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Population Digital Health: Continuous Health Monitoring and Profiling at Scale

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Abstract

This paper introduces population digital health (PDH)—the use of digital health information sourced from health internet of things (IoT) and wearable devices for population health modeling—as an emerging research domain that offers an integrated approach for continuous monitoring and profiling of diseases and health conditions at multiple spatial resolutions. PDH combines health data sourced from health IoT devices, machine learning, and ubiquitous computing or networking infrastructure to increase the scale, coverage, equity, and cost-effectiveness of population health. This contrasts with the traditional population health approach, which relies on data from structured clinical records (eg, electronic health records) or health surveys. We present the overall PDH approach and highlight its key research challenges, provide solutions to key research challenges, and demonstrate the potential of PDH through three case studies that address (1) data inadequacy, (2) inaccuracy of the health IoT devices' sensor measurements, and (3) the spatiotemporal sparsity in the available digital health information. Finally, we discuss the conditions, prerequisites, and barriers for adopting PDH drawing on from real-world examples from different geographic regions.

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KEYWORDS

digital health; population health; modeling, health data; health monitoring; monitoring; wearable devices; wearables; machine learning; networking infrastructure; cost-effectiveness; device; sensor; PDH; equity

Introduction

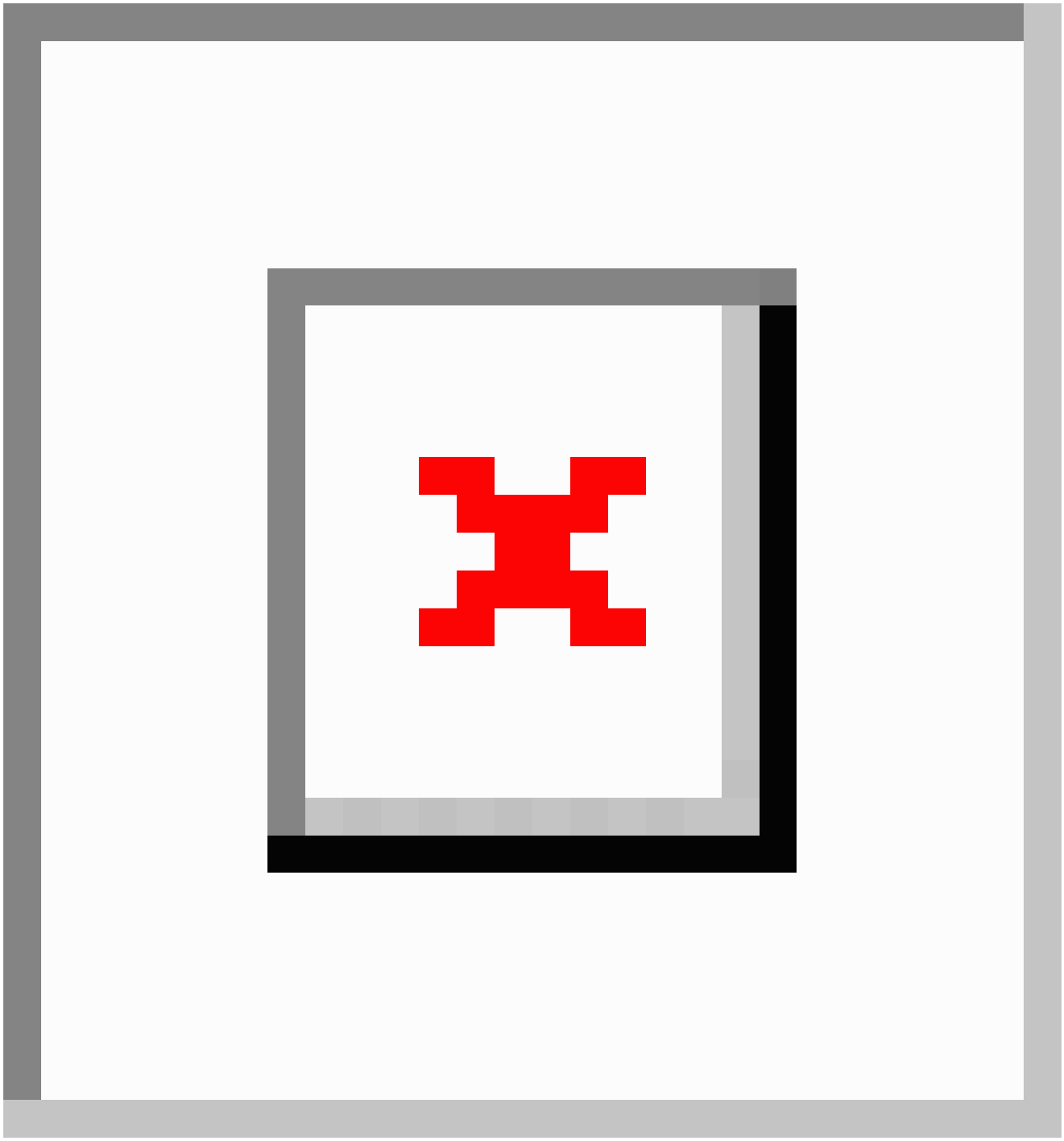
Population health modeling, the monitoring and profiling of spatially fine-grained prevalence of diseases and health conditions, is a critical and key aim for public health [1]. Having accurate and timely information about the citizens' health is essential for informing health policy decision makers, for optimizing care delivery, and in general for improving health outcomes. Detailed profiling and monitoring of diseases can also guide response to emerging health threats such as pandemics, assist in care delivery logistical planning and resource allocation, and the early detection of localized health-related phenomena. A deeper understanding of diseases' interrelationships and epidemiology is also foreseen to play a key role in the future of health care and in sustaining improved health outcomes [2].

Current solutions for monitoring and profiling diseases, such as curating and linking data from electronic health records (EHRs) and health surveys [3], are expensive and have limited spatiotemporal coverage and scale and mostly target developing medical conditions rather than offer insights that can be used to help design policies for their prevention or early detection. These limitations in the availability of information restrict the conclusions that can be drawn. As a result, current solutions are capable of estimating overall disease prevalence and identifying risk factors but unable to offer continuous insights into the current health of the citizens. Improving the scale and coverage of public health models, and consequently the insights about the health of the citizens, requires new ways to cost-effectively collect continuous information about disease onset, health of individuals, and factors affecting them.

This paper introduces *population digital health* (PDH)—the use of digital health information sourced from health internet of things (IoT) and wearable devices for population health modeling—as an emerging research domain that offers an integrated approach for continuous monitoring and profiling of diseases and health conditions at multiple spatial resolutions. PDH is driven by the emergence and widespread adoption of digital personal technologies for health care, including health IoT devices and wearable technology for wellness and personal health monitoring, and advances in machine learning (ML) and artificial intelligence (AI) techniques capable of analyzing and

extracting insights from complex real-world data streams by using powerful edge and cloud computing infrastructure that mobilizes intelligence and delivers requisite computational resources. Figure 1A and B show a high-level illustration of the PDH vision, highlighting the potential of using IoT and personal health devices as an alternative source of data that can modernize (digital) health monitoring, profiling, and reporting to support health care.

Figure 1. High-level overview of the potential of using personal health devices for population health modeling (A). The devices monitor individuals, and their data construct a continuous population health model that can be used as basis for health care and health policy decision-making. The key technical challenges that need to be solved are highlighted in the technical framework (B). AI: artificial intelligence; IoT: internet of things.



Realizing and adopting PDH modeling require addressing challenges in the way data are collected, analyzed, aggregated, and used to derive actionable insights, and lifting the barriers in technical and social hurdles relevant to the development of population health modeling (see section “PDH: A Research Agenda”). These challenges differentiate PDH and drive its research agenda. Specifically, PDH focuses on *population health*, that is, individual subcommunities or groups, instead of the general public, differentiating it from policy making, surveillance, and the modeling of health outcomes for the broader public, as explored by digital public health [4]. PDH targets etiology and identification of disease markers using wearables and other forms of digital data instead of targeting the diagnosis or treatment of diseases, as explored in (digital) precision medicine [5]. Similarly, while data from wearables and health IoT devices are used in mobile and pervasive health

care [6-8], this differs from PDH which harnesses the data for modeling entire populations. Finally, while data are central tenet in many related fields, such as digital epidemiology [9] and precision public health [5,10], PDH specifically targets the challenges in enabling accurate and reliably continuous monitoring and profiling.

We present the overall PDH approach and highlight its key research challenges for PDH to establish a road map for delivering a highly accurate, cost-effective, scalable, equitable, and clinically trusted and actionable population health alternative. We also demonstrate the feasibility of PDH and highlight its benefit through three case studies targeting key challenges: (1) inadequacy of digital health information, (2) inaccuracy of sensor data on health IoT devices, and (3) spatiotemporal data sparsity in digital health information. The results demonstrate that PDH is a promising direction for increasing the scale and coverage of population health information and offers more detailed insights for modeling disease onsets, etiology, and other factors than what current population health modeling approaches can achieve. Eventually, we discuss the conditions and prerequisites that need to be satisfied to adopt PDH and draw examples of different geographic regions to highlight their current readiness.

PDH: A Research Agenda

PDH brings together diverse sources of digital health information and uses it as input for population health modeling and for informing health policy making. Naturally integrating diverse information sources poses technological—and even societal—challenges that must be addressed. We next discuss key dimensions of PDH.

Availability and Management of Digital Health Data

Personal health devices have long been envisioned as a powerful technology for supporting health monitoring [7], and the COVID-19 pandemic has further highlighted their potential as a mechanism to alleviate pressures on public health care delivery systems [11]. Relevant examples include blood pressure monitors, continuous glucose measurement devices, and smartwatches measuring physiological biomarkers, such as heart rate (HR), HR variability, blood oxygen saturation, and body temperature. What makes data from these devices particularly powerful is the diversity of available devices with powerful outreach to all population segments through smartphone apps and smart wearables on youth and work population and at-home medical monitoring devices [12]. At the same time, there are significant challenges in harnessing these data. First, EHRs have emerged over a long period of time and have well-structured representations, whereas currently available digital health information tends to follow proprietary formats and structures. This calls for data structures and algorithms that can consolidate data from different devices [13]. Second, digital health information is sensitive and may be stored and used over a long period of time, which requires combining privacy preservation techniques [14] with secure and tamper-free storage, for example, by taking advantage of distributed ledgers [15]. Finally, availability of digital health information is intrinsically linked to the use of such devices, which is governed by personal preferences, socioeconomic background of individuals, and other factors. As a result, the availability of specific types of information is biased toward certain population segments and there is a need to understand biases governing these divisions to ensure models developed from these data that are generalizable.

Cooperation Between Private and Public Sectors

The integration of data from personal health devices into population health modeling necessitates the consent and cooperation of the companies producing these commercial products. Public-private partnerships (PPPs) present a promising avenue for achieving this as they offer an ethical and effective framework for integrating personal health device data into population health initiatives. These partnerships can be successful, however, only if there are standardized interfaces for integrating data from diverse personal health devices. In addition, the partnerships need to be based on binding and sufficiently long-term contracts to ensure the sustained availability of data from personal health devices. These contracts should outline clear guidelines for data sharing, privacy protection, and ethical data usage, providing a foundation for collaboration between commercial entities and public health systems. There is also a need for cost and profit-sharing models that incentivize the commercial sector to make data available for population health modeling, fostering a mutually beneficial framework for data sharing and utilization.

Data Accuracy

Integrating data from personal devices with health care services requires accurate and reliable data that can be used to make sound policy decisions. Personal health devices, including devices for at-home use, are well known to be susceptible to errors unlike medical-grade devices and equipment [16,17]. Machine learning helps compensate these errors [18,19] and can even reach close to clinical accuracy in some situations [18] but significant challenges remain in ensuring their consistency (ie, robustness) and reliability in a wide range of everyday contexts. For example, in the context of HR monitoring, calibration techniques have been shown to be generally effective during regular physical activity, such as walking or biking but less so in contexts that feature activities with irregular motion patterns (eg, folding clothes). In addition, personal characteristics, such as how the device is used, worn, or the wearer's skin complexion, can impact measurement accuracy [12,16,17]. Public health policies need to be based on accurate information and hence there is a need to understand potential errors and to have effective mechanisms to mitigate them. This requires replicable protocols for evaluating personal health devices for specific use cases. For example, studies on in-home monitoring of elderly people should be assessed with everyday activities they conduct at home as these can cause motion artifacts that distort the signal [20], whereas studies for using personal devices to screen heart conditions (eg, atrial fibrillation using a smartwatch) should be based on clinical criteria. While studies on understanding the performance of personal health devices are increasingly conducted, they tend to rely on different protocols, use different devices, have differing sample populations, and even reference devices [21]. Moreover, these

studies are often anchored at clinical accuracy criteria rather than focusing on specific population health modeling needs, which makes it difficult to aggregate the devices into population health modeling processes. Indeed, showing a 5% error in HR estimates for a specific wearable device in walking and running does not provide sufficient insight into whether the device can be used for profiling or monitoring specific diseases. Replicable protocols anchored at specific population health targets can help make information more useful and easier to integrate.

Regulations and Quality Standards

Ensuring the accuracy and reliability of personal health data is essential for informed decision-making in PDH. However, existing regulatory processes designed for clinical purposes, such as Food and Drug Administration regulations for medical devices, may not fully align with the characteristics and usage of personal health devices for population health purposes. Therefore, there is a need to update regulatory mechanisms to better accommodate personal health devices and to ensure their effectiveness and safe and acceptable use for population health. This may involve introducing more lightweight regulatory alternatives that are specifically tailored for collecting data for personal or population health purposes [22]. Beyond regulation, there is also a need to establish quality standards for data produced by personal health devices. Indeed, rigorous clinical standards, while essential, may not translate to the context of personal health devices due to the inherent variability in data collection procedures and usage contexts. This can be offset by deriving localized and contextualized quality standards that consider the specific contexts of use and the variability relative to the intended application, ultimately ensuring the reliability and validity of the data derived from personal health devices [23]. Failure to provide better regulations and to address the contextualization of data from personal health devices may lead to decreased user trust [24] and limit the potential to harness valuable data for population health.

Digital Biomarker Discoveries

While some diseases and conditions such as cardiovascular diseases, diabetes, pulmonary diseases, and asthma have well-established digital biomarkers used in specialized personal health devices that can monitor their progression, the search is on for the most suitable digital biomarkers for many other diseases and conditions. Understanding the potential of a specific sensor or combinations of sensors and the information that can be gleaned from them in acting as representative digital biomarkers for certain diseases and conditions is currently shaping an exciting discovery pipeline. Such discoveries may exploit repurposing of sensors available in most smartphones, smartwatches, wearables, or at-home IoT devices [25]. For example, microphones from personal devices can sample audio clips to model the coughing sound of respiratory diseases [26]. In fact, speech sensing is currently being extensively researched as a promising source of digital biomarkers in multiple disease areas including Alzheimer disease, Parkinson disease, frontotemporal dementia, depression, and schizophrenia [27]. Motion sensors can also be used to detect early stages of Parkinson disease [28] or to analyze sleep patterns [8]. Research and advances in the digital biomarkers pipeline, through existing or novel sensors, are critically important to enabling PDH.

Data and Service Trustworthiness

Digital population health requires that citizens trust the devices they use and how their data are being handled if they are to engage to guarantee that a critical mass of information is available. This can happen only if sensitive data are protected and there are no concerns about data misuse—a common concern in the use of health data [29].

Federated learning is seen as a potential way to aggregate EHRs [30] and could similarly be adopted for learning insights from health IoT and wearable devices as long as the accuracy of the data can be ensured. Yet, federated learning is vulnerable to poisoning where some of the data used to train the model or the model parameters are manipulated with the aim of misleading the model [31]. AI or ML algorithms are also vulnerable to model biases that may incorporate racial or socioeconomic differences [32] rather than capture the true causes of diseases. Population health and care delivery services will also require trustworthiness in the opposite direction if devices' biomarker data are to be relied on and included within or alongside EHRs. This will require the use of verifiable digital identity for the users, for instance, using the emergent W3C Decentralized Identifiers concept [33] or implementing smart contracts between the concerned parties [34].

AI Models and Data Sparsity

AI models are data-hungry, requiring vast amounts of data and labeled examples to operate effectively and accurately. Even at the population level, the available data tend to be sparse and hence there is a risk of the resulting models being unreliable.

Sparsity can also result in biases as the majority of the data tend to come from specific areas, times-of-day, or specific segments of the population. PDH modeling needs to be aware of these risks and have mechanisms to minimize their effects. For example, our previous work has shown that data reconstruction techniques can be effective at overcoming sparsity in EHRs [35,36] and similar techniques can be used on other forms of digital health data. Another issue related to AI modeling is the untapped opportunity of learning intra- and interdisease correlations brought by the diversity of the conditions and measurements contained in the collected data. Indeed, as outlined, health IoT technology monitors a range of different biometrics and there is a potential to combine and take advantage of such diverse data for constructing unprecedented, sophisticated PDH models.

Data Biases

Bias is pervasive in health care data and has far-reaching implications for studies reliant on observational data, including those on population health modeling. Biases within EHRs often stem from socioeconomic or demographic disparities, such as studies being confined to specific age groups, genders, comorbidity-specific cohorts, or racially skewed populations [13]. The transition to data from personal health devices introduces further biases that are linked to technology and connectivity availability, cost-related barriers limiting access

to specific devices or technology, and spatiotemporal biases arising from varying usage patterns. With PDH drawing on data from personal devices, there is a tangible risk of excluding certain socioeconomic groups from health studies. However, it should be noted that this issue also impacts EHRs as there are notable racial and socioeconomic disparities in the use and accessibility of health services. Addressing biases necessitates stringent reporting guidelines during the profiling and modeling phase to identify and rectify potential biases in modeling [37]. Robust techniques are also required to analyze and establish causal links between observations and population health outcomes [38]. Bias may also be mitigated by harnessing explainable AI techniques as they enable researchers to scrutinize how specific background variables may influence analysis outcomes [39].

Multitier Data Processing

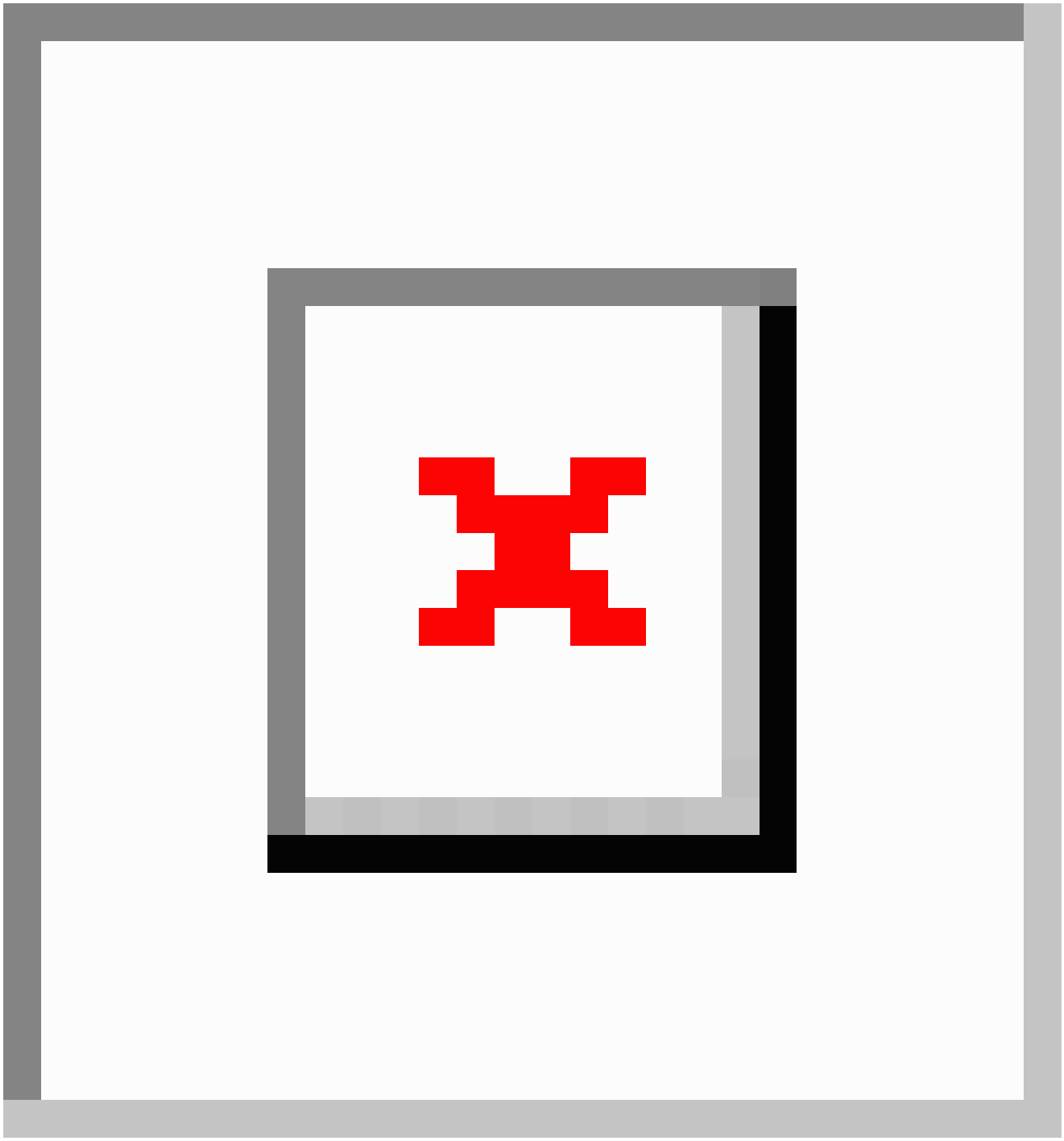
Collecting and analyzing digital health information produce vast amounts of measurements that need to be cleansed, aggregated, and preanalyzed. Low-level data may also need to be folded into digests to reduce data volume and facilitate better use. There is also a need to analyze certain measurements at different spatial and temporal resolutions to identify disease prevalence, for example, to identify risk factors in a specific district. However, the continuous transmission of data to remote servers—or the cloud—requires a lot from both the network and the remote infrastructure, besides posing privacy challenges and risks of unauthorized data access. This demands elasticity from the public health infrastructure to scale to increasing amounts of data volume and velocity. Such elasticity may become cost-prohibitive requiring intelligent use of edge computing [40]. Deploying AI support on the network edge can alleviate the burden and enable localized modeling that is tailored to specific geographic areas (eg, neighborhoods). Unfortunately, edge and fog solutions are neither scalable nor dense enough to provide continuous support for intermediate data processing. This requires multilayer architectures where each of the layers supports and participates in the processing. Advances in network connectivity, smart gateways, and cloud-fog-edge architectures make it possible to optimize and reduce the cost of moving and aggregating data, but this also requires carefully planned deployments. For example, deploying edge support at points-of-entry locations, such as malls, transportation stations, parks, or other similar locations that people frequent, can offer a cost-effective way to connect the majority of the population to the data processing infrastructure scalably (Figure 1). Developing suitable architectures and identifying practically feasible ways to deploy them are important challenges for ensuring large-scale feasibility of the PDH vision.

Case Studies for PDH

Availability of Digital Health Data

Access to health data from health IoT devices and personal wearables is a prerequisite for PDH. We first show how data from health devices are increasing and can indeed significantly increase the scale and coverage of population health models. We use the Google Play Store Apps data set [41] and demonstrate how the number of apps and users per app have grown from 2010 to 2020. As shown in Figure 2A, the release of new applications has increased by an average of 66.9 (34.1%) per year.

Figure 2. Number of smartphone apps released in the Health category between 2010 and 2020 (A) and number of app users (B).



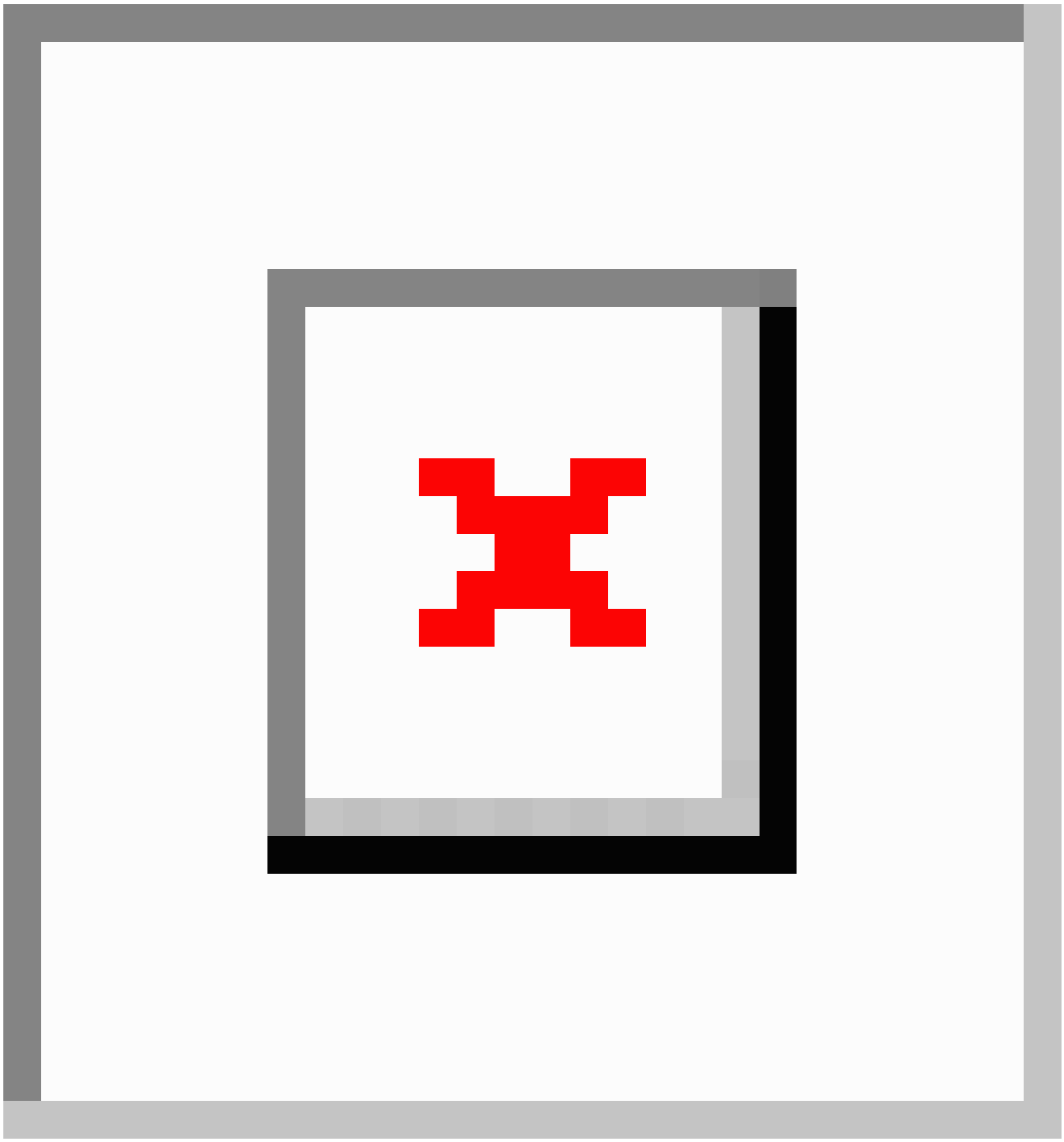
At the same time, the adoption of apps has been very diverse, and the usage base tends to be highly fragmented. Indeed, the vast majority of health apps have fewer than 1000 users (39.1% [24.9%]), with only a small fraction of the apps (39.1% [24.9%]) having more than 100,000 users (Figure 2B). What this means in practice is that there are significant opportunities to take advantage of digital health data, but overall the user base tends to be fragmented and maximally taking advantage of all data can prove challenging. At the same time, a small number of apps garners a large user base and thus integrating data from them would serve as a logical starting point. This integration can harness either public application programming interfaces offered by the companies or, preferably, PPPs that set conditions and boundaries for data use. Beyond data fragmentation, there are naturally other challenges also in the use of the data. For example, all app ecosystems are prone to churn with a wide range of factors affecting the overall retention of apps [42].

The increased availability of digital health data alone is not sufficient as the data need to be suitable for modeling. Population health models commonly analyze records at a fixed spatial resolution (such as a postcode or a grid) but obtaining continuous measurements from personal health devices from all of the areas is next to impossible. We use the Carat [43] Top 1000 Users Long-Term App Usage Dataset [44] to highlight how data from health apps vary across time and depend on the app popularity. We focus specifically on the situation prior to the pandemic as this gives a more stable view of the app usage. Specifically, we analyze the daily collection patterns in 2017

and 2018 of the top three popular health apps used for tracking individual's health in different contexts: (1) Samsung Health, (2) Fitbit, and (3) Sports Tracker Running Cycling.

Figure 3A shows that the usage patterns for the 3 apps generally follow diurnal patterns, which means that nights and mornings tend to have much lower amount of measurements than afternoons. While this tends to be a generic pattern for apps [45], naturally the usage patterns also vary depending on app functionality and other factors. For example, sleep-tracking apps naturally produce more data during nights than physical activity trackers. There are also some activity trackers that continuously collect measurements from different sensors and this is also the reason for the low variation in measurements for the Sports Tracker Running Cycling app. In these cases, most of the produced data do not contain any health-related data and hence there is a need for analyzing and validating which of the measurements are relevant for population health modeling purposes.

Figure 3. Temporal sparsity in Health apps (A). Data inaccuracy when measuring HR from different devices and body parts (B). HR: heart rate



Data Inaccuracy

We next demonstrate potential utilization of digital biomarker data and the effect that data sparsity and its accuracy have on modeling PDH. Personal wellness and health devices do not always meet clinical criteria for accuracy and thus the measurements need to be validated before they are used. We highlight this issue using HR measurements in the PPG-DaLiA

data set [46]. The data contain HR measurements from a chest-worn device and a wrist-worn device to study HR variations during daily life activities [47]. Personal HR trackers are popular examples of devices producing digital health information and they are well known to be subject to inaccuracies [16].

Figure 3B shows the difference in HR measurements for the 2 devices (wrist-worn smartwatch and chest strap monitor) for 9 activities and 15 users. The HR variation is highest in aerobic activities (stairs: 104, SD 19.1 bpm, cycling: 112.4, SD 14.8 bpm, and walking: 93.8, SD 7.9 bpm) compared with activities with little movement (sitting: 53.1, SD 7.5 bpm, table soccer: 80.5, SD 8.6 bpm, driving: 78.7, SD 9 bpm, lunch: 75, SD 8.1 bpm, and working: 73.7, SD 4 bpm). The mean absolute error between the HR measurements collected at the chest and at the wrist is 7.7, SD 5.9 bpm, which is much worse than the reported accuracy of the devices and highlights issues with measurement quality. The discrepancy tends to be highest in activities where both the body and the wrist are moving (eg, stairs, 29.7, SD 13.9 bpm) and low motion activities result in lowest errors (eg, sitting, 2.6, SD 5.2 bpm). Integrating digital health information thus needs to be carried out carefully as otherwise errors in the measurements can result in misleading conclusions. Machine learning techniques can help curb such inaccuracies. Table 1 illustrates how even the simplest ML models can significantly decrease the errors by learning how to calibrate the sensors. The sole exception, in our example, is cycling where all algorithms slightly increase the error as they fail to capture the periodic nature of motion patterns. More complex algorithms, such as deep learning [19], can further reduce HR measurement errors, but they are similarly prone to overfitting on specific types of patterns. Further research is certainly needed to understand and mitigate different biomarker errors and to integrate this information reliably into public health models. At the same time, there is a need for regulations that specify what level of accuracy is needed, and these should be contextualized to consider how the data are being used. For example, using HR data to study the prevalence of obesity does not require the same accuracy as attempting to understand the prevalence of arrhythmia or other health conditions.

Table . Error (mean absolute error) of different heart rate calibration models.

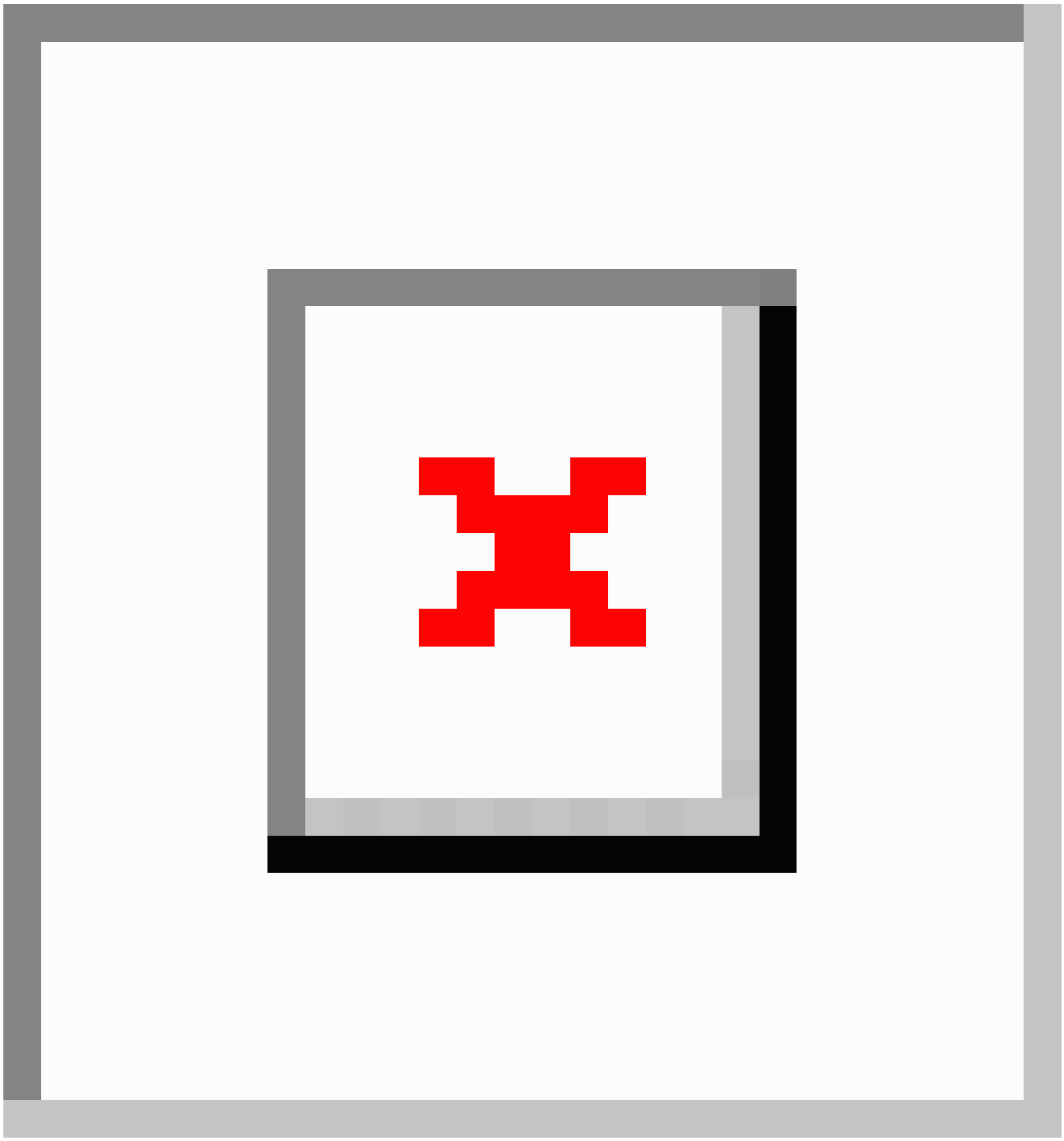
Status	HR[a] at wrist	Logistic regression	Random forest	Gradient boosting
Sitting	0.9 (0.9)	0.5 (0.8)	0.4 (0.7)	0.4 (0.5)
Stairs	34.9 (11.5)	10.2 (5.6)	12.7 (8.2)	10.4 (5.7)
Table soccer	17.9 (5.5)	4.2 (3.2)	3.3 (2.6)	3.0 (2.2)
Cycling	5.5 (9.6)	6.9 (6.2)	6.3 (8.1)	5.7 (6.5)
Driving	2.2 (1.9)	1.9 (1.5)	1.4 (1.2)	1.6 (1.2)
Lunch	2.5 (2.6)	2.4 (1.9)	1.9 (1.7)	1.9 (1.5)
Walking	0.7 (0.6)	0.7 (0.5)	0.5 (0.8)	0.7 (0.6)
Working	2.6 (1.9)	1.3 (1.3)	1.3 (1.2)	1.3 (1.1)
Overall	4.8 (9.2)	2.7 (3.6)	2.5 (4.3)	2.3 (3.4)

[a]HR: heart rate.

Spatiotemporal Sparsity

Finally, we show an application use case of how management and multitier data processing of digital health data can be used to reduce the sparsity of digital biomarker data and improve performance in PDH modeling. Our previous research has addressed spatiotemporal data sparsity in EHRs and developed a methodology that is based on deep learning and data reconstruction to mitigate the effects of sparsity [35,36]. The approach, coined *compressive population health* (CPH), uses intra- and interdisease correlations, convolutional neural networks, and generative adversarial networks to infer (recover) missing prevalence rate entries of different chronic diseases from a sparse population health data set (Figure 4).

Figure 4. Recovery of missing prevalence data of 2 diseases from the London population health data set. Original prevalence data (A) contain many missing entries (blue areas in the left), which are augmented by exploiting spatial intradisease correlations (black arrows) and interdisease correlations between different diseases (orange arrows). This allows to obtain prevalence rate estimates for all geographic areas (B). CNN: convolutional neural network; GAN: generative adversarial network.



Through experiments carried out on a decade of public health data containing 17 chronic diseases and health conditions across 500+ wards in London (the London population health data set [48]), research has shown that CPH is highly effective in modeling disease prevalence. The 2-stage reconstruction and fusion framework of CPH outperformed all baselines and achieved significantly improved accuracy on estimating prevalence rates. The extent of improvements, however, depends on the specific disease or health condition. For example, for obesity, CPH results in an error of 10.5%, an 8.5% improvement over the best baseline. For hypertension, CPH error is 2.7% but the baseline reconstruction techniques also perform well and the CPH improvement is only 5.1%. For diabetes, CPH achieves an error of 8.2%, outperforming the best baseline by 16.9%. In terms of coverage, sampling just 11% of the entire region can result in a lower than 15% reconstruction error for the missing data entries, suggesting that reconstruction can also improve the accuracy of the data. In contrast, other baseline methods need to sample at least 57% of the region to satisfy the same requirement. Overall, the results show that CPH can save more than 90% of resources in data collection while increasing the quality of data and the accuracy of estimates derived from it. Surely, further work is needed to address other factors beyond prevalence. Nevertheless, these results demonstrate the potential

digital population health can have on significantly cutting cost of monitoring while improving coverage (and hence health equity) and data accuracy. From an analytics standpoint, CPH offers increased flexibility compared with traditional spatial epidemiology modeling, which is often limited to parametric-linear approaches and bound to low-dimensional measurement sets.

Adopting PDH

The adoption of PDH is contingent not only on the identified challenges but also on the presence of a comprehensive ecosystem and network to support its implementation. The readiness of different cities, countries, or regions to fully embrace PDH varies significantly and is influenced by factors such as public willingness to share data, the availability of private-public partnerships, trust in the system, the existence of legal frameworks for health data, technological foundations, and the availability of health care providers and institutions to benefit from digital population health.

Regions with established clinical research networks exemplify ecosystems that can readily adopt digital population health, as they possess the necessary legislative frameworks, data and computing frameworks, and connections between stakeholders. An illustrative example is the OneFlorida+ Clinical Research Network [49], which integrates a data trust that offers access to curated EHRs, vital statistics, and Medicaid and Medicare claims. The data representation follows a common model, specifically the PCORnet Common Data Model [50], and adheres to Health Insurance Portability and Accountability Act regulations on health data privacy [51] providing interoperability and legislative protection on privacy. The network has been successfully leveraged to profile and analyze the prevalence of health conditions and diseases in the state of Florida, with examples including studies on hypertension [52] and adult obesity [53].

Another example is the shared European Health Data Space initiative across EU member countries that links curated health data records across EU member countries and aligns the data representation with data governance frameworks such as the General Data Protection Regulation and the EU Data Act [54]. These examples illustrate that regions with established networks for health data usage generally offer a strong starting point for adopting PDH, as they ensure the necessary infrastructure for curating, storing, and representing that the data are available, and that this infrastructure links with health care providers, patients, clinicians, and researchers, while being supported by robust legal frameworks. Smaller-scale examples include Estonia, which has strong data protection laws, widespread public trust in digital services, and a well-developed e-governance infrastructure [55], and Singapore, which has fostered PPPs in the health care sector and focused on creating a robust computing infrastructure [56].

While existing ecosystems provide a strong starting point for adopting PDH, adoption is also possible without such networks, provided that a sufficiently large percentage of the population uses personal health devices and companies consent to their data being used for health purposes, or that suitable PPPs are established. Many developed countries fall into this category, as they have widespread adoption of personal health devices but limited access to health services, let alone having unified data models and data governance models. Thus, the adoption of PDH is not restricted to a specific model or framework, but different models can be followed depending on the structure of the regional health care service networks.

While there are many possibilities to adopt PDH, there are also negative scenarios where adoption may be hampered. First, maintaining a sufficient level of trust among individuals to share their data is crucial, and misuse of personal data can erode this trust. Breaches of health care data have become increasing common, which is degrading the user's willingness to share their personal health data [57]. Similarly, inadequate standards for representing digital health data and the evolving nature of digital health technology pose challenges in integrating data from different providers. Many regions still have inadequate standards for representing digital health data and this can make it hard to integrate data from different provides [23,58]. Regions with existing standards are better positioned to harness digital data, but at the same time digital health technology continues to evolve and new devices and health indicators emerge regularly. Thus, even if standards exist, they need to be updated frequently as new tools and technologies are developed. Regulations and legislative frameworks, while essential for ensuring data safety, also create barriers [59]. Finally, inequity of health access is another concern that can hamper adoption, as certain population segments have unequal opportunities to access digital health tools and technologies. For example, older people and those from lower income brackets tend to use these technologies fewer than other parts of the population [60]. Thus, achieving equitable reach across all population segments may require PDH to coexist with another approach that reaches those segments that personal health devices fail to reach.

Despite these challenges, the increasing use of digital health technologies and the evolving societal attitudes toward their adoption indicate a growing receptiveness to PDH. As long as significant breaches of sensitive health data are avoided, the trend toward adoption is likely to continue, highlighting the inevitability of society becoming increasingly amenable to embracing PDH.

Summary and Conclusion

We presented PDH as an emerging research domain that harnesses digital information provided by wearables and health IoT devices for population health modeling. We highlighted key research challenges for PDH, relating to the availability, readiness, and management of health data; the inaccuracy inherent in these data and the spatiotemporal sparsity of the data measurements; and the trustworthiness of the overall ecosystem. PDH complements existing population health modeling approaches by increasing the scale, coverage, and power of the models to explain onset, causation, and other factors about diseases and health conditions. Through case studies, we demonstrated how PDH can indeed increase the scale and accuracy of population health models. We also demonstrated how ML and AI are essential for tackling issues in data quality.

Finally, we discussed the necessary conditions for transitioning to PDH and how different regions can adopt it. Our research takes the first steps toward establishing the viability of a new approach for public health modeling and demonstrating the role machine intelligence plays in it.

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Conflicts of Interest

None declared.

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Abbreviations

CPH: compressive population health
EHR: electronic health record
IoT: internet of things
ML: machine learning
PDH: population digital health
PPP: public-private partnership

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Viewpoint

Bringing the Public Health Informatics and Technology Workforce Together: The PHIAT Conference

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Abstract

The field of public health informatics has undergone significant evolution in recent years, and advancements in technology and its applications are imperative to address emerging public health challenges. Interdisciplinary approaches and training can assist with these challenges. In 2023, the inaugural Public Health Informatics and Technology (PHIAT) Conference was established as a hybrid 3-day conference at the University of California, San Diego, and online. The conference's goal was to establish a forum for academics and public health organizations to discuss and tackle new opportunities and challenges in public health informatics and technology. This paper provides an overview of the quest for interest, speakers and topics, evaluations from the attendees, and lessons learned to be implemented in future conferences.

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KEYWORDS

public health informatics; health informatics; technology; health technology; digital health; digital intervention; digital interventions; conference; health conference; health conferences; public health workforce; public health worker; public health workers; PHIAT Conference; PHIAT; public health; health surveillance

Introduction

In recent decades, the field of public health informatics has undergone significant evolution, propelled by advancements in technology and the imperative to address emerging public health challenges. From its early beginnings in manual data collection to the widespread adoption of electronic health records and sophisticated data analytics, public health informatics has played a pivotal role in revolutionizing health care data management and surveillance systems. This historical trajectory underscores the continuous efforts to leverage technology and data-driven approaches to enhance public health outcomes and address the complex needs of populations worldwide. As the field continues to grow and adapt, understanding its historical context provides valuable insights into its current state and future directions. Especially after the COVID-19 pandemic, public health informatics has continued to grow as a field, and as expected, workforce needs have and will continue to expand for health information fields [1].

According to the US Bureau of Labor Statistics, health information technologists and medical registrars have a job growth outlook of 16% over the next 10 years, with an average of 3100 position openings per year [2]. This includes specialized positions in public health informatics and technology. However, growing and expanding does not come without workforce issues, such as recruitment, diversity, retention, burnout, and posttraumatic stress disorder among public health, public health informatics, and technology workers, which was especially

exacerbated by COVID-19 [3-5]. In addition to these challenges, although there is rising enrollment in public health programs, there are fewer graduates entering public health agencies [6,7].

There are US-based conferences, such as the American Public Health (APHA) Association Annual Meeting [8], AcademyHealth [9], and other public health conferences [10-13], as well as a range of technology conferences, such as the Associates of Computing Machinery (ACM) [14] and Institute of Electrical and Electronics Engineers (IEEE) [15] conferences; there is also the American Medical Informatics Association (AMIA) [16] conference for biomedical and clinical informatics. Nevertheless, few conferences are available to address the bridge between public health, informatics, and technology.

In 2023, the inaugural Public Health Informatics and Technology (PHIAT) Conference was held as a 3-day hybrid conference. The PHIAT Conference occurred with an in-person option on the third day at the University of California, San Diego. The aim of the conference was to create an environment for academia and public health organizations to discuss and address emerging public health challenges and opportunities specifically in and with informatics and technology [17].

Preliminary Research: Gathering Interest

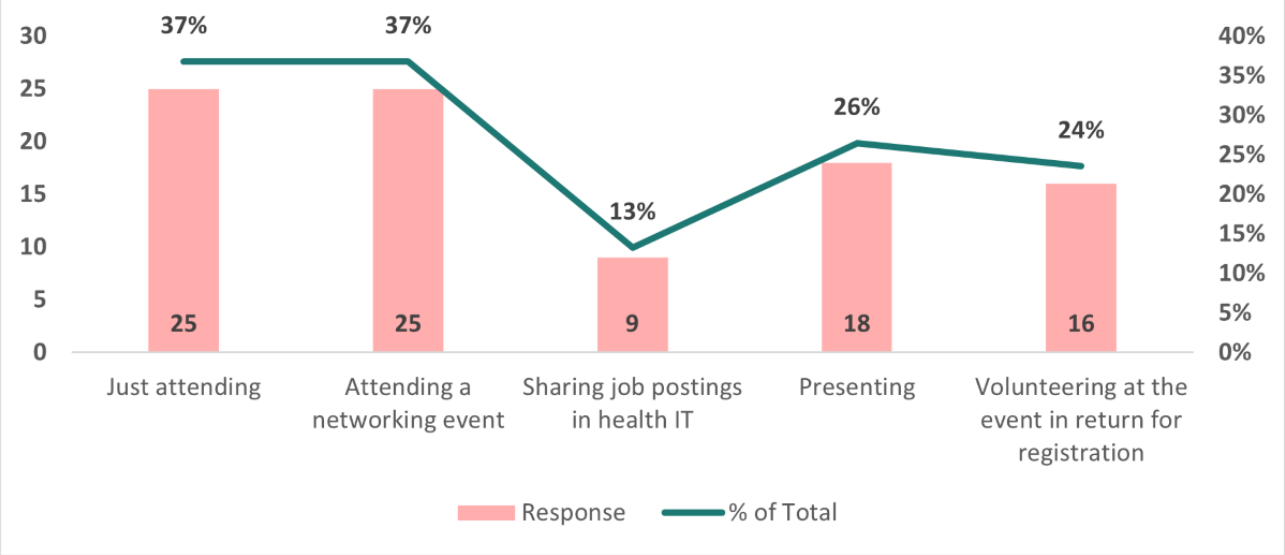
At the time of the first PHIAT Conference, we had not identified any public-facing events directly focused on public health informatics and technology. To gather interest and ideas on how and where to announce the conference, we designed a preliminary survey to understand the feasibility of a conference dedicated specifically to public health informatics and technology. The survey was shared with the AMIA Public Health Informatics Working Group [18], the APHA LinkedIn group [19], and the Chronic Disease Geographic Information Systems Basecamp group of public health agency practitioners [20].

The preliminary survey included both closed- and open-ended questions related to interest in the idea of a public health IT conference, likelihood of attending a conference in June of the same year, rating of specific public health topics, preferred conference format, likelihood of attending the conference in person, and preferred level of participation. The brief survey was fielded from February 2 to 6, 2023, with most responses in the first 2 days.

This initial survey resulted in 46 responses and indicated a strong interest in the conference. Most of the participants had general positive reactions and indicated a willingness to pay for and attend the hybrid conference. The response rates for each question varied because not all respondents answered every question, some of the questions allowed respondents to answer with more than 1 choice, and all questions were optional.

The data presented in Figure 1 use a scale of 1 to 5 to denote interest level (where 5 signifies high interest and 1 signifies low interest) in a public health IT conference. Most of the respondents (23/42, 55%) noted a high level of interest. Additionally, 40% (17/42) of respondents were moderately interested. Importantly, none of the respondents expressed a lack of interest in the public health IT conference. These statistics underscore a substantial demand for hosting more public health IT conferences in the future.

Figure 1. Interest in attending a public health IT conference.



Conclusions regarding the likelihood of attending a conference months after this survey can be drawn from the data displayed in Figure 2. Using a scale of 1 to 5 to indicate interest levels (where 5 denotes strong interest and 1 denotes low interest), 34% of total responses showed a moderate degree of interest in attending the public health IT conference (11/32; n=14 missing values). In addition, 31% (10/32) gave the conference a rating of either 5 or 4 on the scale, demonstrating a strong level of interest. The significant relevance and interest respondents have expressed in attending the public health IT conference are illustrated in Figure 2, which supports the earlier findings.

Figure 2. Likelihood of attending the conference in June 2023.

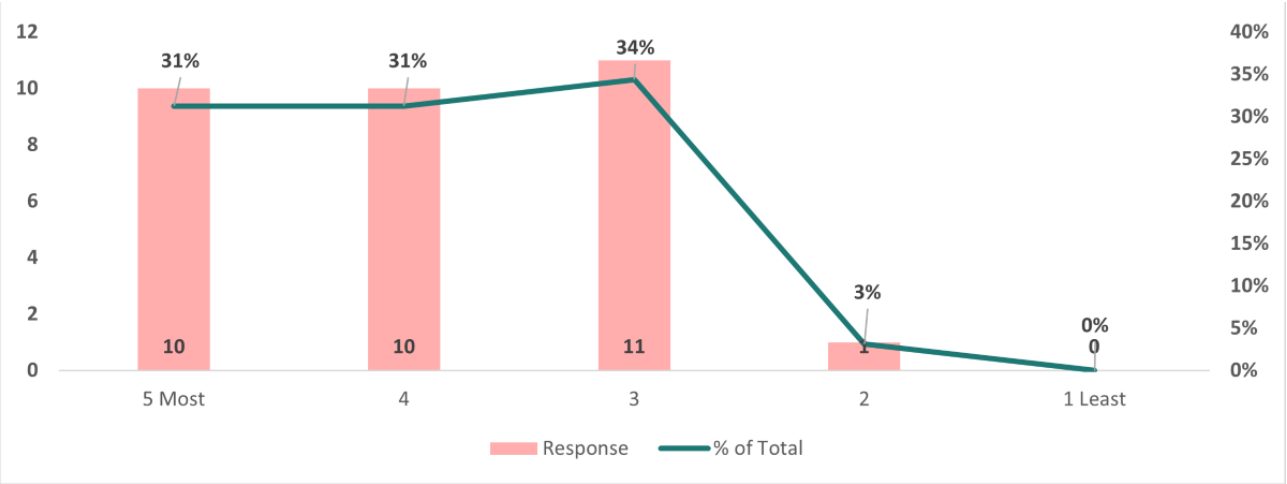
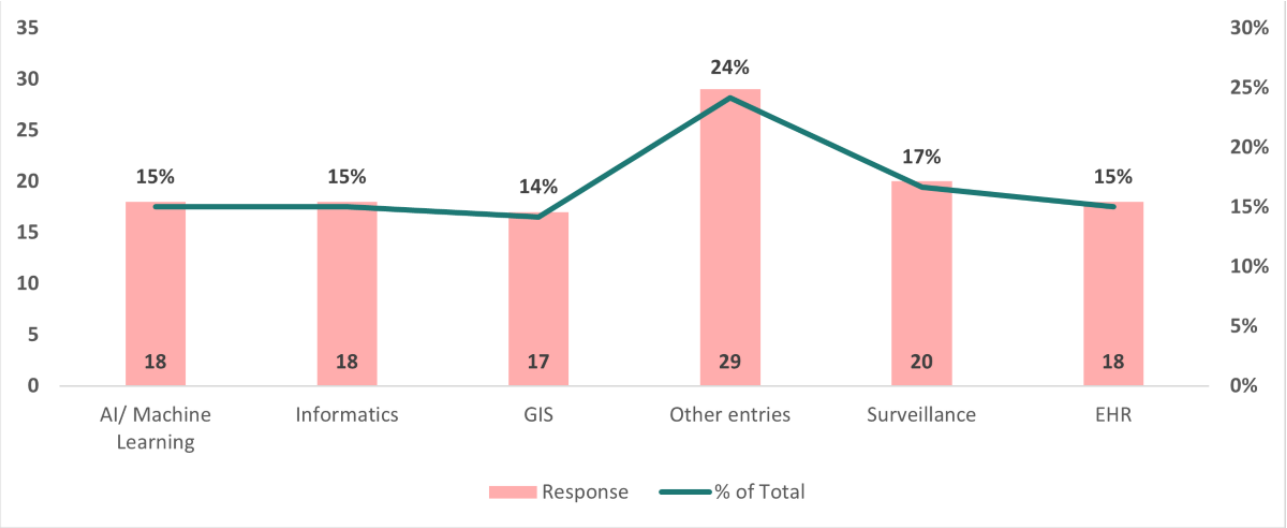


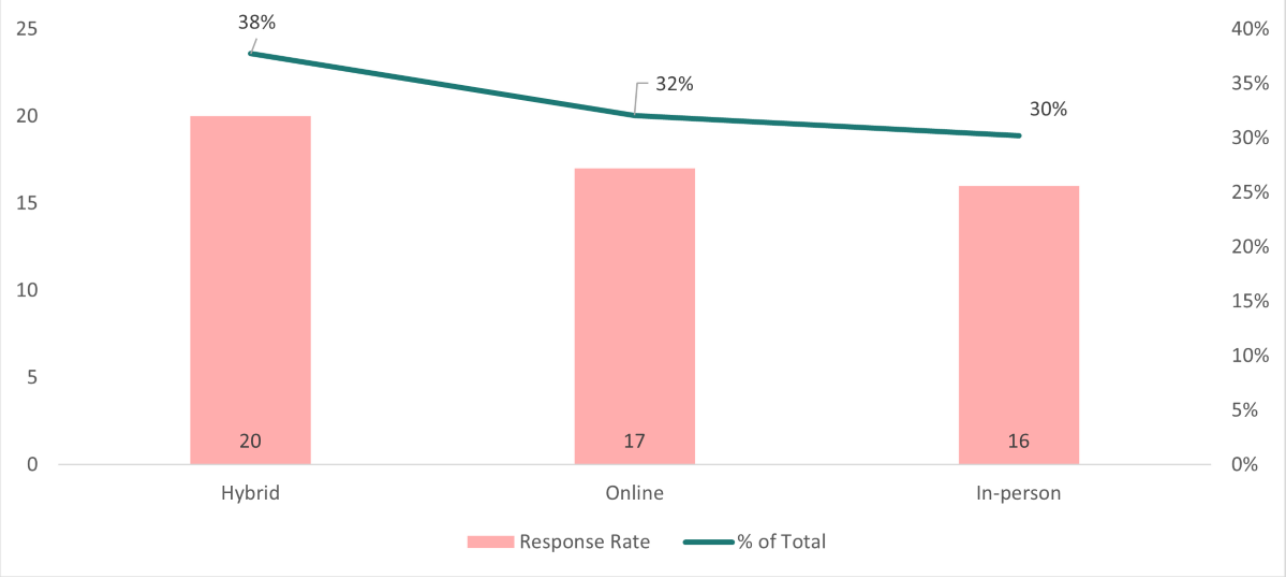
Figure 3 provides insights into the public health IT topics that piqued the interest of the respondents. These findings were valuable for this and future conference planning. The results indicated the following trends: the highest area of interest is categorized as "other entries," such as public safety, alternatives to certain software, health information exchange and data sharing, and standards and guidance. Additionally, topics related to surveillance garnered significant attention, with 20 of 120 (17%) responses showing interest. The remaining topics garnered comparable levels of interest among respondents. Specifically, artificial intelligence (AI) and machine learning, electronic health records (EHRs), informatics, and geographic information systems (GISs) attracted similar levels of interest, each capturing 15% of the responses (18/120). Lastly, GISs received interest in 17 of 120 responses. These insights provide a comprehensive view of the preferences among the respondents for various public health IT topics.

Figure 3. Preferred public health IT conference topics.



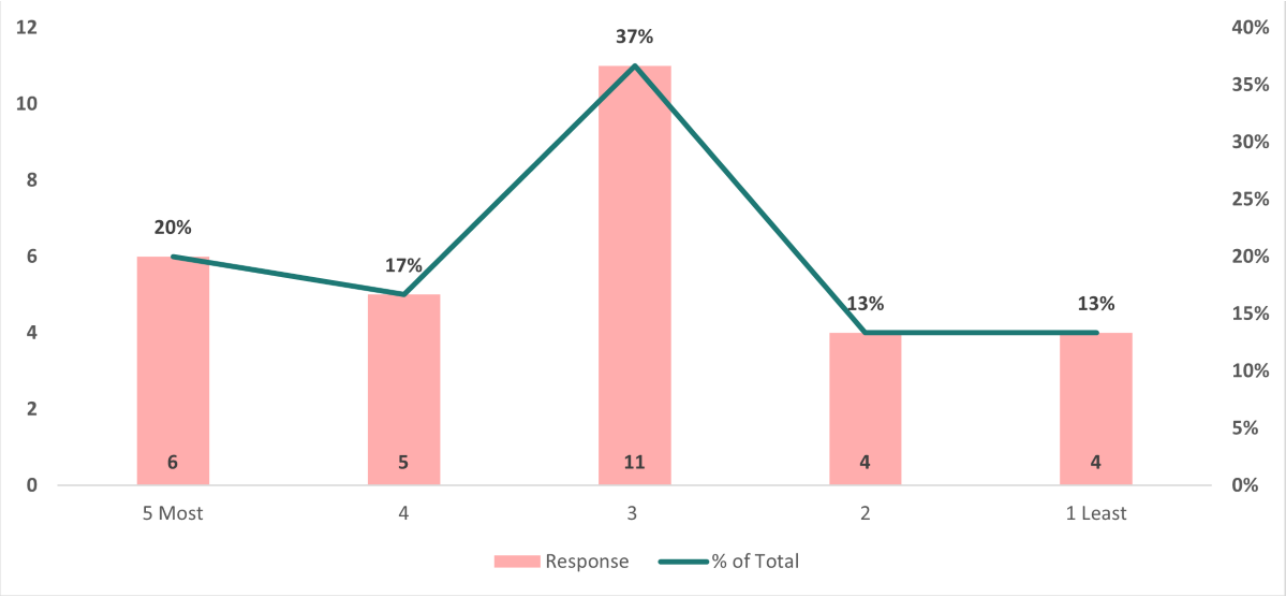
Based on the data presented in Figure 4, valuable insights can be gleaned regarding the potential formats for future public health IT events after the COVID-19 pandemic. These insights could be instrumental in guiding decisions on how to attract a greater number of participants while maintaining optimal learning effectiveness and efficiently budgeting the conference costs. Among the 53 responses, the preferred formats for a public health IT conference were as follows: 20 responses (38%) indicated a preference for a hybrid format; 17 responses (32%) expressed a preference for a web-based format; and 16 responses (30%) favored an in-person format. These findings provided a clearer understanding of the preferences of respondents regarding the format of the public health IT conference, thereby informing future planning and decision-making processes.

Figure 4. Preferred format for the conference.



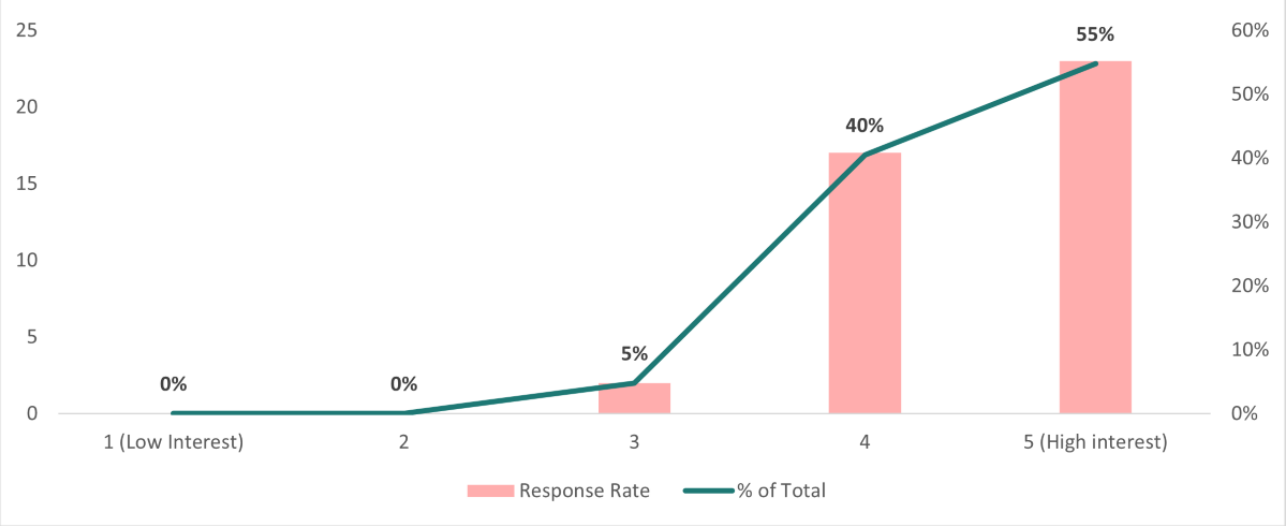
We extended our inquiry by posing a follow-up question based on the previous questions. Figure 5 offers valuable insights into the anticipated participation levels in public health IT events after COVID-19. Over time, this information will facilitate the observation of growth trends in the public health informatics IT conference landscape. Among the 30 total respondents, a majority, 11 individuals (37%), expressed their intention to participate in the conference. Notably, 6 respondents (20%) displayed a high likelihood of joining the conference in person in San Diego, California. Based on the groups that were selected to have access to the survey, these results provide a view of respondents' intentions to participate, aiding in gauging interest and contributing to future conference planning endeavors.

Figure 5. Likelihood of in-person attendance in San Diego, CA.



We polled various public health and technology interest groups to learn about their preferences and interests to further increase the value of a public health IT conference. Five different categories were clarified by the insights (Figure 6). These insights are crucial for tailoring the conference to meet the preferences of the participants. The survey outcomes highlighted the following preferences among the 68 responses: the most popular choice, preferred by 20 individuals (29%), was attending a networking event. Attending the conference exclusively was favored by 16 respondents (24%); 13 respondents (19%) expressed their interest in volunteering at the event in exchange for registration. Additionally, 12 individuals (18%) indicated their desire to present at the conference. Lastly, 7 respondents (10%) expressed interest in sharing job postings during the conference. These findings offer a comprehensive understanding of the attendees' preferences and aspirations, which will contribute to creating a well-rounded and engaging public health IT conference.

Figure 6. Preferred levels of participation.



Description of the Conference

Cross-Sector Collaborations

The PHIAT Conference was designed to include the latest academic research on public health informatics and technology. The event featured public health department representatives, academic researchers, and businesses sharing their innovative approaches to improving public health. We enjoyed providing this space for interaction and communication across these various sectors and look forward to continuing to cultivate these discussions to share public health informatics and technology best practices, policy implementations, case studies, and the latest innovative developments in the field.

Structure of the Conference

The hybrid nature of the conference allowed for academics, organization professionals, and students to attend either via video conferencing or in-person for the day 3 workshops during Pacific Standard Time. We found that this maximized the opportunity for individuals to be able to attend across demographic, socioeconomic, and geographic spaces where time, location, or cost were potentially constraining factors. The option of meeting either online or in person provided more opportunities for internationally based individuals to attend our conference. For example, speakers from other continents were able to present, sleep, and watch the rest of the event online without having to travel. Some were able to share prerecorded presentations and to participate online at a time-zone appropriate time, watch the recording, connect with other speakers, and submit their event feedback later. Additionally, students were able to register at a discounted rate and attend the event remotely if travel funding was a concern. Finally, attendees with logistical challenges were able to attend live for a short period of time, leave, and then return without the need to travel to the event.

Some presenters, such as the national coordinator for health IT and the presenters from Esri Health and Human Services and the Department of Biomedical Informatics of the University of California, San Diego, were personally invited to speak, due to their known expertise and our familiarity with their work. Additionally, many of the presenters were selected through their abstract submissions, quality of presentation, and suitability for the theme of the conference. A team of 5 individuals selected the abstracts, and talks were scheduled based on the theme of the day and time availability of speakers. In cases where the time zones were many hours apart, such as in Australia, presenters were given the opportunity to prerecord their sessions.

Event Overview

The first day of the event included a range of discussions, such as community solutions, AI, machine learning, data sharing, and health equity. There were a variety of organizations and teams represented, such as universities, health centers, community-based agencies, and researchers.

We began the event (Multimedia Appendix 1 includes a link to the agenda) with a presentation led by KSW on the status of the public health informatics workforce and workforce needs now and in the near future. We continued the event with many of our featured invited presenters. The national coordinator for health IT, Micky Tripathi, PhD, MPP, discussed the US federal health IT strategy and goals for interoperable infrastructure under TEFCA (Trusted Exchange Framework and Common Agreement), emphasizing further collaborations with qualified health information networks (QHINs).

As Nanette Star, MPH, of Esri's health and human services team mentioned on day 2 in her keynote speech, "pictures are worth a thousand words and maps are worth a thousand pictures." Her keynote speech was focused on understanding health GISs to answer questions, in addition to sharing some use cases for GISs in public health. Additionally, on day 2 AMA provided a talk on developing strategy for GIS leadership, including important points such as understanding why the map is made, who it is made for, and what is seen and remains unseen in the data provided.

The event provided space for discussion on emerging themes of blockchain technology for public health data security, presented by Tsung-ting Tim Kuo, PhD, of the University of California, San Diego, biomedical informatics department, who shared some of his National Institutes of Health–funded research on blockchain models for health. Findings from opioid-related

disorder research through natural language processing for social media and GISs for health were presented by Anthony Corso, PhD, of California Baptist University.

A broader discussion on technology and innovation for public health was provided by Azizi Seixas, PhD, of the University of Miami Media Innovation Lab. The organizers also led a discussion on public health big data, AI, and ethical challenges, with great insight from attendees. We were very aware that many of our speakers did not have specific backgrounds in public health. Their topics were intentionally welcomed due to their importance and relevance for the possibilities of public health innovation, collaboration, adaptation, and framework development. They were also invited because public health professionals often have not yet been working with these topics.

On the final day of the event, we met in person at the campus of the University of California, San Diego, where we provided 2 workshops that were also available via video conferencing. One workshop was hosted by Ming Hsiang Tsou, PhD, of San Diego State University on big data and GISs for precision public health. This was followed by a workshop on artifact evaluation by Gondy Leroy, PhD, of the University of Arizona, followed by health informatics presentations from researchers at the University of California, San Diego, and a networking reception where participants had the opportunity to discuss their conference reflections, build new partnerships, and share their interest in the future conference next year.

Postconference Feedback

We conducted a postconference survey to gather insights from attendees' experience and feedback, aiming to better understand their preferences and optimize our marketing strategies for the PHIAT Conference in the future. Most of the respondents learned about this conference via email and word of mouth and from the Public Health Podcast Network [21] newsletters and monthly events. Attendees of this inaugural conference were drawn to it for the opportunity to advance their professional development.

The postconference survey asked why participants were interested in attending; their comments, with our responses, are shown in Table 1.

Table 1. Postconference survey comments from participants and our responses.

Comment	Response
"I'm a public health informatics epidemiologist and I am really interested to learn more about how we can make our informatics program more advanced and efficient."	PHIAT was designed with the public health workforce and academia in mind. With innovation and corporate development and academic partnerships, the goal was to improve the quality of public health data processes while fueling innovative ideas for research and development for positive public health implications.
"My position is focused on chronic disease informatics, and I was hoping to see examples of informatics methods and case studies using electronic health records or clinical data."	Developing workflows for electronic health data and building health information exchange infrastructure are continuing goals for public health, and another goal with the PHIAT Conference is to cultivate better processes for building public health informatics infrastructures. The use of informatics is still relatively new for public health departments, and this is often beyond the scope of departmental epidemiological methods. We hope to include more public health informatics professionals to speak at our conferences as the event becomes more established.
"I was very interested in hearing from guest speakers experienced in the IT side of public health and knew there would be a great variety in professionals sharing their knowledge."	There is a small percentage of public health professionals who have been trained in foundational IT skills, such as database development, the software development life cycle, and informatics frameworks, and we were excited to invite and bring these individuals together through the conference. We also intended to welcome new professionals and researchers into this field, either for their own research or professional development interests or to increase institutional knowledge at their public health departments.
"The main reasons for attending this conference were to foster and enhance professional growth and development. This public health informatics conference provides educational sessions (what tools can be used by combining machine learning and GIS), training workshops (how to develop a research question), and tutorials that focus on enhancing technical skills, understanding policy frameworks, and mastering health information technologies. Attending these meetings has allowed me to extend my horizons and keep ahead of the curve in my career."	The decision not to focus on one specific public health technological topic, such as epidemiological surveillance, and to focus on a broad range of topics in informatics and technology for public health professionals provided the opportunity for professionals to learn from a breadth and depth of knowledge. We hope that professionals had the opportunity to learn about ideas, topics, and developments that they had not heard of before. We also hope that attendees left the event with new ideas, approaches, and concepts to advance the quality of their work and their career development.

Respondents indicated an interest in a variety of educational seminars, training workshops, and tutorials at the conference with the goal of improving their personal technical proficiency, comprehending policy frameworks, and mastering health information technologies. They expressed a desire to learn more about developing research questions, using electronic health records and clinical data in informatics approaches and case studies, and merging machine learning and GIS technologies, which were topics covered in our conference sessions. One of the respondents said, "Attending these meetings helped me stay at the forefront of the field as a public health informatics epidemiologist with a focus on chronic illness informatics." In order to progress and refine their organization's informatics program for increased efficiency and effectiveness, attending meaningful conferences has been crucial. One participant indicated that they learned about the conference from other guest speakers well-versed in the IT side of public health, which is driven by an insatiable need for information. They excitedly

embraced the chance to receive insightful knowledge and immerse themselves in a wide range of skills.

Attendee feedback highlighted several key aspects of their experience at the public health informatics conference. They commended Nanette Star's presentation and the use of QR codes in the slides to enhance interactivity. The suggestion to include more presentations of this nature for future events was well received. Additionally, attendees expressed interest in hearing from major health care organizations regarding their use of community health care data and the impact of IT developments on care improvements. In relation to the timing of the conference, we received suggestions that the length of the conference remain 1-3 days with 4-5 hours a day of presentations and 3 hours for practice, questions, and discussions.

In terms of cost, based on the 3 day–long conference in San Diego, which included a valuable networking reception, participants suggested an average registration fee of US $400 per person. In addition, based on the financial considerations that some attendees might have, participants also sought opportunities for a discounted student rate and a reduced rate for professionals currently experiencing unemployment. Further suggestions included hiring professional teams to run the event, which would help us focus on moderating the panels. In order to enhance the conference experience, attendees also suggested adding interactive sessions with explicit discussion questions or expert panels. They observed that several themes appeared to be more concerned with public health than public health informatics, which suggests that the conference's thematic substance can move toward becoming more focused on public health informatics technologies. Partnering with recognized public health informatics leaders or organizations, like the US Centers for Disease Control and Prevention's Office of Informatics and Information Resources Management, was also advised.

Overall, there was general interest in the various topics of public health technology and precision public health and enthusiasm in the discussions.

Conclusion

The inaugural PHIAT Conference was an engaging, informative, and much-needed event providing public health professionals with information that many in the field were not previously familiar with. The technological side of public health is a crucial part of the future of health, yet many professionals are still new to the concepts of how AI, machine learning, and other technologies of precision public health can contribute to their organizations' data and infrastructure capabilities.

Lessons Learned

We found a high level of interest in the topics presented and are looking forward to continuing these discussions to further build, support, and develop public health technological infrastructure. In addition, most attendees appreciated the interactive sessions with discussion questions and expert panels, suggesting that more such sessions be included in future events.

When asked in the postevent survey about their feedback for improvement, attendees provided their feedback, including the statements in Table 1.

We plan to continue the PHIAT Conference yearly and collaborate with additional institutions who work in public health informatics. At this time, we will continue to host the event in the San Diego or southern California area.

Future Plans

For the time being, the conference will be presented in 2 formats in alternate years. For 2024 and even-numbered years, the event will be a 1-day PHIAT summit event to continue with updates in the field by selected leaders in health IT, GISs, machine learning, modeling and simulation, and more to provide interim updates from policy and innovation perspectives. The event will return in odd-numbered years in the 3-day abstract submission format, highlighting new developments in various public health IT and informatics topics with discussion from academics, public health practitioners, and enterprises. To support event accessibility, we will likely continue to use an in-person, 3-day format for the next event, with the option to participate online as well for those who are unable to travel due to logistical or financial concerns. With the expansion of fellowships and programs in public health informatics and technology, we would like to collaborate and partner for a larger discussion on workforce preparedness. Additionally, we are seeking sponsorships to create a space for greater impact and reach in public health informatics and technology.

Acknowledgments

We would like to thank Gerardo Arellano, PhD, and the University of California, San Diego, Raza Resource Centro for providing space for the 2023 Public Health Informatics and Technology Conference (PHIAT) Conference, as well as our student volunteers Diana Carrillo, Joshua Chola, Valeria Vallejo-Montoya, and Rainaclare Sibal for assisting with the event.

Conflicts of Interest

AMA is the founder of the Public Health Media Network, which sponsored this event. The authors have no other conflicts to disclose.

Multimedia Appendix 1
The 2023 Public Health Informatics and Technology Conference Agenda Booklet.

[PDF File (Adobe PDF File), 5268 KB - ojphi_v16i1e55377_app1.pdf]

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Abbreviations

AI: artificial intelligence
EHR: electronic health record
GIS: geographic information system
ML: machine learning
PHIAT: Public Health Informatics and Technology
QHIN: qualified health information network
TEFCA: Trusted Exchange Framework and Common Agreement

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Review

Roles of Health Literacy in Relation to Social Determinants of Health and Recommendations for Informatics-Based Interventions: Systematic Review

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Abstract

Background: Health literacy (HL) is the ability to make informed decisions using health information. As health data and information availability increase due to online clinic notes and patient portals, it is important to understand how HL relates to social determinants of health (SDoH) and the place of informatics in mitigating disparities.

Objective: This systematic literature review aims to examine the role of HL in interactions with SDoH and to identify feasible HL-based interventions that address low patient understanding of health information to improve clinic note-sharing efficacy.

Methods: The review examined 2 databases, Scopus and PubMed, for English-language articles relating to HL and SDoH. We conducted a quantitative analysis of study characteristics and qualitative synthesis to determine the roles of HL and interventions.

Results: The results (n=43) were analyzed quantitatively and qualitatively for study characteristics, the role of HL, and interventions. Most articles (n=23) noted that HL was a result of SDoH, but other articles noted that it could also be a mediator for SdoH (n=6) or a modifiable SdoH (n=14) itself.

Conclusions: The multivariable nature of HL indicates that it could form the basis for many interventions to combat low patient understandability, including 4 interventions using informatics-based solutions. HL is a crucial, multidimensional skill in supporting patient understanding of health materials. Designing interventions aimed at improving HL or addressing poor HL in patients can help increase comprehension of health information, including the information contained in clinic notes shared with patients.

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KEYWORDS

health literacy; social determinants of health; SDoH; social determinants; systematic review; patient education; health education; health information; information needs; information comprehension; patient counseling; barriers to care; language proficiency

Introduction

Overview

In recent decades, medical providers, health systems, and legislators have prioritized increasing patient access to health information. For example, the 21st Century Cures Act mandates that patients must have access to their electronic health records, including clinic notes, in a rapid and convenient manner [1]. However, clinic notes and other health information can contain jargon that is difficult for patients to comprehend, reducing the utility of health information sharing. The Healthy People 2030 initiative, sponsored by the US Department of Health and Human Services, aims to address this issue by increasing patient comprehension of health information received from providers and web-based sources, such as their electronic health records [2].

A key part of health information comprehension is health literacy (HL), the ability to understand, contextualize, and make well-informed decisions based on health information [3]. Reducing HL gaps is crucial to meeting the goals set forth by Healthy People 2030 and maximizing the benefits of the 21st Century Cures Act.

Health Literacy

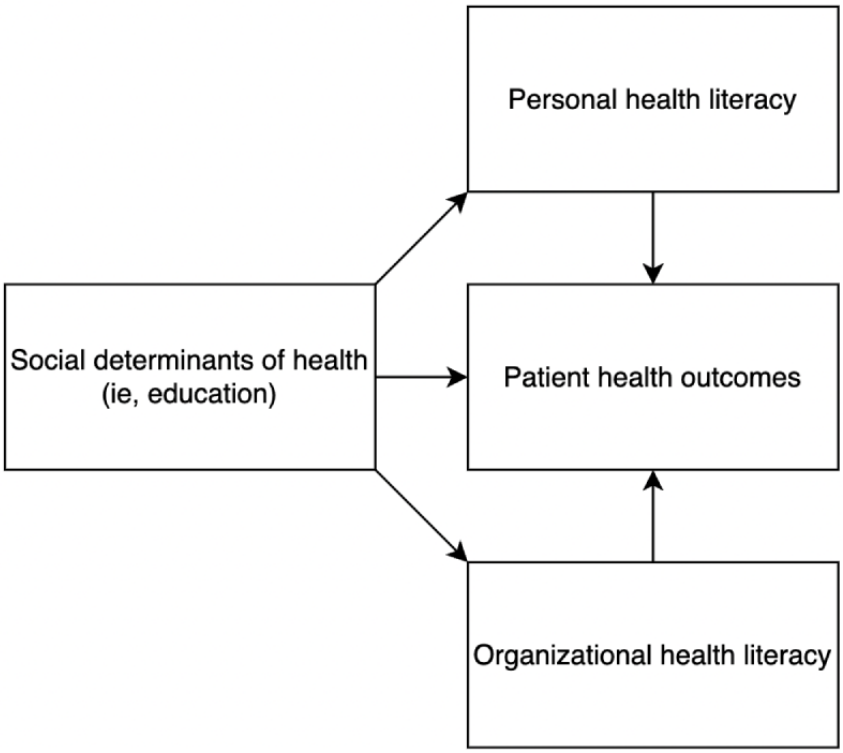
Having high HL correlates with greater shared decision-making between patients and physicians and promotes positive health outcomes because patients can better comprehend and act on the health information they receive [4]. Healthy People 2030 distinguishes between two dimensions of HL: personal, as previously described, and organizational [2]. Organizational HL holds health care systems and providers accountable for providing their patients with comprehensible health information to make informed decisions. This newer understanding of HL raises questions about how HL fits into the public health framework addressing disparities in health comprehension.

Social Determinants of Health and Health Literacy

Social determinants of health (SDoH) are nonmedical social and economic factors that fall into the following 5 domains: economic stability, education, health care and access quality, neighborhood and built environment, as well as social and community context [5,6]. SDoH affects health status and outcomes, and it can generate health disparities between population groups by influencing patient behavior and organizational responses. These determinants are also distinct from social factors or needs that exist at the individual level and instead exist as community- or population-level barriers [7-9].

HL has been categorized in different sources as an SDoH itself and as a midstream consequence of SDoH that can impede or improve patient interactions with health care institutions and health outcomes (ie, vaccination status and screening utilization) [10-12]. For example, a study by Schillinger et al [13] proposes that a higher education level improves HL, which was associated with better glycemic control among patients with diabetes. This is a unidirectional characterization of the relationship between SDoH, HL, and health outcomes, depicted in Figure 1.

Figure 1. Relationships characterized by the influence of social determinants of health on health literacy (personal and organizational), subsequently impacting health outcomes.



However, this may be an oversimplification. HL can evolve through continued exposure to health environments and interventions at the personal and organizational levels [14]. Moreover, even patients with high HL can struggle with comprehension in different contexts. Therefore, this relationship warrants further investigation, as there is a lack of systematic

literature analyses that macroscopically evaluate how SDoH and HL are related across different SDoH domains [15]. Understanding the nature and role of HL in interactions with SDoH can also indicate the most effective approach to designing HL-targeting interventions for patients who struggle to understand health information.

Objectives

Due to the literature gap in examining the complex relationship between HL and SDoH, we aimed to conduct a systematic literature review to (1) understand this relationship and (2) recommend informatics-based interventions to address low HL among patients.

Methods

Search Strategy

We systematically reviewed literature in PubMed and Scopus, two major biomedical and social science literature repositories. The initial database searches were conducted on June 22, 2020. The review followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2009 guidelines to understand the relationship between HL and SDoH [16,17].

The search terms used were "health literacy" AND "social determinants of health." After filtering for non-English articles and articles without abstracts, the remaining 281 articles were compiled in a Microsoft Excel sheet with their title, author, publication year, DOI or PMID, and abstract.

Screening Process

Two researchers (SB and CX) independently screened 281 papers by title and abstract and used the following exclusion criteria: (1) HL is a minor factor in the article; (2) the article is not an empirical study; (3) the article focuses on HL measurement tool development or evaluation; (4) the paper does not examine HL in relation to SDoH; (5) no abstract is available; and (6) the paper is not written in English.

Each researcher independently gave the article a score of "1" for inclusion or "0" for exclusion. The scores were summed; articles scoring "2" were automatically included, and those scoring "0" were excluded from the full article eligibility review. Disagreements (any papers with a total score of "1") were resolved by the authors after the initial screening. The process was repeated for the full-article eligibility review and subsequent reference screening from the included full articles. Reference screening was a precautionary step to ensure the inclusion of articles that may not have been included in the initial database search. Original exclusion criteria were consistently used.

Quality Assessment

Before the information extraction, all included articles were assessed by 2 researchers (SB and TG) for study quality. Using the Agency for Healthcare Research and Quality (AHRQ) guidelines, separate quality assessments were developed for each type of study included in the review—observational studies and randomized clinical trials (RCTs) [18]. Domains included in both study types were study questions, population, interventions, outcome measurement, statistical methods, results, discussion, and disclosure of funding or sponsorship. Domains evaluated in the RCT assessment also included blinding and randomization.

The reviewers created a 3-point scoring system for the quality assessment. Articles were rated by 2 team members (SB and TG) with scores of "good," "fair," and "poor" for each domain and assigned numerical values of 2, 1, and 0, respectively, as per the AHRQ guidelines [18]. Values were averaged and translated back to a rating of "good" (1.50 or higher), "fair" (1-1.49), and "poor" (0-0.99).

Information Extraction

Based on quality assessment results, 43 papers were included for information extraction. Four researchers (CB, CX, AN, and TV) extracted data for the following PRISMA-based criteria: title, author, article ID, year published, location, study design, sample demographics, results, and limitations [16]. To answer the research questions, information specific to SDoH focus, HL measurement, and health outcomes was collected. The information extraction sheet is attached as Multimedia Appendix 1.

Quantitative and Qualitative Data Analysis

Extracted data were analyzed both quantitatively and qualitatively. Location, year of publication, and study design were statistically summarized. AHRQ guidelines were used to categorize studies as RCT, cross-sectional, and qualitative designs, with the last two being types of observational studies [19].

Qualitative analysis was conducted in 2 steps. First, a narrative synthesis of the chosen articles summarized the relationships between SDoH and HL. Narrative synthesis involves analyzing the data from systematic reviews to create textual explanations of observed patterns or trends rather than relying solely on statistical data. This involves developing textual descriptions of the data by extracting key information pertinent to the research question (ie, methods used or results) and exploring commonalities and differences between and within studies (ie, through visually mapping relationships) [20]. These methods were also used in a systematic review previously published by the authors [21]. The included articles were classified by SDoH domains they addressed, per the 5 domains defined by Healthy People 2030: economic stability, education, health care access and quality, neighborhood and built environment, as well as social and community context. Then, information extraction data from article results and discussion sections were used to define roles for HL. Finally, a theme visualization was conducted that plotted HL roles against publication year to understand how HL perception has evolved.

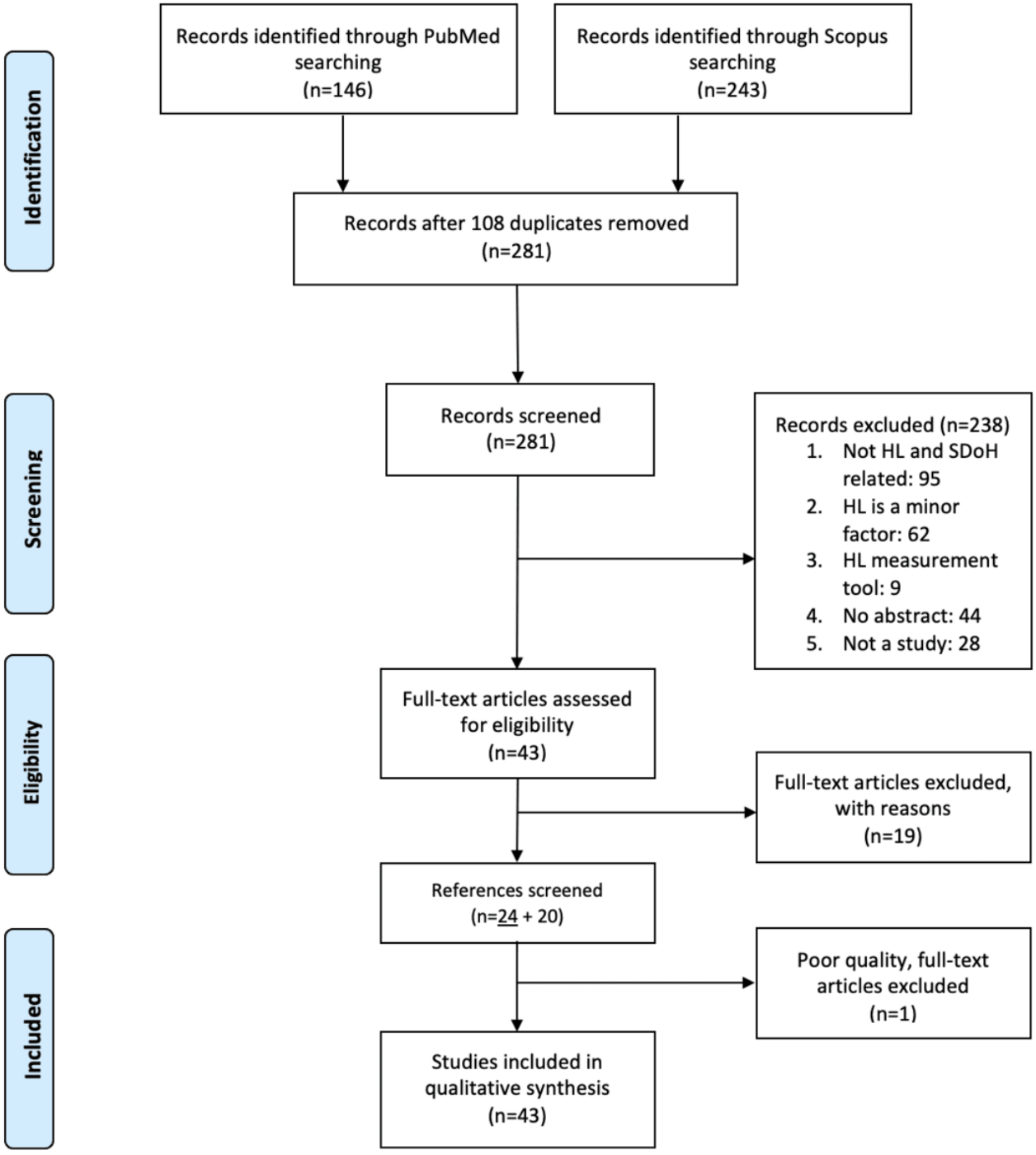
In the second step, lessons learned were summarized regarding HL roles, again using the results and discussion sections. From these same sections, the authors then extrapolated possible interventions that use HL to improve patient comprehension of health information.

Results

Literature Search Results

The PubMed and Scopus searches yielded 389 articles, resulting in 281 unique articles (Figure 2). After screening titles and abstracts, 43 articles remained for full-text eligibility assessment. Not discussing HL and SDoH together (n=95) was the largest cause for exclusion. Other papers were excluded because HL was not a substantial focus of the paper (n=62). A total of 19 articles were excluded from the full-text eligibility, once again for a minor focus on HL. References of the remaining 24 articles were screened for inclusion, yielding 20 additional articles. After the quality assessment, 1 low-quality article was excluded. Information extraction and narrative synthesis were conducted on a final sample of 43 articles.

Figure 2. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram of articles from the PubMed and Scopus search. A total of 24 articles (underlined) were included from the first database search.



Quantitative Analysis

The final 43 articles were analyzed for study location, year of publication, role of HL, and study design (Table 1). A total of 14 (32.6%) studies took place in North America (12 in the United States and 18 in Europe). All articles from South America originated in Brazil (n=4). Publication year trends revealed an increased focus and discussion of the topic in recent years, with 90.7% (n=39) of the articles being published after 2010. Most articles (n=40, 93%) had a cross-sectional design and used surveys, while 4.7% (n=2) used a qualitative design with semistructured interviews and focus questions to assess SDoH and HL.

Table 1. Summary of articles included in the literature review (N=43).

Category	Values, n (%)
Study location	
Europe	18 (41.9)
North America	14 (32.6)
Asia	6 (14)
South America	4 (9.3)
Australia	1 (2.3)
Year published	
2006-2009[a]	4 (9.3)
2010-2013	9 (20.9)
2014-2017	15 (34.9)
2018-2021	15 (34.9)
Study design	
Cross-sectional	40 (93)
Qualitative	2 (4.7)
Randomized controlled trial	1 (2.3)

[a]The search was not limited to 2006 for publication year; this was the earliest date among the 43 articles.

Qualitative Analysis

Narrative Synthesis

The narrative synthesis generated 4 roles for HL in relation to SDoH (Table 2). Most of the articles discussed multiple SDoH domains, but all 43 articles discussed education access and quality [5].

The most common categorization of the HL role was as a "result of SDoH" (n=23), followed by "modifiable SDoH" (n=14), and finally, as a "mediator of SDoH" (n=6). HL can be a "result of SDoH" (n=23), which suggests that SDoH domains contribute to HL levels and that it is a downstream variable [22-44]. As mentioned, 14 studies identified HL as a "modifiable SDoH," where they identified HL as an SDoH, often citing the World Health Organization's categorization of it; these studies suggested that HL can be improved through interventions and is actionable at multiple levels [14,45-57]. Finally, the articles that categorized HL as a "mediator of SDoH" (n=6) discussed how HL is an intermediary between other SDoH domains, such as educational attainment or economic stability, and that high HL levels can compensate for lower domain levels that compromise positive health outcomes [58-63]. Occasionally, the same paper would suggest multiple roles for HL (eg, an article's Results and Discussion sections would inform both modifiable and mediatory roles for HL), but the most prominent relationship that appeared was used to categorize each article.

These 3 roles were plotted against the years of publication in Figure 3. In the few HL-focused articles published before 2010, HL was recognized as having a variety of roles, but only 1 article identified it as a modifiable SDoH. In the next 5-year period, being a result of SDoH was the most common role assigned to HL. In 2013, a total of 5 out of 7 articles identified HL as being a result of SDoH. As the number of published HL-focused articles increased in subsequent years, being a result of SDoH remained the most consistent and most prominent role assigned to HL to appear across all articles. Nevertheless, there has been increasing recognition of HL as a modifiable SDoH in the years 2015, 2018, and 2020, further cementing HL's multidimensional nature.

Table 2. Summary of narrative synthesis themes.

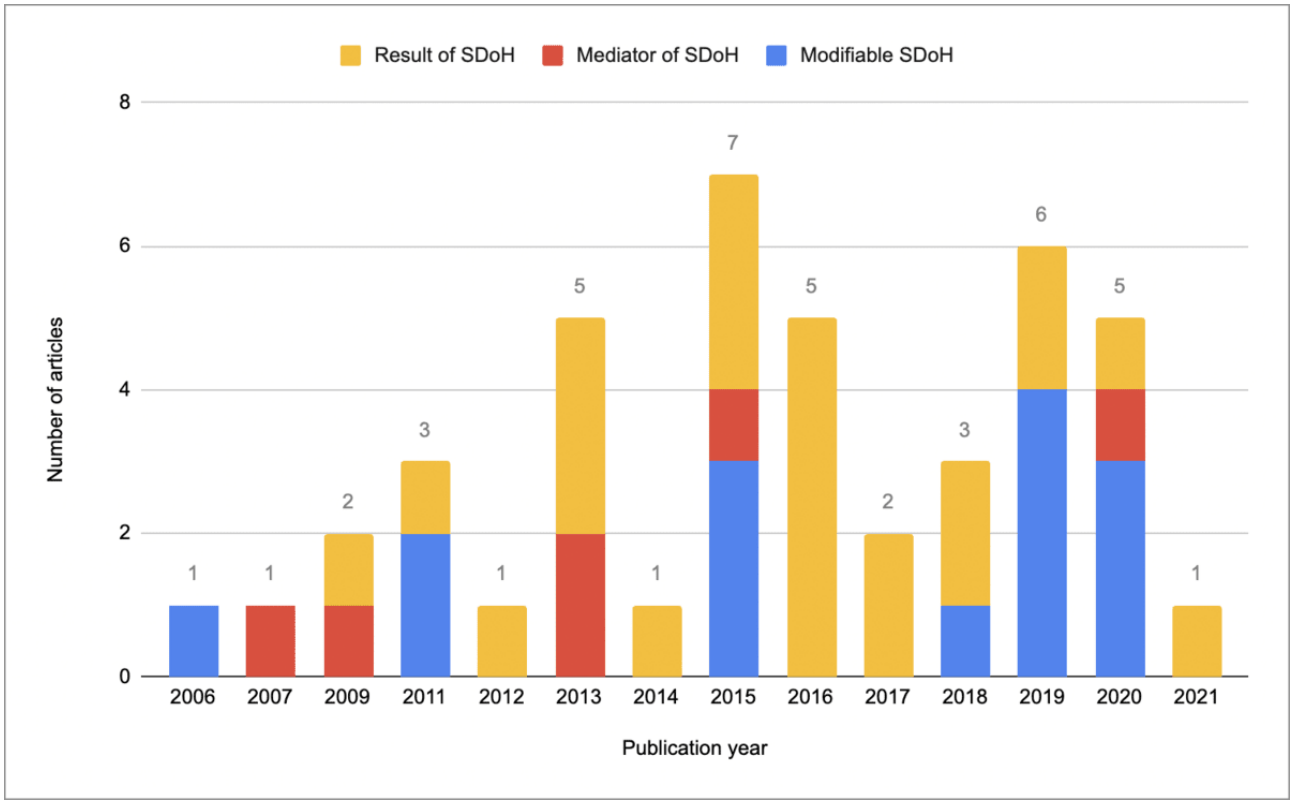
Category	Values, n (%)
SDoH[a] domain[b]	
Education access and quality	43 (100)
Economic stability	38 (88)
Health care and access quality	11 (26)
Social and community context	11 (26)
Neighborhood and built environment	9 (21)
HL[c] role	
Result of SDoH	23 (53)
Modifiable SDoH	14 (33)
Mediator of SDoH	6 (14)

[a]SDoH: social determinant of health.

[b]Most of the articles included more than 1 SDoH domain they studied.

[c]HL: health literacy.

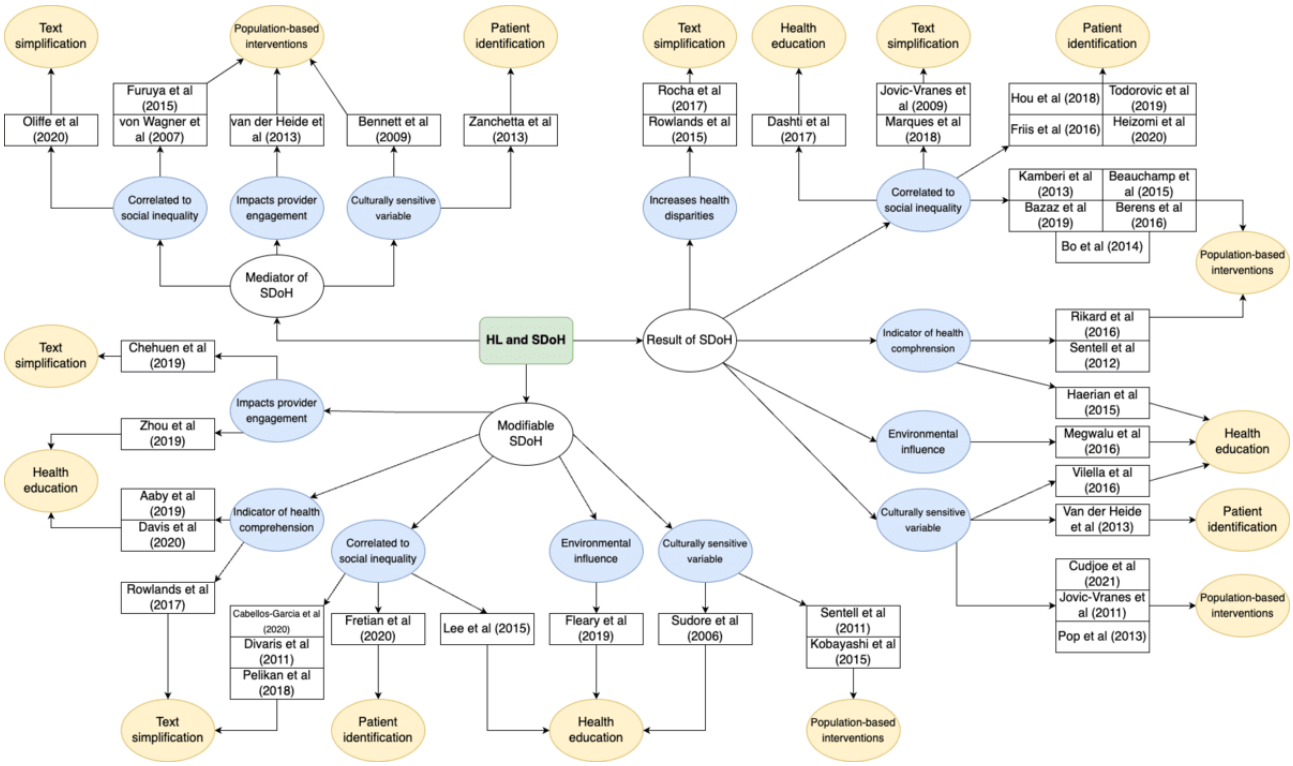
Figure 3. Theme visualization of the evolution of health literacy roles over time. SDoH: social determinants of health.



Lessons Learned

In addition to analyzing articles for the HL role, each article was further examined to determine details about the nature of the relationship between HL and SDoH. These were titled "lessons learned." Figure 4 [14,22-63] shows an idea map that organizes articles by the role of HL and lessons learned. Although most of the articles are cross-sectional and do not always draw a causal relationship between Hl and SDoH, the authors of the articles nevertheless offer hypotheses on factors influencing HL or how it interacts with SDoH and health outcomes.

Figure 4. Idea map of health literacy (HL) roles, lessons learned, and article breakdown. Each role (white oval) is broken down into lessons learned (blue oval) and then into the article title and author (white rectangle) and possible intervention focus (yellow oval). SDoH: social determinants of health [14,22-63].



HL as a Result of SDoH (n=23)

Being a result of SDoH was the most frequent role identified for HL. These articles characterized HL as being associated with, influenced by, or resulting from other SDoH. All articles addressed that a higher level of education, such as high school graduation, had implications on HL levels [22-44]. Bazaz et al [22], Berens et al [24], and Rocha et al [39] have suggested that HL is developed through interactions with health care due to age and disease condition, and more interaction with health care over time leads to an improvement in HL. Hou et al [31], Jovic-Vranes et al [32], Kamberi et al [34], and Todorovic et al [41] also note that lived environments have an important role in HL development. Kamberi et al [34] argue that rural versus urban environments influence SDoH, such as health care access and quality, thereby, impacting HL development [34]. Beauchamp et al [23], Berens et al [24], Cudjoe et al [26], and Sentell et al [40] observed that HL is also influenced by the patient's primary language, especially if the patient's primary language is different from the language of the health system. Bo et al [25] and Pop et al [37] elaborated on the relationship between education and HL; they found that lower levels of language proficiency and self-perceived health can indicate lower HL. Heizomi et al [30] and Dashti et al [27] notice gender disparities in HL among students in Iran, with the latter observing that cultural differences encouraged technology access for men at a younger age, leading to higher HL levels among men compared to women [27,30].

HL as a Modifiable SDoH (n=14)

The 14 articles that classified HL as an SDoH did so following the World Health Organization's classification and previous research or by defining determinants as factors that impact or predict health outcomes. Aaby et al [45] classify HL as an SDoH because it is a combination of "personal competencies and situational resources" that affects individuals' interaction with health care institutions. Some authors, despite describing HL as an SDoH, still note that it is related to other SDoH as well. Cheuhuen et al [47] identify that HL is associated with economic stability and education, and Lee et al [55] and Sentell et al [46] both associate it with the social context. Articles also identified various health outcomes that HL may impact. Cabellos-Garcia et al [48] and Zhou et al [57] identified that poor HL could lead to reduced understanding of disease conditions and engagement with providers. Nevertheless, all 14 articles emphasize that HL is a modifiable SDoH that can change over time through interventions [14,45-57].

HL as a Mediator of SDoH (n=6)

A total of 6 articles established that, as a mediatory variable, HL can both compensate for and contribute to disparities in SDoH. Some articles define HL as an SDoH itself but further classify it as a mediator for other determinants. All 6 articles included education and income as SDoH for which HL could serve as compensation [58-63]. Bennett et al [59] also suggest that having high HL can compensate for racial or ethnic disparities in health outcomes. Zanchetta et al [63] describe that HL mediates between disparities in health care access and quality as well as social cohesion and context. To address poor HL among patients, van der Heide et al [62] recommend simplifying medical jargon. When designing these interventions, Bennett et al [59] emphasize considering complex patient perspectives and unique demographic needs, such as those of

the geriatric population, which differ from those of younger patients.

Informatics Interventions

The secondary objective of the study was to identify informatics-based interventions to improve HL. Articles rarely provided specific intervention recommendations but instead listed several potential problems, such as complicated medical jargon or low health awareness, that complicate patient understanding of health information. Therefore, 4 informatics-based solutions were proposed based on the research team's knowledge and experience for the identified problems, as follows: (1) language or text simplification, (2) population-focused (or policy-based) interventions, (3) health education efforts, and (4) patient identification. Since the included articles were largely not interventional in nature, the following sections extrapolate on the recommendations with references to ongoing studies that have implemented these strategies.

Discussion

Principal Findings

This systematic review included 43 papers and reported the results following the PRISMA guidelines. Most studies were conducted in Europe in the past 5 to 10 years. The studies examined HL in relation to the two themes of SDoH—health-focused and demographic—and generated 3 roles for HL, as follows: a mediator of SDoH, a result of SDoH, and modifiable SDoH. More than half of the studies had a cross-sectional design. However, HL is a complex, actionable variable that may be targeted by various strategies.

Proposed Interventions

As clinical note sharing becomes more popular, generating interventions that address low HL becomes even more crucial. In this vein, we generated 4 recommendations for focused HL interventions based on the key findings of this systematic review.

Interventions with an informatics focus could play a particularly vital role in improving patient comprehension of health information as the health care field becomes increasingly mobile and technology dependent. It is important to consider experimental methods to measure the efficacy of implementing these strategies. Including control groups and validated HL measuring tools can help monitor how different interventions influence patient HL levels. Validated measuring tools include the Rapid Estimate of Adult Literacy in Medicine (REALM), REALM-Short Form, Short Assessment of Health Literacy-Spanish and English (SAHL-S&E), Brief Health Literacy Screen (BHLS), and Test of Functional Health Literacy in Adults (TOFHLA) [64-66]. The REALM, REALM-SF, and SAHL-S&E have all been validated and recommended by the AHRQ. The REALM and SAHL-S&E are recommended for research purposes to assess participant HL, while the REALM-SF, BHLS, and TOFHLA have been validated for use in screenings in clinical settings [66,67]. The REALM-SF is particularly designed to identify limited literacy levels [67]. Therefore, the clinically usable metrics may be more relevant for interventions that take place in health care settings, such as patient identification.

Language and Text Simplification

Text simplification addresses the tendency of clinic notes and health information in general to include medical jargon that exceeds the comprehension levels of most patients [42,44,62]. Even patients with highly educated backgrounds have shown low scores on HL surveys. Therefore, text simplification can benefit patients across all HL competencies by reducing jargon and making health information more easily understandable and usable [62]. Text simplification does not replace the existing clinic note shared between providers; it provides a simplified version for patients in addition to the original note. Current research indicates that the most effective manner of text simplification relies on manual editing techniques using human oversight of a text simplification process, combined with information visualization [68]. Although simplification improves patient comprehension, manual editing could strain health care professionals' workload. Therefore, developing informatics interventions that automate text simplification while retaining the grammatical and logical integrity of the clinical text is important. Current automated simplification methods scored poorly due to grammatical errors, repetition, and inconsistencies in the autogenerated documents [68]. Artificial intelligence–derived text simplification methods may overcome these barriers by matching a document's reading level to the readers' needs, as shown in a study where ChatGPT was able to modify answers to men's health condition questions to accommodate lower reading levels [69,70]. However, popularly used AI tools, such as ChatGPT, need considerable evaluation to minimize inaccurate information delivery and improve comprehensibility. Current studies indicate that these tools lack citations for the information they provide and cannot differentiate between low-quality and high-quality information [70,71].

Population-Based Visualization and Cross-Cultural Communications

HL needs are different across populations and cultural contexts, and interventions should account for these differences. For example, non–English-speaking individuals are overlooked in many HL studies, and interventions targeting English speakers will not always suit those with a limited or nonnative grasp of English [23,72]. Realizing this limitation, the OPHELIA (OPtimising HEalth LIterAcy) [73] project is a multisite study that assesses HL strengths and weaknesses in their patient population at each study site and uses these responses to determine appropriate intervention methods. Equally important is including representatives from the community in intervention design. A systematic review looking at interventions that address HL among Aboriginal and Torres Strait Islander community members noted that many failed to include these patients in the design process and consequently had limited participant retention [74]. Another facet is implementing policy-level changes that increase access to HL support. This is particularly relevant for patients who face health inequity. However, implementing these changes has been slow. In the European Union, challenges such as funding constraints and obstacles to

initiatives have prevented effective execution beyond a few countries [75]. The population-based and policy-level interventions should consider visual analytics to explore meaningful patterns in a large data set and use recent advances in natural language understanding and translation to promote cross-cultural communication [76].

Patient Identification

Although population-focused and policy-level interventions address low HL at the macro level, such methods may overlook the individual HL needs of a patient. Therefore, screening HL levels as a part of standard practices in health care settings can help identify patients who need additional support at the clinic visit and can expedite provider response [36]. For example, Vanderbilt University Medical Center and the University of Arkansas Medical Sciences incorporate HL screening as part of their educational health assessment and have done so since 2010 and 2016, respectively [77]. Screening may also involve various informatics tools. For example, patients can be actively screened using electronic data capture tools (eg, REDCap) [78]. These informatics tools should be integrated into clinical workflow to ensure the quality of data. On the other hand, patient cohorts can be identified by reports or dashboards of electronic health records or medical text search engines (eg, Electronic Medical Record Search Engine [EMERSE]) [79]. Once the patient group is targeted, inclusive HL interventions can be designed and executed. However, implementing screening practices should be done with caution to avoid perpetuating stigma or embarrassment. Integrating screening questions within the clinical workflow and training health professionals on screening administration can help address these concerns [77].

Health Education and Online Community Building

Given the relevance of socialization and environment on HL development, it is important to consider interventions that cultivate HL through health education. Health care providers, such as nurses and community health workers, have important roles in providing education and reinforcing patient understanding of their health conditions [63,80]. However, the burden on health education cannot be placed on providers alone. Health education programs implemented by health care organizations and community health centers can actively and effectively improve HL [81]. It is important to adapt these programs for cultural and demographic sensitivity and patient-provider communications. For example, a recent study targeting older adult needs emphasized the need to include the patient's caregivers and to accommodate barriers in comprehension, especially cognitive ones [82]. Health education intervention should consider developing an online community, such as ImproveCareNow, to promote collaborative care and build repositories of patient education materials with well-designed education programs to help patients improve their HL [83]. Including the input of individuals who are well-integrated into and familiar with the needs of a patient population, such as community health workers, can also be helpful in this process [80].

Limitations

There are a few limitations in the methodology and generalizability of our research. First, we conducted a database search of only PubMed and Scopus, limiting the scope of the article search. However, PubMed and Scopus are two of the most popular and largest databases in biomedical and social science research. During the analysis, it was clear that the results were concise and supported one another. For example, several articles noted multiple roles for HL but tended to focus on one. Second, very few articles included noncorrelated results because of their cross-sectional designs. This prevented researchers from drawing a causative relationship between HL and SDoH, but they nevertheless had hypotheses for relationships that informed our classification. Third, the PRISMA guidelines were updated in 2020 with new standards and recommendations for systematic reviews. As we had already made considerable progress in this project before the revision was published in 2021, we completed the data analysis using the 2015 reporting standards that originally informed our methods. However, in cross-referencing our methods with the 2020 revisions, our research largely adheres to the new guidelines [84].

Conclusions

The articles included in this literature review indicate that HL can adopt various roles in conjunction with SDoH. This flexibility makes HL an appropriate topic for intervention to accommodate poor health outcomes and improve patient autonomy. However, the complex nature of HL means that it warrants further research to understand how HL-targeted interventions impact this process.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Literature search and information extraction.
[XLSX File (Microsoft Excel File), 61 KB - ojphi_v16i1e50898_app1.xlsx]

Multimedia Appendix 2
PRISMA Checklist.
[PDF File (Adobe PDF File), 109 KB - ojphi_v16i1e50898_app2.pdf]

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Abbreviations

AHRQ: Agency for Healthcare Research and Quality
BHLS: Brief Health Literacy Screen
EMERSE: Electronic Medical Record Search Engine
HL: health literacy
OPHELIA: OPtimising HEalth LIterAcy
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT: randomized clinical trial
REALM: Rapid Estimate of Adult Literacy in Medicine
SAHL-S&E: Short Assessment of Health Literacy-Spanish and English
SDoH: social determinants of health
TOFHLA: Test of Functional Health Literacy in Adults

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Review

e-Cigarette Tobacco Flavors, Public Health, and Toxicity: Narrative Review

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Abstract

Background: Recently, the US Food and Drug Administration implemented enforcement priorities against all flavored, cartridge-based e-cigarettes other than menthol and tobacco flavors. This ban undermined the products' appeal to vapers, so e-cigarette manufacturers added flavorants of other attractive flavors into tobacco-flavored e-cigarettes and reestablished appeal.

Objective: This review aims to analyze the impact of the addition of other flavorants in tobacco-flavored e-cigarettes on both human and public health issues and to propose further research as well as potential interventions.

Methods: Searches for relevant literature published between 2018 and 2023 were performed. Cited articles about the toxicity of e-cigarette chemicals included those published before 2018, and governmental websites and documents were also included for crucial information.

Results: Both the sales of e-cigarettes and posts on social media suggested that the manufacturers' strategy was successful. The reestablished appeal causes not only a public health issue but also threats to the health of individual vapers. Research has shown an increase in toxicity associated with the flavorants commonly used in flavored e-cigarettes, which are likely added to tobacco-flavored e-cigarettes based on tobacco-derived and synthetic tobacco-free nicotine, and these other flavors are associated with higher clinical symptoms not often induced solely by natural, traditional tobacco flavors.

Conclusions: The additional health risks posed by the flavorants are pronounced even without considering the toxicological interactions of the different tobacco flavorants, and more research should be done to understand the health risks thoroughly and to take proper actions accordingly for the regulation of these emerging products.

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KEYWORDS

vaping; e-cigarettes; tobacco flavors; toxicity; regulation; tobacco; public health; smoking; menthol; social media; nicotine; symptoms; symptom; risk; risks; toxicology; health risk; regulation

Introduction

Background

Tobacco flavoring is added to e-cigarettes to make them appealing to vapers, specifically by mimicking the taste of traditional cigarettes. Tobacco-flavored e-cigarettes are often advertised as a safer alternative to traditional cigarettes, which allow smokers to enjoy the taste they are familiar with more conveniently and smoothly for harm reduction. Tobacco-flavored e-cigarettes are very popular among various subpopulations of adults in the United States, with around 30% of vapers using these products [1]. However, the prevalence seems to be lower in dual users (vapers who also use traditional cigarettes) and vapers who used e-cigarettes as an attempt to

quit smoking, with the percentages being 28.5% and 20.5%, respectively [2,3].

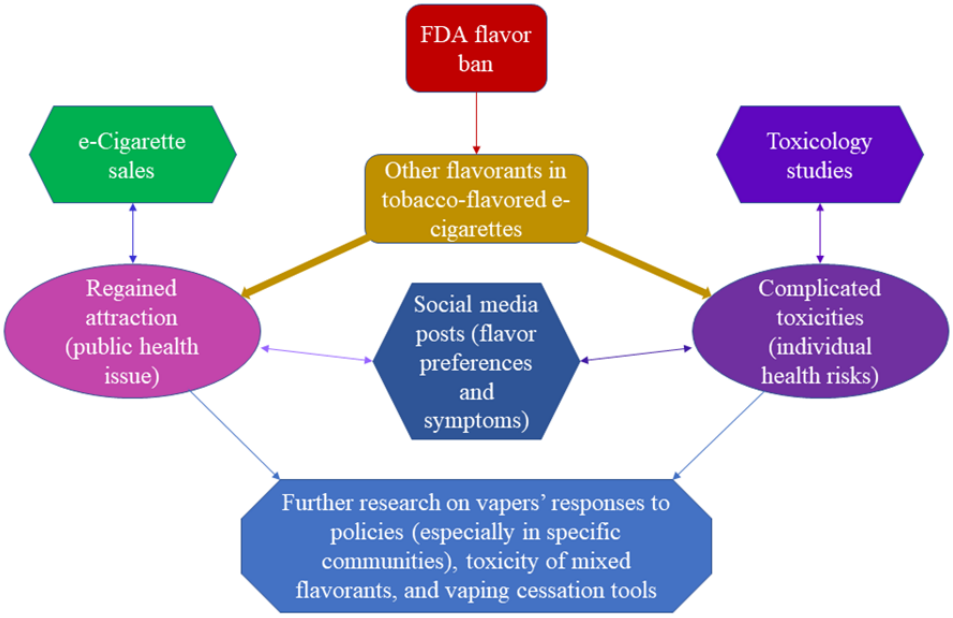
Although the taste of tobacco-flavored e-cigarettes mimics that of traditional cigarettes, the type of nicotine they contain may differ from traditional cigarettes. Recently, e-cigarette products have begun to contain synthetic nicotine or tobacco-free nicotine (TFN), a racemic mixture of both R- and S-nicotine isomers, which is different from the traditionally used tobacco-derived nicotine that is composed of pure S-nicotine [4]. Initially, e-cigarette products began to use TFN since it was not regulated by the US Food and Drug Administration (FDA), and products were able to be brought to the market since these products did not need to go through the premarket tobacco product application for e-cigarettes [4]. Although initially brought to the market without government regulation, in 2022, new legislation expanded the authority of the FDA to regulate TFN products as well [5]. Currently, limited data are available regarding the health effects of TFN, but studies have found that messaging by e-cigarette companies leads to the belief by e-cigarette users that TFN has a lower health risk compared to tobacco-derived nicotine and a higher intention to use TFN products [6]. Young adults between 18 and 25 years of age who were interested in trying TFN believed it to be less addictive than those who were uninterested, and those who have tried TFN reported that TFN products have flavors that taste better and smoother [7]. Similarly, young adults (aged 18-25 years) who were likely to purchase TFN pouches believed that TFN pouches were less harmful to a person's health; less addictive; and tastes smoother, cleaner, and better compared to young adults who would not purchase TFN pouches [8]. Due to the perception in young adults that TFN is less harmful and addictive, there is a need for more research on the health effects of exposure to TFN to aid government regulation and properly educate the public about any potential risks of using these compounds. More recently, Nixodine (ie, (S)-6-methyl nicotine), which is a structural analog of nicotine, and synthetic-free nicotine or tobacco-free nicotine have been introduced into the market as well without much being known about their biological or toxicological effects.

Besides the use of TFN in tobacco-flavored e-cigarettes, another important modification to these products is the addition of flavorants commonly used in other flavors. On February 6, 2020, the FDA implemented enforcement priorities against all flavored, cartridge-based e-cigarettes other than tobacco- and menthol-flavored products [9]. According to Rostron et al [10] in 2020, as much as 93.2% of youth vapers started vaping with a flavored e-cigarette, and among those who are still vaping, 71% reported the flavors of e-cigarettes as a reason for use. It was also indicated that youth vapers preferred fruit and mint flavors to tobacco or menthol flavors [11]. The tobacco flavors of e-cigarettes are made to mimic the flavor of traditional tobacco cigarettes with some variation. There are many different tobacco flavors made from hundreds of brands that can provide the user with different types of tobacco flavors, including "Classic Tobacco," "Smooth/Bold Tobacco," and "Virginia Tobacco." Demographically, tobacco flavors are more popular among adults and less popular among youth [12]. The lack of appeal of tobacco-flavored e-cigarettes to youth allows for fewer regulations. Therefore, we perceived that the ban on flavors other than tobacco and menthol undermined the e-cigarette products' appeal to youth vapers, as their favorite flavors were removed from access, thus largely decreasing the manufacturers' profit. To reverse the impacts brought by the difference in regulations, e-cigarette manufacturers started to blend other flavors into tobacco-flavored e-cigarettes, recreating the appeal for youth vapers [13,14]. For example, we found that an e-cigarette manufacturer has a fourth-generation e-cigarette product with a "Smooth Tobacco" flavor, which contains a combination of tobacco and cream flavors. The same entity also sells an e-liquid of "Tobacco Salt Rich" flavor, which is a mixture of tobacco, smokey vanilla, and creamy caramel flavors. Studies have also extracted flavorants that represent sweets and caramel-like flavors in an e-liquid marked "Smooth & Mild Tobacco" and multiple flavorants that do not belong to tobacco flavors in another tobacco-flavored e-liquid that was deidentified [13,15,16]. Such compounds include ethyl maltol, vanillin, corylone, and ethyl vanillin, which can lead to adverse health effects [14]. Additionally, the volatile organic compounds (VOCs), reactive oxygen species, and other compounds present in the tobacco-flavored e-liquids can pose further health risks.

Objective

The emergence of these new tobacco flavors may serve as a source for public health issues, and information related to them is critical for the establishment of regulations and interventions. Therefore, by analyzing the toxicity, characteristics, sales, social media perception, and public health aspects of tobacco-flavored e-cigarettes, this review aims to inform authorities about this issue and provide information for potential interventions (Figure 1).

Figure 1. A schematic of the discussion of new tobacco-flavored e-cigarettes and their associated problems. FDA: Food and Drug Administration.



Methods

To collect data, searches were conducted on Google Scholar and PubMed for papers published between 2018 and 2023 related to e-cigarette use patterns, toxicity of e-cigarette chemicals, social media posts about e-cigarettes, and public health interventions regarding e-cigarettes. Toxicity information was also included from articles published before 2018, and e-cigarette sales data and related policies were extracted from government websites and documents. The keywords for searching these sources of information included "tobacco-flavored e-cigarettes," "e-cigarette use," "synthetic nicotine," "flavorants," "e-cigarette policy," "social media and vaping," "vaping cessation," and chemical names mentioned in this review.

The extracted information was discussed to identify the appeal of tobacco-flavored e-cigarettes based on sales data, to document the toxicity complications from toxicology studies, and to confirm the impacts of the addition of other flavorants in tobacco-flavored e-cigarettes by analyzing studies on related social media posts (Figure 1).

Results

e-Liquid Constituents Inhaled During Vaping

Tobacco-flavored e-cigarettes have a wide range of chemicals in the e-liquid, and different tobacco flavors have different flavoring agents. However, in general, tobacco-flavored e-cigarettes contain propylene glycol, glycerol, and 0-50 mg/mL of nicotine (in the form of freebase nicotine or nicotine salts), similar to most other e-cigarettes. Tobacco-flavored e-cigarettes have also been shown to have cinnamaldehyde [17]. Additionally, for the popular brands JUUL and Puff Bar, many other chemicals were frequently found to be in their tobacco-flavored e-cigarettes in greater than 1 mg/mL concentrations, including ethyl maltol, corylone, vanillin, and ethyl vanillin [14]. Another study found caffeine, isophorone, tributyl O-acetylcitrate, tributylphosphine oxide, triethyl citrate, and vanillin in tobacco-flavored e-liquids from popular brands such as JUUL, Blu, Smok, and Vuse Alto [18]. There are also many VOCs present in tobacco flavors such as ethanol, toluene, ethylbenzene, and styrene [17]. Moreover, tobacco flavors would also produce reactive oxygen species that cause oxidative stress when used. Overall, there are many different carbonyls, citrates, phenols, VOCs, and other organic compounds present in tobacco-flavored e-liquids and their combustion and degradation products that are inhaled during vaping.

Cellular Toxicities of Tobacco-Flavored e-Cigarette Aerosols

Existing studies have established some knowledge of the toxicities of tobacco-flavored e-cigarettes [16,19-24]. The compounds present in the e-liquid and aerosol of tobacco-flavored e-cigarettes have many toxic effects on cells. For instance, nicotine in tobacco flavors can induce mucus hypersecretion by goblet cells and decrease mucociliary clearance in the lung by suppressing α7 nicotinic acetylcholine receptor activity and cystic fibrosis transmembrane conductance regulators, resulting in a greater risk for chronic lung diseases [19]. It was revealed that tobacco flavorants can induce oxidative stress, inflammation, DNA damage, and higher levels of cell death in lung epithelial cells and inflammatory responses in different types of cells including fibroblasts [20,21]. Overall, reported in either in vivo or in vitro studies, increased reactive oxygen species or oxidative stress and the release of inflammatory cytokines were associated with tobacco flavors, and the conclusions included increased cell death, decreased cell viability, and increased inflammatory responses [22].

Mechanisms of Disease Pathogenesis Related to Toxicities of Tobacco-Flavored e-Cigarette Aerosol

Beyond cells, tobacco-flavored e-cigarettes are harmful to the user's overall health. Inhaling nicotine from tobacco-flavored e-cigarettes can result in hypertension, chronic obstructive pulmonary disease (COPD), increased myocardial infraction

risk, and asthma [23]. The propylene glycol found in tobacco-flavored e-cigarettes can also pose health risks when inhaled, where cough, difficulty breathing, and increased asthma risk are linked to the inhalation of propylene glycol [23]. Moreover, the heating of glycerol found in tobacco-flavored e-liquids can produce formaldehyde, which can act as a carcinogen when inhaled [23]. In another study, it is also shown that tobacco flavor accompanied by the presence of nicotine can induce an allergic inflammatory response, characterized by elevated levels of eotaxin, interleukin-6, and chemokine (C-C motif) ligand 5 (also known as RANTES) [16]. The combination can also increase the level of plasminogen activator inhibitor-1, with a higher level being a risk factor for thrombosis and atherosclerosis [16,24]. Additionally, the reactive oxygen species and VOCs present in tobacco-flavored e-cigarettes can increase exposure to free radicals, resulting in oxidative stress and lung inflammation [19]. Overall, the inhalation of compounds present in tobacco-flavored e-cigarettes poses a serious health risk and can increase lung toxicity and the likelihood of various chronic lung diseases ranging from COPD to cardiovascular disease (Figure 1).

Tobacco-Flavored e-Cigarette Products

Although the flavors are limited to tobacco flavors, there is still a variety of e-cigarette devices with distinct characteristics associated with tobacco flavors [25,26]. Generally, e-cigarette devices are divided into 4 generations, all of which can support tobacco flavors [26].

First-generation e-cigarettes are designed to mimic the appearance of traditional cigarettes and thus are also known as cig-a-likes [25,26]. The major components are a battery, an atomizing unit, and a fluid reservoir (cartridge) [26]. Although outdated, tobacco-flavored e-cigarettes of the first generation can still be found in some web-based and physical vape shops.

In second-generation e-cigarettes, the cartridge is replaced by a "clearomizer" installed in a pen-shaped device, so second-generation e-cigarettes are also called "vape pens" [25,26]. Third-generation e-cigarettes, on the other hand, are highly customizable and contain sub-ohm tanks, which allow even higher wattage due to decreased resistance [25,26]. Both second- and third-generation e-cigarettes use e-liquids for aerosol generation, and tobacco-flavored e-liquids can be easily found in web-based vape shops and are sold in large amounts.

Fourth-generation e-cigarettes are called "Pod-Mods," indicating a modifiable pod cartridge that can be in various shapes [25,26]. Fourth-generation e-cigarettes use nicotine salts instead of the freebase nicotine used in previous generations, allowing a higher concentration of nicotine to be present [25]. A popular variation named "vape bars" is the most popular product in web-based vape shops.

Tobacco-flavored products associated with all the generations discussed above are widely available web-based vape shops for vapers, and the products are sold in large amounts. In web-based vape shops, the best-selling tobacco-flavored e-cigarette products are mostly vape bars (fourth-generation devices), followed by tobacco-flavored e-liquids (used by second- and third-generation devices). First-generation products and prefilled cartridges or pods (second-generation products) can also be found in another vape shop, where it claims that the first-generation product is "the new #1 selling e-cigarette on the market." The vape shop selling primarily fourth-generation e-cigarettes has a better website design with different fonts that may attract young vapers, whereas the vape shop website that sells first- and second-generation e-cigarettes looks relatively old.

Public Perceptions of Tobacco-Flavored e-Cigarettes on Social Media

An examination of the public perceptions of different e-liquid flavors on over 2 million e-cigarette–related Twitter (subsequently rebranded as X) posts from May 31 to August 22, 2019, showed the public had a more negative attitude toward the tobacco flavor (sentiment score=–0.134) using sentiment analysis [27]. Meanwhile, it was also found that the public was positive toward fruit (sentiment score=0.074) and sweets flavors (sentiment score=0.156), and most of the discussions were about these 2 flavors (58.15% and 14.67%, respectively) [27]. Immediately after the flavor ban, only menthol and tobacco flavors were allowed on the market, and an increase in discussion about menthol flavors (from 16.4% to 37%) was observed [9,28]. However, there was no significant increase in discussion about tobacco flavors, indicating that vapers likely did not choose to shift to tobacco flavors immediately after the ban of their favorite flavors [28]. In contrast, the discussion of fruit and sweets flavors remained high after the ban and even increased around 5 months later (from 41% and 22.3% before the ban to 57% and 28% five months after the ban, respectively), signaling that the vapers might have sought other sources for their favorite flavors after they were banned, which indicates continued interest in these flavors [28].

Through applying generalized estimating equation (GEE) models on over 3000 Reddit posts from January 2013 to April 2019 that comention e-cigarette use and health symptoms in the same Reddit post, it was found that tobacco flavor was more likely to be comentioned with respiratory and throat symptoms than other symptoms [29]. A specific examination of the JUUL pod tobacco flavor with health symptoms, using similar GEE models and Reddit posts from September 2016 to April 2019, showed a high probability of the comention of the JUUL tobacco flavor with throat, respiratory, and cardiovascular symptoms [30].

e-Cigarette Sales After Flavor Ban Regulations and Flavorants' Appeal to Vapers

The vast variety of e-cigarette flavorings, such as banana, mango, and cotton candy, are extremely appealing to the younger generation, which supports the nicotine addiction epidemic among today's youth. However, the February 2020 FDA ban on flavored prefilled e-cigarette cartridges, while having the intention of curbing flavored e-cigarette use, also opened new doors for the vaping industry to continue making profits [9]. This was due to 2 loopholes in the FDA policy: the ban did not cover the sale of tobacco- and menthol-flavored prefilled cartridges or the sale of flavored disposable e-cigarettes [31]. For these reasons, e-cigarette users were able to find

alternatives to flavored prefilled cartridges, such as the tobacco-flavored e-cigarettes outlined in this paper.

Centers for Disease Control and Prevention data show that after the FDA policy enactment, the unit share of disposable e-cigarettes went from 29.9% to 49.6%, whereas the respective unit share of prefilled cartridges lowered from 70% to 50.3% between February 2020 and July 2022 [31]. This data show the popularity of flavored e-cigarettes in the vaping population, with them quickly switching to disposable e-cigarettes once flavored prefilled cartridges became unavailable. Additionally, although the FDA ban was supposed to limit prefilled cartridge manufacturers such as JUUL from profiting off of nicotine addiction, it allowed disposable vaping brands, such as Puff Bar, Elf Bar, and Blu, to achieve a massive increase in sales by developing products that filled the "flavoring hole" left by the prefilled cartridge ban. Data showed that in response to these holes, e-cigarette users largely switched to disposable devices rather than continuing to buy the tobacco- and menthol-flavored cartridges still on the market [31]. After the 2020 ban up until July 2022, tobacco-flavored cartridge sales only increased by 11.9%, whereas all other flavor sales increased by 75.6% [31], showing the preference of the vaping population for nontobacco flavorings, which indicates that vapers are likely to be attracted to the new tobacco flavors that contain flavorants from other flavors.

Public Health Interventions Associated With Tobacco Flavors

Flavors have been cited as a key factor for the initiation of vaping by adolescents and young persons and facilitate the ongoing use of vaping products by those of all ages. Flavored vaping products are alluring to both new and established tobacco product users, and a wide variety of flavors are available. This wide variety and the ability to combine different flavors, in this case, the addition of other flavorants into tobacco flavors, could contribute to the ongoing vaping behavior among both youth and adults [12,32].

Per the FDA "Deeming" regulations, the FDA can now regulate the presence and amount of "characterizing flavors" in vaping products [33]. According to former FDA Commissioner Dr. Scott Gottlieb, e-cigarette use among youth can be characterized as an epidemic [34]. Users must be at least 18 years of age to buy vaping products in most states, but those younger than 18 years old are still able to purchase from a variety of retailers and web-based vendors [12,33].

To address the vaping epidemic, especially among youth, in 2021, the FDA implemented a flavor enforcement policy to restrict the sales of all cartridge-based, unauthorized, flavored e-cigarettes other than tobacco and menthol flavors [35,36]. Evaluation of the impact of the FDA flavor enforcement policy on e-cigarette use behavior is in progress. One study assessed the potential impact of the flavor enforcement policy on a specific vaping-related behavior change—quitting vaping—using natural language processing strategies with data collected from the Twitter platform [35]. The proportion of tweets (and Twitter users' mentions) concerning quitting vaping was compared before and after the implementation of the FDA flavor policy [35]. Compared to before the FDA flavor policy, the proportion of tweets and Twitter user mentions after the implementation of the policy was higher [35]. They also reported that after the policy implementation (compared to before), there was an increasing trend in the proportion of female individuals and young adults (18-35 years old) mentioning quitting vaping [35]. They concluded that, as observed on Twitter, the FDA policy did have a positive effect on vaping cessation and therefore a potential influence on broader definitions of vaping behavior [35].

Another public health intervention for vaping cessation is the use of free vaping cessation apps, which have various content, features, and adherence to evidence-based approaches. In 2020, researchers conducted a systematic search of existing smartphone apps for vaping cessation [37]. A total of 8 apps were included in a quality assessment and content analysis. They concluded that the few existing vaping cessation apps use similar approaches to smoking cessation apps but are potentially valuable tools [37].

Discussion

Toxicological Complexities Brought by the Addition of Other Flavorants

Besides the toxicities of tobacco-flavored e-cigarette constituents, the introduction of other previously irrelevant chemicals may inevitably complicate the toxicity of these products. The most commonly used flavorant (in 35% of e-liquids), vanillin, is responsible for vanilla flavors in e-liquids; is likely to be present in the "Tobacco Salt Rich" e-cigarette; and was extracted from the deidentified tobacco-flavored e-cigarette introduced earlier in this paper [16,38,39]. As shown, the presence of vanillin has a positive correlation with the toxicity of e-liquids (R^2=0.62) [38]. The vanillin in tobacco flavors is inflammatory and can irritate airways [19]. Another popular flavorant (in 32% of e-liquids) present in caramel flavors, ethyl maltol, was also present in the deidentified tobacco-flavored e-cigarette and has been shown to be a contributing factor for incidences of kidney lesions in rats and mild hemolytic anemia in dogs [15,16,39,40]. Furthermore, the inhalation of cinnamaldehyde and ethyl maltol, compounds found in tobacco flavors, causes oxidative stress and can lead to inflammation and epithelial barrier dysfunction, increasing the risk of diseases such as COPD [19]. These are only 2 of the flavorants used in e-liquids, and the typical number of different flavorants in a single e-liquid product would be higher than 10 [38]. It was found that the more chemicals there are in the e-liquid, the higher the toxicity that the e-liquid is likely to possess [38]. Therefore, it is predicted that the additional flavorants in tobacco-flavored e-cigarettes, which already contained many kinds of flavorants, would increase the overall toxicity of the product, and it would be hard to figure out the interactions of the toxicity mechanisms related to flavorants that originally belonged to completely unrelated species. More studies are required to fully understand this complexity and take appropriate actions regarding the regulation.

Youth Vapers' Preferences

According to scientific studies, e-cigarette users' preferences for e-cigarette devices were shifting toward newer-generation devices: Fourth-generation devices (prefilled pod cartridges) are the most used devices, although third-generation devices still take up a considerable proportion of use [41]. It was also observed that the shift toward newer generations is faster in youth users than in young adults or older adults [41]. Another study conducted by Lin et al [42] also agrees with this finding, as they found that adolescent and young adults' preference is responsive to advancements in e-cigarette technology. They generally avoid using earlier-generation devices (the percentage of users who usually used disposable or large-size rechargeable e-cigarettes dropped from 88.2% to 33.1% during the study) and prefer more innovative products (the percentage of users who usually used pod-based e-cigarettes, which were only introduced into the market when the study was halfway through, was 22.3% by the end of the study) [42]. The trend found by those studies is likely applicable to tobacco-flavored e-cigarettes, as the characteristics of web-based vape shops discussed above match the trend [41,42]. The fact that youth vapers shifted to pod-based e-cigarettes quickly also made the addition of other flavorants in these products a more significant public health issue.

Implications From Social Media Studies

According to results from the social media studies mentioned earlier, vapers demonstrated continued interest in fruit and sweets flavors immediately after the flavor ban while remaining uninterested in original tobacco flavors [27,28]. Our web-based survey study also showed that most vapers continued using flavored e-cigarettes even after the flavor ban, as disposable e-cigarettes were not covered by the FDA flavor ban [43]. Therefore, when their favorite flavors are integrated back into tobacco flavors, it is expected that they would prefer the mixed flavor. Since the availability of flavors was among the top reasons for vaping and its initiation, especially in adolescents and young adults, the addition of these flavors in tobacco flavors would likely resuscitate the motivation for vapers to continue to vape [44,45].

Social media research that focused on health issues comentioned with flavors discovered that tobacco flavors were generally more likely to be comentioned with respiratory and throat symptoms, and cardiovascular symptoms were also frequently comentioned if the tobacco-flavored e-cigarettes were from JUUL [29,30]. These results are associated with traditional, tobacco-flavored cigarettes prior to the addition of new flavors, and the addition might be associated with more complicated symptoms. In the web-based vape shop, we found that for new tobacco-flavored e-cigarettes, the best-selling ones often contained new flavors categorized as "sweets" flavors or the "crème" flavor in JUUL products [29,30]. According to the same GEE models, "sweets" flavors were comentioned with throat and digestive symptoms, whereas JUUL's "crème" flavor was comentioned with neurological, digestive, and "other" symptoms, which were not observed in the corresponding tobacco flavors [29,30]. However, the comention of flavors with health symptoms does not indicate that vaping will cause these symptoms, as it is also possible that vaping could reduce the health symptoms. Previous study showed that the toxicological effects of the flavorants may interact with each other, and the effects of such interactions are unknown [46]. Therefore, more research should be done to further understand the symptoms associated with the addition of other flavors into tobacco-flavored e-cigarettes.

Overall, as we observed more varieties of tobacco-flavored e-cigarettes sold in vape shops, the public perceptions of tobacco-flavored e-cigarettes and their associations with health symptoms mentioned on social media need to be revisited.

Vaping Communities and Flavor Addition to Tobacco Flavors

Since vapers can belong to a variety of different communities, the addition of other flavors into tobacco-flavored e-cigarettes may have different effects in these communities, and we need to focus on the differences. For example, the vaping behaviors of dual users of both traditional cigarettes and e-cigarettes are different from vapers who only use e-cigarettes [2]. Dual users usually only use e-cigarettes when they are engaging in activities or in places that encourage e-cigarette use, or when they use e-cigarettes as substitutes for traditional cigarettes [47]. This type of difference becomes exceedingly important when there is a relatively high prevalence of vaping in the community (including minority youth) or when the community is our major target of protection (including age groups such as adolescents) [48]. For instance, among young adult e-cigarette users, bisexual women were the most susceptible to e-cigarette use habits with a high level of cigarette use [49]. Such disparities are of importance when public health interventions are tailored, so knowing how specific communities respond to the addition of flavorants in tobacco-flavored e-cigarettes is critical. However, despite this importance, there is minimal data on this issue, and the differential effects remain unknown to us. Further studies should be done on these specific communities for us to comprehensively understand how new tobacco-flavored e-cigarettes impact the entire vaping population and establish regulations accordingly.

Conclusion

After the FDA implemented enforcement priorities against all flavored, cartridge-based e-cigarettes other than tobacco- and menthol-flavored products on February 6, 2020, most e-cigarette products became regulated, leaving only menthol and tobacco flavors to be widely and legally available for vapers [9]. This ban on other flavors impaired e-cigarettes' appeal to vapers, so e-cigarette manufacturers decided to recreate similar flavors by blending the corresponding flavorants into tobacco-flavored e-cigarettes to form variant tobacco flavors, including "Smooth Tobacco" [13,16]. These mixed tobacco flavors are now widely available in web-based vape shops, and the products either come as or can be used in any generation of e-cigarettes to accommodate the preference of vapers in different age groups (it is inferred that younger vapers' preferences switch to more innovative products more easily and they generally use newer-generation devices) [41,42].

Evidence from both the vaping market share and social media posts indicate that the manufacturers' strategy was successful [28,31]. After the FDA regulation, the unit share of prefilled cartridges decreased, and the sales of disposable e-cigarettes of flavors other than tobacco flavors increased dramatically, indicating a strong preference for flavorants in other flavors that motivated the vapers to switch to disposable e-cigarettes [31]. Therefore, the addition of these flavorants into tobacco flavors may establish appeal to the new tobacco flavors. On the other hand, similar trends were found in social media posts, showing that fruit and sweets flavors were still often discussed after the flavor ban policies [28]. The heated discussions indicate the vapers' strong craving for these flavors, so this further confirms that the addition of other flavorants into tobacco flavors may successfully attract vapers.

This strategy by the manufacturers can not only lead to new public health issues but also new health risks and symptoms in individual users, and it even raises issues on harm reduction approaches. The additional flavorants mixed in the new tobacco-flavored e-cigarettes may have unique toxicology mechanisms that are not observed in flavorants used in traditional tobacco flavors. For example, vanillin and ethyl maltol are likely found in a product with the flavor "Tobacco Salt Rich" and another deidentified tobacco-flavored e-cigarette, and these flavorants have been shown to increase the toxicity of e-liquids and induce incidences of kidney lesions in rats and mild hemolytic anemia in dogs, respectively [15,16,38-40]. Other flavorants may also be integrated into the recipe of tobacco-flavored e-cigarettes, and it has been shown that the toxicity of the e-liquids increases as the number of chemicals in its recipe increases [38]. Meanwhile, in the analysis of Reddit posts using GEE models, the "sweets" flavors in e-cigarettes were associated with higher comention of digestive and throat symptoms, which are not demonstrated in traditional tobacco flavors [29]. Therefore, the symptoms associated with e-cigarette use are likely to be more complicated when using the new tobacco-flavored e-cigarettes. However, our predictions of toxicology and symptoms are based on the simple addition of effects, where the interactions between the flavorants were not taken into consideration. More research needs to be done to fully understand the interactions and the overall effects.

Besides the public health issues and personal health risks associated with the addition of flavorants in tobacco-flavored e-cigarettes, the FDA flavor ban policies did have an overall positive effect in helping vapers quit vaping [36]. The use of the new vaping cessation apps is also a potentially important aspect of public health interventions [37]. To further extend the positive effects, more research should be done to analyze the effects brought by the manufacturers' efforts to bypass the regulations and premarketing approval, and emphasis should be placed on vulnerable communities regarding the vaping public health effects.

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Authors' Contributions

YS, DL, PP, RR, SM, and IR contributed to writing—original draft preparation. YS and IR contributed to writing—review and editing and the preparation of schematics and conceptual diagrams. IR contributed to supervision, project administration, and funding acquisition and compilation. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

None declared.

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Abbreviations

COPD: chronic obstructive pulmonary disease
FDA: Food and Drug Administration
GEE: generalized estimating equation
TFN: tobacco-free nicotine
VOC: volatile organic compound

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Review

Predictive Data Analytics in Telecare and Telehealth: Systematic Scoping Review

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Abstract

Background: Telecare and telehealth are important care-at-home services used to support individuals to live more independently at home. Historically, these technologies have reactively responded to issues. However, there has been a recent drive to make better use of the data from these services to facilitate more proactive and predictive care.

Objective: This review seeks to explore the ways in which predictive data analytics techniques have been applied in telecare and telehealth in at-home settings.

Methods: The PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) checklist was adhered to alongside Arksey and O'Malley's methodological framework. English language papers published in MEDLINE, Embase, and Social Science Premium Collection between 2012 and 2022 were considered and results were screened against inclusion or exclusion criteria.

Results: In total, 86 papers were included in this review. The types of analytics featuring in this review can be categorized as anomaly detection (n=21), diagnosis (n=32), prediction (n=22), and activity recognition (n=11). The most common health conditions represented were Parkinson disease (n=12) and cardiovascular conditions (n=11). The main findings include: a lack of use of routinely collected data; a dominance of diagnostic tools; and barriers and opportunities that exist, such as including patient-reported outcomes, for future predictive analytics in telecare and telehealth.

Conclusions: All papers in this review were small-scale pilots and, as such, future research should seek to apply these predictive techniques into larger trials. Additionally, further integration of routinely collected care data and patient-reported outcomes into predictive models in telecare and telehealth offer significant opportunities to improve the analytics being performed and should be explored further. Data sets used must be of suitable size and diversity, ensuring that models are generalizable to a wider population and can be appropriately trained, validated, and tested.

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KEYWORDS

telecare; telehealth; telemedicine; data analytics; predictive models; scoping review; predictive; predict; prediction; predictions; synthesis; review methods; review methodology; search; searches; searching; scoping; home

Introduction

Technologies can play a role in addressing the challenges associated with supporting people to live longer independently at home. Telecare services have existed since the 1970s and are systems designed to support vulnerable individuals living in their homes, enabling them to maintain their autonomy while ensuring protection from any anomalous situations that may arise [1]. Telecare devices have gone through many iterations since their introduction as simple user-triggered alarms and now include, for example, bed occupancy sensors and automatic fall detectors [1]. Today, telecare systems can work as lifestyle monitors, collecting data relating to the individual and their home environment in real time. Telehealth services are used in the management of long-term conditions such as heart disease or diabetes. Users are provided with equipment, such as vital signs monitors, to record blood pressure, heart rate, or blood glucose levels, for example. These data are shared with care providers to allow remote assessment of the well-being of an individual and to intervene if necessary.

Technology-enabled services have been a feature of care at home for a number of years and the demand for these services remains high. In Scotland alone, there are over 129,000 people (2.4% of the total population) who make use of a telecare service or community alarm [2], while an estimated 1.8 million people across the whole of the United Kingdom (2.7% of the total population) use either telecare or telehealth services [3]. In the United States, a total of 2.3 million veterans used telehealth services in 2022, representing more than a third of all veterans receiving care from the Department of Veterans Affairs [4].

Newer telecare and telehealth devices collect increasing amounts of data from a variety of connected sensors and systems. However, most services respond to an anomaly once it has been identified and do not intelligently use the data they receive to identify those at higher risk of an adverse event in order to pre-emptively plan what an individual may require. There are significant benefits to more proactive services, such as a reduction in secondary care use, including ambulance callouts or eventual hospital admissions [5,6].

Recent policy has highlighted a desire to shift telecare and telehealth services toward a more proactive model. The UK Government state—in their plan for Digital Health and Social Care—that anticipatory care promoting prevention through machine learning–facilitated data analysis will be routinely implemented by 2028 [7]. This has similarly been highlighted in a number of other countries including Australia, Canada, and New Zealand [8-10].

This scoping review, therefore, seeks to identify and explore the ways in which predictive data analytics techniques have been applied in the use of community-based telecare and telehealth devices and services in order to identify the current gaps and opportunities that exist for the future use of predictive analytics in telecare and telehealth.

Methods

This review was conducted and presented in accordance with the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) 2020 checklist [11]. The protocol was informed by the methodological framework proposed by Arksey and O'Malley [12].

Inclusion or Exclusion Criteria

This review considered any study using quantitative methods relating to the predictive use of data analytics in the fields of telecare and telehealth. Qualitative studies were excluded. The Population, Concept, and Context (PCC) framework was applied. Database searches were conducted in August 2022 and restricted to papers published within 10 years of the initial searches being conducted. Only papers published in the English language were considered.

Population

Papers focusing on any and all users were included. All populations of users (anyone using a telecare and telehealth device or systems) including both adult and child services were valid for inclusion since the focus of this review was on the methods of analytics being applied, rather than the specific reason for accessing telecare or telehealth.

Concept

Any telecare or telehealth innovation that gathers or generates data and electronically communicates it for use in an analytical manner was valid for inclusion. This could be "passive" technology, such as sensors and wearables, or "active" technology where data are intentionally entered into a device by a user. Papers investigating devices, which do not directly monitor a health element of an individual, such as an educational app, were excluded. Any data analytics that make inference or predictions from the data they receive were included in this review. This includes diagnosis, classification, and anomaly detection and does not exclusively consider predictions of future events. Additionally, this review only considers telecare and telehealth devices related to a somatic condition, that is, physical condition of the body. Papers focused on mental health and loneliness, for example, were excluded because these conditions may require a significantly different management approach.

Context

Any paper which had a "care in the community" setting was suitable for inclusion (patient's own home, assisted living facilities, and sheltered accommodation). In-patient and non–home-based settings were excluded with the exception of papers that focus on technologies clearly designed for at-home use that have thus far only been tested on individuals in an in-patient setting.

Study Type

All reviews (systematic, literature, and scoping) were excluded as this would cause duplicate data to be reviewed and could lead to bias through overreporting. Any paper outlining an entirely conceptual framework and not detailing on how it would

work in practice was excluded. The review also excluded editorials, summaries, and opinion pieces.

Databases Searched

Databases relevant to health and social care—MEDLINE [OVID], Embase [OVID], and Social Science Premium Collection [ProQuest]—were searched.

Search Strategy

The following 2 key domains were identified for inclusion in the search strategy: data analytics and telecare or telehealth (see Table 1). Search terms that were deemed most applicable to each database were applied. MeSH (Medical Subject Headings) terms and free-text entries were considered as appropriate. Boolean operators such as "AND," "OR," and truncation codes were used to refine and improve searches. A copy of the full search strategy employed while searching the Medline database can be found in Multimedia Appendix 1.

Table 1. Synonyms considered during literature searches for review.

Search term domains	Synonyms
Data analytics	• Data analytics • Big data • Health analytics • Electronic data capture • Data management system • Machine learning • Data analysis • Data mining
Telecare or telehealth	• Telecare • Telehealth • Remote health care services • Remote monitoring • Telemonitoring • Telecommunication • Advanced assistive technology

Study Screening

Results from each database search were imported to EndNote [13] where duplicates were removed. Studies were uploaded to Covidence [14] for screening. Title and abstract screening were completed by 6 reviewers (ML, NW, ED, DK, MR, and LL). Every paper was screened independently by at least 2 researchers, with conflicts resolved through discussion. A third reviewer was consulted when agreement could not be reached.

Full-text versions of the accepted papers were obtained for full-text screening. There were 537 papers considered for full-text screening by the lead author. Of these 537, approximately 15% (n=80) were screened collaboratively by the lead author (EA) and 2 other reviewers (NW and DK). Interrater agreement (all 3 reviewers coming to the same conclusion on inclusion or exclusion) was categorized through the following thresholds: <70%=poor, 70%-79%=fair, 80%-89%=good and ≥90%=excellent [15]. Of the papers that were collaboratively reviewed by all 3 researchers, there was an interrater agreement of 81%. This was a sufficient level of agreement for the remaining full-text papers to be independently screened by the primary author only. A second opinion was sought by the primary researcher during full-text screening when required.

Data Charting Process

A data extraction table was created in Microsoft Excel by the primary author. The data extraction table was piloted by the primary author for the first 10 papers before a discussion with secondary authors was conducted to ensure the appropriateness of the data being extracted. These discussions helped shape the table further with modifications made so that all relevant pieces of information were extracted. Data extracted related to key study characteristics, data analyzed in the paper, the technology employed, and the analytics techniques used.

Data Items and Synthesis of Results

Data were collected on paper characteristics (eg, title, authors, year of publication, location of publication, and country of origin) and study characteristics (eg, study design, stage of implementation, study setting, primary or secondary analysis, participant description, duration of study, and dropouts). Data were also captured relating to the technology in use (eg, what the technology is designed to assist with, the technology being employed, and its function), the data used in the analyses (eg, data streams, where the data are sent, and what it is being used for), and the methods of analyses employed (eg, the statistical method of analysis, the actions taken as a result of the analysis and outcome measures). Information on the key findings from each study and any potential limitations with the studies were also collected. A summary of the data extracted for each paper can be found in Multimedia Appendix 2.

Results

A total of 86 published papers were included in the review. A PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the full screening process completed for this review can be found in Figure 1. Of the 86 selected papers, approximately one-third of papers (n=28)

considered telecare services, with the other two-thirds considering telehealth services (n=58).

The data analytics tasks employed in the studies reviewed (with reference to Banaee et al [16]) can generally be categorized into: anomaly detection (n=21, 24%), prediction (n=22, 26%), and diagnosis and decision-making (n=32, 37%). Additionally, this review identified a fourth data analytics task, which relates to activity recognition systems (n=11, 13%). Table 2 provides a breakdown of the papers, categorized by the type of data analytics task applied.

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram outlining the full screening process.

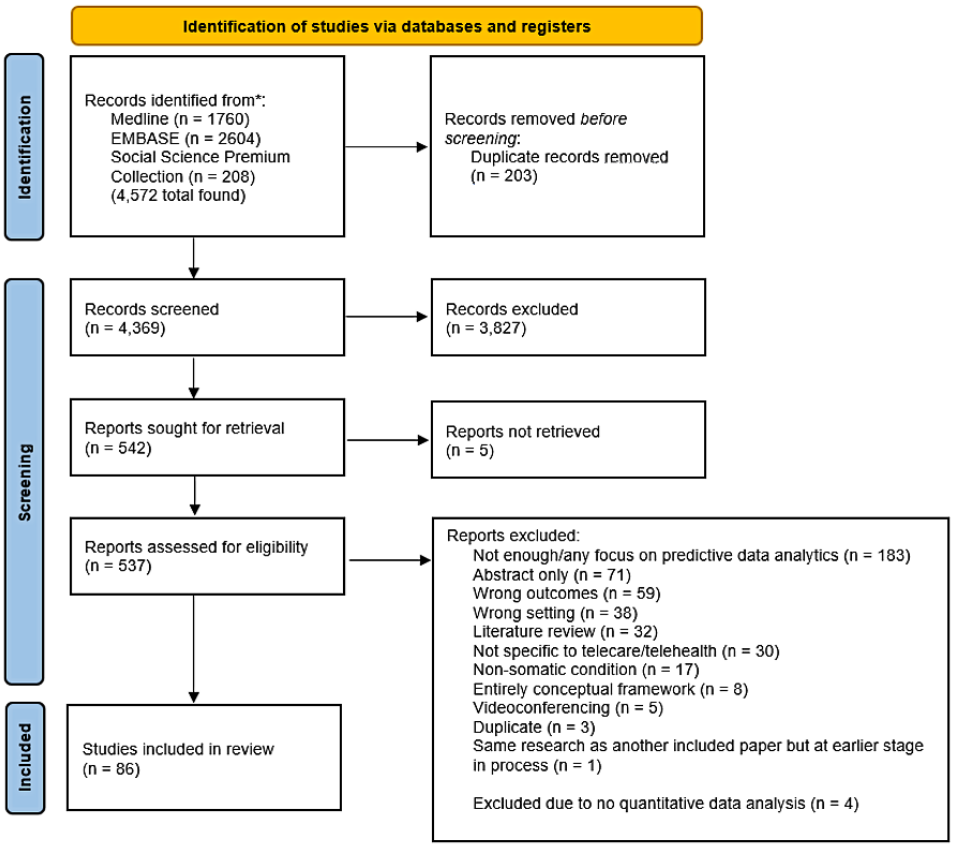

Table 2. Categories of data analytics in included papers.

Type of data analytics applied	Studies, n	References
Diagnosis and decision-making	32	[17-48]
Prediction	22	[49-70]
Anomaly detection	21	[71-91]
Activity recognition	11	[92-102]

The most common areas of focus for overall technology systems were general monitoring systems (n=14, 16%) and activity recognition systems (n=11, 13%). The majority of the included papers focused on the prevention, detection, treatment, or monitoring of a specific health condition (n=53, 62%). Of these, the most commonly studied was Parkinson disease (n=12, 14%), followed by conditions of the cardiovascular (n=11, 13%) and respiratory systems (n=8, 9%). Table 3 lists the number of papers considered by the paper's focus, split between technology systems and by health condition.

Table 3. Focus of papers included in review, grouped by monitoring systems, and by health condition[a].

	Studies, n	References
Focus of Paper (Technology System)		
General monitoring system	14	[30,53,55,59,71,73-75,80,84,85,88,90,91]
Activity recognition system	11	[92-102]
Falls monitoring system	5	[51,70,86,89,100]
Focus of Paper (Health Condition)		
Parkinson disease	12	[20,21,28,32,40,41,43,44,47,48,76,77]
Cardiovascular system (heart disease, heart failure, atrial fibrillation, cardiovascular disease, blood pressure, and anticoagulation)	11	[23,24,27,46,57,63,67,68,70,82,83]
Respiratory system (lung transplant, chronic obstructive pulmonary disease, and asthma)	8	[49,56,58,60-62,69,79]
Sleep apnea	4	[26,29,35,78]
Diabetes (including prediabetes)	4	[39,64,65,81]
Poststroke rehab	3	[22,25,31]
Cognitive assessment or dependence	2	[18,33]
Weight or diet	2	[36,54]
Multiple sclerosis	2	[37,45]
Craniosynostosis	1	[17]
Gait	1	[19]
Pressure injuries	1	[34]
Alzheimer disease	1	[38]
Typhoid	1	[42]
Cancer	1	[50]
Pancreatectomy	1	[52]
COVID-19	1	[66]
Knee arthroplasty	1	[72]
Pain management	1	[87]

[a]Table 3 does not sum to 86 as there are a small number of papers that have more than one area of focus.

Studies featuring primary data sources accounted for just over half of the papers included (n=46, 53%). There were a further 36 papers (42%) that used data originating from secondary sources, such as data gathered over the course of a separate experiment or trial that was then applied to future studies, while 4 papers (5%) used a combination of both primary and secondary sources [27,41,85,99]. There were a total of 3 papers that focused on the predictive analytics of data that has been routinely collected in telehealth practice, while there were no such telecare papers [31,42,68]. Every paper reviewed was either in a pilot or feasibility study or was undergoing proof-of-concept tests.

Table 4 displays the different types of technologies featured in this review. The most common technologies were wearable sensors (n=38, 44%). The majority of the papers (n=68, 79%) used at least 1 type of sensor—be it wearable, environmental or motion or pressure, smartphone, or 3D motion scanners. Other technologies included self-reported symptoms via smartphone apps (n=17, 20%) and vital signs monitoring (n=11, 13%). These technologies do not map neatly onto the data analytics tasks shown in Table 2. For example, wearable sensors feature in papers that consider diagnosis and decision making, anomaly detection, prediction, and activity recognition tasks.

Table 4. Technology featured in papers under review[a].

Technology used	Studies, n
Wearable sensors	38
Patient-reported outcomes via app	17
Environmental/pressure/motion sensors	16
Vital signs monitoring	11
Smartphone sensors	10
3D motion scanners	4
Computer or phone-based testing	2
Virtual glove	2
Virtual knee sleeve	1
Video recording	1
Voice recording	1
Images	1

[a]Table 4 does not sum to 86 as a number of papers featured the usage of more than one technology.

Machine learning (ML) techniques were the most commonly applied method of analysis of the data collected in the studies reviewed (n=76, 88%). Table 5 breaks down the ML techniques that have been reported in at least 2 papers in this review, highlighting the variety of different possible methods of analysis. For papers that consider multiple different ML methods, only the technique found to be most accurate has been selected. Other methods of analysis employed in this review were rules-based inference systems (n=4, 5%) and nonmachine learning algorithms (n=3, 3%). The most commonly applied ML methods were decision trees (n=14, 16%), followed by neural networks (n=12, 14%) and support vector machines (n=11, 13%). Additionally, there are a number of papers (n=16, 21%) that consider highly bespoke algorithms, employed in 1 instance only, which do not feature in Table 5.

Table 5. Machine learning techniques applied in relevant papers.

Machine learning technique	Studies, n
Decision trees	14
Neural networks	12
Support vector machines	11
Random forests	8
Ensemble (combination of models)	6
Logistic regression	5
Hidden Markov Models	2
k-Nearest neighbors	2

There were 68 papers (79%) in this review that reflected on potential limitations with their studies. Of these, 2 limitations were identified across multiple papers: small sample or study sizes (n=32, 47% of papers reporting limitations) and the issue of bias (n=13, 19% of papers reporting limitations). In total, there were only 2 included papers that considered the calculation of suitable sample sizes for their studies [31,79].

The main limitation identified in the papers reviewed is that a significant number of papers are trained on very small data sets or samples. In total, there were 32 papers that acknowledged this as an issue. The other limitation that was identified a significant number of times was the possibility of the introduction of bias to the models. Bias presents a similar issue to small sample sizes as it can invalidate the findings of a study, as the model is trained on a group that is not representative of the wider population of interest. The types of bias identified in this review can be found in Table 6.

Table 6. Sources of bias identified by researchers.

Type of bias	Studies, n	References
Technology trialed on young, healthy individuals	5	[51,71,83,93,100]
Female dominated data set	4	[18,26,39,54]
More complete data received from healthier individuals	1	[24]
Participants almost all White and college educated	1	[44]
Participants all recruited from one church in urban area	1	[59]
Male-dominated data set	1	[67]

Discussion

Within this review, the data analytics approaches can be categorized, with reference to Banaee et al [16], as: anomaly detection, prediction, and diagnosis or decision-making. Additionally, a fourth analytics category, activity recognition systems, has been identified. Table 2 features a breakdown of the analytics approaches employed in the reviewed papers.

Diagnosis and decision-making systems were the most commonly occurring data analytics task performed in the literature (n=32, 37%), while systems designed to identify anomalous events that have already taken place accounted for 21 reviewed papers (24%). Systems designed to make temporal predictions—identifying anomalies or events before they occur—only accounted for 22 of the papers reviewed (26%). This branch of analytics approaches is of critical importance to researchers and care providers due to the potential health care savings that could be made through the timely and proactive identification and resolution of anomalies before they occur. As such, it is expected that in the future, studies focusing on predicting anomalous events will be more frequently applied in the field of telecare and telehealth. This is supported by recent policy documents highlighting aspirations to move toward more proactive and predictive models of care [7-10].

The final identified branch of data analytics tasks is activity recognition systems (n=11, 13%). These systems typically use a classification model to identify the activity performed (eg, walking and falling), which is very relevant in the field of telecare but found rarely in the literature. A few studies show how such systems could be advanced toward more predictive anomaly detection [92,100] but they do not currently have a feedback loop whereby the recognition of an event taking place leads to an action by the care provider. This is of critical importance if aiming to identify people at risk of an adverse event and take preventative measures and is likely to become more commonly applied in telecare and telehealth moving forward.

Analytics Focus

This review also highlighted that there has been significantly more research into predictive analytics in telehealth (n=58) compared to telecare (n=28). Telehealth data may be more suitable to the application of predictive analytics because they are often more structured and numerical in nature whereas social care data more frequently rely on unstructured case notes.

Studies which considered a system or technology aimed at a specific disease or condition made up the majority of papers identified, with the most common disease of focus being Parkinson disease [31-42]. The extensive focus on Parkinson disease in research may be attributed, in part, to its features and symptoms and their suitability for being measured by sensors and then modeled by data analytics techniques. For example, slowness of movement, uncontrollable shaking, and gait problems are very common symptoms of Parkinson disease and are all well suited to being captured through wearable sensors. Such remote monitoring or assessment is also useful in diseases like Parkinson disease where clinical features of the disease may be intermittent in the early stages and thus may not be present during a scheduled assessment [103].

Patient-Reported Outcomes

While patient-reported outcomes (PROs) were one of the more commonly featured tools in this review (n=17, 20%), they are not commonly used in telecare predictive data analytics models (n=3/28 telecare papers, 11%). PROs can provide more nuanced information than solely using clinical indicators which can lead to an underestimation of the impact on a patient in combination with an overestimation of the effectiveness of treatment being provided [104,105]. As such, there is an argument to be made for further use of PROs in predictive data analytics models, especially in the field of telecare.

Including PROs in predictive modeling is challenging as it involves the integrating both objective and subjective data. However, this integration can enhance model results by capturing the true reported experiences and outcomes of patients. Indeed, evidence shows that PRO measurements are of comparable accuracy to many objective clinical measures [106]. Appropriate testing, validation, and re-evaluation of PROs can help improve the quality and consistent collection of data while the move toward standardization of PROs through the use of tools such as the National Institute of Health's Patient-Reported Outcome Measurement Information System (PROMIS) can enable a rise in data quality levels across the board, facilitating a greater integration of PROs in predictive modeling work [107].

Use of Routinely Collected Data

Routinely collected data can be defined as data that has not been specifically captured for research purposes. There are only 3 studies featured in this review using data that have been routinely collected in real-world health and care practice, with all of these papers considering telehealth systems [31,42,68]. From a telehealth perspective, a lack of use of routinely collected

data makes sense due to these systems focusing on highly specific features that need to be extracted about a given condition or illness. As such, the data considered in these systems tend to originate from bespoke, highly targeted data collection methods.

However, a significant amount of data is being generated by providers of telecare services globally as they deliver care, and the application of data analytics in these real-world data sets needs to be explored further than it has been to date. One key barrier to the analytical use of routinely collected telecare data is that these data are typically siloed in different locations, with systems lacking interoperability. For example, call handling data are frequently maintained in a different system than other social care data, resulting in the outcomes of calls being inaccessible to social care organizations. This has been identified by the Scottish Government as being a key issue preventing the use of data-driven care [108].

Additionally, work must be done to improve other issues surrounding the use of routinely collected data such as patient consent and data governance and security [109]. If researchers, care providers, and any commercial suppliers in control of these rich data sources can collaboratively overcome these identified issues, then a whole new avenue for the use of predictive data analytics will be opened.

Limitations Within Studies

Limitations noted by researchers were typically specific to the technology employed. These limitations include low quality data being captured [84]; the technology being uncomfortable to wear and with a short battery life [86], and there being a limited number of sensors employed [93]. Limitations related to the analytics techniques included low impact falls being missed by a model [89], large volumes of missing values [61], and a model that struggled to differentiate between an individual sitting and standing [101].

The main limitation identified in this review is that a significant number of papers are trained on very small data sets or samples. In total, there were 32 papers (47% of the total papers reporting limitations) that acknowledged this as an issue. This is a critical problem as having a small sample size could undermine the legitimacy of the findings of the paper—particularly when the outcome of interest is rare. Small sample sizes make it harder to accurately train, validate, and test ML models with the findings less conclusive and less reliable.

To ensure that the strongest evidence base possible sample size calculations should be conducted prior to the study, however only two of the papers featured in this review reported prior sample size estimation [31,79]. This may be attributed to the pragmatic nature of recruitment, where it is difficult to recruit sufficient numbers of individuals with a certain condition, but it remains critical for ensuring the validity of the findings.

The other limitation that was identified a significant number of times was the possibility of the introduction of bias to the models, as can be seen in Table 6. Bias could invalidate study findings as the model is trained on a group that is not representative (eg, gender, age) of the target population meaning that its performance may not translate in reality. In the field of telecare and telehealth, it is critical that data sets consider individuals of appropriate age—generally elderly—and that disease-specific systems have been trialed on individuals with the illness or condition of interest. For example, a study using young, healthy volunteers to classify falls—and other activities—requires participants to simulate falls [100]. This may have an impact on the accuracy of the model, and a data set featuring genuine falls captured by elderly individuals would be significantly more appropriate. The key sources of bias identified in this review are the use of exclusively young, healthy adults to trial technologies that are designed for an older population and data sets, which are dominated by women.

Limitations of This Review

The quality of the studies selected for inclusion in this review was not assessed using any official appraisal tool. This is typical of a scoping review, which seeks to synthesize the available literature rather than provide a systematic analysis; however, this means that the quality of the papers featured in this review cannot be guaranteed. Another limitation of this review is that it may have missed commercially developed data analytics tools that have been implemented in practice, as these may not necessarily be documented in research literature. Finally, only papers available in the English language were considered, which may preclude a number of relevant papers from this review.

Conclusions

Predictive data analytics have been widely used in the field of telecare and telehealth but all of the studies featured in this review are still small-scale pilot studies and must be extended to larger trials. Additionally, opportunities for predictive analytics revolving around routinely collected data and PROs should be explored further. Using larger and more diverse “real world” data will enable models to be built that have less bias, can predict more accurately, and could be adapted more widely within other telecare or telehealth settings. Ultimately, appropriate consideration of these factors could lead us to more predictive and preventative data driven models of telecare and telehealth.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Example literature search strategy employed in Medline.
[DOCX File , 65 KB - ojphi_v16i1e57618_app1.docx]

Multimedia Appendix 2
A summary of the data extracted for each paper included in this review.
[DOCX File , 80 KB - ojphi_v16i1e57618_app2.docx]

Multimedia Appendix 3
PRISMA-ScR checklist.
[PDF File (Adobe PDF File), 103 KB - ojphi_v16i1e57618_app3.pdf]

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Abbreviations

MeSH: Medical Subject Headings
ML: machine learning
PCC: Population, Concept, and Context
PRO: patient-reported outcome
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews
PROMIS: Patient-Reported Outcome Measurement Information System

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Review

Data Analytics to Support Policy Making for Noncommunicable Diseases: Scoping Review

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Abstract

Background: There is an emerging need for evidence-based approaches harnessing large amounts of health care data and novel technologies (such as artificial intelligence) to optimize public health policy making.

Objective: The aim of this review was to explore the data analytics tools designed specifically for policy making in noncommunicable diseases (NCDs) and their implementation.

Methods: A scoping review was conducted after searching the PubMed and IEEE databases for articles published in the last 10 years.

Results: Nine articles that presented 7 data analytics tools designed to inform policy making for NCDs were reviewed. The tools incorporated descriptive and predictive analytics. Some tools were designed to include recommendations for decision support, but no pilot studies applying prescriptive analytics have been published. The tools were piloted with various conditions, with cancer being the least studied condition. Implementation of the tools included use cases, pilots, or evaluation workshops that involved policy makers. However, our findings demonstrate very limited real-world use of analytics by policy makers, which is in line with previous studies.

Conclusions: Despite the availability of tools designed for different purposes and conditions, data analytics is not widely used to support policy making for NCDs. However, the review demonstrates the value and potential use of data analytics to support policy making. Based on the findings, we make suggestions for researchers developing digital tools to support public health policy making. The findings will also serve as input for the European Union–funded research project ONCODIR developing a policy analytics dashboard for the prevention of colorectal cancer as part of an integrated platform.

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KEYWORDS

policy making; public health; noncommunicable diseases; data analytics; digital tools; descriptive; predictive; decision support; implementation

Introduction

Noncommunicable Diseases as a Public Health Challenge

Noncommunicable diseases (NCDs), such as cardiovascular or chronic respiratory diseases, cancer, and diabetes, account for 74% of all deaths globally [1]. In the European Union (EU), NCDs are responsible for almost 80% of the disease burden and most premature deaths [2]. They affect quality of life and life expectancy, create numerous challenges for patients and their families, and have a large financial impact, costing EU economies more than 100 billion US$ annually. As many NCDs are age-related, their burdens are increasing partly due to the

prolonged lifespan of the population [3]. NCDs are strongly associated with a number of preventable factors, such as smoking, physical inactivity, harmful alcohol use, and unhealthy diet, and environmental factors, such as air, water, soil pollution, and chemical exposure. Interventions for controlling such risk factors and promoting health and well-being have the potential to reduce the prevalence of NCDs by as much as 70% [4]. To this end, the European Commission has launched an initiative to support effective policies and actions to reduce the burden of major NCDs and improve citizens' health and well-being [2].

The successful management of NCDs requires the integration of the best available scientific evidence into decision-making [5]. Effective use and reporting of data can guide the process and empower policy makers to better understand and act [6]. On the other hand, research findings that directly apply to the policy of interest, when available, are often inconsistent, out of date, or of poor quality. As a result, policy making is traditionally based on social context, political agendas, expert opinion, or the media, all of which are usually biased [7]. Currently, this traditional policy-making approach, which abides more to the notion of clinical health services delivery, is simultaneously challenged from various aspects as it appears unable to meet the novel needs of decision makers [8]. From population surveillance data and indicators to big data and time-tagged trends, policy makers' informed decisions nowadays predispose the effective deployment of technological advancements regardless of whether they concern NCD screening and treatment or managing emerging crises. The recent COVID-19 pandemic signaled the transition into the digital health era, where a newfound model of supporting policy makers' decision processes is needed [9].

Harnessing Digital Technologies for Public Health Policy Making

In the last 2 decades, the growth of health care data in quantity and complexity and the rapid advances in the fields of big data analytics (BDA) and artificial intelligence (AI) present an opportunity to transform conventional policy making into a data-driven process, utilizing various health-related data sources such as electronic health records (EHRs), public health databases, and social networking platforms [10-12]. The integration of routinely collected real-world data and use of advanced analytical techniques for improved decision-making is also referred to as "precision public health" as opposed to traditional public health [13].

Reliable data, combined with data analytics, play key roles at various stages of the public health policy-making process by aiding in understanding, priority setting, resource allocation optimization, identification of the optimal intervention, implementation, and evaluation [14]. This capability allows policy makers to base their decisions on empirical evidence by identifying patterns, trends, and correlations that might not be evident otherwise. Such informed decision-making is vital in areas like health care and can lead to more effective outcomes [10]. Specifically, data analytics may improve the delivery of public services, enabling governments to anticipate public health crises, optimize public health initiatives, increase adherence from the public, and enhance the overall responsiveness of services [15]. This iterative process of policy evaluation and adjustment, supported by real-time data monitoring, ensures that strategies are continuously refined to achieve intended goals. Analytics can identify high-impact areas for efficient resource allocation, such as targeting aggressive policies where they are most needed (eg, the outbreak of a pandemic).

Data analytics approaches are commonly categorized into 3 broad types: descriptive, predictive, and prescriptive analytics. The 3 types answer different questions but use similar methodologies that can be applied individually or in combination, depending on the health policy objectives, data availability, and decision-making context. Descriptive analytics summarize past and present trends and patterns in the data to answer the question "What happened?" Predictive analytics use primarily historical data to create models that answer the question "What will happen?" Prescriptive analytics employ data-driven models and optimization algorithms to recommend the most effective actions, interventions, or allocation strategies trying to answer the question "What should I do?"

The use of data analytics in the context of policy making has also been referred to as "policy analytics" by some authors [16]. It has been suggested that policy analytics include data-driven tools that respond to a policy need and use a transparent development process [17]. Examples of policy analytics techniques are statistics, simulations, data mining, machine learning (ML), social networks, and geographic info [18].

Rationale and Aims

Currently, there is no comprehensive overview of the use of data analytics tools to support policy making for NCDs. Such an overview could guide stakeholders and organizations involved in policy making, engineers and companies managing such tools, data analysts, and researchers, and could highlight gaps and unmet needs in the area. The present review has been performed in the context of the Horizon Europe project ONCODIR [19]. The project seeks to identify risk factors associated with colorectal cancer (CRC) and will integrate multidisciplinary research methods and technologies to deliver evidence-based and personalized recommendations on CRC. The findings of this review will serve as an evidence base for the development of the policy analytics component of ONCODIR's integrated platform.

The primary aim of this scoping review is to investigate the landscape of data analytics tools and platforms designed to support evidence-based policy making for NCDs. The secondary aim is to explore the adoption of these tools by policy makers and the factors affecting this.

Methods

Design

A scoping review was selected given the aim of this study. It has been suggested that scoping reviews are more suitable than traditional systematic reviews and meta-analyses when focusing on rapidly evolving topics, as they allow more timely synthesis of evidence. The inclusive and broad nature of scoping reviews also makes them better at looking into the range of evidence on a particular topic [20]. We conducted our review according to

the Joanna Briggs Institute guidelines to ensure quality and reliability [21]. We followed the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) guidelines (Multimedia Appendix 1) and developed a search strategy based on the Population, Concept, and Context framework as follows [22]:

- Population: humans with NCDs
- Concept: digital data analytics tools
- Context: public health policy making

Based on this framework, in December 2023, we searched the PubMed database for publications written in English from 2013 to date. The search was repeated in July 2024. We searched for articles published in the last decade to explore the latest advances in the field. We searched for original research and review articles published in peer-reviewed journals and no other sources to ensure the highest quality of the studies.

A query was first developed in PubMed and was then adapted for IEEE Xplore: ((“health”[Title/Abstract] OR “healthcare”[Title/Abstract] OR “clinical”[Title/Abstract] OR “medical”[Title/Abstract]) AND (“policy”[Title/Abstract] OR “policies”[Title/Abstract] OR “policymaking”[Title/Abstract] OR “policy-making”[Title/Abstract] OR “policy making”[Title/Abstract] OR “decision making”[Title/Abstract] OR “decision-making”[Title/Abstract] OR “decision maker”[Title/Abstract]) AND (“analytics”[Title/Abstract] OR “analytic”[Title/Abstract]) AND (“data”[Title/Abstract] OR “evidence”[Title/Abstract] OR “evidence-based”[Title/Abstract])).

Given that the concept of policy analytics and the associated terminology are not yet well defined, we chose broad terms in the first place to widen the results and assessed eligibility later case by case. For instance, we did not use a term for NCD as it appeared that usually the names of the individual conditions are used. Moreover, we preferred “health” as “public health” is not consistently used in the context of policy making for NCDs.

Study Selection

Title and abstract screening and full-text review were performed according to predefined eligibility criteria (Textbox 1). A snowballing approach was also used to identify any additional articles from the reference lists of the screened articles. We included studies describing data analytics tools or their use in detail. These had to be concrete tools or applications designed specifically with the aim to support policy makers as opposed to models, algorithms, or other theoretical frameworks, such as decision-analytic models or cost-effectiveness analyses. Analytics tools had to be designed for or applied to a specific NCD as these have been defined according to the World Health Organization (WHO) [23]. We excluded analytics not performed on specific conditions or not applied to health data (eg, health care management). We also excluded studies on views or perceptions about analytics.

From all included articles, we extracted data related to the disease studied, purpose of the study and tool, analytics used, implementation, and link with policy making. We performed a narrative, descriptive data synthesis of the techniques used and their implementation.

Textbox 1. Eligibility criteria for article selection.

Inclusion criteria

- Original research or review.
- Study on humans with noncommunicable diseases (NCDs).
- The study includes a concrete digital data analytics tool that can be used by a policy maker.
- The study includes a tool that is designed to support health policy making.
- The study includes analytics performed on health-related data.

Exclusion criteria

- Commentaries, viewpoints, protocols, perspectives, or other study types.
- Study on infectious diseases or no disease (eg, health management).
- The study describes theoretical models, frameworks, or statistical algorithms.
- The study includes tools for clinical decision support, patient benefit, or other purposes.
- The study includes analytics performed on the literature.

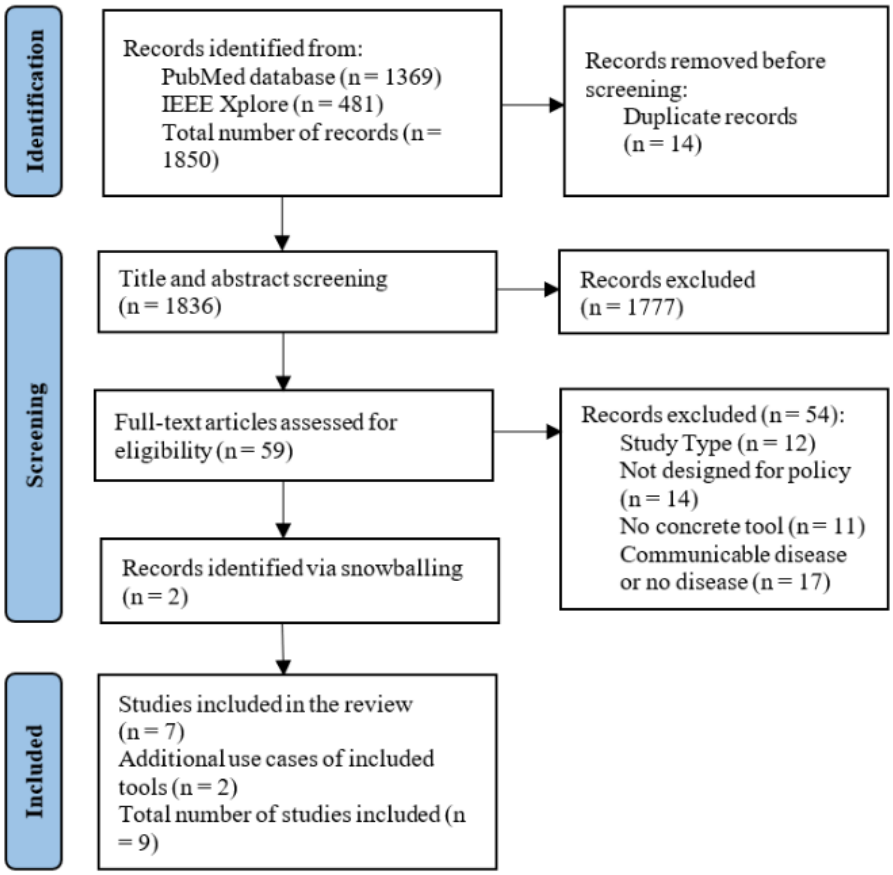
Results

Study Characteristics

The search yielded 1850 articles from the PubMed and IEEE Xplore databases (Figure 1). After article duplicates were removed, 1836 remained for title and abstract screening. A total of 59 articles were identified for full-text review. Five studies met our eligibility criteria and were included in the review. Two more studies were identified via snowballing of the reference lists of screened articles. Furthermore, 2 articles were added that included additional applications of the identified tools, as one of the aims of the review was to explore implementation and uptake. In total, 9 articles were included in this review. Articles were published between 2017 and 2022. The articles described 7 data analytics tools or integrated platforms including a data analytics component. The studies described the tools in detail and included use case scenarios, pilot studies, workshops, and examples of implementation that illustrate how analytics

can be used to support policy making for NCDs. Four studies were conducted in the United States, 1 in Australia, and 1 in Canada. Three studies were conducted in various countries of Europe (ie, Greece, Germany, Slovenia, Spain, United Kingdom, Sweden, Finland, Northern Ireland, Republic of Ireland, and Denmark).

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) flow diagram of the stages of the scoping review.



Tools Overview

The 7 tools reviewed are summarized in Table 1. Three integrated platforms (EVOTION, MIDAS, and CrowdHEALTH) were designed to support public health policy decisions for a range of conditions and include a data analytics component supporting both descriptive and predictive analytics [24-28]. Users can create policy models, define the way in which data should be analyzed in order to produce the evidence useful for public health policy making, and obtain analytical results of how this evidence may support or contradict various policy actions. The other 4 tools (PoPHQ, PoPHR, Social InfoButtons, and RiskScape) were designed for disease monitoring through the integration, descriptive analysis, and visualization of population health data from various sources [29-32].

Two of the 7 tools were designed to address specific NCDs. EVOTION was specifically designed for hearing loss and PoPHQ was designed for obesity prevention. The other platforms were applicable to and piloted with a wide range of conditions, including obesity in adults and children, cardiovascular conditions, chronic kidney disease, chronic respiratory conditions, cancer, mental health, asthma, and diabetes. Three platforms were piloted in obesity, physical activity, and nutrition. Two platforms were piloted with each of the following conditions: respiratory, cardiovascular, and diabetes. CrowdHEALTH was piloted with cancer [25]. Six of the 7 tools were designed for or used with NCDs only, while PoPHR was applicable to infectious diseases as well [30].

Table 1. Overview of the tools included in this review.

Tool	Type	Analytics supported	Implementation reported	Study
EVOTION	Public health policy decision support	Descriptive and predictive	Analytics applied, use case example, and workflow	Prasinos et al [27] and Saunders et al [28]
CrowdHEALTH	Public health policy decision support	Descriptive and predictive	Use case example, workflow, and use cases including health care stakeholders	Moutselos et al [26] and Mavrogiorgou et al [25]
MIDAS	Public health policy decision support	Descriptive and predictive	Pilots with policy makers	Shi et al [24]
PoPHQ	Health informatics tool	Descriptive	Design workshops where stakeholders identified user stories and use cases	Canfell et al [29]
RiskScape	Public health surveillance	Descriptive	Real-life implementation	Canfell et al [29] and Cocoros et al [32]
Social InfoButtons	Public health analytics	Descriptive	Use case scenarios	Ji et al [31]
PoPHR	Visualization of population health data	Descriptive	Description and functionalities with examples, and initial implementation ongoing	Shaban-Nejad et al [30]

Study Settings

Details of the use cases are provided in Table 2. The studies presented the 7 tools using different settings, including descriptions of the functionalities with examples, use case scenarios where authors presented a workflow, pilot studies with actual data from various sources, applications of analytics on data collected using the tool, design workshops with stakeholders, and real-life implementation.

CrowdHEALTH was piloted in 5 different countries and 6 use case scenarios with stakeholders from various health care organizations [25]. Relevant data from patients and healthy adults and children were used to address policy needs on various conditions. For example, the Slovenian pilot used data on physical activity to analyze the physical fitness and weight status of children, assess its development over time, and predict future levels. This provided a basis for the implementation of policies that link school and health data for early intervention monitoring and evaluation. Interestingly, this use case was based on a real-life policy described in the Slovenian National Program on Nutrition and Physical Activity for Health 2015-2025 [26]. MIDAS was piloted in 4 countries using social media, MEDLINE analytics, and news media data on a range of conditions [24]. Ji et al [31] used data on treatments and symptoms posted by patients on social media to evaluate the effectiveness of the Social InfoButtons platform. PoPHR was piloted with a randomly sampled, open cohort of 25% of the Montreal population in Canada [30]. PoPHQ is currently in the mock-up phase but has been designed to integrate anonymized electronic medical record data from Queensland, with a final total sample size of approximately 5 million [29]. No pilot data were reported for Risk Scape, but the Massachusetts Department of Public Health (MDPH) is currently using the platform to monitor conditions of interest using EHR data that are updated monthly from clinical practice groups that cover approximately 20% of the state population [32]. Prasinos et al [27] described the workflow of policy creation, selection, and execution of analytics using the EVOTION platform. Saunders et al [28] reported 3 applications of BDA techniques using a dataset synthesized from the EVOTION data repository.

Table 2. Details of the analytics included in this review.

Study and country	Noncommunicable disease	Analytics	Purpose	Data
Prasinos et al [27]				
Greece, United Kingdom, and Denmark	Hearing loss (HL)	• Basic statistics • Linear regression • Principal component analysis • Inferential statistics	• Investigate the impact of hearing interventions on quality of life (QOL)	Synthetically generated dataset from the EVOTION data repository
Saunders et al [28]				
Greece, United Kingdom, and Denmark	HL	• Predictive modeling • Regression analysis • Generalized linear mixed model • Correlations	• Estimate the risk of noise-induced HL • Predict hearing aid (HA) usage from changes to the sound environment • Examine the association between physical activity and HA usage	Synthetically generated dataset from the EVOTION data repository
Moutselos et al [26]				
Slovenia	Obesity	• Forecasting • Simulation • Causal analysis	• Effectiveness of various interventions for obesity prevention • Early detection of children with increased risk linked to poor physical fitness	Large-scale data from the national surveillance system on the physical and motor development of children
Mavrogiorgou et al [25]				
Spain	Obesity in adults	• Clinical pathway mining • Risk stratification	• Identification of overweight patients	Demographic information, hospitalization, emergency and hospital episodes, and morbidity
Sweden	Cardiovascular and chronic kidney disease	• Clinical pathway mining • Risk stratification • Causal analysis	• Monitor patients	Demographic, drug usage, and practitioners' consultation data
Slovenia	Fitness and obesity in childhood	• Clinical pathway mining • Risk stratification • Causal analysis	• Analyze physical fitness and weight status • Predict future levels of fitness and somatic development	Physical activity, sedentariness, sleep, heart rate, socioeconomic status, and parental physical activity
Greece	Chronic respiratory conditions	• Risk stratification	• Monitor disease progression and health care expenditure for improved chronic disease management of patients	Biosignals from pulse oximeters, blood pressure meters, glucometers, spirometers, weighing scales, and activity trackers
Germany	Nutrition and physical activities	• Clustering analysis • Correlation analysis	• Understand the influence of nutritional habits and physical activity on overall health and QOL	Physical and activity data provided by activity trackers
Greece	Cancer care	• Causal analysis	• Evaluate the impact of online coaching and medical education	Diagnosis, treatment, comorbidities, health behaviors, and side effects
Shi et al [24]				
Spain	Obesity	• Random forests/least absolute shrinkage and selection operator	• Identify the risk factors of childhood obesity	Controlled and open data including social media analysis, MEDLINE analytics, and news media analysis
Finland	Mental health	• Lexis diagram analysis • Descriptive analysis	• Aggregate, summarize, and visualize risk factors • Evaluate health, social, and educational status	Controlled and open data including social media analysis, MEDLINE analytics, and news media analysis

Study and country	Noncommunicable disease	Analytics	Purpose	Data
Northern Ireland	Social care for children	• Markov chain • Long short-term memory (LSTM) network	• Track patterns of behavior over time • Estimate the probability of transition between different types of care • Improve the protection of children	Controlled and open data including social media analysis, MEDLINE analytics, and news media analysis
Republic of Ireland	Diabetes	• Autoregressive integrated moving average (ARIMA) model	• Forecast the consumption of diabetic drugs	Controlled and open data including social media analysis, MEDLINE analytics, and news media analysis
Canfell et al [29]				
Australia	Obesity	• Comparison across age groups • Counts by facility • Counts and percentages • Stratification by suburb and facility	• Target interventions across the life course • Direct resources • Justify the problem • Compare obesity across regions	"Mock-up" without patient data[a]
Canfell et al [29] and Cocoros et al [32]				
United States	Diabetes, hypertension, asthma, and obesity	• Heat maps by zip code • Stratification by demographics and comorbidities • Time series analyses with trend statistics • Data aggregation and visualization	• Review, analyze, map, and trend aggregate data • Prevalence of selected conditions • Identify health disparities	Electronic health records (EHRs) from 3 clinical practice groups that cover approximately 20% of the state population (>1.2 million)
Ji et al [31]				
United States	Posttraumatic stress disorder and asthma	• Statistical • Geospatial • Temporal • Topic investigation • Association discovery • Recommendation discovery • Visualization	• Compute statistical aggregates • Explore data according to a geographic feature • Analyze trends over time • Explore correlations between treatments, side effects, symptoms, and conditions • Discover treatment recommendations • Integrate openly available health data	Openly available health data sources including SMN, Twitter, MedHelp, WebMD, CDC, and PubMed
Shaban-Nejad et al [30]				
Canada	Chronic diseases (eg, diabetes, hypertension, coronary heart disease, and stroke)	• Visualization • Stratification • Filtering • Statistical algorithms to detect changes in an indicator over time and space	• Explore and visualize available indicators • Create coherent portraits of population health and health system performance • Evaluate the effects of public health interventions	No actual data used in this study; initial implementation ongoing[b]

[a]Final total sample size is estimated to be approximately 5 million (anonymized electronic health record data from Queensland).

[b]Initial implementation with a randomly sampled, open cohort of 25% of the population of the Census Metropolitan Area of Montreal, Quebec; in the process of implementation in the entire population of the province of Quebec.

Data Analytics Applied

Table 2 presents the data analytics applied in detail, including the setting, purpose, data used, NCD studied, and country where the study took place. The choice of analytics is strongly linked to the policy need being addressed and the nature of the tool. A wide range of analytical techniques were used, which can be summarized as follows.

Descriptive Analytics

All tools employed descriptive analytics. The first level was data ingestion, integration, cleaning, and preprocessing, such

as removal of duplicates and errors, imputation of missing data, handling of outliers, and standardization of data formats [24,25,30,31]. The next step was data exploration using basic descriptive statistics and inferential statistics, such as the identification of risk factors for a specific condition. Static or interactive visualizations were used, including scatter plots, heat maps, bar or box plots, and pie charts. Three of the tools employed more specialized techniques, including geospatial analytics or mapping (ie, exploration of data in a geographical area), temporal analytics (ie, tracking trends over time), and comparative analytics, which identifies differences between groups of measurements, such as disease prevalence across different age groups [29,30,32]. Other types of analyses used were clustering analysis (ie, grouping of objects based on measures of similarity) and correlation analysis to identify the strength of the linear association between variables. All tools included a visualization dashboard or user interface, although there were differences in the type or level of user interaction.

Predictive Analytics

Three out of the 7 tools employed predictive analytics. Methods included regression analysis and statistical modeling. Contemporary frameworks were also used for prediction and forecasting, including ML, deep learning, and simulation modeling [24,28]. Other types of analyses that were used for predictive purposes included risk stratification analysis; causal analysis, which models the behavior of the target variable of interest; and clinical pathway analysis, which models the process followed during treatment of a patient with respect to a particular condition [25,26].

Prescriptive Analytics

No study implemented a concrete prescriptive methodology. Three out of the 7 tools were decision support systems designed to make policy recommendations. The authors referred to the prescriptive capabilities of the tools and demonstrated the policy creation process [24,27,29]. However, none of them presented a related use case actually applying this type of analytics.

Tool Implementation

Out of the 7 platforms reviewed, 1 has been fully implemented in real life. RiskScape is used by MDPH to monitor conditions of interest using EHR data updated monthly from 3 clinical practice groups that cover approximately 20% of the state population [32]. It has a key role in demonstrating the need and burden for MDPH's applications for funding through the identification of inequitably burdened populations. The authors suggest that the platform unloads analytical burden from health departments, centralizes information in an efficient electronic environment, and offers clinical practices a holistic understanding of disease patterns and management practices. RiskScape is an open-source software and is publicly available [33]. Shaban-Nejad et al [30] reported that PoPHR had been initially implemented and was in the process of being fully implemented in Montreal, Quebec. According to the authors, the platform can be used by policy makers to improve decisions related to the planning, implementation, and evaluation of population health and health system interventions.

For the remaining 5 tools, the reviewed studies included analytics examples, use cases, or pilots. MIDAS was evaluated by policy makers in the pilot studies and successfully achieved all key progress indicators [24]. The platform received positive feedback on its capacity to integrate and analyze data. The pilots demonstrated how custom-tailored analytics produced knowledge and results that are actionable by public health policy makers and gave them insights for possible future interventions. Based on these results, the authors concluded that MIDAS is transferable, sustainable, and scalable across policies, data, and regions. Mavrogiorgou et al [25] reported how each use case of the CrowdHEALTH platform provided insights that can be used in policy making. Stakeholders from various sectors attended a workshop and provided feedback on the purpose, interface, and overall design of PoPHQ [29]. They identified various uses of the platform to create stories for 4 different end users: public health practitioners, systems planners, researchers, and generic users. PoPHQ is planned to be implemented in Queensland with a population of 5 million [29]. Saunders et al [28] reported that a policy maker could use EVOTION analytics as evidence to expand guidelines aimed at preventing noise-induced hearing loss or simulate hearing aid uptake and usage if urban planning organizations were to project an increase in everyday acoustic noise due to changed requirements for official noise prevention initiatives. Finally, Social InfoButtons can be used by governments for disease surveillance [31].

Discussion

Data Analytics for Public Health Policy Making

This scoping review was conducted to explore the data analytics tools designed for public health policy making for NCDs and their implementation. The review was motivated by the emerging need for approaches harnessing BDA, AI, and other novel technologies to improve public health policy making. It was also motivated by the EU-funded research project ONCODIR developing a policy analytics dashboard for the prevention of CRC as part of an integrated platform.

We presented 2 different types of tools enabling data analytics for policy making for NCDs: (1) tools designed for public health monitoring and surveillance that aggregate openly available data or data from electronic medical records and have mainly descriptive analytics and visualization functionalities and (2) integrated platforms designed for policy decision support with both descriptive and predictive analytics functionalities. Previously, Canfell et al [13] reviewed the use of real-world data for precision public health in NCDs and identified surveillance platforms integrating descriptive, comparative, and geospatial analytics. Our review, with its different scope, extends these findings and further demonstrates that predictive analytics can be used for the management of NCDs to inform policy decisions. A variety of ML techniques were used in the studies included in this review for forecasting. Moreover, classic statistical methods, such as logistic regression analysis, were adopted. ML techniques are increasingly used with large population health datasets to improve public health surveillance, disease prediction, and delivery of interventions [34]. On the other hand, prescriptive analytics provide actionable

recommendations to policy makers and can have a key role in precision public health. It must be noted here that even though 3 of the platforms included in this review were designed as policy decision support tools, no prescriptive analytics were actually applied in the pilot studies or use cases that generated policy recommendations. Instead, predictive models, risk estimation, and forecasting provided insights that aimed to support policy makers in making decisions. We could claim that the 3 tools reviewed, which employ predictive analytics, are more advanced toward supporting policy decisions compared to tools with descriptive analytics capabilities only. However, the actual usefulness of a tool for policy makers depends on the specific policy need and scenario.

NCDs Studied

Among the 4 major types of NCDs, cancer appears to be the one that is least studied in the context of data analytics for policy making as only the CrowdHEALTH platform was piloted with cancer. CrowdHEALTH used data from a web platform related to patients' diagnosis, treatment, comorbidities, health behaviors, and side effects to assess the impact of online coaching and medical education and predict future behaviors of cancer patients [25]. The type of cancer supported by the platform was not specified. According to the authors, given the absence of specific policies for the provision of medical information and online coaching and the increased patient support needs, such an approach may be useful for the improvement of resource allocation in the health care system among others. Other studies have explored protocols for mapping breast cancer registry data [35], the use of modeling to optimize cancer screening and predict catchment areas, and the use of AI for risk stratification of cancer patients [36-38]. However, none of these studies included tools designed to be used by policy makers. To the best of our knowledge, no policy-making platform with an analytics component has been designed for or used with cancer.

To address this gap, the EU-funded ONCODIR research project aims to develop an intelligent policy analytics dashboard as part of an integrated platform to support the primary prevention of CRC. The dashboard will incorporate retrospective data on CRC incidence, risk factors, and other relevant data as well as prospective data from a mobile app, and will enable descriptive and predictive analytics to provide insights to inform CRC prevention policies.

Use of Tools by Policy Makers

Our findings show very limited real-world use of analytics by policy makers. This is in line with previous studies showing limited implementation of digital tools for NCDs [13]. Only RiskScape is fully implemented and is also publicly available to use. Shaban-Nejad et al [30] reported that PoPHR had been initially implemented and was in the process of being fully implemented in Montreal, Quebec, but no more reports have been published since then [30]. In a subsequent study from 2020 not included in this review, it was reported that PoPHR was in the process of being deployed in Quebec for routine use by public health professionals [39]. In the same study, the authors reported their plans to extend the use of PoPHR to recommend interventions that are likely to be the most effective.

For most of the other tools' use cases, pilots or evaluation workshops were reported that involved policy makers. For instance, Saunders et al [28] reported some applications of analytics using the EVOTION platform with implications for policy makers [28]. In another study not included in this review, Dritsakis et al [40] reported a series of workshops where EVOTION was demonstrated to stakeholders in 4 countries and evaluated using a Strengths, Weaknesses, Opportunities, and Threats methodology [40]. The study highlighted the potential of the tool together with obstacles and risks that need to be addressed, such as the complicated mechanism of data collection and analysis and the lack of major analytic capabilities required for public health policy decision-making (eg, economic evaluation).

Overall, the 7 tools included in this review have been mostly designed as research prototypes in academic settings. Policy makers were involved in the development or use in some way, and all studies highlight the potential use of analytics to support policy making. However, there is very limited uptake or plans for use by policy makers reported in the reviewed studies. This has implications for the usefulness of the tools as most of them have not been tested in real-life settings. RiskScape (fully implemented) and PoPHR (initially implemented) are currently the most mature data analytics tools that can aid policy making according to the findings of this review. The fact that most tools were developed in the last 4 years could explain the poor uptake to some extent as the tools may not be implemented yet or the implementation may not have been published. Finally, it must be noted that besides RiskScape, it is unclear if the rest of the platforms are accessible and available for use.

Adoption of Digital Health Technologies

Many studies have explored factors influencing the adoption of digital health technologies by policy makers. Innovative solutions are incorporated into health policy functions at a slower pace than health transformation into a digital asset [41]. Lack of advanced infrastructure, low interoperability levels among critical actors, and bureaucracy pose barriers to the acceptance of new technologies that are frequently exacerbated by safety concerns. Other challenges are organizational fragmentation creating siloed data systems, difficulty in data sharing due to privacy and security issues, and concerns around data quality [42]. Moreover, systemic and organizational issues exist owing to the core characteristics of public health authorities as administrative bodies that lack regulatory frameworks and a data governance culture as a whole [43].

A very important obstacle from the perspective of end users is often the poor IT literacy and lack of digital skills by policy makers and public health professionals [44]. Another aspect is whether these tools actually meet the needs of end users. For example, reviews on the use of visual analytics in mental health care planning have shown that despite the availability of advanced visualization tools, such as geographical maps, the majority of experts use simple, familiar, and readily available visualizations, and a very small percentage of digital tools are actually used for policy and planning [45,46]. Despite a clear need to extract information from highly complex data, such barriers and concerns hinder the use of analytics as part of

decision-making and lead policy makers to use approaches that are most familiar to them and widely understood, and keep relying on expert opinion and intuition.

Poor uptake of evidence-based tools is also related to challenges inherent in the policy-making process. Moving evidence into practice will always require political engagement and therefore will be influenced by political agendas [28]. Moreover, there will always be urgent problems and limited funds that will require policy makers to use economics, statistics, and scientific skills to rapidly interpret evidence and provide solutions as the recent COVID-19 pandemic showed. The successful use of data-driven tools for responsive and accurate public health decisions for NCDs requires the optimization and reorganization of the public health sector and workflows [13]. Some priorities that have been reported include investment in modern data management infrastructure, development of strategic partnerships, need for AI transparency and reproducibility, and explicit consideration of equity and bias [47]. To effectively use new technologies and the large amount of health care data that are now becoming available to guide policy decisions, it is necessary to overcome the computational, algorithmic, and technological obstacles of an extremely heterogeneous data landscape, as well as a variety of legal, normative, governance, and policy limitations. Moreover, the transition into the digital health era requires a digital health background and key IT skills to ensure that policy makers have the capacity to make the most out of digital health innovations. A paradigm shift is required for policy makers at local, regional, and national levels to overcome cultural barriers that influence their acceptance and implementation of novel technologies [48].

Recommendations

Moving forward, we recommend that researchers developing advanced data analytics tools for policy making should engage with end users throughout the process, respond to their needs, and present results in a way that is easy to interpret. They should specify the type and purpose of analytics, how policy makers can use it, and what they can achieve with it. They should also secure the required resources to make the tool available and sustainable after it has been launched. Finally, developers must promote the implementation of digital health tools for decision-making as this could positively influence the IT literacy of policy makers. On the other hand, public health professionals should be encouraged by the potential of data analytics tools to inform evidence-based decisions and empower their digital health skills to be able to use the developed IT tools. Overall acceptance of novel technologies in domains and processes where current uptake is limited will facilitate the required paradigm shift.

To unlock the full potential of data analytics, authorities need to prioritize robust data infrastructure, interoperability, data integration, and the initiation of high-quality nationwide data registries (eg, cancer registries) to monitor public health. Training programs for data governance capacity building, hiring of specialists to key positions, and international collaborative efforts on major public health threats could help transition to more informed and responsive public health policy making. Finally, a strong legislative framework on data sharing that focuses on maximizing utility while also preserving privacy could be a major accelerating factor in fostering a data-driven culture. Establishing trust between government authorities and individuals would eventually create a conducive environment that promotes data sharing for the benefit of the public health system as a whole.

Methodology

The scope of the review and the corresponding search strategy were intentionally broad to allow us to explore a relatively new concept that is not yet well defined. The term policy analytics, although present in the literature, was rarely used in the studies reviewed here. Instead, authors used separate terms to refer to (1) the analytics and tools designed (eg, data integration, aggregation, visualization, or analysis; BDA; platform; data-driven; evidence-based; and system) and (2) the use or purpose of the analytics (eg, policy [decision] making, [precision] public health, surveillance, monitoring, and population health). There are differences in the way the applications of tools are reported in the literature. For example, the term “use case” may refer to the actual use of the tool in a particular setting or scenario and examples of how the tool can be used. Various terms are also used to refer to conditions (eg, NCDs, public health, or the name of the individual condition) and end users (eg, policy makers, decision makers, and public health professionals). This highlights the difficulty to comprehensively review all such tools and their applications.

A quality assessment of the included studies was not performed in this review. Quality assessment is an optional step for scoping reviews. Even though it would provide a more robust evaluation of the evidence and help identify any potential biases, it was not considered crucial given the aims of the review (we were not interested in the actual data collected or the findings). However, the different types, aims, and scopes of the included studies have been clearly presented in the Study Characteristics subsection in the Results section.

Finally, we only searched 2 databases compared to other scoping reviews that included more sources of information. However, we selected 2 reliable databases that together cover both the medical and technological fields of literature and are therefore sufficient to explore the concept of data analytics tools and public health policies. The search strategy as a whole ensures the quality of the studies reviewed.

Conclusions

There are many digital tools incorporating descriptive and predictive analytics that can support policy making in different ways for a range of NCDs. However, the majority of these tools are not widely used by policy makers in real-life. We have discussed factors affecting the adoption of digital health technologies as a whole and have also made recommendations on how stakeholders involved in the development and use of data analytics tools for public health policy making can help increase adoption and maximize the impact of such tools in supporting the policy-making process. The effectiveness and actual usefulness of the tools reviewed in this study should be assessed on the basis of the specific policy needs, settings, populations, conditions, and data with which they were tested.

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Authors' Contributions

GD made substantial contributions to the conception and design of the work throughout the manuscript preparation. IG contributed to the parts of the manuscript specific to data analytics. MEP contributed to the parts of the protocol specific to public health policy making. AA reviewed and approved the final manuscript. DD made substantial contributions to the conception and design of the work and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) checklist.
[PDF File (Adobe PDF File), 84 KB - ojphi_v16i1e59906_app1.pdf]

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Abbreviations

AI: artificial intelligence
BDA: big data analytics
CRC: colorectal cancer
EHR: electronic health record
EU: European Union
MDPH: Massachusetts Department of Public Health
ML: machine learning
NCD: noncommunicable disease

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Corrigenda and Addenda

Correction: Making Metadata Machine-Readable as the First Step to Providing Findable, Accessible, Interoperable, and Reusable Population Health Data: Framework Development and Implementation Study

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In “Making Metadata Machine-Readable as the First Step to Providing Findable, Accessible, Interoperable, and Reusable Population Health Data: Framework Development and Implementation Study” (Online J Public Health Inform 2024;16:e56237) the authors noted one error.

The group author “INSPIRE INSPIRE network” has been removed from the end of the authorship list.

The correction will appear in the online version of the paper on the JMIR Publications website on August 14, 2024, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

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Corrigenda and Addenda

Correction: Vaccine Hesitancy in Taiwan: Temporal, Multilayer Network Study of Echo Chambers Shaped by Influential Users

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In "Vaccine Hesitancy in Taiwan: Temporal, Multilayer Network Study of Echo Chambers Shaped by Influential Users" (Online J Public Health Inform 2024;16:e55104) the following information has been added:

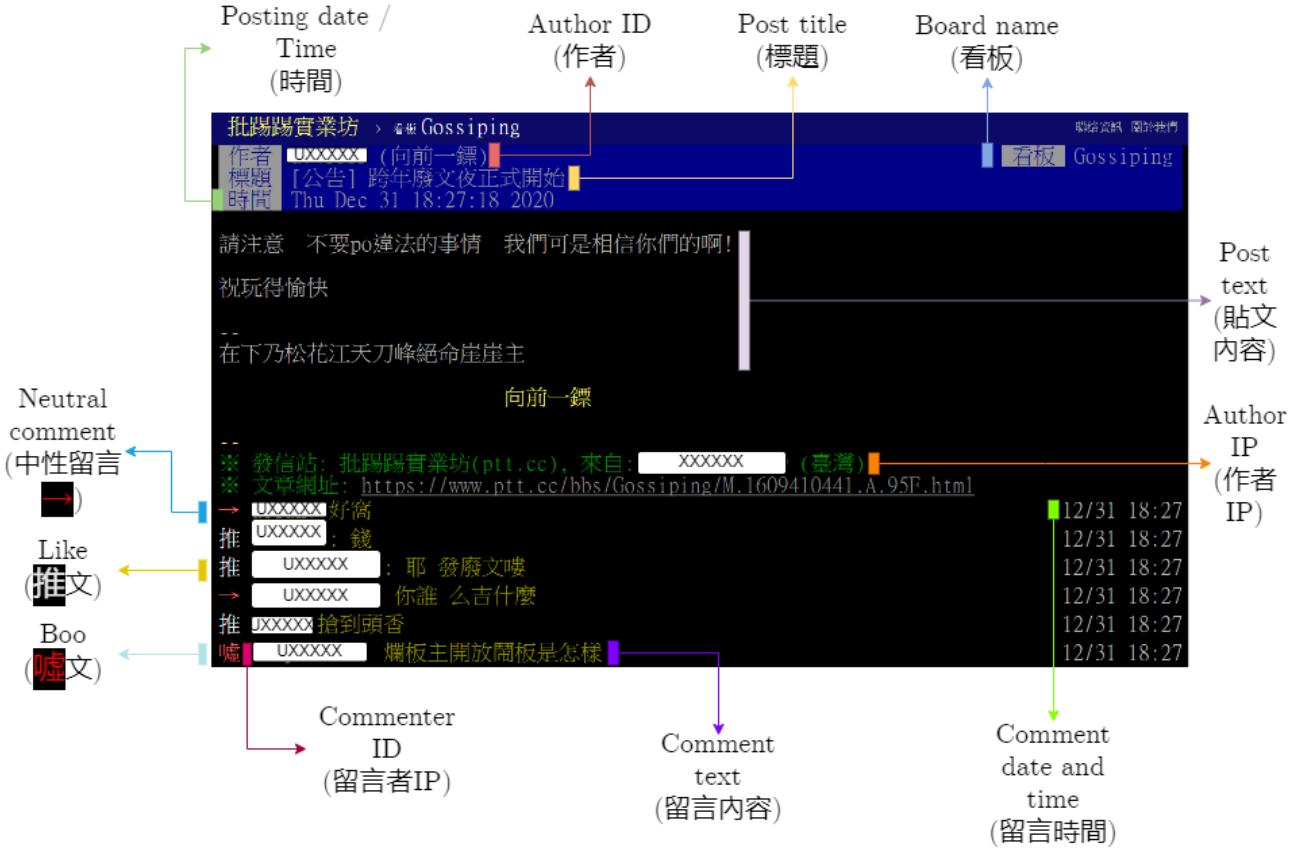
The "Ethical Considerations" section has been changed to read as follows:

> *All data from PTT are open and publicly available. All data from PTT in its raw form include usernames. These usernames are deidentified and anonymised during the research process to ensure they cannot be traced back to individuals. To do this, a 6 digit alphanumeric temporary username is generated for each unique user. Data is available upon request.*

Figure 1 will now appear as the following image, with updated caption:

> *Figure 1. Chinese and English labelling of 1 thread of the PTT forum to show its structure. Usernames omitted for protecting individual identity.*

Figure 1. Chinese and English labelling of 1 thread of the PTT forum to show its structure. Usernames omitted for protecting individual identity.



The Data Availability statement has been amended to read as follows:

> *Data from PTT are publicly available. Data used for this analysis are available upon reasonable requests made to the author of this paper.*

Finally, the file previously present as Multimedia Appendix 1 was removed.

The correction will appear in the online version of the paper on the JMIR Publications website on August 15, 2024, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

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Corrigenda and Addenda

Correction: Machine Learning Model for Predicting Mortality Risk in Patients With Complex Chronic Conditions: Retrospective Analysis

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In "Machine Learning Model for Predicting Mortality Risk in Patients With Complex Chronic Conditions: Retrospective Analysis" (Online J Public Health Inform 2023;15:e52782) the authors noted one error.

The Corresponding Author's address previously appeared as:

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Original Paper

Intention to Use Mobile-Based Partograph and Its Predictors Among Obstetric Health Care Providers Working at Public Referral Hospitals in the Oromia Region of Ethiopia in 2022: Cross-Sectional Questionnaire Study

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Abstract

Background: A partograph is a pictorial representation of the relationship between cervical dilatation and the time used to diagnose prolonged and obstructed labor. However, the utilization of paper-based partograph is low and it is prone to documentation errors, which can be avoided with the use of electronic partographs. There is only limited information on the proportion of intention to use mobile-based partographs and its predictors.

Objective: The objective of this study was to determine the proportion of obstetric health care providers at public referral hospitals in Oromia, Ethiopia, in 2022 who had the intention to use mobile-based partographs and to determine the predictors of their intention to use mobile-based partographs.

Methods: We performed an institution-based cross-sectional study from June 1 to July 1, 2022. Census was conducted on 649 participants. A self-administered structured English questionnaire was used, and a 5% pretest was performed. Data were entered into EpiData version 4.6 and exported to SPSS version 25 for descriptive analysis and AMOS (analysis of moment structure; version 23) for structural and measurement model assessment. Descriptive and structural equation modeling analyses were performed. The hypotheses developed based on a modified Technology Acceptance Model were tested using path coefficients and *P* values <.05.

Results: About 65.7% (414/630; 95% CI 61.9%-69.4%) of the participants intended to use mobile-based electronic partographs, with a 97% (630/649) response rate. Perceived usefulness had a positive influence on intention to use (β=.184; *P*=.02) and attitude (β=.521; *P*=.002). Perceived ease of use had a positive influence on attitude (β=.382; *P*=.003), perceived usefulness (β=.503; *P*=.002), and intention to use (β=.369; *P*=.001). Job relevance had a positive influence on perceived usefulness (β=.408; *P*=.001) and intention to use (β=.185; *P*=.008). Attitude positively influenced intention to use (β=.309; *P*=.002). Subjective norms did not have a significant influence on perceived usefulness (β=.020; *P*=.61) and intention to use (β=–.066; *P*=.07).

Conclusions: Two-thirds of the obstetric health care providers in our study intended to use mobile-based partographs. Perceived usefulness, perceived ease of use, job relevance, and attitude positively and significantly influenced their intention to use mobile-based electronic partographs. The development of a user-friendly mobile-based partograph that meets job and user expectations can enhance the intention to use.

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KEYWORDS

mobile-based partograph; mHealth; mobile health; cross-sectional; questionnaire; questionnaires; survey; surveys; modified TAM; technology acceptance model; intention to use; obstetric health care providers; Ethiopia; intent; intention; TAM; experience; experiences; attitude; attitudes; opinion; opinions; perception; perceptions; perspective; perspectives; acceptance; adoption; partograph; digital health; health technology; birth; women's health; obstetrics; obstetric; obstetric health care; labor monitoring

Introduction

Background

Globally, maternal mortality remains a persistent and potentially preventable issue of great concern. In 2020, every 2 minutes, a woman died due to pregnancy-related preventable causes, indicating that about 800 women died every day, resulting in a maternal mortality ratio of 223 deaths per 100,000 live births [1]. By lessening maternal mortality to roughly 70 per 100,000 live births between 2016 and 2030, the Sustainable Development Goal initiatives hope to avert the maternal mortality rates [2]. Contrary to goals set according to the Sustainable Development Goals 3.1, the global maternal mortality rate increased from 151 in 2019 to 152 per 100,000 live births in 2020 [3]. In Ethiopia, maternal death rate was 412 per 100,000 live births in 2016 [4]. It stayed high, accounting for 412 per 100,000 live births in 2019 [5]. In Ethiopia, prolonged and obstructed labor account for 22% of all maternal deaths [6]. Although prolonged and obstructed labors are among the leading causes of death in resource-poor settings, they can be diagnosed and averted with correct partograph use [7,8]. A partograph is a graphic representation of the labor's progress that includes pertinent information about the mother and the fetus [9]. In this regard, one of the most important ways in assuring high-quality care for both the mother and the newborn during labor is to use the partograph [10].

Despite its significance, partograph use by obstetric health care providers is still low in Ethiopia [6,7,11-15]. In addition to this, the paper-based approach is prone to recording errors due to health care providers' overburdened and retrospective data entry [16]. Paper-based partographs are also exposed to incomplete reporting of parameters. In Uganda, only 24.6% of the partograph parameters demonstrated complete details [17]. In a study in Jigjiga and Degehabur, about 64% of the partograph characteristics were only partially recorded [11]. A study in the West Shoa zone revealed that only 3% of the partographs examined was recorded according to the standard [7]. The rapid progress of technology is one of the many drivers now impacting health care systems [18], and offering health care services via mobile devices is now seen as a promising technological advancement [19]. The widespread availability of smartphones and tablets provides an opportunity for the use of a well-designed electronic partograph [16]. Digitizing the partograph improves adherence and overcomes the limitation of paper-based partographs [10,16,20-22]. The electronic partograph is a contemporary instrument for capturing labor data in real time, which can improve mother and infant outcomes [23]. Electronic partographs make it possible to improve the labor management system's record of labor progress statistics and care given to mother and fetus, especially in low-income nations [10,20,24,25]. Electronic partographs also result in a significant reduction in the rate of prolonged labor from 42% to 29% and have a far greater usage rate than paper-based partographs [21]. In addition, electronic partographs are preferred over paper-based partographs by clinicians due to their ease of use and less time, improved performance, decreased referral rates, assured prompt referral when necessary, facilitation of reporting obligations, and enhancement of service quality [26,27].

Studies show that using mobile-based health services in the health sector have the potential to increment health service access, quality, adherence, and efficiency [28-35]. However, the technological benefit obtained depends on the rate of use and adherence of users. Human activities mainly depend on their behavioral intention, and the intention to use digital tools is a determinant factor of actual user behavior. Therefore, determining the behavioral intention to use and its predictors before the adoption of technology is important and prevents implementation failure [36]. Behavioral intention is the degree to which a person has made intentional plans to engage or abstain from engaging in a specific future conduct [37]. To facilitate future implementation, it is vital to ascertain the degree of intention to employ any digital tools in the health sector [36]. A variety of Technology Acceptance Models (TAMs) have been applied to identify and predict end user behavioral intention to utilize technology. Among these, Davis's TAM is significant and effective at predicting users' intent to use [38].

To increase understanding of the factors affecting behavioral intention, different scholars have modified the original TAM [39-45]. Therefore, we modified the TAM to increase the understanding of the predictors that influence the behavioral intention of obstetric health care providers to use mobile-based partographs because information on the proportion of intention to use mobile-based partographs and its predictors is limited. This study was intended to fill this gap.

Theoretical Model and Hypothesis Development

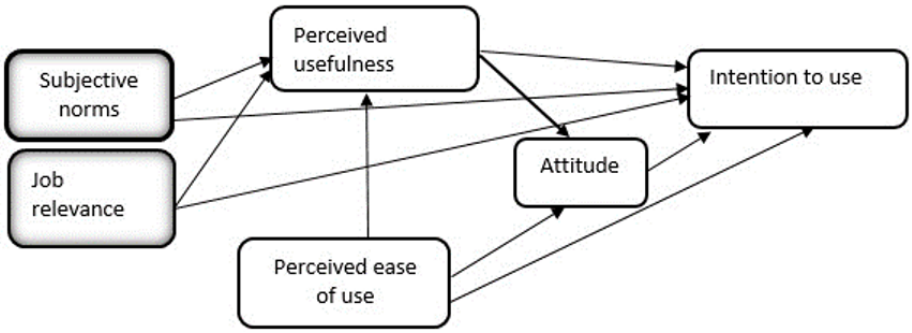
TAM is the most well-known methodology for establishing and evaluating each person's intent to embrace new technology [46]. It is a commonly used model that is used to anticipate possible users' behavioral intentions to use a technological innovation [47]. TAM had been altered, nevertheless, to boost its capacity for predicting variations in usage intention. Studies on doctors' approval of digital personal aids in Turkey [48], smart health care services among medical practitioners in China [49], health information system acceptance by hospital personnel in Greece [50], intention to use technology to attend to clients by health professionals in Ghana [51], and sustainable adoption of eHealth systems by health care professionals in Ethiopia [39] by using modified TAM report about 71%,71.5%, 87%, 97%, and 56% of variance in intention to use, respectively.

TAM was initially established with 2 key dimensions termed as perceived utility and perceived ease of use to identify the potential drivers of intention. The extent to which a person

thinks using a given system would improve his or her performance at work is known as perceived usefulness [38]. According to studies [18,38,39,48,52] in health care settings, perceived usefulness had a significant and positive influence on intention to use. Perceived ease of use is another factor that establishes the end users' behavioral intentions. The degree to which someone perceives a system to be simple to use is known as perceived ease of use [38]. The greater the user's propensity to use something, the friendlier is the user experience [53]. Perceived ease of use significantly and positively influences intention to use [39,48,50,54] and end users' attitudes toward using a particular approach or technology [55]. The attitude is described as an individual's impression of the positive or negative implications of embracing technology [56]. Attitude toward using positively and significantly influences intention to use [52,57,58] and is influenced by perceived usefulness [58,59] and ease of use [39].

According to the core construct of TAM, it is possible to add antecedents to improve the predictive power and understand the potential factors influencing behavioral intention. To this end, subjective norms and job relevance are important predictors added to the original TAM. Subjective norms refer to "a person's view that the majority of influential individuals in his life believe he should or should not engage in the behavior in question" [60]. Studies have shown that subjective norms influence perceived usefulness [61] and intention to use [49,62]. The perception of whether a technology is suitable for their jobs can also have an impact on whether they intend to use it. Job relevance examines how users view using the system for work and is found to influence perceived usefulness and intention to use [44,45,63]. Whether the specified concept will mediate the link between constructs is another key factor to consider. The mediators act as a channel for latent concept effects to reach the dependent variables [64]. Perceived usefulness [65,66] and attitude [53,67,68] have been reported to act as mediators in TAM studies. The following hypotheses are formed in light of the information presented above (Figure 1).

Figure 1. Our proposed modified Technology Acceptance Model based on the original Technology Acceptance Model of Davis et al [69].



Hypothesis 1: Perceived usefulness will have a positive effect on the intention to use mobile-based partographs.

Hypothesis 2: Perceived usefulness will have a positive effect on obstetric health care providers' attitudes toward mobile-based partographs.

Hypothesis 3: Perceived ease of use will have a positive effect on obstetric health care providers' attitudes toward mobile-based partographs.

Hypothesis 4: Perceived ease of use will have a positive effect on the perceived usefulness of mobile-based partographs.

Hypothesis 5: Perceived ease of use will have a positive influence on the intention to use mobile-based partographs.

Hypothesis 6: Obstetric health care providers' attitudes toward using mobile-based partographs will positively influence intention to use.

Hypothesis 7: Job relevance will have a positive effect on the intention to use mobile-based partographs.

Hypothesis 8: Job relevance will have a positive effect on the perceived usefulness of mobile-based electronic partographs.

Hypothesis 9: Subjective norms will have a positive effect on the perceived usefulness of mobile-based partographs.

Hypothesis 10: Subjective norms will have a positive effect on the intention to use mobile-based partographs.

Hypothesis 11: Perceived usefulness mediates the relationship between job relevance and intention to use.

Hypothesis 12: Perceived usefulness mediates the relationship between subjective norms and intention to use.

Hypothesis 13: Perceived usefulness mediates the relationship between perceived ease of use and intention to use.

Hypothesis 14: Attitude mediates the relationship between perceived usefulness and intention to use.

Hypothesis 15: Attitude mediates the relationship between perceived ease of use and intention to use.

Methods

Study Design and Setting

An institution-based cross-sectional study was conducted from June 1 to July 1, 2022, at public referral hospitals in the Oromia region of Ethiopia. There are 30 municipal administrations and 23 zones in the Oromia region. Thirteen public referral hospitals, 33 general hospitals, 67 primary hospitals, 1383 health centers, and 6797 health posts are located in the Oromia region. In the 13 public referral hospitals, there were about 649 obstetric health care professionals employed. The midwives, nurses, integrated

emergency obstetrics and surgery professionals, general practitioners, obstetricians, and gynecologists are trained obstetric health care professionals.

Study Participants and Sample Size Determination

All obstetric health care providers who were working at Oromia region public referral hospitals and were available at the time of data collection were the source and study population of this study. The sample size for this study was calculated based on the rule of thumb of structural equation modeling. The most widely used rule of thumb is that for 1 free parameter, 10 observations are required [70,71]. The proposed model of this study had 55 free parameters. Therefore, n (number of free parameters × 10; 55 × 10) = 550, where n represents the sample size. Considering a 10% nonresponse rate, the final minimum sample size was 605.

Sampling Procedure

In the 13 public referral hospitals of the Oromia region, there were 649 obstetric health care providers. From the onset, this study required a large sample size to test the developed hypothesis using the maximum likelihood estimator of the structural equation model. However, the number of study participants involved in this study was not adequate for sampling. For this reason, a census was conducted.

Study Variables

The outcome variable of this study was the intention to use mobile-based partograph, whereas the mediator variables were attitude toward using and perceived usefulness. The independent variables of this study included technology acceptance–related exogenous latent variables (perceived ease of use, subjective norm, and job relevance), sociodemographic and other related factors of obstetric health care providers (age, sex, marital status, religion, profession, qualification, and years of experience), access to mobile devices, partograph learning, in-service training, and computer courses.

Operational Definition

Behavioral intention is the extent to which an individual has made intentional plans to engage in or refrain from engaging in a specific future conduct [37]. The intention to use, in this case, refers to the likelihood of obstetric health care providers whether they intended to use mobile-based partograph if they will be offered. The construct had 4 items, and each was measured with a 5-point Likert scale response. The median score was used as a cutoff point. The obstetric health care provider who scored median and above on intention to use construct was considered as intended to use a mobile-based partograph otherwise unintended.

Data Collection and Procedure

A self-administered structured English questionnaire was used to collect data. Regarding the latent variable, the questionnaire was adapted from different literatures [44,53,63,72-77]. The adapted questionnaire was modified to fit the context of this study. The structured questionnaire had 4 parts: the first part included the sociodemographic characteristics of the obstetric health care providers, the second part related to access to mobile devices, the third part related to partograph and computer courses, and the fourth part included technology acceptance–related parameters (perceived usefulness, perceived ease of use, intention to use, attitude, job relevance, and subjective norm). A total of 21 items were used in this study to test the proposed hypothesis. A Likert scale ranging from strongly disagree (1) to strongly agree (5) was used to rate the level of participant agreement toward the prepared close-ended questions.

Data Quality Assurance

A pretest was done on 5% of the sample size among obstetric health care providers who were working out of the study area. One day of training was given to 4 data collectors and 4 supervisors on the objective of the study, data collection procedures, data confidentiality, and respondents' rights. The data collectors were BSc graduates: 3 midwives, 2 health officers, and 3 nurses. Supervision was continuous and made by the supervisors and principal investigator throughout the data collection. After data collection, completeness was checked.

Data Processing and Analysis

Before data analysis, the coded data were entered into EpiData (version 4.6) and finally exported into SPSS (version 25; IBM Corp) for descriptive analysis and AMOS (analysis of moment structure; version 23) for structural and measurement model assessment. Structural equation modeling is a multivariate statistical analysis technique that is used to analyze structural relationships. The data set was checked for missing values, and there were no missing data. The sociodemographic data were analyzed descriptively using SPSS, and the results were presented using a frequency table. Descriptive statistics was used to compute the proportion of intention to use mobile-based partographs, and the result was presented using the bar graph. The maximum likelihood estimation method was considered, and the assumption was checked. One assumption is the presence of multiple measurements for a construct. Perceived ease of use, perceived usefulness, and intention to use each have 4 items. However, attitude, subjective norms, and job relevance each have 3 items. Multicollinearity among the independent variables was assessed using the variance inflation factor. The result obtained (variance inflation factor ranged from 1.6 to 2.027) proved that there was no multicollinearity among independent variables.

Another assumption was univariate normality, which was assessed using kurtosis and skewness values, and the result shows there was univariate normality. The kurtosis value of less than 5, a critical ratio between –1.96 and +1.96, was used to declare the presence of multivariate normality. Unfortunately, the assumption of multivariate normality was not fulfilled. Therefore, bootstrapping technique was used to manage multivariate nonnormality.

Confirmatory factor analysis was used to perform measurement model assessment. Construct reliability was tested using Cronbach α and composite reliability. A cutoff point greater than .7 was used to declare the presence of internal consistency of the item that measured construct [78]. The recommended Cronbach α value should be .7 and above [79,80]. Furthermore, the composite reliability should be greater than .7 [36]. The

average variance extracted and factor loading was used to measure convergent validity. In the measurement model assessment, the average variance extracted value greater than 0.50 [45,64] and factor loading of at least 0.6 [75] should be used to establish convergent validity. Discriminant validity assesses the distinctness of construct when measured by their respective items. The discriminant validity was determined using the square root of average variance extracted, and the value should be greater than the interconstruct correlations to declare whether the discriminant validity of the construct was achieved [64]. The degree to which one construct differs from every other construct in the instrument is indicated by its discriminant validity [81].

Model goodness of fit was checked both for measurement and structural model assessment. A model fit index of the ratio of chi-square to degrees of freedom ≤3 [36], comparative fit index >0.90, goodness-of-fit index >0.90, adjusted goodness-of-fit index >0.85, normalized fit index >0.90, standardized root mean square residual <0.08, and root means square error of approximation <0.008 index value were used to measure and declare the model's goodness of fit [39,50]. We planned to perform model modification to improve the model fitness if the initial model did not fit by deleting the factor loading value with<0.5 covariate error terms [82]. In this regard, even if the measurement model fitness was achieved initially, the model modification was performed since the chi-square to the degree of freedom for the structural model was 3.128. Therefore, to increase the model fitness, we covariate the error term 15 and 16 on the intention to use the latent variable. Finally, the overall model fitted the data well.

After measurement model assessment, structural model fitness was checked and the model fit the data well. Then, the structural model assessment was performed. Based on AMOS output, the standardized path coefficient and the level of significance were used to test the developed hypothesis and determine the association between the latent variables of the study. The standardized regression weights showed the strength of association between latent variables [83], and *P* values less than .05 showed the level of significance considered. The square multiple correlations were used to report the proportion of variances in endogenous latent variables explained by exogenous variables. The bootstrap method was used to test the mediation effect.

Ethics Approval

Ethical clearance was obtained from the University of Gondar, and this study was approved by its ethics review board (Ref/IPH/2129/2014). A letter of support was obtained from the Department of Health Informatics, and written consent was taken from each study participant.

Results

Sociodemographic Characteristics of the Participants

A total of 649 participants were planned to be included in this study from all public referral hospitals in the Oromia region for the assessment of their intention to use mobile-based partographs and the predictors for their intention to use. Among them, 97% (630/649) gave their consent and completed the questionnaire. The results of this study show that almost more than half (344/630, 54.6%) of the study participants were males, while 45.4% (286/630) of the participants were females. The median age of the study participants was 32 (IQR 9) years. The majority of the participants were in the age group of 30-39 years. About 34.4% (217/630) of the respondents were Orthodox Christians in religion. Among the study participants, 371 (58.9%) respondents were married and 218 (36.4%) were single. Regarding their profession, more than half (351/630, 55.7%) were midwives, 96 (15.2%) were nurses, and 95 (15.1%) were general practitioners. Of the total study participants, 497 (78.9%) were bachelor's degree holders and 78 (12.5%) were a specialist in their qualifications. Almost half (328/630, 52.1%) of the study participants had ≤4 years of working experience with the qualification they had. All the sociodemographic characteristics of the study participants are shown in Table 1.

Table 1. Sociodemographic characteristics of the obstetric health care providers who were working at public referral hospitals in the Oromia region of Ethiopia in 2022 (N=630).

Demographic characteristics	Values, n (%)
Sex	
Male	344 (54.6)
Female	286 (45.4)
Age (years)	
20-29	232 (36.8)
30-39	299 (47.5)
>40	99 (15.7)
Religion	
Orthodox Christian	217 (34.4)
Muslim	167 (26.5)
Protestant	208 (33)
Others[a]	38 (6)
Marital status	
Married	371 (58.9)
Single	218 (34.6)
Divorced	25 (4)
Separated	10 (1.6)
Widowed	2 (0.3)
Others[b]	4 (0.6)
Profession	
Midwives	351 (55.7)
Nurses	96 (15.2)
General Practitioner	95 (15.1)
Obstetrician and Gynecologist	78 (12.4)
Others[c]	10 (1.6)
Level of qualification	
Bachelors	497 (78.9)
Masters	48 (7.6)
Specialists	79 (12.5)
Others[d]	6 (1)
Years of working experience	
≤4	328 (52)
5-9	195 (31)
≥10	107 (17)

[a]Waaqeffanna, Adventist, and Catholic.

[b]In a relationship.

[c]Integrated Emergency Obstetric Surgery professionals.

[d]Diploma.

Access to Mobile Devices and Partographs

In this study, of the 630 participants, 625 (99.2%) had access to mobile devices (Table 2). Approximately 93.1% (582/630) of the obstetric health care providers had access to a smartphone. About 77.8% (490/630) of the study participants had a partograph. However, only 326 (51.7%) study participants had taken in-service training for using paper-based partographs.

Regarding the computer course, 310 (80.7%) took basic computer training. Table 2 shows the frequency of access to mobile devices, partograph learning, partograph in-service training, and computer courses.

Table 2. Access to mobile devices, partograph training, and computer courses by obstetric health care providers who were working at the public referral hospitals in the Oromia region of Ethiopia in 2022 (N=630).

Variables	Values, n (%)
Access to mobile devices	
Yes	625 (99.2)
No	5 (0.8)
Mobile device type	
Smartphone	582 (93.1)
Tablet	33 (5.3)
Others[a]	10 (1.6)
Study partograph	
Yes	490 (77.8)
No	140 (22.2)
In-service training on paper-based partograph	
Yes	326 (51.7)
No	304 (48.3)
Computer courses	
Yes	384 (61)
No	246 (39)
Computer course level	
Basic course	310 (80.7)
Advanced training	74 (19.3)

[a]Basic phones or feature phone.

Intention to Use Mobile-Based Partographs

Among the 630 obstetric health care providers, 414 had intention to use mobile-based partographs. Thus, about 65.7% (414/630; 95% CI 61.9%-69.4%) or two-thirds of the study participants scored median and above of intention to use. The median score of intention to use mobile-based partograph was 16 (IQR 1.5). The minimum and maximum scores for intention to use were 4 and 20, respectively. Figure S1 of Multimedia Appendix 1 shows the proportion of intended and unintended use of mobile-based electronic partographs among obstetric health care providers who were working at public referral hospitals in the Oromia region in 2022. In this study, Cronbach α and composite reliability values were greater than .9. All the factor loading values were found in the range of 0.843 to 0.946, and the average variance extracted value was found in the range of 0.761 to 0.840. Hence, construct reliability and convergent validity of the measurement model were achieved.

Discriminant Validity

The finding of this study indicates that the square root of the average variance extracted value was greater than the value of the interconstruct correlations. Therefore, the discriminant validity of the measurement model was achieved. Table S2 of Multimedia Appendix 1 demonstrates the discriminant validity of the model. The bold values in the table represent the square root of the average variance extracted.

Measurement Indices of the Goodness of Fit of Model

In this study, all the obtained values of the measurement model fit indices were in an acceptable range. Hence, the result of this study indicated that the modified proposed model fitted the data well. Table 3 shows the result of model fit indices [36,39,50].

Table 3. Results of the indices of goodness of fit of the measurement model assessment.

Model fit indices, citation	Cutoff point	Result obtained[a]	Fit decision
Chi-square to degree of freedom [36]	≤3	2.245	Accepted
Goodness-of-fit index [50]	>0.9	0.945	Accepted
Adjusted goodness-of-fit index [50]	>0.85	0.927	Accepted
Normed fit index [50]	>0.9	0.974	Accepted
Comparative fit index [39,50]	>0.9	0.985	Accepted
Root mean square residuals [39,50]	<0.08	0.022	Accepted
Root mean square error of approximation [50]	<0.08	0.044	Accepted

[a]The result is obtained from the measurement model assessment using AMOS (analysis of moment structure; version 23) software to check model fitness.

Structural Model Assessment

Among the 10 proposed hypotheses of the direct relationship, 8 were supported by the collected data. However, hypothesis 9 and hypothesis 10 failed to support the proposed hypothesis. Our study shows that perceived usefulness positively influences intention to use (β=.184; *P*=.02). In addition, perceived usefulness had a positive influence on attitude (β=.512; *P*=.002). According to our finding, perceived ease of use positively influenced attitude (β=.382; *P*=.003), perceived usefulness (β=.503; *P*=.002), and intention to use (β=.369; *P*=.001). Perceived ease of use had the strongest path coefficient in influencing intention to use mobile-based partographs.

Job relevance in the structural model had a positive and significant influence (β=.408; *P*=.002) on perceived usefulness. In addition, job relevance (β=.185; *P*=.008) positively and significantly influenced the intention to use. The results of this study also indicated that attitude (β=.309; *P*=.002) positively and significantly influenced intention to use.

Subjective norms had insignificant influences on perceived usefulness (β=.02; *P*=.61) and intention to use (β=–.066; *P*=.07). Therefore, hypotheses 9 and 10 failed to support the developed hypothesis. Perceived ease of use, attitude, and job relevance had a 0.369, 0.309, and 0.185 path coefficient in association with intention to use, respectively. Results from the AMOS output of the proposed model showed that perceived usefulness was influenced by both job relevance and perceived ease of use (Figure 2). However, perceived ease of use (β=.503) had higher path coefficient than job relevance (β=.408) in influencing perceived usefulness. Perceived usefulness and perceived ease of use influenced the attitude toward using electronic partographs. Perceived usefulness (β=.521) had a higher path coefficient than perceived ease of use (β=.382) in influencing attitude toward using electronic partographs. Table 4 shows the results of the hypothesis testing of the direct path analysis of the proposed model.

Figure 2. AMOS (analysis of moment structure; version 23) output of the standardized estimate. AT: attitude; ITU: intention to use; JR: job relevance; PEOU: perceived ease of use; PU: perceived usefulness; SN: subjective norms.

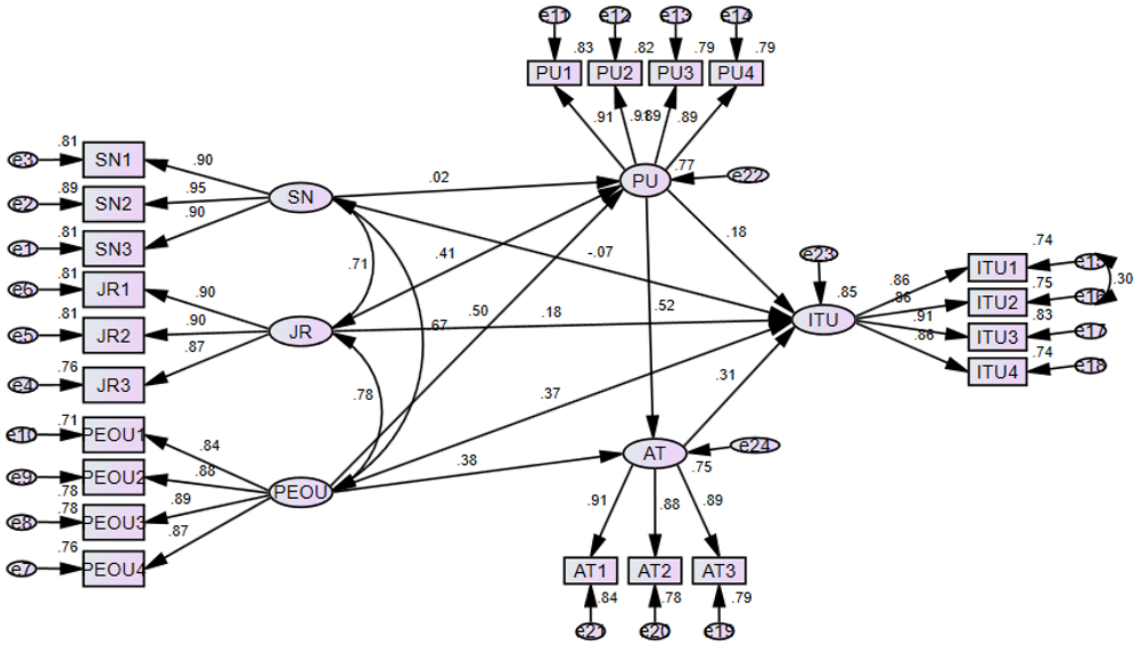


Table 4. The results of the hypothesis testing of the proposed model.

Hypothesis	Causal path	β (path coefficient)	Critical ratio	*P* value	Decision
1	ITU[a]←PU[b]	.184	3.294	.02	Supported
2	AT[c]←PU	.521	9.918	.002	Supported
3	AT←PEOU[d]	.382	7.279	.003	Supported
4	PU←PEOU	.503	11.097	.002	Supported
5	ITU←PEOU	.369	7.160	.001	Supported
6	ITU←AT	.309	6.351	.002	Supported
7	ITU←JR[e]	.185	3.969	.008	Supported
8	PU←JR	.408	8.476	.002	Supported
9	PU←SN[f]	.020	0.540	.61	Not supported
10	ITU←SN	–.066	–2.060	.07	Not supported

[a]ITU: intention to use.

[b]PU: perceived usefulness.

[c]AT: attitude.

[d]PEOU: perceived ease of use.

[e]JR: job relevance.

[f]SN: subjective norms.

Among the 15 developed hypotheses, 5 of them deal with the mediation effect of perceived usefulness and attitude between the exogenous latent variables and outcome variable in this study. Table S3 of Multimedia Appendix 1 shows the result of the mediation analysis using the bootstrapping method. The 95% biased confidence interval and *P* value level were used to test the presence of a mediation. Our results showed that perceived usefulness partially mediates between job relevance and intention to use. Hence, hypothesis 11 was supported. However, perceived usefulness did not mediate the relationship between subjective norms and intention to use. Therefore, hypothesis 12 was not supported. However, perceived usefulness partially mediated perceived ease of use and intention to use. Therefore, hypothesis 13 was supported. Furthermore, attitude partially mediated the relationship between perceived usefulness and intention to use as well as perceived ease of use and intention to use. Consequently, hypothesis 14 and hypothesis 15 were supported. Table S3 of Multimedia Appendix 1 illustrates the result of the mediation analysis.

The squared multiple correlations indicate the predictive power of the model. In this study, the proposed model explained 85% of the variance in intention to use a mobile-based partograph. Perceived ease of use and job relevance aggregately explained 77% of the variance in perceived usefulness. However, perceived ease of use and perceived usefulness explained about 75% of the variance in attitude toward use. Table S4 of Multimedia Appendix 1 shows the result of the predictive power of the proposed model.

Discussion

Principal Findings

This study examines the proportion of obstetric health care providers in the Oromia region of Ethiopia who had the intention to use mobile-based partographs and the predictors for their intention to use. The result of our study revealed that about two-thirds (414/630, 65.7%) of the obstetric health care providers had the intention to use mobile-based partographs. Even if no similar study was conducted on the intention to use a mobile-based partograph, ascertaining the end user's level of acceptance to use technology before execution serves as a prerequisite to judging the accomplishment of the execution [39]. In this regard, a study in north Gondar reported that 44% of the obstetric health care providers were willing to use mobile-based partographs [84]. The findings of [84] assist our study in promoting the execution of mobile-based partographs in clinical settings for enhancing the care given during the management of labor.

The results of our study regarding TAM were in line with those of the original TAM [69]. In this study, perceived ease of use (β=.503; *P*=.002) significantly and positively influenced the perceived usefulness of mobile-based partographs by obstetric health care providers. This study's finding is in line with a study in Omaha on telemedicine acceptance (β=.56) [18] and that in Ethiopia on eHealth acceptance (β=.385) [39]. Further, this study finding is supported by a study conducted in Tanzania in which skilled birth attendants found that electronic partograph was useful, easy to use, and improved the quality of care [24]. This indicates that obstetric health care providers who perceive that mobile-based partograph is easy to use, easy to interact with, and easy to learn are more likely to perceive it as useful, and consequently, this will lead to a high intention to use it [39].

Another association in this study was that perceived usefulness (β=.184; *P*=.02) positively influenced intention to use. This positive and significant relationship of the construct is in agreement with a study in Turkey on personal digital assistant acceptance (β=.41) [48], a study in Uganda on mobile phone

adoption in maternal health care (β=.186) [54], and a study in Ethiopia on eHealth adoption (β=.387) [39]. Thus, obstetric health care providers' perception of mobile-based partograph usefulness is a valuable predictor of behavioral intention to use. It is important to find out how users measure the usefulness of the technology because the more the obstetric health care providers perceive that a mobile-based partograph improves productivity, performance, and effectiveness, and decreases the duration of recording, the more likely they will intend to use it. Our study shows that perceived ease of use positively (β=.382) and significantly (*P*=.003) influenced attitude toward using electronic partographs. This direct effect of perceived ease of use on attitude is in line with a study in Ethiopia (β=.347) [39]. These findings indicate that if users perceive that the use of electronic partograph is easy, they will develop a positive attitude toward using it, consequently impacting their behavioral intention to use it.

We found that perceived ease of use of mobile-based partographs significantly affected intention to use (β=.369; *P*=.001). This showed that the likelihood of intention to use the mobile-based partograph will increase with an increase in the impression of ease of use. This outcome is consistent with a study on the adoption of health information systems that was conducted in Greece (β=.29) [50] and in Ethiopia (β=.339) [39], demonstrating that requiring less effort will boost the system's ability to influence people's intentions to use eHealth systems. Perceived ease of use in this study had the highest path coefficient and a significant impact on usage intention. The more obstetric health care professionals are intentional to use the mobile-based partograph, the less effort it is thought to take to operate it on both a mental and physical level. To meet user expectations, electronic partograph developers should concentrate on the device's user-friendliness. This might increase the uptake and ongoing use of mobile-based partographs. Additionally, we found that attitudes about adopting mobile-based partographs are influenced by perceived usefulness (β=.521; *P*=.002). This finding is consistent with studies on telemedicine acceptability done in China (β=.43) [85] and Ethiopia (β=.26) [39]. The obstetric health care providers' attitude toward use was impacted by how much they believed this technology improves performance and productivity in their job. Thus, intention to use is directly influenced by attitude toward use (β=.309; *P*=.002). Our study's conclusion is consistent with that in a study on the intention of health professionals in Ethiopia to use eHealth (β=.526) and indicates that actions that improve perspectives, such as ongoing training and support and information sharing on eHealth innovations, should be prioritized heavily [39]. The more positive perception the obstetric health care providers developed and had, the higher they intended to use eHealth.

In this study, job relevance significantly and positively (β=.408; *P*=.002) influenced perceived usefulness. This study path relationship is in line with a study that focused on the adoption of technology using modified TAM [44,86]. There should be adequate information provision strategies for end users about the applicability and usefulness of mobile-based partographs in labor management. A study on personal digital assistant acceptance by health care professionals supports this evidence in a way that information provision about the technology applicability by health care institutions promotes technology acceptance [80]. Additionally, job relevance significantly influenced intention to use (β=.185; *P*=.008). This finding is in line with a study conducted on health information technology acceptance [44]. This means that the more probable obstetric health care professionals expected to use a mobile-based partograph, the more they believed it was appropriate, relevant, and vital to their work. Because of this, it is crucial to let obstetric health care professionals know about the use of mobile-based partographs in labor management.

According to this study, subjective norms had an insignificant impact on perceived usefulness (β=.020; *P*=.61). This insignificant influence is in line with the findings of a study on hospital information systems (β=–.18; *P*>.05) [87]. This might be because obstetric health care professionals are more likely to establish their independent judgments and may therefore pay less heed to what other people think. Another factor is that regardless of what is important, others may think all obstetric health care providers will be forced to use mobile-based partographs as long as the government mandates their usage in health care facilities for labor management. Subjective norms also insignificantly influence intention to use (β=–.066; *P*=.07). The result of this study is inconsistent with those of other studies [34,62,75]. Because of the time-consuming and detailed recording in paper-based partographs, obstetric health care providers could record incorrect and incomplete data and they could perform retrograde documentation to avoid accountability. However, in case of the digital partographs, retrograde documentation is not allowed and accountability is assured. To affect the belief that most significant others consider he or she should utilize the mobile-based partograph, the health care system should strengthen the concept of teamwork.

In contrast to a study on the adoption of eHealth in the Amhara region, where attitude was the strongest predictor of intention, in this study, perceived ease of use was the strongest predictor of intention to use [39]. To maximize the likelihood of initial and ongoing usage, mobile-based partographs should be provided with an easy function. The association between job relevance and intention to use as well as the relationship between perceived ease of use and intention to use is partially mediated by perceived usefulness in the study's proposed model, which is consistent with [88]. However, perceived utility is unable to buffer the link between subjective norms and usage intention.

Perceived ease of use and intention to use were partially mediated by attitude and consistent with the study conducted using modified TAM [83]. Attitude toward using mediates the relationship between perceived usefulness and intention to use. To maximize the benefits of the additional capabilities, makers of eHealth platforms should actively work to change how physicians feel about using them [68]. The proposed modified TAM explained about 85% variance in the obstetric health care providers' intention to use mobile-based partographs. This shows that the model's overall predictive ability was high, and the variance in this study was almost equivalent to a study [50] utilizing modified TAM in a health care scenario.

Limitations of This Study

First, it is difficult to discuss whether the proportion of intention to use mobile-based partographs among obstetric health care providers is high or low due to the lack of similar previous studies. This study was a one-time study. Second, it is difficult to establish a cause-effect relationship in this study due to the cross-sectional nature of this study. Third, as the respondents were only from the government and tertiary care levels, caution must be exercised when applying these findings to all obstetric health care providers in the area.

Conclusion

In our study, two-thirds of the obstetric health care providers had the intention to use mobile-based partographs. Perceived usefulness, perceived ease of use, job relevance, and attitude positively and significantly influenced their intention to use mobile-based electronic partographs. Among these, perceived ease of use was the strongest potential predictor of intention to use. The connection between exogenous latent variables and intention to use was partially mediated by perceived usefulness and attitude toward usage, except for subjective norms. The modified TAM is an effective model for forecasting the intention of an obstetric health care professional to use a mobile-based partograph.

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Data Availability

The data set used for the analysis in this study can be obtained on request from the corresponding author.

Authors' Contributions

All the authors of this study contributed to problem identification, proposal development, data collection and analysis, and thesis write-up to final approval for publication. They accept responsibility for this study.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Supplementary data.
[DOCX File , 226 KB - ojphi_v16i1e51601_app1.docx]

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Abbreviations

AMOS: analysis of moment structure
TAM: Technology Acceptance Model

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Original Paper

Harnessing Generalizable Real-World Ophthalmic Big Data: Descriptive Analysis of the Bodhya Eye Consortium Model for Collaborative Research

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Abstract

Background: Eye care organizations and professionals worldwide are increasingly focusing on bridging the gap between population health and medical practice. Recent advances in genomics and anthropology have revealed that most Indian groups trace their ancestry to a blend of 2 genetically distinct populations: Ancestral North Indians, who share genetic affinities with Central Asians, Middle Easterners, Caucasians, and Europeans; and Ancestral South Indians, genetically distinct from groups outside the Indian subcontinent. Studies conducted among North Indian populations can therefore offer insights that are potentially applicable to these diverse global populations, underscoring significant implications for global health.

Objective: The Bodhya Eye Consortium is a collaboration among 8 high-volume nonprofit eyecare organizations from across North India. The consortium aims to harness real-world data consistently and with assured quality for collaborative research. This paper outlines the formation of the consortium as a proposed model for controlled collaborative research among the leading eyecare organizations of North India.

Methods: We detail the creation and effective implementation of a consortium following a structured road map that included planning and assessment, establishing an exploratory task force, defining specialty areas, setting objectives and priorities, and conducting a SWOT (strengths, weaknesses, opportunities, and threats) analysis. Central to this process was a comprehensive data audit aimed at standardizing data collection across all participating organizations.

Results: The consortium currently comprises 9 organizations, each represented in the governance structure by the Governing Council. Scientific standards for published research are established and overseen by the Scientific Committee, while the Conflict Resolution Committee manages any unresolved disputes. The consortium’s working groups, organized by various eyecare

specialties, collaborate on research projects through virtual interactions. A foundational step in this process was the organizationwide data audit, which revealed that most organizations complied with accurate and standardized data collection practices. Organizations with deficiencies in data completeness developed action plans to address them. Subsequently, the consortium adopted data collection proformas, contributing to the publication of high-quality manuscripts characterized by low dropout rates.

Conclusions: The collaborative research conducted by the Bodhya Eye Consortium—a group of high-volume eyecare organizations primarily from North India—offers a unique opportunity to contribute to scientific knowledge across various domains of eyecare. By leveraging the established heterogeneity of anthropological and genomic origins within the population, the findings can be generalizable, to some extent, to European, Middle Eastern, and European American populations. This access to potentially invaluable, generalizable data has significant global health implications and opens possibilities for broader collaboration. The model outlined in this descriptive paper can serve as a blueprint for other health care organizations looking to develop similar collaborations for research and knowledge sharing.

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KEYWORDS

anthropological and genomic heterogeneity; big data; consortium; collaborative research; generalizability; global health impact; North India

Introduction

Eyecare organizations and professionals worldwide are increasingly focused on bridging the gap between public health and medical practice. There has been a recent emphasis on forming alliances to enhance capacity [1], resulting in the rise of public-private partnerships and collaborations between governmental policy makers and high-volume nonprofit eyecare organizations [2].

Central to deriving generalizable knowledge for public health initiatives from any data is understanding the population under study. In India, the majority of nonprofit eyecare organizations conducting clinical and epidemiological research, and establishing baselines for nearly every ocular condition [3-6], are concentrated in the southern region of the country. Although these data are invaluable, their generalisability to other populations outside India may be limited. Recent advances in anthropology and genomics confirm a long-held suspicion: the majority of Indian groups trace their ancestry to a blend of 2 genetically distinct populations. Ancestral North Indians share genetic affinities with Central Asians, Middle Easterners, Caucasians, and Europeans, while ancestral South Indians exhibit genetic ties predominantly within the Indian subcontinent, distinct from groups outside it [7]. In contrast to the relatively homogeneous population of South India, North Indian populations exhibit greater heterogeneity, sharing genetic similarities with Middle Easterners, Central Asians, and Europeans [7], and by extension, with Euro-Americans. As a result, studies conducted on North Indian populations may hold broader applicability to these diverse groups, potentially carrying significant global health implications. This unique genomic diversity found in North India distinguishes it on a global scale. Establishing a network of institutions across North India for collaborative research presents an ideal opportunity to leverage the unique anthropological and genomic diversity of the region to gather substantial real-world ocular data [8]. Real-world data refer to observational data, in contrast to data obtained from randomized controlled trials. Bian et al [9] demonstrated through a systematic scoping review that the quality of real-world data is often inconsistent due to its complex and heterogeneous nature.

The Bodhya Eye Consortium (BEC) is a collaboration among 8 high-volume nonprofit eyecare organizations across North India. This paper describes the formation of the BEC as a proposed model for controlled collaborative research among these leading eyecare organizations. The consortium aims to harness real-world data in a consistent, quality-assured manner.

Methods

Planning and Assessment

We used a comprehensive road map consisting of several key components. The idea for the consortium originated from a global eye genetics consortium in which a few organizations such as ours were participants. Therefore, the organizations approached for the BEC were those with similar structures that were already interacting with each other at various common forums, such as the genetics consortium. These organizations had been involved in such settings for at least 10 years before joining the consortium. Ten high-patient-volume organizations from North India were invited to form the consortium, selected based on the location of their main eye hospitals and catchment areas. Initial discussions were conducted on digital platforms, with joint weekly virtual meetings held over a 12-month period.

Setting Up an Exploratory Task Force

Following these discussions, an exploratory task force was formed to establish shared goals, define the necessary commitments to achieve them, and secure leadership commitment from the institutions. Subsequently, an in-person meeting was held at a mutually convenient eye hospital in Delhi, where the consortium's scope and structure were finalized. Discussions also centered on the legal framework for the consortium, forming a clear governance structure for clinical and research endeavors, as well as for future project and funding applications.

Defining Specialty Areas

Within ophthalmology, specialty areas include cataract, cornea, retina, pediatric ophthalmology, glaucoma, oculoplastics, public

health, and ocular microbiology. Working groups were established based on these specialties, with each group comprising representatives specializing in the respective fields from each member organization.

Setting Objectives/Prioritizing

The objectives outlined in the initial discussions were to build research capacity and facilitate knowledge sharing. A consensus was reached to prioritize conducting high-quality research with the goal of publishing scientific papers in top-ranked ophthalmological journals. The selection criteria for these journals were evaluating both the h-index and the median h-index of each MEDLINE-cited ophthalmology journal, along with their published impact factors. Additional objectives were organizing funding for research and ensuring the robustness of data collected and shared among consortium organizations through a comprehensive data audit.

The data audit was conducted across all participating hospitals to verify the accuracy of patient information entered on the face sheet (first page) of the patient files. The audit followed established protocols and was carried out by trained auditors at each center using a standardized proforma. Twenty files from each of the 10 organizations were selected using a predefined methodology to ensure randomization. Each day, a random number was generated, and the patient corresponding to that number accessing services at the hospital had their file selected, over 5 working days per week. This process was repeated over 4 weeks, resulting in a total of 5 patient files selected per week.

Basic patient information such as unique identifier, name, age, gender, contact number, address, and date of examination was recorded. Additionally, the presence of primary and secondary diagnoses, International Classification of Diseases (ICD) coding, procedures or surgeries performed, complications, and consent for procedures were noted. The variables and their coding are detailed in Multimedia Appendix 1. Proportional analysis was conducted and results are presented in percentages.

Defining Strengths, Weaknesses, Opportunities, and Threats

A SWOT (strengths, weaknesses, opportunities, and threats) analysis of the BEC and its workings was conducted.

Ethical Considerations

As this is a theoretical/modeling paper that does not use or discuss any patient data, no ethics approval was required. The article adheres to the Declaration of Helsinki.

Results

Planning and Assessment

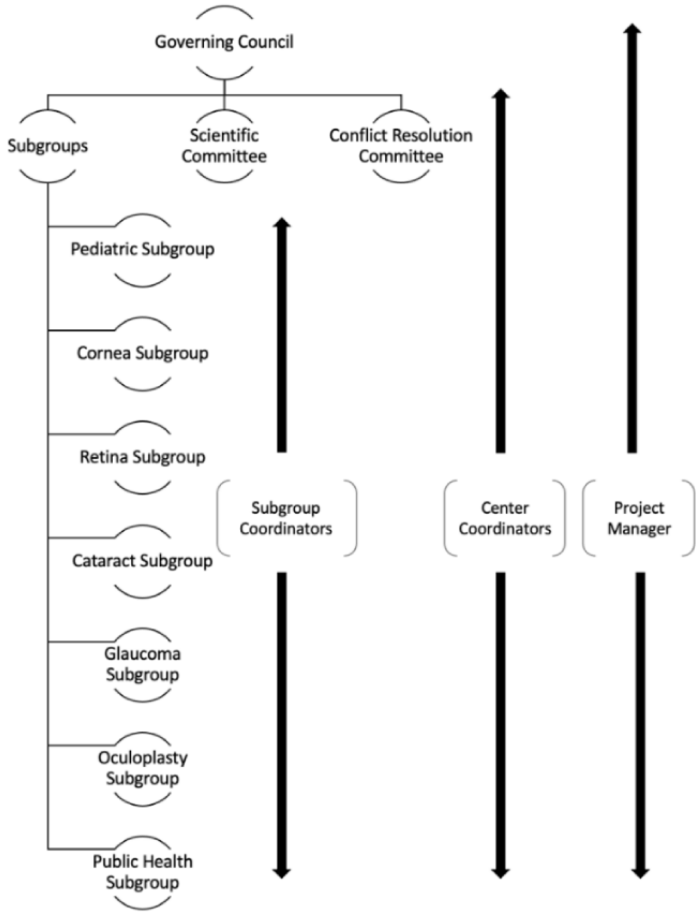
During the initial tele-discussions, 2 organizations dropped out, citing their inability to sustain contributions. However, approximately 4 years later, 1 of these organizations rejoined the consortium after establishing their catchment area and demonstrating the ability to provide sustained input. In recent years, additional organizations from across India—not just North India—have been included in the consortium. These new additions differ from existing members in terms of research capacity, geographic location, or community experience. This diversity enhances the consortium's research validity by extending its applicability to populations beyond North India.

Setting Up an Exploratory Task Force

The governance structure of the BEC was established (Figure 1). At each level of governance, all organizations are equally represented, ensuring similar roles across all members. The Governing Council comprises the Heads of Institutions from each member organization of the BEC. The Scientific Committee, which sets research standards and guidelines for ethics and authorship in collaboration with the Governing Council, includes 2 appropriately trained members from each organization. These members are nominated by the head of each institution and possess a keen interest and experience in research. The Scientific Committee also includes members from diverse backgrounds, including clinical specialists from various subspecialties, public health experts, and basic scientists, including those specializing in genetics. This diversity ensures that research topics remain relevant and innovative. The Scientific Committee is overseen by the Lead Coordinator (a nonvoting member). Additionally, a BEC Project Manager monitors project timelines and ensures ongoing progress, reporting directly to the Governing Council. The Scientific Committee and Governing Council play crucial roles in upholding research standards and quality assurance, serving as the primary decision-making and regulatory bodies of the BEC. Consequently, their responsibilities include ensuring compliance with all legal requirements. Members of both committees hold senior positions within their respective organizations, making it integral to their daily operations to uphold these standards.

To address potential conflicts related to intellectual property and data sharing among multiple organizations, and to ensure appropriate credit allocation, particularly regarding authorship, a Conflict Management Committee was established. This committee reports to the Governing Council and is chaired by an external member of the consortium, who is not affiliated with any of the collaborating organizations within the consortium. The primary role of this committee is to arbitrate disputes within subgroups that cannot be resolved through discussion, particularly regarding authorship concerns. Additionally, the presence and structure of institutional review boards and ethics committees were confirmed across all organizations.

Figure 1. Governance structure of the Bodhya Eye Consortium (BEC).



Defining Specialty Areas

The specialty-focused working groups serve as virtual forums where members discuss, develop, and conduct research. Research topic selection is determined at the working group level, comprising specialists in the respective fields.

Typically, a member of an organization pitches a research topic to the group along with a brief write-up. This proposal is circulated among subgroup members who review it, suggest modifications, and assess their centers' capacity to participate. Once the participating centers are finalized, they create a data collection proforma and initiate institutional review board approval processes at their respective centers before beginning data collection.

The overall standardization and quality of research topics within the consortium are ensured by the Scientific Committee through thorough reviews of study proposals. The study is spearheaded by the member or center proposing the research, and once the proposal is finalized and the lead center obtains institutional review board approval, the study lead submits the proposal to the Scientific Committee for review. After receiving feedback from the Scientific Committee, the study lead revises their proposal accordingly and resubmits it for further review. Once approved by the Scientific Committee, the data collection process commences.

This process enables each subgroup to conduct multiple studies simultaneously, allowing different centers flexibility in determining their contributions and enabling various members to lead and complete their own studies. The Scientific Committee's establishment of research processes and authorship guidelines reinforces this approach. Additionally, the Scientific Committee reviews each study's final manuscript before submission, assessing its scientific relevance, the added value of multicenter involvement, and how these aspects are presented in the manuscript.

Each working group is led by conveners chosen from within the group, who rotate every 3 months to oversee adherence to research guidelines and task deadlines. Administrative support for the working groups is provided by coordinators, 1 from each center, responsible for recording meeting minutes, tracking tasks, and coordinating with other consortium centers and stakeholders. Quarterly updates from conveners to all consortium members regarding subgroup progress encourage the cross-pollination of ideas.

Virtual monthly interactions foster cooperation, collaboration, and mutual respect among all participants through real-time discussions and debates. These interactions also facilitate knowledge exchange and capacity building within member organizations, exemplified by the establishment of virtual grand rounds and research workshops. Virtual grand rounds serve as a monthly knowledge-sharing platform open to all clinical personnel from member organizations, conducted on a rotating basis across each specialty area. Research workshops are conducted to foster a research culture, providing training to staff on research fundamentals such as formulating research questions, conducting literature reviews, interpreting statistical

analyses, and reading journal articles. These workshops are open to all clinical and research staff of consortium hospitals, encouraging both in-person and virtual discussions. Workshops are held at member organizations on a rotating basis. One impactful example is the microbiology training, where 2-3 paramedical personnel from each partner institution attended a 6-day training at the microbiology department of one of the founding consortium members. The training included theoretical materials and starter kits with stains and slides, aimed at establishing basic microbiology services to enhance keratitis diagnosis at their hospitals and to set up a network for future research projects.

Setting Objectives/Prioritizing

One of the primary activities aimed at ensuring data robustness was a file audit, conducted to standardize routine data collection processes across member organizations before formally initiating research and data sharing within the consortium. A total of 200 randomly selected files were audited across all 10 participating organizations at the time.

All 200 files (100%) included the patient's name, age, gender, contact number, address, and date of examination. Of these, 130 files (65%) reported both primary and specialty diagnoses, while 50 files (25%) reported only the primary diagnosis, with the specialty diagnosis available in detailed clinical records but missing from the diagnosis field; 2 files (1%) had incomplete diagnoses with the critical information entered, 1 file (0.50%) had incomplete diagnosis with critical information missing, and 7 files (3.5%) had no diagnosis entered. Among the 200 files audited, 162 (81%) files had complete and accurate ICD coding. Additionally, 10 (5%) files had complete but inaccurate coding, and 8 (4%) files had incomplete coding. Furthermore, 22 (11%) files did not have any ICD coding at all. Regarding procedure or surgery reporting, 158 (79%) files fully documented the procedure or surgery undergone by the patient, including the date. In 4 (2%) files, the procedure or surgery was noted without the date, and in 2 (1%) files, it was incomplete. Moreover, 38 (19%) files did not have the procedure or surgery entered at all. Concerning patient consent, 184 (92%) files indicated that patients had consented to undergo the procedure or surgery, while 16 (8%) files did not document patient consent.

All organizations participating in the BEC collect and store data using electronic medical records. Fields with more than 10% missing data were identified and highlighted to improve practices for clinical data–based studies. Each organization identified its deficiencies, developed action plans to address them, and implemented solutions. Future consortium members undergo the same data audit process upon joining.

This initiative subsequently introduced the use of proformas to facilitate the recording of reproducible and accessible data within working groups. For instance, in pediatrics, proformas were utilized to capture not only a patient's vision data but also the method of acquisition. Additionally, proformas were used to gather information from patient notes, and a feasibility form was circulated before proposing studies to assess the clinical and research capabilities at each center. Based on this approach, each center assessed its ability and capacity to participate in studies proposed through the consortium's subgroups. As a result, not all centers participate in every study. This strategy enabled us to plan, execute, and publish our first study [10], which involved participation from 3 of the consortium centers. While some variations are natural in clinical practice, we ensure that all planned research maintains uniform diagnostic and treatment practices across participating centers. Currently, data heterogeneity is addressed at the outset of each research endeavor, which may result in excluding centers unable to meet required standards.

With the objective of publishing a high-quality manuscript, the first study conducted under the consortium describes the clinical features, visual acuity, and causes of ocular morbidity in 532 children (0-18 years) from North India with microphthalmos, anophthalmos, and coloboma. This study has been published in a major international journal [10]; however, 3.2% (17/532) of the data needed to be excluded as a result of quality issues. Since then, collaborative efforts have successfully completed various research projects based on both retrospective and prospectively collected data. A total of 8 peer-reviewed studies have been published (n=6) or accepted (n=2) in international and national journals [11-16]. Currently, the consortium's research effectiveness is gauged by its capacity to consistently publish high-quality research.

Define Strengths, Weaknesses, Opportunities, and Threats

The SWOT analysis is detailed in Table 1.

Table 1. Strengths, weaknesses, opportunities, and threats of the Bodhya Eye Consortium.

Strengths	Weaknesses	Opportunities	Threats
• Abundance of talented providers and scientists within member hospitals. • High-volume clinics allowing access to big data. • Determination to establish a strong pedigree of research and clinical excellence. • Extraction of quality retrospective data.	• Time as a limiting factor in terms of planning and conducting organized research. • Stresses that come with working in regular eyecare service delivery organizations. • Lack of a central monetary source. • Lack of a data-sharing agreement.	• Funding for research and administration.	• Dependence on social media platforms and security of conducting regular communications and sharing medical data.

Discussion

Principal Findings

The BEC was established through a formal collaboration among existing high-volume clinical eye centers in North India. There is limited literature on the formation of such collaborative processes, particularly in eyecare [17]. The BEC was founded using a standardized approach that included developing organizational structures; standardizing data collection systems [18]; establishing research protocols and guidelines; training personnel appropriately; and using advanced tools, techniques, and technology to enhance operational efficiency and knowledge advancement. The value of such a consortium lies in its diverse geographic locations and strong interinstitutional collaboration.

As a diverse country representing populations of varying demographics, India offers a rich pool for genetic analysis with the potential to deliver significant global impact [8]. The unique geographical spread of the BEC enables studies with globally generalizable data (excluding Africa) [8], leveraging the large patient numbers and high-quality big data collected through this collaboration of nonprofit eyecare organizations. This plays a significant role in advocacy and has the potential to influence government priorities in allocating funds for research and disease control, particularly in eyecare and specific conditions.

The collaboration has been facilitated through the use of digital platforms, which streamlined communication and enabled the BEC to maintain operations during the COVID-19 pandemic and subsequent lockdown [19]. Collaborative multicenter research aims to enhance patient care through improved data quality [20], driven by the commitment and engagement of clinical researchers dedicated to translational work.

Grand rounds and workshops have improved skill and knowledge levels, fostering a better understanding of research methodology. Once the consortium's bank account is established, pooled funds will enable us to promote these events on our website and open them to the broader public based on demand. This progressive approach has already enabled collaboration with organizations such as the Global Eye Genetics Consortium [21], facilitating access to resources such as guest speakers and subject experts from around the world—opening new avenues of thought and fostering network development.

The Scientific Committee is also actively developing advanced policies for authorship, data sharing, and research processes. Increasing in-person meetings and collaborative sessions would further enhance interdisciplinary collaboration among member organizations of the consortium. Member organizations already include scientists, geneticists, public health specialists, and microbiologists as part of their representation in subgroups, complementing clinicians. This diversity enables the consortium to explore new interdisciplinary studies, leveraging different perspectives.

To ensure proficiency in research methodologies and data management among all personnel, the Scientific Committee conducts regular workshops to enhance these skills. Plans are underway for a series of continuous online workshops and activities for ongoing skill development. Discussions are also ongoing to mandate that principal investigators undergo training and certification from selected institutions before their study proposals are approved by the Scientific Committee.

As a foundational activity, the data audit has proven especially beneficial for ensuring the quality and accuracy of data during collection, addressing persisting drawbacks even in retrospective studies [22,23]. Once the consortium establishes a joint bank account and begins sharing finances, it plans to hire a traveling manager. This manager will travel across organizations to ensure standardization in data collection practices, quality, storage, and consent procedures. This initiative will enhance the consortium's data collection methods, ensuring better standardization and consistent quality across all member organizations [24]. Currently, the analysis for consortium studies is conducted by a biostatistician from 1 of the participating centers, dedicating approximately 20% of their time to consortium studies, including those not led directly by their center. Similar to the traveling manager, there are plans to hire a dedicated biostatistician for the BEC in the long run.

Upon acceptance of the first publication under the BEC's auspices [10], editors emphasized that the paper's key strengths included its high-quality multicentric data and the inclusion of a large number of patients within a short time frame. Furthermore, the use of proforma-driven data recorded during consultations ensured a low patient exclusion rate (17/532, 3.2%) in this retrospective study, enhancing its value in the field and minimizing the need for techniques to address data "missingness" [25]. Currently, there are nearly 30 ongoing studies at various stages of the writing and submission process, with 6 already published [11-16] and 2 more accepted. While the consortium is currently in a nascent stage and its research impact is primarily measured through publications, in the medium to long term, as we become more influential in health policy and behavior change, we will broaden our evaluation criteria to include not only impact factors but also other relevant indicators. Furthermore, as we establish a mechanism to create a shared pool of resources, we aim to publish in higher impact factor open-access journals, many of which require publication fees. This initiative will enable us to monitor impact factors and citation counts as quality indicators for journal reach, prestige, and impact. Currently, all current members of the BEC have undergone standardization audits, and scaling up will inevitably introduce additional variables into consideration.

Although initial efforts have begun with retrospective "data-only" studies and a limited number of prospective studies, future endeavors involving extensive prospective studies and biological sample collection will increase research costs, necessitating groundwork in terms of protocols and monitoring activities. While there is encouragement to initiate large prospective studies and collect biological samples, the consortium requires an expansive and reliable framework to streamline public health and clinical studies before embarking on larger studies involving biological tissue collection.

As consortium research intensifies, strategies can be implemented to address time constraints faced by researchers and clinicians. These strategies may include incentivizing participation in research by allocating dedicated time to senior

faculty, as well as providing administrative support to ensure clinicians can focus solely on research activities. Additionally, the consortium's current community engagement is primarily through research endeavors, such as a study to assess the awareness, knowledge, and challenges faced by beneficiaries and nonbeneficiaries of Ayushman Bharat—Pradhan Mantri Jan Arogya Yojana, which has been accepted for publication in a renowned peer-reviewed journal. However, as we conduct more studies actively engaging with local communities, such as needs assessments and qualitative studies, we aim to gather evidence to strengthen the impact and relevance of our work. Therefore, more of these studies are being initiated within the BEC. An example of this is our Glaucoma Subgroup, which is studying awareness of glaucoma, and our Public Health Subgroup, which is investigating awareness of eye health among rural women. As we conduct more studies like these, we plan to utilize various platforms to disseminate our findings and use the evidence for advocacy purposes.

Moreover, in today's dynamic environment, with social media platforms frequently updating their privacy and encryption policies, the sharing of anonymized medical data raises significant concerns. However, we maintain strict monitoring of communications, ensuring that patient data are never discussed over social media. Despite this, given the evolving landscape of social media privacy policies and the introduction of the new Digital Personal Data Protection Act of 2023 [23], there is an urgent need for a more robust and secure data-sharing platform. The new act allows for the legitimate use of medical data when patients voluntarily enroll themselves [26]. However, because research is exempt from legitimate use under the act, updating patient consent forms to include data sharing for collaborative consortium research among member organizations becomes crucial to ensure compliance. In the medium to long term, the BEC can address the necessity for a secure data-sharing and communication platform. Working with relevant professionals, it can develop a digital infrastructure tailored to its specific requirements. Our aspiration is to establish a dedicated platform for medical and health research, ensuring encrypted communication and strict adherence to privacy regulations for sharing medical data. A member organization is currently testing such a platform at an individual level, and based on their feedback, we plan to integrate it into consortiumwide use. These resources are critical for maintaining data validity and quality in research, and for enhancing the impact of prospective studies.

The initial step toward securing sustainable funding for ongoing and future research projects involves establishing a formal data-sharing agreement and subsequently opening a joint bank account to facilitate shared financial management. This process has already begun and will enable the consortium to pursue collaborative applications for national and international research grants. Additionally, we plan to approach funders already associated with these organizations for service delivery. The programmatic sustainability of the consortium is currently ensured through regular meetings of its subgroups and other bodies, quarterly meetings, and established monitoring and motivating mechanisms. Financial sustainability will become crucial in the medium to long term once the consortium opens a joint bank account and establishes a Finance Committee. Therefore, establishing appropriate financial mechanisms, including processes for collective fund contributions, fundraising for grants, and their disbursement, will be a priority. Additionally, funding efforts will be bolstered by publishing a descriptive methodology paper to position the consortium in scientific forums.

Currently, the Heads of Institutions are working to finalize and sign a comprehensive legal and financial agreement. With the Indian Ministry of Law and Justice introducing an Act to govern and regulate health care data [26], it is imperative to expedite this process in accordance with the new regulations. We continuously update our practices in line with the latest Data Protection Act and its modifications. Some organizations are already conducting regular Good Clinical Practice training for all researchers. We plan to extend this training to all member organizations once we have the necessary resources. Until a uniform data-sharing agreement can be adopted, each research endeavor collects only anonymized data through proformas to facilitate ease of operation at the subgroup level. Each institution obtains separate approvals from its respective institutional review boards and ethics committees—a time-consuming process from start to finish [27]. Furthermore, the study lead must also apply for and obtain approval from the Scientific Committee, which evaluates the proposal's relevance as a multicentric study and the consortium's role within it. To streamline this process, we are working to credential Scientific Committee members as representatives of each member organization with institutional review boards. We also aim to include external members from the United Kingdom and the United States. This approach will allow principal investigators of consortium studies to receive uniform central-level approval and detailed feedback before proceeding with individual organization-level applications.

In the short to long term, adopting sound financial practices and implementing well-structured, transparent systems, coupled with significant publications such as those already secured, could attract global research grants. This approach would also enable the consortium to establish a financial reserve to support its activities and implement secure, encrypted data-sharing structures. The consortium can also focus on expanding its reach and impact on global health beyond its current genomic and anthropological focus. Given its diverse group of collaborators, including basic scientists, clinicians, public health researchers, and epidemiologists, the consortium is well-positioned for this expansion. Consortiumwide collaborations with existing partners at the International Centre for Eye Health, the London School of Hygiene and Tropical Medicine, the University of Wisconsin–Madison, the University of Iowa, and the University of Pittsburgh can also be planned and executed. These are the administrative objectives of the consortium.

The consortium also has future scientific objectives aligned with the global health research agenda [28,29], particularly focusing on priorities set by the World Health Organization and the International Agency for the Prevention of Blindness, such as effective cataract surgical coverage, refractive error, and myopia. Collaborative studies are already underway on these topics across various subgroups. Long-term goals include

advancing into advocacy and policy influence through high-quality, high-volume research.

Conclusions

Our consortium offers a distinctive opportunity for members to advance scientific knowledge across various domains of eyecare. The population diversity in North India, encompassing heterogeneity in anthropological and genomic origins, allows findings from our studies to be somewhat generalizable to European, Middle Eastern, and European American populations. The consortium holds significant global health implications, and the model outlined in this descriptive paper could serve as a blueprint for other health care organizations seeking to establish similar collaborations for research and knowledge sharing.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Variables and their coding for the data robustness analysis.
[DOCX File , 14 KB - ojphi_v16i1e53370_app1.docx]

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Abbreviations

BEC: Bodhya Eye Consortium
ICD: International Classification of Diseases
SWOT: strengths, weaknesses, opportunities, and threats

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Original Paper

The Association of Broadband Internet Use With Drug Overdose Mortality Rates in the United States: Cross-Sectional Analysis

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Abstract

Background: The availability and use of broadband internet play an increasingly important role in health care and public health.

Objective: This study examined the associations between broadband internet availability and use with drug overdose deaths in the United States.

Methods: We linked 2019 county-level drug overdose death data in restricted-access multiple causes of death files from the National Vital Statistics System at the US Centers for Disease Control and Prevention with the 2019 county-level broadband internet rollout data from the Federal Communications Commission and the 2019 county-level broadband usage data available from Microsoft's Airband Initiative. Cross-sectional analysis was performed with the fixed-effects regression method to assess the association of broadband internet availability and usage with opioid overdose deaths. Our model also controlled for county-level socioeconomic characteristics and county-level health policy variables.

Results: Overall, a 1% increase in broadband internet use was linked with a 1.2% increase in overall drug overdose deaths. No significant association was observed for broadband internet availability. Although similar positive associations were found for both male and female populations, the association varied across different age subgroups. The positive association on overall drug overdose deaths was the greatest among Hispanic and Non-Hispanic White populations.

Conclusions: Broadband internet use was positively associated with increased drug overdose deaths among the overall US population and some subpopulations, even after controlling for broadband availability, sociodemographic characteristics, unemployment, and median household income.

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KEYWORDS

opioids; broadband internet; mortality; public health; digital divide; access; availability; causal; association; correlation; overdose; drug abuse; addiction; substance abuse; demographic; United States; population

Introduction

Over 900,000 individuals have died from drug overdoses within the last 2 decades, posing a significant public health concern in the United States [1,2]. Opioids, either obtained illicitly or as a prescription, accounted for approximately 75% of the total drug overdose deaths in 2020 [1,2]. Recent numbers suggest an acceleration of both drug and opioid overdose deaths during the COVID-19 pandemic, with the United States experiencing the largest number of drug overdose deaths during this period (93,300 deaths) compared to that reported in any given year within the last 2 decades.

Internet access alongside digital literacy in general have been increasingly recognized as a "super" social determinant of health [3,4]. Access to broadband internet has been identified as a crucial public health issue (including its effect on the domain of access to credible information [5]) and a critical infrastructure for equitable access to health care, especially for underserved communities [6,7]. More specifically, the widening availability of broadband internet could potentially worsen the health inequalities in the United States, as it disproportionately impacts already marginalized groups such as racial/ethnic minorities, the older population, individuals with lower incomes, those with less education, and residents of rural areas [5]. According to the Federal Communications Commission (FCC), approximately 19 million individuals in the United States do not have access to a reliable broadband service, often referred to as reliable high-speed internet. This issue, termed the digital divide, primarily targets rural regions but also encompasses "segments of segregated urban areas that remain disconnected" [4]. Individuals with reduced income and less formal education are less inclined to possess a home broadband service or a mobile data plan subscription, necessitating their reliance on limited cell plan data or local public Wi-Fi hot spots [8,9].

Broadband internet access has been linked with disparities in various health outcomes, ranging from health information–seeking and health communication [10] to access to care during public health emergencies requiring remote care [11]. A recent US study demonstrated an association between lack of broadband coverage and adverse mental health outcomes [12]. In addition, access to broadband internet could affect drug and substance use through several channels. For instance, purchase of drugs via the internet is faster, anonymous, and less risky, which makes overall access to drugs easier; accordingly, the internet has been deemed a "pipeline for narcotics" [13]. Existing research indicates that in instances where drugs are easily accessible on the internet, there is a notable surge in the number of new and first-time users regardless of socioeconomic status [13]. Although, theoretically, increases in knowledge and information should lead to more optimal consumer choices, substantial networking opportunities may result in peers having a significant influence over health behaviors [14]. This raises the possibility that the marked growth in US drug abuse may have partially stemmed from the wider availability of illicit drugs on the internet [15].

The availability of telehealth through broadband internet is likely to reduce health disparities by connecting providers with individuals living in remote areas [6,7,16]. Telehealth brings specialized health care to communities where it was previously unavailable [17,18]. Thus, having access to and the ability to use broadband internet services can affect major public health outcomes such as drug overdose deaths.

Furthermore, access and usage data sets are critically important in building a full and accurate broadband internet map. Access data show current and future plans, while usage data help to understand how access translates into consumption. The aim of our study was to explore how broadband access and usage intersect with drug abuse by using access and usage data to elucidate the association of broadband internet with drug overdose mortality rates. In addition, given that in this time and age almost all counties have internet/mobile data plans in place, our study aimed to explore whether the emphasis should shift from broadband availability to actual usage, which is potentially the more relevant metric from a public health perspective.

Methods

Data Sources

Primary data for the study were obtained from three main sources: (1) 2019 county-level drug overdose death data from restricted-access multiple causes of death files available from the National Vital Statistics System (NVSS) at the US Centers for Disease Control and Prevention (CDC); (2) 2019 county-level broadband internet rollout data from the FCC; and (3) 2019 county-level broadband usage data available from Microsoft's Airband Initiative. In addition, county-level socioeconomic and demographic characteristics were gathered from the US Census Bureau and US Bureau of Labor Statistics.

All drug overdose deaths were measured per 10,000 persons per year by county. Following the CDC and NVSS guidelines, we used the Tenth Revision of the *International Classification of Diseases Clinical Modification* codes X40-X44 (unintentional), X60-X64 (intentional), X85 (homicide), and Y10-Y14 (undetermined) to identify all drug overdose deaths.

Ethical Considerations

As this was a secondary data analysis, there was no requirement of approval from an institutional review board.

Statistical Analysis

Data analysis was performed using descriptive analysis and a cross-sectional regression analysis. In addition to examining the effects of broadband availability and usage on drug overdose deaths, we investigated how these effects vary based on different subpopulations and location characteristics.

The one-way fixed-effects regression equation used for this analysis was:

$$Y_j = \alpha_0 + \partial BB_j + \beta X_j + \delta_s + \varepsilon_s$$

where Y_j is the outcome variable for county j. The BB_j vector indicates the broadband internet availability and usage in a given county during 2019. Internet availability was measured as the percentage of people per county with access to fixed terrestrial broadband at minimum speeds of 25 Mbps/3 Mbps. Internet

usage was measured as the percentage of people per county that use the internet at broadband speeds based on the methodology provided by Microsoft.

Microsoft estimates broadband usage by combining data from multiple Microsoft services. These data are combined with the number of households per county and zip code. While Microsoft suppresses any location with less than 20 devices in zip code–level data, this is not an issue for the county-level data used in our study. Every time a device receives an update or connects to a Microsoft service, Microsoft estimates the throughput speed of a machine. To calculate the broadband speed, they use the size of the package sent to the computer and the total time of the download. They determine the zip code–level location data via the reverse IP. Therefore, they can count the number of devices that have connected to the internet at broadband speed for each zip code based on the FCC's definition of broadband, which is 25 Mbps per download. The zip code–level data were then aggregated to the county level. Microsoft's data might be more representative in regions where its products are more widely used and less representative in regions where its products have lower penetration rates. Since Microsoft's data primarily come from devices running Windows operating systems and services such as Bing, Edge browser, and Xbox, this might skew the data toward certain types of devices and services and may not capture the full spectrum of internet-connected devices or platforms.

The coefficient on these variables (∂) captures the direct effect of broadband availability and usage on the outcome. X_j is a vector of observed socioeconomic and demographic characteristics of county j and ε_s is the error term. State fixed effects eliminate the omitted variable bias that may result from the time-invariant differences between states. The analysis was performed using robust Huber-White standard errors to capture arbitrary within-county heteroscedasticity.

Results

The descriptive statistics showed that 1.71 drug overdose deaths occurred per 10,000 county population in 2019 in the United States. Although approximately 76.6% of people in a given county had access to broadband internet in 2019, only approximately 28% of people were using the internet at broadband speeds (Table 1).

Table 1. Summary statistics.

Variable	Counties, n	Mean (SD)
Outcome variables		
Drug overdose deaths[a]	3104	1.71 (1.48)
Internet availability (% of county population with access to broadband internet)	3104	76.627 (23.88)
Internet usage (% of county population using internet at broadband speeds)	3104	28.133 (19.027)
Kidney deaths[a]	3103	2.179 (1.721)
Non-Hispanic White deaths[a]	3104	1.917 (1.739)
Non-Hispanic Black deaths[a]	3093	2.718 (45.691)
Non-Hispanic other deaths[a]	3104	8.354 (35.53)
Hispanic deaths[a]	3104	0.844 (3.17)
Deaths for those with less than high school education[a]	3104	2.889 (4.101)
Deaths for those with some college education[a]	3104	4.173 (4.033)
Deaths for those with college education or higher[a]	3103	0.486 (1.446)
Male deaths[a]	3104	2.165 (2.138)
Female deaths[a]	3104	1.264 (1.446)
Deaths among those aged ≤19 years[a]	3103	0.1 (0.447)
Deaths among those aged 20-29 years[a]	3103	2.205 (3.554)
Deaths among those aged 30-39 years[a]	3104	3.796 (5.117)
Deaths among those age 40-49 years[a]	3104	3.244 (4.866)
Deaths among those aged 50-64 years[a]	3104	2.39 (3.048)
Deaths among those aged ≥65 years[a]	3104	3.108 (12.245)
Control variables		
Percent county poverty	3103	14.429 (5.772)
Percent population with no health insurance	3103	11.903 (5.108)
Net migration (the number of immigrants minus the number of emigrants in the county)	3104	192.543 (2937.949)
Percent of county population with a college degree or higher	3104	22.018 (9.566)
Median household income (US $)	3103	55,707.34 (14,456.62)
Percent of county population that is unemployed	3103	3.977 (1.41)
Share of population aged 20-34 years	3104	0.18 (0.037)
Share of population aged 35-49 years	3104	0.175 (0.019)
Share of population aged 50-64 years	3104	0.203 (0.024)
Share of population aged ≥65 years	3104	0.198 (0.047)
Share of the female population	3104	0.499 (0.022)
Share of the Black population	3104	0.094 (0.144)
Share of the Hispanic population	3104	0.097 (0.138)
Share of the Asian population	3104	0.015 (0.028)
Counties with population of ≥50,000 (dummy variable)	3104	0.319 (0.466)
Metro counties (dummy variable)	3104	0.374 (0.484)
Adjacent to an urban area (dummy variable)	3104	0.424 (0.494)
Rural county (dummy variable)	3104	0.201 (0.401)

[a]Measured per 10,000 of the total or specific subpopulation indicated.

The regression analysis results in Table 2 show that a 1% increase in broadband internet usage is significantly associated with a 1.2% increase in overall drug overdose deaths among the general population.

Table 2. Associations between broadband internet usage and drug overdose deaths.[a]

Variables	Drug overdose (full sample)	Drug overdose in counties with a population over 50,000	Drug overdose in counties with a population less than 50,000	Kidney disease–related deaths (full sample)
Internet usage, coefficient (robust SE)	0.012 (0.002)[b]	0.008 (0.004)[c]	0.008 (0.003)[d]	0.004 (0.003)[e]
Internet availability	Yes[f]	Yes	Yes	Yes
Socioeconomic variables	Yes	Yes	Yes	Yes
Demographic variables	Yes	Yes	Yes	Yes
State controls	Yes	Yes	Yes	Yes
Robust standard errors	Yes	Yes	Yes	Yes
Number of observations	3103	990	2113	3103
Adjusted R^2	0.296	0.456	0.232	0.214

[a]The regression analysis includes the set of full control variables shown in Table 1.

[b]$P<.001$.

[c]$P=.05$.

[d]$P=.007$.

[e]$P=.18$.

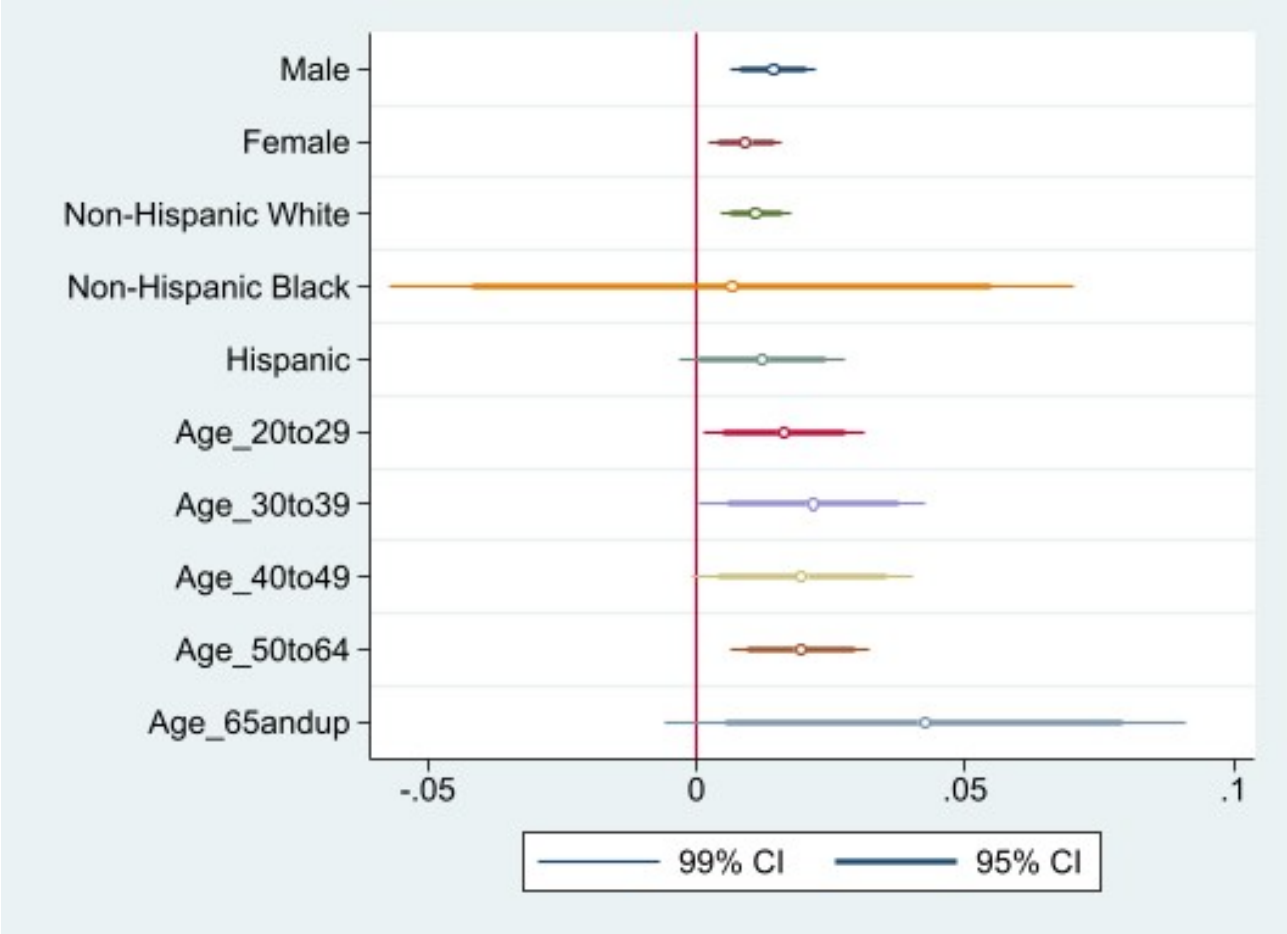
[f]Indicates inclusion of the variable as a control in the regression model; coefficients for subpopulations and the full set of controls are provided in Multimedia Appendix 1.

Splitting the sample into counties with a population more and less than 50,000 showed that the association result was primarily driven by the relationship between these variables in the less populated counties.

This association could result from the fact that the internet encourages greater consumption of drugs by making illegal drugs more accessible. Internet purchasing is more convenient and less risky because of anonymity. Furthermore, online drug sales could also be less risky for suppliers than offline sales. Thus, it is reasonable to expect broadband internet usage to improve market liquidity and spur both the demand and supply of illicit drugs. If this is the case, we would expect no significant association between broadband internet and mortality rates from chronic conditions. To test our assumption, we considered mortality rates associated with kidney disease, which is a chronic condition and should not be associated with internet availability. There was no association between internet availability/usage rates and kidney disease–related mortality rates (Table 2).

Further analysis revealed that different subpopulations are disproportionately affected by the associations between internet usage and drug-related deaths (see Figure 1). More specifically, Figure 1 shows that a 1% increase in internet usage is associated with a 1.1% increase in drug overdose deaths among the non-Hispanic White population, a 1.2% increase among the Hispanic population, a 1.4% increase among the male population, and a 1% increase among the female population. There appears to be no statistically significant association for the Non-Hispanic Black population, although the coefficient's SE is wide for this population because of the small sample size. Additionally, a 1% increase in broadband internet usage was significantly associated with a 1.7% increase in drug overdose deaths among those aged 20-29 years, a 2.2% increase among those aged 30-39 years, a 2% increase among those aged 40-49 years, a 1.9% increase among those aged 50-64 years, and a 4.3% increase among those 65 years and older compared with those 19 years and younger.

Figure 1. Associations between broadband internet usage and drug overdose deaths for different subpopulations. The figure presents the estimates of regression analysis where each variable is the dependent variable and the estimate shown is the coefficient of internet use as a dummy variable. Each regression includes the full controls shown in Table 1.



Discussion

Principal Findings

The findings of this study show that increased usage of broadband internet is positively and significantly associated with increased drug overdose deaths in the general US population as well as in several subpopulation categories, with the largest increase observed among the population 65 years and older compared with those 19 years and younger.

Our approach is novel in carefully distinguishing two different existing definitions of "broadband internet access" that are critical for studying its equity and potential impact on individual and community health outcomes: (1) its physical availability to individuals and communities (broadband availability) and (2) its adoption and effective use by those individuals and communities (broadband usage) [7,19,20]. Although no previous studies have examined the link between broadband internet usage and drug overdose deaths to our knowledge, there have been a few studies examining the link between drug abuse and the internet using the rollout of Craigslist [15], broadband internet subscription rates and opioid prescribing via telemedicine during COVID-19 [21], broadband internet and youth mental health [22], and broadband internet access and treatment admissions to substance use programs [23].

Specifically, one of the earliest studies examining the link between broadband internet access and drug abuse found that every 10% increase in the number of residential high-speed internet lines per capita at the state level was associated with a 1% increase in admissions to treatment programs for substance abuse [23]. Another study, using the phased rollout of Craigslist, a major web-based platform, found that Craigslist's entry was associated with a 14.9% increase in drug abuse treatment admissions, a 5.7% increase in drug abuse violations, and a 6.0% increase in drug overdose deaths in the United States [15]. Although different in magnitude, these previous findings are in line with the results of this study, especially in terms of the direction of the effects of the internet on the health outcomes examined. Other researchers examining the link between broadband internet and youth mental health found similar directional effects of internet access. In particular, access to high-speed internet resulted in an increase in diagnoses of depression, anxiety, drug abuse, and personality disorders for the younger cohorts of both males and females but not for the older cohort [22]. In contrast, Oyler et al [21] found that broadband subscription rates (low and high) did not affect opioid prescriptions dispensed in Kentucky counties during the time period of Executive Order 2020-243 issued by the state's governor on March 22, 2020, which limited nonurgent medical procedures in Kentucky to conserve personal protective equipment and medical supplies for patients with COVID-19.

These findings suggest that access to broadband internet may not affect legal prescriptions of opioids. Despite the heterogeneity, if taken together with previous research, our findings suggest that broadband internet usage may be contributing to the drug epidemic in the United States.

Strengths and Limitations

We should acknowledge that our measure of broadband internet availability does not include internet access via mobile phones. Unfortunately, these data are currently not available; thus, our estimation of the effect of broadband availability would be an underestimation. To obtain information on internet access via mobile use, we downloaded the American Community Survey (ACS) census data for 2021 and 2022, which were the two most recent years (along with 2016) with data available on two relevant questions. The first question was whether or not someone in the household uses or connects to the internet, regardless of whether or not they pay for the service. The second was whether or not anyone in the household has a data plan for a smartphone or other mobile device. Since the ACS does not provide the county Federal Information Processing Standard (FIPS) code for all observations, we could only identify the county FIPS codes for a subset of the respondents and only data for 2022 included FIPS codes for rural counties. Using the Economic Research Service–US Department of Agriculture rural-urban continuum codes [24] to classify rural counties, we found that 94.30% (n=21,733) of households in rural counties and 95.37% (n=1,897,961) in metro and urban counties had a household member with a data plan. Using the same sample and definition of rural, we also found that 97.22% (n=22,657) of households in rural counties and 96.71% (n=1,999,196) of households in metro and urban counties had a household member that uses or connects to the internet. Thus, the use of data plans and internet connection in rural areas is very similar to those in metro and urban areas. Another limitation is that we do not have data for a longitudinal study that could provide opportunities for examining causal relationships.

These limitations notwithstanding, the findings of this study underscore the importance of curbing illegal drug sales via web-based pharmacies and social networks. In addition, it is important for the Food and Drug Administration to monitor the shipping of medications to the United States from other countries. The results of this study emphasize the importance of tracking prescription drug use and sales on web-based platforms to better understand the amount and the types of transactions of prescription drugs taking place on these platforms and the role these platforms play in prescription drug abuse in the United States.

Finally, we have included controls in the regression model that mediate the association between internet connectivity and overdose rates, such as the percentage of uninsured population in a county, which, as expected, was negatively associated with overdose rates although not significantly. Even though determining the mediating effects of such variables was not within the scope of this study, research on the mediating effects of insurance availability, distance from medical resources, and other factors may be an important area for future research.

Conclusions

Broadband internet usage is positively associated with increased drug overdose deaths among the overall US population and some subpopulations, even after controlling for broadband availability, sociodemographic characteristics, unemployment, and median household income. These findings merit further investigation and can assist in policy shaping and thoughtful resource allocation to susceptible populations, especially in areas with recently improved broadband internet access.

Authors' Contributions

GK and VZH had full access to all the data in the study. These authors take full responsibility for the accuracy and integrity of the data and the analysis. IK and KT contributed substantially in writing the manuscript and interpreting the findings. All authors contributed to study concept and design; acquisition, analysis, or interpretation of data; and drafting of the manuscript. IK and KT critically reviewed the manuscript for important intellectual content. GK and VZH performed the statistical analysis.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Table S1: Associations between broadband internet usage and drug and overdose deaths; Table S2: Associations between broadband internet usage and drug and overdose deaths with coefficients for the full set of controls; Table S3: Associations between broadband internet usage and drug overdose deaths for different subpopulations with coefficients for the full set of controls.
[DOCX File , 34 KB - ojphi_v16i1e52686_app1.docx]

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Abbreviations

ACS: American Community Survey
CDC: Centers for Disease Control and Prevention
FCC: Federal Communications Commission
FIPS: Federal Information Processing Standard

NVSS: National Vital Statistics System

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Original Paper

Making Metadata Machine-Readable as the First Step to Providing Findable, Accessible, Interoperable, and Reusable Population Health Data: Framework Development and Implementation Study

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Abstract

Background: Metadata describe and provide context for other data, playing a pivotal role in enabling findability, accessibility, interoperability, and reusability (FAIR) data principles. By providing comprehensive and machine-readable descriptions of digital resources, metadata empower both machines and human users to seamlessly discover, access, integrate, and reuse data or content across diverse platforms and applications. However, the limited accessibility and machine-interpretability of existing metadata for population health data hinder effective data discovery and reuse.

Objective: To address these challenges, we propose a comprehensive framework using standardized formats, vocabularies, and protocols to render population health data machine-readable, significantly enhancing their FAIRness and enabling seamless discovery, access, and integration across diverse platforms and research applications.

Methods: The framework implements a 3-stage approach. The first stage is Data Documentation Initiative (DDI) integration, which involves leveraging the DDI Codebook metadata and documentation of detailed information for data and associated assets, while ensuring transparency and comprehensiveness. The second stage is Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) standardization. In this stage, the data are harmonized and standardized into the OMOP CDM, facilitating unified analysis across heterogeneous data sets. The third stage involves the integration of Schema.org and JavaScript Object Notation for Linked Data (JSON-LD), in which machine-readable metadata are generated using Schema.org entities and embedded within the data using JSON-LD, boosting discoverability and comprehension for both machines and human users. We demonstrated the implementation of these 3 stages using the Integrated Disease Surveillance and Response (IDSR) data from Malawi and Kenya.

Results: The implementation of our framework significantly enhanced the FAIRness of population health data, resulting in improved discoverability through seamless integration with platforms such as Google Dataset Search. The adoption of standardized formats and protocols streamlined data accessibility and integration across various research environments, fostering collaboration and knowledge sharing. Additionally, the use of machine-interpretable metadata empowered researchers to efficiently reuse data for targeted analyses and insights, thereby maximizing the overall value of population health resources. The JSON-LD codes are accessible via a GitHub repository and the HTML code integrated with JSON-LD is available on the Implementation Network for Sharing Population Information from Research Entities website.

Conclusions: The adoption of machine-readable metadata standards is essential for ensuring the FAIRness of population health data. By embracing these standards, organizations can enhance diverse resource visibility, accessibility, and utility, leading to a broader impact, particularly in low- and middle-income countries. Machine-readable metadata can accelerate research, improve health care decision-making, and ultimately promote better health outcomes for populations worldwide.

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KEYWORDS

FAIR data principles; metadata; machine-readable metadata; DDI; Data Documentation Initiative; standardization; JSON-LD; JavaScript Object Notation for Linked Data; OMOP CDM; Observational Medical Outcomes Partnership Common Data Model; data science; data models

Introduction

Population health data play a crucial role in understanding the dynamics of public health and informing evidence-based policies and interventions [1]. In low- and middle-income countries (LMICs), two common approaches for systematically and continuously monitoring health indicators in the population over time are disease surveillance systems and health and demographic surveillance systems (HDSSs). Surveillance systems are designed to detect and respond to outbreaks of infectious diseases, whereas HDSSs are longitudinal systems that collect health and demographic data for a defined population [2,3].

Despite the availability of valuable population health data from these systems, there remains a significant challenge in effectively sharing this information across research entities. Finding data and knowledge or information about population health requires accurate and comprehensive documentation of metadata, often referred to as “data about data”; however, the best way to achieve this remains unclear [4]. Disease surveillance metadata encompass crucial details, including the diseases under surveillance, geographical areas covered, and variables measured, each with defined formats and explanations. For example, variables may include disease incidence rates, demographic characteristics, and health care utilization. Additionally, a data dictionary provides comprehensive definitions and formats for each variable, aiding in the interpretation and use of surveillance data [5].

Metadata are a critical component of achieving the findable, accessible, interoperable, and reusable (FAIR) data principles [6]. The integration of these principles into data science aligns with the original vision of Wilkinson et al [6], which goes beyond the traditional reuse of data but also other digital research components such as inputs, outputs, algorithms, tools, and workflows that generate data [7]. Realizing this vision requires the use of not only one but several standards, depending on the use case [6]. The FAIRness of a data collection process can be ensured by using metadata standards such as the Data Documentation Initiative (DDI), Dublin Core, and Common Data Model (CDM) for representing exposures and outcomes, along with a domain-specific vocabulary for annotating these standards [8,9].

The DDI Codebook and DDI Lifecycle serve as international standards for systematically detailing data generated through surveys and observational methods, ensuring consistent documentation of content, structure, and provenance. This enhances the accessibility, discovery, and preservation of data and consistency in representation of the data by users [10]. Notable portals such as INDEPTH Data Repository (iSHARE), SAPRIN Data, and the African Population Health Research Center’s microdata portal employ the DDI for public data dissemination [11-13].

The Observational Medical Outcomes Partnership (OMOP) CDM addresses the challenge of integrating and analyzing diverse health care data by providing a standardized information model. This model acts as a universal language, enabling seamless integration and consistent analysis of data from various home and clinic encounters [14,15].

The core of the OMOP CDM lies in its well-defined structure comprising 39 tables categorized into relevant health care domains [16]. These domains include standardized vocabularies, person-centric data (eg, demographics and diagnoses), and standardized health system data (eg, procedures and medications). This organization ensures consistency throughout the data and facilitates downstream analyses [15].

Furthermore, the standardized structure allows efficient data preparation through extraction, transformation, and loading (ETL) processes for analysis with various tools. This facilitates uniform analysis techniques across studies. Additionally, a standardized vocabulary enables domain-specific labeling of interventions and outcomes, which is crucial for machine learning and metadata documentation within the CDM framework [17].

The OMOP CDM prioritizes ethical considerations by sharing deidentified and aggregated data, enabling network-wide analysis without sharing patient-level information. This

promotes transparency, reduces bias, and aligns with data protection regulations while enabling autonomous data sharing and safeguarding individual privacy with data remaining secure at the source [18].

While data standardization and harmonization are essential for FAIR compliance, they are not sufficient on their own [6]. Another step involves rendering metadata machine-readable and more findable online, aligning with the objectives of Schema.org, a collaborative project among major search engines such as Google. Schema.org was established to create a schema or shared vocabulary dedicated to developing and establishing metadata standards that enhance the discoverability and indexing of online content, including assets in population health and clinical data [19]. Although Schema.org has applicability across a vast range of domains, its use in population health data remains underexplored. Nevertheless, harnessing Schema.org offers the potential to significantly streamline data discovery efforts, as evidenced by its adoption by over 10 million websites [19].

For this reason, we are considering using JavaScript Object Notation for Linked Data (JSON-LD), a lightweight linked data format capable of marking up internet content with metadata. JSON-LD initially used Schema.org entities such as Action, BioChemEntity, CreativeWork, Event, MedicalEntity, Organization, Person, and Place; however, its capabilities extend beyond these entities. JSON-LD can create complex machine-readable documents that can seamlessly transition between different sets of metadata objects. In our use case and others, JSON-LD demonstrated the potential to FAIRify the arc of data science by enabling seamless interoperability and data sharing across diverse systems and platforms [20].

However, the current practice of FAIR implementation in population health faces substantial barriers. Obstacles include the limited availability of mature FAIR technology, the proliferation of diverse digital tools, and data often being locked within local formats or proprietary standards imposed by electronic health record vendors. Moreover, these challenges are compounded by a prevailing siloed data mindset among the key stakeholders collecting population health data [21].

We here propose an approach to bridge the gap between FAIR principles and practice in population health data by incorporating machine-readable metadata for data and nondata digital assets, including platforms, into the population health data set. We use the Integrated Disease Surveillance and Response (IDSR) data as a case study to demonstrate the proposed processes. Despite its critical role in public health, the current structure of IDSR data presents a challenge in adhering to FAIR principles. Key information regarding data collection methodologies, access restrictions, and updates often lacks proper documentation or resides scattered across diverse formats. This fragmentation severely hinders the findability, accessibility, and interoperability of the data, posing substantial obstacles to its effective use and compliance with FAIR standards. To address this, we leverage established standards such as the DDI and OMOP CDM and explore the potential of Schema.org entities alongside other standards using JSON-LD to extend and adapt these principles. This strategic combination of machine-readable metadata and standards such as Schema.org and others coupled with JSON-LD is a crucial step toward achieving *comprehensive* FAIR compliance in population health data.

The proposed approach integrates the collaborative frameworks of the GO-FAIR and WorldFAIR initiatives to promote interdisciplinary collaboration, culture change, and technology integration for the effective implementation of FAIR principles [22,23]. This effort addresses the long-standing challenge of restricted data discoverability, which hinders the effective use, reuse, integration, and knowledge integration of data [24]. Data stewardship plans mandating the data, along with all assets generated from public funds, should be publicly accessible [25]. Good data stewardship practices, particularly those adhering to FAIR principles, significantly enhance data discoverability and facilitate their improved reuse. Universal access to health research data, regardless of location or resource limitations, is crucial for advancing research and supports the broader goal of promoting healthy lives and well-being for all at all ages, as outlined in Sustainable Development Goal (SDG) 3, for improving global health and achieving SDGs [26,27].

Methods

Framework

We propose a step-by-step guide to making metadata FAIR using the IDSR database, including data collected in population settings and HDSS sites in Africa, as a demonstration of our use case. Our methodology is built upon a flexible, multilevel, domain-agnostic FAIRification framework, providing practical guidance to improve the FAIRness for both existing and future data sets. This framework encompasses 3 stages: (1) integration of DDI metadata, (2) implementation of the OMOP CDM, and (3) leveraging of Schema.org to refine the metadata structure and accessibility [28]. We use the IDSR data as a case study, which is recommended by the World Health Organization (WHO) but may be implemented differently from one country to another.

To effectively implement the DDI framework for population health data, we first selected the National Data Archive (NADA) online catalog. This metadata repository adheres to the DDI 2 Codebook and Dublin Core XML metadata standards [29]. NADA serves as a comprehensive platform for searching, comparing, applying for access to, and downloading metadata, data sets, questionnaires, and reports. NADA plays a pivotal role in ensuring the accessibility, discoverability, reusability, and collaboration of population health data. This is achieved by configuring the open-source web-based data cataloging application according to the guidelines provided in the NADA documentation [30].

Nesstar Publisher is used to create the DDI Codebook, a structured and descriptive document that captures essential metadata elements, which integrates the DDI framework into the IDSR data set [31]. With the help of the International Household Survey Network metadata template and the step-by-step guide, we describe the attributes of the IDSR data in the codebook, providing a rich and informative metadata record, including document description, study description, data file description, variable description, and additional materials

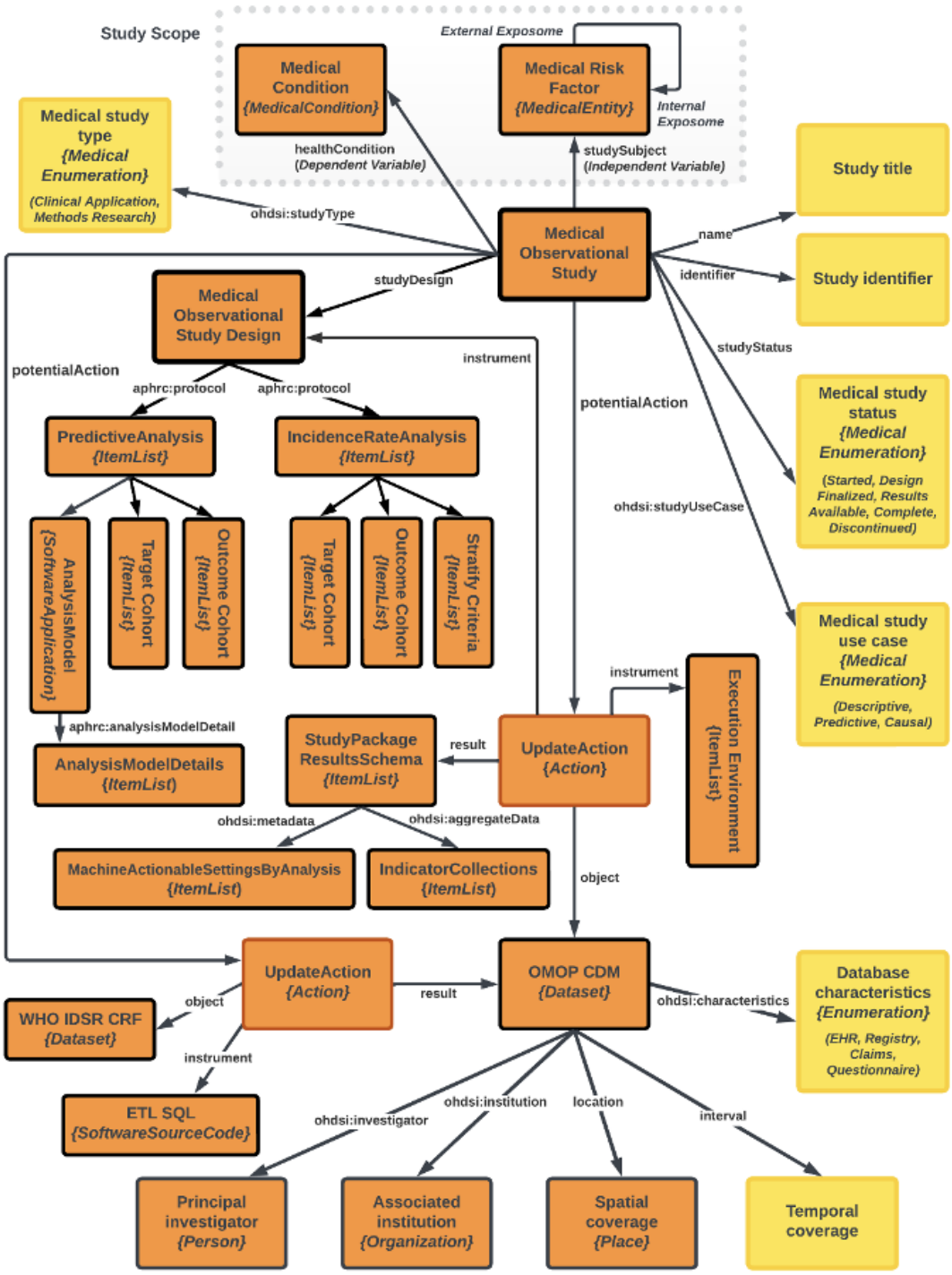
[32,33]. More advanced versions of the DDI, such as the DDI Lifecycle, have the potential to extend this integration to longitudinal studies such as the HDSS and other cohort studies, accommodating distinct waves or rounds of data collection [34,35].

The Implementation Network for Sharing Population Information from Research Entities (INSPIRE) developed ETL programs to upload the source data and metadata into the OMOP CDM, harmonizing and standardizing the data for unified data analysis in research using open-source Observational Health Data Sciences and Informatics (OHDSI) tools, which extend beyond their conventional use in clinical data [36,37].

This framework builds on the methods introduced by the European Health Data & Evidence Network [38] to grow the description of the IDSR data and metadata as a use case within the OMOP CDM. The process of FAIRification begins by identifying various digital resources present within the OHDSI artifacts, including *protocols*, *databases*, *study results*, *controlled vocabularies*, *software libraries*, and any other relevant digital assets. The metadata are described using Schema.org, expressed in JSON-LD format.

The standard CDM has the structure shown in Figure 1. The yellow boxes are literals that describe elements of the Schema.org MedicalObservationalStudy category, including the title, identifier, database, study status, and type. The orange boxes describe a set of classes or concepts that are contained in the data set. These classes use standard vocabulary concepts that describe variables in the study, including the risk factors and exposures (schema: MedicalEntity) and the conditions reported (schema: MedicalCondition) in connection with them. The left of the figure shows the analyses carried out on the data. The lower part of the model outlines the initial step of generating the OMOP CDM instance through an action that uses the ETL process leveraging the Pentaho platform and SQL to integrate and process data from the IDSR source data set or synthetic data.

Figure 1. Structure of the Implementation Network for Sharing Population Information from Research Entities (INSPIRE) model. aphrc: African Population Health Research Center; CRF: cloud raster format; EHR electronic health record; ETL: extraction, transform, load; IDSR: Integrated Disease Surveillance and Response; ohdsi: Observational Health Data Sciences and Informatics; OMOP CDM: Observational Medical Outcomes Partnership Common Data Model; WHO: World Health Organization.



The validity of the generated JSON-LD files can be verified using the Schema.org validator, a user-friendly tool capable of validating JSON-LD code. Validation can be done by either submitting a URL that points to the JSON-LD file or by directly pasting the JSON-LD code into the tool. The JSON-LD is then embedded within the HTML code, enabling search engines such as Google [39] to effectively use these structured data for enhanced data discovery and comprehension purposes.

Ethical Considerations

This research centers on implementing the FAIR principles. As there was no involvement of human subjects in our research, ethical approval from a local ethics committee is not applicable.

Results

DDI Codebook

The DDI codebook presented through the NADA repository provides a comprehensive and structured documentation framework for the IDSR source data. This resource is essential for researchers seeking a comprehensive understanding of the data set. For the complete IDSR codebook, please refer to Multimedia Appendix 1. The codebook is logically organized into four main sections, as outlined in Table 1.

Table 1. Catalog sections of the Data Documentation Initiative (DDI) codebook for Integrated Disease Surveillance and Response (IDSR) source data.

Section	Description
Study description	The Study section of the DDI codebook provides a comprehensive overview of the IDSR study, including its title, purpose, methodology, coverage, producers and sponsors, disclaimer and copyright, and contact details.
Documentation	This section of the DDI codebook includes the World Health Organization IDSR questionnaire for Malawi, Kenya, and Uganda, as well as other relevant documentation for the IDSR study, such as the study protocol.
Data description	Provides a detailed description of the IDSR data set, including the data files from Malawi, Kenya, and Uganda. The codebook provides detailed descriptions of all variables in the data set, including their names, labels, definitions, and coding schemes.
Microdata	This section provides information about the IDSR source data, including the number of variables, their corresponding format, and a description of each variable. The raw microdata are not currently shared, but have been ETLed[a] into the OMOP CDM[b] and the results are accessible through ATLAS [40].

[a]ETLed: extracted, transformed, and loaded.

[b]OMOP CDM: Observational Medical Outcomes Partnership Common Data Model.

The detailed description of the IDSR study offers a deep understanding of the data set, ensuring clarity for researchers. Accessible questionnaires further enrich the resource, providing invaluable insights into the data collection process.

The user interface is intuitively designed, offering seamless navigation and search capabilities. Researchers can effortlessly locate codebooks through keyword, title, or author searches. The availability of multiple download formats, including XML, PDF, and HTML, enhances accessibility.

A notable feature is that the support for the repository extends its accessibility through multilingual metadata support, accommodating researchers from diverse linguistic backgrounds. This inclusivity further bolsters the codebook's utility and accessibility.

Additionally, the codebook maintains a detailed history of versions and updates made to the data set. This feature ensures transparency and aids researchers in understanding potential impacts on their analyses.

JSON-LD Representation

JSON-LD was used to create a structured representation of the IDSR data. This format leverages the Schema.org vocabulary, a common language for describing things on the internet. Specifically, we used properties from the MedicalObservationalStudy schema to capture essential information about the public health study, such as the study design (eg, case series, cohort, observational, cross-sectional, longitudinal, or registry). Additionally, properties such as schema.org/healthCondition, schema.org/studyLocation, schema.org/studySubject, and schema.org/guideline are used to describe patient population characteristics (eg, inclusion criteria, age range), exposure or outcome measures of interest, and relevant health conditions or guidelines. Furthermore, this approach aligns with the efforts of OHDSI, which has adopted Schema.org as a FAIRifying standard and extended its usage through OHDSI extension.

This structured representation benefits both human users and machine processing. For public health users familiar with Schema.org, the data are easier to understand and interpret. Additionally, the use of a common vocabulary facilitates data exchange and integration with other systems that leverage Schema.org. Figure 2 showcases a snippet of the JSON-LD code, illustrating how specific data elements are mapped to Schema.org properties. Table 2 provides a more detailed tabular view of the IDSR JSON-LD class structure, including corresponding properties and their values.

Figure 2. Syntax example: MedicalObservationalStudy.

Table 2. Javascript Object Notation–Linked Data (JSON-LD) class description.

Class	Description
MedicalObservationalStudy	This represents the core IDSR[a] study being described. It includes the Study Title, Identifier, Status, and Use Case.
MedicalRiskFactor	Describes both internal and external exposomes (ie, the exposure of individuals in their environment).
DatabaseCharacteristics	This class describes the IDSR data set, which is implemented using the OMOP CDM[b] v5.4.4. The IDSR data set is a federated system that includes data from Malawi, Kenya, and Uganda. The data set is stored in a relational database with the following tables: Person, Condition_Occurrence, Observation, Drug_Exposure, Procedure_Occurrence, and Measurement.
MedicalCondition	This class describes the medical conditions in the IDSR data, including their descriptions and OMOP CDM concept IDs.
MedicalObservationalStudyDesign	Provides detailed information on the study's design, including types of analyses (eg, predictive analysis, incident rate analysis).
UpdateAction	UpdateActions describe the workflow in the MedicalObservationStudy beginning with an action that takes the source data as input (object) and produces an OMOP CDM instance as output (result) using an ETL[c] SQL as an instrument. A second UpdateAction takes the OMOP CDM as an object and populates the OMOP CDM Results Schema as a result using both the MedicalObservationalStudyDesign and its execution environment as instruments.

[a]ISDR: Integrated Disease Surveillance and Response.

[b]OMOP CM: Observational Medical Outcomes Partnership Common Data Model.

[c]ETL: extraction, transformation, and loading.

Our structured representation methodology makes the IDSR data set easily discoverable through platforms such as Google Dataset Search. The JSON-LD codes are available on the GitHub repository [41]. Additionally, the HTML code, embedded with JSON-LD, can be found on the INSPIRE website [42]. This open-source approach promotes transparency, reproducibility, and further development of our work.

Discussion

Prospects and Challenges

The integration of the OMOP CDM, DDI, and Schema.org with JSON-LD provides access to the metadata within the IDSR framework. This led to substantial improvements in the FAIRness, standardization, interoperability, and analytical capabilities of the IDSR data, reinforcing the critical role of machine readability in this domain. Notably, the efficient sharing of vital metadata enables seamless data integration, collaborative research, and advanced analysis across diverse contexts, which

is essential for improving public health outcomes. The model may also be used to promote the discoverability, accessibility, and reusability of observational research. One of the main benefits of this integration effort is that IDSR data can become more visible and accessible on the search engine results pages, which can increase the click-through rate [41]. Moreover, sharing nondata research objects such as analytical workflows and code can significantly enrich the research ecosystem by enabling others to replicate, validate, and extend existing findings, fostering transparency and reproducibility.

However, the adoption of Schema.org with JSON-LD in the context of population health data presents certain challenges. Specifically, OHDSI vocabulary predominantly consists of medical terms, lacking comprehensive coverage of population health–related concepts such as HDSSs and IDSRs. Standard vocabularies such as Systematized Nomenclature of Medicine–Clinical Terms (SNOMED-CT) and Logical Observation Identifiers Names and Codes (LOINC) often miss tests and questionnaires common in LMICs, which is particularly evident in capturing stages and public health–clinical interactions for diseases like AIDS. Terminologies such as those of the Columbia International eHealth Laboratory, already integrated into OHDSI, offer significant potential as independent standard vocabularies to address these gaps [43].

To effectively address the specific gaps identified within the MedicalObservationalStudy model for African contexts, it is crucial to focus on enhancing vocabularies tailored to the region. This entails prioritizing risk factors and exposures currently inadequately captured by existing OHDSI standards. Particularly, OHDSI lacks vocabularies encompassing physical/chemical and social determinants of health as well as mental health factors. Our participation in an OHDSI Working Group directly addresses these deficiencies by examining the relationships between diverse exposure histories (eg, climate variations, pharmaceutical accessibility, and health care availability for vulnerable populations such as pregnant women) and the medical conditions presented by study participants.

Importantly, technical expertise is necessary to optimize web pages for search engine optimization, ensuring effective implementation of Schema.org with JSON-LD. This highlights the importance of community support in developing and refining the necessary resources and expertise to overcome these challenges and maximize the benefits of adopting Schema.org with JSON-LD for population health data in Africa.

While the DDI codebook is a valuable tool for metadata documentation, it may not be as effective as the DDI Lifecycle for promoting reuse under FAIR principles, as noted by Kanjala et al [35]. The DDI codebook is a static document that describes the data in a study at a single point in time, whereas the dynamic DDI Lifecycle can be used to describe the data throughout their life cycle, from collection to dissemination. Moreover, the DDI Lifecycle is more machine-actionable, automating tasks such as data validation and interoperability. As a result, adoption of the DDI Lifecycle presents a promising avenue for future research to further enhance the accessibility and reusability of population health data in LMIC contexts.

The study's findings underscore the substantial benefits of adopting OMOP CDM, DDI, and Schema.org with JSON-LD and suggest that these benefits outweigh the accompanying challenges. However, it is imperative to proactively address these challenges to ensure the successful implementation and adoption of these technologies. By actively tackling the challenges and offering robust support to users, the IDSR or HDSS community can significantly enhance the FAIRness and accessibility of their data and digital assets, enabling a broader spectrum of users to leverage their potential for research, decision-making, and public health interventions.

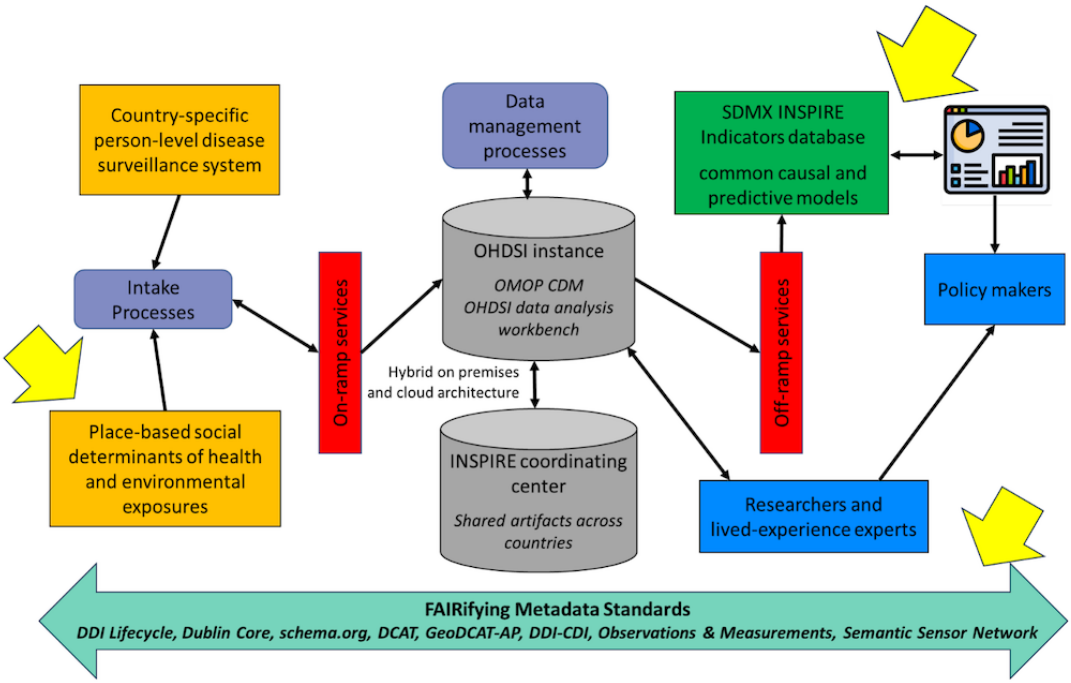
Future Directions

In future strategies, the FAIRification process will emphasize the adoption of Schema.org and JSON-LD MedicalObservationStudy as a standard within the Cross-Domain Interoperability Framework. This framework is capable of describing a workflow that includes the WHO IDSR platform, the OMOP CDM, and the OHDSI data analysis workbench. Regardless of whether each locality has its own platform, the data stay at home and only methods and aggregate results are shared or the data are pooled and move through the entire workflow at once. Indeed, because the MedicalObservationalStudy can describe the entire arc of clinical and population health research, it more or less guarantees the reproducibility of studies.

In the future, our aim is to expand the capabilities of MedicalObservationalStudy in several ways. First, we intend for it to describe a workflow that includes climate events and social determinants of health, which is crucial for understanding outcomes [44]. Furthermore, we seek to enhance the MedicalObservationalStudy to describe a workflow that terminates in a data cube in which each cell disaggregates an aggregate result by many dimensions [45] . This would be a workflow that INSPIRE augments with a Statistical Data and Metadata eXchange (SDMX) instance to present the OMOP CDM Results schema as an indicator repository [46]. This addition to the workflow mirrors the United Nations SDG platform and ensures broader utilization.

While SDMX is prominent, the DDI–Comprehensive Data Integration offers arguably a more capable format that statistical organizations may adopt in the future [45]. In addition, the ongoing integration of Fast Healthcare Interoperability Resources with OHDSI may provide other paths for a future workflow to follow [47]. Through the navigation of these evolving platforms and their standards, our work with the MedicalObservationalStudy aims to achieve compatibility, relevance, and interoperability within the public health community. The arrows in Figure 3 show where machine-readable and machine-actionable metadata are still needed.

Figure 3. Next steps to achieving machine-readable and machine-actionable metadata for public health. CDI: Comprehensive Data Integration; DCAT: Data Catalog Vocabulary; DDI: Data Documentation Initiative; FAIR: findable, accessible, interoperable, reusable; GeoDCAT-AP: a geospatial extension for the DCAT application profile for data portals in Europe; INSPIRE: Implementation Network for Sharing Population Information with Research Entities; OHDSI: Observational Health Data Sciences and Informatics; OMOP CDM: Observational Medical Outcomes Partnership Common Data Model; SDMX: Statistical Data and Metadata Exchange.



Finally, as new and emerging data formats emerge, Schema.org's flexibility and extensibility will play a crucial role in accommodating these formats, ensuring continued compatibility and interoperability within the evolving landscape of population health data.

Conclusions

The use of machine-readable metadata plays a vital role in ensuring the FAIRification of population health data. By embracing universal standards such as those of Schema.org, organizations can not only enhance their search engine optimization but also make their data more discoverable on the internet. This will maximize the impact and utility of population health data, particularly in LMICs. This paper highlights the importance of promoting and adopting machine-readable metadata standards in LMICs to advance the FAIRification and accessibility of population health data.

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Authors' Contributions

DA designed the study and authored the original manuscript. JG oversaw the study's implementation. JT, JG, SKM, AT, and TB played key roles in conceptualization and methodology. JT, KT, JG, TB, AK, AG, MO, CK, and SKM reviewed and edited the manuscript. All authors contributed to the article and approved the submitted version.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Data Documentation Initiative (DDI) documentation.
[PDF File (Adobe PDF File), 112 KB - ojphi_v16i1e56237_app1.pdf]

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Abbreviations

CDM: Common Data Model
DDI: Data Documentation Initiative
ETL: extraction, transform, load
FAIR: findable, accessible, interoperable, reusable
HDSS: health and demographic surveillance system
IDSR: Integrated Disease Surveillance and Response
INSPIRE: Implementation Network for Sharing Population Information with Research Entities
JSON-LD: Javascript Object Notation–Linked Data
LMIC: low- and middle-income country
LOINC: Logical Observation Identifiers Names and Codes
NADA: National Data Archive
OHDSI: Observational Health Data Sciences and Informatics
OMOP: Observational Medical Outcomes Partnership
SDG: Sustainable Development Goal
SDMX: Statistical Data and Metadata Exchange
SNOMED-CT: Systematized Nomenclature of Medicine–Clinical Terms
WHO: World Health Organization

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Original Paper

Public Perceptions of Treating Opioid Use Disorder With Deep Brain Stimulation: Comment Analysis Study

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Abstract

Background: The number of opioid-related deaths in the United States has more than tripled over the past 7 years, with a steep increase beginning at the same time as the COVID-19 pandemic. There is an urgent need for novel treatment options that can help alleviate the individual and social effects of refractory opioid use disorder (OUD). Deep brain stimulation (DBS), an intervention that involves implanting electrodes in the brain to deliver electrical impulses, is one potential treatment. Currently in clinical trials for many psychiatric conditions, including OUD, DBS's use for psychiatric indications is not without controversy. Several studies have examined ethical issues raised by using DBS to counter treatment-resistant depression, obsessive-compulsive disorder, and eating disorders. In contrast, there has been limited literature regarding the use of DBS for OUD.

Objective: This study aims to gain empirical neuroethical insights into public perceptions regarding the use of DBS for OUD, specifically via the analysis of web-based comments on news media stories about the topic.

Methods: Qualitative thematic content analysis was performed on 2 Washington Post newspaper stories that described a case of DBS being used to treat OUD. A total of 292 comments were included in the analysis, 146 comments from each story, to identify predominant themes raised by commenters.

Results: Predominant themes raised by commenters across the 2 samples included the hopes and expectations with treatment outcomes, whether addiction is a mental health disorder, and issues related to resource allocation. Controversial comments regarding DBS as a treatment method for OUD seemingly decreased when comparing the first printed newspaper story to the second. In comparison, the number of comments relating to therapeutic need increased over time.

Conclusions: The general public's perspectives on DBS as a treatment method for OUD elucidated themes via this qualitative thematic content analysis that include overarching sociopolitical issues, positions on the use of technology, and technological and scientific issues. A better understanding of the public perceptions around the use of DBS for OUD can help address misinformation and misperceptions about the use of DBS for OUD, and identify similarities and differences regarding ethical concerns when DBS is used specifically for OUD compared to other psychiatric disorders.

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KEYWORDS

deep brain stimulation; DBS; comment analysis; refractory opioid use disorder; substance abuse; opioid addiction; opioid; substance use; opioid use; treatment; addiction; mental health; therapeutic; psychiatric disorder

Introduction

As early as the late 1950s, lobbyists began pursuing pain medication legislation throughout the United States [1-3]. Based on the idea that chronic pain should be treated by physicians, US laws included the lack of prosecution of physicians prescribing pain medications in the 1980s [1,2]. In the United States, the prescription of opioids to provide pain relief has been debated since the mid-1990s, when the US Food and Drug Administration (FDA) approved oxycodone as a chronic pain medication, after which the overprescription of opioids and subsequent substance abuse became more prevalent [4]. There is evidence that the number of overdose deaths per year has increased significantly since 2010 [5], with a 3-fold increase in the United States between 2015 and 2021 [6,7], specifically affecting those in lower socioeconomic status regions of the United States [8-12]. Many countries, including the United States, recognize the psychological, social, and economic burdens of opioid addiction [13,14]. Several of these countries have implemented preventative measures, like prescription restrictions and prescription drug monitoring programs, to minimize refractory opioid use disorder (OUD) [15,16] mortality rates [17,18].

OUD is defined by the *DSM-5* (*Diagnostic and Statistical Manual of Mental Disorders* [Fifth Edition]), as a compulsive dependence on opioid consumption that negatively impacts a person's life [15,16]. OUD is considered to be refractory when patients do not show a decrease in drug use after being treated by all FDA-approved treatments including buprenorphine, methadone, behavioral counseling, and behavioral interventions [15,16].

Deep brain stimulation (DBS) has been proposed as a potential treatment for refractory OUD [19-21]. DBS involves the implantation of electrodes into the brain to regulate abnormal neural activity. It is FDA-approved for various movement disorders, such as Parkinson disease, and under investigation for psychiatric conditions [22,23]. There are currently 8 clinical trials listed in the US National Institutes of Health's clinical trial database focused on "opioid addiction" (the term used by international studies [21]) or "OUD" (US studies [24]), including the pilot study discussed in the news stories we address here.

The use of DBS for psychiatric conditions raises ethical considerations including concerns about informed consent [25], treatment safety [26], threats to patient agency [27], and the treatment being too intrusive [28,29]. Ethical discussion of the use of DBS for addiction [30] must also consider the stigmatization and criminalization of OUD [31]. While a number of empirical studies assess public perceptions of the use of DBS for psychiatric disorders [28,29,32], ours is the first, to our knowledge, to focus on public perceptions of DBS to treat OUD. The analysis of reader comments on web-based media stories offers valuable insights into public opinions and the factors that shape these opinions [33]. A better understanding of these perceptions can help address misinformation and misperceptions about the use of DBS and OUD [34,35]. This paper aims to provide insight into public perceptions of and concerns about using DBS to treat OUD, using public comments on web-based news stories about this therapy.

Methods

Source of Content Analysis

We used qualitative thematic content analysis [36,37] to examine and compare public comments on 2 Washington Post stories that described the case of an individual who entered a DBS pilot study for refractory OUD [38,39]. The first story [38] was published in 2019, directly preceding the procedure, while the second story [39] followed up with the same study participant's results in 2021. The second story reported that the patient had been in sustained remission for over 600 days post implantation [39]. To our knowledge, these are the only news stories in major news outlets focusing on DBS and OUD that have been published with an extensive number of public comments. Our queries to verify this information have included sources, such as BBC News [40], CNN [41], and local news stories [42-44], focusing on the US clinical trials. All queried stories did not have publicly available comments [45] directly below the stories.

Ethical Considerations

Publicly available information used for commentary analysis is generally exempt from institutional review board (IRB) review because it involves data that are already accessible to the general public and does not involve direct interaction with or personal data from individuals. Since this type of information, including news stories, social media content, and public records, is disseminated openly and is not subject to privacy restrictions, it typically does not pose the ethical concerns that IRB reviews are designed to address. The data used in this study was deidentified. We did not apply for an ethics board review assessment, as according to a Common Rule exemption criteria, "research uses of identifiable private information" (including information found on the web) are exempt from typical Common Rule protections, such as full board or expedited IRB review if such information is "publicly available" without restriction (45 Code of Federal Regulations 46.104(4)(i)). However, it is essential to remain mindful of ethical considerations, such as ensuring that interpretations are accurate and that the use of such data adheres to principles of fairness and respect.

Qualitative Analysis

Our analysis is based on 292 comments. This includes all 146 comments from the 2019 story. For the 2021 story, 146 (of a total of 579) comments were randomly selected to facilitate a comparison of the themes found in the two sets of comments and to avoid biasing the quantification of comments toward the 2021 story [46]. Excel (Microsoft Corp) was used to organize and code the data, as well as to randomize the comments included in the second story. Each comment was treated as a single unit of analysis, even when the same commenter had multiple comments for the same piece. Comments were coded according to the theme or themes they elicited. After curating the data set to eliminate "not relevant" comments, our final number of comments for the 2019 story was 101, and 80 comments for the 2021 story.

Comments coded as "not relevant" included comments not addressing DBS for OUD or OUD itself. For example, some comments only discussed topics related to Alcoholics Anonymous and were therefore considered off-topic.

An example of a comment that shows how a comment can be still "on-topic" but not directly relevant to our codebook's themes.

> *GOP needs electrodes implanted to vote the correct way.* [2019 story, ID 45]

This comment showcases the Alcoholics Anonymous "sidebar conversation" that was prominent throughout our 2021 story sample.

> *My experience with 12 step programs is that they are not terribly helpful.* [2021 story, ID 444]

Our qualitative thematic analysis used the codebook adapted from a previous study, based on web-based public comments on stories about treatments for psychiatric conditions, which included DBS [46], with the addition of several novel themes that emerged during the analysis of this data set and that reflected concerns specific to DBS for OUD. Coding was conducted by 2 independent coders (RB and JK), using iterative review and agreement after the coders discussed differences in codes.

Statistical Analysis

We used descriptive and inferential statistics to characterize the composition and properties of the samples. Data were analyzed using SPSS (version 26; IBM Corp). Major themes were defined as themes that had cumulative percentages of comments greater than 10%. The threshold of $P<.05$ was set for statistical significance for the comparison of comments across the 2 stories.

Results

Major Themes Across Both Stories

Overview

In what follows, we examine themes commonly appearing in both stories. The percentage

of comments for all themes in both stories is found in Table 1. Four themes showed no significant differences between the 2019 and 2021 stories, as displayed in Table 2.

Table 1. Comparison of the percentage of themes per relevant comments in Bernstein (2019) and Bernstein (2021).

Theme	Percent of coded theme per relevant comment, %	
	Bernstein (2019)	Bernstein (2021)
Controversial[a]	37	5
Overall Therapeutic Need[a]	10	30
Is Addiction a Mental Disorder?	14	24
Overall Social Issues[a]	8	18
Resource Allocation[a]	19	7
Personal Anecdote (Patient)[a]	9	13
Cautionary Realism[a]	17	4
Hopes and Expectations	9	11
Scientific Validity	18	1
Stigma	5	11
Sarcastic Humor	10	4
Medical Professional Issues[a]	3	11
Optimism	5	5
Direct Modification of the Brain	6	4
Questioning Effectiveness of the Intervention	0	10
Industry Related Issues	6	3
Risk/Safety	8	0
Pop Culture References	6	1
Historical Lesions	6	1
Overall Disadvantages	6	0

[a]χ^2_1 with a 2-tailed Fisher Exact test showed statistically significant results ($P<.05$) for relevant themed comments with cumulative percentages greater than 10% (Table 2).

Table 2. Results from χ^2_1 (N=382) with a 2-tailed Fisher Exact test for relevant themed comments with cumulative percentages greater than 10%.

Theme	Fisher Exact 2-tailed *P* value (comparing 2019 and 2021)
Controversial	<.001
Resource Allocation	.09
Scientific Validity	.02
Cautionary Realism	.02
Is Addiction a Mental Disorder?	.15
Overall Therapeutic Need	<.001
Personal Anecdote	.01
Hopes and Expectations	.48
Overall Social Issues	.04
Stigma	.18
Medical Professional Issues	.03

Resource Allocation

The financial cost of undergoing DBS surgery, together with considerations about insurance coverage, were concerns captured under this theme. The availability of both the treatment and of qualified physicians was described as a limited resource. A comparison of the cost of saved lives to the financial cost of getting DBS was made in a few of the comments in the 2019 story. Other comments discussed the question of who should pay the financial cost of getting DBS (eg, the general public, the creators of opioids, or the families of patients with OUD).

A comment that mentions that health insurance is needed to cover the cost of DBS.

> *I'm sure most have insurance to cover the cost of treating opioid addiction with brain surgery. That's absurd.* [2019 story, ID 4]

This comment elaborates on how limited the number of health care providers and facilities are in different regions.

> *It was only recently that treatment options were more readily available (in some parts of the country) ... And still. It's hard to find good help. Even in a place that doesn't have a shortage of therapists, psychiatrists, and x-waivered prescribers (those who can prescribe buprenorphine) it's difficult to find a qualified clinician.* [2021 story, ID 45]

Is Addiction a Mental Disorder?

Commenters disagreed about whether OUD should be considered a mental disorder. Several commenters expressed that addiction, in their view, is not a medical problem. Comments on whether addiction can be mitigated by self-control occurred for both stories but were more frequently made in the 2021 story, as shown in Table 1.

This comment illustrates the perspective that OUD should be considered a decision and not an illness.

> *It's not a moral issue. Simply a matter of deciding what you want to do, then doing it. Battery powered Nirvana is not Nirvana. Nor is a marathon record made by driving a motorcycle, a real marathon record.* [2019 story, ID 21]

This comment shares the potential implications of categorizing addiction as a choice, instead of an illness.

> *Addiction is the result of disease. It's not pretty, but as long as we consider it a social issue instead of a medical one, it will be ignored, stigmatized and improperly treated.* [2021 story, ID 93]

This comment includes the perspective that people with addiction have to want to get better.

> *I do believe addiction, for the most part, is a decision. Yes, treat it as a health issue, but one that the dependent person is willing to heal...* [2021 story, ID 97]

Hopes and Expectations

This theme captures comments expressing hope for positive outcomes for the research or for the specific patient discussed in both stories or a strong belief that DBS can be successful in the treatment of refractory OUD.

This comment shows a positive perspective on treatments evolving with OUD or addiction.

> *Hopefully, technology and medical techniques like this will help provide some relief for people like [the patient], who desperately want to get clean, but are being constantly and actively undermined by countless years of neurochemical evolution.* [2019 story, ID 66]

This comment cheers on the success of DBS in the 2021 story.

> *I mean it seems like one of many tools in this guy's arsenal of sobriety. Either way, though, I am grateful for his success and his giving back to the community.* [2021 story, ID 126]

Stigma

Comments coded under this theme referred to the stigma associated with DBS as a potential treatment for OUD and with

OUD itself. Using DBS as a treatment method for OUD was described as potentially treating one problem by creating another problem, electrical stimulation addiction replacing OUD. A handful of comments supported the destigmatization of those with OUD.

This flippant comment illustrates the perspective on DBS by suggesting that the user will become addicted to the electrical stimulation.

> *Oh, great ... now they'll be addicted to electrodes.* [2019 story, ID 34]

This comment includes a bigger picture of how a person with addiction might behave with something other than substance abuse or OUD.

> *...Addicts don't choose to be addicts. They suffer from an inability to delay gratification no matter how inconsequential the delay. The "addictive personality" can be spotted at a very young age. The addict will always choose an immediate reward even if delaying the reward by a mere ten seconds will earn them a double reward.* [2021 story, ID 461]

Key Areas of Difference Between Stories' Comments

In what follows, we examine statistically different themes. In particular, we found that 7 themes showed significant differences between the 2019 and 2021 stories.

Controversial

Comments were coded as controversial when they included snarky comments or sparked passionate discussion and disagreement. This theme had the largest difference in the percentage of coded comments between the two stories. There were significantly more comments coded in this theme for the 2019 story. Most comments on this theme blamed corporations, physicians, political associations, or the legal system for the prevalence of OUD.

This comment includes a discussion of the conflict innately in the rate of OUD's potential original cause.

> *Most addicts probably do not get their drugs from official/legal sources. But Wow ... Did the "corporation" tie the person to a bed and force them to become addicts? Where is the inalienable right to make personal choice we generally hold dear as a fundamental freedom? Or are choices good ... only until we can blame someone else for the bad choices we make? Sue all chocolate factories for my cravins?* [2019 story, ID 117]

This comment blames health care providers for their part in the current rate of OUD in the United States.

> *At the time, doctors knew little about the opioid disaster they were unleashing, which has since claimed half a million lives. They didn't know that heroin was addictive? Or they were just making too much money by getting people addicted to ask questions?"* [2021 story, ID 171]

Scientific Validity

This theme captures the mention of either questioning or asserting scientific evidence. For example, the mention of there not being enough research, issues regarding the premature use of DBS, or comments that question the effectiveness of intervention were coded under this theme. Comments often had a tone of disbelief toward the potential benefits of DBS, however, comments on the scientific process of testing novel treatments were also included.

This comment questions the effectiveness of DBS as a treatment for OUD.

> *A fix that's too quick and easy to be true, likely is too quick and easy to be true.* [2019 story, ID 21]

This comment includes the rigor of clinical trials, such as the DBS trial for OUD.

> *You might also understand that there is no treatment without research testing and clinical trials. This is research.* [2019 story, ID 61]

This commenter questioned the validity of using DBS as a treatment for OUD.

> *This is medical quackery.* [2021 story, ID 430]

Cautionary Realism

This theme captures comments that see the potential promise of the treatment but give cautionary warnings for the future. Comments made by readers of the 2019 story expressed "Cautionary Realism" more than twice as frequently compared to the later story, as shown clearly in Table 1.

This comment includes positive and uncertainty toward DBS as a treatment method for OUD.

> *This is terrifying and exciting all at once. This guy is very brave to try this. I hope that it helps him stay sober, as he obviously wants to.* [2019 story, ID 121]

This comment gives credence to DBS as a treatment method, while including a sense of hesitancy regarding the number of times it has been implemented.

> *...The surgical implant route, while radical and infrequent, deserves the detailed exploration given in this article.* [2021 story, ID 649]

Therapeutic Need

Commenters frequently mentioned that there are few therapies available to persons with OUD, emphasizing the need for novel treatments in this space. The percentage of comments in this category was much larger for the 2021 story than for the 2019 story. Many comments discussed potential alternatives to DBS, which were not described as options in the stories themselves. Another topic included in the comments involved the variability of needs of different people with OUD.

This comment touches upon the resistant portion of refractory OUD when describing the lack of treatment options and therefore hope.

> *Amazing to turn to this type of drastic invasive treatment, unless it's truly for those who have no other*

> *hope at all. And where is the discussion of psychedelic drugs, which have been showing the greatest benefit with the least down side?* [2019 story, ID 140]

This comment points out the variations of OUD and how given those variations, not all treatments work the same for all.

> *Addiction is insidious and no one size fits all approach has been discovered.* [2021 story, ID 7]

Personal Anecdote

Comments coded under this theme capture stories from commenters who have struggled with addiction and are sharing their story to sympathize with the story, or who have had DBS or similar interventions for another disorder, or commenters who are giving accounts of friends or family on their experiences with addiction. This theme contained significantly more comments on the 2021 story.

This comment includes the commenter's somewhat surreal experience after receiving DBS.

> *Had DBS for a tremor disorder. Worked like a charm. I hope this is successful for this person. And yes, it's pretty wild to be awake during brain surgery. We were all talking about a TV show we liked and then they wanted me to draw a spiral. Oh, so you've already put the wire in?* [2019 story, ID 1]

This comment includes an experience making the decision to not take prescribed opioid painkillers.

> *Before the awareness of the over-prescription of opioids, I have had doctors recommend Codeine and Oxycontin for various needs. They also said I could just try more milligrams of an over-the-counter painkiller to get by. I am so glad I always chose the later.* [2021 story, ID 533]

Overall Social Issues

This code was used for a variety of comments on social issues not captured by other codes covering social themes. Comparing OUD to other diseases, generational differences in perspective on DBS and OUD, government regulation of OUD and DBS, economic drivers, and access to health care were a few of the social issue topics described in these comments. More comments on the 2021 story were coded with this theme.

This comment focuses on society's potential response to making opioids more available.

> *Perhaps your arguments would be effective for the supply side of the equation, but they do nothing to reduce the demand side. Legalizing it would mean that opioids are more available, and more people would become addicted.* [2019 story, ID 80]

This comment includes various other implications of changing behavior with the use of neurotechnology such as DBS.

> *If brain stimulation can be used to curb addictive impulses, then maybe it can also be used to alter other kinds of behavior as well. Maybe someday convicted criminals will be given the opportunity to allow implantation of the probes as an alternative to serving time in prison. Think of all the possible uses of such a technology!* [2021 story, ID 216]

Medical Professional Issues

These comments included any mention of professional inertia, physicians as gatekeepers to care, doctor-patient relationships, conflicts of interest, and the management of patient care. A higher percentage of comments were coded under this theme for the 2021 story.

This comment includes a negative perspective on health care providers and opioid prescription.

> *He knows more than you Mr. Handout for Treatment Money. The opiates ARE MEDICINE for SEVERE pain and TRUE addiction is RARE. 996 in 1000 new to an opiate WILL NEVER ADDICT. Good health to you, they are now almost completely unavailable in therapeutic doses from any Doctor of Medicine.* [2019 story, ID 75]

This comment includes a potential future policy to require more vigilante follow-up from health care providers prescribing opioids.

> *The solution is for the doctor to closely monitor opioids post-op and refuse to refill the prescription and move the patient to an alternative as soon as possible.* [2021 story, ID 580]

Discussion

Principal Results

Overall, our results indicate that members of the public regard the treatment of refractory OUD using DBS with both some optimism and some concern. In addition to discussing the therapy, a number of comments addressed OUD itself, making it clear that both the disorder and its treatment shape commenters' views.

A number of themes were commonly raised in comments on both of the Washington Post stories, while others were common for only one of them. Here, we consider these common themes in the context of the broader discussion of the ethics of DBS. Where applicable, we also address the differences in comment frequency in light of the framing of each of the original stories.

When relatively new medical interventions, such as DBS, appear on the horizon for disorders that have had such a toll on families and society, there are "Hopes and Expectations" that arise surrounding them. Considering the social [47-49], psychological [34,43], and economic [11,18] toll of OUD, these public comments portraying hope and expectation might mirror the desire to find something that can finally help with the toll that OUD takes on individuals, their loved ones, and society. The prevalence of this theme may also be attributed to the expectation that the public has about the scientific community finding treatments for various conditions in an efficient manner [50], but also to the often optimistic way in which novel treatments are portrayed in the media. In Cabrera et al [46], "Optimism" was a broader theme that encapsulated many of the same ideas as "Hopes and Expectations." Much like "Hopes and Expectations," the theme "Optimism" was found in multiple

stories regarding DBS. For example, DBS is sometimes described in an overly optimistic manner in scientific journal studies [51,52], and it has been noted that the tone of media coverage of DBS is becoming increasingly more positive as time goes on [53]. This is important because the media acts as an intermediary between clinical researchers and the public [54]. Therefore, if the media continues to portray DBS in an overly optimistic way, focusing primarily on its benefits rather than offering a more balanced account of its pros and cons, this can create further misunderstandings and unfounded hopes for the general public [52].

"Stigma," another major theme raised in both stories' comments, reinforces barriers to the implementation of evidence-based interventions to prevent opioid overdose deaths [31,34,55-57]. Stigma has 2 important components. There is a stigma around psychiatric disorders in general [29,45,55,58], as well as a particular stigma related to treating OUD with DBS [34,55,57,58]. For example, almost half of the news stories included in the 10-year analysis by McGinty et al [57] use language that depicts opioid use in a stigmatizing manner. Furthermore, the way some media stories frame those with OUD as criminals instead of people needing treatment [56,59], further stigmatizes those with OUD. The stigma associated with receiving treatment for OUD can also be found with regard to other addiction-related diseases, as measured by the Shatterproof Addiction Stigma Index [55,58]. The Shatterproof Addiction Stigma Index was created to help measure levels of stigma, and to help combat stigma, discrimination, and barriers to care associated with substance use disorder [55,58]. There is also a stigma associated with DBS. Lack of awareness of what DBS treatment is, as well as its distinction from electroconvulsive therapy, has been shown to influence public attitudes and views about it when considering it as a potential treatment option [26,28,29,53].

Part of the perspective on whether DBS is acceptable for people with OUD is dependent on whether addiction is considered a mental disorder, a theme that clearly intersects with stigma. The medical field has classified OUD as a mental health disorder [60], but that does not mean that society sees it that way. If the public does not agree that OUD is a mental disorder, they are less likely to agree with supplying treatments that are more costly (such as DBS) [61,62], as we saw with comments coded under "Is Addiction a Mental Disorder?" These overlapping topics feed into the comments coded under "Resource Allocation" and "Medical Professional Issues." For example, similar to a previous publication [46], comments under the "Resource Allocation" theme focused on access to health care as a topic of conversation, with several comments shaped by whether or not psychiatric disorders are considered medical conditions. Likewise, past abuses by the medical profession with psychiatric interventions resonate in this analysis and previous work examining psychiatric interventions.

For the themes that appeared more frequently in comments on one of the two stories, it is possible that the framing of each story shaped the relevance of certain themes for comments in one but not the other. For the 2019 story, significantly more comments were coded with the themes "Controversial," "Scientific Validity," and "Cautionary Realism." A previous study examining psychiatric neurosurgical interventions, including DBS [46], found a similarly large number of comments coded under these themes. It is possible that the experimental nature of DBS in psychiatry shapes these comments. Interventions directly affecting the brain are not without controversy, however, the difference in frequency of this theme between 2019 and 2021 could be the result of increasing awareness of DBS for other disorders, and as such it was not viewed as being as controversial for the later story. Readers of the 2019 story may have been skeptical that refractory OUD could be treated at all and surprised that the patient was willing to participate in this clinical trial, which would be why so many comments were coded as "Cautionary Realism." By contrast, the second story provided the anecdotal story of the patient having had success with DBS, giving "Scientific Validity" to the procedure; this framing might have alleviated some of the hesitancies about using this neuromodulating technology reflected in comments referring to the 2019 story.

"Overall Therapeutic Need," "Overall Social Issues," and "Personal Anecdote" were major themes in the 2021 story. While it is the case that not all treatments work for all patients [20,23], for OUD in particular there has been a clear need to find effective alternatives [63]. The theme of "Overall Therapeutic Need" may have been more prevalent for the 2021 story because commenters raised awareness about the lack of effective treatments for OUD. The description of the FDA's requirements for enrollment into this clinical trial in the 2021 story, as well as the title, may have contributed to this theme [38]. In addition, "Therapeutic Need," a prevalent theme in previous studies examining psychiatric neurosurgical interventions [46], resonates with the scientific push to find novel treatments for refractory psychiatric conditions. "Overall Social Issues" reflected the complexity of social issues entangled with the application of neurotechnology as a treatment option for psychiatric disorders. Finally, as we have seen with previous news comments analysis [46,64], readers take the opportunity to share their own stories related to the topics covered in the story giving context to their perspectives on both the disorder and the treatment at hand. This makes the theme "Personal Anecdote" particularly helpful in hearing the voices of those who have been affected by OUD or treated with DBS.

Limitations

This study was limited by the number of comments that exist in response to each story, and by the fact that only 2 stories were available to analyze. In addition, the comments reflect the opinions of readers of web-based stories in newspapers, such as the Washington Post, and more specifically, those who choose to comment on the story. As such, they may not be representative of the concerns of other groups. Comment analysis also has an inherent limitation related to the interpretability of comments with a limited amount of context. Because the data was anonymized and commenters only used usernames, the analysis did not take into consideration potential commenters' access to clinical information, demographics, or socioeconomic status. In addition, one commenter could comment several times with a similar perspective on the topic, which could have skewed the frequency of themes.

Conclusions

Comments containing the perspectives and attitudes of society on DBS as a treatment method for OUD elucidated themes that include sociopolitical issues, positions on the use of technology, and technological and scientific issues. Future work may include further exploration of the public's perception of the use of DBS as a novel treatment for OUD, as well as other key public views (including patients) on the use of DBS as a potential treatment method for OUD.

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Data Availability

The data sets generated during and analyzed during this study are based on publicly available data.

Authors' Contributions

LYC and RB conceptualized the project, conducted data curation, performed supervision of students, and reviewed and edited the original draft. PH wrote the manuscript and together with all authors carried out formal analyses. All authors reviewed the final manuscript.

Conflicts of Interest

None declared.

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Abbreviations

DBS: deep brain stimulation
***DSM-5*:** *Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition)*
FDA: Food and Drug Administration
IRB: institutional review board
OUD: opioid use disorder

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Original Paper

Contact Tracing Different Age Groups During the COVID-19 Pandemic: Retrospective Study From South-West Germany

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Abstract

Background: Contact tracing was implemented in many countries during the COVID-19 pandemic to prevent disease spread, reduce mortality, and avoid overburdening health care systems. In several countries, including Germany, new systems were needed to trace potentially infected individuals.

Objective: Using data collected in the Rhine-Neckar and Heidelberg (RNK/HD) districts in southwest Germany (population: 706,974), this study examines the overall effectiveness and efficiency of contact tracing in different age groups and stages of the pandemic.

Methods: From January 27, 2020, to April 30, 2022, the RNK/HD Health Authority collected data on COVID-19 infections, quarantines, and deaths. Data on infection, quarantine, and death was grouped by age (young: 0-19 years; adult: 20-65 years; and senior citizens: >65 years) and pandemic phase (infectious wave plus subsequent lull periods) and analyzed for proportion, risk, and relative risk (RR). The overall effectiveness and efficiency of contact tracing were determined by calculating quarantine sensitivity (proportion of the infected population captured in quarantine), positive predictive value (PPV; proportion of the quarantined population that was infected), and the weighted Fβ-score (combined predictive performance).

Results: Of 706,974 persons living in RNK/HD during the study period, 192,175 (27.2%) tested positive for SARS-CoV-2, 74,810 (10.4%) were quarantined, and 932 (0.132%) died following infection. Compared with adults, the RR of infection was lower among senior citizens (0.401, 95% CI 0.395-0.407) and while initially lower for young people, was ultimately higher for young people across all 5 phases (first-phase RR 0.502, 95% CI 0.438-0.575; all phases RR 1.35, 95% CI 1.34-1.36). Of 932 COVID-19–associated deaths during the study period, 852 were senior citizens (91.4%), with no deaths reported among young people. Relative to adults, senior citizens had the lowest risk of quarantine (RR 0.436, 95% CI 0.424-0.448), while young people had the highest RR (2.94, 95% CI 2.90-2.98). The predictive performance of contact tracing was highest during the second and third phases of the pandemic (Fβ-score=0.272 and 0.338, respectively). In the second phase of the pandemic, 5810 of 16,814 COVID-19 infections were captured within a total quarantine population of 39,687 (sensitivity 34.6%; PPV 14.6%). In the third phase of the pandemic, 3492 of 8803 infections were captured within a total quarantine population of 16,462 (sensitivity 39.7%; PPV 21.2%).

Conclusions: The use of quarantine aligned with increasing risks of COVID-19 infection and death. High levels of quarantine sensitivity before the introduction of the vaccine show how contact tracing systems became increasingly effective at capturing and quarantining the infected population. High levels of PPV and Fβ-scores indicate, moreover, that contact tracing became more efficient at identifying infected individuals. Additional analysis of transmission pathways is needed to evaluate the application of quarantine in relation to infection and death risks within specific age groups.

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KEYWORDS

COVID-19; SARS-CoV-2; pandemic; quarantine; contact tracing; contact tracing effectiveness; demographics; mortality; case fatality; public health surveillance; public health systems

Introduction

Background

SARS-CoV-2 was first identified as the causative agent of the respiratory disease COVID-19 in Wuhan, Hubei Province, China, in December 2019 [1,2]. As of April 30, 2022, over half a billion cases of COVID-19 and more than 6 million COVID-19–related deaths have been reported worldwide [3].

COVID-19 in Germany

The first COVID-19 case in Germany was identified in Munich on January 27, 2020. By the end of April 2022, Germany, with a population of approximately 83 million, had registered over 24 million COVID-19 cases and more than 135,000 COVID-19–related fatalities. While the disease affected all age groups, nearly 90% of all COVID-19–related deaths in Germany were among individuals aged over 60 years, and over 98% were among those aged over 50 years [4]. According to Germany's national public health institute, the Robert Koch Institute (RKI), the majority of the initial SARS-CoV-2 infections in Germany occurred in 6 distinct waves, each primarily dominated by 1 of 4 virus variants [5].

During the first 2 waves of the COVID-19 pandemic, which were predominantly driven by the wild-type variant, studies generally reported a higher risk of infection in adults compared with younger individuals [6-8]. Additionally, there was a higher risk of infection in school-aged children (6-14 years) compared with those in childcare and kindergarten (0-5 years) [9]. Subsequent seroprevalence studies, however, have suggested that COVID-19 infections among younger individuals may have been underreported, as children and adolescents were often asymptomatic during a period of limited testing capacity [10,11]. Conversely, reduced transmission rates may have contributed to lower infection rates in younger people during the first 2 waves of the pandemic dominated by the wild-type variant [12-14]. Data from the Corona-KiTa report, published by the RKI and the German Youth Institute (DJI), also indicate that during the first 2 infection waves, the incidence of disease among children and adolescents, particularly those aged 0-5 years, was not only lower but also exhibited a delayed peak compared with older populations. The infection wave for this specific age group rose later and declined earlier than in older age groups [9].

Contact Tracing and Vaccination as Infection Control Measures

Infection control measures are specific actions designed to stop or reduce the spread of disease, thereby decreasing associated morbidity, mortality, and the burden on health care systems. During the COVID-19 pandemic in Germany, these measures were defined at both the federal and state levels and implemented by district health authorities. In addition to contact tracing and vaccination, which were critical control measures throughout the pandemic, other measures included lockdown periods, travel restrictions, and nightly curfews; temporary closure of schools, businesses, and religious institutions; prohibition of social, cultural, and sporting events; personal hygiene measures (eg, handwashing and sanitization); limitations on social contacts and physical distancing (1.5 m); and case isolation [15].

Most infection control measures were applied broadly across the entire population and often specifically targeted young people due to concerns about severe outcomes [16-21], including "long COVID" [22] and the risk of transmission to high-risk groups based on social contact data [23-26]. While these measures were generally effective, they were associated with increased levels of stress [27], language difficulties, weight gain [28], anxiety [29], stigmatization [30], depression [31], reduced sleep quality [9,28,32], and lower intelligence test scores [33]. Particularly among children and young people, the proportion of individuals with mental health problems dramatically increased during the pandemic [31,34,35]. Young people also experienced decreased social and physical activity [32], coupled with increased media consumption [36], as well as higher rates of overweight and obesity [37-39]. Further studies reported declines in language development and fine motor skills in children [28]. Among adults and senior citizens, studies have highlighted increases in economic difficulties, such as loss of income or savings, and reduced access to health and other essential services [32]. For parents of young children, limited access to childcare facilities was identified as a significant factor contributing to increased stress and anxiety [9]. Reports indicated rises in all forms of domestic violence, including sexual violence [40,41], amid concerns that prolonged confinement could be a risk factor for heightened family conflicts and child mistreatment [15,42]. German authorities closely monitored the negative impacts of infection control measures, particularly on children and adolescents' education, fitness, social adjustment, and mental health [15,43].

Contact tracing and quarantine are specific infection control measures that involve identifying and isolating individuals who have been in close contact with someone diagnosed with a transmissible disease. This differs from isolating a known or confirmed case. Unlike many countries, Germany's well-defined infection surveillance processes [44,45] were shown to have detected and reported close to the true number of COVID-19 cases during the pandemic [46,47]. This was achieved through a broad range of measures, including disease education campaigns and daily status updates to raise awareness of periods of heightened infectivity; automated contact tracing solutions, such as the Corona Warn App (SAP/Deutsche Telekom), which alerted users to their proximity to a known infection; event check-in systems, including mobile apps (eg, Luca app, culture4life GmbH), to identify potential disease transmission;

and subsidized home testing along with widespread free antigen and PCR testing sites that facilitated easy access to infection status information. While antigen test results were not used for reporting or contact tracing during the pandemic in Germany, a positive result from an antigen test generally prompted subsequent PCR testing. This process increased the detection of confirmed cases within the community and among quarantined populations.

Laboratories were required, under the Infectious Disease Protection Act (Infektionsschutzgesetz, §§ 7 to 9 IfSG [48]), to report each confirmed case to local health authorities. Specially trained contact tracing staff then attempted to contact and conduct telephone interviews with all COVID-19 cases to identify close contacts, also known as contact persons. They also informed individuals of their legal requirement to isolate and collected additional medical information. If the health authority was unable to establish contact with a known case, the local regulatory authority was notified, and an officer was dispatched to make contact. Ultimately, the Rhein-Neckar-Kreis/Heidelberg (RNK/HD) Health Authority estimated that during the period of active contact tracing, it successfully established contact with 85% of COVID-19 cases, with an additional 5% reached through the local regulatory authority. Additional contact tracing measures were implemented by specialist teams to protect senior citizens in care facilities and young people in kindergartens and schools. Once identified, close contacts were reached by contact tracing staff and informed of their legal obligation to quarantine in their residence, ideally in a separate room away from other coinhabitants, for a period ranging from 5 to 14 days. The definition of close contact and the duration of quarantine were specified and updated throughout the pandemic by state governments in accordance with national RKI guidelines [49]. To ensure compliance, officers from the local regulatory authority investigated reports of potential breaches and conducted spot inspections of disease case isolations and quarantined individuals. Although rarely issued in RNK/HD, regulatory officers had the authority to impose fines of up to €25,000 (~US $27731) or impose prison sentences of up to 5 years in extreme cases where there was a significant risk of harm to others (§ 74, 75 IfSG [48]).

Vaccines to prevent the spread and minimize the impact of COVID-19 were approved for emergency use in Germany on December 21, 2020, following recommendations from the European Medicines Agency (EMA; Table 1). The RNK/HD Health Authority administered the first doses in the district on December 27, 2020 [50].

As part of a national strategy to prioritize limited vaccine supply for senior citizens and high-risk individuals [50], the RNK/HD Health Authority initially administered vaccinations through 3 immunization centers in the RNK/HD district and mobile teams focused on aged care facilities and other vulnerable groups. Vaccines became more broadly available through medical practices starting April 7, 2021, and were later offered in pharmacies beginning February 8, 2022. Prioritized distribution of the vaccine ended, and young people over the age of 12 years were granted access starting June 7, 2021, following approval by the EMA [51], despite a lack of recommendation from the National Vaccine Advisory Authority (Standing Committee on Vaccination [STIKO]) [52]. While vaccination was mandatory for individuals working in medical or aged care facilities, the general population was encouraged to get vaccinated through social responsibility education programs and incentive schemes (Figure 1; also see [53]).

Contact tracing efforts and quarantine measures in RNK/HD were scaled back toward the end of 2021, following the widespread adoption of the COVID-19 vaccine. By this time, many other infection control measures that limited social contact had been lifted for individuals who could demonstrate a negative test result, proof of vaccination, or evidence of a recent infection within the last 90 days. As case fatalities remained relatively low following the Omicron-dominated fifth wave and hospital and intensive care unit capacities were no longer critical in 2022, most institutions and businesses gradually resumed normal operations while adhering to remaining infection control measures. At the end of March 2022, the RNK/HD Health Authority ceased active contact tracing, and on November 15, 2022, the state government of Baden-Württemberg lifted the legal requirement for quarantine (Figure 2).

Table 1. COVID-19 vaccine approvals.

Registered name	Manufacturer	Technology	Approval date
Comirnaty	BioNTech/Pfizer	mRNA[a]	December 21, 2020
Spikevax	Moderna	mRNA	January 6, 2021
Vaxzevria	Oxford/AstraZeneca	Adenovirus vector	January 29, 2021
Ad26.COV2.S	Janssen (Johnson & Johnson)	Adenovirus vector	March 11, 2021
Nuvaxovid	Novavax	NVX-CoV2373	December 20, 2021

[a]mRNA: messenger RNA.

Figure 1. COVID-19 vaccination coverage in RNK/HD from January 2021 to May 2022 [52]. HD: Heidelberg; RNK: Rhine-Neckar.

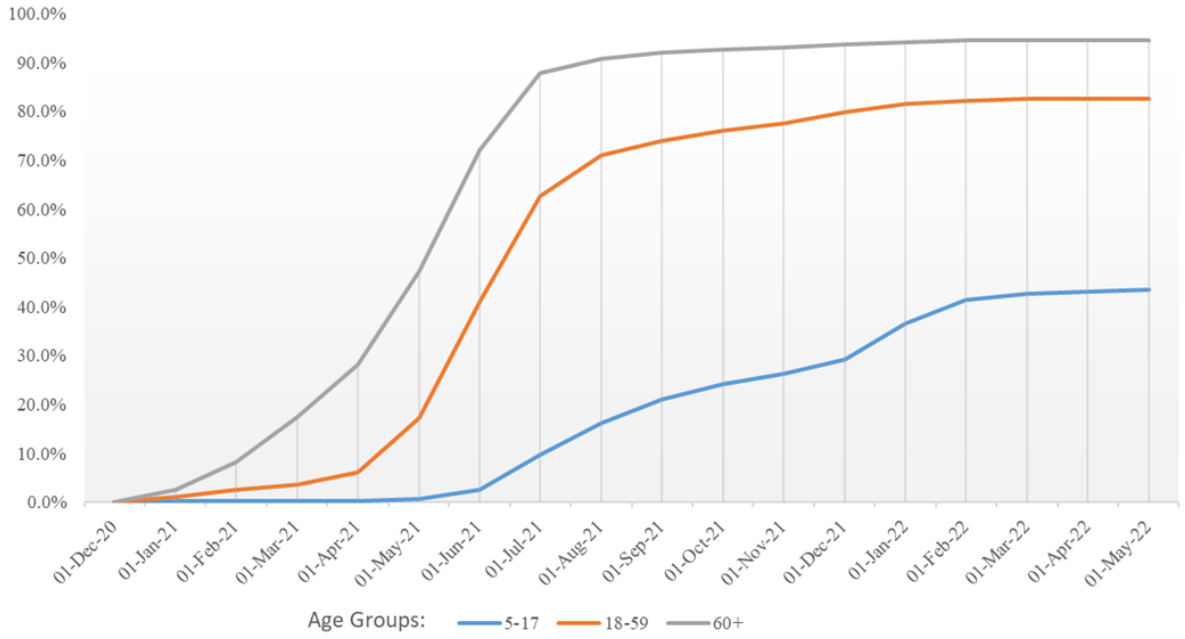
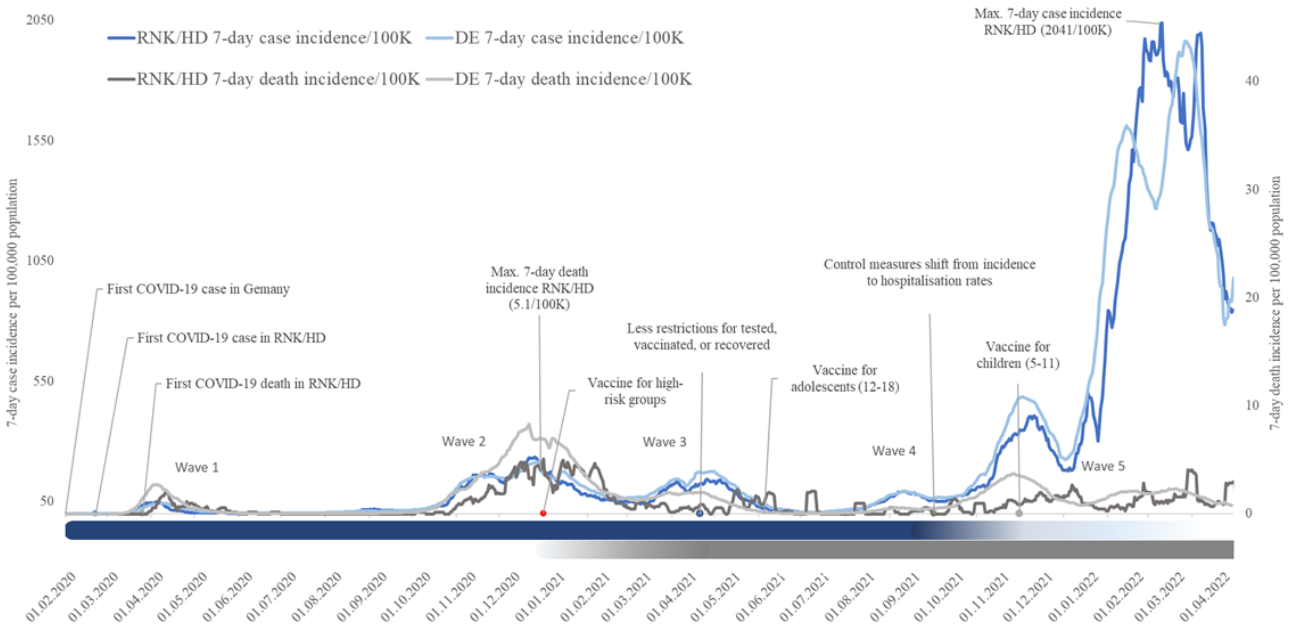


Figure 2. Timeline of initial COVID-19 disease incidence (morbidity) and death (mortality), with critical events including period of contact tracing and the introduction of the vaccine in RNK/HD, Germany. DE: Germany; HD: Heidelberg; RNK: Rhein-Neckar-Kreis.



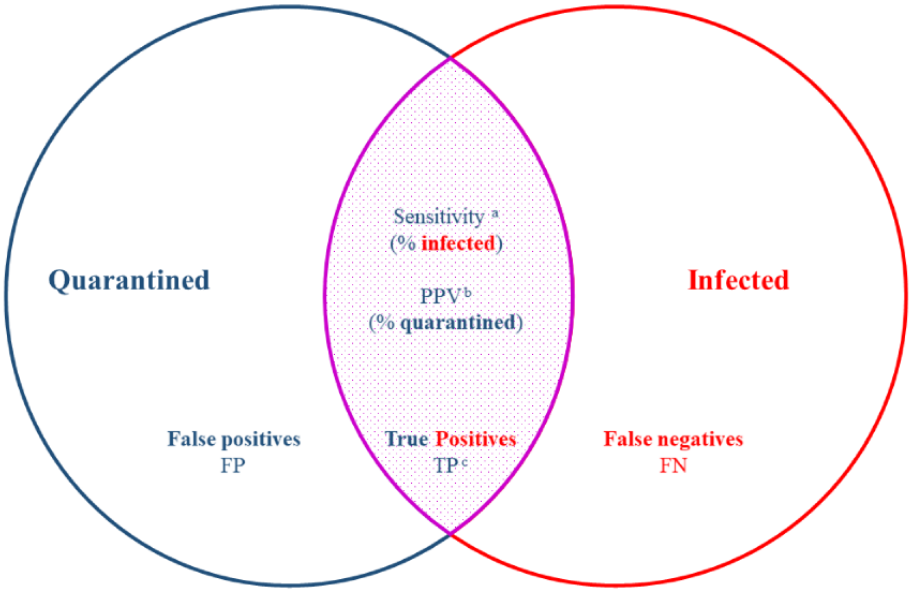
Measuring Contact Tracing Effectiveness and Efficiency

A Cochrane rapid review on quarantine during the COVID-19 pandemic concluded that, while broadly accepted as effective, there is a notable lack of agreed-upon metrics and data to demonstrate its effectiveness [54]. This finding was supported by a subsequent systematic review of observational and modeling studies of COVID-19, which concluded that the spread of the disease could be stopped if at least 80% of cases were captured in quarantine, or slowed if the capture rate was below 80% [55].

This paper examines the use of quarantine as an infection control measure in RNK/HD from the initial disease outbreak until the introduction of the vaccine. To assess overall effectiveness in a real-life setting, we propose using "quarantine sensitivity," defined as the proportion of the infected population captured in quarantine (Figure 3). To assess overall efficiency, we propose using the positive predictive value (PPV), defined as the proportion of the quarantined population that tested positive

while in quarantine. To evaluate predictive performance as a combined measure of sensitivity and PPV, we propose using an F_β-score, with an arbitrary weight that values sensitivity more than PPV. Ideally, all infected individuals would be quarantined (sensitivity 100%) and only infected individuals would be quarantined (PPV 100%), resulting in perfect predictive performance (F_β-score=1). In practice, quarantine can be considered overall effective if it captures a sufficient proportion of the infected population to limit or reduce disease spread. It is deemed efficient if the number of healthy individuals placed in quarantine is kept to tolerable levels.

Figure 3. Quarantine sensitivity, PPV, and predictive performance. [a]Sensitivity = cases captured in quarantine/total number of infected cases. [b]PPV = cases captured in quarantine/total number of people quarantined. [c]Predictive performance (F$_\beta$-score) = ([1+β^2]TP)/([1+β2]TP+β2FN+FP). FN: false negative; FP: false positive; PPV: positive predictive value; TP: true positive.



Study Objectives

The study focuses on contact tracing and the use of quarantine within 3 distinct age groups during the initial 5 phases of the COVID-19 pandemic. In particular, did the use of quarantine reflect variations in COVID-19 infection and mortality between the different age groups and at different time points? Was contact tracing effective in identifying and capturing potentially infected individuals in quarantine? How efficient was contact tracing in capturing only infected individuals in quarantine? Were there differences between age groups and across the different phases of the pandemic?

Methods

Data Collection and Storage

All known COVID-19 cases, including the first cases reported in RNK on February 27, 2020, and in HD on February 28, 2020, were reported to district health authorities within 24 hours. The RNK/HD District Health Authority then transmitted case data to the RKI while managing the infectious disease control process. Initial containment measures were managed largely through ad hoc systems until a dedicated COVID-19 monitoring and containment system, including an operational database, was developed and launched on March 8, 2020. A database for research purposes was subsequently created from the comprehensive outputs (CSV files) of the operational database, which were archived daily until November 2022.

Until August 2021 (the end of the third phase), the RNK/HD Health Authority contacted each confirmed case via telephone and regular email to inform them of their legal obligation to isolate, collect medical information, and identify potentially infected contacts. RNK/HD contact tracing staff received specialized training and followed a standardized procedure to collect and document case details for national reporting, contact tracing, and other operational purposes.

This study includes data from the first documented infection on February 27, 2020, until the cessation of contact tracing in the region on April 30, 2022. Medical records collected by the RNK/HD Health Authority without informed consent were anonymized, aggregated, and analyzed in accordance with the EU General Data Protection Regulation (GDPR 2016/679), specifically recitals 1, 4, 26, and 159 [56], and the Treaty on the Functioning of the European Union, Title XIX, Research and Technological Development Space, Article 179 [57].

Ethics Approval

The use of patient data records by health authority staff without informed consent was approved for this study by the University of Heidelberg Medical Faculty Ethics Committee on September 30, 2022 (reference number S-488/2022).

Additional national COVID-19 data and statistics, including vaccination levels, were accessed from the RKI national database on February 1, 2023, and other publicly released sources [4]. Population data for RNK/HD, valid as of December 31, 2020, were obtained from the Baden-Württemberg Office for Statistics web page, accessed on October 6, 2022 [58].

Documentation and Outcomes

For reporting purposes, a confirmed COVID-19 case was defined as an individual with a positive SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) test, regardless of symptoms [59]. Individuals who were in close contact with a confirmed case and were legally required to undergo quarantine were contacted separately and documented as noncases within the COVID-19 monitoring and containment system. A death was documented as COVID-19 related if the person tested positive for COVID-19 via RT-PCR either before or immediately after death, and if medical professionals assessed that COVID-19 contributed to or caused the death.

In the research database, a confirmed case was documented with the date of disease onset as the testing date, or with the date of the first positive PCR result if no actual test date was recorded in the operational database. Contact persons were documented as nonconfirmed cases, with a quarantine start date based on when they were first entered into the operational database, and an end date determined by the median duration of quarantine for each specific day during the study period. Infected contact persons were identified if the date of disease onset occurred during the quarantine period. Noninfected contact persons were those who did not become infected during the quarantine period, although they may have been infected at another time. To avoid double counting across study phases, records of infected contact persons who were quarantined in one phase but tested positive or died in another phase were included only in the phase during which they were quarantined. Similarly, for nonquarantined persons, if death occurred in a subsequent study phase after the infection, the record was included only once, in the phase of the infection.

Statistical Analysis

This publication presents data collected by the RNK/HD Health Authority, the sixth-largest district health authority in Germany, which serves a combined population of 706,974 registered residents as of December 31, 2020 [58].

Data were included from the first case in the RNK/HD area, recorded on February 27, 2020, until April 30, 2022, by which time many infection control measures, including contact tracing, had been relaxed. The study timeframe was divided into 5 phases (Table 2), with each phase beginning at the start of a calendar week in which incidence rates increased due to a new virus variant or following a summer lull in infection levels, according to RKI retrospective classification [5]. Lulls are included at the end of a phase because quarantine measures, infections, deaths, and the emergence of new virus variants were more frequently initiated during infection waves that extended into lulls, rather than during lulls that extended into waves.

Data were further categorized into 3 age groups: (1) young people, which included predominantly those attending kindergarten and school (aged 0-19 years, n=130,387); (2) adults, which included predominantly higher education students, parents, and those engaged in the workforce (retirement age in Germany: 65 years, aged 20-65 years, n=437,581); and (3) senior citizens, which included predominantly retired persons, including those in aged care facilities and individuals at high risk of hospitalization and fatal outcomes from COVID-19 [60] (aged ≥66 years, n=139,006).

The risks of COVID-19–related quarantine, infection, and death were calculated as follows: the number of individuals who were quarantined, infected, or who died with or of COVID-19 during the specified period was divided by the relevant subpopulation as of December 31, 2020 [58]. All risk calculations consider only single instances during the specified time and exclude additional instances where an individual may have been quarantined or infected multiple times. Reinfections and/or multiple quarantine events were counted as separate events. The adult age group, which constitutes 61.89% (437,581/706,974) of the population, was used as the reference group to calculate the relative risk (RR). The corresponding 95% CI was calculated using a Wald test with bivariable logistic regression, assuming a normal distribution.

Using a contingency table to evaluate binary classifiers, the sensitivity of contact tracing or quarantine decisions was calculated as the percentage of COVID-19 cases captured in quarantine (true positives [TPs]/(TPs + false negatives [FNs]). The PPV of quarantine was calculated as the percentage of persons quarantined who tested positive for COVID-19 during the quarantine period (TP/(TP + false positive [FP]). As a combined measure of predictive performance, F_β-scores were weighted toward sensitivity rather than PPV ($\beta=2$), and calculated as the weighted product of PPV and sensitivity divided by weighted PPV plus sensitivity, which can be simplified as follows: $([1+\beta^2]TP)/([1+\beta2]TP+\beta2FN+FP)$. It was not possible to calculate test accuracy because the number of true negatives (contacts, but not close contracts, of infected persons) was not documented.

Records without birth dates or with implausible birth dates were excluded from age-related analyses, including 988 of 78,641 quarantine records (1.26%) and 34 of 198,148 case records (0.02%).

To validate the results, supplementary risk analyses for infection, quarantine, or death were conducted by grouping data based on gender and location (HD city vs surrounding RNK district). No statistically significant differences (within 95% CI) were expected between males and females, but some variations were anticipated between RNK and HD due to demographic differences.

In this report, comparable output values ranging from 0.001 to 999 were rounded to 3 significant digits (eg, 12.3, 1.23, 0.123, 0.012, and 0.001). A decimal 0 was added to natural numbers to indicate that rounding had occurred (eg, 12.0, 1.20).

Data processing and analysis for this report were conducted using MS-SQL (Microsoft Corporation) and Python version 3.12 (Python Foundation) [61]. All statistical assessments were performed using pandas version 2.1.1 [62], statsmodels version 0.14.0 [63], scipy version 1.11.3 [64], and matplotlib version 3.8.4, with matplotlib-venn version 0.11.10 [65] for Venn diagrams. Additional graphs and tables were prepared using MS Excel 2016 (Microsoft Corporation) [66].

Table 2. The initial 5 phases of the COVID-19 pandemic in Germany [5].

Study phase (period) and RKI[a] phase description	Dominant viral strain
1: February 27, 2020 to September 27, 2020	
Sporadic cases	Wild type
First wave	Wild type
Summer lull	Wild type
2: September 28, 2020 to February 28, 2021	
Second wave	Wild type
3: March 1, 2021 to August 1, 2021	
Third wave	Alpha
Summer lull	Alpha
4: August 2, 2021 to December 26, 2021	
Fourth wave	Delta
5: December 27, 2021 to April 30, 2022	
Sixth wave	Omicron

[a]RKI: Robert Koch Institute.

Results

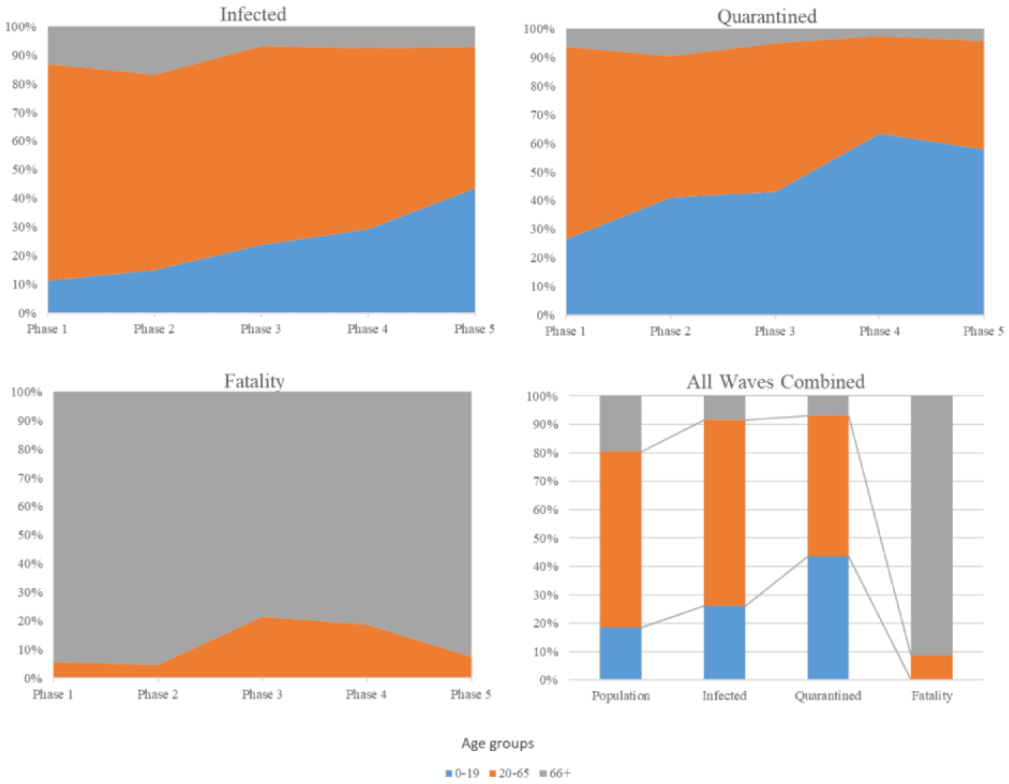
Age Group Proportion of Infection, Quarantine, and Case Fatalities

Within the total population of 706,974 people, young people aged 0-19 years account for 18.41% of the population (n=130,137) and were underrepresented among cases during the first 2 phases of the pandemic, comprising 11.23% (phase 1, 234/2083) and 15.02% (phase 2, 2513/16,730) of confirmed cases (Figure 4; Supplementary Table S2 in Multimedia Appendix 1). However, over the course of the 5 pandemic phases, young people became overrepresented as cases, eventually accounting for 26.31% (50,560/192,141) of COVID-19 infections. Adults aged 20-65 years, who account for 61.9% (n=437,581) of the total population, were slightly overrepresented in the infected population, accounting for 65.48% (125,822/192,141) of cases. This overrepresentation was particularly pronounced in the first phase of the pandemic, where they made up 75.5% (1574/2083) of COVID-19 infections. By contrast, senior citizens aged over 65 years, who account for 19.7% (n=139,006) of the total population were underrepresented in the infected population, comprising 8.46% (16,263/192,141) of cases.

Young people, as 18.4% of the local population, were overrepresented in the quarantined population, making up 43.47% (32,092/73,822) of those quarantined (Figure 4; Supplementary Table S2 in Multimedia Appendix 1). This overrepresentation increased from 26.56% (2046/7702) in the first phase to a peak of 63.43% (5178/8163) in the fourth phase. By contrast, both adults and senior citizens were underrepresented in the quarantined population. Adults, 61.9% of the population, accounted for 49.46% (36,510/73,822) of those quarantined and senior citizens, 19.7% of the population, accounted for 7.07% (5220/73,822) of quarantines. This underrepresentation was particularly pronounced in the fourth phase, where adults made up 34.13% (2786/8163) of those quarantined and senior citizens just 2.44% (199/8163) of those quarantined.

The vast majority of COVID-19–associated deaths documented by the RNK/HD Health Authority occurred within the population of senior citizens, aged over 65 years, accounting for 91.4% (852/932) of all COVID-19 deaths across all study phases (Figure 4; Supplementary Table S2 in Multimedia Appendix 1). The remaining deaths occurred in adults aged 20-65 years (80/932, 8.6%), with no deaths reported among younger people aged 0-19 years. During the third and fourth phases, adults represented relatively higher proportions of the COVID-19 deaths: 22% (14/65) and 19% (26/140), respectively, compared with the first, second, and fifth phases, where they accounted for 5.7% (3/53), 4.7% (22/469), and 7.3% (15/205) of deaths, respectively.

Figure 4. Proportion of COVID-19-related infections, quarantine, and death cases, by age group and pandemic phase (stacked areas) from January 27, 2020, to April 30, 2022.



Risks of Infection, Quarantine, Mortality, and Case Fatality

Within the RNK/HD population of 706,974 people, a total of 198,148 SARS-CoV-2 infections were documented during the study period (Supplementary Table S1 in Multimedia Appendix 1). The lowest risk of infection occurred during the first phase of the pandemic (infections, n=2083, risk 0.295%). In this phase, the risk of COVID-19 infection was 0.181% for young people (infections, n=236), 0.361% for adults (infections, n=1578), and 0.196% for senior citizens people (infections, n=273; Figure 5; Supplementary Table S3 in Multimedia Appendix 1). The risk of infection reached its highest level of 20.8% (infections, n=147,866), which occurred during the omicron-dominated fifth phase. In this phase, 31.0% of young people (n=40,476), 22.0% of adults (n=96,273), and 7.98% of senior citizens (n=11,093) tested positive for COVID-19. During the period of active contact tracing (phases 1-3) in RNK/HD, the highest infection risk for all age groups was observed in the second phase of the pandemic.

For each age group, the lowest risk of infection occurred during the first phase of the pandemic, while the greatest risks were observed in the fifth phase (Figure 5). During the initial 2 phases, young people had a lower risk of infection compared with adults (RR 0.502 in phase 1 and 0.745 in phase 2; Supplementary Table S3 in Multimedia Appendix 1). However, across all phases, young people experienced a higher risk of infection than adults (RR 1.35, 95% CI 1.34-1.36). Senior citizens consistently maintained a significantly lower risk of infection compared with adults throughout all 5 phases (RR 0.401, 95% CI 0.395-0.407).

The risk of being placed in quarantine during the first five phases of the pandemic in the RNK/HD area was just over 10% (quarantines, n=78,641; risk 10.4%). The greatest risk of being quarantined occurred in the second phase of the pandemic (quarantines, n=39,687, 5.32%; Figure 6; Supplementary Table S3 in Multimedia Appendix 1). The ratio of quarantine events to confirmed cases was highest in phase 1, decreasing in each successive phase of the pandemic from 4.10 in phase 1 to 0.036 in phase 5; and highest for young people (ranging from 8.97 to 0.077; Figure 7). The population of senior citizens consistently had the lowest ratio of quarantine events to confirmed cases across all phases of the pandemic, ranging from 1.78 in phase 1 to 0.020 in phase 5. Young people had the highest risk of quarantine (quarantines, n=33,761; risk 5.9%) compared with adults (quarantines, n=38,553; risk 8.81%) and senior citizens (quarantines, n=5339; risk 3.84%). Relative to adults, the risk of quarantine for young people was nearly 3 times higher (RR 2.94, 95% CI 2.90-2.98), while the risk of quarantine for senior citizens was less than half (RR 0.436, 95% CI 0.424-0.448).

The overall risk of death following infection (case fatality) was 0.485% (deaths, n=932; infections, n=192,141) during the study period, with a notable decline across successive phases of the pandemic, from 2.54% in phase 1 (deaths, n=53; infections, n=2083) to 0.139% in phase 5 (deaths, n=205; infections, n=147,050; Figure 8; Supplementary Table S3 in Multimedia Appendix 1). For the senior citizen population, the case fatality risk dropped significantly, from 18.3% in phase 1 (deaths, n=50; infections, n=273) to 1.72% in phase 5 (deaths, n=190; infections, n=11,037). Within the population of 706,974 people, the population-wide mortality risk during the first five waves of the pandemic was 0.132% (deaths, n=932), with senior

citizens experiencing a higher mortality risk at 0.613% (deaths, n=852; senior citizen populations, n=139,006). The mortality risk peaked during the second phase of the pandemic, with 0.066% for all age groups (deaths, n=469) and 0.322% for senior citizens (deaths, n=447; Figure 9). Senior citizens had a significantly higher risk of COVID-19 mortality compared with adults, with the risk being between 11.5 and 64.0 times greater across the study phases. The lowest RR for senior citizens was observed in the third phase of the pandemic, which followed the targeted release of the vaccine to senior citizens and high-risk individuals.

Supplementary analyses aimed at validating the results indicated no significant differences between males (population, n=345,903; infections, n=94,993; risk 27.46%) and females (population, n=362,072; infections, n=102,328; risk 28.26%) in terms of infection risk (RR infection female relative to male 1.03, 95% CI 1.02-1.04), quarantine risk (male quarantines, n=36,499, male risk 10.55%, female quarantines, n=39,724, female risk 10.97%; RR quarantine female relative to male 1.04, 95% CI 1.03-1.06), or death risk (male deaths, n=447, male risk 0.13%; female deaths, n=479, female risk 0.13%; RR death female relative to male 1.03, 95% CI 0.903-1.17; Supplementary Table S4 in Multimedia Appendix 1). Compared with 158,741 residents of HD, those 548,233 persons living in the surrounding RNK district had slightly higher risks of infection (HD infections, n=39,637, HD risk 24.97%; RNK infections, n=157,084, RNK risk 28.65%; RNK RR to HD 1.15, 95% CI 1.14-1.16), quarantine (HD quarantine, n=14,317, HD risk 9.02%; RNK risk 114%; RNK RR to HD 1.26, 95% CI 1.24-1.29), and death (HD deaths 145, HD risk 0.09%; RNK deaths 774, risk 0.14%; RNK RR to HD 1.55, 95% CI 1.30-1.85).

An additional analysis of RNK/HD data confirmed results from the RKI Corona-KiTa study [9], showing that the risk of infection in young children (aged 0-5 years) remained below the risk of infection in adults in each phase of the pandemic until April 30, 2022 (Supplementary Table S5 in Multimedia Appendix 1). Despite having a lower risk of infection than adults and no associated deaths, young children aged 0-5 years had the highest risk of being placed in quarantine (risk 28.5%; RR to adults 3.23, 95% CI 3.18-3.29).

Figure 5. Age group risk of COVID-19 infection during the intial 5 phases of the pandemic.

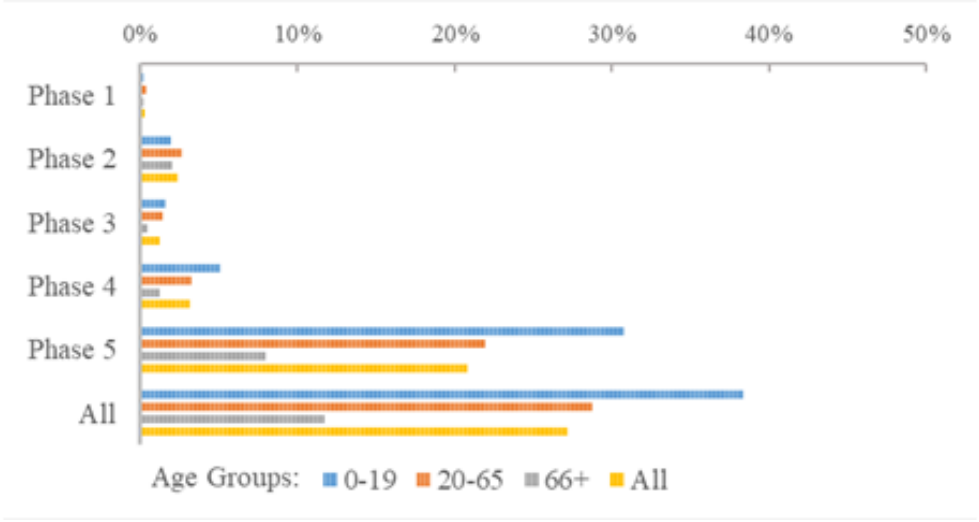


Figure 6. Age group risk of quarantine during the initial 5 phases of the COVID-19 pandemic.

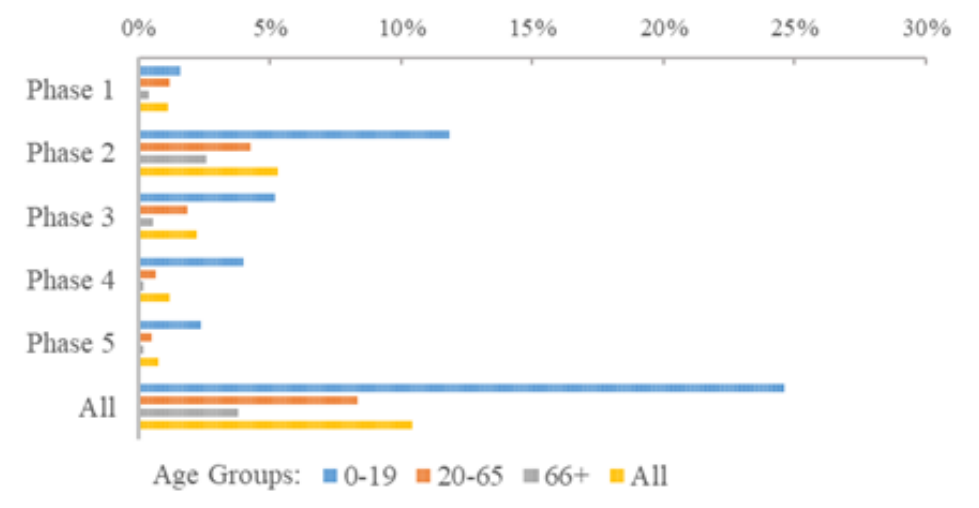


Figure 7. Ratio of quarantine events to COVID-19 cases during the initial 5 phases of the pandemic.

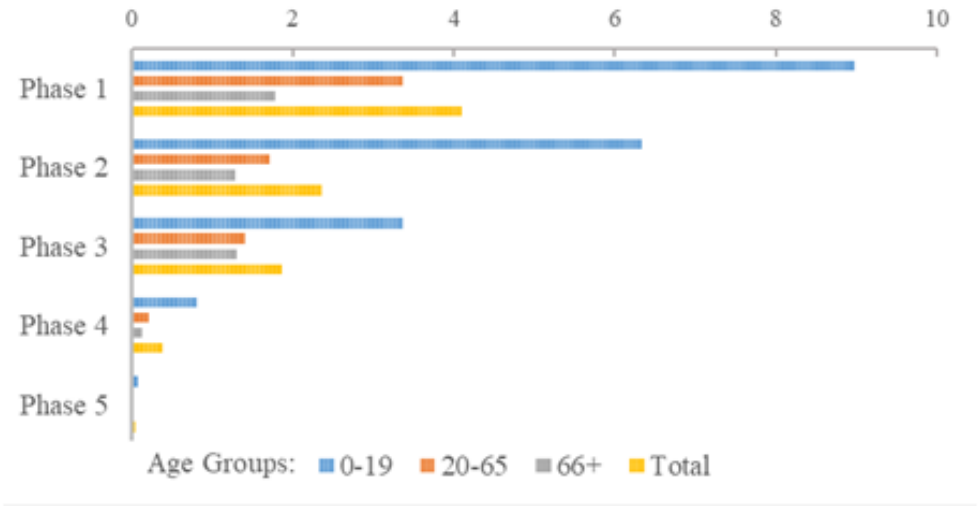


Figure 8. Age group risk of death following COVID-19 infection (case fatality) during the initial 5 phases of the pandemic.

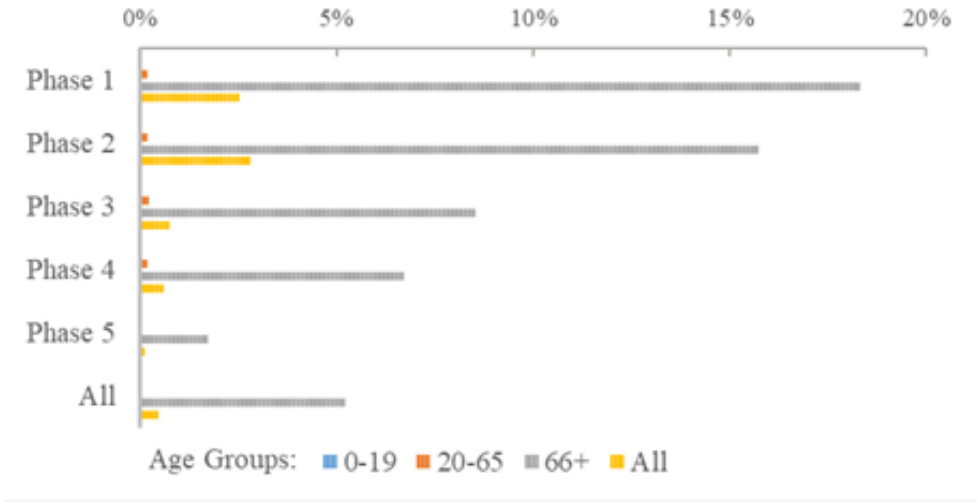
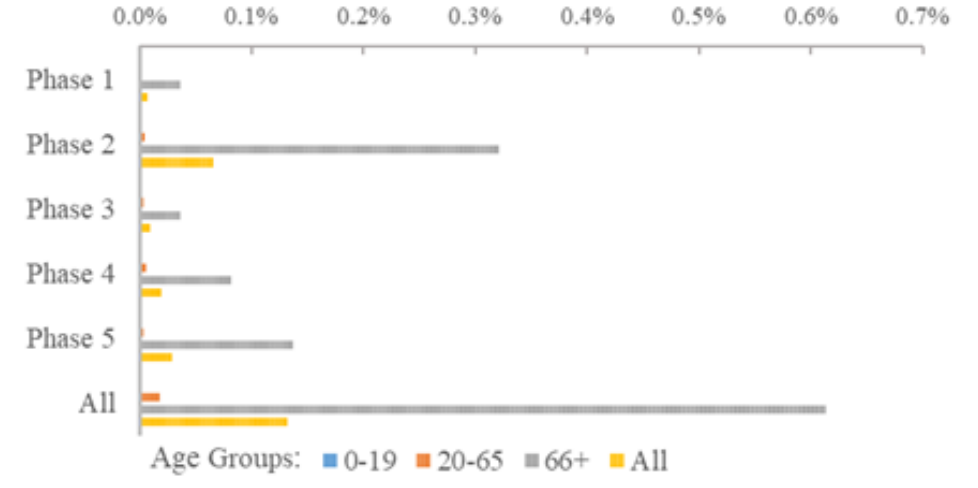


Figure 9. Age group risk of COVID-19–related death (mortality) during the initial 5 phases of the pandemic.



Quarantine Sensitivity, Positive Predictive Value, and Predictive Performance

The size of the quarantine population was larger than the size of the infected population during the first 3 phases of the pandemic, with increasing overlap, particularly for young people, between the 2 populations (sensitivity, PPV, and predictive performance; Figure 10). During the first phase of the pandemic, around one-fifth of all cases in RNK/HD were captured in quarantine (sensitivity 19.2%; Multimedia Appendix 2), and only 1 in 20 quarantined individuals tested positive during quarantine (PPV 4.69%). Taken together, this resulted in a low predictive performance: β-weighted (2) F_β-score=0.119. During phases 2 and 3 of the pandemic, sensitivity increased to 34.6% and 39.7%, and PPV increased to 14.2% and 21.2%, with F_β-scores improving to 0.272 and 0.338, respectively. As contact tracing efforts were scaled back in phases 4 and 5, sensitivity decreased progressively to 9.83% and 0.693%, respectively. PPV, by contrast, continued to increase and peaked in phase 4 (25.9%) before reducing in phase 5 (19.0%). Predictive performance (F_β-score weighted toward sensitivity, β=2) reduced in both the fourth (0.112) and fifth (0.009) phases.

Comparing age groups during the period of active contact tracing (phases 1-3), quarantine sensitivity was highest in the younger population, capturing from around one-third of the infected population in quarantine in phase 1 (33.1%) to nearly two-thirds in phases 2 and 3 (59.8% and 56.0%, respectively; Figure 11; Supplementary Table S6 in Multimedia Appendix 1). Quarantine sensitivity for adults and senior citizens started at around one-tenth in phase 1 (adults 12.8%; senior citizens 8.36%), increasing to almost one-third in phase 3 (adults 34.8%; senior citizens 32.3%). Contact tracing sensitivity was lowest for senior citizens in each study phase. As contact tracing efforts were reduced in phases 4 and 5, the proportion of the infected population captured in quarantine decreased for all age groups (young: from 17.6% to 1.33%; adults: from 6.85% to 0.473%; senior citizens: from 4.36% to 0.288%).

Comparing the proportion of the quarantine population that tested positive (PPV) across different age groups, a higher proportion of adults and senior citizens in quarantine tested positive compared with younger persons in almost every study phase (Figure 12). In phase 4, when PPV was highest, 36.8% (74/201) of senior citizens placed in quarantine tested positive, 33.15% (976/2944) of adults, and 21.62% (1168/5403) of young people in quarantine tested positive (Supplementary Table S6 in Multimedia Appendix 1). In phase 3, during the period of active contact tracing, 24.9% (193/776) of senior citizens in quarantine tested positive, 24.66% (2127/8624) of adults, and 16.60% (1172/7059) of young people in quarantine tested positive.

The predictive performance of contact tracing (F_β-weighted toward sensitivity, β=2) increased during the first 3 phases of the pandemic and decreased rapidly in the fourth and fifth phases as contact tracing efforts were reduced (F_β-scores for phases 1-5=0.119, 0.272, 0.338, 0.112, and 0.009, respectively; Figure 13; Supplementary Table S6 in Multimedia Appendix 1). The predictive performance of contact tracing was consistently higher for young people compared with other age groups throughout the study phases, peaking at 0.380 in phase 3.

Figure 10. Proportional Venn diagrams of COVID-19 infections captured in quarantine (sensitivity) and within quarantined population (PPV) providing elements for predictive performance (Fβ-score) calculations in age groups and phases of the pandemic. PPV: positive predictive value.

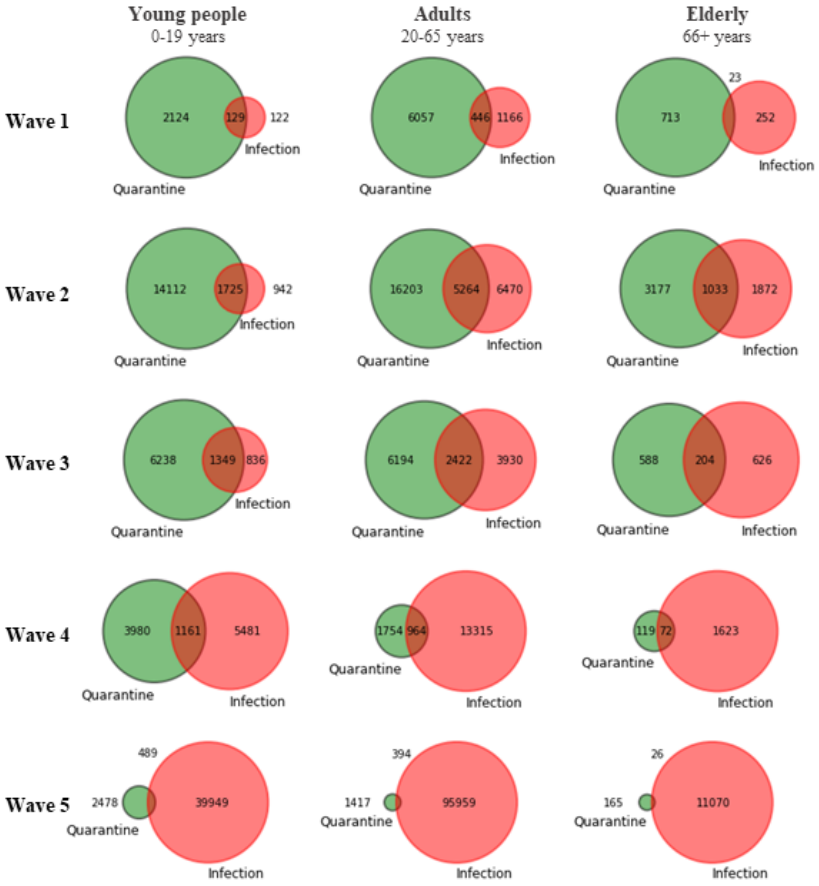


Figure 11. Age group quarantine sensitivity (% cases captured in quarantine) during the first 5 phases of the COVID-19 pandemic.

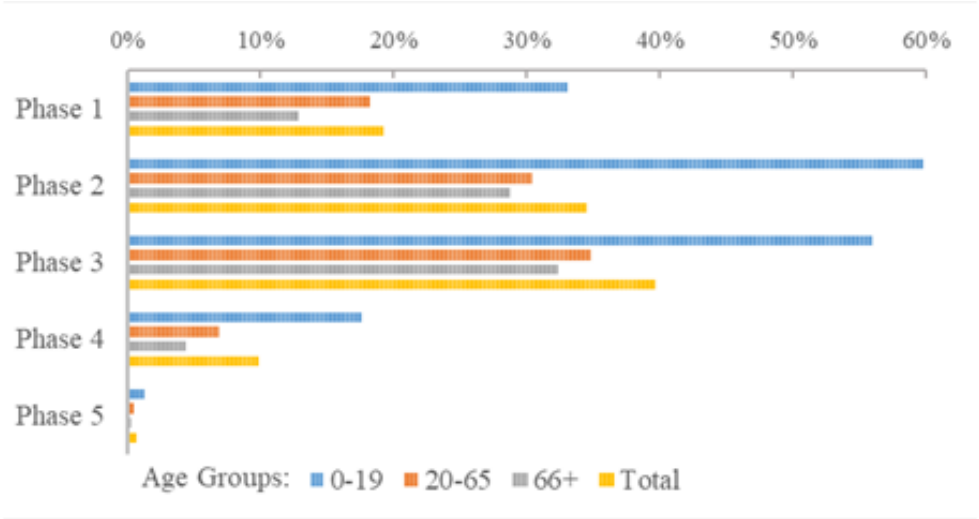


Figure 12. Age group quarantine PPV (% quarantine population infected) during the first 5 phases of the COVID-19 pandemic. PPV: positive predictive value.

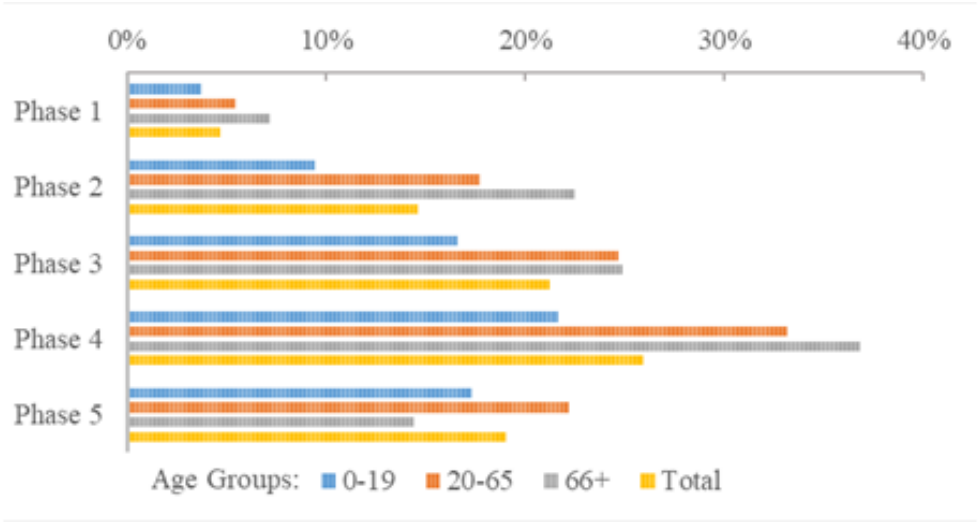
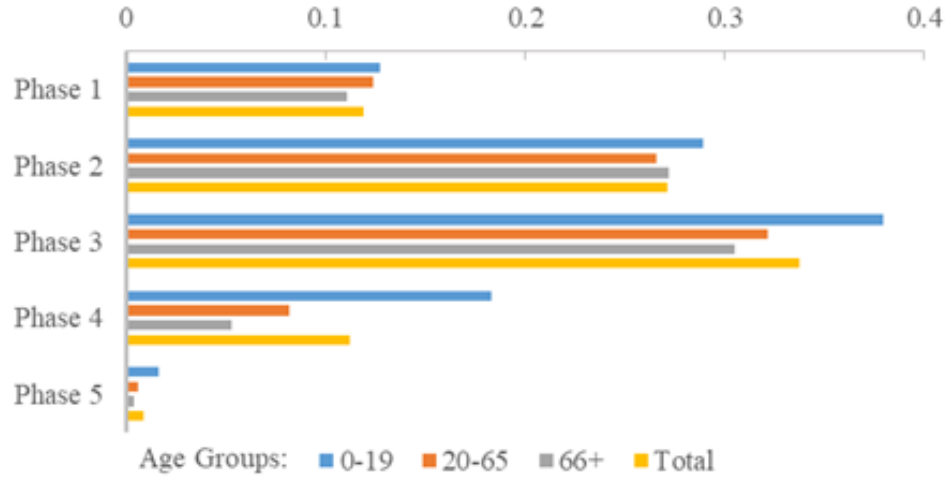


Figure 13. Age group quarantine predictive performance (Fβ score, weighted toward sensitivity β=2) during the first 5 phases of the COVID-19 pandemic.



Discussion

Principal Findings

The data on SARS-CoV-2 infections and case fatalities from the RNK/HD Health Authority align with national statistics in terms of scale [3,36] and the timing of infection waves and lull periods [5]. The risks of infection, quarantine, and case fatality varied significantly across age groups. Young people exhibited the highest risks of infection and quarantine, whereas mortality and case fatalities were predominantly observed in the senior citizen population.

The overall effectiveness of contact tracing, measured by the proportion of cases captured in quarantine (sensitivity), did not reach the 80% threshold predicted to halt further COVID-19 transmission. However, the sensitivity of around 40% observed in the second and third phases of the pandemic likely contributed to reducing transmission [55,67,68]. This reduction in transmission would have helped in lowering the incidence of severe and potentially fatal infections, thus alleviating the burden on health care systems. The overall efficiency of contact tracing, measured by the proportion of quarantine cases that tested positive (PPV), improved significantly across 4 of the 5 study phases. This improvement helped to reduce the burden on noninfected individuals. The F_β-score offers a consolidated measure of both the effectiveness (sensitivity) and efficiency (PPV) of contact tracing, providing a comprehensive assessment of its performance throughout the pandemic.

Variations in Disease Outcomes

Much of the variation in COVID-19 incidence and mortality observed in RNK/HD can be attributed to the targeted release of vaccines to senior citizens and changes in the infectivity of virus variants [69,70]. Initially, when vaccine supplies were limited and prioritized for high-risk adults and senior citizens, there was a notable reduction in the risk of death among the latter group, as evidenced by decreases in both mortality and case fatality rates. At the same time, however, the increased proportion of deaths among adults suggests that the targeted vaccination efforts may not have effectively reached high-risk individuals within this age group (eg, those with preexisting conditions such as diabetes, obesity, heart failure, lung disease,

or dementia). Additionally, senior citizens are known to engage more frequently in disease-preventative behaviors, both in general [71,72] and during the COVID-19 pandemic [73], which may have also contributed to better outcomes within this group.

Consistent with other published research, data from RNK/HD indicate that relatively fewer infections were reported in young people compared with adults or senior citizens during the first 2 phases of the pandemic [2,6-9]. This trend may partly be attributed to a lack of testing within this age group [10,11]. Alternatively, recent data from human challenge experiments suggest a strong correlation between symptoms and wild-type disease transmission [12]. This supports findings from other studies indicating that the initial contagion predominantly spread within the adult population where the disease was first established [9,23]. Data from the German RKI Corona-KiTa study also show that the risk of infection in young children aged 0-5 years was lower compared with other age groups during the initial phases of the pandemic [9]. An additional subanalysis of RNK/HD data confirmed that, during the early wild-type phases of the pandemic, young children aged 0-5 years had the lowest risk of infection.

Contact Tracing and Quarantine Effectiveness and Efficiency

Data from RNK/HD show that quarantine sensitivity, PPV, and the F_β-score can serve as indicators of the overall effectiveness and efficiency of contact tracing efforts. Sensitivity offers a clear measure of how effectively contact tracing captured the infected population in quarantine. To demonstrate that this success was not merely due to an increased number of people placed in quarantine, PPV (the proportion of the quarantined population who tested positive) provides a complementary measure of contact tracing efficiency. F_β-scores, weighted toward sensitivity (β=2), indicate that an optimal balance between effectiveness and efficiency was achieved during the third phase of the pandemic, with the highest F_β-score of 0.338, when 39.67% (3492/8803) of all infections were captured in quarantine and 21.21% (3492/16,462) of the quarantined population tested positive (Supplementary Table S6 in Multimedia Appendix 1). Unweighted *F*-scores showed similar results, but were less reliable for identifying the reduction in sensitivity between phases 3 and 4 (Supplementary Table S7 in Multimedia Appendix 1).

As a measure of overall effectiveness, quarantine sensitivity was initially low during the first study phase, likely due to the ongoing development of systems. Sensitivity increased as the risks associated with COVID-19 infection peaked, capturing nearly half of all confirmed cases during the second phase of the pandemic. As contact tracing and quarantine measures were reduced in phases 4 and 5, leading to decreased sensitivity, other infection control measures—such as widely available antigen and PCR testing—continued to help individuals identify when to self-isolate after an infection and to self-quarantine after contact with an infected person.

As a measure of overall efficiency, the PPV increased from around 5% to 27% during the first 4 phases of the pandemic. This improvement can be attributed to the increased availability of free PCR testing and the fine-tuning of other policy and operational practices. Policies exempting fully vaccinated individuals from quarantine may have also contributed to the rise in PPV. However, the PPV improved for young people despite limited vaccine availability in phases 3 and 4. Additionally, factors such as the experience and expertise of contact tracing staff and policy makers may have further enhanced the proportion of infections captured within the quarantine population.

As a combined measure of predictive performance, weighted to prioritize sensitivity over PPV, the increasing F_β-scores indicate simultaneous expansion and improvement of contact tracing processes during the first 3 phases of the pandemic. Conversely, the decreasing F_β-scores in phases 4 and 5 reflect the reduction in contact tracing efforts, which particularly impacted sensitivity. By incorporating both sensitivity and PPV, F_β-scores offer a comprehensive measure of the overall efficiency and effectiveness of contact tracing measures.

Higher levels of quarantine sensitivity, but lower PPV and F_β-scores for young people compared with adults and senior citizens, highlight the disproportionate application of quarantine measures across different age groups. One reason suggested for the higher quarantine rates among young people is their increased social interactions, such as in classroom or kindergarten settings [26]. Additionally, the conditions of quarantine for young children were often less stringent due to practical reasons, including exemptions from mask usage and the difficulty in enforcing hygiene and social distancing rules for this age group. By contrast, school closures and other restrictions were implemented to reduce such social contacts during the initial phases of the COVID-19 pandemic [74]. As schools and kindergartens reopened, additional hygiene and infection control measures were introduced to protect children from infection and minimize the need for widespread quarantine [75].

Quarantining Young People

The decision to quarantine young people to prevent disease transmission to higher-risk groups was initially supported by contact pattern data, which suggested that young people could be a source of transmission for broader outbreaks, similar to patterns observed in influenza [25]. However, transmission data from contact tracing studies have since shown that SARS-CoV-2 transmission occurs predominantly within specific age groups and, unlike influenza, is more common in households and other settings rather than in schools [69,76-78]. This observation is supported by data from the RNK/HD area (manuscript in preparation). Additionally, data from the Corona-KiTa study indicated that infections in young adults, rather than in children or adolescents, preceded each of the early phases of infection [9].

Although the vaccine is likely to have reduced the risk of mortality and quarantine for the population of senior citizens, it seems that this protective benefit did not influence decisions regarding the quarantine of younger people. The higher levels of quarantine for younger individuals, and the apparent need to capture a greater proportion of them, were initially driven by

concerns for the children themselves. These concerns included reports of unexpected pathology [16] and "long COVID" [79]. However, these complications were only anecdotally associated with children and were quickly identified as being of low incidence [14,19,22,80-84]. Relatively little attention was given to the reports of young people experiencing negative effects from quarantine [15,28,34,35,37-39,42,43], although these reports may have influenced decisions to keep schools and kindergartens open.

Limitations

As in other locations, failures to identify cases or underreporting make it challenging to ascertain the true number of COVID-19 infections and deaths, which are likely to have been higher than reported [85]. Many cases, particularly asymptomatic and mild ones, were less likely to be tested, diagnosed, and reported. This issue was especially pertinent at the beginning of the pandemic when testing capacities were limited. Data collected for operational purposes may contain more errors and exclusions (eg, missing birth dates) due to limited validation, compared with data collected specifically for research purposes. Although case reporting in Germany was reportedly high, quarantine sensitivity, PPV, and F_β-scores may still be influenced by undetected cases within the community and the quarantine population.

Measures of sensitivity, PPV, and F_β-scores reported in this paper do not account for delays between testing and the notification of cases, nor the identification and notification of contact persons. Delays in case isolation and quarantine can increase the risk of disease transmission, thereby undermining the assumption that cases captured in quarantine (sensitivity) prevent all subsequent infections. To address this issue, delays would need to be quantified, along with the likelihood of resulting infections.

The size and nature of the domicile where individuals were quarantined may influence quarantine sensitivity, PPV, and F_β-scores. For instance, individuals living alone may be less likely to identify or infect contact persons compared with those residing in larger families or shared living arrangements, such as aged care facilities. Institutions where staff frequently enter and exit quarantine areas and then interact with other residents may be particularly susceptible to disease transmission. Further research is needed to assess the impact of living arrangements, such as occupant density and type of domicile, on these effects.

The contribution of automated processes, such as mobile apps for detecting proximity to known cases, to the overall effectiveness or efficiency of contact tracing cannot be separately assessed from the contact tracing processes used by the RNK/HD Health Authority. A distinct evaluation of the quarantine sensitivity, PPV, and F_β-score of automated or digital solutions would be valuable for comparing different contact tracing methods.

Conclusions

During the first 3 phases of the pandemic, up to August 2021, contact tracing in the RNK/HD area played a crucial role in infection control, initially helping to limit the spread of SARS-CoV-2 and associated fatalities. During this period, high levels of quarantine sensitivity and PPV were effective in reducing virus transmission and preventing the health system from becoming overwhelmed. Especially during phases 2 and 3 of the pandemic, the availability of testing and ongoing improvements in contact tracing processes ensured that a greater proportion of the infected population was captured in quarantine (sensitivity) and that a higher percentage of those quarantined were actually infected (PPV).

The impacts of COVID-19—regarding infection, quarantine, and death—varied significantly across different age groups. Even during phases when the incidence of infection was lower in young people compared with adults, they were still significantly more likely to be placed in quarantine. Despite being up to 56 times more likely to die from an infection than adults before the introduction of the vaccine, senior citizens were significantly less likely to be placed in quarantine compared with adults or children. Urgent follow-up research is needed to clarify whether transmission predominantly occurs within specific age groups rather than between them, as has been suggested elsewhere.

In future disease outbreaks, understanding the COVID-19 pandemic and the infection control measures used will provide a valuable foundation. However, a key lesson from this pandemic is that infection control measures must be regularly adapted based on emerging information. State and federal decision makers, along with local authorities implementing policies, benefit from up-to-date data, concurrent analyses, and rapid assessments of specific risks.

This research highlights that a retrospective assessment of health authority data can offer valuable insights into past policies and their practical applications. Further analysis of contact tracing data from RNK/HD could help clarify the transmission pathways of SARS-CoV-2 within and between different age groups and social groups.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Data analysis.
[DOCX File , 76 KB - ojphi_v16i1e54578_app1.docx]

Multimedia Appendix 2
Infection and quarantine contingency tables with quarantine sensitivity, positive predictive value, and predictive performance.
[PPTX File , 48 KB - ojphi_v16i1e54578_app2.pptx]

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Abbreviations

DJI: German Youth Institute
EMA: European Medicines Agency
FN: false negative
FP: false positive
GDPR: General Data Protection Regulation
IfSG: Infektionsschutzgesetz
PPV: positive predictive value
RKI: Robert Koch Institute
RNK/HD: Rhein-Neckar-Kreis/Heidelberg
RR: relative risk
RT-PCR: reverse transcription-polymerase chain reaction
STIKO: Standing Committee on Vaccination
TP: true positive

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Original Paper

Rank Ordered Design Attributes for Health Care Dashboards Including Artificial Intelligence: Usability Study

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Abstract

Background: On average, people in the United States visit a doctor 4 times a year, and many of them have chronic illnesses. Because of the increased use of technology, people frequently rely on the internet to access health information and statistics. People use health care information to make better-educated decisions for themselves and others. Health care dashboards should provide pertinent and easily understood data, such as information on timely cancer screenings, so the public can make better-informed decisions. In order to enhance health outcomes, effective dashboards should provide precise data in an accessible and easily digestible manner.

Objective: This study identifies the top 15 attributes of a health care dashboard. The objective of this research is to enhance health care dashboards to benefit the public by making better health care information available for more informed decisions by the public and to improve population-level health care outcomes.

Methods: The authors conducted a survey of health care dashboards with 218 individuals identifying the best practices to consider when creating a public health care dashboard. The data collection was conducted from June 2023 to August 2023. The analyses performed were descriptive statistics, frequencies, and a comparison to a prior study.

Results: From May 2023 to June 2023, we collected 3259 responses in multiple different states around the United States from 218 people aged 18 years or older. The features ranking in descending order of importance are as follows: (1) easy navigation, (2) historical data, (3) simplicity of design, (4) high usability, (5) use of clear descriptions, (6) consistency of data, (7) use of diverse chart types, (8) compliance with the Americans with Disabilities Act, (9) incorporated user feedback, (10) mobile compatibility, (11) comparison data with other entities, (12) storytelling, (13) predictive analytics with artificial intelligence, (14) adjustable thresholds, and (15) charts with tabulated data.

Conclusions: Future studies can extend the research to other types of dashboards such as bioinformatics, financial, and managerial dashboards as well as confirm these top 15 best practices for medical dashboards with further evidentiary support. The medical informatics community may benefit from standardization to improve efficiency and effectiveness as dashboards can communicate vital information to patients worldwide on critically prominent issues. Furthermore, health care professionals should use these best practices to help increase population health care outcomes by informing health care consumers to make better decisions with better data.

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KEYWORDS

data visualization; dashboards; public health; population health; informed decisions; consumer decision-making; health data; usability

Introduction

Overview

A health care dashboard is a visual representation of vital health care data designed to emphasize key information for individuals and organizations, aiding them in making informed decisions [1]. These dashboards are increasingly used worldwide to track and report emerging and widespread diseases, trends, and other information to allow the public to make better health care decisions. [2,3]. Some examples include the Johns Hopkins COVID-19 dashboard, the Centers for Disease Control and Prevention FluView Interactive dashboard, the World Health Organization mpox dashboard, and the State of Pennsylvania's Cancer Statistics dashboard.

Dashboards can effectively communicate health information to allow the public to make better health care decisions for themselves [4-6]. On the other hand, if health care dashboards are presented poorly or without the proper information, they can be ineffective tools for the public [7].

The research team conducted an observational review and surveys on the effectiveness of health care dashboards in the United States to better understand and improve their design elements. As a part of this research, the team reviewed over 250 US city, county, and state health care dashboards as an observational assessment of whether their designs were favorable or not. Along with the observational study, the team conducted 2 surveys with the public about the favorability of the top 15 best practices for both COVID-19 and health care dashboards. The COVID-19 dashboard survey had 118 people participating and the health care dashboard survey had 218 participants. The latter is the focus of this research article.

From these surveys and subsequent analysis, the authors were able to develop and confirm the top 15 best practices of health care dashboard design. These 15 top best practices were assessed as the most important aspects of a health care dashboard's effectiveness.

There is a wide range of qualities when it comes to health care dashboard design. Some dashboards are confusing and difficult to read while others are clear and easily comprehensible. This study attempts to quantify what makes an effective health care dashboard.

With these best practices, practitioners can build upon these key elements to design and disseminate effective health care dashboards allowing the public to make better health care decisions and in turn, help improve health care outcomes.

The aim of this study is to rank and explain the relative importance of aspects of health care dashboards so that they can be more easily usable and understandable.

Background

The average person in the United States visits a doctor 4 times a year, and 6 in 10 adults in the United States have a chronic disease [8]. In total, 61% of all US adults have searched for health or medical information on the internet [9]. In addition, 49% have accessed a website that provides information about a specific medical condition or problem [3]. Therefore, it is important that health care information used by the public is both informative and easily understood, since many people are constantly searching for new health care information.

The public makes health care decisions based on available information, either sourced from the internet or received in-person. Public health tools such as health care dashboards play a key role in the health care decision-making process because they can be readily available and provide real-time information instantly. Doctors and patients can benefit from health care dashboards, if they are designed in the best interest of the public and health care officials.

An effective health care dashboard should effectively display relevant and comprehensible information to its users [10,11]. For instance, a health care dashboard on cancer that provides data promoting timely screenings for breast and colon cancer can not only contribute to reducing the prevalence of these cancers, but also may influence patients in the consideration of appropriate therapy, enabling them to make well-informed decisions in a collaborative manner. It is also important that information and data are offered through assorted designs to help all demographics, including minorities and ethnically diverse populations that are more susceptible or at risk of specific public health issues [1]. For example, Hispanic individuals are about 50% more likely to die from diabetes or liver disease [12]. Dashboards that prioritize population-specific data for screening and prevention in the Spanish language may enhance usability leading to improved prevention strategies.

Furthermore, broadening the conversation regarding the application of these design features in various health care settings, such as managing chronic diseases, tracking epidemics, and incorporating artificial intelligence (AI) and predictive analytics, could further enhance the practical implications and overall impact of this research in the health informatics field.

Role of AI and Predictive Analytics

Furthermore, the use of AI to display dynamic on-demand predictive analytics in a health care dashboard can have a significant potential future impact. Its incorporation in dashboard design is especially helpful for analyzing and displaying data, identifying trends, forecasting future health scenarios, and providing personalized recommendations based on historical data and current health indicators.

The integration of AI significantly impacts usability by offering enhanced decision support, improving efficiency, personalizing user experiences, increasing accessibility, and enabling data-driven health interventions. These factors make health care

dashboards more powerful tools for helping individuals and organizations make informed health decisions, leading to better health care outcomes. By addressing the effective integration and potential effects of AI, this research offers important perspectives on the future of dashboard advancement in the health care industry.

The study aims to provide a reliable assessment of the key attributes that make health care dashboards effective tools for public health decision-making including the use of AI for predictive analytics and other prominent features.

Methods

Overview

We initially examined over 250 public-facing health care dashboards from both the US government and commercial sources such as the Johns Hopkins COVID-19 dashboard, the Centers for Disease Control and Prevention FluView Interactive dashboard, the World Health Organization Healthcare mpox dashboard, and the State of Pennsylvania's Cancer Statistics dashboard. After the review of these health care dashboards, the authors identified key design elements for health care dashboards and then conducted a survey validating the top 15 attributes to produce a rank-ordered list.

The attributes surveyed are as follows: (1) easy navigation, (2) high usability, (3) use of diverse chart types, (4) mobile compatibility, (5) predictive analytics with AI, (6) incorporated historical data, (7) use of clear descriptions, (8) compliance with the Americans with Disabilities Act (ADA), (9) comparison data with other entities, (10) adjustable thresholds, (11) simplicity of design, (12) consistency of data, (13) incorporated user feedback, (14) storytelling, and (15) charts with tabulated data.

In a previous study, we gathered responses from 118 individuals for 10 key elements on COVID-19 dashboards [2]. For this new and expanded survey, we surveyed 218 participants and introduced 5 additional attributes not previously explored in our research. These newer attributes are storytelling, predictive analytics leveraging AI, mobile compatibility, incorporated historical data, and consistency of data.

This survey was distributed using a combination of web-based platforms and direct outreach to ensure a wide and diverse demographic representation. The anonymous Google Forms survey was administered to the public by either providing a tablet device to employees and patients in medical clinics in Germantown, MD, Rockville, MD, Charlestown, WV, and Lansdowne, VA as well as an email sent to participants nationwide. The online survey stated the benefits of the healthcare dashboard study and informed the participants that the results collected were anonymous. The target population was adults over the age of 18 in the United States.

Data Analysis

This survey was distributed using a combination of web-based platforms and direct outreach to ensure a wide and diverse demographic representation. Participants who did not respond were sent a follow-up email. Measures were taken to minimize response biases by ensuring anonymity, randomizing the order of questions, and providing clear and neutral question wording. In addition, the survey was pretested with a small group to identify and rectify any potential sources of bias or confusion. The survey consisted of 15 questions. Responses of "yes" counted as 1 point, while responses of "no" counted as 0 points. The data from the survey was imported into Excel and online calculators by two different operators to perform the statistical analysis. These analyses were frequencies, descriptive statistics, and a comparison of design attributes with a prior study.

Demographic Information

Demographic data including county, state, and gender were included for all survey participants. Survey respondents represented a diverse range of 10 US states, including Maryland, Virginia, and Texas. The team aimed to ensure that they included at least 5 different US states. In accordance, the selection process satisfied the team's candidate attributes, as data were collected from a larger number of states than originally contemplated.

Ethical Considerations

Online data collected from this study were anonymous. A waiver from the Bullis School ethics committee was granted retrospectively.

Results

Overview

The survey aimed to help the impact of web-based learning through data dashboards on all health care information. Previous studies have highlighted how to easily read dashboards instead of the specific dashboard designs that would benefit users. The survey was developed using credible questionnaire resources, such as Google Forms and Survey Monkey, and tailored to our study needs. This survey was pretested with a small group of students to receive feedback and improve clarity and flow. The inclusion criteria were that all participants had to be aged 18 years or older and a total of 3259 responses were recorded (Table 1). The number of questionnaire respondents was 218 and the response rate was 89% (244/218). The authors conducted a survey of 218 individuals aged 18 years or older. The authors calculated a total of 3259 responses with 2945 responses of "yes" and 314 responses of "no."

The "use of charts with tabulated data" had the lowest percent agreement of "yes" responses of 83% (182/218), whereas "easy navigation" had the highest percent agreement of "yes" responses of 96% (209/218), and the "use of predictive analytics using AI" had "yes" responses of 87% (188/218), ranking at the 13th most popular attribute (Table 2).

Textbox 1 shows the five new dashboard attributes added to this study in comparison to the prior Malkani study on dashboards. These new attributes incorporate new technologies, such as mobile and artificial intelligence and 3 other attributes comprising the top 15 attributes design attributes for health care dashboards. The following sections provide a discussion for each of the 15 design attributes.

Table 1. Demographic results of the public health dashboard design survey, 2023 (N=218).

Measure and item	Individuals, n (%)
Sex	
Male	82 (61.9)
Female	135 (37.6)
Gender	
Nonbinary	1 (0.5)
Age (years)	
18-29	61 (28.1)
30-39	25 (11.5)
40-49	54 (24.9)
50-59	26 (12)
60-69	18 (8.3)
70-79	26 (12)
80-89	6 (2.8)
90+	1 (0.5)
State of residence	
Maryland	46 (21.2)
West Virginia	70 (32.4)
Virginia	45 (20.8)
New Jersey	22 (10.1)
Pennsylvania	12 (0.056)
Missouri	8 (0.037)
Iowa	3 (0.014)
Texas	2 (0.009)
Ohio	2 (0.009)
South Carolina	3 (0.014)
Indiana	1 (0.005)
Florida	1 (0.005)
Tennessee	1 (0.005)

Table 2. Results of health dashboard design survey, 2023 (N=218).

Rank	Dashboard feature	"No" (0; mean 21, SD 8, range 9-36; median 21, IQR 15-25)	"Yes" (1; mean 197, SD 8, range 182-209; median 195, IQR 193-202)	Total points (mean 217, SD 1, range 215-218; median 217, IQR 217-218)	Percentage of agreement (%; mean 91%, SD 4%, range 83%-96%; median 91%, IQR 88%-94%)
1	Easy navigation	9	209	218	96
2	Incorporated historical data	10	207	217	95
3	Simplicity of design	14	204	218	94
4	High usability	14	204	218	94
5	Use of clear descriptions	16	201	217	93
6	Consistency of data	16	201	217	93
7	Use of diverse chart types	23	195	218	91
8	Compliance with the Americans with Disabilities Act	20	195	215	91
9	Incorporated user feedback	21	195	216	91
10	Mobile compatibility	23	194	217	89
11	Comparison data with other entities	26	192	218	88
12	Storytelling	24	193	217	88
13	Predictive analytics with artificial intelligence	29	188	217	87
14	Adjustable thresholds	33	185	218	85
15	Charts with tabulated data	36	182	218	83
Total		314	2945	3259	90

Textbox 1. Key design attributes for public facing health care dashboards including 5 new attributes as bolded in a usability study, 2023 (N=218).

The top 15 medical dashboard design attributes (N=218)

- Easy navigation
- Incorporated historical data
- Simplicity of design
- High usability
- Use of clear descriptions
- Consistency of data
- Use of diverse chart types
- Compliance with the Americans with Disabilities Act
- Incorporated user feedback
- Mobile compatibility
- Comparison data with other entities
- Storytelling
- Predictive analytics with artificial intelligence
- Adjustable thresholds
- Charts with tabulated data

Easy Navigation

The ability to navigate through various pages and windows of a health care dashboard with ease is an essential and top-rated element of a health care dashboard. Users of health care dashboards should be able to navigate fully throughout the dashboard regardless of education level or background [13,14]. While reviewing over 250 different health care dashboards, it was noted that many of the dashboards were difficult to navigate due to erroneous navigation features such as unclickable links

and no scroll bars. We noted that several modifications could be introduced in some of the dashboards regarding the dimensions and positioning of the navigation elements, aligning them more closely with the more efficient dashboards or data services like those found in Apple or Samsung mobile phones. In addition, a health care dashboard should allow a user to hover over a data element to review additional information regarding that element of data, known as a "focus mode" [15] for a data dashboard or website. Easy navigation can be a major key to the success of health care dashboards and should be advanced further in many health care dashboards. It ranked as the #1 design attribute out of 15 design attributes based on the 218-person survey.

High Usability

High usability for health care dashboards is a key concept for dashboard design. The attribute of high usability can be achieved through faster loading speeds, consistent labeling, simpler layouts, and optimization for multiple devices. Poor responsiveness of the dashboard can negatively affect the perception of the quality and reliability of your dashboard. Using simple, clear, and consistently labeled data with highly readable fonts and text, effective labeling, and avoiding clutter and distortion helps optimize usability [16-18].

A good dashboard should have a simple layout with a logical and coherent structure, with a clear hierarchy, flow, and balance. Using grids, white space, borders, and headings to create visual separation and alignment among elements can help create harmony and proportion on the dashboard, helping the user process the information quickly. Finally, health care dashboards with high usability should have accurate, clear, and concise information to increase the adoption and use of the dashboard and its information.

Use of Adjustable Thresholds

An adjustable threshold customizes the level of specificity that a graph or other charts show and makes the dashboard more interactive. The use of interactive and adjustable thresholds is a principal factor to incorporate in health care dashboards. They are advantageous as users can interact with the dashboard and modify its parameters through these adjustable thresholds. For example, a short 10-day period may not be able to capture noticeable fluctuations in COVID-19 or mpox cases [15,19]. Expanding the view, a 90-day threshold, for example, brings benefits when assessing the dashboard more comprehensively. Incorporating adjustable thresholds based on percentages offers greater flexibility enabling easier and effective evaluation of the data. Transitioning from daily to monthly statistics or changing data trends over an extended period helps improve insights. This method proves significantly more potent, helping streamline data evaluation.

The interactivity of the dashboards makes the experience more intuitive, responsive, and meaningful, allowing the user to filter, drill down, zoom, highlight, and compare data as needed.

Use of Diverse Types of Charts

In a health care dashboard, incorporating a diverse set of chart types offers many advantages. To diversify visualization options and expand the scope of the information presented, it is important to offer a variety of chart types such as bar, line, and pie charts. Considering the diverse range of dashboard users, the addition of elements other than line charts, such as heat maps, can add variety, and help with comprehension by different user groups. Studies show that users prefer to review various chart types. In addition, interactive graphs that allow users to explore data from different perspectives can be valuable additions.

Use of Charts With Tabulated Data

The use of charts with tabulated data can be immensely helpful because it improves data comprehension, enables the ability to see and track trends in the data, and promotes data exploration. Tables allow a deeper dive into the numbers and help examine exact values instead of focusing on approximations or visualizations. For example, displaying the number of illnesses diagnosed over a specific period may be easier to accomplish with a chart by simply showing numbers and locations. However, a tabulated format is more useful when it is necessary to communicate other additional variables as well such as causes, outcomes, and even specifics about the length of the illness, number of relapses, and more.

Incorporated User Feedback

Health care dashboards are powerful tools, but they are not static. As a best practice, they should be constantly updated and improved based on feedback from the user [13]. User satisfaction and feedback are important concepts for the design of health care dashboards. While the designers of dashboards try to anticipate the concerns of users, it is vital to have a quick and simple system for users to express their suggestions about the dashboard. With a similar system, designers can incorporate feedback into their dashboards and attract more user activity. By applying user feedback, designers of health care dashboards can optimize the comprehensibility of their information. User feedback provides designers with valuable insights into user perspectives, helping them identify potential enhancements, and rendering data more accessible and comprehensive. Designs that incorporate feedback from the user and continuously monitor and evaluate the feedback data help keep the dashboard updated, relevant, and user-friendly.

Simplicity of Design

Simplicity of design is a key factor for creating a well-designed health care dashboard. Users should be able to navigate any health care dashboard easily and effectively. Based on the authors' survey of 218 adults, the design of health care dashboards should not be complex. The amount of text on each page should be kept to a minimum and information should be presented simply and concisely. The most important and urgent information should be shown on the first pages while less relevant information should be displayed later. Users should be able to search for more details as they navigate the dashboard. The simplicity of design allows all users, regardless of their age or background, to easily interpret and analyze data.

Adding Clear Descriptions for Charts

Since data displayed in charts can be overwhelming, complicated, or difficult to understand, it is important that there

are clear and concise descriptions for charts. Descriptions should be simple, while still getting the information across. With clear axis labels, units, and scales of measure, as well as titles, the users can easily comprehend the data.

Compliance With the ADA

To ensure equal access to information to all people across the United States, health care dashboards should make efforts to abide by the ADA. For example, there are an estimated 300 million people in the world with color vision deficiency and red-green color blindness is the most common form of color blindness [20]. To address this issue, health care dashboards should refrain from using red and green colors. The dashboards should make sure that the alerting system is also differentiated in some other way besides color, for example, pairing light and dark colors or light and dark variations of individual colors. Health care professionals' dashboards should use the ADA website to ensure equal access to health care dashboards for all people across the United States.

Comparison of Data With Other Entities

Comparison of data with other reference groups is essential for a health care dashboard to be easily read and understood. By comparing and displaying different elements such as demographics users can compare their own experiences with other groups in similar situations, proving a valuable tool toward better comprehension. For example, the number of mpox cases in Canada versus the United States displayed on a dashboard allows users to understand the prevalence and potential risk of mpox in the context of their own lives and locality. It can also warn or help make educated predictions about what could potentially arise in the future due to the number of cases or deaths in a neighboring area. Dashboards are intended to inform the public about information that should help them make informed decisions not only about the current situation but also the future.

Historical Data

Comparison with historical data on a health care dashboard is highly effective because it allows for meaningful comparisons in terms of any changes. Providing historical data on health care dashboards will enable users to identify and analyze specific trends and patterns to make their own decisions based on past experiences. Being able to track data throughout the years and using it to make future decisions makes historical data important in a variety of health care–related situations.

Storytelling

When presenting data, storytelling is vital for building relevance and aiding in comprehension. When a person reviews a chart or selection of data in a limited and isolated manner it can lead to a lack of comprehension. Converting the data within the context of the background helps create a narrative helping in relevance and comprehension. For example, a story can be presented through points on the graph, explaining a particular event and why it affected the data, or through creating a section outside of the data to explain all factors that could have created trends that were shown. Through storytelling, a viewer can fully grasp and better understand the information. It also helps create a "timeline" of events, as well as a link to future events or actions that may affect the data in question.

Consistency of Data

The consistency of data in health care dashboards is crucial for accurate and reliable information. Consistency refers to the quality of the data and in reference to data being accurate, uniform, dependable, and up-to-date throughout. Maintaining consistency ensures that the data presented on the dashboard are trustworthy and can be used for informed decisions. Throughout health care dashboards, data are collected from complicated systems and sources, and consistency becomes one of the most crucial factors to help in comprehension. As an example, consistency should be shown through the different axes of the charts having the same scale of measure. Consistency of data enables health care professionals, policymakers, and researchers to analyze trends and make informed decisions based on accurate, comparable, and reasonable data. Most importantly the consistency of data in health care dashboards affirms the credibility of the information provided and improves the effectiveness of the data.

Predictive Analytics With AI

As our world continues to develop, predictive analytics based on AI technology is increasingly relevant and beneficial. It is only fitting that predictive analytics using AI should be applied to the field of health care informatics research. If the user can input certain individual parameters, the dashboards should be able to provide predictive analytics for any parameter or question. Using predictive analytics, analysts can examine how data trends may fare in the future, and a user can review a detailed example of future data [21]. Predictive analytics of potential future trends are important for dashboards and data as they allow users to make decisions for themselves beyond the expectation of a linear trend. When viewing data for even a few past years, consumers assume linear trends and make predictions based on their perception of what data will look like in the future. Performing a similar analysis with predictive analytics with AI will provide more accurate predictions and allow people to make better medical decisions.

Mobile Compatibility

The best health care dashboards are designed with mobile compatibility. Health informaticians increasingly aim to make health care dashboards accessible and usable on diverse types of devices. Mobile compatibility is important given that most users spend a great deal of time viewing and accessing information on their mobile devices. Mobile compatibility is important for 3 reasons. First, mobile compatibility empowers users with the ability to access critical data anytime and anywhere allowing real-time data tracking, timely updates, and retrieval. Second, mobile compatibility ensures that charts and graphs seamlessly adjust to the screen dimensions of the user's device. This adaptation optimizes data visualization and user experience by presenting data in an easily comprehensible format, regardless of the screen size. Finally, mobile compatibility enables health care dashboards to leverage the unique functionalities of different devices. For instance, when data are accessed on a smartphone, these dashboards can use

features like “push notifications” to provide users with instant updates and keep them informed about the latest health care information. Given the widespread use of mobile devices in society, it is imperative to publish health care dashboards compatible with a range of devices, from large public displays to compact cell phones, thereby promoting broader accessibility to health care data.

Discussion

Principal Findings

Health dashboards are an important part of the health-data world which provides insight into health information through easily accessible images, charts, and representations. We found that the top 5 most important design attributes for an effective health care dashboard are easy navigation, simplicity of design, high usability, use of clear descriptions, and use of diverse chart types. The results from this research produce the top 15 design attributes for an effective health care dashboard. As health care dashboards are better designed, the idea is that the public will make better-informed health care decisions which will in turn increase health care outcomes. These specific 15 design attributes have been generally discussed in previous literature for health care dashboards, but this is the first time they have been specifically identified for health care dashboards. Similar studies have supported this overall research stream but do not compete with or overlap with these results. AI-generated dashboards in particular may have certain ethical biases that would lead to potentially incorrect conclusions by the public. The user of the dashboard should be informed if AI has been used in predictive analytics, for example, and the characteristics of the data (ie, size, type, kind, and location) should be available for the user to access to address the ethical concerns about the use of AI in health care.

The findings add to the prior literature on the design attributes for healthcare dashboards [2, 10, 15, 19, 21, 22]. As prior publications emphasize the importance of healthcare dashboards [4, 6, 17], this study focused on the design characteristics of healthcare dashboards.

Ansari et al [21] stated that usability problems exist with public health dashboards. Their checklist can be used in concert with these best practices for the healthcare dashboards. Karami at al [10] developed 7 key concepts and criteria for effective dashboards, whereas this study provides 15 best practices for healthcare dashboards. Murphy et al [13] stated that informatics and human factors principles should be incorporated into dashboard design. We provide human factor and informatics factors in the best practices for the design of dashboards. Malkani et al [2] developed best practices for the design of COVID dashboards. This study builds on those results and is focused on the broader topic of healthcare dashboards. Khodaveisi at al [19] provided the characteristics of COVID dashboards like Malkani. Finally, Martins et al [15] provide the best practices for dashboards for business management. These studies are consistent with this study and the prior literature is not in conflict with the results.

Limitations

Over 70% of the study’s participants (161/218) were from the 3 US states including Maryland, West Virginia, and Virginia. The study, therefore, is limited as far as the generalizability across the entire United States is concerned. Furthermore, with only 218 participants the study could have had a greater impact if it were for example over 1000 participants with at least 5 to 10 participants per state. Beyond the number and location of the participants, this study is limited in scope as it is based on self-reporting by the public for what they consider a positive dashboard design. It does not measure whether a better dashboard design, for example, results in a better actual health care decision. Beyond these limitations, this study is important as it attempts to quantify the top 15 elements of health care dashboard design which is undocumented in this context in previous literature.

Conclusion

As technology evolves, the availability of resources and data has become increasingly easier and better. With a click or a quick search, consumers have access to an abundance of health care data and data dashboards which aid in making informed health care decisions. However, health care dashboards may not be of the highest quality or as easily understood. Through our observational review and multiple surveys, we evaluated the effectiveness of health care dashboards in the United States to better understand and improve their design elements. From our analysis, we were able to develop and confirm the top 15 best practices of health care dashboard design from the ease of navigation to the use of predictive analytics. These 15 top best practices were assessed as the most important aspects of a health care dashboard’s effectiveness. The studies validated and concluded that the top 5 attributes of health care dashboards, such as easy navigation, simplicity of design, high usability, use of clear descriptions, and use of diverse chart types. As identified and analyzed, best practices can be incorporated in order to design and disseminate effective health care dashboards making valuable health care information available to the public. The availability of better health care dashboards will help consumers make better and more informed health care decisions resulting in better health care outcomes.

Conflicts of Interest

None declared.

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Abbreviations

ADA: Americans with Disabilities Act
AI: artificial intelligence

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Viewpoint

Applying Machine Learning Techniques to Implementation Science

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Abstract

Machine learning (ML) approaches could expand the usefulness and application of implementation science methods in clinical medicine and public health settings. The aim of this viewpoint is to introduce a roadmap for applying ML techniques to address implementation science questions, such as predicting what will work best, for whom, under what circumstances, and with what predicted level of support, and what and when adaptation or deimplementation are needed. We describe how ML approaches could be used and discuss challenges that implementation scientists and methodologists will need to consider when using ML throughout the stages of implementation.

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KEYWORDS

implementation science; machine learning; implementation strategies; techniques; implementation; prediction; adaptation; acceptance; challenges; scientist

Introduction

Implementation science is a research field developing and testing methods and strategies that can improve the uptake of evidence-based interventions (EBIs) and practices into routine use in targeted settings [1]. It has important applications in both clinical and public health settings, such as health care facilities, public health departments, schools, and workplaces [2-4]. For example, the RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance) framework, which was proposed by implementation scientists to guide the planning and evaluation of programs, has been used for health care– and community-based programs promoting chronic disease prevention and management, healthy aging, mental health, and health behavior change [5]. In addition, implementation science methods have been applied in clinical settings (eg, clinic-initiated cancer screening, tobacco cessation, and mental health programs) to scale up effective interventions to improve population health [4].

Implementation strategies are the methods, actions, and activities that aim to enhance the adoption, implementation, and sustainability of EBIs in clinical and public health practice. Implementation strategies can target multiple levels (eg, communities, hospitals, health care clinics, public health

departments, clinical and public health practitioners, and individual patients and community members) and may involve multiple components (eg, information technology tools, workflow changes, and policies mandating services) and activities (eg, training and incentives) [6,7]. Numerous factors, such as target populations and targeted behavior change, varied uptake of strategies across settings, the actors that deliver the implementation strategies, and the timing of the EBI implementation, can influence the implementation processes and outcomes [6-8]. Further, there is often a need to tailor or adapt implementation strategies and the associated activities to the local, dynamic context to increase implementation success. Given the multifactorial drivers and their complex relationships, implementation science could benefit from advanced data analytics frameworks and methods for artificial intelligence and machine learning (ML).

As a subfield of artificial intelligence, ML [9,10] develops automated methods and algorithms that learn from data. With this learning, it can then perform tasks such as prediction and pattern discovery. To date, ML applications in health care settings have been focused on supplementing clinical work, predicting health-related outcomes (eg, disease severity and prognosis) [11-14], and supporting clinical decisions (eg, tailoring medications and other treatments) [15-17]. Applications of ML in public health include population health surveillance and outbreak mitigation, evaluating the effectiveness of public health strategies and campaign and disaster and emergency alleviation [18-22]. Existing literature on the application of ML in the field of implementation science is sparse [23]. However, ML has great potential to be applied in areas such as tailoring strategies and support activities, supporting decision-making on the selection of actors or settings, and predicting and understanding the impact of implementation strategies on the adoption of EBIs across different settings and target populations. The aim of this viewpoint is to introduce a roadmap for applying ML techniques to address implementation science questions, describe a few limited real-world applications of ML related to implementation science, and discuss challenges that implementation scientists and methodologists may face along the way when using ML as a strategy to monitor EBI adoption or to inform the need for interventions.

A Roadmap for Applying ML in Implementation Science

ML approaches can be applied across the continuum of EBI implementation. Here, we use the strategic implementation framework (SIF) [24] as a roadmap to illustrate the potential application of ML at different stages of implementation, as summarized in Table 1. The SIF depicts 3 stages of implementation (ie, setting the stage; active implementation; and monitor, support, and sustain) and the distinct types of strategies needed for practice change in each stage to ensure that improvements are supported and sustained.

Table 1. Roadmap for implementation scientists and methodologists to use ML[a].

	Strategic implementation framework stages		
	Setting the stage	Active implementation	Monitor, support, and sustain
Implementation goals and activities	• Understand the local context to select implementation strategies and prepare for implementation	• Implement strategies and support activities to improve EBI[b]	• Monitor the sustained adoption of strategy and EBI improvements
Implementation challenges	• Limited data available or used • The context is not static • End users with differing priorities	• The context is not static • End users with differing priorities • Need to adapt to setting and targeted population	• The context is not static (new guidelines, policy, and care delivery)
Opportunities for ML application	• Predict who will adopt an EBI • Determine the level of support needed • Identify the need for change	• ML as a strategy	• Monitor progress • Inform need for deimplementation • Inform need for support
Considerations when using ML across the 3 stages	• Setting characteristics • Time period • Data completeness • Multilevel strategy	• N/A[c]	• Risk prediction bias • Recalibration of ML • Adaptation of ML • Deimplementation of ML

[a]ML: machine learning.

[b]EBI: evidence-based intervention.

[c]N/A: not applicable.

Setting the Stage

Setting the stage refers to preimplementation activities such as assessing readiness to change, identifying barriers and facilitators to implementing EBIs, selecting or developing strategies to support implementation, and identifying and acquiring resources. Implementation scientists often find that an effective strategy in one setting may not work well in other settings and that some may need more or different types of support (eg, hours of training, intensity of coaching support, or remote vs in-person training). As such, one of the biggest implementation science challenges is to identify what works,

for whom, under what circumstances, and with what level of support.

Typical approaches for selecting and tailoring implementation strategies to fit the local context (eg, process mapping, intervention mapping, and coincidence analysis) address this challenge at the organization or population levels [25]. Often, data to inform the selection of an implementation strategy are limited to surveys, qualitative interviews, and organization-level data. However, clinical or public health data (eg, electronic health records [EHRs], administrative data, claims data, patient or disease registries, immunization registries, and health surveys), data linkages (eg, EHR data linked across practice sites, water quality, and air quality), and data related to implementation processes (eg, responses of patients, community members, and practitioners to a specific implementation science strategy from prior studies) are increasingly available. Implementation scientists could use ML to analyze large-scale, individual-level data to identify or predict who (individuals or subpopulations) is most likely (or least likely) to engage or respond to the intervention [26,27]. Specifically, the application of ML in the preimplementation stage could assist with the selection of the settings or actors, refinement of implementation strategies, and decisions about support activities. ML techniques could predict which sites, practitioners, or target populations will most likely respond well to certain implementation strategies (such as a training session or a health information technology tool), are most likely to need extra support, or might respond better to different strategies. These analyses could be based on prior engagement with strategies that led to increased adoption of EBIs or known characteristics of community (eg, census and environmental health), health systems (eg, geographic location), providers (eg, years of practice), patients (eg, race and ethnicity), and other targeted users.

There are currently no studies using ML approaches to tailor implementation strategies or support needs in the preimplementation stage. A few studies have used unsupervised statistical learning methods, such as latent class analysis and latent profile analysis [28], to identify subgroups of health care providers [27] and patients [26] responding differently to implementation strategies that promote provider-patient communication on critical illness or patients' physical activities for weight reduction. For example, one study identified 3 groups (or phenotypes) of oncologists based on demographics, practice patterns, and patient panel information [27]. These phenotypes showed different responses to an EHR-based intervention (EHR nudges) aimed at improving advance care planning (ACP) discussion. Oncologists with the lowest volume of patients and a higher rate of baseline ACP discussion showed the greatest improvement compared to those with higher volume or lowest baseline ACP and intermediate volume or baseline ACP. One study used a supervised learning model to identify areas where the implementation of HIV prevention programs should be prioritized. Using state surveillance data on substance use, sexually transmitted diseases, and community characteristics (eg, percent living in poverty), ML modeling identified high-priority areas, of which 79% did not have implemented syringe services programs [29]. Similar modeling approaches could be used to better identify who will adopt what implementation strategies with what supports and tailor resource allocation before an implementation program is launched to improve the adoption and sustainability of EBIs.

Further, ML applications during the setting the stage could also facilitate monitoring when interventions are needed. For instance, using continuously collected clinical or public health data and ML-based phenotyping methods [27], it is possible to prioritize target populations who need the EBIs most at different time points or stages of the implementation of an intervention. Modeling could also trigger notifications to local clinics and public health departments about changes in quality metrics that require improvement, the resources needed to make an improvement (eg, additional staff), or changes in an environmental context (eg, climate change) [30] that could impact disease incidences and health care needs.

Active Implementation

During the active implementation stage, strategies and support activities are implemented to promote the adoption of an EBI (eg, disease surveillance, prescribing shingles vaccination, and lung cancer screening). During this stage, ML techniques could be incorporated as an implementation strategy. ML-based algorithms relating to the active implementation stage are currently being used to support making accurate diagnoses, disease risk estimation and surveillance, public health campaigns, and clinical decision-making. One example is the use of an ML model to identify foodborne illness in real time (FINDER). This model was developed, implemented, and tested in 2 US cities. FINDER would provide a daily list of restaurants identified as unsafe (likely to have health code violation). Health departments would then conduct an inspection in the restaurants identified by FINDER. The model identified accurately more unsafe restaurants than the previous system or reported complaints [31]. Examples in palliative care include a deep learning model that incorporates patients' EHR data to predict mortality (those patients most likely to die within 3-12 months). The model-generated estimates were used to inform providers' care recommendations and decisions about referring patients to palliative care [32,33]. In the context of cancer screening, ML models based on reinforcement learning or ensemble learning are being developed to more accurately identify patients with high risk of cancer [34,35]. These models could be used for cancer screening to balance the benefits of early detection and the costs of overscreening.

Further, in clinical care, clinical decision support (CDS) tools [36,37], including EHR alerts, are common implementation strategies used to promote guideline-concordant practice. ML can be used to develop "smarter" CDS tools to reduce alert fatigue. For example, an ML model was developed to predict whether a provider would respond to shingles vaccination alerts based on the provider's characteristics (eg, demographics and clinical roles), patient's demographics, and history of the provider's interaction with the alerts [38]. The ML model was shown to reduce over 45% of shingles vaccination alerts without reducing weekly shingles vaccination orders [38].

Monitor, Support, and Sustain

This stage focuses on activities that ensure the sustainability of an intervention. During the monitor, support, and sustain stage, ML can inform changes needed to ensure the adoption and sustainability of practice changes. ML-based methods can leverage vast amounts of data to inform more flexible and adaptive implementation strategies. ML can also facilitate the evaluation and adaptation of strategies and inform where deimplementation is needed. For instance, ML could be used to identify when public health campaigns have reached saturation, need to be refocused, or are missing the target population. For example, during the COVID-19 pandemic, studies use ML models to identify people at greatest risk for COVID-19 death and who should be prioritized for vaccination. Different studies using different populations showed variations in who should be prioritized in informing local public health efforts [39-42]. For example, in clinical practice, implementation scientists leveraged both EHR audit logs and innovative ML-based approaches to monitor the impact of implementing a tobacco control CDS tool in the EHR system [43-45]. According to the Health Information Portability and Accountability Act (HIPAA) [46] and the 2014 release of the Meaningful Use regulations [47], all the EHRs in the United States are required to implement audit logs to unobtrusively track users' EHR use. In a recent study, a latent-variable statistical ML model was developed to infer EHR-use activities from EHR audit log data [44]. Specifically, the ML model identified topics from EHR log data, where each topic was represented by a probability distribution of microlevel EHR actions such as loading a flow sheet, viewing a problem list, and using a favorite phrase predefined in EHR. Domain experts (3 physicians and 1 EHR specialist) reviewed these topics (eg, the top-ranked microlevel EHR actions belonging to each topic and example EHR sessions representative for each topic) and assigned an EHR-use activity (eg, visit documentation with record review and address CDS alerts) to each topic. This domain expert–informed model was then applied to EHR logs for 3703 encounters (before CDS implementation: n=2633 and after CDS implementation: n=1070) in 4 cancer clinics to monitor changes in providers' EHR-use between 2019 and 2020 [45]. This study found that clinicians spent more time addressing CDS (more than 32-35 seconds) during a patient visit after CDS implementation (vs before CDS implementation), with compensatory unintended reductions in time spent reviewing patient vital data (less than 61 seconds) and modifying EHR (less than 7-24 seconds) [45]. These findings pointed to potential adaptations of the CDS to improve efficacy and reduce burden [43]. These data-driven findings can inform qualitative studies that aim to understand the causes of the unintended consequences and further inform the decision on refining or deimplementing certain features of the CDS tool.

In summary, despite very few real-world applications of ML in implementation science, there are many options and opportunities to use ML at different stages of implementation; however, some factors are important to take into consideration.

What Are the Factors to Consider in Using ML for Implementation Science?

As illustrated earlier, ML applications can potentially benefit implementation science across each of the SIF stages. However, many factors can impact the use or validity of these ML-based applications in real-world settings, including achieving equitable outcomes across multiple settings or subpopulations [48].

There are various techniques used in ML [49]. Supervised learning methods can be used to build predictive models (eg, prediction of patients' risks in illness or poor prognosis and responses of community members, patients, or providers to EBIs and implementation science strategies). Unsupervised learning methods can be used to mine data to identify patterns (eg, identify subgroups of population, patients, and health systems who have different responses to EBIs and implementation strategies). A common practice to develop and validate supervised ML models includes two stages: (1) using a data set to develop and validate (ie, internal validation) the model and (2) using a separate data set (obtained from other similar settings or from a withheld sample) to validate (ie, external validation) the developed model [50,51]. In the first stage, the model can be trained or validated through cross-validation or using a random split of the data set (eg, training or development or validation sets). The model's parameters and hyperparameters are tuned or set using the training and development sets. In the second stage, the model's performance is further assessed on the external validation set. Different from supervised learning, there is no ground truth (eg, labels for clusters or subgroups identified by unsupervised learning) to validate results from unsupervised learning in a real-world setting. Consequently, the evaluation process for unsupervised learning is less standard than supervised learning, and the choice of evaluation measures often depends on the unsupervised learning algorithms that are used [52,53]. In general, the quality of clustering results can be measured in 2 aspects when no external references (ie, ground truth) are available: coherence (ie, the similarity of objects falling into the same cluster) and separation (ie, the separation between clusters). Manual chart review is also useful or even necessary for qualitatively validating the clustering results in clinical settings [54]. Both supervised and unsupervised models developed on a specific sample or data set may not be readily applicable to other samples or data sets—the issue with generalizing ML models to different settings [55,56]. This issue has important implications on the use of ML in implementation science and requires paying special attention to model design, development, and validation.

The first factor to consider is that implementation strategies can be implemented at multiple levels (eg, state, county, community, population, health systems, clinicians, and patients), which would determine at which level the ML models would be based. Models developed and validated using data from one level (eg, clinic or community) need further validation and adaptation before being used for predicting outcomes at another level (eg, patient) or an intervention implemented at multiple levels [57]. For example, within the setting the stage phase, a model could

be developed using clinician and clinic characteristics (eg, specialty, provider type, and clinic geographic location) to predict which clinicians or clinics will be most likely to adopt a CDS tool. This model, however, is unlikely to be sufficient or valid in predicting the adoption of a multilevel intervention that targets both clinicians and patients (using provider nudges via EHR and patient nudges via SMS text messages). Similarly, public health programs (eg, a tobacco control or vaccination program) often use strategies targeting various levels within a public health jurisdiction (eg, individual, city, county, and state). An ML model predicting the adoption or success of such programs needs to take into account multilevel factors.

Second, the setting (eg, type of clinic and social culture of a specific community), its geographic location, and the time period used in validating the ML model are important factors to consider. These contextual factors are important in implementation science as they impact which strategy or combination of strategies are selected to scale up or modify to ensure the adoption and sustainability of EBI. Models that predict the adoption or sustainability of an implementation strategy developed in primary care clinics are unlikely to have an adequate prediction in specialty clinics in the setting the stage phase. Similarly, an ML-based strategy to improve an EBI in a rural community setting will likely need adaptation to be valid in an urban community setting. Additionally, the time period in which the model was developed needs to be taken into account. For instance, ML-based CDS developed prior to the COVID-19 pandemic may be obsolete or invalid after the pandemic in view of the widespread adoption of telehealth.

Third, when using ML models as an implementation strategy for risk prediction, they should be designed to predict the actual targeted outcome rather than the outcome that is easiest to obtain. For example, consider a risk prediction model being used to direct palliative care interventions. It is easier to train an ML-based tool to predict mortality, as a surrogate for palliative care needs, because mortality is less susceptible to measurement error and is available in palliative care medical records [58,59]. However, training an algorithm on mortality may not identify the individuals with high symptomatic or psychosocial needs who would benefit from palliative care the most. Targeting the risk prediction to the outcome that is most likely to matter for the EBI being implemented is imperative.

Finally, it is critically important to develop and validate models with equity in mind. Many of the algorithms developed in medicine are based on trials with nonrepresentative samples [60]. A recent publication examining various race-biased algorithms used for medical risk predictions demonstrated the potentially harmful consequences of biased algorithms [61]. Within implementation science, as noted earlier, strategies may not work for all. ML models validated in a specific population (eg, pediatric patients) within a specific setting (eg, hospital) could be misused and inequitable if used in a different population (eg, Latino pediatric patients receiving care in a community health center). The learning here is that ML-based implementation strategies need to be tested, validated, and adapted to fit the context of the targeted population to ensure health equity.

What Are the Challenges?

Overview

Despite the large amount of clinical data and data from pragmatic implementation trials, there are many challenges associated with data access and data quality. Further, the tools and resources needed to extract and preprocess these data for developing ML may not be easily accessible. For example, extracting and harmonizing patient-level data from the EHRs from multiple health systems to develop a preimplementation ML model could be particularly difficult and time-consuming if these health systems have different EHR vendors. Furthermore, the application of ML in implementation science may result in unintended consequences, and issues related to the sustainability and scalability of the model need to be addressed.

Data: Quality, Availability, and Type

Public health data and information systems vary with regard to data quality, completeness, collection methods by systems, sampling bias, and underreporting [62-64]. In addition, the collection and generation of public health data are often time-consuming, resulting in delays in data reporting. Similarly, clinical-related data, such as EHR or health insurance claims data, are not designed for research and as such may not be collected and recorded in a systematic standard way. For example, comprehensiveness, completeness, and availability of patient demographic information (eg, race or ethnicity), health insurance data, and clinician data vary greatly by health systems and EHR vendors [65-71]. Additionally, some information that can be critical in the accuracy of ML prediction may reside in unstructured data (eg, a scanned PDF and free text of an encounter note) and, therefore, would require additional preprocessing steps, such as natural language processing [72]. Missing clinical-related data are unlikely to be random [70]. Specifically, EHR data come from a combination of clinician notes, test orders and results, documentation of diagnoses, and patient-reported information. The accuracy and completeness of these data are dependent on the source of the information. For example, the history of a cancer diagnosis can be derived from clinician diagnosis, clinical exchange systems, and patient self-reported history. A study linked EHR data with cancer registry to assess the accuracy of cancer diagnosis in the EHR [66]. Authors found that approximately 45% of cases recorded in the registry did not have a cancer history in their EHR. This information may have been in unstructured data such as in encounter notes. Data used for training an ML model may underrepresent certain patient subgroups [71]. For example, the use of insurance claims data excludes patients without health insurance, and these patients are often socioeconomically disadvantaged individuals. Variation in data documentation and completeness impact not only predictor variables used in the ML models but also the outcome variables. For example, predictive models of emergency department admissions using claims data would miss patients who are uninsured and are more likely to rely on the emergency department for care [73]. Moreover, ML models designed to develop an intervention targeting health system, school system, or community-based

organization change may require data on staffing, supplies, or organizational capacity, which could be challenging to obtain.

Potential for Unintended Consequences

ML models, whether designed for predicting disease risk or for supporting clinical care management and decision-making, are susceptible to bias. Bias can be introduced at multiple points in the development and application process of ML [61,74,75]. As noted earlier, data sources and data representativeness (eg, the population, inclusion or exclusion of diseases, comorbidities, and health risk factors) can greatly influence the ML model and consequently the actions based on the ML model. Further, because ML models can generate data for other ML models, bias can be amplified and can lead to unintended consequences [76]. Char et al [77] proposed a framework for examining ethical considerations of ML models in health care settings, which poses questions about the values and ethics at multiple steps of the model development and implementation. This framework can guide decision-making to minimize bias and can promote accountability and transparency in model development.

Sustainability and Scalability of the Model

Public health interventions and campaigns are moving targets. For instance, climate change is leading public health departments to adapt or develop new initiatives for disaster preparedness efforts, disease surveillance, and carbon footprint reduction [78-80]. For instance, there is growing evidence of the mental health toll of climate-related events [81], yet strategies to monitor and intervene climate-related mental health burden are scarce [78]. Analogously, health care systems are ever-changing [82] as they must adapt to new clinical care guidelines, changes in reimbursement policies, care delivery modality (ie, telemedicine), quality improvement efforts, and local, state, or federal law amendments. For example, in April 2020, the American Society of Colposcopy and Cervical Pathology released new guidelines to provide recommendations on cervical cancer screening frequency and follow-up tests for abnormal cervical cancer results [83]. These guidelines significantly differ from the previous 2012 version [84]. Any implementation strategies designed to facilitate the adoption of the 2012 guidelines became obsolete and needed to be revised. For another example, EHR-based patient portals are efficient systems for communication between patients and health care providers and platforms for health information exchange. These portals can be a platform for patient-centered implementation strategies to improve the uptake of evidence-based practice. Patient portal tools have been used to improve the uptake of ACP or lung cancer screening [85]. Patient portal adoption before the COVID-19 pandemic, however, remained relatively low and varied widely across patient subgroups (eg, by age and socioeconomic status), diminishing the effectiveness of strategies implemented within the portal [86,87]. The need for social distancing and the uptake of telemedicine during the COVID-19 pandemic led to a rise in patient portal use, which could improve the reach of such strategies [88]. The uptake in patient portal during the pandemic was also associated with a rise in “e-visits,” which were communications between patients and clinicians between in-person visits [89,90]. This led to health care systems to bill for these messages following existing federal rules [90,91], which in turn may limit the use of patient portals and impact their effectiveness as an implementation strategy. This example illustrates how the changes in the health care system can impact a specific implementation strategy. Consequently, the reach, adoption, and sustainability of the EBI it aimed to improve are also impacted. These ever-changing systems pose a significant complication when using ML models [92,93]. How frequently should an ML model be adapted or recalibrated to ensure that it has accurate predictions and is unbiased and ethical? This is a critical factor impacting the use of ML in implementation science and across the 3 stages of implementation and remains to be answered by future studies.

Conclusions

ML can assist with predicting what will work best, for whom, under what circumstances, and with what level of support, or what and when adaptation and deimplementation are needed. However, there are many remaining challenges with integrating ML into various stages of implementation, which require further research and investigation. Tackling these challenges has the potential to render ML as an innovative and useful tool in implementation science in years to come.

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Authors' Contributions

All authors substantially contributed to the conceptualization and edits of this viewpoint and approved the final version.

Conflicts of Interest

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Abbreviations

ACP: advance care planning
CDS: clinical decision support
EBI: evidence-based intervention
EHR: electronic health record
FINDER: foodborne illness in real time
HIPAA: Health Information Portability and Accountability Act
ML: machine learning
RE-AIM: Reach, Effectiveness, Adoption, Implementation, and Maintenance
SIF: strategic implementation framework

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Original Paper

Discussions With End Users to Inform the Vision for a Shared Care Record in Ontario: Qualitative Interview Study

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Abstract

Background: Improving the health outcomes of populations of individuals through population health management requires the use of electronic health records that can exchange real-time digital information using an accurate and complete shared care record that is accessible to health care providers, services, and patients.

Objective: The aims of this study were to understand end users' (health care providers) experiences, attitudes, and insights using current electronic health records; their expectations of what is required to establish a shared care record; and how they anticipate adapting to the use of a shared care record in daily practice. This work is the result of a quality improvement initiative deemed not to require ethics approval according to the Western research ethics board checklist.

Methods: Clinicians were contacted using voluntary response sampling and interviewed via Zoom (Zoom Video Communications) between June 2022 and July 2022. The participants were from various health care sectors and at various stages of career development.

Results: Overall, adaptation to the use of a shared care record was viewed positively by health care providers, highlighting the benefits of a centralized, shared, and accessible location for real-time data, promoting patient continuity of care. The main concerns included the privacy, confidentiality, and security of the record along with patients' ability to interpret their own medical information found in a patient portal. The resources requested by end users included multifaceted ongoing training on the use of a shared care record.

Conclusions: This study provides practical findings that will help emphasize factors that facilitate clinicians' practical use and process of adaptation to the use of a shared care record.

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KEYWORDS

population health management; shared care record; health information exchange

Introduction

Population Health Management

Defining population health management (PHM) requires taking a step back and thinking of the bigger picture. The Population Health Alliance PHM framework explains that "a population health management program strives to address health needs at all points along the continuum of health and wellbeing through the participation of, engagement with and targeted interventions for the population" [1]. Their definition specifies that the goal of PHM is to uphold or improve the "physical and psychosocial wellbeing of individuals through cost-effective and tailored health solutions." Breaking it down, PHM involves the use of data to proactively manage the health and well-being of an identified population of individuals while considering the diversities within that population along with their social determinants of health [2]. PHM is a constantly progressing concept that is increasing in popularity worldwide. For example, in Ontario, PHM has been characterized as a fundamental element in Ontario's health system transformation. In the Netherlands, several PHM initiatives are working to tackle the health-related social needs of residents by building partnerships among medical care, public health, social services, and community-based organizations [3]. Managing populations of patients based on their diagnosis while maintaining their health and keeping them out of dangerous circumstances has recently become popular as it affords the ability to deliver high-quality and efficient care that is satisfying to everyone involved [4]. Examples of leaders in PHM and integrated health care delivery include those in Denmark, Spain, and the United States, such as Geisinger, Memorial Hermann, the Department of Veterans Affairs, and Kaiser Permanente. Another important mention is Epic, a widely used software company among hospitals that allows for the exchange of medical records across organizations in the United States and beyond. They are all highly regarded for high-quality and efficient health care through integrated care delivery processes [5].

PHM can be viewed as improving the health outcomes of a population using appropriately coordinated care and proper patient engagement, which is sustained through adequate economic and care models [6]. The question then becomes how to best support the entire population clinically and financially. According to the *Health IT Playbook* [7], examples of PHM services involve efforts to proactively help people improve their health, guarantee they obtain preventive screenings, and help them effectively manage their chronic conditions. A vital feature of this approach to care delivery is that the population whose health is being managed is a complete group of people, not only those who are pursuing health care. This population can be defined in ways such as all the employees of an employer, members of a health insurance plan, or residents of a community, but the key feature in PHM is that the health of all members of this population is considered [7].

Another crucial aspect of PHM is coordinating a diverse and progressive group of stakeholders who work together to provide programs, services, and tools for interoperable care for patients in various health care settings [8]. This is also where the integration of services occurs, such as financing and delivery of health care working together [4]. According to Jones and Smith [4], an entirely integrated care system is defined as both horizontally and vertically integrated. Vertical integration combines provider and care delivery, financing, and support services such as IT. Horizontal integration combines provider services, home health services, hospitalization (tertiary and secondary), and ambulatory care, entailing continuous and seamless care [4].

Health Data

The growing burden of chronic diseases challenges health care system sustainability in countries worldwide. Working toward coordinating care to prevent unnecessary hospitalizations is a crucial solution to limiting increasing health care costs. According to Burnel [9], to reach this goal, clinicians and professionals must be able to exchange information using electronic health records (EHRs). An EHR is a real-time digital form of a patient's health care record, allowing information to be available to providers authorized to access it across different health care organizations instantly and safely [10]. Beyond providing a patient's collected medical data, an EHR offers a comprehensive view of a patient's care. An EHR contains information from all providers involved in a patient's care concerning admission documents, diagnostics, ongoing assessments, and health care plans and can be shared with other health care providers; caregivers; patients; and organizations, including laboratories, medical imaging facilities, specialists, pharmacies, and clinics [10]. EHRs make it possible to reduce medical errors, increase health care provider communication, and improve care coordination [11]. The broad implementation of EHR systems in primary care has permitted the compilation of enormous amounts of clinical data that have the potential for secondary use, such as improving clinical programs, system management, and population health research [12].

Shared Care Record

With EHRs in mind, the concept of the *shared care record* is introduced. A shared care record is an enabler that helps allow PHM to be possible. According to the Patient, Family, and Caregiver Declaration of Values for Ontario [13], to enable integrated care, each resident in Ontario ought to have access to their health-related information record, which is "accurate, complete, available and accessible across the provincial health system at [their] request." The record should be accessible to health care team members and patients as required and in a manner that encourages appropriate care and positive experiences. A complete and accurate shared care record includes up-to-date information about the person and their demographic information, the administrative services they use, their medical or clinical information, and additional health-related information involving the social determinants of health.

Shared care records permit all primary and secondary care providers to view and use a single dependable source of documentation that is up to date and provides accurate clinical information in real time about a patient [14]. It is about giving everyone access to the information they need but does not require everyone to be on one common information system.

Patient records from a variety of care providers and sources can be linked through a health information exchange (HIE) system. The vision of the shared care record would give providers, in the home database system they work in daily, access to information captured about their patients from other care providers and other systems. For example, a provider (or patient) can view medications prescribed by provider A alongside those prescribed by provider B in the same place even if providers A and B use different EHR technologies. This information could come from their primary care records, home and community care records, community mental health and addiction records, or hospital systems. Systems worldwide are using this approach to link information on allergies, laboratory test results, procedures, appointments, and much more. The HIE simply enables information exchange between systems, for example, between hospitals and primary care [15]. Moving this information between the systems aims to help the care team locate and use the correct information to provide safe, efficient, and equitable patient-centered care. This means that a patient only needs to describe their health care history once instead of sharing it multiple times at each health care encounter. If done properly, information from this system can also provide information to public health teams to understand the health and health needs of the population [15].

The Need to Reform Service Integration in Ontario

The current health care system in Ontario is experiencing increasing strain from the aging demographic, overloaded hospitals and emergency departments, and a significant increase in chronic diseases, putting our care delivery model at risk [16,17]. Completely changing the Ontario model of health care delivery is not feasible; therefore, we must work with the existing structures. One example is health IT systems that can be better connected to improve workflows; centralize health data; and deliver information to health care providers, patients, and families where and when they need it. Ontario is not alone; fragmented care exists among health care systems worldwide involving a lack of communication between primary care physicians, other health care providers, specialists, patients, and families, leading to negative impacts on patients and gaps in continuity of care. Many systems have realized the benefits of interoperability, "defined as the ability of different health information systems to cooperatively access, integrate and exchange data to advance effective delivery of health care" [16]. Several obstacles must be kept in mind when it comes to the electronic exchange of health information, such as technical, financial, legal, and privacy barriers that can impede the implementation of interoperability. Nonetheless, as health care providers request continuous integration of information and patients stress the need for access to health data, health care organizations will be forced to share information appropriately. This may require funding for information management technology such as EHRs and IT to enable care across the continuum [4,17].

The concepts of integrated care, digital health, interoperability software, and centralized health data, exemplified by the shared care record, are crucial to exposing the benefits of a restructured and better coordinated health care system. Collectively working toward a shared care record can help reduce medical errors, health care costs, and redundant and unproductive work while improving communication among health care providers, quality of patient care, and seamless transitions of patients across health care providers and settings to create a resourceful system [17,18].

Aim of the Study

This qualitative study used semistructured interviews to improve the understanding of end users' (health care providers) perspectives and insights regarding how they anticipate adapting to the use of a shared care record. Information gathered from the interviews will support the development of use case storyboards to inform various stakeholders across Ontario of considerations for developing a shared care record across the province. Talking with end users will help understand what a range of clinicians from different specialties believe is required to establish a shared care record and how they will adapt to its use over time.

Methods

Setting

Middlesex County is in Ontario's Southwestern region, covering a geographical area of 2800 km^2 and home to >450,000 people. This region consists of a mix of urban and rural residents. London is the largest metropolitan area within Middlesex County and is home to >450,000 residents. The region also surrounds 3 sovereign First Nations: the Chippewas of the Thames, Oneida Nation of the Thames, and Munsee-Delaware Nation. For several years, legislators in Canada's most populated province, Ontario, have endeavored to change the local health care system to create a more coordinated and financially united system [19]. This initiative resulted in the Government of Ontario Ministry of Health formation of 54 approved Ontario Health Teams (OHTs) within specific geographic areas across the province. OHTs modify how health care is financed and delivered and concentrate on collaborative partnerships in which providers and organizations such as primary care, mental health services, hospitals, and home and community care work as one synchronized team [20,21]. The Middlesex London OHT is specifically responsible for supporting the health of the population residing in the Southwestern Ontario region [22]. Using OHTs, the provincial government is assembling sustainable systems that will respond to local populations' short- and long-term needs, support local services, and enable straightforward system navigation and transition among providers [19,23]. Another critical player providing guidance and regulation is Ontario Health, a government-formed agency working to coordinate and connect the province's health care system [24]. This new visualization of Ontario's health care system is aligned with the Quadruple Aim, a framework internationally understood to design and provide a system that improves patient and caregiver experiences, patient and population health outcomes, and provider experiences while reducing total costs [23].

Participants and Recruitment

Using voluntary response sampling, clinicians were contacted via email based on preexisting professional relationships. A

total of 14 health care providers were interviewed, comprising those who volunteered or agreed to participate upon request. These health care providers hold positions in various care sectors, including nursing, community care, primary care, emergency medicine, dietetics, practice specialties, occupational therapy, and physiotherapy. The list of health care provider interviewees who agreed to participate in the data collection, organized by occupation, is shown in Table 1. The providers also ranged widely across stages of career development and duration, from new graduates to experienced employees.

Table 1. Interviewees.

Professional title	Care setting	Professionals (N=14), n (%)
Registered nurse	Inpatient acute care	3 (21)
Registered nurse	Cardiac outpatient clinic	1 (7)
Registered nurse	NSWOC[a]	1 (7)
Clinical nurse specialist	Chronic diseases and clinical informatics	1 (7)
Clinical dietician	Bariatric outpatient clinic	1 (7)
Physician	Emergency medicine	1 (7)
Physician	Primary care practitioner	1 (7)
Registered physiotherapist	Outpatient clinic and inpatient acute care	1 (7)
Registered practical nurse	Home and community care	1 (7)
Clinical practice specialist	Occupational therapy	1 (7)
Clinical practice specialist	Palliative care and oncology	1 (7)
Occupational therapist	Home and community care	1 (7)

[a]NSWOC: Nurse Specialized in Wound, Ostomy and Continence.

Data Collection

Participants in the study were first introduced to the concept of a shared care record verbally and through a video demonstrating its functionality. All participant questions about a shared care record were answered before the interviews. A semistructured question guide ensured that each interview covered essential topics and allowed participants to disclose issues and stories as they saw relevant. The use of a prepared guide also worked to decrease interviewer bias by decreasing interviewer involvement. Confidentiality and anonymity were established at the beginning of the interviews. Verbal consent was obtained from each participant to potentially use quotes from the discussions in future publications or presentation materials that result from the initiative. The semistructured interviews averaged 15 (SD 2.56) minutes and were web-based via Zoom (Zoom Video Communications) between June 2022 and July 2022.

The interview format was chosen, as opposed to focus groups, as it allowed for direct, individual engagement with each end user. Stokes and Bergin [25] discussed the opportunity for the interviewee to truly analyze their motivations for a particular action while being given a feeling of empowerment because of the anonymity in the individual interview setting without the pressures of a group setting that may lead to a consensus view. The interviews were designed to elicit the health care providers' understanding of and experiences with the EHRs they currently use along with their attitudes, beliefs, and expectations regarding the future use of a shared care record in their daily practice. The sequence of interview questions used and additional instructions to guide the interview are shown in Table 2. The interviews were audio recorded with permission from the participants, transcribed using web-based software, checked for accuracy, and then analyzed to develop a report. The results present the participants' initial reactions to the concept of a shared care record and then transition to their interpretation and reflections on the use of and adaptation to a shared care record.

Table 2. Interview guide.

Interview portion	To do	Additional notes
Warm-up	• Introduce and explain the purpose of the interview. Obtain consent to use quotes from the interview and to record the interview.	• Introduce the idea of the shared care record and how it works.

Interview questions	• Consider your electronic health record today (name the record), what additional health or social information regarding your patient would you like to have access to in this new shared care record or would make a difference for you, when providing care for that patient?
	  • Prompt: tell interviewee more about what a shared care record could offer them.
	• So, for you, tell us how this information would impact or change the care you provide (or can) to your patients?
	  • Prompt: what difference would it make if you had access to all of your patient's information (the type of information you just listed) on the shared care record?
	  • Prompt: would you look at it more or make use of that information?
	• This would be a change and change is never easy, but what do you think you and your colleagues would need to do to adapt to using a shared care record in your day-to-day practice?
	  • Prompt: what would help your colleagues benefit from this change?
	  • Prompt: what support or resources would help you with the introduction to and adaptation to this system?
	• Do you have any concerns with the concept of a shared care record?
	  • Prompt: Overall, what factors or conditions challenge or serve as barriers to your personal use of a shared care record? How might this change that?
	• In closing, do you have any concluding thoughts or comments related to the shared care record that you would like to convey?
		• Build each question off the previous one and rearrange the order as needed according to the flow of the conversation. Use the prompts to further stimulate conversation.

Closing	• Thank the interviewee for their time. Let them know not to hesitate to reach out if they have anything else they would like to discuss.	• Ask interviewee whether they give permission to be contacted in the future.

Data Analysis

The interviewer first read and interpreted the individual transcripts to become well acquainted with the data collected. After developing the initial semantic codes based on the data, the interviewer grouped the codes into categories and themes and then reviewed, named, and discovered various connections between the themes to write the analysis. The themes were modified using an iterative process, adjusted, and grouped, with categories and subcategories added as they arose from the data analysis. The interviewer used a qualitative interpretative approach, the framework method, to analyze the data by joining thematic analysis with comparison so that the data were surveyed for known literature themes and emerging themes. The interview findings are presented in the *Results* section of this paper; quotes are included from the interview transcripts to illustrate the generated themes. End users are identified by their health professions in each quote.

Ethical Considerations

This publication is the result of a quality improvement initiative deemed not to require ethics approval according to the Western research ethics board checklist.

Results

Participants' Reflections on the Shared Care Record

Theme 1: Opportunities for Using a Shared Care Record

Lack of Communication Affecting Care Delivery

A lack of adequate communication among health care providers, services, and health care facilities across the care system was a common response among participants. Discussions with end users highlighted frustrations across the care continuum, such as entering care encounters with inadequate or lacking information, more difficult care management and planning, and delays in access to information causing delays in care. Registered nurse 4 stated the following:

> *Why are we doing the same assessments over and over again? Patients are forced to repeat tests because the results are not passed between the health care providers, which in the end only delays their [the patients'] treatment.*

The introduction of a shared care record could drastically improve communication among health care providers, potentially decreasing the current workload, increasing confidence in decisions, and affecting patient safety and continuity of care:

> *...with a client that I'm seeing, he's a cancer patient, so he'll go to London, and then he'll go to Stratford for example. The two hospitals they don't communicate very well...the communication between the two kind of gets lost in between...it's all of these extra steps between myself and this patients' daughter. We are trying to figure out when was his last treatment? And was the medication provided? What was that medication? And how long was he supposed to take that? So, you have Stratford asking this and trying to get through to London to get those questions answered, the whole process becomes very difficult.* [Registered practical nurse]

End-user discussions touched on the impact of poor communication on patient satisfaction, trust, and their subsequent health care journeys. Occupational therapist 1 described how enhanced communication between providers could affect the patient care experience:

> *From a patient perspective, it might be one less time they have to answer the same questions. Not being asked the same questions all over again seems trivial, but if you're the patient who's had to answer the same question twenty times you think people aren't listening to you...we could just kind of summarize what we know, which I think also makes the patients feel like we're all a team speaking with each other. So, we're communicating what we know about the patient, as opposed to having to ask them the same information over and over and over again.*

The retrieval of information to provide proper care was deemed exceptionally crucial among end users working in community settings, where some may not have any connections to EHRs:

> *I mean our nurses are walking in really with very minimal information. Again, relying on the family a lot of the time to tell us, even as far as medications that they're on, you know, we're going through all of their bottles and discharge lists, and lists they pull out of their wallet, and trying to reconcile it. So, it's really pieces of information.* [Clinical practice specialist]

Real-Time Information

End users collectively admired that one of the most critical advantages of the record would be the access to real-time information as it changes and becomes updated. A clinical nurse specialist described information access as "very much a game changer for clinicians," with other participants agreeing, describing it as "taking the legwork" out of obtaining essential patient information. The shared care record real-time information feature "would not only help the patients but also the healthcare team be up to date, and they wouldn't have to take so long to find the information they need" (registered nurse 3). Considering their daily practice allowed the end users to visualize clinical patient data being stored in one central location where the information could be accessed, analyzed, uploaded, and used, with one process going to everybody involved in the patient's care:

> *I'm really intrigued by receiving information in real time, I find that especially in the community if there has been a medication that's been added, I don't always receive that information, unless I'm at the client's home and I see the new bottle because they don't typically tell me if they are on a new medication, and the doctors just prescribe it, they definitely don't inform us. That would be information would be very helpful for me when trying to figure out why they're having a change in their health status, or maybe a cognitive change or something along those lines.* [Registered practical nurse]

Theme 2: Perceived Benefits of Using a Shared Care Record

Effective Use of Time

Access to clinical information through the shared care record was described as promoting the effective use of time and resources. End users felt that the record would provide "an accurate picture of what's going on," and it would be "a lot less doubling and tripling of assessments." Registered nurse 1 recalled a common scenario occurring in their inpatient hospital unit:

> *...on my floor patients come up with a bag of medications or just a list of medication names and dosages that they have scribbled onto a piece of paper...the time we are spending on doing something very basic like manually inputting medication information that should be available through the pharmacy or from a physicians list would save so much time and then you would be able to spend more time doing a proper assessment on the patient, providing care or starting a treatment.*

Within the complex and fast-paced acute care setting in which several of the interviewed end users worked, the ability to save time was the most significant determinant of efficiency. Effective care must be provided with often limited resources and high workloads. Occupational therapist 1 discussed the vision of the shared care record as a benefit to their work:

> *...we're always looking in acute care for efficiencies. The length of stay is already very short, and the more information that we have access to when we are doing our initial triage or chart review, the earlier we can start to at least reflect on what the likely plan is.*

Informed Circle of Care That Promotes Continuity of Care

The vision of the shared care record would allow the patients' circle of care, everyone involved in the patients' care, to be well informed, leading to better care, time savings, and less frustration. According to registered nurse 1, "it would promote continuity of care and keep everybody in the loop and informed, which is so important in healthcare in general." End users discussed the benefit of being able to collaborate with other clinicians and share more information in general:

> *...even when our clients go into hospital, they [the hospital occupational therapists] have no idea what we have been working on at home. And then if they*

> *go to discharge the client, sometimes they'll put in new OT and PT services without realizing there's already different things in place. There's just poor communication, so I think this idea would make a huge difference.* [Occupational therapist 2]

The consensus among the participants was that this vision becoming reality would change the way they practice, offering the ability to connect with everyone that the patients are in contact with:

> *...everything is just in silos right now, and I think anyone that's had any contact with the healthcare system knows that. I think it's very prominent in community...it is not practical how it is right now, so I think any move in that direction [access to a shared care record], would help immensely.* [Registered nurse 4]

With regard to the patient-provider relationship, providers indicated that patients in the hospital setting can feel vulnerable and left out of conversations and might not know what is going on:

> *If we could retrieve those records...it would help the patients feel comfortable, they would be able to ask more questions during their stay and obtain answers from us as providers.*
>
> *No one wants to be in the hospital as it is, so when they [the patient] come in, and they notice that their cardiologist has no idea that so and so [other healthcare providers] prescribed a certain medication, patients tend to become annoyed, and rightfully so...having that information prior to their visit would make their visit a lot easier, faster, and more efficient for them and for everyone involved.* [Registered nurse 5]

Overview of Patient Health Status

The increased amount of health and health-related information accessible to health care providers would help them understand their patients' medical requirements. A physiotherapist discussed how treatment of his patients would be enhanced "by helping me know and understand their timeline for recovery." The record would "help understand other areas they [the patient] need help with because patients forget things and don't always understand what other healthcare providers tell them when it comes to their injury." Participants noted a lack of patient awareness regarding what providers are involved in their care, medication management, or even their diagnoses. Physicians discussed situations in which, unless their patients informed them, they were unaware of new allergies or changes to medication dosing made by other physicians. Registered nurse 2 discussed that, when noticing a new irregular sign or symptom, the shared care record would allow for "a quick reference, if that's something they [the patient] have at baseline or if you need to look into it further, and just kind of base your actions on that information":

> *...especially going into people's homes, it would just make me more aware of things. People won't always tell you the truth about things or they'll leave out things they don't feel are important but are impacting how they are managing at home...If you knew the information, walking into it, you kind of have a more holistic picture before moving forwards with them.* [Occupational therapist 2]

Adaptation

Theme 3: Factors That Promote Use of the Record

Positive Outlook on Adaptation

Overall, the participants revealed an incredibly positive outlook when considering their own and their colleagues' adjustment to the record. Participants made comments such as "it wouldn't be a challenge for me and my colleague's personally" (registered nurse 3) and "I don't think there would be a large change-related level of concern or anxiety" (occupational therapist 1). End users acknowledged that technology is on the rise, with many individuals of all ages using digital solutions in their daily lives:

> *...even just logging in and seeing their bloodwork online, people are more comfortable doing that...even if they're older or they haven't done that they're comfortable reaching out to their neighbor or their child to help them with that...I think it would be easier than you know even 5 years ago.* [Registered nurse 4]

Health Care Provider Requests for Health Information Access

When end users were asked what other patient health or social information they would like access to when providing patient care, most made remarks regarding the difficulty of obtaining access to clinical data documented beyond the organization they worked within. The most common request among end users was access to a verified list of medications. Often, providers must rely on medication bottles, discharge lists, and family members to reconcile patient prescriptions:

> *...patients might know the name of the drug, or what the pill looks like, but they have no idea what it does, or why one of their physicians ordered it. For example, when they come into the clinic telling us that their nephrologist ordered something to bring their blood pressure down because their kidneys are failing, their cardiologist might just be finding out about the medication and realizing the medication could be affecting their heart. So being able to see what was ordered and when it was ordered would be such a big help.* [Registered nurse 5]

The lack of integrated health IT was found to cause duplication of efforts and lack of comparison across documentation from the hospital versus the community or across organizations or different regions:

> *I cannot see pictures of x-rays that they [patients] get in the community. So, people get sent in with a break and I need a picture to see if I need to push on it, to put a cast on it and get it in the right place. We often repeat x-rays that probably wouldn't need repeating if we could just see the original picture.* [Physician 1]

Interoperability between organizations can reduce redundant tests, save time and costs, and result in better continuity of care. Participants regarded patient diagnostic imaging as the information they would like to access, including the actual pictures and not just the reports of x-rays, ultrasounds, computed tomography scans, echocardiograms, and other imaging modalities. Furthermore, patient exposure to radiation or contrast dye would decrease without the need to repeat tests and scans:

> *...it would help me if I had access to imaging without having to rely on what the patient tells me or what they can even remember. Sometimes patients don't even know what type of imaging they had done or even what that imaging was for.* [Physiotherapist]

Participants listed patient medical-related appointments as the information they wanted to see on the record. Many patients have complicated cases and multiple teams following them in the community, which can be overwhelming to manage independently. Family physician records or membership in a family health team was another common request, along with up-to-date access to all referrals sent out and specialist information:

> *Knowing what doctor the patient was referred to...a lot of time people will come in and will say "well my doctor sent me to a cardiologist, but I haven't heard anything in three months" So then I'm like "well I'll send you to a cardiologist as well." Am I sending them to a different cardiologist? I have no idea.* [Physician 1]

Access to patient social history information was highly requested, including living arrangements, home care reports, and community support or professional services that patients were using as this information significantly affects patient care planning and discharge planning. According to physician 2, "it would be nice if the patient could update things like occupation, substances, family members, consent to family members":

> *In many cases, we don't have a true understanding, at least initially on chart review, without speaking with our team about the exact specifics of what type of services or equipment or programs they are [the patient] currently involved in, in the community. A true understanding of that social and community history allows us to initially strike off maybe some options that we may not have at our disposal, or start to plan out some of the gaps that we anticipate based on what we know that they already have.* [Occupational therapist 1]

End users discussed situations requiring access to patients' medical histories and complete health records. Requests for clinical data access included a complete list of diagnoses and when the patient was assessed for them; laboratory test results; previous rehabilitation journeys; surgeries; and conversations that had taken place, which could indicate the patient's understanding of their illness or where they are at:

> *Almost every single clinician that I have spoken to would say, we wish we had more, or the information is just a very brief summary...especially with acute care, the length of stay is so short, we're trying to piece together as much as we can...so the more the more understanding of the patient's history and journey through the healthcare system, the more efficient we can be as occupational therapists.* [Occupational therapist 1]

Ongoing Training

The most common suggestion among end users was the provision of proper education and training on the new system. As one of the primary objectives of an EHR is to improve collaboration among health care providers, it only makes sense that they are offered the chance to provide feedback on the system they use daily:

> *From a training perspective, it's nice to first of all be part of the process of building the system, or having some input on that system, which helps with the engagement and integration when we're actually putting the rubber to the road...it definitely would help with the connection to the implementation.* [Clinical nurse specialist]

Most participants suggested that they would benefit from getting to know the new system through proper training on the layout of the information and how to find the information that they could use. End users visualized the benefits they could obtain from an introduction to and familiarization with the system before it becomes implemented in practice:

> *...obviously, there needs to be training, and along with that comes the resources. Not only do the training but pay for them [the end users] to attend, which is always an issue. And then I think even support along the way, for example IT support, do we need to build that internally in our IT department...up front, it's just really the education and making sure it is ongoing...in healthcare in general, there is a lot of turnover, so how do we sustain the education moving forward.* [Clinical practice specialist]

Many participants discussed "multi-pronged approaches" as the most effective method for introducing and adapting to the record. Resources mentioned by the participants included a chat or live support option for immediate questions, videos on how to use the system, a toolkit or tip sheet developed by the system creators, and in-person and web-based computer sessions. Occupational therapist 2 described the introduction to their current EHR system as they recalled:

> *Clinicians felt more comfortable using the system if they had some test patients to go through trial cases of what a daily patient intervention might look like prior to the go live.*

Several participants mentioned the idea of "super users":

> *...our nurse colleagues on the floor, who had additional training and were more familiar with the record so that we could reach out to them if we needed help or if we had questions.* [Registered nurse 1]

These super users would function to support their colleagues in the transition while helping others learn to use the record to the fullest extent.

Another resource identified was the use of clinical educators who already work to support staff with clinical updates to rules, procedures, policies, and methods of accessing information.

Record Accessibility

Several questions from end users concerned how to physically access the clinical data on record and the timeliness of finding information. Questions included the following: "where do we need to click?" "Under what icon?" "How do I add things to the shared care record?" "Do I have to do it manually?" "Does it just happen automatically?":

> *The biggest adaptation would be how to access the information, like opening the charting system will look different, so getting used to the new layout and the new system and knowing where to find things.* [Physiotherapist]

A key finding among participants included statements regarding the user interface or usability of the shared care record. Participants used terms such as "seamless," "simple," "accessed quickly," "user friendly," and "easy to follow" to describe how they envisioned the software to function:

> *But we need to really limit where they're [frontline staff] finding their information, if they need to upload, that they are not having to do it to all of the people we need to report to. There are so many layers and rules, and we just need to make it as simple as possible.* [Clinical practice specialist]

Participants considered the least amount of clicking and integration with their current systems to obtain data or add to their assessments as crucial features of the record. Information being uploaded automatically was considered foundational, with physician 1 commenting the following:

> *If we have to do an additional step at the end to get it uploaded, you're going to get way less uptake...as long as in the back end of things, my EHR links it all up.*

Regarding user-friendliness, the physicians explained that they would not appreciate retyping a password to access the charting or repeated verification of the designation upon entering the system:

> *I don't want to have to log into something else, I'm already logging into so many things every day...and so there's that information that sits somewhere but that it gets pushed to all the different places and then shared between the different places.* [Physician 2]

Theme 4: System-Dependent Considerations and Concerns

Clinical Data Consistency, Accuracy, and Organization

Although participants recognized numerous potential benefits, they also discussed fundamental considerations of functional practicality, such as the consistency and accuracy of data across the record. To present clinical data across different EHR systems uniformly, health care providers must be consistent with the documentation methods and upload the documentation to the record:

> *I would be concerned about it being unorganized or messy, um if everyone has different styles and systems of taking notes or recording, maybe it would be difficult to find one particular piece of information that you are looking for.* [Physiotherapist]

Understanding patient rostering or enrollment was discussed as a critical element of the record, understanding who is involved in a patient's care, and participating providers can change or adjust that if needed:

> *I changed my practice maybe three years ago, but I am still on some people's charts at the hospital. I have requested to have my name taken off, but unless the patient calls and changes that, nothing can happen. And so that becomes a privacy issue, I keep getting files for people who I am not actually taking care of.* [Physician 2]

Beyond consistency, participants identified the importance of double-checking the information obtained from the record with the patients themselves. Updates may not be revised, data could be deleted, and mistakes can still occur:

> *If you have a medication record from two years ago, you would still have to do your due diligence to make sure the information you are using is accurate.* [Registered nurse 1]

An auditing system of the record was suggested that could review charting to help ensure that health care providers input the required information to maximize the utility and reliability of the clinical data. According to registered nurse 5, "that way people have to take responsibility for what they're changing or what they're contributing towards this shared documentation."

Change in Workflows

Uncertainty regarding daily practice workflows came up as a barrier to overcome when participants discussed adaptation to the use of the record. Visualizing the details of the change to their current EHR system interface was difficult for certain participants:

> *It's hard to know what the change management strategy would be.* [Clinical practice specialist]
>
> *My hope is that there would be very little that we would actually have to change...everything else I would expect to be kind of behind the scenes where I do my normal process, that it would just sort of happen in the background.* [Physician 2]

Discussions held with professionals in the community setting revealed that there would be an adjustment to their current workflow, with the additional time spent reviewing history, reports, and other data accessible in the record before going in to see the patients:

> *Right now...I really only check [name of EHR] to look at when appointments are confirmed, phone numbers, names, and then I find out a lot more information from the patient once I get there [to their place of*

> *residence]...for home care, that's just kind of how it's been. If I am seeing four or five people every day and driving between these destinations, it would take time maybe at the beginning before getting used to it as part of the routine.* [Occupational therapist 2]

Upon introducing the idea for the record, a statement from the Ontario Patient, Family, and Caregiver Declaration of Values [10] was presented to participants explaining the vision for transparency in patient access to their health records. Wondering how patients would interpret seeing physicians no longer in the patient's circle of care re-entering their medical information and whether this would be concerning, physician 1 stated the following:

> *...Most of us [physicians] require understanding of, did the treatment I gave actually have a good effect? And what did the follow up doctor think? So, we will access records a few weeks later to see what happened so that we can learn...that's how I learn and how I can change how I practice, which is super important...we are expected to do continuing professional development and take courses, but then it's always read and learn around your cases. How am I supposed to learn around my cases when I can't find out what the specialists thought of this unique situation that I can't just open a textbook and read about.*

Privacy, Confidentiality, and Security of the Record

The most common concern among participants regarded privacy and confidentiality. The extensive personal health information or personal information accessible in a central location, this being the record, increases the risk of a privacy breach:

> *I think about it, not only as a clinician, but as a user of healthcare as well.* [Occupational therapist 1]

According to registered nurse 1, with "a lot more information that is available to you as the healthcare provider, it would have to be ensured that only people who are part of the patient's circle of care are accessing this information and that you are only accessing records that are applicable to the care that you are providing." Nevertheless, most providers, including the nurses, physiotherapist, and occupational therapist, agreed that the benefits of the shared care record would outweigh the risks, and everyone could work together to make it as secure as possible.

Patient Portal Access

The concept of a patient portal, as described in the video shown to the participants, raised many questions and some hesitation among them. According to physician 1, "if the patients can see all of the notes that I write, that might change the way I document and I may be less comfortable putting the note in [to the record]." Understanding that patients will have access to their health data, questions revolved around the extent of access provided, whether to their entire chart and complete provider documentation or solely to scheduled appointments and their care plan:

> *...For instance, the other day I was printing a note for a patient knowing that her family member was going to be sitting with her reading it, she [the patient] asked me not to tell her family that she smokes weed...So, now I am changing my note, instead I copy and paste into a discharge note and then kept in my actual note all the facts so that I have that in her chart for other doctors to see because that's important medical information.* [Physician 1]

Several end users expected that there would be system controls or protocols surrounding what information the patient could see or change themselves and what information the patient would not be able to change. Further discussions covered the documentation of sensitive patient information and how patients might respond to the presentation of such information:

> *...there might be certain things...in the record that maybe patients themselves would not want to see...if the patient was confused after a surgery and there was an episode of violence that was documented. It may almost be triggering or upsetting to them [the patients].* [Registered nurse 2]

Regardless, health care providers considered the inclusion of these types of documentation to be vital to the patient's record:

> *I have a suspicion that this might be going on and I need to share that with my colleagues, because if they have a similar suspicion and it's a pattern that's important.* [Physician 1]

When considering patient access to records, participants emphasized the importance of patients being able to interpret the information correctly and objectively, especially regarding medical jargon. Participants suggested that clinicians may be inclined to use different terminology or a different writing style or reformulate the information in a meaningful way for patients:

> *...kind of helping socialize the clinicians to the new reality of the patients being able to read their notes more readily or easily. I think there would be value in having a discussion as a team about those types of changes.* [Occupational therapist 1]

Discussion

Overview

Concepts such as PHM, data security, and privacy can be complex to explain to individuals; however, they will become progressively essential to the design and delivery of health care. PHM is founded on interoperability, data sharing, and integration with diverse health sectors and services. Although people tend to understand the role and significance of EHRs, they may neglect the value of inputting accurate and high-quality data into them. PHM and primary health care strive for many of the same features, including person-centeredness; continuity; accessibility; and consideration of physical, mental, cultural, and social aspects of health, among others [2]. Health care providers commonly have a good understanding of the population that they serve, often living within the community themselves, and appreciate the needs and some of the determinants of health of these populations. A PHM approach rooted in quality data quantifies this understanding and enables an even deeper level of understanding [2,17]. As the vision for a shared care record using HIE technology starts coming to life,

obtaining end users' opinions and ideas will be imperative. End-user involvement in the record's design; development; and, ultimately, operation will help simplify the adoption of changes and attain the goals of proactive and coordinated care that actively engages patients.

Principal Findings

This study provides practical findings that will help emphasize factors that facilitate clinicians' process of adaptation to the use of a shared care record. Considering the fast pace of health care, clinicians highly commended and admired a central location for real-time information availability that could promote efficiency through the effective use of time. The benefits of accessible retrieval of information were especially highlighted among end users practicing in the community setting. Discussions with end users brought forth the importance of an informed circle of care, promoting patient continuity of care, and more effective provision of care. Health care providers requested access to additional information that would help them in their practice, from medication lists and diagnostic imaging to social community and home care support, laboratory test results, and referrals. Discussions also brought forth questions regarding the interoperability of the record, its functional usability, and changes in workflows.

Adaptation to a shared care record was viewed positively by health care providers. Several end users spoke about the benefits of getting to know the new system through proper ongoing training using multifaceted approaches. Some of the approaches considered included videos, in-person and web-based computer sessions, and live user support options. The idea termed "super users" was brought forth, whereby colleagues who would be more acquainted with the software would function as support for their coworkers in the transition and adaptation to use of the record. End users wanted to understand the functionality of the record, the impact of changes on their daily workflows, and the consistency and accuracy of data across the record to maximize the utility and reliability of the clinical data. The main concerns of participants were the privacy, confidentiality, and security of the record and patient information interpretation through the patient portal.

A growing body of literature on the topic of patient access to health care provider electronic visit notes suggests that the active involvement of patients at the point of care can foster stronger patient-provider therapeutic partnerships. A study by Wolff et al [26] suggested that most patients reported benefits of reading provider notes, such as more agreement concerning treatment care plans, increased ability to formulate questions to ask their care providers, and more productive care discussions. Walker et al [27] brought forth challenges such as patients not being registered on portals to allow for access to notes or patients being unaware of provider notes being available to access. Nevertheless, the benefits of expanded patient access to clinical notes have been established, holding the potential to better support and involve patients in care, increase communication, and provide feelings of control and preparation for health care visits [26-28].

Limitations

This study was limited in certain ways. The range of clinicians could have included various other providers within diverse health care settings to broaden the perspectives included. Furthermore, the application of voluntary response sampling in the recruitment of health care providers for this study is a limitation because of the possible sampling bias of respondents who volunteered, meaning that the study could have involved EHR advocates. Future research should involve a subsequent round of health care provider interviews once the record has a fully developed user interface design functioning across several systems involved with the HIE initial demonstration project. At this stage, health care provider interviews may offer further understanding of the functional usability of the shared care record once the providers can visualize and use it within the home database system they work in daily. These interviews could be geared toward comprehending how information design principles align with clinician workflows, patient information examinations, or decision-making in the medical environment. Building on this effort can help populations receive high-quality care while ensuring that it meets community needs.

Conclusions

This study provided insights into health care providers' perceptions of a shared care record and presented their reflections on the practical use and adaptation to the use of a shared care record. It is essential to bring end-user perspectives into the shared care record's development, introduction, and maintenance, along with the training necessary to permit the use of the system. There is an urgent demand for high-quality, integrated, and timely health data allowing individuals, health care providers, and communities to be involved and informed partners in the provision and attainment of health care [17].

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Conflicts of Interest

None declared.

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Abbreviations

EHR: electronic health record
HIE: health information exchange
OHT: Ontario Health Team
PHM: population health management

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Attitudes of Health Professionals Toward Digital Health Data Security in Northwest Ethiopia: Cross-Sectional Study

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Abstract

Background: Digital health is a new health field initiative. Health professionals require security in digital places because cybercriminals target health care professionals. Therefore, millions of medical records have been breached for money. Regarding digital security, there is a gap in studies in limited-resource countries. Therefore, surveying health professionals' attitudes toward digital health data security has a significant purpose for interventions.

Objective: This study aimed to assess the attitudes of health professionals toward digital health data security and their associated factors in a resource-limited country.

Methods: A cross-sectional study was conducted to measure health professionals' attitudes toward digital health data security. The sample size was calculated using a single population. A pretest was conducted to measure consistency. Binary logistic regression was used to identify associated factors. For multivariable logistic analysis, a *P* value ≤.20 was selected using Stata software (version 16; StataCorp LP).

Results: Of the total sample, 95% (402/423) of health professionals participated in the study. Of all participants, 63.2% (254/402) were male, and the mean age of the respondents was 34.5 (SD 5.87) years. The proportion of health professionals who had a favorable attitude toward digital health data security at specialized teaching hospitals was 60.9% (95% CI 56.0% - 65.6%). Educational status (adjusted odds ratio [AOR] 3.292, 95% CI 1.16 - 9.34), basic computer skills (AOR 1.807, 95% CI 1.11 - 2.938), knowledge (AOR 3.238, 95% CI 2.0 - 5.218), and perceived usefulness (AOR 1.965, 95% CI 1.063 - 3.632) were factors associated with attitudes toward digital health data security.

Conclusions: This study aimed to assess health professionals' attitudes toward digital health data security. Interventions on educational status, basic computer skills, knowledge, and perceived usefulness are important for improving health professionals' attitudes. Improving the attitudes of health professionals related to digital data security is necessary for digitalization in the health care arena.

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KEYWORDS

health; profession; digital; attitude; security; data

Introduction

Health care digitalization has empowered and enabled health care professionals to achieve positive health care outcomes [1,2]. The World Health Organization (WHO) has released guidance for digital health after a critical review of available evidence for the benefits, harms, acceptability, feasibility, resource use, and equity considerations of digital health interventions [3]. The growth of digital technology in the health sector has changed the relationship between health care professionals and patients. It helps to bring new attitudes toward health care or medical data. However, these new ways of thinking have been raising concerns about digital security [4].

Digital security in health care has an ultimate impact on an individual's quality of life [5,6] because the storage, processing, transmission, and analysis of data are major health care activities. In electronic health transactions, the privacy regulations required by the Health Insurance Portability and

Accountability Act tried to assure consumers that as their health records became fully electronic and networked, their information would be protected [5]. Therefore, digital health security is vital in the internet age for professionals and organizations to keep their information assets safe [7].

However, there is a matter of using digital health security countermeasures, particularly as sensitive electronically protected health information has been at risk because it is accessed by every health care service in various ways digitally [6]. As mentioned by many studies, among the major impediments to the adoption of digital health by users are security concerns [3,4]. Numerous health care data security breaches have occurred owing to a lack of attitude by the user [8]. Most prominently, digital health data were the victim of phishing, ransomware, and malware [9].

As studies elucidated, the attitudes of health professionals toward digital health data security were prominent factors in determining the consequences of adopting digital technology to secure health care data [3]. According to studies, these attitudes influence people's comprehension of and use of data-security measures [10,11]. Henceforth, digital health data users desire to know more about security measures [12]. However, human error is the main driving force behind security problems. According to a study by a security organization, about 88% of data breaches are caused by employee error [13]. This revealed that health professionals have an inadequate attitude toward digital data security [14]. Various studies elaborated that the contributing factors to attitudes toward security were age, frequent use of digital technology [15], education, and the types of work manners or jobs [16,17]. Therefore, improving the attitudes of health professionals toward data security is the backbone of health care institutions. Another study suggested that improving their knowledge, computer skills, and education level was the best approach to developing a favorable attitude toward digital security [18-20].

Digital technologies used by health care organizations uniquely have the ultimate purpose of processing lifelong and sensitive data. In resource-limited countries, including Ethiopia, health information technology is at a developmental level; some digital health applications have run in health care settings to ease the handling of health information. These applications are smart care, district health information systems, and wearable and wireless health care devices operating in each health care field. As a result, in resource-limited countries, some health organizations have used digital technology. However, there are limitations to using digital health data security tools regarding health professionals' attitudes. This issue has not yet been addressed. Therefore, the main aim of this research was to assess health care professionals' attitudes toward digital data security in a limited-resource country. Identifying the factors associated with attitudes toward digital health data security will serve as a baseline for further studies and guide security strategies for health care digitalization.

Methods

Study Design and Settings

This study was conducted at a specialized teaching hospital in a resource-limited country in Northwest Ethiopia. All hospitals play an academic and referral role for more than 3.5 million people. For this study, a cross-sectional study design was an appropriate method to assess health professionals' attitudes toward digital data security. The study was conducted from May 30 to June 20, 2022, at a specialized teaching hospital in Northwest Ethiopia. Appropriate informed consent was taken to administer the study.

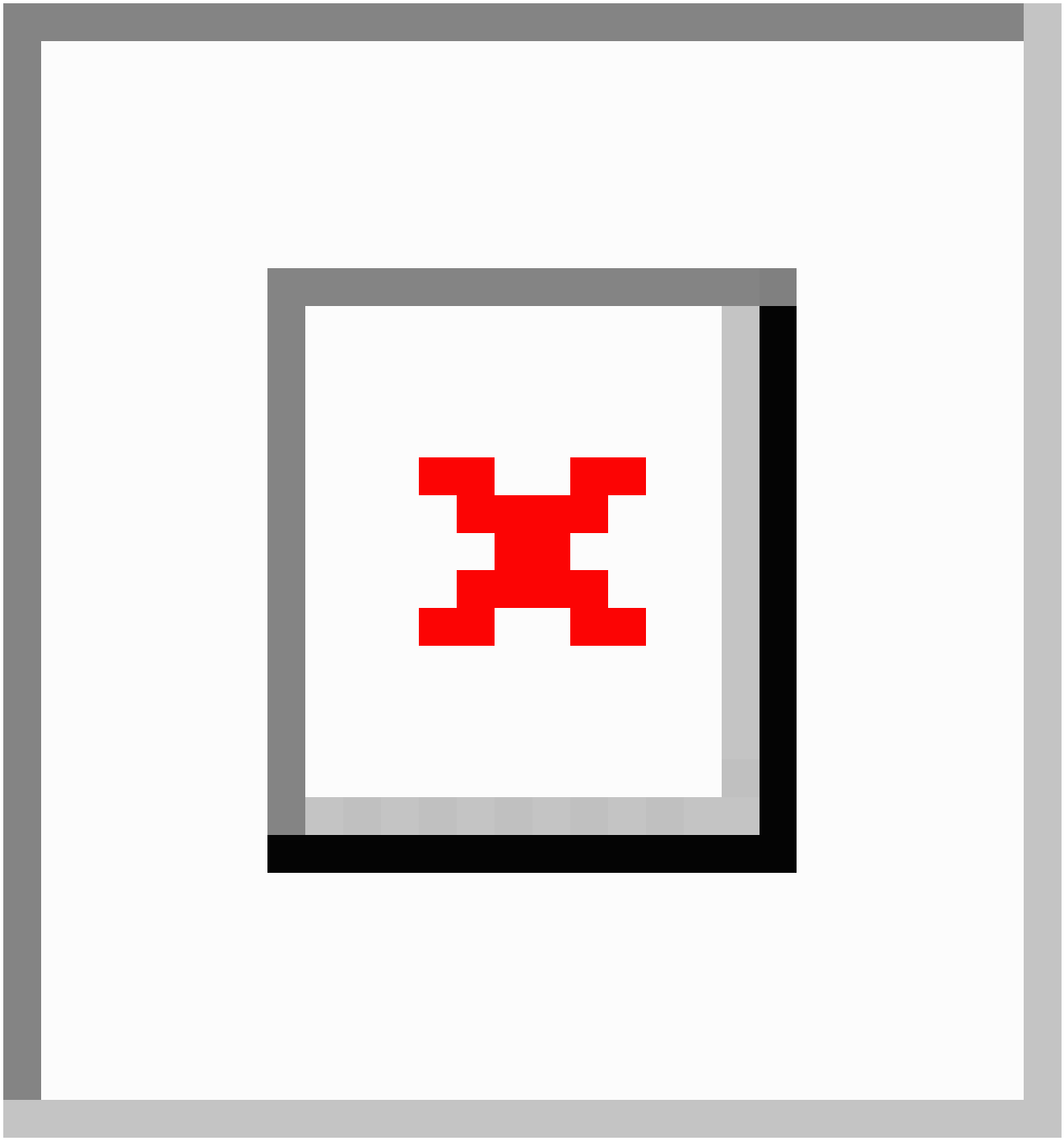
Study Sample and Eligibility Criteria

The source population of the study was health professionals working in specialized teaching hospitals. Health professionals who had used digital devices in those hospitals were selected for the sample population. On the contrary, health professionals who had no experience in digital health and who were not in health care settings during the period of data collection were excluded from the study.

Sample Size Determination and Sampling Procedure

The sample size was determined using single-population proportions and a nonresponse rate of 10%. The sample size was calculated assuming a 95% significance level, 5% marginal errors, and a 50% population proportion, which is recommended by biostatistician experts [21]. In this case, the total sample size was 423. Proportional allocations were made for each health care institution. Then, based on the sampling frame of the list of health professionals obtained from human resources management, simple random sampling was used to pick the study participants who were working in specialized teaching and referral hospitals. These steps are illustrated in Figure 1.

Figure 1. Sampling procedure of the study



Study Variables

The outcome variable of this study was the attitudes of health professionals toward digital health data security. Other characteristics such as sociodemographics (age, gender, educational status, work experience, and monthly salary), behavioral and technological characteristics (computer skills, knowledge of digital health data security, use of the internet, use of social media, perceived ease of use, and perceived usefulness), and organizational characteristics (training and health care workload) were the explanatory variables of the study.

Measuring Instruments

Digital health data security refers to digital health data techniques to safeguard health care data from illegitimate or unauthorized access, alteration, and destruction.

Knowledge of digital health data security refers to the know-how of health professionals to use security tools while processing health data, which we measured using a 10-item Likert scale. The data were not normally distributed, as shown using the Shapiro-Wilk test (P value <.05), skewness, and kurtosis. Therefore, knowledge was determined based on the median; a score above the median value of 35 (IQR 31 - 40) indicated good knowledge, and a score below the median score indicated poor knowledge [22,23].

Attitudes toward digital health data security refer to the feelings of health professionals about digital security tools (data encryption, antivirus, etc) and while processing health data using digital devices, which have been measured using a 10-item Likert scale. The data were asymmetrically distributed and categorized by the median. A score above the median value of 31 (IQR 27 - 33) indicated a favorable attitude, and a score below the median indicated an unfavorable attitude [15,23,24].

Data Collection Tool and Quality Assurance

A structured self-administered questionnaire was adopted and modified using information from various publications [15,22,24-27]. The questionnaire was written in the English language. A pretest was conducted to ensure reliability before conducting the study. Trained medical professionals collected the data. Finally, the investigators took over overall supervision. Validated forms were then completed using statistical software to minimize errors and verify missing values or incompleteness. To ensure the quality of our surveys, we conducted research consultations and a pretest to check the tool. Based on suggestions from medical experts, word corrections were made to facilitate comprehension, and Cronbach α scores of 60% or higher were used. The pretest showed that the Cronbach α scores of attitude and knowledge were 0.83 and 0.86, respectively.

Statistical Analysis

Data were input into EpiData version 4.6 software (EpiData Association) and exported to Stata (version 16; StataCorp LP). χ^2 assumptions, collinearity, and other assumptions, such as incomplete values, were checked and tested by presenting the data via summary statistics. After generating the cleaned data, further analysis was performed using the Stata software. The means, medians, SDs, percentages, and frequencies were used to illustrate the results in tables and graphs. We also used binary logistic regression to identify the relevant factors. Variables with *P* values less than or equal to .20 were candidates for multivariate analysis. Multicollinearity was checked using the variable inflation rate. Finally, an odds ratio with a 95% CI and a *P* value less than .05 were used to determine the outcome variable by adjusting for confounding effects. Model fit was checked using the Hosmer-Lemeshow test.

Ethical Considerations

Ethical approval was received from the Institutional Review Board of the University of Gondar, College of Medicine and Health Science, the Institution of Public Health Ethical Review Committee (no. IPH/2013/2014). The procedures used in this study obey the rules of the Declaration of Helsinki. A formal letter was received from each specialized teaching hospital unit coordinator (no. 1061/90/13). Finally, written consent forms were delivered with each questionnaire, and appropriate written consent was taken from the respondents.

Results

Sociodemographic Characteristics

Of the 423 health professionals, 95% (n=402) participated in this study, whereas 5% (n=21) of participants did not complete the survey due to various situations. In terms of sociodemographic characteristics, out of 402 health professionals, 254 (63.2%) were male, and 148 (36.8%) were female, with a mean age of 34.5 (SD 5.87) years. Among all study participants, 131 (32.6%) were aged between 20 and 30 years, 214 (53.2%) were in the range of ages between 31 and 40 years, and 57 (14.2%) were above 40 years. In the case of marital status, 166 (41.3%) were single, 191 (47.5%) health professionals were married, and the remaining 45 (11.2%) were others who might be separated or widowed. Regarding educational status, 293 (72.9%) health professionals had bachelor's degrees, 55 (13.7%) had master's degrees, and 54 (13.4%) had postmaster's degrees (specialist and subspecialist). Further, 224 (55.7%) and 178 (44.3%) health professionals had 1-5 years of work experience and above 5 years of work experience, respectively. Regarding monthly salary, the majority of health professionals were paid below 10,000 Ethiopian birr (US $82.95; Table 1).

Table . Sociodemographic characteristics of health professionals' attitudes on digital health data security at specialized teaching hospitals in Northwest Ethiopia in 2022 (n=402).

Variables	Frequency	Percent
Gender		
Male	254	63.2
Female	148	36.8
Age (years)		
20 - 30	131	32.6
31 - 40	214	53.2
>40	57	14.2
Marital status		
Single	166	41.3
Married	191	47.5
Other[a]	45	11.2
Educational status		
Bachelor degree	293	72.9
Master's degree	55	13.7
Postmaster's degree[b]	54	13.4
Work experience		
1 - 5 years	224	55.7
>5 years	178	44.3
Monthly salary in Ethiopian birr (1 Ethiopian birr=US $0.008)		
≤10,000	273	67.9
>10,000	129	32.1

[a]Other (separated, widowed).

[b]Postmaster's degree (specialist, subspecialist).

Behavioral and Organizational Characteristics

Based on organizational characteristics, the results illustrate that 58% (n=233) of health professionals agreed that there is a workload in the health care organization, while 42% (n=169) agreed that there is no workload in the health care settings. In the case of digital training, 57% (n=229) of health professionals had taken basic computer training, whereas 43% (n=173) of the participants had not taken training delivered by their health care institutions. In terms of behavioral characteristics, 54.7% (n=220) of health professionals perceived digital health security tools as easy to use, while 45.3% (n=182) perceived digital health security tools as not easy to use. Regarding usefulness, 23.1% (n=93) of health professionals perceived digital health security tools as useful to use, whereas 76.9% (n=309) perceived that their usefulness was not adequate for digital health data security, as shown in Table 2.

Table . Behavioral, organizational, and technological characteristics of health professionals regarding digital health data security at specialized teaching hospitals in Northwest Ethiopia in 2022 (n=402).

Variables	Frequency	Percent
Health care workload		
Low workload	169	42
Have workload	233	58
Use internet		
Yes	394	98
No	8	2
Use social media		
Yes	390	97
No	12	3
Taken computer training		
Yes	229	57
No	173	43
Trained in digital data security		
Yes	75	18.7
No	327	81.3
Digital literacy		
Poor literacy	148	36.8
Good literacy	254	63.2
Perceived ease of use		
Not easy	220	54.7
Easy	182	45.3
Perceived usefulness		
Inadequate usefulness	309	76.9
Usefulness	93	23.1

Technological Characteristics

The study shows that according to technical characteristics, 63.2% (n=254) of health professionals were digitally literate, whereas 36.8% (n=148) of the participants did not have adequate digital literacy. Concerning digital security, 18.7% (n=75) of health professionals were trained in digital security, whereas the majority of participants, which accounted for 81.3% (n=327), were not adequate in digital security. Related to internet and social media accessibility, the majority of health professionals, which accounted for 98% (n=394), had used the internet, and 97% (n=390) had used social media. A few participants had limited access to the internet and social media (Table 2).

Health Professionals' Attitudes Toward Digital Health Data Security

Overview

The first and main aim of this study was to find out the prevalence of health professionals' attitudes toward digital health data security in a limited-resource country. Using the median score, those above the median value of 31 (IQR 27 - 33) have favorable attitudes, whereas those below the median value have unfavorable attitudes [23]. Based on that, from a total of 402 health professionals, 245 participants had a favorable attitude, which accounted for 60.9%. In contrast, 157 (39.1%) participants had an unfavorable attitude toward digital health data security countermeasures. This indicates that out of 5 health professionals, 3 need an intervention to improve their attitudes and reach an optimal level of security to minimize risk for digital health data.

Factors Associated With Attitudes Toward Digital Health Data Security

According to the context of a limited-resource country, the significant factors of health professionals' attitudes toward digital health data security were identified using logistic regression analysis. After identifying the variable using binary logistic analysis, the candidate variables were adjusted for final analysis and interpretations. Therefore, education status, computer skills, knowledge, and perceived usefulness were determined as associated factors for health professionals' attitudes toward digital health data security.

This study revealed that educational status was a significant factor and that the professionals with a postmaster's degree

were 3.29 (adjusted odds ratio [AOR] 3.292, 95% CI 1.16 - 9.34) times more likely to have a favorable attitude toward digital data security, and this difference was statistically significant at a *P* value of .03. Second, health professionals with basic computer skills were 1.8 (AOR 1.807, 95% CI 1.11 - 2.938) times more likely to have a favorable attitude toward digital data security, with a statistically significant *P* value of .02. The findings also show that health professionals with good knowledge of data security were 3.238 (AOR 3.238, 95% CI 2.0 - 5.218) times more likely to have a favorable attitude toward digital data security, with a statistically significant *P* value of 0.00. Similarly, the professionals who perceived the usefulness of digital data security were 1.965 (AOR 1.965, 95% CI 1.063 - 3.632) times more likely to have a favorable attitude toward digital health data security, with a statistically significant at a *P* value of .03 (Table 3).

Table . Bivariable and multivariable analysis of factors associated with the attitudes toward digital health data security among health professionals working at specialized teaching hospitals in Northwest Ethiopia (n=402).

Variables	Unfavorable attitude, n (%)	Favorable attitude, n (%)	COR[a] (95% CI)	AOR[b] (95% CI)
Educational status				
BSc degree	130 (32.3)	163 (40.6)	1	1
Master's	21 (5.2)	34 (8.5)	1.29 (0.715 - 2.33)	0.96 (0.488 - 1.886)
Postmaster's	6 (1.5)	48 (11.9)	6.38 (2.65 - 15.37)	3.292 (1.16 - 9.34)[c]
Monthly salary in Ethiopian birr (1 Ethiopian birr=US $0.008)				
≤10,000	121 (30.1)	152 (37.8)	1	1
>10,000	36 (9)	93 (23.1)	0.763 (0.563-1.035)	1.166 (0.646 - 2.105)
Taken computer training				
No	85 (21.1)	88 (21.9)	1	1
Yes	72 (17.9)	157 (39.1)	2.106 (1.4 - 3.168)	1.498 (0.936 - 2.397)
Use email				
No	15 (3.7)	13 (3.2)	1	1
Yes	142 (35.3)	232 (57.7)	1.885 (0.872 - 4.078)	1.01 (0.426-2.4)
Basic computer skills				
Poor	85 (21.1)	63 (15.7)	1	1
Good	72 (17.9)	182 (45.3)	3.41 (2.23 - 5.217)	1.807(1.11-2.938)[c]
Knowledge of digital data security				
Poor	115 (28.6)	91 (22.6)	1	1
Good	42 (10.5)	154 (38.3)	4.634 (2.99 - 7.182)	3.238 (2.009-5.218)[d]
Perceived usefulness				
Inadequate usefulness	136 (33.8)	173 (43)	1	1
Useful	21 (5.2)	72 (17.9)	2.695 (1.578 - 4.604)	1.965 (1.063-3.632)[c]
Perceived ease of use				
Not easy	103 (25.6)	117 (29.1)	1	1
Easy	54 (13.4)	128 (31.8)	2.087 (1.38 - 3.156)	1.289 (0.789-2.106)

[a]COR: crude odds ratio.

[b]AOR: adjusted odds ratio.

[c]*P*<.05.

[d]*P*<.01.

Discussion

Principal Findings

The main aim of this study was to assess health professionals' attitudes toward digital health security in health care in a limited-resource country. The proportion of health professionals who had a favorable attitude toward digital health data security was 60.95% (95% CI 56.0% - 65.6%). While comparing this finding with resourceful countries however, this was contrary to studies conducted in Portugal [4], Norway [14], Turkey [28], and Sweden [29]. The majority, which accounted for 81.7% (1283/1569) of the participants, had a favorable attitude, which entails that health professionals have trust in data security

techniques and believe that worthy health needs virtuous digital data security measures. In rich countries, there may be sufficient resources to give training on digital health security techniques and be actively involved in health care technology compared with resource-limited country.

The findings of this study identified educational status as a significant factor; professionals with postmaster degrees were 3.29 times more likely to have a favorable attitude toward digital data security. This denotes that the level of health professional educational status has an enormous effect on attitude toward digital data security techniques. This finding is in line with the studies conducted in European countries that show education status has a significant effect on attitudes toward digital health data security [16]. This is because, through the life of education, nearly developed digital security tools are accessed by health data users to be authenticated.

Professionals with basic computer or digital literacy were 1.807 times more likely to have a favorable attitude toward digital data security. This suggests that taking basic literacy courses related to digital technology influences a favorable attitude toward the use of digital security techniques. This finding is evidenced in Turkey, where acquiring digital literacy skills has improved attitudes toward data security [30]. However, in this study, only 63.2% (254/402) of health professionals had good computer skills. This indicates that there was a low level of involvement of health professionals in the use of digital technology to facilitate daily health care tasks.

The findings also showed that the knowledge of health professionals is 3.238 times more likely to have a favorable attitude toward digital data security. This revealed that health professionals' knowledge of digital security significantly influences their attitude toward digital data security, and this is consistent with a study in Norway that found that the knowledge of health care professionals significantly enhances their attitude in health care settings [14]. Similarly, a study conducted in Indonesia indicates that the workforce's knowledge of digital security has a beneficial effect on their attitude, resulting in a strong and enthusiastic data security culture [20].

Finally, professionals who perceived the usefulness of digital data security were 1.965 times more likely to have a favorable attitude toward digital data security. This explains why well-perceived usefulness in digital security has a significant association with attitudes toward digital health data security. This result is supported by a study conducted in Korea that used the Technology Acceptance Model, which showed that perceived usefulness made a great difference in digital security [31].

Overall, the contribution of this study to the research on attitudes toward digital health security is as follows. First, the study revealed that the education level and digital literacy of health professionals have positively influenced their attitudes toward digital health data security. Second, perceived usefulness and knowledge about data security are also important to improve their attitude toward digital data security. These findings are essential and contribute to studies on digital health.

Strength and Limitation

Digital health security is an urgent issue in the digital health environment. Especially, the findings of health professionals' attitudes toward digital data security are the basis for expanding the installation of digital health in resource-limited countries. Therefore, the findings of this study will serve as a guide for interventions in digital health development. This cross-sectional study may have introduced bias in identifying the cause-and-effect relationship.

Conclusions

According to the results of this study, the attitudes of health professionals toward digital health data security in a limited-resource country were inadequate. To improve the attitudes of health professionals, working on the significant factors, which are updating educational status, improving computer skills and knowledge toward digital security, and increasing perceived digital health security usefulness, is the basis for improving attitudes and ultimately has the purpose of safeguarding digital health data. Therefore, improving health care professionals' attitudes toward digital data security will guide the development of health care digitalization.

The findings will be forwarded to referral hospitals, the Regional Health Bureau, the Federal Minister of Health, and other institutions. The outcomes may help to improve health professionals' attitudes toward digital health data security by motivating them to improve their computer skills and enhance their educational level. Health care institutions shall be changing the attitudes of health professionals toward digital data security to create a safe digital environment. Finally, the Regional Health Bureau and the Minister of Health will formulate a plan to ensure the optimum use of digital security measures.

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Data Availability

The datasets analyzed in the study are not available due to confidentiality.

Authors' Contributions

The authors confirm their contributions to the study as follows: ASG, ZRW, and MBM contributed to study conception and design; ASG, AAM, AAS, ADW, MBM, and SBT contributed to data collection, analysis, and interpretation of results; and ASG, GH, FWB, MKT, BTA, AFS, AWS, and FWB contributed to draft manuscript preparation. All authors reviewed the results and approved the final version of the manuscript.

Conflicts of Interest

None declared.

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Abbreviations

AOR: adjusted odds ratio
WHO: World Health Organization

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Original Paper

Patient Characteristics Associated With Phone and Video Visits at a Tele-Urgent Care Center During the Initial COVID-19 Response: Cross-Sectional Study

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Abstract

Background: Health systems rapidly adopted telemedicine as an alternative health care delivery modality in response to the COVID-19 pandemic. Demographic factors, such as age and gender, may play a role in patients' choice of a phone or video visit. However, it is unknown whether there are differences in utilization between phone and video visits.

Objective: This study aimed to investigate patients' characteristics, patient utilization, and service characteristics of a tele-urgent care clinic during the initial response to the pandemic.

Methods: We conducted a cross-sectional study of urgent care patients using a statewide, on-demand telemedicine clinic with board-certified physicians during the initial phases of the pandemic. The study data were collected from March 3, 2020, through May 3, 2020.

Results: Of 1803 telemedicine visits, 1278 (70.9%) patients were women, 730 (40.5%) were aged 18 to 34 years, and 1423 (78.9%) were uninsured. There were significant differences between telemedicine modalities and gender ($P<.001$), age ($P<.001$), insurance status ($P<.001$), prescriptions given ($P<.001$), and wait times ($P<.001$). Phone visits provided significantly more access to rural areas than video visits ($P<.001$).

Conclusions: Our findings suggest that offering patients a combination of phone and video options provided additional flexibility for various patient subgroups, particularly patients living in rural regions with limited internet bandwidth. Differences in utilization were significant based on patient gender, age, and insurance status. We also found differences in prescription administration between phone and video visits that require additional investigation.

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KEYWORDS

telehealth; telemedicine; tele-urgent care; virtual urgent care; nonemergency care; televisit; phone visit; video visit; urgent care; health services research; COVID-19; health disparities; insurance status; cross-sectional study

Introduction

Health systems rapidly adopted telemedicine as an alternative health care delivery modality in response to the COVID-19 pandemic. Demographic factors, such as age and gender, may play a role in patients' choice of a phone or video visit [1-3]. However, it is unknown whether there are utilization differences between phone and video visits.

The pandemic led to a rise in phone and video consultations, providing an opportunity to study their usage across demographics and outcomes, such as medication prescriptions. Telemedicine can help improve health access and reduce disparities for vulnerable populations [4-7]. Although we know that medication prescription differs between in-person and video visits [8], there is a gap in the knowledge regarding differences in prescription administration, whether medication was prescribed or not, between telephone and video visits. Driven by prior differences in prescription administration among providers based on gender and specialty [7], we hypothesized that prescription administration, a service outcome of telemedicine, may differ between phone and video visits.

Phone-based treatment has been found feasible, acceptable, and effective compared to face-to-face visits. It is a promising alternative in telemedicine, offering tailored interventions [9]. Phone visits have taken less time and have been used more frequently, but there have not been significant differences in patient perceptions or other clinical outcomes [10].

Telemedicine's growth during the pandemic has led to a need for understanding the limitations of telephone-based versus video-based consultations for clinical care [11,12]. Patients reported that video consultations were more favorable compared to phone consultations, claiming that video visits led to improved outcomes, better diagnostic accuracy, and patient satisfaction [13-18].

Previous studies have looked at the impact of phone or video visits on vulnerable patients [19-23], but there is a lack of research on the differences in patient characteristics between the 2 modes of telemedicine-based care. Understanding these differences can help health organizations and policy makers tailor telehealth options to better suit patients.

Telemedicine use during the pandemic has been examined in various clinical environments, such as primary care, geriatrics, and subspecialties [5,22,23]. It is unclear how phone and video health care delivery in urgent care clinics was affected during the initial phases of the COVID-19 pandemic, especially regarding wait times and visit duration. The demand for urgent care clinics increased due to emergency department overcrowding, cost increase, and long wait times [24,25]. Therefore, it is important to understand the changes in urgent care practices considering telemedicine deployment postpandemic.

In this exploratory study, we examined patient and service characteristics of on-demand telehealth utilization and whether they differed by modality during the initial phase of the pandemic when the health care system suspended all in-clinic visits. We used the Donabedian framework of structure-process-outcome to inform this study design [26].

Methods

Study Overview

We conducted a descriptive analysis on a cross-sectional study of patients using a statewide, on-demand tele-urgent care clinic in the southeastern United States region. The Virtual Urgent Clinic (VUC) is an on-demand clinic open for nonemergency concerns 24 hours a day and 7 days a week. Regardless of whether they are new or existing patients, any individuals can register and access the virtual clinic through the web-based portal. To use the telemedicine service, individuals must create an account, input their medical history, and request a virtual care visit. Individuals can choose their telemedicine modality—telephone or video—through a computer, tablet, or phone.

The cost of the visit was the same for phone and video visits. The clinic provides on-demand service such that individuals can log on to the web-based portal and choose to have a visit immediately or schedule a visit for a later date. Board-certified physicians are available 24 hours every day of the week to provide care for patients. If an individual is an existing patient, documentation of the virtual visit is integrated into the electronic medical record after the visit is completed.

Data Collection

VUC monthly data were collected from March 3, 2020, through May 3, 2020, using the institutional data warehouse. The data set included patient information, such as age, gender, insurance status, and residential address, and service characteristics, such as telemedicine modality, wait time, visit duration, and medication prescription outcomes. To avoid double counting of patients or visits, each patient and each visit received a unique identifier. Incomplete encounters were recorded in the data set as incomplete if the call was not completed for any reason. The rate of incomplete encounters was only 7.9% (142/1803) of the total visit volume in this study and was included to better understand the characteristics of patients who sought care via telehealth.

Outcomes

Our primary endpoints were the characterization of telemedicine modalities (phone vs video) on patient characteristics measured by demographics and insurance status, utilization measured by the volume of visits; and service characteristics measured by medication prescriptions and visit wait times. The secondary endpoint was utilization, which was measured by the number of visits from rural and urban neighborhoods.

Statistical Analysis

The study data included patient age, gender, health insurance status, address, number of medication prescriptions, number of visits, and choice of telemedicine modality. For each of these variables, we calculated descriptive statistics for each demographic category stratified by modality (phone or video) and the total of both groups. A χ^2 test was calculated to check for significant differences between telemedicine visits and these

variables. Additionally, we calculated the average wait time and visit duration for phone and video visits. A 2-sample *t* test assuming unequal variances (Welch *t* test) was also conducted to determine if there was a statistically significant difference in the average wait times and visit duration lengths between phone and video telemedicine visits.

To examine the predictors of prescription administration, we constructed a logistic regression model with a dichotomous dependent variable of prescription administration (0=no prescription=0 and 1=at least 1 prescription given) as a dependent outcome variable and patient age, gender, insurance status, location, and telemedicine modality as independent variables in the model predictors. We used a *P* value level of .05 to indicate statistical significance.

Geospatial Analysis

Geographical locations for patients with VUC visits over the phone or video were examined to assess the urban-rural spread of the patients in this data set. Using the US Census definition, cities with populations of 50,000 people or more were designated as urban, and those with less than 50,000 people were designated as rural. In the telemedicine data set, 198 places in North Carolina were found, of which 179 were classified as rural and 19 were classified as urban, which was used to develop the health access map. A χ^2 analysis was used to determine the significance between an encounter from an individual in an urban or rural area and the encounter modality.

To understand the association between telehealth modality and location, we used ArcGIS (Esri) to map zip code–level populations, as reported in the 2010 US Census Bureau data, with VUC visits based on Zip Code Tabulation Areas (ZCTAs). We used the 2016 American Community Service (ACS) to calculate the percentage of households with internet access by ZCTA. We then mapped the ACS data and visit counts from the VUC by modality on the North Carolina (NC) map to better understand the preference of patients for modalities based on internet availability.

We used natural breakdowns to quantify the percentage of households with internet in each NC zip code to determine the threshold for low, medium, and high categories based on the 2016 ACS data set. The colors along the bottom row (gray to light blue to teal) represent ZCTAs with a low percentage (0%-71%) of households with internet access and an increasing number of phone (or video) visits. The colors in the middle row (light pink to light purple to blue) represent ZCTAs with a medium percentage (72%-82%) of households with internet access and an increasing number of phone (or video) visits. The colors along the top row (pink to purple to dark purple) represent ZCTAs with a high percentage (83%-100%) of households with internet access and an increasing number of phone (or video) visits. The colors along the diagonal (gray to light purple to dark purple) represent ZCTAs with low internet access and low telemedicine visits, medium internet access and medium telemedicine visits, and high internet access and high telemedicine visits. For phone visits, the breaks were 1-2 (low), 3-6 (medium), and 7-37 (high). For video visits, the breaks were 1 (low), 2-3 (medium), and 4-15 (high). We used quantiles to determine the threshold for low, medium, and high categories based on the ACS 5-year estimates from 2015-2019.

Ethical Considerations

University of North Carolina at Chapel Hill institutional review board approval was obtained prior to conducting this study (18-1628).

Results

Telemedicine Visit Overview

Table 1 shows a series of visit counts of the patients who used the telemedicine service during the observed period categorized by the patient characteristics captured in this study. It also indicates the χ^2 and *P* values for significance tests for the differences between these observed characteristics.

Table 1. Percentage statistics and χ^2 values for phone and video telemedicine visits.

Demographic	Phone visits (n=1414)	Video visits (n=389)	Total visits (N=1803)	Chi-square (df)	*P* value
Visits per day, mean (SD)	22.8 (9)	6.3 (3.1)	29.1 (10.7)	N/A[a]	N/A
Gender, n (%)				16.79 (2)	<.001
Women	1033 (73)	245 (63)	1278 (70.9)		
Men	377 (26.7)	144 (37)	521 (28.9)		
Nonbinary	4 (0.3)	0 (0)	4 (0.2)		
Age (years), n (%)				24.99 (4)	<.001
<18	96 (6.8)	57 (14.7)	153 (8.5)		
18-34	579 (40.9)	151 (38.8)	730 (40.5)		
35-50	486 (34.4)	123 (31.6)	609 (33.8)		
51-64	185 (13.1)	44 (11.3)	229 (12.7)		
≥65	68 (4.8)	14 (3.6)	82 (4.5)		
Health insurance status, n (%)				18.91 (1)	<.001
Insured	329 (23.3)	51 (13.1)	380 (21.1)		
Uninsured	1085 (76.7)	338 (86.9)	1423 (78.9)		
Residence, n/N (%)				6.74 (1)	.009
Rural	782/1370 (57.1)	189/381 (49.6)	971/1751 (55.5)		
Urban	588/1370 (42.9)	192 /381 (50.4)	780/1751 (44.5)		
Prescriptions per visit, n (%)				24.07 (1)	<.001
Received	980 (69.3)	218 (56)	1198 (66.4)		
Did not receive	434 (30.7)	171 (44)	605 (33.6)		

[a]N/A: not applicable.

Patient Characteristics

Phone visits constituted most of the 1803 total visits (n=1414, 78.4%), with an average of 22.8 (SD 9) daily visits, while video visits accounted for the remaining visits (n=389), with a daily average of 6.3 (SD 3.1) visits. Most of the patients were women across both phone and video modalities (phone visits: n=1033, 73%; video visits: n=245, 63%). Among age groups, patients aged 18 to 34 years had the most visits (phone visits: n=579, 40.9%; video visits: n=151, 38.8%), with patients aged 35 to 50 years being the next most represented age group (phone visits: n=486, 34.4%; video visits: n=123, 31.6%). Across both modalities, the least present age group included patients older than 65 years (phone visits: n=68, 4.8%; video visits: n=14, 3.6%). Most patients across both modalities were uninsured (phone visits: n=1085, 76.7%; video visits: n=338, 86.9%).

Significant differences between telemedicine modalities and gender (*P*<.001), age (*P*<.001), insurance status (*P*<.001), health access (*P*=.009), and prescriptions given (*P*<.001). This suggests that men, patients younger than 18 years, uninsured patients, and patients residing in urban areas preferred the video modality for telemedicine visits, and video visits were more associated with not getting prescriptions.

Telemedicine Service Characteristics

Prescription Administration

More patients received at least 1 prescription (phone visits: n=980, 69.3%; video visits: n=218, 56%) from a telemedicine visit rather than no prescription. Video visits were more associated with no prescriptions than phone visits (*P*<.001). Significant differences were found in medication prescription administration between phone and video visits (*P*<.001; Table 1).

For phone visits, of a total of 1414 phone visits, 980 (69.3%) resulted in at least 1 prescription given, while the other 434 did not receive any prescriptions. On average (SD), patients received 1 (1.02) prescription per encounter. Of all phone visits, 434 (30.7%) patients did not receive a prescription, 944 (66.8%) patients received 1-3 prescriptions in an encounter, and 36 (2.5%) patients received 4-7 prescriptions in an encounter.

For video visits, from a total of 389 video visits, 218 (56%) resulted in at least 1 prescription given, while the other 171 did not receive any. The average (SD) number of prescriptions per encounter was 0.84 (1.00). Of all video visits, 171 (43.9%) patients did not receive a prescription, 210 (54%) patients received 1-3 prescriptions in an encounter, and 8 (2.1%) patients received 4-7 prescriptions in an encounter.

We found that 5 patient characteristics were strong predictors of telemedicine prescription administration (Table 2). Predictors

that were positively associated with prescription administration were patients aged 18 to 34 years (β=.62, *P*<.001), 35 to 50 years (β=.81, *P*<.001), and older than 65 years (β=.94, *P*=.002). Predictors that were negatively associated with prescription administrations were video visits (β=–.47, *P*<.001) and male patients (β=–.38, *P*<.001). There was no significant relationship between patients' insurance status and prescription rates.

Table 2. Logistic regression model showing patient demographic associations with telemedicine prescription administration. The independent variables were modality, age, gender, and insurance status. The depended variable was prescriptions given.

	Estimate	SE	*z* score	Pr(>|z|)[a]	R^2
Model intercept	0.2711	0.1853	1.463	.14	0.027269
Modality					
Video	-0.4724	0.1204	-3.922	<.001	N/A[b]
Gender					
Men	-0.3878	0.1108	-3.5	<.001	N/A
Nonbinary	0.4606	1.1715	0.393	.69	N/A
Health insurance status					
Insured	0.1629	0.1308	1.245	.21	N/A
Age (years)					
18-34	0.6227	0.1858	3.351	<.001	N/A
35-50	0.8057	0.19	4.241	<.001	N/A
51-64	0.3573	0.2173	1.644	0.10	N/A
≥65	0.9421	0.3045	3.094	0.002	N/A

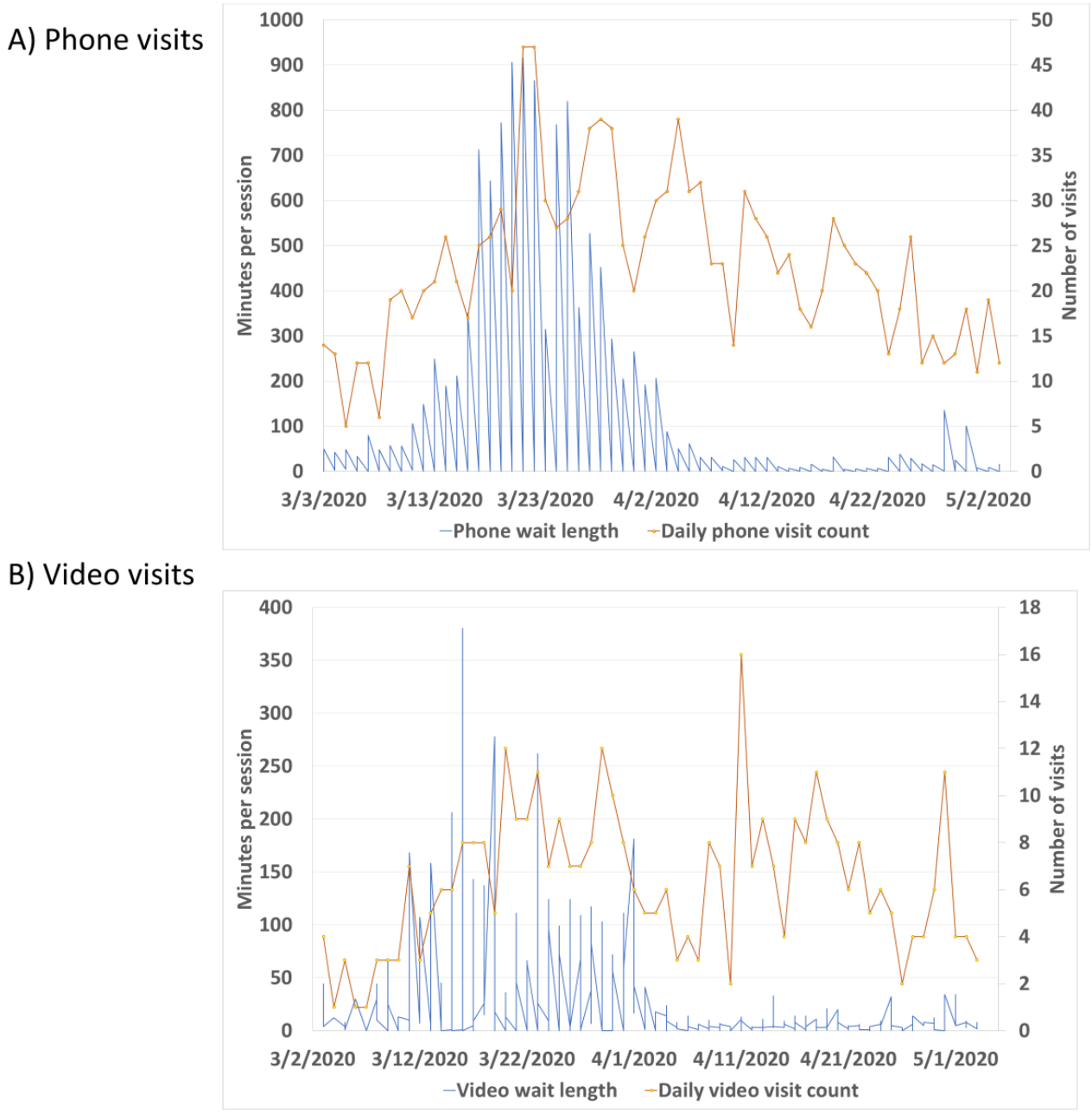
[a]Pr(>|z|): *P* value associated with the value in the z score column.

[b]N/A: not applicable.

Wait Times and Visit Duration

The average wait time for patients to start their phone visits was 64.1 (SD 129.9) minutes, while the average wait time for patients with video visits was 24.6 (SD 45.6) minutes. The average visit duration for phone visits was 7.3 (SD 4.4) minutes, while the average visit duration for patients in video visits was 9.0 (SD 5.9) minutes. Significant differences existed between the average wait times and durations for phone and video visits (Welch *t* test *P*<.001 for both wait times and duration). For phone and video visits in this data set, the daily wait times for patients to see a physician across each modality are indicated in Figures 1A and 1B, respectively. The number of physicians working daily shown in these figures peaked at a maximum of 33 physicians on March 21 and 22. The number of phone sessions facilitated was also at its peak on these days at 47 phone visits. Phone users experienced the longest wait times in the second half of March, but both phone and video users experienced extended wait times in this same period compared to April.

Figure 1. Comparison of (A) phone visit and (B) video visit wait times with a count of daily visits and physicians working.

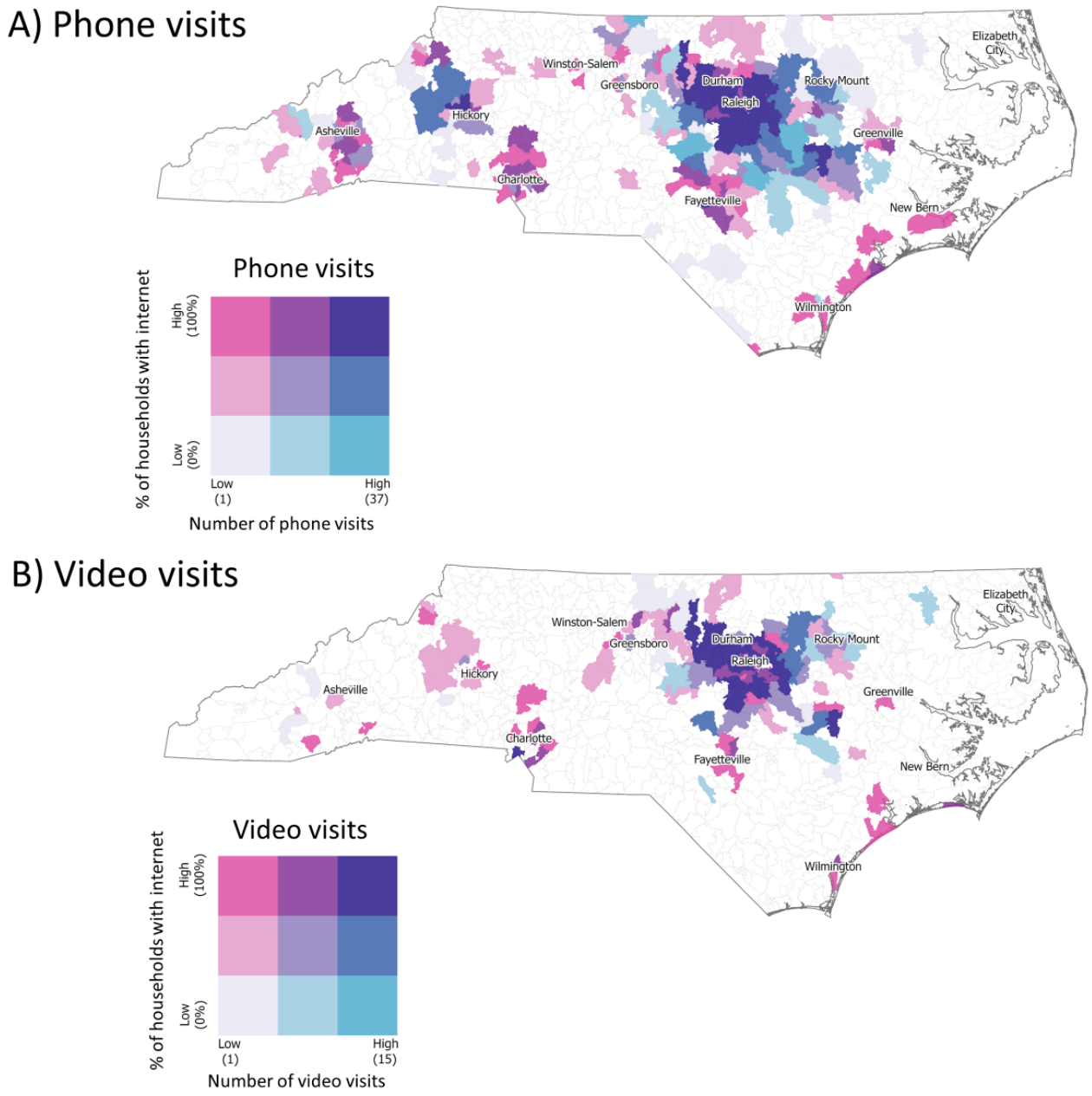


Telemedicine Utilization in Rural and Urban Areas

Of the 1080 NC zip codes, 262 (24.3%) had a low percentage of households with internet access, 277 (25.6%) had a medium percentage of households with internet access, and 269 (24.9%) had a high percentage of households with internet access. There were 272 (25.3%) zip codes with no internet access.

The overall utilization of video visits was higher in areas with high percentages of households having internet access (Figure 2). Among the individuals from zip codes with low internet access there were 127 (83.5%) phone visits and 25 (16.5%) video visits. Zip codes with medium internet access had 367 (80.8%) phone visits and 87 (19.2%) video visits, and those with high internet access were 879 (76.2%) phone visits and 274 (23.8%) video visits.

Figure 2. Comparison of (A) phone and (B) video telemedicine visits and the percentage of households in North Carolina with internet access based on American Community Service data.



Visits to the telemedicine-based clinic came from 431 (40%) unique NC zip codes. Of these, 251 (58.2%) were rural zip codes and 180 (41.8%) were urban zip codes (Figure 2). The density of the visits, shown in larger icons in Figure 2, originated mostly from major metropolitan areas like the state capitol or the Research Triangle Park. Phone visits provided further reach into areas with low internet access, while video visits mainly occurred in urban settings with high access to internet services.

Phone visits provided significantly more access to rural areas than video visits (P<.001). There were 1363 phone visits from patients in NC, with 780 (56.8%) being from rural areas and 583 (42.5%) from urban settings. There were 383 video visits from patients in NC, with 190 (49.2%) being from rural areas and 193 (50%) from urban settings.

Phone visits originated from 290 (26.9%) unique NC zip codes, of which 170 (58.6%) were from rural areas, 80 (27.6%) were from urban areas, and 40 (13.8%) were from out of state. Video visits occurred in 141 (32.4%) unique NC zip codes, of which 80 (56.7%) were from rural areas, 56 (39.7%) were from urban areas, and 5 (3.6%) were from out of state. Phone visits provided better reach into rural areas; however, video visits had widespread coverage, demonstrating the potential to complement phone visits in rural areas. Both phone and video visits within urban areas provided comparable coverage as expected.

Discussion

Principal Findings

We conducted a cross-sectional study of telemedicine urgent care visits completed through phone or video using a statewide,

on-demand urgent care telemedicine clinic, focusing on demographics, utilization, and service characteristics. We observed significant differences in service characteristics between phone and video visits. The rate of medication prescription was much higher among phone visits compared to video visits. Patients had a higher probability of receiving a prescription during a phone visit, while the probability of receiving a prescription was lower during a video visit. Differences in gender, age, and telemedicine modality were associated with significant variations in prescription administration.

Similarly, significant differences in wait time and visit duration were observed between phone and video visits, where phone visits had higher wait times and longer visit durations. The high volume of requests for phone visits can justify the long wait. It was unclear if providers compensated for the long wait times by providing more visit time or if patients who waited longer had more questions based on the differences in visit durations.

Utilization of phone and video visits differed significantly. Women, insured patients, and those residing in rural areas preferred phone visits, while men, uninsured patients, and those residing in urban areas preferred video visits. Patients older than 65 years were equally split. The increase in video visits was due to pandemic-related cancellations of in-person appointments. Video visits were more common for children due to the need for clinical examination. Phone visits were more common in rural areas with no internet access for video visits. Rural patients preferred phone visits while urban patients preferred video visits. The reason for this preference is unclear. We suspect that a combination of privacy concerns, lack of confidence in their internet connection, and a lack of awareness may drive patients' decisions; however, more investigation is needed [27,28].

Tying our findings to similar studies in the literature was a challenge because of a gap in studying the differences between telephone and video visits on the same outcomes [29]. Comparative studies have indicated that there has not been a meaningful difference between these modalities, having similar consultation session lengths, content, and perceived quality [30-32]. One study reported that older, rural, and ethnic minority patients were associated with lower utilization rates of video visits compared to phone visits [23]. A previous study reported that patients who had telephone visits had longer visit durations than those who had video visits [32], which contradicts our finding where video visits were longer in duration. A few studies have indicated increased utilization of telemedicine to trend toward women, with women being more likely to attend telephone-based interventions and to benefit from such interventions in the context of addiction treatment [33,34]. Moreover, another study showed that no major differences in utilization were found between video and telephone visits [31], which contradicts our findings demonstrating higher utilization of telephone visits compared to video visits.

Other studies explored telemedicine modalities separately demonstrating limitations due to selection bias in patient populations, such as including patients from a single hospital or clinic setting [13,14,16]. There is also concern that these studies often cater to specialized medical concerns or treatment options, which limits the demographic diversity of the patients recruited regarding factors such as age or gender, making the findings less generalizable [17,30]. Little was known regarding the patient characteristics of telephone or video telemedicine modalities across the rural-urban divide, patient insurance statuses, and prescriptions provided to the patients.

The COVID-19 policy waivers by the Center of Medicaid and Medicare and private insurers to include phone and video visits appear to be an effective decision that increased access and reduced disparities [35,36]. Additionally, this study shows that internet access is still limited in rural areas, which may limit the ability to conduct patient video visits, resulting in more phone visits. We recommend policymakers to continue to support video and phone visits equally, and we highlight the importance of building internet capacity within rural and vulnerable communities to expand the effective use of telemedicine.

Limitations

This study had several limitations. We conducted a cross-sectional study as we could not randomize patients to a telemedicine modality due to the complexity of the process and given the sensitivity of COVID-19. In addition, the study was conducted over 2 months (March 3, 2020, to May 3, 2020) at the height of the pandemic with a limited amount of data; however, this reflected the initial response to the pandemic when telemedicine was the primary option for care. A large proportion of patients in this study were uninsured. Uninsured patients preferred telehealth during the initial phase of the pandemic due to the suspension of in-person visits and the shutdown of health care systems and primary care clinics, which are more expensive for uninsured patients compared to emergency departments [37]. This study did not include a comparison to in-person consultations because the health care system suspended all nonessential visits during the observed study period, starting on March 20, 2020. There were no data collected on race, ethnicity, or type of insurance used or covered, which could have added value to the findings of this study. The diagnosis type may confound the difference in prescription administration of phone and video visits. We could not merge the telemedicine data with the electronic health record data to assess the difference in documentation quality between phone and video visits. No information was available to determine if the visit wait times in the data set included those seeking a telemedicine visit immediately as opposed to at a later date. Wait times could be separated for those seeking immediate appointments to improve our findings. Physician-level data was not accessible, limiting our assessment of factors such as clinician preparedness. Finally, the study findings were limited to 1 site, and so the generalizability to other settings is limited.

Conclusion

Our study analyzed the use of phone and video visits at a telemedicine clinic during the COVID-19 pandemic. We discovered that providing patients with a variety of phone and video options was beneficial for many patient groups, especially those in rural or low-bandwidth areas. Gender, age, and insurance status were also factors affecting usage. Moreover,

we observed differences in prescription administration between the 2 modalities that require further investigation. Our findings indicate that phone visits were more prevalent in rural regions compared to urban areas. To promote telemedicine adoption and quality, we must work toward improving internet infrastructure in rural areas, educating patients on selecting the appropriate modality, and establishing equitable service policies for phone and video visits.

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Authors' Contributions

SK contributed to the data collection, study design, analysis, and manuscript writing. RJ contributed to the data analysis and manuscript writing. MP contributed to data analysis and manuscript writing. PM contributed to map creation and manuscript revision. BE contributed to the study design and data collection. All authors have reviewed and agreed to submitting the manuscript.

Conflicts of Interest

None declared.

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Abbreviations

ACS: American Community Service
NC: North Carolina
VUC: Virtual Urgent Clinic
ZCTA: Zip Code Tabulation Area

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Original Paper

A Semantic Approach to Describe Social and Economic Characteristics That Impact Health Outcomes (Social Determinants of Health): Ontology Development Study

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Abstract

Background: Social determinants of health (SDoH) have been described by the World Health Organization as the conditions in which individuals are born, live, work, and age. These conditions can be grouped into 3 interrelated levels known as macrolevel (societal), mesolevel (community), and microlevel (individual) determinants. The scope of SDoH expands beyond the biomedical level, and there remains a need to connect other areas such as economics, public policy, and social factors.

Objective: Providing a computable artifact that can link health data to concepts involving the different levels of determinants may improve our understanding of the impact SDoH have on human populations. Modeling SDoH may help to reduce existing gaps in the literature through explicit links between the determinants and biological factors. This in turn can allow researchers and clinicians to make better sense of data and discover new knowledge through the use of semantic links.

Methods: An experimental ontology was developed to represent knowledge of the social and economic characteristics of SDoH. Information from 27 literature sources was analyzed to gather concepts and encoded using Web Ontology Language, version 2 (OWL2) and Protégé. Four evaluators independently reviewed the ontology axioms using natural language translation. The analyses from the evaluations and selected terminologies from the Basic Formal Ontology were used to create a revised ontology with a broad spectrum of knowledge concepts ranging from the macrolevel to the microlevel determinants.

Results: The literature search identified several topics of discussion for each determinant level. Publications for the macrolevel determinants centered around health policy, income inequality, welfare, and the environment. Articles relating to the mesolevel determinants discussed work, work conditions, psychosocial factors, socioeconomic position, outcomes, food, poverty, housing, and crime. Finally, sources found for the microlevel determinants examined gender, ethnicity, race, and behavior. Concepts were gathered from the literature and used to produce an ontology consisting of 383 classes, 109 object properties, and 748 logical axioms. A reasoning test revealed no inconsistent axioms.

Conclusions: This ontology models heterogeneous social and economic concepts to represent aspects of SDoH. The scope of SDoH is expansive, and although the ontology is broad, it is still in its early stages. To our current understanding, this ontology represents the first attempt to concentrate on knowledge concepts that are currently not covered by existing ontologies. Future

direction will include further expanding the ontology to link with other biomedical ontologies, including alignment for granular semantics.

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KEYWORDS

social determinants of health; ontology; semantics; knowledge representation

Introduction

Background

Ontologies are an important resource that have advanced the biomedical sciences. Originating from the philosophical domain and later incorporated into the computing and information sciences, ontologies represent and model our physical reality using semantics to describe domain entities (ie, knowledge base) [1]. These artifacts can be used to house vocabularies to generate inferences with the help of software reasoners such as HermiT [2], ELK [3], and FaCT++ [4]. Logically structured vocabularies can be used with reasoning tools to implement problem-solving software in clinical settings. In addition, biomedical researchers have advanced and wielded ontologies to be used in applications for artificial intelligence, natural language processing, information retrieval, and indexing (eg, data integration, harmonization, and exchange) [5]. Some impactful examples of ontologies include the Systematized Nomenclature of Medicine–Clinical Terms [6] and Gene Ontology [7], which are hosted on the National Center for Biomedical Ontology [8] and the OBO Foundry [9]; for example, the National Center for Biomedical Ontology BioPortal is an open repository of >700 biomedical ontologies [8], whereas the OBO Foundry hosts interoperable biomedical and health ontologies that share a common framework [9]. All the OBO Foundry–approved ontologies are built upon the Basic Formal Ontology (BFO), a common upper-level ontology, for interoperability and reuse. More than ever, there is a strong need to use ontologies for social health behavior sciences with the downstream goal of harmonizing biological and behavioral data [10].

Social Determinants of Health

Since the early 19th century, the public health community has sought to determine how social determinants are associated with behavior, health outcomes, and health inequalities [11]. Factors such as social position can influence an individual's health status and thus lead to disease-inducing behaviors [11]. The link between social determinants and disease is a central point for public health research [11]. Over the years, public health researchers have classified these determinants as social determinants of health (SDoH). SDoH have been described by the World Health Organization as the conditions in which individuals are born, live, work, and age [12]. These nonbiological factors influence health outcomes in terms of health status, well-being, mortality, and life expectancy.

SDoH encompass many different areas, such as social and political context, governance, physical and living environment, community, safety, education, occupation, income, cultural and social values, biological and behavioral factors, wellness, food, and the health care system [12]. These categories can be represented by 3 levels of organization: macrolevel, mesolevel, and microlevel determinants [12]. Macrolevel determinants consist of socioeconomic hierarchies that govern access to resources in society through policy making [11]. Mesolevel determinants include concepts such as environment, neighborhood quality, occupation, and crime. This intermediate level is also concerned with psychosocial risk factors such as a stressful environment, the quality of social networks, and high physical or social demand [11]. Finally, microlevel determinants describe individual interactions, behaviors, lifestyle, and genetics [11]. Associated with these determinants are health inequalities, or the unfair and avoidable differences in health status among individuals [12], including inequities caused by structural or systemic factors.

Research Objective

The overarching goal of this research was to develop a biomedical ontology to model and represent knowledge on SDoH. More specifically, this work attempted to provide a broad spectrum of concepts ranging from the macrolevel to microlevel determinants focusing on social and economic characteristics as well as social-related health policies. By developing an ontology for SDoH, we can standardize the current scientific knowledge of this area based on a lightweight literature review and consensus from domain experts. Accomplishing this may help provide a computable ontology artifact that can link health data to concepts involving SDoH and advance informatics methods and tools to understand the impact each determinant has on human populations. In addition, modeling SDoH may also help to reduce existing gaps in the literature through explicit links between the determinants and biological factors. This in turn can allow researchers and clinicians to make better sense of data and discover new knowledge through the use of semantic links.

Existing relevant ontologies usually focus on biology and biomedicine; however, the scope of SDoH expands beyond the biomedical level (ie, microlevel) and relates to aspects that are not necessarily biology based, such as economics, public policy, social factors, and so on. Some of the more mature ontologies, such as the ones hosted on the OBO Foundry, have some interoperability due to a shared framework, but there remains a need to connect the heterogeneous SDoH concepts within the biomedical level and elucidate meaning from the knowledge. We therefore put forth the following research objective: *using ontological methods, we can represent, formalize, and connect concepts pertaining to social, policy, and economic factors of SDoH*. The output of this effort is an initial ontology artifact that models the social, policy, and economic concepts and their relationships in composing the scope of SDoH to build future work. To accomplish this, we (1) analyzed the literature on the 3 aspects and the aforementioned concepts within these aspects

and (2) produced an evaluated ontology artifact that reflects the intricate connections of the social and economic concepts of SDoH. This final experimental ontology artifact will be logically consistent with evaluation from domain experts and reasoning tools, grounded from a review of the literature to determine high-level concepts that stretch across SDoH, and aligned with a shared framework for biomedical ontologies to enable interoperability and reusability.

Methods

Overview

A brief yet comprehensive review was conducted to develop ontology terminology that effectively captures the concepts related to SDoH. This review served as a foundation for structuring and defining the key elements within the ontology. The literature reviewed aimed to examine how human health is affected by nonbiological factors that are associated with SDoH. The concepts were curated in concept map drafts from the review of SDoH, and the determinant of health model was used as a guide for concept development [13]. Later, we used Web Ontology Language, version 2 (OWL2) [14], the BFO [15-17], and semantic reasoners to construct and validate the ontology artifact.

Review of Social and Economic Factors Impacting Health

Peer-reviewed articles were searched and evaluated by the primary author on PubMed from September 17 to October 8, 2021. Boolean operators and MeSH (Medical Subject Headings) terms were used to refine literature searches conducted using the advanced search feature on PubMed. Multiple concepts and relationships were combined through Boolean expressions, that is, “Social determinants of health AND (health policy OR health care system),” to broaden the search. Certain phrases were enclosed in parentheses to isolate parts of the search query for precision and specificity. MeSH terms with regard to SDoH were provided by PubMed and used to construct the queries. A summary of each search is described in Table 1.

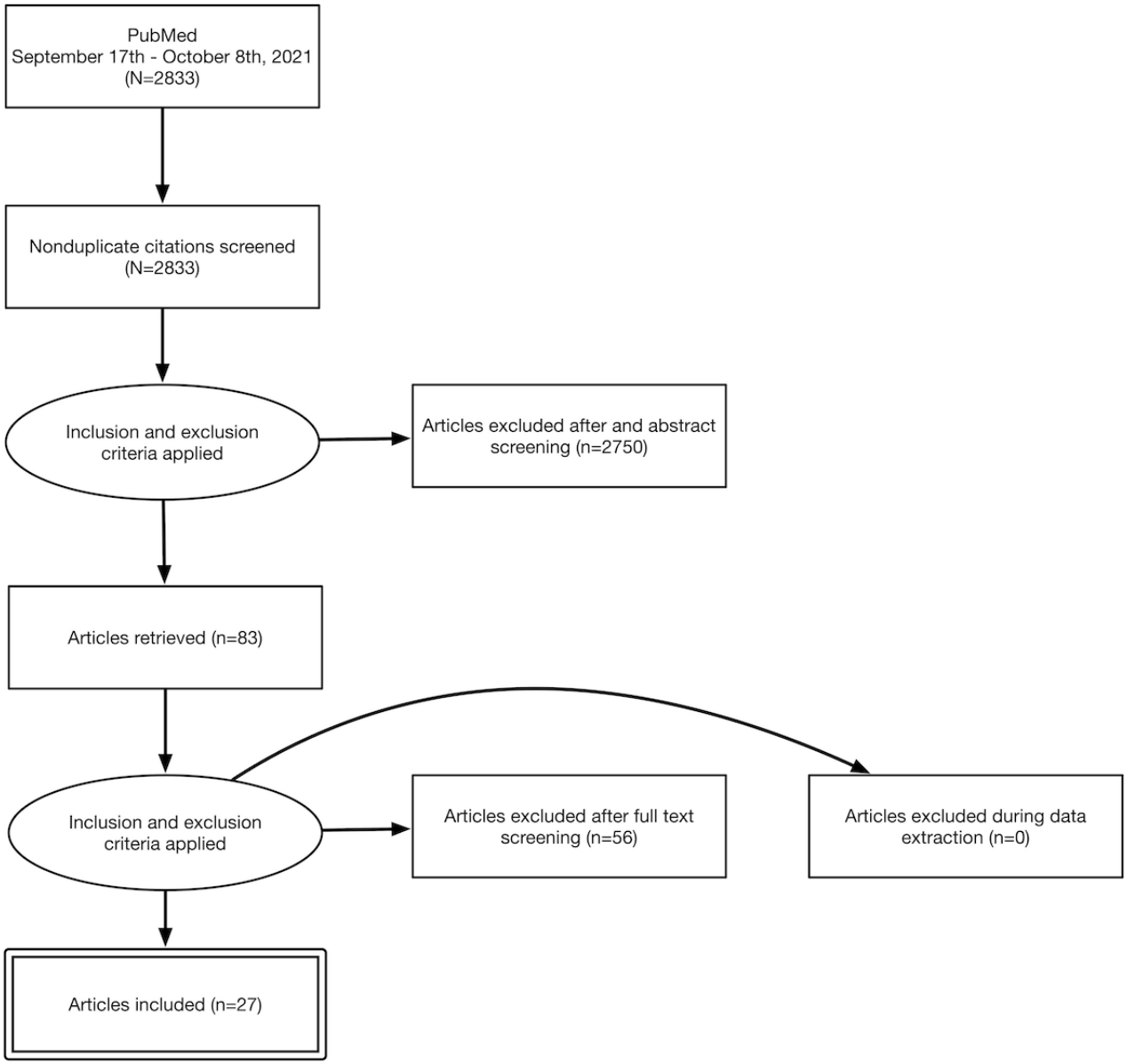
Table 1. Literature search overview. Advanced search queries for each level of the social determinants of health were searched on the PubMed database between September 17 and October 8, 2021. The table displays the query, applied filter, and number of results each search yielded (N=2833).

Level	Search query	Results, n (%)
Macrolevel	“Social determinants of health AND (health policy OR health care system OR health disparities)”	721 (25.45)
Macrolevel	“Income inequality AND welfare AND health policy”	10 (0.35)
Macrolevel	“Environmental determinants of health AND climate change”	216 (7.62)
Mesolevel	“Work OR socioeconomic position AND (health inequalities)”	300 (10.59)
Mesolevel	“Socioeconomic outcomes AND (housing OR food)”	291 (10.27)
Mesolevel	Food OR poverty AND (health inequalities)”	250 (8.82)
Mesolevel	“Social determinants of health AND (crime rate OR domestic violence)”	14 (0.49)
Microlevel	“Social determinants of health (gender OR age OR ethnicity OR race OR inequalities OR education)”	1031 (36.39)

Articles of interest must have met the following criteria: free full text available, publication date <10 years ago, and published in English. With accessibility in mind, free full text was included as an eligibility criterion. Older publications may have been relevant to this paper but were not considered because they may not reflect current knowledge. Thus, the publication date was set to <10 years ago. As English is the primary language of all authors of this study, it was included as an eligibility criterion for the literature search. Finally, the article type must have been a book or document, systematic review, journal article, observational study, case report, or clinical study. Collectively, the search queries yielded a total of 2833 nonduplicate citations.

The first step of the inclusion and exclusion process involved removing articles that did not incorporate, or relate to, the MeSH terms identified in the search queries within their abstract or title. After this evaluation, of the 2833 articles, 2750 (97.07%) were immediately excluded, and 83 (2.93%) remained for a second assessment. Articles that did not precisely align with the research topic were once again removed. As a result, of the 83 articles, 56 (67%) were excluded, and thus 27 (33%) articles remained. Of these 28 articles, 9 (33%) were included for the macrolevel determinants, 10 (37%) addressed the mesolevel determinants, and 9 (33%) focused on the microlevel determinants. The inclusion and exclusion processes are depicted in Figure 1.

Figure 1. Iterative process for gathering the articles of interest. The PubMed searches produced 2833 nonduplicate citations; by applying the inclusion and exclusion criteria described in the main text, we removed 2805 (99.01%) citations, leaving 27 (0.95%) articles for review.



Ontology Design and Development

The review helped us capture some basic salient high-level knowledge that we can encode into ontology from concept maps. The motivation is to gain a *bird's-eye view* of SDoH and proceed from a top-down approach in developing the experimental ontology. We developed iterative multiple concept maps using draw.io [18] to identify concepts and relationship links among the concepts. Our analysis of the concept maps revealed 4 generalized relationships that bridged the various concepts: *type of, part of, dependency,* and *causal*. Figures 2-5 reveal the final drafted concept maps.

Figure 2. Determinants that impact health outcomes and behaviors. Dotted concept ovals indicate additional child concepts that are further described in Figures 3-5.

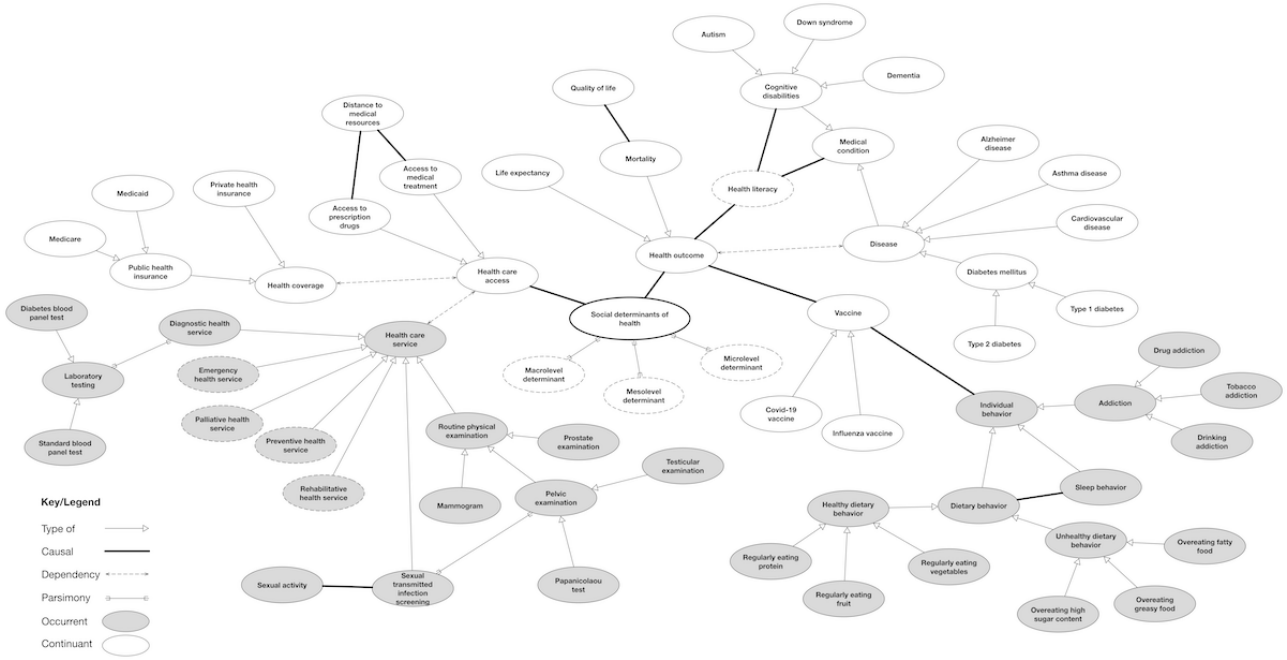


Figure 3. The relationship of concepts associated with macrolevel determinants. Concepts were derived from literature keywords, such as “health policy,” “income inequality,” “welfare,” and “environment.” Dotted concept ovals indicate additional child concepts.

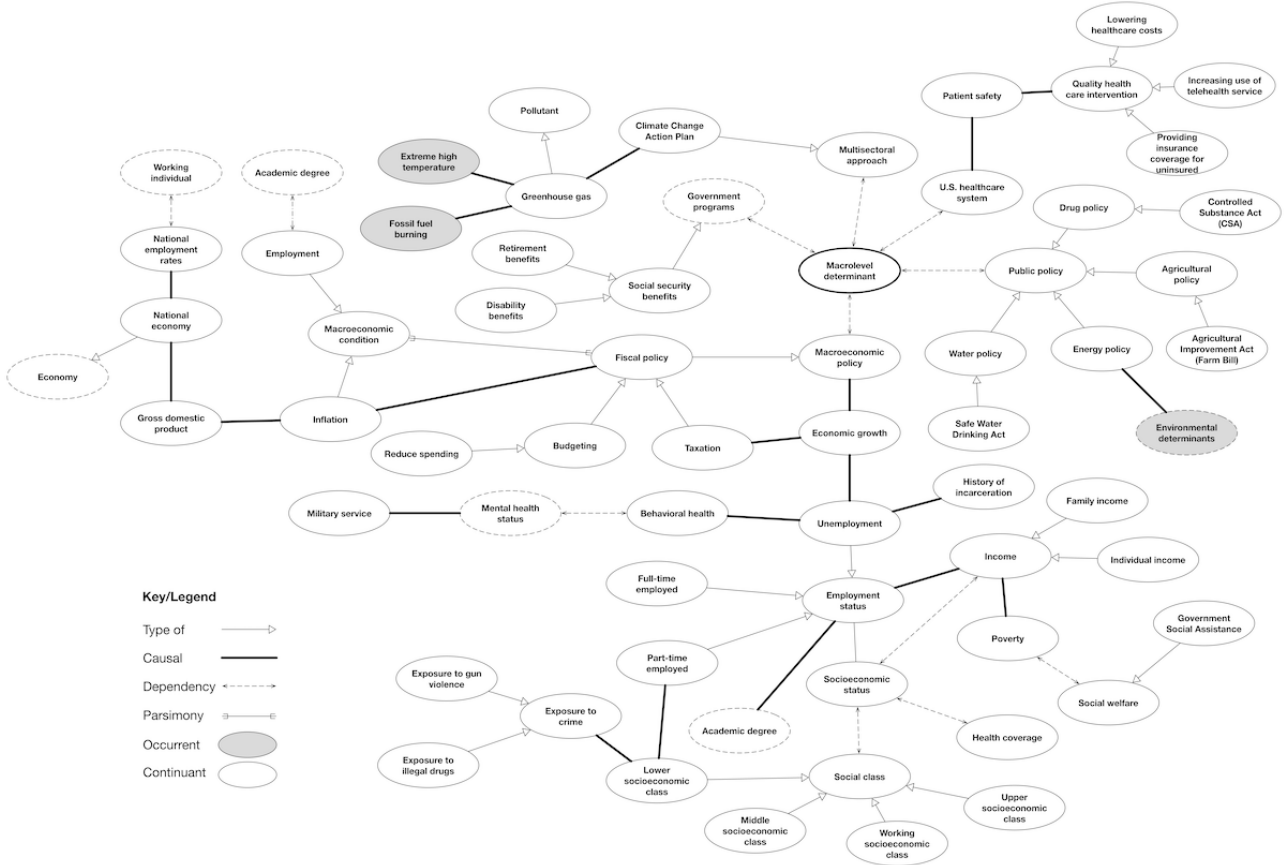


Figure 4. The relationship of concepts associated with mesolevel determinants. This map displays the most detailed network of relationships and was formed from the following keywords: "work," "work conditions," "psychosocial work factors," "socioeconomic position," "socioeconomic outcomes," "food," "poverty," "housing," and "crime." Dotted concept ovals indicate additional child concepts.

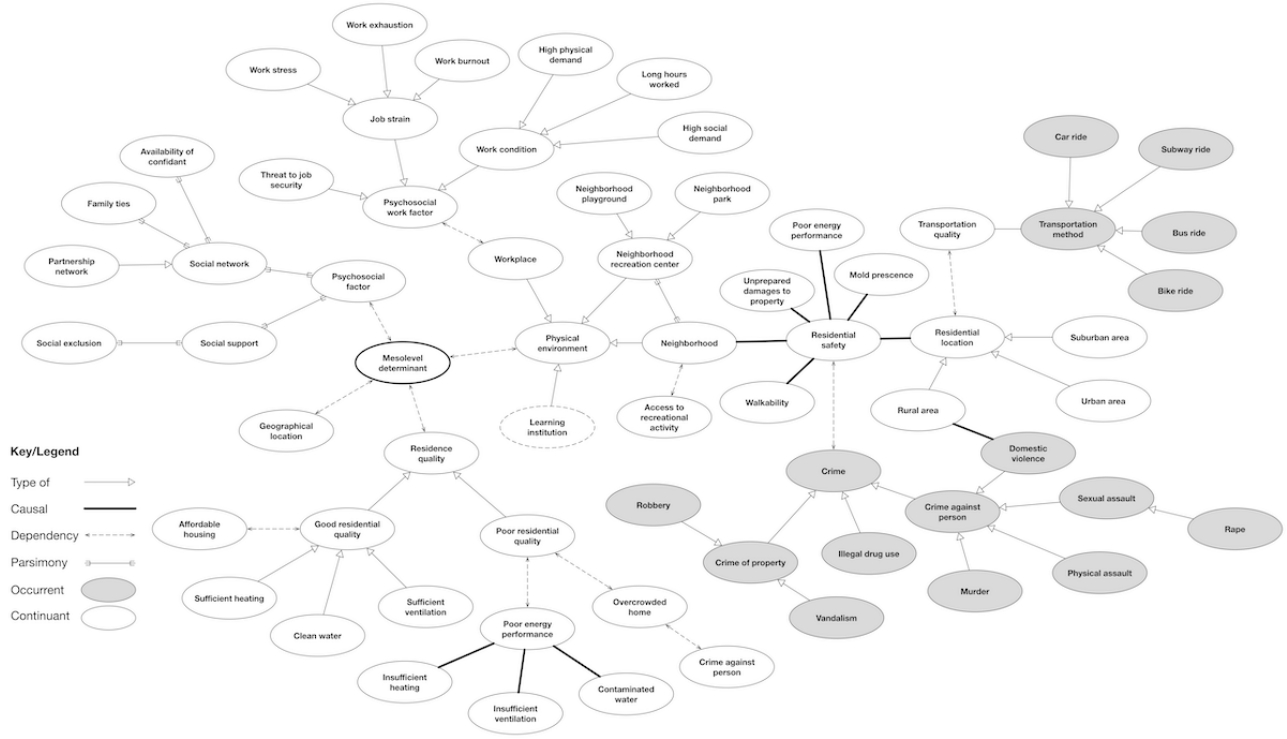
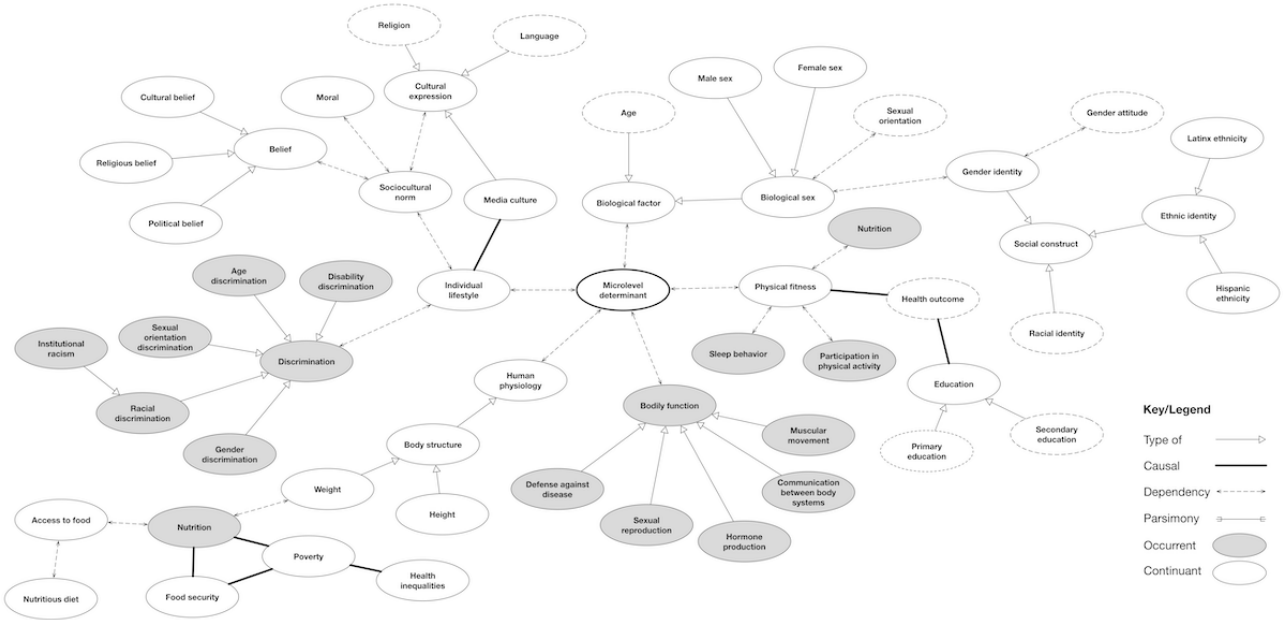


Figure 5. The relationship of concepts associated with microlevel determinants. Key elements of this map were gathered from keywords such as "physiology," "gender," "ethnicity," "race," and "behavior." Dotted concept ovals indicate additional child concepts.



The *part of* relationship is illustrated with a forked link connection and indicates that 2 concepts were part of each other; for example, this is demonstrated in Figure 2 between the concepts "Macrolevel determinants" and "Social determinants of health," where macrolevel determinants are one part (meronym) of the composition of SDoH (holonym). A *dependency* relationship was demonstrated as a dotted-line link connection and referred to concepts that were dependent on each other. This can be seen in Figure 3 between the concepts "Behavioral health" and "Mental health status," where an individual's behavioral health is dependent on the status of their mental health.

A *causal* relationship was represented as a thick line link connection and described 2 concepts that had a cause-and-effect relationship. An example of this is demonstrated with the concepts "greenhouse gas" and "extreme high temperature," where there is a causal relationship between greenhouse gas and increased temperatures. Finally, a *type of* relation was illustrated as an open arrowhead similar to Unified Modeling

Language notation. This was used to represent inheritance, or parent and child concepts. All child objects inherit the functionality specified by the parent. This included relationship types; for example, as seen in Figure 2, the concept "Health outcome" was described to have a causal relationship with "Vaccine," where "Vaccine" could have child entities such as "COVID-19 vaccine" and "Influenza vaccine." As health has a causal relationship with vaccine, it also shares this relationship with its child objects.

Ontology Encoding and Natural Language Evaluation

Items from the visualization concept modes were authored as an OWL2-based ontology [14] using the open-source ontology editor, Protégé [19]. Natural language translation was used to produce statements from the ontology for evaluation using Hootation, an experimental software library that extracts ontology axioms and produces human-friendly natural language statements for expert evaluation [20]. Statements were represented as sentences based on ontology class axioms and object properties; for instance, Hootation produced existential-type statements for subclass axioms such as "Every bus ride is a type of transportation method." The evaluations were used to determine whether classes and their relationships were expressed correctly. To assess the quality of the ontology, 4 evaluators were asked to assess each statement on an Excel (Microsoft Corp) spreadsheet. Two of the evaluators are social behavioral scientists (ie, social work), and 1 of the evaluators is a biomedical ontology scientist. Furthermore, each evaluator was asked to rate a statement as (1) "Yes, this is accurate," (2) "No, this is not accurate," or (3) "Do not know if this is accurate." The Results section discusses details of our analysis from the collected evaluation data.

Alignment With the BFO

To ensure semantic interoperability, we aligned our ontology with the BFO [15,17,21]. The BFO is an upper-level ontology that models entities using metalevel categories based on philosophical realism [16]. It is a widely regarded standard framework for creating biomedical and health reference ontologies that enable sharing, interoperability, and consistency with other ontologies by way of the metalevel categories and properties. To advance this work further, we aligned our exploratory ontology with a few of the metalevel concepts from the BFO. Currently, we have made some early attempts to align the object properties with OBO Foundry properties.

Earlier, we identified 4 basic relationships that connect the concepts from our ontology model. We reviewed the BFO model and identified object property relationships that semantically correspond with our 4 relationship connections. The OBO Foundry's p*art of* or *has part* (BFO_0000050 [22]) object property was used to reflect the *part of* relationship [23]. The OBO Foundry's *causally related to* (RO_0002410 [24]) object property reflected a causal relationship, and the OBO Foundry *depends on* (RO_0002502 [25]) object property was used to reflect the dependency relationship [23]. Naturally, the type of relationship was handled by OWL2's *SubClassOf* axiom.

In addition to the identified property relationships, we settled on classifying the concepts using the 2 basic categories *continuant* (BFO_0000002 [26]) and *occurrent* (BFO_0000003 [27]). A *continuant* is defined as "an entity that persists, endures, or continues to exist through time while maintaining its identity" [26], essentially an entity or object. An *occurrent* is defined as "an entity that unfolds itself in time or it is the instantaneous boundary of such an entity (for example a beginning or an ending) or it is a temporal or spatiotemporal region which such an entity occupies_temporal_region or occupies_spatiotemporal_region" [27], basically an event or process. Each of the concepts in our model was classified into these 2 very basic classes from the BFO. Classifying these concepts into these BFO categories helped leverage the aforementioned property relationships because they were dependent on whether the connecting concepts were aligned with the BFO concepts.

We used ROBOT (a recursive acronym for "ROBOT is an OBO Tool") [28], an OBO Foundry command line software tool, to perform development tasks with OBO Foundry ontologies. We extracted the 2 BFO categories, and the 3 object properties (along with their corresponding axioms via the STAR [situation, task, action, and result] method) using ROBOT to generate a light import of the essential BFO terms. The exported import was used to encode alignment of the concepts in our ontology with the BFO, and FaCT++ [4] was the software reasoner of choice, due to its fast performance, to test whether our ontology model was logically satisfiable. The finalized reviewed ontology, named 3M (microlevel, mesolevel, and macrolevel) Ontology, was published in our GitHub repository [29].

Results

Overview

The literature search identified several topics of discussion for each determinant level. For macrolevel determinants, topics included health policy, income inequality, welfare, and the environment. For mesolevel determinants, the selected articles investigated areas such as work, work conditions, psychosocial work factors, socioeconomic position (SEP), socioeconomic outcomes, food, poverty, housing, and crime. Among all 3 levels, the highest number of articles for discussion were available for mesolevel determinants. Finally, the articles found for microlevel determinants examined gender, ethnicity, race, and behavior. In the following paragraphs, we discuss SDoH in detail.

Policy Making

Social policies and programs, fair employment and working conditions, and living environment are all likely to have the greatest impact on SDoH [30]. Social protection measures, increased coverage and quality of early years care, parental employment support, and gender equality in employment and education may improve early childhood development and even help to reduce child poverty. Affordable housing can be met through minimum housing standards and government actions [30]. Air quality legislation may have some benefits on air pollution and overall living [30].

The effects of climate change may be reduced by improving early warning systems and extreme weather preparedness.

Without action, climate change has the potential to raise agricultural prices, and this may threaten food security in low-income regions [31]. Families and individuals with low-income status are most susceptible to climate-related diseases such as malaria. Providing universal health care coupled with climate resilience measures is needed to reduce climate change impact on those with low-income status [31]. Bouzid et al [32] point out that several systematic reviews discuss diseases associated with climate change, but more focus should go toward the management of droughts, floods, air pollution, and food safety. The lack of research in these areas is likely due to the unpredictable nature of, for example, floods and government bodies that are primarily concerned with disaster response rather than research [32].

Policy Outcomes and Interventions

Health policies are fundamental for health and safety and are designed to improve quality of life. The most common types of implementation measures used to assess health policy outcomes include acceptability, feasibility, appropriateness, and compliance [33]. Well-tested quantitative measures are not used enough, and this may directly affect policy outcomes [33]. Most policy intervention tools at the school, district, state, or province level assess wellness policies from high-income countries such as the United States. Data from a systematic review showed that low- and middle-income countries lacked policy intervention initiatives [34]. Similar studies have investigated the relationship between income inequality and subjective well-being.

Evidence on the impact of social assistance on human health remains unclear [35]. Not enough articles discuss the differences between social assistance recipients and nonrecipients [35]. There is a lack of strong methods and study designs to evaluate the health effects of policies mainly in part due to insufficient data. Population-based health surveys do not provide enough information on respondent characteristics [35]. The available methods used to evaluate policy interventions require researchers to identify instances of large-scale policy change when social assistance programs are hardly ever affected by big changes. Instead, areas to be looked at are tobacco, food labeling, greater income redistribution, and labor market regulations [35].

A systematic review assessed randomized social experiments on social policy interventions for health outcomes in the United States and found that investments in early life, income support, and health insurance interventions may hold the potential to improve mental health and health in general [36]. The authors' power analyses suggested that the models that were used were underpowered to detect health effects and outcomes. The authors noted that policy-related experiments should focus on design to accurately measure the relationship between health outcomes and policy interventions.

Income Inequality and Low SEP

According to a meta-analysis, income inequality was not influenced by measures used to assess subjective well-being or geographic region [37]. Instead, the level of country development, more specifically job opportunities, may be linked to income inequality in low- and middle-income countries. This serves as an indicator to government policy makers that reducing income inequality may lead to an improvement in subjective well-being [37]. While income inequality may have some effect on well-being, political economy may also influence population health. A systematic review revealed that there is a gap in the literature on many aspects of political economy, and it is unclear whether there is a relationship between political economy and population health [38]. Although there is no evidence, it seems that social democratic states with higher public spending tend to have better population health, but there is still no significant relationship between welfare state type and health inequalities [38].

In addition to income inequality, a low SEP may also contribute to poor health outcomes. There is consistent evidence that individuals who have a low SEP are often associated with hospital death and poor-quality end-of-life care [39]. Individuals with a poor education and who resided in impoverished neighborhoods were most likely to die in the hospital, receive acute-based care, and not receive specialized palliative care [39]. Future research on end-of-life interventions should consider SEP and its effects across the social strata [39].

Physical Environment and Health

A systematic review conducted by Lago et al [40] analyzed the relationship between health and physical environment, lifestyle, and social and economic conditions. On the basis of their evidence, the authors concluded that the main factor linking socioeconomic status and health status was income. Individuals with a higher level of income, as opposed to those with lower income, were associated with a lower chance of negative health outcomes [40]. The current association between income distribution and health is the general conclusion because individuals belonging to a lower social class have been shown to have worse average health. Different variables such as education may also play a role in determining health status because it is usually correlated to individuals' social class [40]. Warmth and energy interventions may lead to improvements in respiratory health, mental health, and overall health for individuals with low-income status. Studies that targeted existing chronic respiratory diseases linked to inadequate warmth were most likely to see health improvement [41].

A mixed methods study demonstrated that energy performance interventions reduced energy use and helped raise indoor temperatures [42]. Despite there being a lack of evidence that suggests that energy performance investments improve health, data did show that improvements in social and economic conditions are better for overall well-being and health [42]. Economic conditions such as a low SEP are linked to poor health outcomes [42]. Individuals with a low SEP had an increased risk of cardiometabolic disorders and mortality according to Petrovic et al [43], who examined the role of health behaviors in socioeconomic equality in health. Behaviors such as smoking, alcohol consumption, physical activity, and diet were considered, as well as health outcomes such as cardiometabolic disorders and mortality. Of all behaviors examined, smoking contributed to the most social inequalities in health. The authors conclude that health behaviors may contribute to socioeconomic

inequalities, but this is dependent on population and study characteristics [43].

Impact of Food Availability on Nutrition

Individuals with low- and middle-income status are subject to food scarcity and poor nutritional health [44]. Supplementary feeding had a positive effect on weight and growth in low- and middle-income countries and was most beneficial to individuals who were poorly nourished. There were moderate positive effects on psychomotor development and mixed evidence on improved cognitive development [44]. Groups with lower income tend to select energy-dense diets that do not consist of vegetables or fruit [45]. Fats, refined grains, and added sugars are less expensive than nutrient-dense foods [45]. As a result, there may be a link between high obesity rates and low-cost calories [45]. Pregnant or postnatal women had an increased intake of fruits and vegetables after being enrolled in a food subsidy program [46]. Mean birth weight was slightly higher in 2 high-quality studies [46]. There is currently not enough evidence on the true impact of food subsidy programs for both children and adults [46].

Work Conditions and Occupational Health

Currently, no data suggest that workplace health promotion programs (WHPPs) increase socioeconomic inequalities in health, and there is not enough quantitative data on the ability of WHPPs to reduce social inequalities [47]. WHPPs seem to be the most helpful for working individuals who have a low SEP, but most of the programs were equally effective for groups from lower and higher socioeconomic backgrounds [47]. Most studies on working conditions supported the notion that adverse working conditions can mediate the association between SEP and well-being [48]. Studies that examined occupational categories or employment grades as indicators of SEP had the strongest findings in comparison to those that used education or income [48].

There is strong evidence that both physical and psychosocial factors are the cause of approximately one-third of the socioeconomic inequalities in health [49]. Despite limited longitudinal studies, cross-sectional evidence consistently showed that both physical and psychosocial work factors contributed to socioeconomic differences in self-rated health. Work factors may also play a role in inequalities, but there is not enough evidence to determine specific types of work factors [49]. In comparison to men, women experienced worse working conditions and higher job insecurity and also experienced poorer self-perceived physical and mental health [49,50]. Employed men had less emotional support, worked longer hours, and faced higher physical demands; however, they also held higher job statuses and had greater levels of effort-reward imbalance [50]. Although men were subject to more physically demanding tasks, women reported more musculoskeletal symptoms [50]. Health disparities between genders may stem from less favorable working conditions experienced by women [50]. Women are more commonly exposed to repetitive movements with low loads and awkward working positions than men [50]. Anthropometric differences in bone mass, fatty tissue, and muscle may also influence these health outcomes [50].

Socioeconomic Factors and Domestic Violence

Employment, income, social class, ethnicity, race, and living conditions all make up socioeconomic factors that may contribute to domestic violence [51]. The highest frequency of violence against women is found in a family environment, with the spouse being the most common perpetrator, and is most prevalent in low-income countries [51]. Individuals who experienced sexual dissatisfaction, unsatisfactory environmental conditions, and mental disorders tend to partake in acts of violence [51]. Certain countries have established laws to better protect women, but there needs to be an integrated approach for both national and international government organizations to achieve social change [51].

Discrimination and Poor Health Outcomes

The literature has shown a significant relationship between poor health and racism and a relationship with even higher significance between poor mental health and poor physical health [52]. Health outcomes indicated an association between racism and suicidal ideation, planning, and attempts. Depression was the most reported health outcome and had the same magnitude of association as racism [52]. Health care providers with different training, experience, and specialty backgrounds may hold implicit bias against racial and ethnic minority people [53]. A systematic review revealed that bias is associated with patient-provider interactions rather than health outcomes [53]. This indicates that patient-provider interaction can mediate the relationship between provider bias and patient health outcomes [53].

Institutionalized racism refers to the macrolevel systems, social forces, institutions, ideologies, and processes that interact with one another to cause inequities among racial or ethnic groups [54]. Although public health literature mentions the term *institutionalized racism*, it does not always engage with the concept or dive deep into the mechanisms through which health injustice is perpetuated [54]. To better understand racial and ethnic groups considered disadvantaged, the term should be explicitly mentioned in public health research as a central concept of health inequities [54]. Disparities in the neonatal intensive care unit exist in structure, process, and outcomes and generally disadvantage infants from racial and ethnic minority groups [55]. Hispanic and Black infants are most likely to receive care in poor-quality hospitals. In addition, hospitals serving racial and ethnic minority groups are underresourced and may lack quality improvement infrastructure. Quality improvement initiatives may have the best effect on populations considered disadvantaged who experience poor-quality care [55].

Gender Attitude and Sociocultural Norm

There may be several factors that can shape gender attitudes in early adolescence. In a study conducted in 29 countries, data demonstrated that young adolescents from varying cultures all express similar stereotypes and gender attitudes [56]. A gender study demonstrated that adolescents commonly endorsed norms that perpetuated gender inequalities such as masculinity established on toughness and skills or femininity based on physical appearance and shaming of sexuality [56].

Sociodemographic characteristics such as gender, race, immigration status, and age cause a variation in the results; however, family and peers are the central influences in building gender attitudes [56].

Statistical Analysis

Initial metrics from the ontology exhibited 245 classes, 47 object properties, and 346 logical axioms. Four evaluators independently reviewed 232 statements, specifically SubClassOf axioms, produced by the Hootation natural language translation software. Each statement was categorized as a *0* or a *1* to indicate expression accuracy. Statements that were not accurate were annotated as *0*, and accurate statements were annotated as *1*. Unsure responses were annotated as *0*. The levels of agreement for each evaluator were calculated using a web-based program called ReCal3 ("Reliability Calculator for 3 or more coders") [57]. Intercoder reliability was assessed through an average pairwise agreement and an average pairwise Cohen κ value [58].

Individual levels of agreement were as follows: evaluator 1=54%, evaluator 2=58%, evaluator 3=56%, and evaluator 4=76%. The average percentage agreement in terms of the average number of shared responses was 60.85% (SD 10.13%). The pairwise agreement also demonstrated that evaluator 2 and evaluator 4 had the highest similarity (74.14%) among shared responses, and the lowest percentage for shared responses was between evaluator 1 and evaluator 3 (48.71%). The pairwise agreements between evaluator 1 and 2 (56.47%), evaluator 1 and 4 (70.26%), evaluator 2 and 3 (60.35%), and evaluator 3 and 4 (55.17%) were recorded. The relationship among these results is demonstrated more accurately through the average pairwise Cohen κ value (0.19), which determined the interrater reliability. The results are presented in Table 2.

Table 2. Evaluation of subclass accuracy in percentage. Evaluators were asked to rate expression accuracy with 0 (no and unsure) and 1 (yes). The individual levels of agreement and disagreement are shown for each evaluator.

	Agreed (*yes*[a]; %)	Disagreed (*no*[a] and *unsure*; %)
Evaluator 1	54	46
Evaluator 2	58	42
Evaluator 3	56	44
Evaluator 4	76	24

[a]*Yes* indicates the evaluator denoted a knowledge statement from the ontology was true, whereas, *no* indicates the evaluator assessed it to be false and unsure for if the statement was unknown to the evaluator to be true or false.

The average Cohen κ value was extremely low (0.19), as was the pairwise Cohen κ value for evaluators 1 and 3 (−0.04). The other Cohen κ values between evaluators 1 and 2 (0.12), evaluators 1 and 4 (0.38), evaluators 2 and 3 (0.19), evaluators 2 and 4 (0.44), evaluators 3 and 4 (0.04) were recorded. The statistical analyses helped identify concepts that required revision or omission. Statements that were classified as *0* were reviewed for analysis and possible error. Concepts with high levels of disagreement were revised, and new concepts were added to create a more logically structured ontology.

Discussion

Principal Findings

The ontology that was developed attempted to model the macrolevel and mesolevel conceptualizations of SDoH in more detail. Interpretations from the literature demonstrated that macrolevel factors are crucial determinants of health and health inequities. Individuals considered disadvantaged are almost always at risk for poor health and poor health outcomes. The main drivers of health inequalities seem to be a lack of education, affordable housing, basic housing needs, income, and access to health care. More specifically, women and racial and ethnic minority people are subject to these determinants, and this is the same for individuals living in low- and middle-income countries. Data from the articles also identified gaps in the literature for current research on low- and middle-income societies. Moreover, policy outcomes determined by SDoH can be measured in many ways; yet, there is little quantitative data on their validity. Finally, findings from the literature provided a solid foundation of knowledge and analysis that guided the design and development of the ontology.

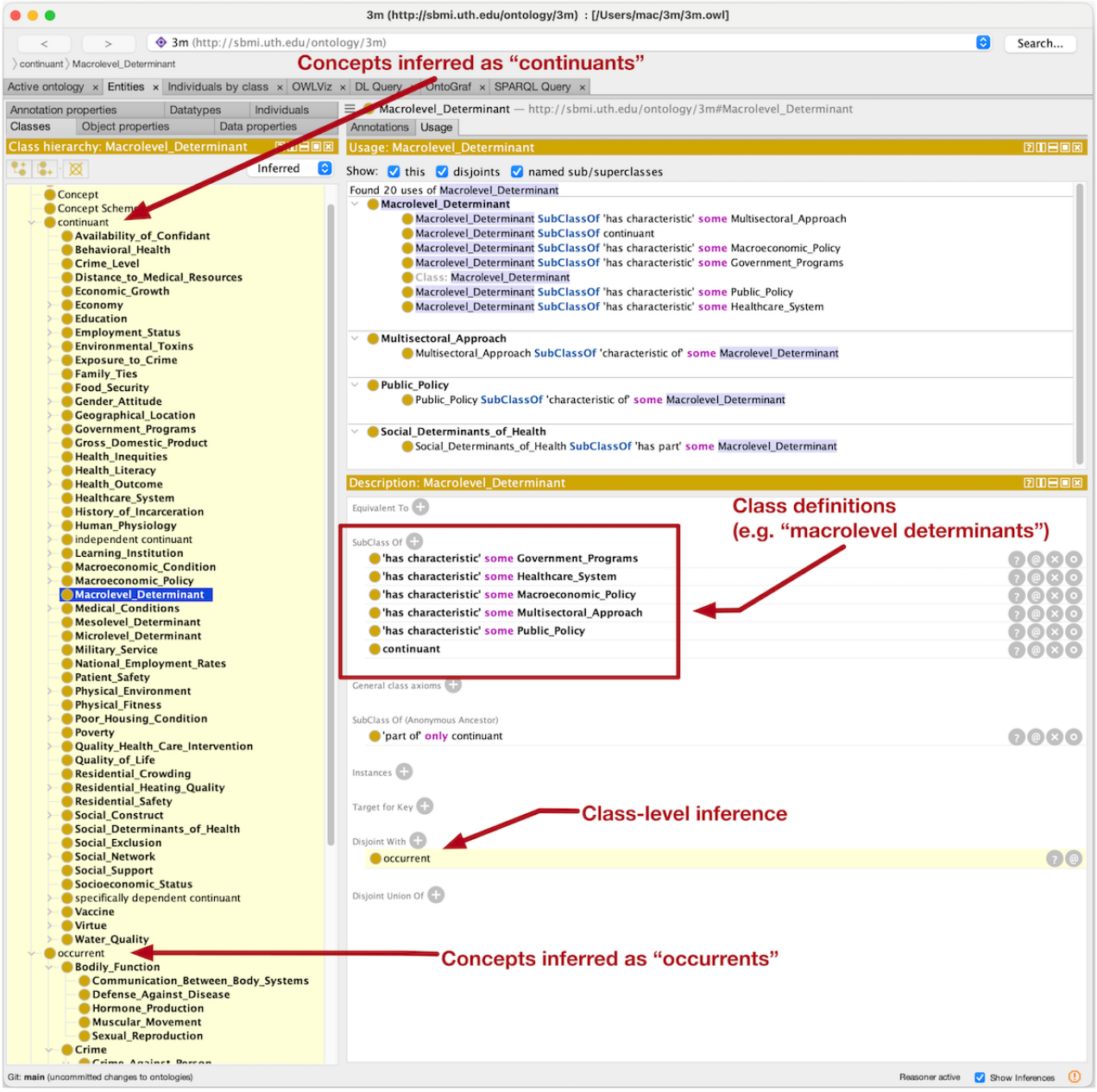
Each of the 3 determinant levels interacts with, and dynamically influences, the other 2; therefore, delineation among the micro-, meso-, and macrolevel determinants is not always clear [59]; for example, the primary effects of discrimination are microlevel factors, such as the imposed psychological context from the individual enacting the discrimination and the individual experiencing it. However, the act of discrimination also has effects on the meso- and macrolevel determinants. The willingness of providers to live and work in underserved communities is considered a mesolevel factor, while the ability of the health care system to create recruitment and retention policies is a macrolevel factor. For an adequate transformation of these complex systems to occur, there will need to be an emphasis on the interactions among the levels and their interdependence [60]. Our work is imperative to the understanding of the ontology of SDoH because it will further the scholarly understanding of public health, lead to the development of necessary policy and interventional changes, and reduce the gap in health care literacy.

The statistical analyses from the evaluations were used to create a revised version of the ontology with a broad spectrum of knowledge concepts ranging from the macrolevel to microlevel determinants. Interpretation of the statements varied, and this may have posed a potential challenge for proper ontology evaluation; for example, the average Cohen κ values indicated that there was no effective agreement, implying that statements from the ontology were not accurate. The low levels of

agreement were mostly attributed to poor labeling and poor association between class and subclass axioms. Poor labeling referred to items that were not specific enough (eg, burnout→job strain, translated to "every burnout is a job strain"). Poor associations among expressions were found to be untrue or mislabeled (eg, poor→income inequality, translated to "every poor is an income inequality"). Personal opinions on statement evaluations were considered but not always incorporated for revision; for example, the concept poor energy performance was not understood by the first 3 evaluators, but it was cited in the literature and described poor energy efficiency in homes, such as poor heating or poor insulation [42].

After some iterative revisions of the ontology, we imported the minimal BFO concepts and property relationships discussed earlier into the Protégé environment and encoded the concept alignment with the BFO terms. We used the FaCT++ reasoner to perform a check of the logical consistency of our final aligned ontology model, and it revealed no inconsistent axioms. At the time of this writing, the core ontology exhibited 383 classes, 109 object properties, and 748 logical axioms, and we included an import of the Simple Knowledge Organization System ontology for additional annotation properties [61]. This preliminary ontology is currently hosted on GitHub [62]. Figure 6 shows a screenshot of the ontology in the Protégé tool with all essential concepts aligned (by assertion and inference) with the BFO categories and properties.

Figure 6. Screenshot of the experimental ontology in Protégé with alignment with Basic Formal Ontology concepts and properties.



Determining the accuracy of ontology concepts may help to produce a well-structured ontology. Moreover, appropriately addressing SDoH is fundamental for improving health and reducing long-standing inequalities. Modeling concepts transform metadata into a knowledge domain, which facilitates new knowledge discovery. By linking this ontology of SDoH

with other biomedical ontologies, researchers can make use of shared data for data exchange and information integration for biomedical tools such as computer-aided reasoning or decision support applications, enhance existing ontology knowledge bases, produce precise definitions of SDoH concepts in natural language, and provide a better understanding of the terminology associated with SDoH to reduce gaps in the literature.

Several concepts exist beyond the macro-, meso-, and microlevel determinants, which are included in the final version of the ontology. Concepts that impact or contribute to SDoH include academic degree, access to food, access to health care, behavioral health, discrimination, distance to medical resources, economic growth, economy, employment status, environmental determinants, exposure to crime, disease, food security, gross domestic product, gender attitude, gender identity, health inequities, health literacy, health outcomes, health services, health care coverage, history of incarceration, income, individual behavior, media culture, medical conditions, military service, national employment rates, nutritious diet, patient engagement, patient safety, personal health management, quality health care interventions, quality of life, sexual activity, sexual orientation, social class, social constructs, and vaccine. Each of these items contains additional subclasses (Figures 2-5).

Macrolevel Determinants

Class axioms for the macrolevel determinants included government programs, health care system, income inequality, macroeconomic conditions, macroeconomic policies, multisectoral approach, public policy, social security benefits, and social welfare. Each of these classes has been broken down further, as illustrated in Figure 3. Government programs, social security benefits, and social welfare were created to assist individuals who belong to a low social class, have a secondary-level education or less, and who are unemployed or work minimum wage jobs [30]. Both national and local governments intend to improve overall health by formulating macroeconomic policies and implementing multisectoral action initiatives to develop comprehensive strategies for addressing SDoH, promote inclusion and transparency in decision-making, and adopt equity-focused approaches in planning and resource allocation [30].

Currently, the US federal government mandates several public policies to improve the quality of life through the drug policy, agricultural policy, water policy, and energy policy [12]. Macroeconomic conditions such as employment and inflation can help regulate the economy, but these are highly dependent on current national employment rates [38]. Likewise, fiscal policies may help to reduce government spending, control debt, and regulate taxation, which in turn controls the economy [38]. Findings from the literature are reported on adult populations and rarely focused on children.

Mesolevel Determinants

The focal point for the mesolevel determinants is the physical environment. It is the level that contained the highest number of classes and subclass axioms. In addition to physical environment, classes included access to recreational activity, affordable housing, crime level, geographic location, psychosocial factor, psychosocial work factor, residence quality, residential location, residential safety, transportation, transportation quality, and walkability. The concepts that warrant the most discussion are physical environment, residence quality, and psychosocial work factor. The environment in which an individual lives and works affects their ability to function and socialize. The quality of housing has major implications on health outcomes [41]. Evidence suggests that poverty and low income affect housing circumstances.

Poor residence quality, such as insufficient heating or insufficient ventilation, may lead to illness [42]. Likewise, poor housing conditions such as mold presence, overcrowding, and unrepaired damage to property may also affect healthy living. Negative health outcomes are associated not only with residence quality but also with work environment. Exposure to psychosocial work factors was linked to poor mental health status [49]. Working long hours and being subject to high physical demands can result in depression, burnout, or work exhaustion [49]. Undesirable working conditions may affect job performance and ultimately employment status [48]. Occupations differ in both psychosocial work factors and work conditions; therefore, these concepts could be elaborated further. Mesolevel factors are presented in Figure 4.

Microlevel Determinants

Microlevel determinant class axioms were identified as biological factor, bodily function, human physiology, individual factor, individual lifestyle, nutrition, participation in physical activity, and physical fitness. Each of these concepts has subclasses that are illustrated in Figure 5. The relationship between individual factors such as education and health is complex. Low educational attainment may result in poor health. Cognitive disabilities and health conditions may affect educational outcomes, which in turn affect health literacy [63]. Low health literacy is associated with poor health outcomes and mortality. Individuals who do not understand the severity of their health conditions are less likely to seek medical care [63]. Poor operation of bodily functions may also result in undesired health outcomes. Likewise, poor management of diet and nutrition can affect physical fitness [45]. Individuals with a low SEP are subject to food insecurity and often malnourished [44]. Their inability to purchase food or healthy food options reflects their diet and nutritional status, resulting in illness [44].

Another microlevel factor that disrupts healthy living is discrimination. Individuals who are discriminated against for their race, gender, sexual orientation, disability, or age may experience depression and suicidal ideation. Discrimination that occurs in a hospital setting is prominent against African American and Hispanic individuals and results in poor or delayed treatment [53]. Negative gender attitudes may elicit aggressive behavior and lead to domestic or physical violence [56]. Attitudes toward gender may be attributed to sociocultural norms or individual beliefs; for example, individuals living in low- and middle-income countries with a high poverty rate often express toxic masculinity [56].

Individuals who identify as lesbian, gay, bisexual, transgender, or queer are targets for discrimination, bullying, isolation, and violence [64]. This is true even in the health care system, where

transgender women are commonly admitted as men, despite them expressing their gender [64]. Similarly, the normalized societal attitude toward individuals with disabilities is often exclusionary [64]. As health systems are often not designed with the needs of individuals with disabilities in mind, these individuals frequently face challenges, requiring them to navigate and challenge established norms [64]. Overall, findings from the literature emphasized that microlevel factors play a large role in human behavior and health outcomes.

Conclusions

In this paper, we examined the range of social and economic factors covering SDoH and modeled these aspects using ontology-based methods and tools to create a representational artifact. With this artifact, data and resources can be linked and aggregated to address clinical research that could analyze the link between the aforementioned factors and possible biological factors sourced in published bioinformatics ontologies. To our knowledge, this is the first ontology to focus on knowledge concepts that are not addressed by current biomedical ontologies for SDoH. The latest version of this ontology is available on GitHub [62] for public early release and future updates. Overall, this preliminary work is a demonstration of the possibility to model these heterogeneous social and economic concepts that can be aligned with the greater body of biomedical ontologies.

However, the social and economic scope of SDoH is expansive, and although the ontology is broad, it is still in its early stages and could be expanded further with more granular social and economic concepts. Future consideration will be given to developing specific subdomains that can act as federated modules that can integrate with this ontology. Finally, we will include further aligning of this work with the BFO, using more precise semantic properties to accurately reflect the relationships among the concepts, which will provide further alignment with the existing validated biomedical ontologies.

Acknowledgments

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Data Availability

The data sets generated during and analyzed during this study are available in the 3M Ontology repository [29].

Conflicts of Interest

None declared.

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Abbreviations

BFO: Basic Formal Ontology
MeSH: Medical Subject Headings
OWL2: Web Ontology Language, version 2
SDoH: social determinants of health
SEP: socioeconomic position
STAR: situation, task, action, and result
WHPP: workplace health promotion program

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Viewpoint

Vaping: Public Health, Social Media, and Toxicity

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Abstract

This viewpoint aims to provide a comprehensive understanding of vaping from various perspectives that contribute to the invention, development, spread, and consequences of e-cigarette products and vaping. Our analysis showed that the specific characteristics of e-cigarette products as well as marketing strategies, especially social media marketing, fostered the spread of vaping and the subsequent effects on human health and toxicity. We analyzed the components of e-cigarette devices and e-liquids, including the latest variants whose impacts were often overlooked. The different forms of nicotine, including salts and freebase nicotine, tobacco-derived nicotine, tobacco-free nicotine, and cooling agents (WS3 and WS23), have brought more choices for vapers along with more ways for e-cigarette manufacturers to advertise false understandings and present a greater threat to vapers' health. Our work emphasized the products of brands that have gained significant influence recently, which are contributing to severe public health issues. On the other hand, we also discussed in detail the toxicity of e-liquid components and proposed a toxicity mechanism. We also noticed that nicotine and other chemicals in e-liquids promote each other's negative effects through the oxidative stress and inflammatory nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway, a mechanism leading to pulmonary symptoms and addiction. The impact of government regulations on the products themselves, including flavor bans or regulations, has been limited. Therefore, we proposed further interventions or harm reduction strategies from a public health perspective.

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KEYWORDS

addiction; behavior; behaviors; device; devices; e-cigarette; e-cigarettes; effect; effects; e-liquid; flavors; nicotine; public health; social media; human health; toxicity; vape user; vape; vaper; vapers; vaping

Vaping: A Public Health Issue

Recently, e-cigarette use among the adolescent population has become a concerning public health challenge in the United States. The popularity of the relatively new invention of e-cigarettes reversed the nation's effort to reduce tobacco use among youths in the past 30 years [1]. According to data collected in 2021 in the United States, 11% of young adults aged 18-24 years currently use e-cigarettes, and 24% of 12th-grade students reported having engaged in vaping activities in the past 30 days [1,2]. This public health issue is not limited to the United States, however, as the prevalence of past 30-day vaping among adolescents aged 12-16 years in 68 different countries worldwide was 9.2% (2021) [3]. This is especially concerning, as e-cigarette use among early-adolescent smokers is a predictor of any smoking and more frequent cigarette smoking in late adolescence [4]. Besides the impact on smoking behaviors, adolescents who vape can develop severe respiratory symptoms that may even require ventilation, and other symptoms, including gastrointestinal tract symptoms, coughing, and hypoxemia, can also arise throughout the body [5].

e-Cigarette use has become a worldwide public health issue that demands our attention. To gather information and present it to the public, this paper has taken literature from PubMed and Google Scholar into consideration and introduced the advantages and disadvantages of vaping based on current literature by

including conflicting reports and potential biases on social media and public health.

e-Cigarette Brands and Characteristics

Due to the public impact of e-cigarette use, it is important to understand the characteristics of popular e-cigarette products. According to the 2022 National Youth Tobacco Survey, Puff Bar (29.7%), Vuse (23.6%), JUUL (22%), SMOK (13.5%), NJOY (8.3%), Hyde (7.3%), and Blu (6.5%) were found to be the most popular brands among youth [6]. Another study by Ali et al [7] showed that during the 4-week period that ended December 25, 2022, the top 5 brands with the highest e-cigarette unit sales were Vuse, JUUL, Elf Bars (Funky Vape or EB Design), NJOY, and Breeze Smoke. Among the products from all the brands mentioned above, only products from SMOK were third-generation e-cigarettes (also known as mods, a type of highly customizable aerosol-generating devices that use e-liquids and have subohm tanks that allow for higher wattage), while all other products were fourth-generation e-cigarettes (also known as pod mods, a type of modifiable pod cartridges including vape bars that use nicotine salts and can come in different shapes). Most fourth-generation e-cigarettes introduced above contain salt-form tobacco-derived nicotine (TDN) with a concentration of ≤5% and a volume below 2 mL. The products from Hyde are unique in that some of them contain larger volumes (up to 10 mL) that support a higher number of puffs, and these products may contain tobacco-free nicotine (TFN). The characteristics of TDN and TFN are discussed in a subsequent section.

In 2023, however, several new brands became more popular, including Elf Bars (EB Design, Lost Mary, Funky Vape, BC5000, and BC 7000), all from iMiracle Associates (originated from Shenzhen, China), FLUM float bars, ESCO bars, and Tyson. All of the products within these brands are fourth-generation e-cigarettes with nicotine salts as the source of nicotine. All the products contain a larger volume (up to 13 mL) and thus more puffs (≥2500 puffs). Only some products from iMiracle contained TFN, while the other brands only used TDN.

Among all the popular brands, Elf Bars (Funky Vape or EB Design, now rechargeable with pods) from iMiracle requires the most attention due to worries of it becoming the next "JUUL" that produces massive public health issues (e-cigarettes by JUUL were extremely popular from 2017 to 2020 and caused massive public health issues) [8]. In the youth population in England, around 50% of past 30-day vapers reported the use of Elf Bars (EB Design) [9]. Researchers have also suggested that the increase in vaping frequency and the shifted interest toward disposable e-cigarettes among English vapers could have been driven by the popularity of Elf Bars (EB Design) [9]. Moreover, an analysis of data from the National Poison Data System showed that 60.8% of e-cigarette–associated cases in poison centers with reported brand information were related to Elf Bars (EB Design) [10]. Therefore, its popularity, its ability to change vapers' vaping behaviors that were demonstrated by the shift in vapers' interests, and its potential for causing severe health issues all make Elf Bars (EB Design) a dangerous brand from a public health perspective, and public health interventions should be applied to prevent another "JUUL" from emerging and causing severe issues.

In addition to the most popular brands on the market, another set of brands also requires our attention, despite not being as popular. Both freebase nicotine and nicotine salts are used in brands including EC Blend (uses TDN), Halo (TDN), Coastal Clouds (TDN), Bad Drips (TDN and TFN), Naked (TDN and TFN), Cloud Nurdz (TFN), and Primus (TDN); however, these compositions change regularly. e-Cigarettes originally used freebase nicotine, while more recent e-cigarettes started using nicotine salts, which have a lower pH and therefore are less irritating to the throat and allow for higher doses [11].

The difference between freebase nicotine and nicotine salts is not restricted to user experience, as different physiological and toxic properties were observed. Research in pharmacokinetics has shown that nicotine salts are absorbed more rapidly and can reach higher concentrations, while freebase nicotine is metabolized more slowly, causing it to remain at higher concentrations in male rats, which may be generalizable to humans [12]. As advertised, these characteristics allow vapers to experience an instant nicotine "hit" or a prolonged sensation, or they can even achieve both by using both types of products. However, the availability of both types of products in these brands allows vapers to encounter the different adverse effects of either type. Generally, nicotine salts produce changes in levels of more types of proinflammatory cytokines and have more complicated effects on human nasal epithelial cells, but freebase nicotine can also cause unique changes, including increased secretion of interleukin-7 [13]. The results above were yielded with the same nicotine concentration, while nicotine salt products often have double the nicotine concentration than freebase nicotine products [14]. Therefore, the toxicity of nicotine salt products should be more serious than that of freebase nicotine products, but the threat of the availability of freebase nicotine along with nicotine salt is also not neglectable.

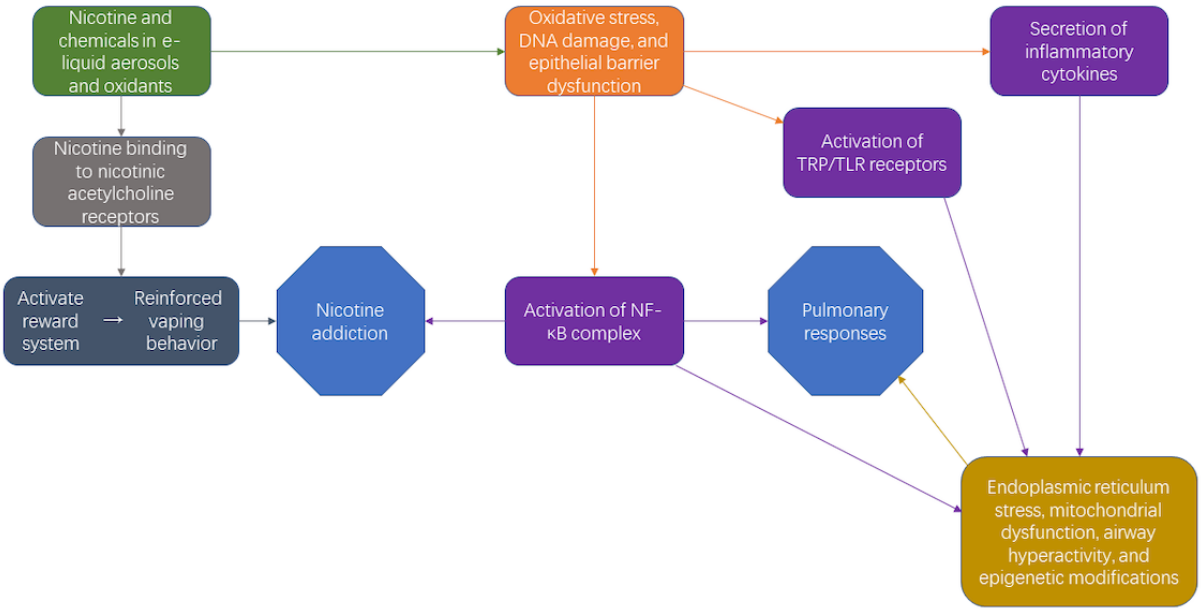
e-Liquids Composition, Toxicology, and Associated Pulmonary Symptoms or Responses

Besides the toxicities specific to nicotine salts, there are various toxic effects of almost all the components in the e-liquids [15-24]. The most abundant chemicals, propylene glycol, and vegetable glycerin, can negatively affect cell viability as they can cause decreases in cell growth to a similar degree to dimethyl sulfoxide [15]. Propylene glycol is known to cause respiratory arrest in rats after administration of 25 mg/kg/day for 3 days [16]. Chronic propylene glycol exposures are associated with reported symptoms of chronic wheezing, chest tightness, and weaker lung function, while acute exposures are associated with coughs and other upper airway symptoms as well as ocular irritations [17,18]. Heating vegetable glycerin in the presence of other acids may cause it to undergo pyrolysis reactions, releasing acrolein, which can cause nasal cavity irritations, lung lining damage, and even contribute to the onset of cardiovascular diseases [19-21]. Furthermore, the chemical

that vapers are addicted to (ie, nicotine) can induce health issues by increasing reactive oxygen species, causing lipid peroxidation, and damaging human DNA [22] (Figure 1).

The most commonly used flavorants in e-liquids mentioned above also have pronounced toxicities [15,23,24]. Vanillin, the flavorant used in 35% of e-liquids, is positively correlated with the toxicity of the e-liquids (R^2=0.62) [15]. Meanwhile, ethyl maltol leads to incidences of kidney lesions in rats and mild hemolytic anemia in dogs [23]. Ethyl butyrate, a type of ethyl ester flavor additive, can be broken down under high temperatures (may be achieved by atomizers) into carboxylic acids [24]. These carboxylic acids can then decompose into ketene, a chemical known to be a strong respiratory poison that can cause severe lung damage even at lower concentrations [24]. Generally, it is shown that the more chemicals there are in an e-liquid and vaporized (aerosols), the higher toxicity that e-liquid is likely to have [15].

Figure 1. Biological pathways to pulmonary responses and nicotine addiction. NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells; TLR: toll-like receptors; TRP: transient receptor potential-like channels.



Another group of deleterious chemicals that are present in e-liquids and aerosols are volatile organic chemicals (VOCs), including benzene, aldehydes, toluene, and ethylbenzene [25]. VOCs are significant risk factors for asthma among children [26]. In fact, the risk for asthma doubles for every 10 μg/m^3 increase in the concentration of toluene, and it even triples for benzene [26]. Meanwhile, VOCs are also associated with reduced lung function in all age groups [27].

Besides the chemicals in the e-liquids themselves, vapers may inhale other toxic chemicals, including heavy metals (cadmium, lead, nickel, copper, arsenic, and chromium), while vaping and experience health risks, including increased oxidative stress, DNA damage, and decreased cellular viability in tissues [28,29]. It is observed that later puffs contain higher concentrations of toxic metals, and these higher concentrations can lead to a 30% increase in DNA damage after a 7-day exposure [28]. The commonly used flavorant, ethyl maltol, can also enhance the absorption and toxicity of copper in lung epithelial cells, as apoptosis, DNA damage, and oxidative stress occurred after coexposure to ethyl maltol and copper at low concentrations, which cannot initiate toxic effects individually [30]. Such toxicities can be applicable to most vapers, as higher cadmium, lead, silver, vanadium, nickel, and chromium concentrations were found in the urine or serum of e-cigarette users [31-33].

Due to the toxicity of these chemicals, although e-cigarettes are potentially less harmful than traditional cigarettes (less nitric oxide, oxidants, aldehydes, and no carbon monoxide inhaled), they are not as safe as expected by vapers [34]. Moreover, studies that demonstrated less harmful effects for e-cigarettes mostly focused on short-term effects, so whether the long-term health effects of e-cigarettes are also lower remains unclear [34]. More longitudinal studies should be conducted to confirm the long-term, chronic effects of e-cigarette use.

Tobacco-Free and Tobacco-Derived Nicotine

In addition to the toxic effects brought by the presence of certain chemicals, the source of such chemicals may have an effect as well. The source of nicotine in e-liquids can be divided into 2 categories: TDN and TFN (nicotine that is not derived from tobacco plants). The type of nicotine originally used in e-cigarettes was TDN, but TFN started to be used in e-cigarettes since products containing TFN were not defined as tobacco products by the Federal Food, Drug, and Cosmetic Act and thus could evade regulations. e-Cigarette manufacturers have also advertised TFN as safer and with smoother flavors, causing vapers to believe that TFN has lower risks and to be willing to use and even pay more for TFN products [35]. Similarly, young adults have an overall positive perception of TFN products' flavors, and those who are willing to try TFN products believe that TFN products are less addictive [36]. Fortunately, on April 14, 2022, new legislation took TFN into consideration and

granted the Food and Drug Administration the authority to regulate TFN products, and TFN products are no longer a viable way to evade regulations [37].

Considering the chemical composition of TDN and TFN, the fundamental difference between them is chirality. The nicotine in TDN products is mostly S-nicotine (only 0.1%-1.2% is R-nicotine), while the nicotine in TFN products is a racemic mixture of R- and S-nicotine (50% R-nicotine and 50% S-nicotine) [38,39]. There is limited information on how the chirality of nicotine may impact its health effects, but it is stated that TFN is pharmaceutically pure and does not contain impurities found in TDN, including tobacco-specific nitrosamines, which may contribute to negative health effects [40,41]. Research has shown that TFN products of beverages or minty or iced (containing cooling agents, such as WS3 and WS23) flavors generate significantly less reactive oxygen species (ROS) than their TDN counterparts, which concurs with the statement earlier [42]. However, no significant difference was detected with fruity or tobacco flavors, indicating that flavorants also play a role in the process of generating ROS [42]. Therefore, more research should be done to confirm the difference posed by TFN itself, and cellular experiments are also crucial to understanding the inflammatory response of humans to the different forms of nicotine.

Mechanism of Toxicity

Overall, the inhalation of e-liquid aerosols can lead to lung injuries, and Kaur et al [43] proposed mechanisms for this process. In this mechanism, the chemicals in the aerosol produce ROS in the lungs and induce oxidative stress, DNA damage, and epithelial barrier dysfunction. These cellular toxicities then trigger the transient receptor potential-like channels or toll-like receptors, activate the NF-κB complex, and stimulate the release of inflammatory cytokines, including interleukin-1 beta, interleukin-6, and tumor necrosis factor-alpha, which are all parts of inflammatory responses [43]. These inflammatory responses then manifest as symptoms by inducing endoplasmic reticulum stress, mitochondrial dysfunction, airway hyperactivity, epigenetic modifications, and other disease-developing mechanisms [43].

Besides the inflammatory aspects of the activation of the NF-κB complex, such activation can also contribute to the addiction to e-cigarettes [43-45]. The NF-κB complex is known to facilitate the positive reinforcing effect of drugs through reward sensitization in the nucleus accumbens, thus exacerbating the development and maintenance of nicotine addiction in vapers [44]. The major addiction development pathway, on the other hand, originates from the binding of nicotinic acetylcholine receptors with nicotine [45]. Signals are then sent to the reward system in the central nervous system, including the nucleus accumbens, to reinforce the behavior and eventually lead to addiction [45]. Figure 1 describes the known biological pathways of the toxicity of and addiction to e-cigarettes.

As a result of these pathways, the addiction potential of e-cigarettes is not lower than that of traditional cigarettes [46]. A study that used the Fagerström test for nicotine dependence showed that exclusive e-cigarette users (mean 3.5) have a nicotine dependence level more than 2 times higher than that of traditional cigarette smokers (mean 1.6) [46]. Dual users also demonstrated higher dependence when using e-cigarettes (mean 4.7) than when using traditional cigarettes (mean 3.2) [46]. The high addiction potential of e-cigarettes may make them unsuitable for being used as smoke cessation tools, especially in young adults who have a higher risk of addiction to e-cigarettes, as demonstrated in the study [46].

Social Media and Vaping

In 2022, the number of social media users in the United States reached over 302 million. Around 90% of the US population used social media as of 2023. Social media platforms, such as Twitter, Reddit, Instagram, TikTok, YouTube, and Facebook, have become increasingly popular, especially among youth and young adults. Instagram and YouTube are the most broadly used social media platforms among youth in the United States, with 80% of youth using YouTube and 72% of youth using Instagram [47].

With the increasing popularity of social media platforms in the United States, e-cigarette companies and vape shops have aggressively marketed vaping products on social media [48-52]. Vaping marketing and promotion posts dominate vaping-related social media posts with more user engagement [47,50,52]. Social media accounts of e-cigarette companies or vape shops usually post well-designed pictures with vaping products, images linking vaping with luxury lifestyles, price promotions, discounts, and product giveaways [53-55]. Examples of extensive use of such strategies include the “Doit4juul” campaign on social media platforms, including Instagram and YouTube, initiated by the JUUL manufacturer, and the campaign largely contributed to the rapid growth of the brand [56]. They also sponsor influencers with many followers to help them market vaping products [57,58]. Around US $75 million (inflation-adjusted 2021) was spent on marketing vaping products by the vaping industry in the third quarter of 2019, including marketing and promotion on various social media platforms that reach most of the US population, including youth under 18 years [57,59,60]. The massive marketing and promotions of vaping products on social media resulted in the misperception of vaping as a harmless activity [58]. They also increased the risk of vaping initiation, especially among youth and young adults [61-63]. Research also found that the initiation of vaping is associated with subsequent cigarette smoking [64,65]. However, a recent epidemiological longitudinal survey study using Population Assessment of Tobacco and Health Wave 1-5 data (2013-2019) implicates that baseline vaping is not associated with subsequent cigarette smoking initiation in youth who have never smoked before after adjusting for behavior risk factors, such as alcohol, marijuana, and other tobacco product use [66]. Fortunately, the advertisements for combustible cigarettes are more restricted by the government, and combustible cigarette companies can only focus on marketing at the point of sale and product packaging [67,68].

Besides the massive marketing and promotion activities of vaping industries, the public also uses social media platforms to share their opinions and user experiences on vaping products

[48,50,69]. Our longitudinal examination of the vaping flavors mentioned in 2.8 million Reddit posts from January 2013 to April 2019 showed that the top 2 flavors were fruit and sweet, consistent with previous survey results during a similar period [50]. A further examination of the association of vaping with health symptoms mentioned in the same Reddit posts showed a significant comentioning of fruit-flavored vaping products and cardiovascular symptoms [48]. A sentiment analysis of over 2.7 million vaping-related Twitter posts (tweets) from May 31 to August 22, 2019, found the fruit, mint, and sweet flavors were more positively perceived, and the beverage and tobacco flavors were more negatively perceived by the public [50]. A systematic review of the vaping-related social media studies from 2007 to 2017 found the major topics related to vaping on social media included the health effects of vaping, vaper testimony, benefits and risks associated with vaping, regulations of vaping products, and vaping as smoking cessation aids [69]. Being exposed to antivaping content on social media was associated with reduced vaping activities among young people [70].

Vaping-related social media posts could also be used to examine the impact of vaping product regulation policies on public attitudes toward vaping [71-73]. With the high prevalence of vaping in youth and young adults and the e-cigarette or vaping use-associated lung injury (EVALI) outbreak in 2019, many state governments and the FDA started to ban flavored vaping products.

Overall, social media plays an important role in vaping product marketing, promotion, and communication with the public about the potential harms of vaping. Regulations on social media marketing of vaping products can help reduce vaping initiation in youth and young adults. Meanwhile, social media platforms could also be used to provide education to the public about the potential harms of vaping and deliver vaping cessation interventions or harm reductions to reduce the uptake of vaping in youth and young adults. An example of such an application is the Real Cost e-Cigarette Prevention Campaign [74]. However, the low frequency of educational posts and the lack of appeal to youth social media users may impact the efficacy of the intervention, and more research should be done to address these issues and improve its efficacy [74].

Health Effects of Vaping

Due to the recent and fast e-cigarette popularization with the contributions of social media, there is limited scientific evidence regarding its exact long-term effects. However, e-cigarette use has caused the onset of respiratory symptoms among consumers, labeled EVALI, the etiology of which involves the inhalation of vitamin E acetate (VEA) along with other chemicals emitted from e-cigarettes [75]. Patients with EVALI present to the hospital with sterile exogenous pneumonitis and the symptoms of cough, chest pain, dyspnea, nausea, gastrointestinal tract symptoms, fatigue, and fever [76]. Although the identification of VEA in bronchoalveolar lavage fluid is commonly associated with EVALI, sampling and identifying VEA from bronchoalveolar lavage fluid are not widely available, so the diagnosis of EVALI remains to be done through exclusion [77]. Nevertheless, as of 2020, almost 3000 cases of lung injury hospitalizations related to vaping have been reported in the United States [78]. Lung biopsies taken from 8 of these patients in various centers revealed acute lung injuries, including organizing pneumonia, diffuse alveolar damage, or interstitial inflammation [79]. In addition to respiratory damage, e-cigarette use can have effects elsewhere. In a recent study, researchers noticed an association between e-cigarette use and seizures in youth, perhaps due to the high levels of nicotine or flavoring chemicals inhaled when vaping—this finding also raises concerns about the impacts of e-cigarette use on brain development and other neurological complications in the youth population [80]. e-Cigarettes have been shown to produce an increase in blood pressure and aortic stiffness, lending themselves to further cardiovascular stress [81], and can also be potentially carcinogenic due to formaldehyde-releasing agent formation during the vaporization process [82] and high levels of nitrosamines present in e-cigarette flavorings [83].

If used as a cessation method for traditional smoking, e-cigarettes have the potential to limit traditional smoking. However, e-cigarette corporations' decision to expand their consumer base past quitting smokers ushered in a new generation plagued by nicotine addiction. Since 1999, combustible nicotine intake has been steadily decreasing among high schoolers, down from an average of 5 days per month to only 1; however, after the popularization of e-cigarettes among school-aged children in 2015-2017 (coinciding with the release and rapid growth of the JUUL corporation), these numbers have begun to rise, once again approaching 5 days [84]. While nicotine addiction in youth may be lucrative for e-cigarette corporations, it perpetuates a cycle of toxicant inhalation, leading to the dangerous symptoms described above.

Public Health Interventions Against Toxicity

The serious health effects and the wide spread of e-cigarettes led to the urgent need to address the public health issue. However, the sole motivation of the tobacco industry is to maximize profit, so it is unlikely it will ever be motivated to abandon profit and help address the public health issue of tobacco product use [85]. Historically and to this day, this profit has clearly been at the expense of public health. Such expenses include the use of aggressive tactics, including lobbying for industry-favorable laws and regulations [86], marketing directly and indirectly to youth [87], targeting many channels and subpopulations with evolving marketing strategies [88], and advanced public relations approaches to undermine and misrepresent evidence-based science by inflating scientific uncertainty to undercut public health initiatives and regulatory actions [85,89]. Many industries have subsequently adopted this game plan of disrupting normative science, which leads to an assertion of personal accountability for what are actually industrially generated health hazards [86,90].

Despite overall drops in rates of smoking (including mentholated products), menthol product use has increased, especially among young adults, female individuals, and Black users. Bans on menthol, a flavoring that has historically been disproportionately

marketed to African American communities and associated with a lower likelihood of cessation among persons from these communities, were thought to have a high potential for increasing cessation in the communities [91]. Governments have taken steps to outlaw the retail sale of flavored tobacco products, including menthol cigarettes. The regulations primarily include the requirement of premarket tobacco product applications for e-cigarettes (as in traditional cigarettes), raising the age restriction of e-cigarette purchases to 21 years, broadening smoke-free policies and high taxation (originally only against traditional cigarettes) to e-cigarettes, and flavor bans [1]. These regulations target different aspects of e-cigarette use, but they all have imperfections in that the implementation of such regulations has a long processing time and not all states and jurisdictions would choose to implement such policies [1]. Therefore, e-cigarette sales are still largely underregulated.

On the other hand, the tobacco industry has once again aggressively fueled erroneous information about these policies, including the claim that such flavor bans target African American smokers' freedom of choice, in service of their goals to protect profit [92]. The example demonstrated that the industries would exert all their effort and resources to oppose such prohibitions [92].

Telephone quitlines have demonstrated effectiveness for smoking cessation for more than 20 years [88]. They can produce both short-term and long-term intervention effects [88]. It has also been shown that promotions through television and radio have tripled call rates [88]. It is reasonable to infer that such promotions and best practices can be effective for vaping cessation, especially when promoted on social media. Since young adults and adolescents are the most vulnerable to nicotine addiction and the other negative effects of vaping, it is important to analyze the quitlines' effectiveness in these understudied populations [89]. More research is needed to analyze the effectiveness of quitlines on adolescent and young adult vape users, including analysis of the effects of quitline-related treatment modalities such as websites, user chat rooms, and SMS text messaging. Additionally, it is needed to analyze the reach and efficacy of social media promotion of such eHealth intervention platforms.

Summary and Conclusion

Overall, we have discussed the various aspects of vaping and its related toxicity. Social media marketing is an essential part of the companies' strategies due to its high influence among youth. Their strategies are successful for their companies, as they gained substantial growth in their sales, while causing almost 3000 hospitalizations associated with vaping in the United States [78]. The most popular and most problem-causing brands discussed in the study should be monitored, especially Elf Bars (EB Design or Funky Vape or Funky Land), which is responsible for 60.8% of e-cigarette–associated cases in poison centers with reported brand information [10]. The toxicity mechanism of and addiction to e-liquids was also proposed in this study, including the chemicals' contributions to nicotine addiction in vapers (Figure 1). More research should be done on the newer variants of e-liquid components to address the lack of understanding of these components and their potential to cause public health issues (ie, chronic effects on toxicities and health effects). In addition, a lack of knowledge about the long-term effects of vaping may undermine the determination of e-cigarette regulations, so longitudinal studies should be conducted to acquire the crucial information [34]. Investigations on the potential effectiveness of vaping cessation on the mitigation of both short- and long-term health effects would also be crucial in combating the vaping epidemic.

Considering the complexity of the toxicity that stemmed from the new e-liquid formula (bars and e-liquids with devices) and subsequent health issues, vaping cessation interventions or harm reduction should also address all these concerns. From a public health perspective, social media marketing of vaping products should be prohibited, and social media should instead be leveraged to provide education and cessation resources to the public. Government or federal regulations alone on flavored tobacco products may have a limited impact since corporations can bypass such regulations with their resources [87]. Viable intervention strategies should include telephone quitlines and related eHealth interventions, such as websites and SMS text messaging, which should be promoted to and tailored for adolescent and young adult populations.

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Disclaimer

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Authors' Contributions

YS, PP, DL, SM, and IR contributed to the writing and original draft preparation. YS, PP, and IR were responsible for writing, reviewing, and editing. YS and IR prepared schematics and conceptual diagrams. IR contributed to supervision, editing, project administration, acquisition, and compilation. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

None declared.

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Abbreviations

EVALI: e-cigarette or vaping use-associated lung injury
NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells
ROS: reactive oxygen species
TDN: tobacco-derived nicotine
TFN: tobacco-free nicotine
VEA: vitamin E acetate
VOC: volatile organic chemical

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Review

Facilitators, Barriers, and Potential Impacts of Implementation of e-Pharmacy in India and its Potential Impact on Cost, Quality, and Access to Medicines: Scoping Review

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Abstract

Background: e-Pharmacy can potentially solve problems related to the quality of services and products, cost, and access to medicines in low- and middle-income countries. This review aims to understand the facilitators and barriers to the implementation of e-pharmacy in India.

Objective: This scoping review aimed (1) to understand the facilitators and barriers to the use of e-pharmacy in India and (2) to estimate the potential for e-pharmacy in India for improving access to medication, improving the quality of services and medicines, and decreasing costs of medications.

Methods: All published and gray literature from July 1, 2011, to June 30, 2021, relating to e-pharmacy, was searched from MEDLINE, Scopus, ProQuest, and Google using a systematic search strategy.

Results: In total, 1464 titles and abstracts were screened, of which 47 full-texts were included in the review. e-Pharmacy can potentially improve access to medications for remote areas, and old and debilitated individuals. e-Pharmacies can enable lean supply chain management, lower cost, and allow easy tracking of dispensed medicines. There is potential for integration of e-pharmacy services into the national program of Bhartiya Jan Aushadhi Pariyojana. However, the country is not adequately regulated to prevent the growth of illicit e-pharmacies. Lack of global accreditation and internet coverage, digital literacy, and transnational access are other challenges.

Conclusions: E-pharmacy has the potential to improve universal health coverage in India by improving access to medicines and lowering the overall cost of health care. However, future growth will need specific regulations and accreditation mechanisms.

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KEYWORDS

online pharmacy; internet pharmacy; telepharmacy; ePharmacy; prescribing systems; drug prescribing; prescriptions; medications

Introduction

e-Pharmacy has been defined as the "business of distribution or sale, stock, exhibit, or offer for sale of medicines through the web portal or any other electronic mode" [1]. In recent times, there has been a substantial increase in the use of e-pharmacy in India due to the growth of the e-commerce sector, increasing internet penetration, and the use of smartphones [2]. During the COVID-19 pandemic, health care in India witnessed a substantial transformation due to the wide use of telemedicine services, including online prescriptions and e-pharmacies [3]. The Indian e-pharmacy market stood at US $344.78 million in 2021 and is expected to witness 21.28% growth by 2027 [4]. Soon, the e-pharmacy model may account for 5%-15% of the total medicine sales in India and thus may contribute to health care substantially along with the traditional brick-and-mortar pharmacies [5].

e-Pharmacy platforms offer a convenient, doorstep delivery of medicines to consumers, resulting in a rising global demand for the model [6]. e-Pharmacy can, therefore, prove to be an important tool in the armamentarium of Indian health policy makers to improve universal health coverage [7]. On the other hand, the growth of rogue e-pharmacies is a significant concern worldwide, especially in low- and middle-income countries (LMICs), which often lack specific regulations for the online sale of medicines [8,9]. The proliferation of e-pharmacy in India so far has been largely beyond existing regulatory mechanisms with issues related to the quality of medicines and dispensing errors [10,11,12].

There is a lack of systematic evidence on the status of e-pharmacy in India and its potential in the near future to improve health access. The present scoping review was undertaken to (1) understand the facilitators and barriers to the use of e-pharmacy in India and (2) estimate the potential for e-pharmacy in India for improving access to medication, improving the quality of services and medicines, and decreasing costs of medications.

Methods

Protocol Registration

The review was carried out in accordance with the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines [13]. The protocol was registered with the Open Science Framework (OSF).

Search Strategy and Selection Criteria

MEDLINE, Scopus, ProQuest, and Google were searched for scientific literature, and Google and ProQuest were searched for gray literature published from July 1, 2011, to June 30, 2021, which were written in English or Hindi were included. Relevant literature published from June 30, 2021, till September 30, 2022, has been added after the completion of the initial search and data extraction to keep the readers updated about recent developments. Original papers, review papers, newspaper articles, reports from government or nongovernmental organizations, guidelines and policy documents, newsletters, web pages, blogs, and PowerPoint (Microsoft Corp) presentations were included.

Inclusion criteria were original papers and other publications, as mentioned above, related to the technologies used for e-pharmacy; regulations for controlling e-pharmacy in India and other countries; the impact of e-pharmacy on access, supply chain management, quality of services, availability of essential medicines, and cost (especially in the context of primary health care). Global literature on facilitators and barriers to e-pharmacy deemed important to the Indian context was included. Literature from developed countries that did not fit in the context of developing nations was excluded from the review. Literature related to telemedicine without any relevance to e-pharmacy was excluded from the review.

A 3-step search strategy as defined in the standard Joanna Briggs Institute (JBI) systematic reviews was used for this purpose. As a first step, a limited search of the relevant databases was done, following which analysis of the key terms used in the title, abstract, or index was done. In step 2, keywords were extracted from the literature identified during the first step. Variants and combinations of search terms relating to these keywords (e-pharmacy, facilitators and barriers, access, quality, cost, and regulations) were used for searching (Table S1 in Multimedia Appendix 1). In step 3, reference lists of the identified articles were searched for relevant references.

Publication Selection

The title and abstract of the available search results were screened using DistillerSR (Distiller Inc) simultaneously but independently by 2 authors (HRB and SK) based on the given eligibility criteria. In case of any uncertainty regarding the inclusion of the article, a third author (AA) was consulted. The full texts were then procured for the selected number of articles, which were screened independently by 2 authors (AA and HRB), and for any conflicts between the 2 authors, a third author (SJC) was consulted.

Data Charting

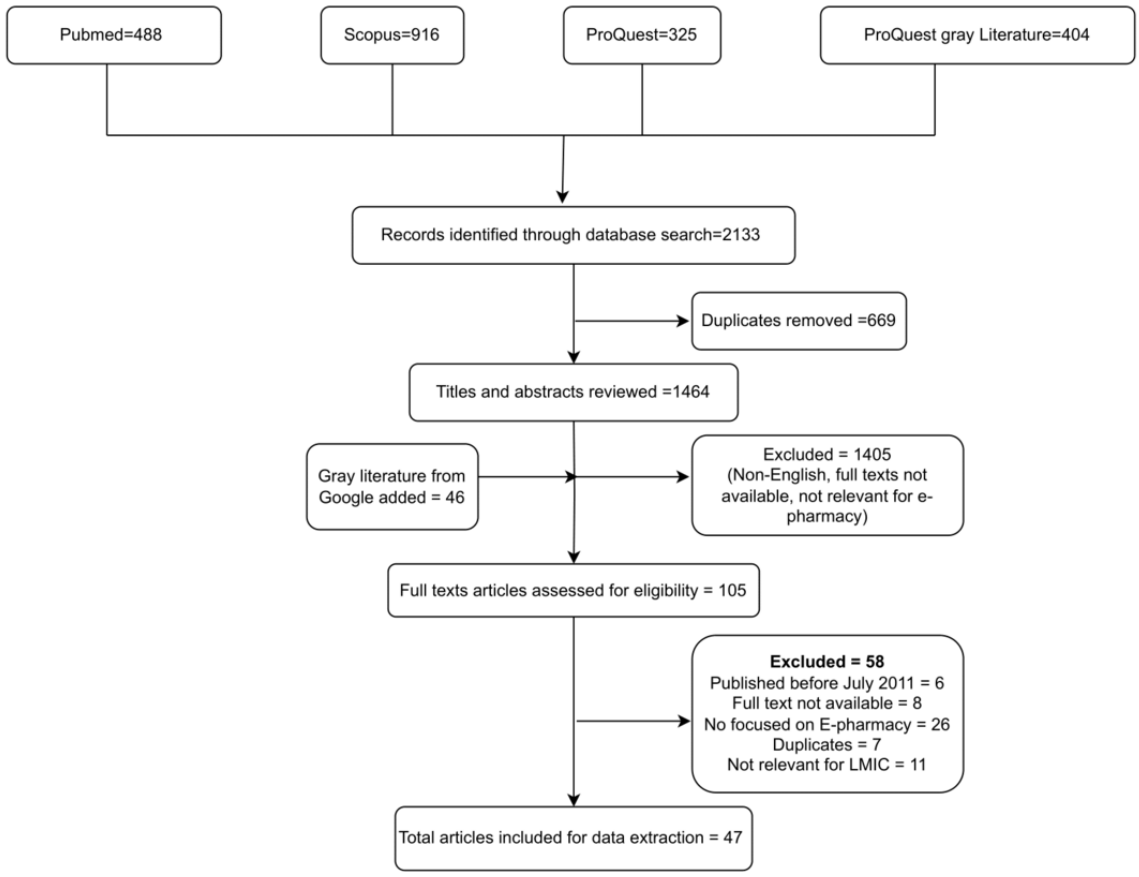
Data charting for the selected full-text articles was carried out by 3 authors (AA, SK, and HRB) using data collection forms generated using DistillerSR software. Charting performed by one author was verified by one more author. The data extracted included information on the study characteristics (author, year of publication, country, type of publication, and focus group) and outcomes (Technology used for e-pharmacy, advantages, disadvantages, regulations, access or availability, cost, affordability, and quality of service). The final datasheet was exported as an Excel file from the software, which was used for the compilation of results.

Results

The search yielded 2133 records from MEDLINE, Scopus, ProQuest, and ProQuest Gray literature. After removing 669 duplicates, 1464 abstracts were screened for inclusion in the review. Of these, 47 full-text articles were included in the scoping review (Figure 1). These included 13 original papers, 11 literature reviews, 5 newspaper articles, 6 newsletters, 3 guidelines or reports from nongovernment organizations, 3

policy documents or government guidelines, 1 case study, 1 viewpoint, 1 PowerPoint presentation, 1 systematic review, and 2 blogs. Of these 47 articles, 32 were focused on India. In addition, 5 were focused on other Asian countries (China, Bangladesh, Taiwan, and Saudi Arabia).

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.



Study Characteristics

The study characteristics for original papers are provided in Table 1, which mainly comprised surveys done among consumers or pharmacists and observational studies using e-pharmacy websites. Table S2 in Multimedia Appendix 2 shows a summary of findings from other papers, including literature reviews, reports, guidelines, web pages, and newspaper articles.

Table 1. Study characteristics of the original studies included in the scoping review.

Author (year)	Country	Methods	Sample size	Findings
Jain et al (2019) [14]	India	Survey	80	Good awareness of online pharmacies; however, there is a chance of delivering wrong medicines and delayed delivery; there is less chance of unavailability of medicines.
Miller et al (2021) [11]	Kenya, India, and Nigeria	Literature review and key informant interviews	18 key informant interviews	None of the study countries had yet enacted a regulatory framework for e-pharmacy; Key regulatory challenges included the lack of consensus on regulatory models, lack of regulatory capacity, regulating sales across borders, and risks of overregulation.
Mulani et al (2018) [15]	India	Literature review and self-administered survey	100 retail pharmacists	All respondents were aware of e-pharmacy in India, and most of them expressed a positive attitude toward it.
Srivastava and Raina (2020) [16]	India	e-survey	184 consumers	Performance expectancy, effort expectancy, social influence, and hedonic motivation had a positive correlation with e-pharmacy adoption and the intention to recommend. Gender and educational background did not correlate.
Aithal and Shabaraya (2019) [17]	India	e-survey	258 (general public)	91% of the respondents purchased medicines offline almost always and 46% of respondents were happy with offline medicine purchases; 32.63% of the respondents who also purchase medicines online feel that attractive discounts on prices and offers are major factors in their decision.
Sabbir et al (2020) [18]	Bangladesh	e-survey	285 consumers	Perceived trust and health literacy were found significant in determining consumers' intention to adopt e-pharmacy, while perceived risk and innovativeness were found insignificant.
Yan-Kwang et al (2019) [19]	Taiwan	Development of a sustainable inventory model	N/A[a]	This study proposes a single-period visual-attention-dependent demand (VADD) inventory model for e-pharmacies to cope with the sales growth of online marketing while reducing the cost of excessive inventory.
Yin et al (2016) [20]	China	Survey	274 consumers	Performance expectancy, social influence, perceived trust, and perceived risk have directly significant influences on consumers' adoption intention of online medicine purchases.
Ma (2021) [21]	China	Survey	459 nonadopters of online pharmacy	Perceived usefulness and trustworthiness significantly affected nonadopters intention; perceived ease of use positively impacted perceived usefulness and trustworthiness; perceived risk negatively affected trustworthiness.
Brijnath et al (2014) [22]	Australia	Semistructured face-to-face interviews	28 Indian-Australians and 30 Anglo-Australians	Cost, convenience, and dissatisfaction with local health services were the main reasons for buying medicines online. Increased availability of medicines online raises important issues for the safe use of medicines.
Fittler et al (2013) [23]	Hungary	Observational study	136 online pharmacy websites	Only 41.2% of included websites were operational for up to 4 years; 44.1% were rogue, and 16.9% were unapproved; long-term continuous operation strongly correlated with explicit illegal activity.
Alwon et al (2015) [24]	United Kingdom	Observational study	113 websites selling diazepam, fluoxetine, and simvastatin	Less than a quarter of the websites were regulated; prescription was not mandatory in 80 websites; unregulated websites were found to adhere more closely to the clinical criteria and less likely to disclose the identity.
Bate et al (2014) [25]	United States	Email survey	2907 members of RxRights	61.54% purchase drugs online and mostly from foreign websites, citing cost savings as the leading reason.

[a]N/A: not applicable.

The results are described under the following subthemes.

Regulations for e-Pharmacy in India

Out of 47 publications, 22 included information about regulations on e-pharmacy, and of these, 17 articles were written in the context of Indian settings (Table 1 and Table S2 in Multimedia Appendix 2).

In India, the Drugs and Cosmetics Act (1940), the Drugs and Cosmetic Rules (1945) [26], and the Pharmacy Act (1948) [27] are inadequate for the regulation of e-pharmacies [1]. Hence, a subcommittee of the Drugs Consultative Committee of the Drug Controller General of India (DCGI) suggested a draft amendment to the Drugs and Cosmetic Act, of 1945 (draft general safety regulation (GSR) from the Ministry of Health and Family Welfare, Government of India dated August 20, 2018) [1]. As per this amendment, for e-pharmacy, compliance with the Information Technology Act, 2000 [28] is required in addition to the 1945 rules.

As per these draft rules, the e-pharmacy needs to be registered with the DCGI, and the e-pharmacy portal should mention the registration details, official logo, the name of the registered pharmacist with the registration number, contact numbers, and return policy of dispensed medicines, details of the logistic service provider for the e-pharmacy. The premises or facility for the e-pharmacy business can be audited once in 2 years by the central licensing authority as per these rules [1]. In addition, the e-pharmacy portals should maintain the confidentiality of all the customer information except for regulatory audits and should not advertise in any print or digital media. Data thus collected should not be shared or stored outside the country [1,12]. There is no provision in the draft rules for the consumers to verify the authenticity of e-pharmacies. The sale of narcotics and psychotropics, tranquilizers, and Schedule X medicines through e-pharmacy is prohibited.

However, implementation of the draft rules has been pending for more than 5 years now. There is strong opposition to the growth of the e-pharmacy model in India by brick-and-mortar pharmacies. This is due to discrepancies in the rules for both and possibly because of vested interests in preventing the growth of e-pharmacies [11]. There have been public interest litigations in the Delhi and Madras high courts stating that in the absence of a monitoring system, the online sale of medicines can pose risks to doctors and patients [29]. The white paper published by the Indian Medical Association in 2015 opposed e-pharmacy due to the increased risk of drug abuse and drug misuse, including indiscriminate use of antibiotics and self-medication, as well as the proliferation of illicit pharmacies. Some of these concerns have been addressed in the current draft rules. However, the following issues need further action: the e-pharmacy portals can be used by children who cannot legally purchase medicines from a pharmacist; there is no mechanism to check the storage conditions of the medicines sold by e-pharmacies; mechanisms for recall of drugs sold through e-pharmacy are unclear [30]. With the increasing use of e-pharmacy in the country, online pharmacy retailers have come together to establish an association, the Indian Internet Pharmacy Association (IIPA). The association aims to protect and promote public health by maintaining harmony with regulators regarding the implementation of e-pharmacy in India. The IIPA is now renamed as Digital Health Platform (DHP) and is currently working actively with the Government to bring in changes to the regulations, including the use of Aadhar-linked prescriptions to appropriate use of e-pharmacy [31].

Despite these limitations, the e-pharmacy sector has grown by leaps and bounds in the last few years, especially with the advent of the COVID-19 pandemic, where doorstep delivery of medicines has been considered essential. Due to this, the Union Ministry, on March 24, 2020, mentioned pharmaceutical products as essential goods and delivery of medicines as essential services [32]. Recently, the department-related Parliamentary Standing Committee on Commerce Ministry, in its report presented to the Chairman of Rajya Sabha on June 15, 2022, recommended that the central government, in its draft e-pharmacy rules, should be finalized without any further delay. The committee expressed displeasure over the undue delay in the finalization of these rules, which is not conducive to the fast-paced digital markets [33].

Other regulatory challenges for the implementation of e-pharmacy in India include a lack of qualified personnel in the regulatory system, understaffing, corruption, and a lack of expertise to monitor online transactions. The e-pharmacy markets often operate beyond national borders, and regulators have no control over the purchase of medicines from pharmacies operating outside the country. Despite the presence of the rule that a doctor's prescription must accompany a medicine, this rule is rarely enforced [11]. Furthermore, there is a lack of specific regulations for the sale of herbal medicines, which are easily available through the internet without a prescription and are often consumed under the popular belief that herbal drugs do not have adverse effects [34].

e-Pharmacy and Access to Medicines

Access to medicines was mentioned in 14 publications included in the review. Except for 1 qualitative study, all publications were either reviews, blog posts, opinions, or reports (Table 1 and Table S2 in Multimedia Appendix 2). In one of the studies, which was conducted in Australia, patients (including Indo-Australians) taking antidepressants reported easy access through e-pharmacies to complementary and alternative medicines that were either not available or quite expensive in conventional pharmacies [22]. However, this was not the case with allopathic medicines, which were heavily subsidized and easily accessible from conventional pharmacies through the Pharmaceutical Benefits Scheme (PBS) in Australia.

The original evidence is scarce on what impact e-pharmacies may have on access to medicines in India. Nevertheless, there were a few studies on important facets of the access issue [35]. A narrative review highlighted the wide disparity in access to medicines by geographic area in India, probably due to the lack of conventional pharmacies and pharmacists in many parts. Although the distribution time in remote areas is delayed, certain e-pharmacies are known to reach and serve at least 90% of pin codes in the country. According to a report, e-pharmacies can aggregate supplies, making otherwise hard-to-find medicines available to patients across the country [5,36]. However, for an internet-naïve vulnerable population residing in remote areas with limited internet access, Deepika et al [37] believe that e-pharmacies may not increase access to medicines. Presently, internet penetration in India, which is essential for e-pharmacy ordering, is relatively low at 50% with better access in the urban as compared with rural areas [38]. According to the National Sample Survey Office's 75th round national survey (2017-2018), only 8.5% of women in rural India can use the internet as compared with 17.1% of males. For urban areas, the percentage of internet users is significantly higher [39].

In urban India, e-pharmacies may help medicines reach the older adult population in particular. This group is often isolated due to the increasing adoption of the nuclear family structure. However, despite the convenience offered by e-pharmacies, there is considerable resistance from consumers in India [5,32]. A recent review reported that only 6% of respondents purchased medicines online, although more than 85% knew about e-pharmacies [14]. An expert opinion recommended that

e-pharmacies establish logistics channels to reach out to patients in remote areas with less medical access [40]. It has also been suggested that the government should encourage generics to ensure the reach of medicines in remote areas [36].

Quality of e-Pharmacy Services and Supply Chain-Related Issues

Quality of service or supply chain issues as well as products were studied or discussed in 6 original papers and 6 other publications (Table 1 and Table S2 in Multimedia Appendix 2).

A 2011 global systematic review found that only 12%-28% of e-pharmacies had at least 1 quality certification, and up to 17% of e-pharmacies did not have a secure website [41]. A global study on the quality of e-pharmacies found that 41% of e-pharmacies were in continuous operation for the 4-year study period [23]. However, 30% of the long-lived e-pharmacies were unapproved, and 64% were rogue. Though the physical location was disclosed by 54% of e-pharmacies, only 10% of e-pharmacies operated their server within the borders of the given location. Consumers were required to produce prescriptions and information on health status by 6% and 62% of e-pharmacies, respectively. These findings corroborate with another similar study from the United Kingdom published a year later [24].

Globally, the quality of e-pharmacy services is regulated using verification standards and professional certifications [23-25] by bodies such as the General Pharmaceutical Council (GPhC) in the United Kingdon and the National Association of Boards of Pharmacy (NABP) in the United States [42]. e-Pharmacies in the European Union (EU) should obtain a common logo that is displayed on their respective websites. Tapping on the logo would lead to a page where the authenticity of respective e-pharmacies can be verified [43]. Third-party certification agencies such as LegitScript accredit e-pharmacies worldwide and are endorsed by several regulatory authorities across the world.

India currently lacks any accreditation or certification body required to ensure the safety and health of consumers. The evidence comparing the quality of medicines purchased from e-pharmacies and conventional pharmacies is lacking in India. Certain e-pharmacies in India offer discounts, loyalty programs, and cashback to retain patients, and this effort may have an impact on the quality of medicines supplied or services provided [40]. Public perception of the quality of products supplied by e-pharmacies in India varies. In an e-survey, 26% of respondents believed that the quality of medicines would be compromised if medicines were traded online [5]. Conversely, in another survey, relatively more respondents believed that the quality of products supplied by e-pharmacies is better than that of conventional pharmacies [44].

Green supply chain management is increasingly considered globally and is adopted in Indian e-pharmacies [14,19]. E-pharmacies can reach out to local medicine stores for partnerships to cancel out supply chain issues in remote areas [36]. With certain e-pharmacies, medicines can be traced back to the channel, manufacturer, or supplier enabling quality checks [32]. Frost and Sullivan [12] suggest that substandard and fake medicines could be sold through conventional pharmacies, whereas e-pharmacies could prevent the sale of poor-quality medicines through their efficient tracking mechanism. However, as highlighted before, there are instances of suboptimal supply through e-pharmacy [36,45].

Cost and Affordability of Pharmacy Services Using e-Pharmacy

Several published papers indicate that e-pharmacies can offer medicines at a lower cost as compared to conventional pharmacies (Table 1 and Table S2 in Multimedia Appendix 2). An e-pharmacy does not require a physical store for selling its merchandise and thus saves on both infrastructure costs and recurring costs like electricity and maintenance. This would result in significant cost reduction as most large pharmacies need to operate 12 hours a day, incurring huge maintenance and electrical costs. There is a cost involved in maintaining the infrastructure that consists of the hardware and software that run the e-pharmacy, shipping, and delivery costs. The reduced procurement and transactional costs are passed onto consumers at lower prices [8,40]. A study from the United States found that the cost of purchasing medications online for Parkinson disease ranged from 7% to 58% less for brand names and 31% to 76% less for generic medications compared with the community pharmacy [6,23].

A survey from India reports that 32.63% of respondents who purchase medicines online feel that discounts on prices and offers are major attractive factors for the use of e-pharmacy [17]. However, there are no studies from India comparing the cost-effectiveness of e-pharmacies.

Advantages and Facilitators of e-Pharmacy

Global literature shows several advantages of e-pharmacies over brick-and-mortar pharmacies, such as improved access and reduced cost [46]. However, although the access is round-the-clock for the patients, the benefits offered by the round-the-clock access are not comparable with 24-hour brick-and-mortar pharmacies as the patients have to wait for a few hours or days till the medicines arrive [47]. Central stocks and digital accountability of stocks of e-pharmacy facilitate tracking of the supply chain and ensure easier access as compared with retail pharmacies [12,14,19]. Patients perceive less intimidation or embarrassment when they order medicines online rather than speaking directly to a pharmacist in a busy community pharmacy [47]. The anonymity offered by the internet encourages patients to seek information about medicines that they would otherwise avoid asking their physician or at an offline pharmacy, particularly for contraceptives, psychiatric diseases, erectile dysfunction, acne, sexually transmitted diseases, hair loss, etc. In a review of more credible Internet pharmacies, 1 study found that the quality of medical information was variable but generally more comprehensive than that provided by conventional pharmacy drugstores [48]. The e-pharmacies also offer cost comparisons across the internet databases thus empowering the consumers.

Advantages for the regulators and health system include the audit trail for all transactions including all details of medicines,

prescribers, and e-pharmacy holders. These datasets can be used to inform public health policy; with increased transparency of transactions, 100% payment of applicable government taxes can be facilitated [5,11] and also facilitate back-tracing the channel or manufacturer or supplier of counterfeit and falsified medicines, thereby making the market a lot more transparent and authentic [46].

Recent literature shows good acceptance of e-pharmacy by users and physicians. In a survey by the Federation of Indian Chamber of Commerce and Industry (FICCI), almost 90% of Indian physicians perceived it as an acceptable means of sale and purchase of pharmaceutical products. The easy access and convenience of e-pharmacies are major determinants for attracting consumers in the view of medical practitioners, as mentioned by 85% and 75% of respondents, respectively [5]. A systematic review of e-pharmacy services in community pharmacy settings showed no difference in medication safety and adherence, conflicting evidence on patient satisfaction, and inadequate evidence on inappropriate medication use [49]. Recent literature shows that the use of e-pharmacy during COVID-19 was associated with a positive perception among pharmacists [50], was beneficial, especially in settings with a shortage of pharmacists [51], and could even reduce hospitalization due to COVID-19 [52].

Disadvantages and Barriers to e-Pharmacy in India

Due to the absence of a physical structure and poorly evolved regulations, especially in the LMICs, including India, rogue pharmacies may outnumber legitimate pharmacies. Dispensing of substandard, falsified, or counterfeit medicines has been reported from such pharmacies due to a lack of oversight in e-pharmacy supply chains, and this may, at times, pose a life risk for patients [8]. Such pharmacies may allow the sale of medicines, including schedule-H medicines without a valid prescription. With the availability of health information on the internet, patients often self-diagnose and can get attracted by rogue e-pharmacies to self-medicate [10,53]. For example, toxicity associated with the self-administration of Zolpidem has been reported in the United Kingdom [45]. Although rogue pharmacies can prevail in brick-and-mortar pharmacies, the risk increases multifold with e-pharmacies as, in the absence of proper regulations, these can be run without the presence of a physical structure and qualified pharmacist and are thus less likely to get monitored. Studies conducted on the sale of psychiatric medicines found that patients with mental illness used online pharmacies to stock medicines believed to be effective in managing their condition. In addition, even when a prescription is available for the medicines, the consumer might still misuse it by sending a single prescription to multiple online pharmacies [54]. Additional disadvantages include delays in the delivery of medicines, lack of confidentiality, and medical supervision [55]. In a recent survey conducted among the general population in Chandigarh, India, most of the respondents preferred to consult their physicians before buying a drug online [56].

The pros and cons associated with e-pharmacy in the Indian context have been summarized in Table 2.

Table 2. Pros and cons of e-pharmacy in India.

Pros	Cons
Improved access: Available 24 hours a day, seven days a week.	No patient-pharmacist interaction: Lack of medical supervision or availability of registered pharmacists to answer essential questions through questions[a].
The convenience of doorstep delivery: important for debilitated and older people, useful in pandemic conditions.	Risk of getting counterfeit, substandard, or incorrect medicines.
Offers anonymity to patients: Less intimidation while obtaining drugs for embarrassing health conditions[a].	Concerns about privacy and confidentiality of personal information[a].
Availability of drug-related information on the website[a].	It may not be feasible for technology-naïve or illiterate people[a].
Price comparisons are easy with searchable databases[a].	Risk of misuse especially by using rogue pharmacies leading to adverse drug reactions or substance abuse.
Medicines can be offered at a considerably low cost.	Many rogue pharmacies provide drugs without valid prescriptions.
Can provide better access to medicines in remote and rural areas.	Lack of a national accreditation body to distinguish between authentic and rogue pharmacies[a].
Potentially beneficial for chronic diseases to improve compliance with medicines[a].	Lack of awareness about e-pharmacies among physicians and the general public[a].
Ensured drug availability due to central stocks.	Limited participation by third-party payers.

[a]These factors are specific to e-pharmacies.

Discussion

Principal Findings

The present review summarizes available evidence from published and gray literature related to the implementation of e-pharmacy in India. The review shows clear benefits of e-pharmacy introduction in India in terms of improved access and delivery of medicines, especially in remote areas, for the older adult population and reduced costs of medicines. This is especially important in Indian settings considering the diverse

pharmacist-patient ratios across various states [35] and the fact that medicines account for 70% of the health care costs in India [6]. E-pharmacy can also provide transparency in drug purchase and audit purposes. With the increasing use of e-pharmacy, to integrate clinical skills with the virtual environment, it has been suggested adding tele-pharmacy to pharmacy education [57]. Gil-Candel et al [58] showed that it is feasible to develop an e-pharmacy program within an outpatient pharmacy department of a tertiary hospital with home delivery of medicines.

The lack of clear regulations for e-pharmacy in India, lack of internet penetration, and digital literacy were found to be some of the important barriers to implementation. To combat the issue of internet connectivity and digital literacy, the Government of India has set up Common Services Centers (CSC) across the country to deliver the government's e-services to rural and remote locations. According to the report, the Department of Pharmaceuticals aims to use CSCs for offering e-pharmacy services such as Jan Aushadhi medicines (generic medicines made available through the national program Bharatiya Jan Aushadhi Pariyojana). Patients may also search for and order their medications from Jan Aushadhi stores using the mobile or web-based applications that are being developed [5].

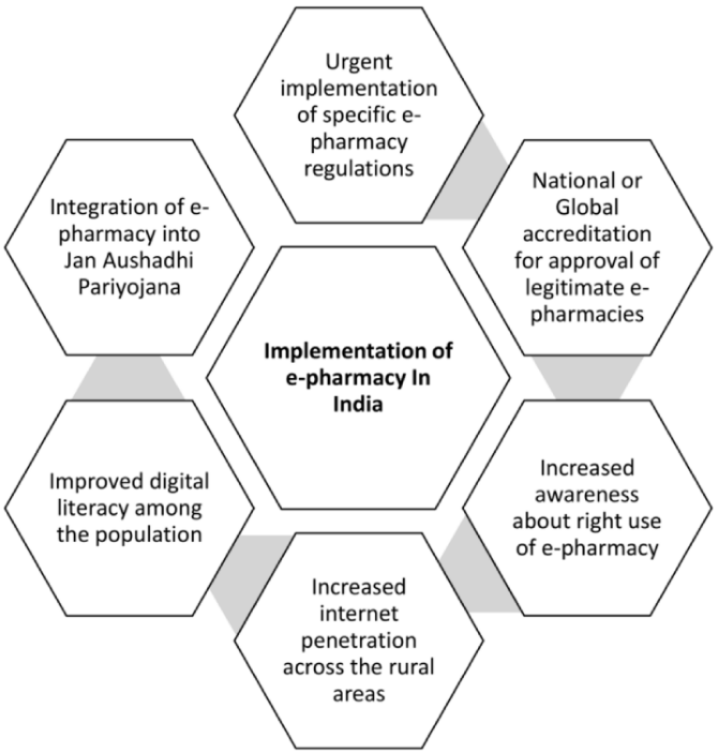
Specific regulation for e-pharmacy is a key step to propagating future investment and growth of e-pharmacy in India and curbing the unregulated growth of rogue pharmacies across the country. The introduction of these laws is possibly delayed as a result of hostility and litigations by retail pharmacist associations in the country [1]. The absence of comprehensive regulations on e-pharmacy in India is a possible loophole for selling substandard and counterfeit medicines [59]. An approved regulatory framework for e-pharmacy is keenly awaited to prevent confusion among the stakeholders and to increase investment in this sector. To expedite and smoothen the implementation of laws for e-pharmacy, policy makers should initiate dialogue with key stakeholders such as major pharmaceutical companies, IT companies, pharmacists, and physician associations. This can also help to resolve the issues responsible for the delay and thereby ensure the forward movement of the implementation of e-pharmacy in the country.

In addition, a national accreditation system should be in place to weed out rogue pharmacies, having robust technology solutions to interrupt the financial transactions of illicit pharmacies. As suggested by Miller et al [11], the presence of a global regulatory network may be the next step for the regulation of e-pharmacies due to the risk of the sale of medicines across national borders.

Improved literacy and awareness among consumers and health care providers about the use of legitimate pharmacies has been suggested to channel the e-pharmacy growth, and physicians should educate their patients about the dos and don'ts of online purchase of medicines [12,24].

The key steps in facilitating the implementation of e-pharmacies in India have been summarized in Figure 2.

Figure 2. Key steps in the implementation of e-pharmacy in India.



The findings of our review are similar to recently published reviews on e-pharmacy from developing countries. A review of the effectiveness of e-pharmacy in rural Africa shows that e-pharmacy can improve health care access; lack of infrastructure, inadequate funding, and regulatory challenges are important hurdles in the implementation [60].

The review has certain limitations. We have used global literature with reference to the Indian context due to the scarcity of published literature. Furthermore, the gray literature including

newsletters or data blogs is not peer-reviewed. In addition, due to delays in the peer review process, the review fails to include the most recent literature. Nonetheless, the review provides a consolidated overview of the status of e-pharmacy in India and key recommendations for the policy makers to consider during the implementation of e-pharmacy in India.

Conclusion

Overall, e-pharmacy has the potential to improve access and affordability of medicines for Indian consumers by unleashing the power of technology for better health. However, there is an urgent need to implement a strong regulatory and accreditation network for the implementation of e-pharmacies in India to provide quality services and products through this model. In addition, increased internet penetration, improved digital literacy, raised awareness about legitimate e-pharmacies among doctors and patients, and integration into the public health program of Jan Aushadhi Yojana are needed to reap the real benefits of this technology.

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Authors' Contributions

AA, HRB, SJC, SK, and TDS together conceptualized the idea. AA, in consultation with others, developed the protocol for the scoping review. HRB, SK, and AA were involved in the screening of titles and abstracts. HRB, AA, and SJC were involved in the selection of full-text articles. AA, HRB, and SK completed data extraction. AA, with support from HRB and SK, prepared the first draft and revised it. AA, HRB, SJC, SK, and TDS were involved in the critical review and editing of the manuscript. All authors reviewed and approved the final version.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Key themes and search strategies.
[DOCX File , 15 KB - ojphi_v16i1e51080_app1.docx]

Multimedia Appendix 2
Summary of literature reviews and gray literature included in the scoping review.
[DOCX File , 117 KB - ojphi_v16i1e51080_app2.docx]

Multimedia Appendix 3
PRISMA ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) checklist.
[PDF File (Adobe PDF File), 497 KB - ojphi_v16i1e51080_app3.pdf]

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Abbreviations

CSC: Common Services Centers
DCGI: Drug Controller General of India
DHP: Digital Health Platform
EU: European Union
FICCI: Federation of Indian Chamber of Commerce and Industry
GSR: general safety regulation
GPhC: General Pharmaceutical Council
IIPA: Indian Internet Pharmacy Association
JBI: Joanna Briggs Institute
LMIC: low- and middle-income country
NABP: National Association of Boards of Pharmacy
OSF: Open Science Framework
PBS: Pharmaceutical Benefits Scheme
PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews

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Psychometric Properties of Measuring Antiretroviral Therapy Adherence Among Young Latino Sexual Minority Men With HIV: Ecological Momentary Assessment and Electronic Pill Dispenser Study

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Abstract

Background: Increasing HIV rates among young Latino sexual minority men (YLSMM) warrant innovative and rigorous studies to assess prevention and treatment strategies. Ecological momentary assessments (EMAs) and electronic pill dispensers (EPDs) have been used to measure antiretroviral therapy (ART) adherence repeatedly in real time and in participants' natural environments, but their psychometric properties among YLSMM are unknown.

Objective: The study's objective was to assess the concurrent validity, acceptability, compliance, and behavioral reactivity of EMAs and EPDs among YLSMM with HIV.

Methods: A convenience sample of 56 YLSMM with HIV with suboptimal ART adherence, aged 18 - 34 years, was recruited into a 28-consecutive-day EMA study. Concurrent validity was analyzed by comparing median ART adherence rates and calculating Spearman correlations between ART adherence measured by EMA, EPD, and baseline retrospective validated 3-item and single-item measures. Acceptability was assessed in exit interviews asking participants to rate EMA and EPD burden. Compliance was assessed by computing the percent lost to follow-up, the percent of EMAs missed, and the percentage of days the EPD was not opened that had corresponding EMA data self-reporting adherence to ARTs. Behavioral reactivity was assessed by computing the median change in ART adherence during the study period, using generalized mixed models to assess whether the cumulative number of EMAs completed and days of EPD use predicted ART adherence over time, and by asking participants to rate perceived reactivity using a Likert scale.

Results: EMA ART adherence was significantly correlated with baseline validated 3-item (r=0.41, P=.003) and single-item (r=0.52, P<.001) measures, but correlations were only significant for participants that reported EMA was not burdensome. Correlations for EPD ART adherence were weaker but significant (r=0.36, P=.009; r=0.34, P=.01, respectively). Acceptability was high for EMAs (48/54, 89%) and EPDs (52/54, 96%) per self-report. Loss to follow-up was 4% (2/56), with the remaining participants completing 88.6% (1339/1512) of study-prompted EMAs. The percentage of missed EMA surveys increased from 5.8% (22/378) in week 1 of the study to 16.7% (63/378) in week 4. Of 260 days when EPDs were not opened, 68.8% (179) had a corresponding EMA survey self-reporting ART adherence. Reactivity inferred from the median change in ART adherence over time was 8.8% for EMAs and −0.8% for EPDs. Each completed EMA was associated with 1.03 odds (95% CI 1 - 1.07) of EMA ART adherence over time, and each day of EPD use with 0.97 odds (95% CI 0.96 - 0.99) of EPD ART adherence over time. Self-reported perceived behavioral reactivity was 39% for EMAs and 35% for EPDs.

Conclusions: This study provides evidence of concurrent validity with retrospective validated measures for EMA- and EPD-measured ART adherence among YLSMM, when participant burden is carefully considered, without significant behavioral reactivity. While acceptability and compliance of EMAs and EPDs were high overall, noncompliance increased over time, suggesting respondent fatigue.

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KEYWORDS

human immunodeficiency virus; HIV; MSM; sexual minority; antiretroviral therapy; Latino; Hispanic; adherence; psychometric; ecological momentary assessment; electronic pill dispenser; validity; acceptability; compliance; medication dispenser; reminder; alert; digital health; young adult

Introduction

In 2020, Latinos accounted for 27% of new HIV diagnoses in the United States and 31% of new HIV diagnoses among sexual minority men (SMM) [1]. In the same year, Latino SMM accounted for 23% (n=246,097) of people with HIV in the United States [1]. Despite viral suppression being critical to prevent new cases of HIV and preserve the health of people with HIV [2], only 66% of Latino SMM with HIV in the United States achieved viral suppression in 2020, compared with 73% among non-Latino White SMM [3]. Low rates of viral suppression are partially due to suboptimal antiretroviral therapy (ART) adherence. The US representative sample data from 2015 to 2019 showed only 57% of Latino SMM with diagnosed HIV reported taking all their ART doses in the previous month, with younger (<40 years old) Latino SMM less likely to report being adherent [4].

Ecological momentary assessments (EMAs) collect data on behaviors and experiences repeatedly in real time and in the participant's natural environment [5]. Electronic pill dispensers (EPDs) are pillboxes designed to monitor pill-taking by recording timestamped signals when the device is opened [6]. EPDs have been used for nearly 2 decades as an objective measure of ART adherence in rigorous HIV and pre-exposure prophylaxis clinical trials that have had significant implications [7-10]. While the validity, acceptability, and compliance of EMA and EPD have been evaluated in some studies suggesting they are valid and acceptable tools to measure outcomes among the general population of people with HIV [11-15], the psychometric properties of EMA and EPD among young (18 - 34 years old) SMM are unknown. Acceptability and compliance of these demanding protocols may be lower for those experiencing socioeconomic and structural barriers [13] such as young SMM, which may compromise the validity of the data collected. A 2019 study of young SMM and trans women in San Francisco showed those reporting housing instability, foregoing HIV medications to afford basic needs, or reporting lower educational levels were more likely to miss EMA surveys [13].

Both EMA- and EPD-measured ART adherence pose the additional psychometric concern of reactivity, or the potential effect that repeated and frequent measurements of adherence behavior will have on the observed outcome despite a lack of intervention [16]. Behavioral reactivity has been examined more extensively in EMA studies of drinking and smoking, which have shown no or small reactivity effects, that is, none or a small decrease in drinking or smoking over the course of the EMA study assumed to be due to repeated real-time monitoring of the behavior [17-20]. Studies of behavioral reactivity from the use of EPD to monitor medication adherence across various health conditions have also reported no or minimal reactivity when used without additional intervention components, suggesting minimal concern about its use in observational research [21,22]. However, we were unable to identify any studies assessing the behavioral reactivity of EMAs or EPDs when used to measure ART adherence among Latino SMM, suggesting an important gap in the literature.

In this study, we report findings of 3 study objectives that assess the rigor and use of EMA and EPD and inform methodological and analytical choices in the study of ART adherence among young (18 - 34 years old) Latino SMM (YLSMM). Our first objective was to assess the concurrent validity of EMA- and EPD-measured ART adherence by comparing their agreement with retrospective self-reported validated and single-item measures of ART adherence taken at baseline. Based on previous research, we hypothesized that EMA and EPD ART adherence would be significantly correlated with validated baseline ART adherence measures [23,24]. Our second objective was to assess acceptability and compliance with EMA and EPD ART adherence protocols among this population. We hypothesized that acceptability and compliance with daily EMAs and EPD use would be moderate, given previous research showing high acceptance, but cautioned by potentially added barriers experienced by our population [13,25]. Our final objective was to assess behavioral reactivity to daily ART adherence monitoring. We hypothesized improvements in ART adherence over the course of the study and that participants would self-report a change in ART adherence behaviors due to their participation in the EMA and EPD protocols [21,22].

Methods

Study Design and Procedures

We conducted an EMA study of YLSMM with HIV to examine ART adherence behaviors and barriers to daily ART adherence [26]. After consent, participants completed an online self-administered baseline questionnaire, followed by 28 days of EMAs, and a telephone mixed methods (qualitative and quantitative) exit interview. EMAs consisted of 25 questions that took participants 4 - 6 minutes to complete daily and were delivered via a link in an SMS text message at 5 PM with 2 subsequent reminders 30 minutes apart. We chose to deliver the EMAs at 5 PM for all participants to ensure that the survey questions were answered in a similar way, with the same relative time point as a reference, in mind. For example, when answering questions about their mood, they were all referring primarily to their mood that day, versus the previous day if the EMA was delivered in the early morning for some. Study staff monitored incoming EMAs daily, and participants who did not complete 3 or more consecutive surveys were contacted via phone to remind them or troubleshoot issues. Similar to other studies, during enrolment, participants were offered an additional incentive if at least 80% of surveys were completed [27,28].

Baseline, EMA, and exit surveys were completed in the participant's preferred language (English or Spanish). When available, validated translations were used. If not available, questions were translated by a native Spanish speaker team member and reviewed by 2 additional Spanish speakers from different countries of origin, and differences were discussed until a consensus was reached. In addition, participants were given a Wisepill 3G RT2000 Dispenser with a 7-compartment cartridge (fitting at least 7 pills at a time per 1 week of ARTs) and a charger and asked to use the EPD daily to store their ARTs throughout the 28-day protocol. EPDs recorded date, time, and geolocation when opened. EPDs were monitored daily by study staff for battery power and signal; if a signal was not detected, study staff contacted participants via phone to troubleshoot or exchange the EPD, if needed.

Recruitment

A convenience sample of 56 YLSMM was recruited from the South Florida area between February 2021 and May 2022. The sample size was calculated to provide 80% power to detect meaningful odds ratios for the association between time-varying discrete covariates in the primary aims of the parent study and ART adherence as a binary outcome. Participants were recruited via referrals from case managers, linkage specialists, and physicians at 3 community HIV clinics, by posting flyers at local clinics and social service agencies serving people with HIV, and through paid targeted online advertising on search engines (eg, Google) and social media platforms (eg, Facebook). Eligible participants included individuals aged 18 - 34 years who self-identified as Latino; who self-identified as gay, bisexual, or other SMM; who spoke either English or Spanish; whose HIV was confirmed through a case manager referral, by submission of an HIV laboratory test, or ART prescription by the participant; who had a current ART prescription; who had no AIDS diagnosis; and who had no activity restrictions. Additionally, eligible participants needed to meet one of two criteria for suboptimal ART adherence: evidence of at least one detectable viral load test (≥20 copies/mL) in the past 24 months, or self-report ART adherence of less than "excellent" or "very good" in a 6-point Likert rating scale.

Measures

We measured adherence in 4 ways. First, we calculated *EMA ART adherence* using responses to the following question on daily EMAs—"Since the last survey, have you missed a dose of your HIV medication?" (yes/no)—and defined it as the total number of days that ARTs were taken divided by the total number of days a survey was submitted, setting missed surveys (173/1512) to missing. Second, we calculated *EPD ART adherence* as the total number of days the EPD was opened divided by the total number of days the EPD was on and receiving a signal, setting days when the EPDs were out of signal range (11/1512) to missing [7]. Third, we calculated *validated 3-item self-reported retrospective ART adherence* at baseline using Wilson et al's [29] ART adherence scale. Extensive research has been conducted to validate self-reported ART adherence by assessing its relationship with HIV viral load, suggesting self-report is a valid way to measure ART adherence [8,14,23,29,30]. Wilson et al's [29] scale has been shown to have a positive linear association with viral suppression in clinical and research settings. The three questions in the scale are as follows. (1) "In the past 30 days, on how many days did you miss at least one dose of any of your HIV medicines?" (2) "In the past 30 days, how good a job did you do at taking your HIV medicines in the way you were supposed to?" (6-point Likert from "very poor" to "excellent"). (3) "In the past 30 days, how often did you take your HIV medicines in the way you were supposed to?" (6-point Likert scale from "always" to "never"). We coded each question in Wilson et al's [29] scale so that higher numbers corresponded to greater adherence, then transformed responses to a 0 - 100 scale and took the mean of the 3 transformed items. Finally, we calculated *single-item retrospective ART adherence* using only question one of the Wilson et al [29] scale because it was adapted to be used in the EMAs. Median percent adherent was used for all measures due to the skewness of the data.

Measures of acceptability were gathered from the exit interview by asking participants to state their level of agreement (5-point Likert scale from "strongly agree" to "strongly disagree") with the following 2 statements: "It was burdensome to complete the surveys daily" and "It was burdensome to use the electronic pillbox daily." Self-reported measures of behavioral reactivity were also obtained from the exit interview by asking participants to state their level of agreement (5-point Likert scale from "strongly agree" to "strongly disagree") to the following 2 statements: "The daily surveys affected my HIV medication adherence" and "The use of the electronic pillbox affected my HIV medication adherence." We categorized acceptability and reactivity measures as "yes" burdensome or "yes" affected adherence if they responded, "strongly agree" or "agree."

Data Analysis

We assessed concurrent validity, acceptability, compliance, and behavioral reactivity of EMAs and EPDs among YLSMM with HIV. *Concurrent validity* was assessed by comparing median adherence rates and computing Spearman correlations for the whole sample and partial correlations by age, race, education, and US-born status between EMA-EPD-ART adherence and both the validated 3-item and single-item retrospective ART adherence measures [29]. We also stratified our correlation analysis by reporting the burden of EMAs and EPDs to capture if validity was impacted by the acceptability of EMA and EPD protocols. The tetrachoric correlation between EMAs and EPDs was calculated to assess the day-to-day agreement between the EMAs and EPDs across all participants and all 1512 observations. Correlations were considered significant if the *P* value was <.05 [8]. We conducted sensitivity analyses to understand the impact of missing EMA and EPD data on validity by replacing missing EMA adherence data with EPD data for the same day, if available. Similarly, we assessed the impact of replacing days without an "open" signal in the EPD (originally coded as nonadherent days) with EMA data for the same day, if available.

Acceptability was analyzed as the proportion of participants who reported the EMA and EPD to be burdensome. To assess *compliance*, we computed the percent of missed EMA surveys for the 28-day period and by study week, the percent of days

the EPD was not opened that had corresponding EMA data self-reporting adherence to ARTs, and the percent lost to follow-up. Finally, *behavioral reactivity* was assessed objectively by computing the median change in EMA- and EPD-measured ART adherence over the 28-day period and by using generalized mixed models to assess whether the cumulative number of EMAs completed predicted ART adherence over time. Behavioral reactivity was also assessed subjectively as the proportion of participants who self-reported that the use of the EMA and EPD affected their ART adherence behavior.

Ethical Considerations

The Florida International University institutional review board approved this study (IRB-18-0296). Informed consent was obtained from all participants in their preferred language (English/Spanish) prior to their participation in this study. Measures to protect the privacy and confidentiality of the data and participants included removing personally identifiable information from all data collection instruments, encrypting data during transfer and storage, storing data on secure systems with restricted access, and limiting access to identifiable information to the study coordinator and principal investigator. Participants were compensated US $35 for completing the baseline questionnaire, US $150 for participating in the 28-day EMA, US $35 for completing the exit interview, and US $30 if they completed at least 80% of EMA surveys for a maximum total of US $250.

Results

Participants

Of 56 participants who consented to be part of the study and completed the baseline questionnaire, 54 began the EMA and EPD portion of the study and were considered in the current analyses (details provided in the *Acceptability and Compliance* section). Twenty-four participants completed the EMAs in Spanish. Participants (n=54) had a mean age of 28.8 (SD 3.4) years and predominantly reported their gender identity to be male (52/54, 96%) and sexual identity to be gay (47/54, 87%) (Table 1). Participant's Latino origin was predominantly from South America (22/54, 41%) and Cuba (16/54, 30%), most self-identified as White (30/54, 56%) or multiracial or other (20/54, 37%), and most were foreign-born (37/54, 69%). About 44% (24/54) were single, 37% (20/54) had a college degree, and 50% (27/54) were working full-time.

Table . Characteristics of young Latino sexual minority men with HIV who participated in a 28-day EMA[a] and EPD[b] ART[c] adherence monitoring study (N=54[d]).

Characteristics		Values
Age (year), mean (SD)		28.8 (3.4)
Gender identity, n (%)		
	Male	52 (96)
	Other	2 (4)
Sexual identity, n (%)		
	Gay	47 (87)
	Bisexual	2 (4)
	Other	5 (9)
Latino origin, n (%)		
	Cuban	16 (31)
	South American	22 (42)
	Central American	8 (15)
	Other or mixed	6 (12)
Race, n (%)		
	White	30 (56)
	Black	4 (7)
	Other or multiracial	20 (37)
Immigrant generation, n (%)		
	First generation (foreign-born)	37 (71)
	Second or third generation (US-born)	14 (27)
	Don’t know or prefer not to respond	1 (2)
Year of stay in the United States (if foreign-born), n (%)		
	1 - 5 years	22 (41)
	6 - 10 years	13 (24)
	>10 years	19 (35)
Marital status, n (%)		
	Same-sex partner, married	11 (20)
	Same-sex partner, unmarried	19 (35)
	Single	24 (44)
Education, n (%)		
	High school diploma or less[e]	9 (17)
	Some college or vocational school	17 (31)
	Bachelor’s degree	20 (37)
	Master’s or doctoral degree	4 (7)
	Unknown or prefer not to respond	4 (7)
Employment status, n (%)		
	Full-time	27 (50)
	Part-time	11 (20)
	Self-employed	4 (7)
	Student	3 (6)
	Unemployed	8 (15)

Characteristics	Values
Don’t know or prefer not to respond	1 (2)

[a]EMA: ecological momentary assessment.

[b]EPD: electronic pill dispenser.

[c]ART: antiretroviral therapy.

[d]Two participants were excluded because they did not start the EMA or EPD protocol.

[e]One participant reported completing grades 1 - 11 but no high school diploma.

Validity

Of the 54 participants who started the EMA and EPD protocol, 52 had reliable data to be used in the assessment of validity (details provided in the *Acceptability and Compliance* section). All 52 participants reported being on once-daily ART regimens. Median EMA ART adherence was highest (100%, IQR 95.2%-100%), followed by single-item retrospective ART adherence (96.7%, IQR 93.3%-100%) (Table 2). Median adherence was lowest and nearly identical between the validated 3-item retrospective measure (89.2%, IQR 82.9%-95.4%) and the EPD (89.3%, IQR 75%-96.4%). EMA ART adherence was significantly correlated with the validated 3-item retrospective ART adherence measure (0.41, *P*=.003), the single-item retrospective ART adherence measure (0.52, *P*<.001), and the EPD measure (0.45, *P*<.001). The correlations between EPD ART adherence and both baseline ART adherence measures were weaker but also significant (validated 3-item measure=0.36, *P*=.009; single-item measure=0.34, *P*=.01). Partial correlations controlling for age, race, education, and US-born status were not appreciably different (not shown in the table). The tetrachoric correlation coefficient between EMA ART adherence and EPD ART adherence for all observations (n=1306) across the whole sample (n=52) was 0.41 (*P*=.003).

In sensitivity analyses, when we imputed missing EMA ART adherence data with EPD data, the correlation between EMA ART adherence and validated 3-item ART adherence (0.46, *P*<.001) and single-item ART adherence (0.54, *P*<.001) remained nearly the same. When we imputed data for days where the EPD was not opened with EMA data, the correlation between EPD ART adherence and validated 3-item ART adherence (0.35, *P*=.01) remained the same, but the correlation with the single-item ART adherence measure improved from 0.34 (*P*=.01) to 0.42 (*P*=.002).

To assess whether validity was a function of EMA or EPD acceptability, we assessed validity by the reported burden of EMA and EPD use. The Spearman correlation coefficient between EMA ART adherence and validated 3-item retrospective ART adherence was significant and positive (0.49, *P*<.001) among those who reported participating in daily EMAs was not burdensome compared to not significant for those who reported the EMAs were burdensome (−0.71, *P*=.12). A similar pattern was found when comparing EMA ART adherence with the single-item retrospective ART adherence measure by reported burden (not burdensome: 0.55, *P*<.001; burdensome: 0.09, *P*=.86). Among those who found the EPD not to be burdensome, the Spearman correlations between EPD ART adherence and validated 3-item retrospective ART adherence and single-item retrospective ART adherence were nearly unchanged compared to the overall sample. We were unable to assess the validity of EPD for those who found the EPD to be burdensome due to the small number of participants who reported the EPD to be burdensome (n=2).

Table . Validity of EMA[a] and EPD[b] ART[c] adherence among young Latino sexual minority men with HIV.

	Total, n	Median percent ART adherence[d] (IQR)	Spearman correlation coefficients (*P* value)		
			Validated 3-item retrospective ART adherence	Single-item retrospective ART adherence	EPD ART adherence
Daily prospective measures					
EMA ART adherence	52[e]	100.00 (95.24-100)	0.41 (.003)	0.52 (<.001)	0.45 (<.001)[f]
Not burdensome	49	—[g]	0.49 (<.001)	0.55 (<.001)	—
Burdensome	6	—	−0.71 (.12)	0.09 (.86)	—
EPD ART adherence	52[e]	89.29 (75.00-96.43)	0.36 (.009)	0.34 (.01)	—
Not burdensome	53	—	0.37 (.009)	0.35 (.01)	—
Burdensome	2	—	N/A[h]	N/A	—
Baseline retrospective measures					
Validated 3-item ART adherence scale	—	89.17 (82.92-95.42)	—	0.76 (<.001)	—
Single-item ART adherence	—	96.67 (93.34-100)	—	—	—

[a]EMA: ecological momentary assessment.

[b]EPD: electronic pill dispenser.

[c]ART: antiretroviral therapy.

[d]Median of within-person 28-day percent adherence.

[e]Two participants were excluded for not initiating the EMA and EPD protocol, 1 participant was excluded because of missing data on 23 of 28 EMA days, and another 1 participant was excluded for providing identical responses on 22 of 28 EMA days.

[f]Tetrachoric correlation coefficient between daily EMA ART adherence responses (dichotomized, yes=1, no=0) and daily EPD recorded adherence (dichotomized, yes=1, no=0) for all observations (n=1306) across the whole sample (n=52) was 0.41 (*P*=.003).

[g]Not applicable.

[h]N/A: not available; only 2 participants reported the electronic pill dispenser to be burdensome, thus correlations coefficients were not able to be computed.

Acceptability and Compliance

Approximately 89% (48/54) of participants self-reported that the daily EMA surveys were not burdensome, 96% (52/54) reported that using the EPD was not burdensome, and 98% (53/54) that they would participate in a similar study in the future (Table 3). Participants were highly compliant with the EMA protocol. Among 56 participants, 2 were lost to follow-up prior to starting the EMA or EPD protocol. The remaining 54 participants responded to 1339 (88.6%) of 1512 study-prompted EMA surveys over the 28-day study protocol. The EMA nonresponse rate ranged from 0 to 23 days, with a median number of days missed of 2. The number of participants who did not respond to the EMA survey increased from 1 participant on the first EMA day to 10 participants on day 28, with some inconsistency in days 16 and 19. The percentage of missed EMA surveys increased from 5.8% (22/378) in week 1, to 10.6% (40/378) in week 2, 12.2% (46/378) in week 3, and 16.7% (63/378) in week 4. Regarding data quality, 1 participant had missing data on 23 EMA days, and a second participant had identical responses on 22 of 28 EMA days and the responses were inconsistent across questions within the same survey. EPD devices recorded a signal (ie, they were on, charged, and recording data) for 1501 (99.3%) of 1512 days of data collection across all participants. EPD devices were recording data but not opened on a total of 260 (17.3%) of 1501 days. Among days when the EPDs were not opened, 179 (68.8%) had EMA data self-reporting adhering to ART, 23 (8.8%) had EMA data reporting not adhering to ART, and 58 (22.3%) had missing EMA data. Moreover, the proportion of days when EPDs were not opened but ART adherence was reported on EMA surveys increased steadily from 80% in week 1, to 89.7% in week 2, 91.1% in week 3, and 92.7% in week 4. In post hoc analyses, to assess potential changes in the use of the EPD, we examined the tetrachoric correlation between EMA ART adherence and EPD ART adherence by study week. The correlation was highest in week 1 (0.54) and lowest in week 4 (0.34) but fluctuated in the middle weeks (week 2=0.36; week 3=0.42).

Table . Self-reported acceptability and behavioral reactivity of EMA[a] and EPD[b] ART[c] adherence monitoring among young Latino sexual minority men with HIV (N=54[d]).

Statement	Participants, n (%)
Acceptability	
"It was burdensome to complete the surveys daily"	
Yes[e]	6 (11)
No[f]	48 (89)
"It was burdensome to use the electronic pillbox daily"	
Yes	2 (4)
No	52 (96)
"I would participate in a similar study again"	
Yes	53 (98)
No	1 (2)
Reactivity	
"The daily surveys affected my HIV medication adherence"	
Yes	21 (39)
No	33 (61)
"The use of the electronic pillbox affected my HIV medication adherence"	
Yes	19 (35)
No	35 (65)
"I changed the way I take my medication as a result of participating in this study"	
Yes	40 (74)
No	14 (26)

[a]EMA: ecological momentary assessment.

[b]EPD: electronic pill dispenser.

[c]ART: antiretroviral therapy.

[d]Two participants were excluded because they did not start the EMA or EPD protocol. The participant who did not complete 23 of 28 EMAs and another participant who had identical responses on 22 of 28 EMA surveys were included in the analysis of acceptability and compliance.

[e]Yes: "strongly agree" and "agree."

[f]No: "neither agree nor disagree," "disagree," and "strongly disagree."

Behavioral Reactivity

The median change between baseline (validated 3-item retrospective ART adherence) and end-of-study EMA adherence (difference between the measures) was 8.75% (IQR 1.36%-16.14%); using single-item retrospective ART adherence, the median change was 0% (IQR -1.99%-1.99%). The median change between baseline and end-of-study EPD adherence was −0.8% (IQR -9.7%-8.1%) using the validated 3-item measure and −7.14% (IQR -16.54%-2.26%) using the single-item measure. When we assessed whether the number of surveys completed predicted EMA ART adherence in a generalized mixed model, each increasing day of EMAs completed was associated with a 1.03 (95% CI 1 - 1.07) increased odds of ART adherence over time. Controlling for baseline adherence (3-item scale) did not change this association. Each increasing day of EPD use was associated with 0.97 (95% CI 0.96 - 0.99) decreasing odds of EPD ART adherence over time, without change when controlling for baseline adherence. Self-reported reactivity is reported in Table 3. Approximately, 39% (21/54) of participants self-reported that their ART adherence changed over the course of the study due to the EMAs, and 35% (19/54) due to their use of the EPD. The relationship between EMA surveys submitted or days of EPD use and ART adherence was not different by self-reported reactivity level.

Discussion

Principal Findings

This comprehensive study had several primary findings in 3 key methodological areas: validity, acceptability and compliance, and behavioral reactivity. This study provided evidence of concurrent validity of baseline retrospective validated ART adherence measures for EMA- and EPD-measured ART adherence among YLSMM. The strength of the correlation between EMA-measured ART adherence and our baseline measures was lower than the relatively high correlation (0.7) found in a study using a 14-day EMA protocol among adults with HIV [11]. Our study may have observed a

lower correlation because of the additional burden of completing 28 days of EMA, as we only found concurrent validity to be significant among participants who reported the EMA protocol was not burdensome. However, the strength of the correlation between EPD-measured ART adherence and baseline measures in our study was similar to 2 other studies comparing EPD-measured ART adherence to baseline measures, pharmacy records, and viral load [8,14]. Validity did not appreciably improve when combining EMA and EPD data (imputing missing values across these 2 data collection modalities), except for a small increase in the correlation between EPD-measured ART adherence and the single-item retrospective measure, suggesting a potential benefit of using EMA data to impute missing EPD values.

Self-reported acceptability of both the EMA and EPD was high among YLSMM in this study. While compliance overall reached the suggested 80% target [31] and mirrored or surpassed the high compliance in previous studies [31,32], noncompliance with EMA surveys nearly tripled in a 4-week period suggesting respondent fatigue. Interestingly, a meta-analysis by Jones et al [31] of EMA studies among substance users did not find evidence that EMA compliance was associated with the daily frequency of EMAs or length of assessments. However, the structure of financial incentives may influence compliance. Our study offered an additional incentive at the end of the study if at least 80% of EMAs were completed which may have helped to reach overall high compliance, but other incentive structures used in previous research, such as weekly disbursements of payments, or payments associated with each completed survey [33], may have helped to maintain high compliance across time. It is worth noting the discrepancy between high self-reported acceptability of EMA expressed during the exit interviews and decreasing EMA compliance over time, as this inconsistency was also found in a study of YLSMM and trans women in San Francisco [13]. Our finding that participants self-reported ART adherence in EMA surveys on nearly 70% of days that EPDs were not opened, that this discrepancy increased over time, and that concurrent validity of EPD-measured ART adherence improved when supplemented with self-reported EMA data, suggest that some participants were not using the EPD every day. It is possible that even though participants did not perceive the EMA or EPD as "burdensome," they still forgot or chose not to complete the EMA surveys on some days and not use the EPD. In an earlier qualitative phase of this study [26] used, in part, to obtain feedback on the EMA or EPD protocols, some participants expressed concerns about the size of the EPD, the feasibility of carrying it with them, and the potential for disclosing their HIV status if it was seen.

Similar to previous research, our study did not find evidence of behavioral reactivity from the use of EMA, as ART adherence did not increase with the increasing number of completed EMA surveys [21,22]. While we found an association between the increasing number of days of EPD use and decreases in ART adherence over time, the effect was small and only marginally significant (odds ratio 0.97, 95% CI 0.96 - 0.99). This seemingly paradoxical association provides additional evidence of decreases in the use of EPD over time and is consistent with our EPD compliance data that suggests participants are in fact adhering to their ARTs even on days when they do not open the EPD. For example, participants may remove more than 1 pill at a time from the EPD for later dosing and thus not open the EPD daily, a behavior referred to as "pocket dosing" [34,35]. Although about a third of participants self-reported that their ART adherence changed because of the use of EMA or EPD, we did not find that behavioral reactivity measured objectively was stronger for those that self-reported behavioral reactivity, suggesting self-reflection of ART adherence changes may not necessarily concur with actual ART adherence changes measured via EMA or EPD.

Limitations

Our study findings have some limitations. For our assessment of validity, we compared EMA or EPD ART adherence to baseline past 30-day ART adherence; thus, the time periods of measurement did not overlap. This limitation would have been especially problematic if we had found significant behavioral reactivity from the use of the EMA or EPD, but we did not find this to be the case in our sample. Further, our study did not ask participants to report ART doses taken outside while not using the EPD, a limitation reflected in the high proportion of days when the EPD was not opened but a dose was reported as taken in the same day's EMA survey. Additionally, as indicated by 1 participant with the same responses for all survey questions across 23 EMA surveys, asking the same questions each day for 28 days may fatigue participants, and although EMA compliance was high, the quality of the responses may have decreased over time; this limitation would be especially problematic when measuring factors expected to vary daily such as mental health or substance use indicators. Future studies may want to consider randomizing the order of questions daily or creating a variable schedule of questions with a larger sample of YLSMM. It is worth noting that our participants started the study on varying days of the week and compliance with EMA or EPD may differ by day of the week (weekdays vs weekends). Finally, the convenience sample recruited at clinics and online limits the generalizability of the findings, and the very high ART adherence and few missed doses in the sample may have limited power in our analyses, particularly in our evaluation of behavioral reactivity.

Implications for Research

Our findings highlight the importance of developing EMA protocols that are not burdensome for participants to ensure the validity of ART adherence measurements and compliance with protocols over time. Our findings also imply the need to carefully track compliance of EMA or EPD protocols over time objectively, and not only with perceived acceptability measures, and the need to consider decreases in compliance in the analysis of findings. As suggested by others, the choice of an EPD may enhance or diminish compliance, and study and participant characteristics should be considered when selecting an appropriate device for the target population [36]. Additionally, our findings imply that measuring ART adherence via EMAs or EPDs among YLSMM is not associated with unintentional changes in behaviors in observational studies and that these protocols on their own may not be sufficient to obtain ART adherence improvements in experimental settings. Ecological

momentary interventions seeking to increase ART adherence among YLSMM should consider building additional intervention components on top of a simple 1-way text message question about ART adherence behavior. Two-way text message ART adherence reminders have shown promise with youth and may be worth testing among YLSMM [37], as well as interventions that address other adherence barriers such as unmet basic needs, substance use, and mental health conditions [38]. Combined, these interventions can address the primary reasons for missed ART doses among YLSMM including forgetting to take medication, a change in routine, oversleeping, drug use, depression, and lack of needed ancillary services [4,26]. The low cost and easy implementation of self-reported measures of medication adherence using mobile health, such as the one used in our EMA, make it a potentially critical tool for large-scale studies, clinical settings, or for scaling interventions to the community [6,39,40]. Conversely, medication adherence monitoring technologies can be costly, making their application and broad applicability to clinical and community settings limited [6]. In choosing a method for adherence monitoring, EMAs may be better suited for short-term monitoring of larger populations, or in studies where the target population is likely to find EPD challenging (eg, people who are homeless, or in communities with high levels of HIV stigma). EPDs may be more useful for long-term monitoring of adherence in smaller samples.

Conclusions

In conclusion, this study provides evidence of concurrent validity with retrospective validated measures for EMA- and EPD-measured ART adherence among YLSMM, when participant burden is carefully considered, without significant behavioral reactivity. While acceptability and compliance of EMAs and EPDs were high overall, noncompliance increased over time, suggesting respondent fatigue. To ensure rigor and data quality, compliance with EMA and EPD protocols should be carefully tracked, incentivized, and incorporated into the data analysis plan.

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Conflicts of Interest

None declared.

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Abbreviations

ART: antiretroviral therapy
EMA: ecological momentary assessment
EPD: electronic pill dispenser
SMM: sexual minority men
YLSMM: young Latino sexual minority men

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Original Paper

Acceptability of a Digital Adherence Tool Among Patients With Tuberculosis and Tuberculosis Care Providers in Kilimanjaro Region, Tanzania: Mixed Methods Study

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Abstract

Background: The World Health Organization has recommended digital adherence tools (DATs) as a promising intervention to improve antituberculosis drug adherence. However, the acceptability of DATs in resource-limited settings is not adequately studied.

Objective: We investigated the acceptability of a DAT among patients with tuberculosis (TB) and TB care providers in Kilimanjaro, Tanzania.

Methods: We conducted a convergent parallel mixed methods study among patients with TB and TB care providers participating in our 2-arm cluster randomized trial (REMIND-TB). The trial aimed to investigate whether the evriMED pillbox with reminder cues and adherence feedback effectively improves adherence to anti-TB treatment among patients with TB in Kilimanjaro, Tanzania. We conducted exit and in-depth interviews among patients as well as in-depth interviews among TB care providers in the intervention arm. We conducted a descriptive analysis of the quantitative data from exit interviews. Translated transcripts and memos were organized using NVivo software. We employed inductive and deductive thematic framework analysis, guided by Sekhon's theoretical framework of acceptability.

Results: Out of the 245 patients who completed treatment, 100 (40.8%) were interviewed during exit interviews, and 18 patients and 15 TB care providers were interviewed in-depth. Our findings showed that the DAT was highly accepted: 83% (83/100) expressed satisfaction, 98% (98/100) reported positive experiences with DAT use, 78% (78/100) understood how the intervention works, and 92% (92/100) successfully used the pillbox. Good perceived effectiveness was reported by 84% (84/100) of the participants who noticed improved adherence, and many preferred continuing receiving reminders through SMS text messages, indicating high levels of self-efficacy. Ethical concerns were minimal, as 85 (85%) participants did not worry about remote monitoring. However, some participants felt burdened using DATs; 9 (9%) faced difficulties keeping the device at home, 12 (12%) were not pleased with receiving daily reminder SMS text messages, and 30 (30%) reported challenges related to mobile network connectivity issues. TB care providers accepted the intervention due to its perceived impact on treatment outcomes and behavior change in adherence counseling, and they demonstrated high level of intervention coherence.

Conclusions: DATs are highly acceptable in Tanzania. However, some barriers such as TB-related stigma and mobile network connectivity issues may limit acceptance.

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KEYWORDS

acceptability; digital adherence tool; medication reminder monitors; patients with tuberculosis; TB; adherence; TB care provider

Introduction

Tuberculosis (TB) is a significant public health problem and the second leading infectious killer after COVID-19 [1]. The World Health Organization has set a target in its "end TB strategy" to reduce TB deaths by 75% in 2025 and 90% in 2030 [2]. Tanzania is among the 30 countries with high TB burden and is estimated to have had a TB incidence of 208 per 100,000 persons and 1.3% of multidrug-resistant TB cases in 2021 [1]. In 2020, Tanzania reported that about 26,800 people died from TB [3]. TB is a curable disease if adequate treatment is implemented [4]. However, treatment adherence is a major challenge that hinders TB treatment efforts [5]. Insufficient adherence to TB medication is contributed by multiple factors such as the social context, health system, economic factors, patient-related factors (forgetfulness, low knowledge), health service accessibility, and drug-related factors such as drug side effects [6,7].

The World Health Organization has recommended digital adherence tools (DATs) that include SMS text messages, medication event monitoring devices, and video-observed treatment as promising interventions for improving TB adherence [8]. DATs can remind patients to take their medications, offer dose information, alert health care practitioners to risky behavior patterns, and allow health care practitioners to intervene when treatment is interrupted [9]. Furthermore, digital devices provide baseline information for health care providers during adherence counseling, patient motivation, replacement of interrupted medication, and scheduling clinic visits [8].

DATs have proven feasible in high- and low-resource settings [9-11]. Further, studies have shown that these devices have relatively high acceptability in Tanzania among people living with HIV, in Uganda and China among patients with drug-susceptible TB, and in South Africa among patients with multidrug-resistant TB [12-15]. However, literature indicates that the wide implementation of DATs in China has shown challenges, such that 11.3% refused to use DATs at enrollment and 8.2% refused to use DATs during treatment [16]. Another study in Vietnam showed that participants could not use the pillbox as required because they could not carry it to their workplace [17]. More evidence on the acceptability of DATs is needed to inform its large-scale implementation in resource-limited settings.

Investigating implementation research outcomes such as acceptability, feasibility, sustainability, and adoption is essential for identifying implementation bottlenecks that may hamper intervention effectiveness in a real-world setting [18]. In addition, when a health care intervention is not considered acceptable, it may affect health care providers' perception and treatment delivery [19]. In this study, we aimed to investigate the acceptability of DATs among patients and TB care providers for improving adherence to anti-TB drugs among patients with TB in Kilimanjaro, Tanzania.

Methods

Study Design

We conducted a convergent parallel mixed methods study, which was embedded in our cluster randomized trial (REMIND-TB), among patients with TB and TB care providers.

Ethics Approval

This study was approved by the Kilimanjaro Christian Medical College research ethics and review committee (approval 1157, dated December 10, 2018) and the National Health Research ethics subcommittee (ref NIMR/HQ/R.8a/VolIX/2992, dated January 14, 2019). We registered the trial at the Pan African Clinical Trials Registry under PACTR201811755733759 on November 8, 2018.

REMIND-TB Trial

From 2019 to 2021, we conducted a 2-arm cluster randomized trial to investigate whether the evriMED pillbox with reminder cues and adherence feedback effectively improved adherence to anti-TB treatment among patients with TB in Kilimanjaro region in Tanzania. Study sites were randomized into 12 clusters: 6 intervention arms and 6 control arms. The inclusion criteria for the trial were patients' diagnosis with presumptive sensitive TB, aged 18-65 years, attending care at any of the TB centers in the Kilimanjaro region of Tanzania, willing to use the evriMED pillbox, able to read and understand SMS text messages, and able to understand and willing to sign informed consent. Exclusion criteria were hospitalized patients and those who previously participated in similar studies. We provided each participant in the intervention arm with an evriMED1000 pillbox for their medication storage and intake. In the control arm, participants followed the standard of care procedures. In both arms, we followed participants for 6 months of treatment. In the evriMED arm, participants received a reminder SMS text message every day 30 minutes before their set time of taking medication. Detailed information about the REMIND-TB trial and the DAT can be found elsewhere [20].

evriMED Pillbox

The evriMED1000 is a type of tablet dispenser with a SIM card produced by Wisepill, based in South Africa. The pillbox records the opening of the box and stores the so-called medication events on a chip, along with the date and time whenever it is opened. This information is transmitted to a centralized server when one opens the device. Additionally, the evriMED1000 delivers a daily heartbeat event that includes information about the device's identification, battery life, and signal quality. If the pillbox is not opened on a particular day, any pending events will be transmitted during the next heartbeat.

The evriMED1000 sends a reminder SMS text message to an individual's mobile phone 30 minutes before intake time. If the individual does not take the medication within 1 hour of the intake period, a second reminder SMS text message is generated and sent. The patient does not require internet connectivity to receive the reminder SMS text message. The Wisepill pillbox uses a global roaming SIM chip that will connect to the best available mobile network in the area. These devices are designed to work in low-network resource settings (see Multimedia Appendix 1).

As the trial was an implementation study, TB care providers took full responsibility for participant care within their regular duties. They had to explain and demonstrate the use of the evriMED device to patients, provide medication through the device, and discuss adherence reports generated by the device during follow-up clinics. Participants were trained on device usage upon enrollment and were required to stay with it for the entire 6-month treatment period. Any challenges related to device functionality or misunderstandings were addressed through ongoing discussions between patients and care providers during follow-up visits.

Mixed Methods Study on Acceptability of DATs

Study Procedures

Enrolled participants from the intervention arm of the REMIND-TB trial who completed 6 months of treatment were called for a phone interview. One inclusion criterion for this study was that participants had to be randomized into the intervention arm, while we excluded all the participants randomized into the control arm. The other inclusion and exclusion criteria were the same as in the trial. In addition, we purposively selected 18 patients with TB for an in-depth interview. Considering that this was an implementation study in which all the activities were performed by TB care providers, we purposively selected 15 TB care providers to understand the acceptability pattern of evriMED. We aimed at a heterogenic sample for both patients and health care workers by considering patients with good and poor adherence as well as diverse professional experiences among TB care providers. We obtained written informed consent from all individuals who participated in the acceptability study. After completing the follow-up of all participants in the REMIND-TB trial, we purposively selected TB treatment centers with their respective care providers in each cluster, who were called for an in-depth interview. Interviews were performed by trained research assistants using a topic guide in the Swahili language. Audio recordings of the interviews were transcribed and translated by experienced research assistants.

Theoretical Framework of Acceptability

The theoretical framework of acceptability (TFA) is a theoretical framework that helps to evaluate the intervention acceptability based on the lived or perceived experiences of individuals who deliver or receive an intervention [19]. The TFA has 7 constructs that can evaluate acceptability before, during, and after implementation performance (Table 1). In this study, we used TFA to investigate the acceptability of DATs among patients with TB and TB care providers. We believe that this theoretical framework is the best to use for this study due to its robustness in integrating the comprehensive concept of acceptability derived from diverse theories in health psychology and behavior change. To our knowledge, this inherent strength makes TFA the best theory of acceptability when compared to other theories. In addition to that, several studies have employed this theory to evaluate the acceptability of health care interventions [15,21-23].

Table 1. Constructs and description of the theoretical framework of acceptability.

Constructs	Description
Affective attitude	How an individual feels about the intervention
Burden	The perceived amount of effort that was required to participate in the intervention
Ethicality	The extent to which the intervention has a good fit with an individual's value system
Intervention coherence	The extent to which the participant understands the intervention and how it works
Opportunity costs	The extent to which benefits, profits, or values were given up to engage in the intervention
Perceived effectiveness	The extent to which the intervention is perceived to have achieved its intended purpose
Self-efficacy	The participant's confidence that they can perform the behavior(s) required to participate in the intervention

Data Collection Tools

Exit Survey

We conducted an exit survey after a participant completed the treatment. The survey was conducted by phone by trained research assistants. We performed the survey by using a semistructured questionnaire that we developed using the 7 constructs of the acceptability framework (affective attitude, perceived burden, ethicality, perceived effectiveness, intervention coherence, self-efficacy, and opportunity cost).

In-Depth Interviews

We conducted in-depth interviews with patients and TB care providers from the intervention clusters. Patients and TB care providers were interviewed at their respective health facilities at the agreed time. All interviews were conducted by 2 experienced researchers led by the first author (AEM). We used different topic guides for in-depth interviews with patients and care providers, respectively. We used the Sekhon framework for acceptability to define the guide [19]. Questions mainly focused on the 7 constructs of TFA. The questionnaires were adapted if new topics came up during interviews.

Data Analyses

To answer the objective regarding the acceptability of evriMED among patients with TB and TB care providers, we conducted a descriptive analysis of the exit survey responses using STATA (version 15; Stata Corp LLC). The results of the exit survey provided an overview of the frequency and percentages of each element of acceptability. In addition, we analyzed the qualitative responses of participants and TB care providers inductively and deductively by using thematic framework analyses. Three researchers independently read the transcripts (AEM, MSdB, and RAM). We developed memos and subthemes inductively based on the narratives and deductively by adopting preidentified themes from the theoretical framework constructs. We uploaded transcripts and memos in NVivo software (Lumivero) for coding and data organization. Narratives from the transcripts were then coded based on the predefined subthemes.

Results

Description of the Patients

We enrolled 280 patients in the intervention arm; of these, 21 (7.5%) died before study completion, and 14 (5%) were excluded due to either being transferred to other regions or lost to follow-up. Of the 245 (87.5%) patients who completed treatment, 145 (59.2%) were not interviewed because their phone numbers were unreachable. We interviewed 100 (40.8%) patients. The details of the demographic characteristics of the patients with TB are shown below in Table 2.

In addition, we in-depth interviewed 18 patients and 15 TB care providers or directly observed therapy, and we reached data saturation in these interviews. Among the 18 patients, 12 (67%) were males and 6 (33%) were females. Detailed demographic characteristic are shown in Table 3. Of the 15 TB care providers who were interviewed, 3 (20%) were males and 12 (80%) were females, of whom 4 (27%) were clinicians, 1 (6%) was a pharmacist, 4 (27%) were medical attendants, and 6 (40%) were registered nurses.

Table 2. Demographic characteristics and treatment outcomes of the patients with tuberculosis (N=280).

Characteristics	Values, n (%)
Sex	
Male	207 (73.9)
Female	73 (26.1)
Inclusion clusters	
Moshi rural district hospital	21 (7.5)
Moshi rural health center	115 (41)
Moshi urban district hospital	3 (1.1)
Moshi urban health center	42 (15)
Same and Mwanga health facilities	49 (17.5)
Kibongoto National Infectious Disease hospital	50 (17.9)
Age (years)	
<20	2 (0.7)
20-29	50 (17.9)
30-29	57 (20.4)
40-49	89 (31.8)
50-59	52 (18.6)
≥60	30 (10.7)
Education level	
None	9 (3.2)
Primary	213 (76.1)
Secondary	56 (20)
Tertiary	2 (0.7)
Marital status	
Married	155 (55.4)
Single	79 (28.2)
Separated or divorced	35 (12.5)
Widowed	11 (3.9)
Treatment outcome	
Cured/completed treatment	245 (87.5)
Transferred and lost	14 (5)
Dead	21 (7.5)

Table 3. Demographic and adherence characteristics of the in-depth interviews with individuals diagnosed with tuberculosis.

	Sex	Age (years)	Education	Marital status	Participant's adherence as shown by DAT[a] (%)[b]
1	Female	30	Secondary	Married	10
2	Male	40	Primary	Married	24
3	Male	58	Primary	Married	21
4	Male	55	Primary	Married	38
5	Female	53	Primary	Single	99
6	Male	48	Primary	Married	99
7	Male	56	Primary	Married	21
8	Female	38	Primary	Single	0
9	Female	49	Primary	Married	100
10	Male	63	Secondary	Married	100
11	Female	45	Primary	Separated	68
12	Male	52	Primary	Married	90
14	Male	59	Primary	Married	99
14	Male	41	Primary	Married	99
15	Female	45	Primary	Divorced	41
16	Male	52	Primary	Married	93
17	Male	40	Primary	Married	96
18	Male	60	Secondary	Married	98

[a]DAT: digital adherence tool.

[b]Absolute values of the percentages are not provided because the adherence score in the evriMED monitor is automatically generated by the pillbox based on the patient's daily medication intake behavior.

Patients' and TB Care Providers' Acceptability of DAT

The table summarizing the quantitative survey findings can be found in Multimedia Appendix 2.

Affective Attitude

Many participants described positive views concerning the use of the intervention. In the exit interview, 98% (98/100) of the participants indicated their general experience with the pillbox was either good or very good, 83% (83/100) reported that the intervention was satisfactory, and 85% (85/100) had either a good or very good attitude toward the content of the reminder SMS text messages. Of the 20 people who saw their adherence graphs, 18 (90%) had a good or very good attitude toward graphs.

In the in-depth interviews, participants expressed positive opinions about the appearance and attractiveness of the pillboxes. They were particularly impressed with the white color of the pillbox. TB care providers and patients acknowledged the appropriateness of the pillbox's size, stating that it allowed for hygienic medication storage. However, some TB care providers suggested increasing the pillbox size to accommodate patients' cards. Furthermore, some participants appreciated the pillbox's size as it matched the size of TB drug blisters. Additionally, participants with comorbidities (TB-HIV) found the large size of the pillbox advantageous for storing drugs for other diseases. This is illustrated in the following quotes.

> *…From my point of view, the device is good. Even from looking at it. Even the color itself is not bad.* [Patient, 42-year-old male]

> *…it reminds him. Even though he doesn't have his phone, it helps him think he should take medication. The second thing I see is that drugs stay safe. Thirdly, it helped patients to be alert. They were swallowing the medicine on time, and if they forgot, it reminded them.* [TB directly observed therapy, registered nurse]

Participants and TB care providers highlighted the benefits they experienced from using the intervention, particularly regarding medication reminders and storage. TB care providers expressed satisfaction with attending to patients utilizing the intervention, as it enabled them to monitor progress through adherence reports. However, a few participants expressed negative sentiments. One participant suggested that having pillboxes in different colors would be more attractive, as the white color could quickly get dirty. Another participant felt the pillbox size was too large to carry and recommended reducing its size by half, as also mentioned by some other participants.

> *…It alerted us that why this guy/patient has this problem. Let us call him and sit to talk with him about what the problem is.* [TB directly observed therapy, medical attendant]

> *…The first advantage is to be reminded. You understand me. It reminds you. I have been reminded many times because I also like to sleep; if I do not go*

out, I always like to sleep at home. Also, drug storage. [Patient, 30-year-old female]

…It's good, but when it's new. If it is new, it is very attractive. Now, it shows it has been used. It is clean, but not attractive anymore. [Patient, 56-year-old male]

…I don't know…the size should be reduced to half! I see it is big. [Patient, 30-year-old female]

Perceived Burden

We examined the perceived effort involved in using the intervention. During the exit interview, some participants (n=100) faced challenges when using the intervention. Specifically, 10 (10%) respondents mentioned experiencing TB-related stigma, 12 (12%) expressed discomfort with receiving daily SMS text message reminders, 7 (7%) found it challenging to use the device, 9 (9%) encountered difficulties keeping it at home, and 3 (3%) reported issues with charging the device. Additionally, 30 (30%) reported experiencing challenges with mobile network connections.

In-depth interviews revealed a few aspects that participants and TB care providers were experiencing in using the intervention. Few participants expressed challenges in travelling with the pillbox. TB care providers mentioned that the intervention increased their workload, as it required extensive discussions with patients about various aspects of adherence. Moreover, mobile network–related issues caused delays in the system's signal transmission when the pillbox was opened, leading to poor adherence reports for some patients and incorrect SMS text message notifications. Some participants suggested that the system should not send reminder SMS text messages to treatment supporters, as the device occasionally failed to detect events due to network problems. This can be seen from the following quotes.

…I did not feel comfortable going with it because others would suspect me [of being sick]. [Patient, 56-year-old male]

…But the time was insufficient according to the working environment. So, once you get a patient in this environment, it is a bit of a challenge to sit with them. You must be brief because the time is insufficient, and you might need to work in the OPD wards simultaneously. So, if you sit with that patient for a long time, you will cause a jam in another unit. [TB directly observed therapy, medical attendant]

…If the network is fine, the adherence is good. But, if he goes to a place without a network, the device is not communicating even if he has taken the medicine. [TB directly observed therapy, medical attendant]

Ethicality

Many participants and care providers described the intervention as fitting well with their value system. Exit interviews with participants revealed that 85% (85/100) did not worry about being monitored remotely, and 77% (77/100) said they did not experience any form of stigma. Similar findings were observed in the in-depth interviews. Many participants considered the pillbox morally acceptable and appreciated how it helped maintain their confidentiality. TB care providers also found the content of the reminder SMS text messages to be beneficial for their patients, as illustrated in the quotes below.

…I saw the benefits of hiding the secret of my illness. The device is acceptable for my side. I do not know for others. [Patient, 56-year-old male]

…It is morally right to use the device. [Patient, 42-year-old male]

…I think the SMS contents were fine. [TB directly observed therapy, medical attendant]

Furthermore, participants emphasized that the pillbox and SMS text messages aligned with their social values within their families. They highlighted that the intervention facilitated ongoing support from their families throughout the medication period, as described by the following participants.

…even my wife told me: "The time to take the medicine is near. Go and take the medicine." Even if the hours have not arrived, she remembers. [Patient, 42-year-old male]

…They supported me well. For example, giving me milk food. Even, sometimes, when they do cleaning, they wipe the device. [Patient, 48-year-old female]

Intervention Coherence

Most participants and TB care providers claimed to understand the intervention and how it works. The findings from the exit interview revealed that 78% (78/100) of the respondents indicated they understood the intervention, 92% (92/100) mentioned they could use the intervention without any challenge, and 84% (84/100) could charge the device without problems. However, only 20% (20/100) of the participants were shown their adherence graphs during their counseling sessions with care providers.

Similar findings emerged during the in-depth interviews, where many participants and TB care providers effectively communicated the purpose of the intervention and its operational processes. During the interview, we asked health care providers to show how they had informed participants about intervention objectives and how it worked. The in-depth interviews revealed that health care workers understood the intervention's objectives and were adept at conveying this information to their patients. Furthermore, participants and care providers were able to explain how different components of the pillbox, such as the alarm, lights, charging system, and reminder system, communicate with the server. However, the interviews revealed that most participants did not remember the name of the pillbox. Instead, they used to call it by their local name, kiboksi, which means "the box." This is demonstrated in the following quotes.

…It reminds you to swallow the medicine, so when you open it, it indicates someone has opened the device and swallowed it. When you do not open it, it means you have not swallowed it. So, you will be sent a reminder message. [TB directly observed therapy, registered nurse]

…This device, first, is the one we use to store medicine. Second, when you open this device, it turns

on the lights and gives an alarm. Once you have taken out the medicine inside and used the one you need, the other ones you must put back in. When you put them back inside the device, you close this device. If you close it properly, the lights turn off. One thing I have noticed is that it gets to the point where you open it, and then the lights turn on and off. The moment it turns on and off, it does not show the indicator again. [Patient, 63-year-old male]

…Honestly, the graph has never been shown to me. [Patient, 30-year-old female]

Perceived Effectiveness

Participants and TB care providers expressed that the intervention successfully achieved its intended goal. In the exit interviews, 84% (84/100) of the respondents acknowledged that the intervention improved their treatment adherence. Similar findings were observed in the in-depth interviews with both participants and TB care providers. Participants mentioned that the intervention facilitated adherence by providing timely reminders, enabling them to stick to their scheduled intake times. They found the SMS text message reminders especially helpful when occupied with other activities and when prone to forgetfulness. Furthermore, TB care providers reported that the intervention significantly improved the treatment outcomes for patients compared to those who did not use the pillbox, as described in the following quotations.

…Receiving the message that says "the time of intake is near." That has helped me a lot because you are probably far from home. So, you will estimate I have 20 minutes or half an hour to be home. [Patient, 63-year-old male]

…I thank God, to be honest, no patients could stop medication or even die. [TB directly observed therapy, medical attendant]

…Honestly, I have been successful because many patients have recovered; they didn't get resistance. [TB directly observed therapy, clinician]

Health care providers expressed that the intervention improved their rapport with patients by providing feedback on adherence counseling, fostering a sense of compassion and love. They found the adherence report valuable in effectively monitoring the patients' progress. Moreover, the intervention resulted in positive behavioral changes among TB care providers. Many providers mentioned that the feedback in adherence counseling sessions helped them refine their approach when attending to patients with TB, and they gained a better understanding of the significance of adherence in time of medication, which had previously been given less attention, as described in the following quotations.

…It helps to keep the closeness…among the patients…You even get time to talk to him and discover what's happening with him. Many positive patients have come out completely healed. [TB directly observed therapy, registered nurse]

…For us care providers, it was helpful because we are not doing one work, but also doing other work. So, once we get the patient's information for reference from the devices, it helps us to know if the patients are in good care compared to those who are not using the devices. [TB directly observed therapy, medical attendant]

…in the past, we were giving drugs, but we did not emphasize that if a patient should swallow medicine at 8 AM, it should be taken at 8 AM every day. We used to tell them to take drugs in the morning regardless of the time. For this study, we dispensed and told them to choose whether it was 8 or 9 o'clock. He will choose and should take the drug at the same time every day. And we have seen that it has brought great success. [TB directly observed therapy, clinician]

Opportunity Costs

Few participants mentioned that they had to give up something valuable to participate in this study. Exit interview results show that 6% (6/100) of the respondents incurred extra costs while using the intervention. From the in-depth interviews, 1 participant expressed that he incurred higher costs because he received a reminder when he was away from home and did not want to ruin his intake report. Therefore, he decided to take a quick transport to get home on time. Another participant mentioned working fewer hours than usual to get home early to take medication on time.

…There was a period when I was receiving messages, but if I went somewhere and became late, I had to take a quick motorcycle. [Patient, 63-year-old male]

…That happens once in a while because you may find that you are working somewhere, and then you still have time, but you have to leave early. [Patient, 42-year-old male]

Self-Efficacy

Many participants and TB care providers said they were confident to engage in the intervention. In the exit interviews with participants, 84% (84/100) of the respondents said they were comfortable to continue receiving reminder SMS text messages every day. The same was reported in the in-depth interviews, in which some of the participants expressed that they preferred the device to be given to many patients and not to a few just for research. Others mentioned that they were confident in explaining the pillbox to their families and relatives. TB care providers expressed that the intervention would be suitable to be adopted in their care and, if possible, include patients experiencing other diseases such as HIV, as illustrated in the quotations below.

…For my part, I advise this research project to continue. Not just for research purposes only and end there. It should continue because it is a good thing, and the scope should be expanded to get more people to use this device. [TB directly observed therapy, registered nurse]

…This device is so good to the extent that I liked it and wished I could remain with it. [Patient, 53-year-old male]

Discussion

Principal Findings

This study aims to evaluate the acceptability of a DAT (evriMED1000 pillbox) among patients and TB care providers to improve adherence to anti-TB drugs in Kilimanjaro, Tanzania. The overall findings of this study indicate high acceptance of DAT among patients with TB and TB care providers. We found that the high acceptance of DATs was based on the positive attitude toward using the DAT (affective attitude), wherein 83% (83/100) of the participants were satisfied with the intervention, 98% (98/100) expressed good experiences, 78% (78/100) understood how the intervention works, and 92% (92/100) could use the pillbox, such as opening the device, refilling the pills, and recharging the box (intervention coherence). Of the 100 participants, 84 reported improved adherence (perceived effectiveness), and they preferred to continue receiving reminder SMS text messages (self-efficacy). A few participants reported experiencing difficulties while using DATs. Some participants reported experiencing TB-related stigma; 12% (12/100) were not happy being reminded daily, and 9% (9/100) reported experiencing difficulties keeping the device at home. Additionally, 30% (30/100) reported experiencing challenges with mobile network connectivity issues.

Comparison With Prior Work

Our findings support similar studies reporting on the acceptability of DATs among patients and health care providers [12,13,15,24]. The potential benefit of DAT, such as its ability to monitor medication adherence or ease of use, was deemed valuable by patients and TB care providers. A study done in South Africa reported that the acceptability of DAT was highly associated with its ease of use among patients [12]. The real-time medication monitoring reports and feedback on adherence helped patients understand their health conditions and led to improved patient and health care provider relationships [12,24,25]. In addition, it led to improved care practice and behavior change among TB care providers. Many health care providers reported feeling more accountable for patient follow-up and motivating patients to adhere to the time of medication intake. Feedback on adherence counseling also generated a sense of care among patients, which had an impact on the psychosocial life of the patients.

However, participants reported several challenges with DATs, such as incorrect sending of SMS text messages due to network failure, large size of the pillbox, and existence of the reminder alarm, which led to fear of disclosure and, consequently, nonuse of the device during travelling. Similar challenges have been reported in other studies [14,26], which, if not well addressed, might contribute significantly to the nonuse of DATs and less uptake of DATs [24]. TB care providers reported increased workload during the use of DATs. Similar findings were reported in a study done in China, where health care providers reported a moderate workload increase during DAT implementation [16]. However, this contradicts a study in India, which reported a decreased health care workload [24]. We found that the increased workload by health care workers was reported as a major concern in settings with shortage of care staff—mainly dispensaries and health centers. Larger facilities such as hospitals reported a slight increase in the workload. In addition, 48% (48/100) of the participants stated that adherence reports from the device were not shown nor utilized in their conversations with health care workers. The health care provider was likely to have little knowledge of the value of adherence reports as a tool for counseling. Regular training should be conducted to reinforce their understanding of the intervention for effective scale-up. Fear of TB stigma and unwanted disclosure should be considered for effective intervention scale-up.

Limitations and Strengths

This study had certain limitations. One significant limitation was that because of the COVID-19 pandemic, all exit interviews were conducted via phone calls, which posed challenges related to network connectivity and potential interruptions during the questioning process. Mitigation strategies were employed, such as recapping participant responses to ensure accurate information capture. Another limitation was the small sample size in the exit survey compared to the total number of enrolled participants in the trial. The small sample size can be attributed to the public policy implemented in July 2021, wherein unregistered SIM cards were blocked, making it difficult to reach most participants. Nonetheless, we found that the demographic characteristics of the participants who were interviewed (100/245) did not differ from those of the participants who were not interviewed due to the change in the government policy, indicating that the interviewed participants were likely representative of those who were not interviewed. Additionally, 59.2% (145/245) of the participants who were not reached due to the change in the government policy were not affected during the medication period. The change in the government policy regarding SIM card registration occurred when many of our participants had already completed the treatment follow-up and were waiting for the exit survey. In this case, the change in the government policy impacted the exit survey process rather than the intervention itself.

This study has notable strengths that enhance its significance and scope. First, we enrolled participants from all TB-providing facilities in the Kilimanjaro region, thereby offering a comprehensive understanding of acceptability from a broader perspective. Notably, our research pioneers the investigation of the evriMED reminder pillbox's acceptability among patients with TB in East Africa, providing valuable insights on the acceptance. Additionally, using the TFA facilitated a robust understanding of the acceptability of the evriMED reminder pillbox among patients with TB.

Conclusion

Our study demonstrates the positive acceptance of a DAT (evriMED) among patients and TB care providers for improving anti-TB drug adherence in Kilimanjaro, Tanzania. Although the potential acceptability of DATs is evident, addressing concerns related to mobile network connectivity and participants' preferences regarding the number of reminder SMS text messages, and providing adequate training and technical support to health care providers are critical for successful

implementation. Future research should explore the impact of evriMED on large-scale implementation in different settings.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
EvriMED monitor and its associated intervention.
[PDF File (Adobe PDF File), 188 KB - ojphi_v16i1e51662_app1.pdf]

Multimedia Appendix 2
Exit survey findings.
[PDF File (Adobe PDF File), 87 KB - ojphi_v16i1e51662_app2.pdf]

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Abbreviations

DAT: digital adherence tool
TB: tuberculosis
TFA: theoretical framework of acceptability

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Original Paper

Mobile Apps for Vaccination Services: Content Analysis and Quality Assessment

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Abstract

Background: Vaccination services are increasingly in demand by the public, and mobile apps are an effective tool to meet that demand. However, the characteristics and quality of these apps are unknown.

Objective: Commonly used vaccination service apps on the market were surveyed with regard to quality, service content, and user experience to evaluate and guide users.

Methods: The Qimai Data mobile app data analytics platform was used to search for common vaccination service apps by keyword, and the WeChat and Alipay platforms were searched for apps. The apps included in the study were independently evaluated by two reviewers using the Mobile Application Rating Scale, and the service content and user experience of the apps were analyzed. The intragroup correlation coefficient between raters was used to measure interrater reliability.

Results: In the app stores of the four major Android platforms and the iOS app store, 1092 and 207 apps were found, respectively; 189 WeChat applets and 30 Alipay applets were also found. A total of 29 apps was ultimately included in this study according to the inclusion criteria, including 21 independent apps, 4 WeChat applets, and 4 Alipay applets. Significant differences were found between independent apps and applets in terms of the quality score ($t_{449.57}$=–5.301; P<.001) and the subjective quality score (z=–4.753; P<.001). No significant differences were found between iOS and Android platforms in terms of the quality score (t_{1404}=–2.55; P=.80) and the subjective quality score (z=–0.137; P=.89). There was good intragroup consistency among the raters.

Conclusions: In this study, independent apps and nonindependent apps that rely on social and payment platforms for implementation were included in the vaccination services category. The overall quality of these apps was acceptable. Nonindependent running apps were found to have slightly lower scores and showed room for improvement, and scores for the participatory apps were found to be generally low overall.

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KEYWORDS

vaccination service app; Mobile Application Rating Scale; MARS; quality evaluation; app; apps; application; applications; quality; evaluation; rating; mHealth; mobile health; service; services; service content; user evaluation; vaccine; vaccines; public health

Introduction

Vaccination is the most effective primary prevention for infectious diseases. At birth and while breastfeeding, infants can acquire antibodies against infectious diseases from their mothers, but as children grow older, the effectiveness of these antibodies gradually diminishes and disappears [1,2]. Therefore, a detailed immunization program has been developed for children by the Chinese government. It is important to maintain children's health by ensuring that they receive the required

vaccinations in a timely manner. The traditional vaccine consulting service model cannot ensure that the various indicators of immunization planning meet the national requirements [2]. Many preventive vaccination clinics are gradually implementing digital management, and the flow of information incorporates networked automated distribution management. The use of the internet and vaccination platforms presents a new model for preventive vaccination that is gradually being accepted by parents [3].

Since 2021, China has been the country with the largest number of smartphone users in the world, with more than 950 million [4]. The development of smartphones has increased the development of vaccination service apps. Vaccination units can send vaccination appointment information, notifications about necessary vaccines, and publicity and educational articles on preventive vaccination through apps, which can save the expenses of SMS text messaging notifications and publicity costs [5]. Children's parents can keep abreast of their children's vaccination status, vaccine appointment schedules, inventory information of the vaccination unit, online consultations on vaccination-related knowledge, independent booking of vaccination appointments, and other convenient and user-friendly services [6]. These apps are accessible, optimize the efficiency of services [7-9], enhance the motivation to vaccinate, and improve vaccination rates [7,10,11]. These findings are widely recognized in academia. In a needs assessment survey of vaccination service apps, participants expressed their interest in using such apps [12]. In a study by Zaidi et al [13], such apps were more operational, acceptable, and practical. Wei et al [14] found that parents of children using mobile apps for vaccine advocacy scored significantly higher in knowledge and trust than those who used traditional methods. To a certain extent, the vaccination capacity of the population has been enhanced by vaccination service apps [9]. While vaccination service apps are critical to increasing vaccination rates. The essential prerequisite is to ensure that they are of high-quality. A review of relevant studies on such apps reveals that past studies have mainly focused on service content and improving vaccination rates, and there is a lack of research related to quality assessment and user experience.

The Mobile Application Rating Scale (MARS) was developed by a multidisciplinary team of experts as a simple, objective, and reliable tool for researchers, developers, and health professionals to assess the quality of apps. The scale is widely used for apps for weight management [15], disease [16,17], mental health [18], and pain [19]. In China, mobile terminals consist of two main areas: independent apps and nonindependent apps that rely on social or payment platforms (Alipay applets and WeChat applets). Retrieval strategies were designed for each of these two types.

In this study, the commonly used vaccination service apps on the market were investigated, assessed for quality using MARS, and analyzed for service content and user ratings, assisting in the development and improvement of such apps and popularizing their use. At the same time, this information will also provide valuable suggestions for users when choosing apps.

Methods

App Search Strategy

Regarding independent apps, the iOS app store was searched using the keywords "vaccine," "vaccine service," "immunization," and "vaccination." Apps for Android phones were screened by entering the keywords "vaccine," "vaccine service," "immunization," and "vaccination" on the website QiMai Data. The keywords "immunization" and "vaccination" were used to screen for apps on the Huawei, Xiaomi, OPPO, and VIVO smartphones. The top 50 apps found in the search that met the requirements were extracted and ranked according to the number of downloads. Data related to all apps in the App Store, Google Play, and nine major domestic Android marketplaces (Huawei, Xiaomi, OPPO, VIVO, Meizu, Baidu, 360 App Store, and Pea Pod) were provided by QiMai Data.

Platform-Dependent Applets

WeChat applets were searched by entering the keywords "vaccine," "vaccine service," "immunization," and "vaccination" in the WeChat search window. Alipay applets were searched by entering the keywords "vaccine," "vaccine service," "immunization," and "vaccination" in the Alipay search window.

App Filter

For the two different types of apps/applets with vaccination services, the type of functions were noted, and two sets of exclusion criteria were designed. For independent apps, the exclusion criteria were as follows: apps that were not related to the theme, apps that have not been updated for 1 year, apps that have been downloaded <100,000, apps that were not in simplified Chinese, apps with a rating of <2, and apps that cannot be downloaded and used normally. For platform-dependent applets, the exclusion criteria were as follows: applets that were not related to the theme, applets that did not work properly, applets on WeChat with <10,000 recent users, and applets on Alipay with <100,000 recent users.

Assessment Tools

In this study, MARS was used to complete the evaluation of mobile apps. MARS includes five core components: engagement, functionality, aesthetics, information, and subjective quality. The rating scale was a 5-point scale: inadequate (1), poor (2), acceptable (3), good (4), and excellent (5). The subjective quality section comprised four subjective evaluation questions [20].

Review Process

The review process consisted of three steps. In the first step, the basic description and technical information of these 29 apps were collected from the app stores (iOS and Android) and the Alipay and WeChat applet platforms in accordance with the requirements of the first part of MARS. In the second step, all reviewers studied the instructional video training provided by the MARS developers together [15] and discussed and reached a consensus on the content of the queries. The evaluation was performed by three reviewers with two apps; two WeChat applets and two Alipay applets were randomly selected for pre-evaluation. The scores were discussed to agree on the

evaluation criteria as much as possible. In the third step, all 29 apps were installed on a phone (Android device: Xiaomi Mi11Lite, version MIUI13.0.12 stable version; iPhone device: iPad mini, version: 15.6). The quality of the included apps were evaluated using MARS. The evaluation was performed by two independent raters assessing the same app at the same time.

User Experience

The qualitative analysis software NVivo 14.0 (Lumivero) was used for data entry and coding, which followed the process of grounded theory with open coding, spindle coding, and selective coding. Open coding refers to the process of discovering conceptual categories from the data and then naming and generalizing the phenomena under study; spindle coding refers to the process of establishing categories through inductive deduction on the open-coded categories; selective coding is the process of linking the core categories to other main categories around the core categories to construct a new theoretical framework in the form of a storyline [21]. The specific steps of this operation were as follows. First, one researcher completed the extraction and analysis of the basic categories and concepts, and another researcher conducted a theoretical protection test on the coding. In case of disagreement, a third person was invited to participate in the discussion to ensure that all conclusions were agreed upon. Grounded theory is a qualitative approach that emphasizes the generalization or emergence of information from data to build a theory or model [22].

Statistical Analysis

Data were analyzed using descriptive and analytical statistics, with numerical variables describing the means and SDs and categorical variables describing the frequencies of use and percentages of market share. Data collection and collation were completed using Excel 2016 (Microsoft Corporation). Data analysis was conducted with SPSS Statistics version 26 (IBM Corp). The intragroup correlation coefficient was used to measure interrater agreement. A 1-way analysis of the apps on different platforms was performed using *t* tests and *Z* tests. *T* tests were used if the data conformed to a normal distribution; otherwise, the *Z* test was used. The correlation between app quality scores, reviews, and MARS quality scores was analyzed using Pearson correlation analysis.

Results

Overview

A flowchart of the app screening is shown in Figure 1.

Of the 29 eligible apps, 21 were from app stores, 4 were Alipay applets, and 4 were WeChat applets. All apps were free to download, and the number of downloads and ratings were provided by the search platform.

The largest percentage of the apps with a user star rating of 4-5 were on Android (10/18, 56%), followed by iOS (6/13, 46%). Of the 18 apps for Android, 8 (44%) had more than 10 million downloads. Among the types of apps, the medical and sports health categories accounted for the largest proportion (11/31, 35.4% and 8/31, 25.9%, respectively), while the learning and education and convenient life categories accounted for the smallest proportion (both at 1/31, 3.2%; Table 1).

Figure 1. App screening flowchart.

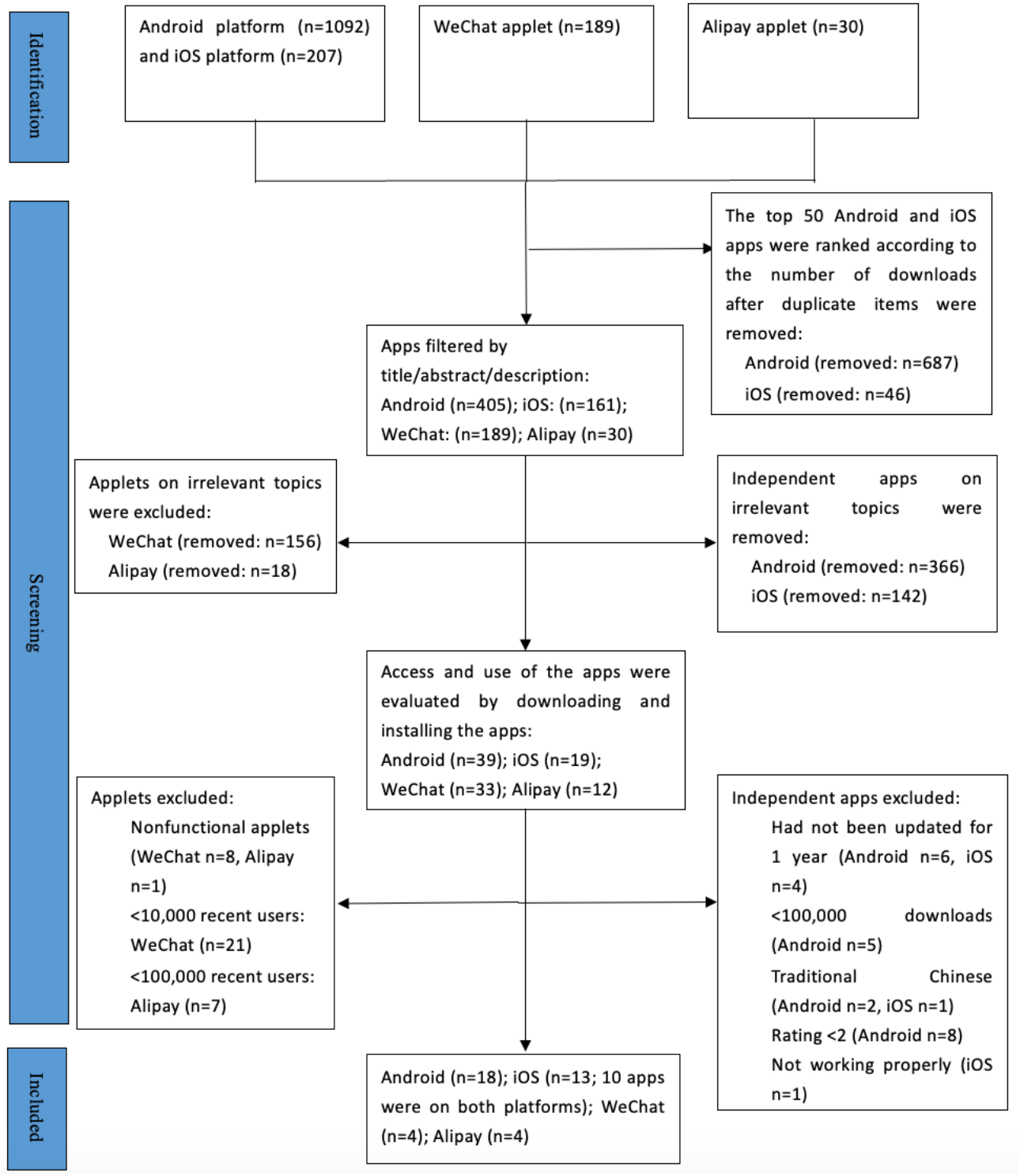

Table 1. Basic app characteristics.

Properties	Apps (N=39), n (%)
Platform	
Apple	13 (33)
Android	18 (46)
Apple + Android	10 (26)
Alipay applet	4 (10)
WeChat applet	4 (10)
Category	
Sports health	8 (26)
Medical	11 (35)
Medical health	5 (16)
Health and fitness class	2 (7)
Children's class	3 (10)
Learning and education class	1 (3)
Convenient life class	1 (3)
Downloads[a] (Android: n=18)	
<999,999	3 (17)
999,999-10,000,000	7 (39)
>10,000,000	8 (44)
User star rating[b]	
Android (n=18)	
2.0-2.9	3 (17)
3-3.9	5 (28)
4-5	10 (56)
iOS (n=13)	
2.0-2.9	2 (15)
3-3.9	5 (39)
4-5	6 (46)

[a]No download descriptions were provided for iOS or the Alipay and WeChat applets.

[b]The Alipay and WeChat applets do not provide user star ratings.

Service Content of the App

There were 10 categories covered by the apps: vaccination appointment management, vaccination record management, vaccination information service, internet hospital, science knowledge, drug administration, health management, family doctor, specialist consultation, and peer support and feedback. Among the 21 apps, the most used service on iOS was the science knowledge category (n=10, 48%), followed by the vaccination appointment management (n=9, 43%) and vaccination information service (n=8, 38%) categories, and the least used service was the health management category, followed by the family doctor and the specialist consultation categories (both n=1, 5%). The most used service on the Android platform was the science knowledge category (n=14, 67%), and the least used service was the vaccination record management category, followed by the health management, family doctor, specialist consultation, and peer support and feedback categories (all n=2, 10%). Among the 8 applets, WeChat applets accounted for the highest percentage of the vaccination appointment management, vaccination information service, and science knowledge categories (all n=4, 50%). Among the Alipay applets, the most often used service was the science knowledge category (n=4, 50%), while the vaccination record management, internet hospital, and health management categories accounted for the least used services (all n=1, 13%; Table 2).

Table 2. Service categories of the apps.

Categories	App (n=21), n (%)		Applet (n=8), n (%)	
	iOS	Android	WeChat	Alipay
Vaccination appointment management	9 (43)	11 (52)	4 (50)	3 (38)
Vaccination record management	2 (10)	2 (10)	1 (13)	1 (13)
Vaccination information service	8 (38)	13 (62)	4 (50)	3 (38)
Internet hospital	6 (29)	8 (38)	2 (25)	1 (13)
Science knowledge	10 (48)	14 (67)	4 (50)	4 (50)
Drug administration	5 (24)	7 (33)	0 (0)	0 (0)
Health management	1 (5)	2 (10)	2 (25)	1 (13)
Family doctor	1 (5)	2 (10)	0 (0)	0 (0)
Specialist consultation	1 (5)	2 (10)	0 (0)	0 (0)
Peer support and feedback	2 (5)	2 (10)	0 (0)	0 (0)

MARS Quality Score

Two independent researchers calculated the scores for each part of all apps according to the MARS evaluation criteria, as detailed in Multimedia Appendices 1 and 2 and Table 3. The interrater reliability intragroup correlation coefficient for each component between the two MARS raters was 0.840 for participatory, 0.733 for functionality, 0.769 for aesthetics, 0.968 for information, 0.943 for app quality score, and 0.637 for subjective quality score, as detailed in Table 4. Significant differences were found between independent apps and applets in terms of quality score ($t_{449.57}$=–5.301; P<.001) and subjective quality score (z=–4.753; P<.001). No significant differences were found between iOS and Android platforms in terms of quality score (t_{1404}=–2.55; P=.80) and subjective quality score (z=–0.137; P=.89; Table 5).

Correlations between individual app quality scores, subjective quality scores, app ratings, and numbers of reviews were analyzed, and significant correlations were found between the app rating and number of reviews (r=0.364; P=.04), rating and subjective quality score (r=0.47; P=.006), and app quality score and subjective quality score (r=0.816; P<.001; Table 6).

Table 3. Applet quality rating scale.

Applet	Section A: participatory, mean (SD)	Section B: functionality, mean (SD)	Section C: aesthetics, mean (SD)	Section D: information, mean (SD)	App quality score, mean (SD)	Section E: subjective quality score, mean (SD)
Alipay						
Vaccination Services	2.84 (0.48)	4.00 (0)	3.33 (0.52)	2.79 (1.37)	3.00 (1.07)	2.88 (1.07)
Vaccination Quaicha	1.70 (0.48)	3.88 (0.35)	3.00 (0)	2.21 (1.58)	2.55 (1.27)	2.13 (0.64)
Medical Health Channel	2.10 (0.57)	3.88 (0.35)	3.33 (0.52)	3.07 (1.49)	3.03 (1.05)	3.25 (0.46)
XinYun Vaccination Inquiry	1.90 (0.57)	3.88 (0.35)	3.33 (0.52)	2.29 (1.64)	2.68 (1.30)	3.00 (0)
WeChat						
Tengxun Health	2.10 (0.57)	4.00 (0)	3.67 (0.52)	2.93 (1.44)	3.05 (1.16)	3.38 (0.52)
Rainbow Doctor	2.50 (0.71)	4.00 (0)	3.67 (0.52)	2.86 (1.41)	3.13 (1.09)	3.13 (0.35)
Baby Plan Vaccination Assistant	2.10 (0.32)	3.88 (0.35)	3.83 (0.41)	2.93 (1.44)	3.05 (1.14)	3.13 (0.35)
Shekangtong	2.10 (0.32)	3.88 (0.35)	3.50 (0.55)	2.93 (1.33)	3.00 (1.07)	3 (0)

Table 4. Interrater reliability table for each component of the two raters.

Quality	Rater 1, mean (SD)	Rater 2, mean (SD)	Intragroup correlation coefficient (95% CI)
Participatory	2.66 (0.73)	2.70 (0.74)	0.840 (0.785-0.882)
Functionality	4.13 (0.57)	4.19 (0.47)	0.733 (0.636-0.807)
Aesthetics	3.46 (0.52)	3.48 (0.52)	0.769 (0.667-0.843)
Information	3.00 (1.39)	3.00 (1.39)	0.968 (0.958-0.976)
App quality score	3.23 (1.11)	3.23 (1.11)	0.943 (0.933-0.952)
Subjective quality score	3.26 (0.62)	3.38 (0.64)	0.637 (0.513-0.735)

Table 5. Univariate analysis of the quality of apps based on the Mobile Application Rating Scale (MARS).

MARS quality evaluation	Score, mean (SD)	*t* test (*df*)	*P* value
App quality score		–5.301 (449.57)	<.001
Applet	2.94 (1.16)		
App	3.33 (1.07)		
Platform		–2.550 (1404)	.80
iOS	3.35 (1.10)		
Android	3.34 (1.08)		
Subjective quality score		–4.753[a]	<.001
Applet	2.98 (0.52)		
App	3.41 (0.63)		
Platform		–0.137[a]	.89
iOS	3.45 (0.650)		
Android	3.46 (0.637)		

[a]*Z* score.

Table 6. Correlation analysis of ratings, reviews, and Mobile Application Rating Scale quality scores.

	Number of reviews	App quality score	Subjective quality score
Rating			
r	0.364	0.348	0.478
P value	.04	.06	.006
Number of reviews			
r	—[a]	0.230	0.155
P value	—	.21	.40
App quality score			
r	0.230	—	0.816
P value	.21	—	<.001

[a]Not applicable.

User Experience

The first 20 reviews of each app were analyzed, and grounded theory was used to analyze, classify, and code the reviews. The user concerns were divided into five topics: content, functionality, experience, service attitude, and privacy. In general, users who rated the first four aspects were partly satisfied and partly dissatisfied. However, users who rated privacy were not satisfied.

Users who evaluated the content gave satisfactory ratings for rich medical knowledge, while dissatisfaction was expressed for lost user data and vaccination record inquiries.

> *Quite useful, you can acquire vaccination-related knowledge...With this software, it's more convenient for my baby to get vaccinated.* [N1]
>
> *The new page is too cluttered...dense with words, the block is not obvious...There is no desire to see, floating ads are also an eyesore.* [N3]

Users who rated the app in terms of functionality gave poor ratings to the software's forced updates, flashbacks, and customer service features, and were satisfied with the app's ability to make vaccination appointments and provide vaccination knowledge.

> *Forced to update, nonstop flashbacks, point in and flashback...cannot access any feature.* [N4]
>
> *The product did not go online after rigorous testing, as a software test engineer seeing this product, I really want to laugh...There were a lot of mistakes when using the software, and even the basic master rod flow could not be used.* [N5]

In terms of the experience, some patients found the app to be very helpful. However, there was the problem of unreliable registered hospitals.

> *The user experience is very good, online consultation is very convenient, medical examination appointment, medical examination report view, report interpretation, etc...experience is very good.* [N6]
>
> *Poor experience, please take this software down, don't let it cheat people. The customer service inside seems to be the same, just as fake...no one responded when I spoke to them, and there was no refund page when it came time to refund.* [N7]

For users of the service attitude evaluation, some questioned the accuracy and quality of the response to questions, while some thought the doctor was professional and quick to review their queries.

> *The doctor's response is slow and perfunctory...No one answers after half a day of waiting, the response is not timely even if the question asked is not detailed... and the charge is not refundable.* [N8]
>
> *Very efficient, there are three opportunities to ask questions... doctor will also give you an answer, give the appropriate explanation, and make a clearer diagnosis later. Very efficient.* [N9]

Users said they were not satisfied with the privacy of the evaluation because the software needed too many permissions, and they were concerned for the security of their personal information.

> *Leakage of personal information...did not place an order, received an SMS notification of a refund, customer service is difficult to deal with and is delinquent in intervening.* [N10]
>
> *The information security of the user is not well done, the child vaccination hospital has inexplicably become other places, and my vaccination records have been altered.* [N11]

Discussion

Principal Findings

In this study, commonly used vaccination service apps on the market were investigated, assessed for quality using MARS, and analyzed for service content and user ratings. The results found the apps to be of good overall quality, with no significant differences between the iOS and Android platforms. This study also found that the apps were classified according to their service content into the following categories: vaccination appointment management, vaccination information service, vaccination record management, internet hospital, science knowledge, drug administration, health management, family doctor, specialist consultation, and peer support and feedback. The service with the highest frequency of use was scientific knowledge. Users were mainly concerned with five issues in the use of this type of app: content, functionality, experience, privacy, and service attitude. The majority of users were not satisfied with the privacy aspects of the apps.

A total of 29 apps were ultimately evaluated in-depth through a search and screening of over 1000 apps. The largest percentage of apps with a user star rating of 4-5 reflects, to some extent, that most users were satisfied with such apps. For Android, 44% of the apps had more than 10 million downloads, which also indicates the popularity of the apps.

MARS Quality Score

In this study, MARS was used as a quality assessment tool. Based on a comprehensive assessment of apps using MARS, Android and iOS were found to be nonsignificantly different in terms of app scores, with overall good quality but room for improvement. Overall, this type of app scored highest in functionality but not in engagement. Therefore, developers are advised to focus on meeting users' needs in all aspects of functionality, multidimensionality, and depth while also paying attention to the design of the app in terms of entertainment, fun, interactivity, and other engagement aspects. Regarding the evidence base category in the scale, among the apps, only the Xiaodou Miao app was validated by evidence in published scientific literature, while the remaining apps scored 0 in this category. This suggests that there was a lack of studies validating these apps and that in-depth studies should be conducted in this area in the future.

Service Content of the App

The apps were classified according to their service content into vaccination appointment management, vaccination information service, vaccination record management, internet hospital, science knowledge, drug administration, health management, family doctor, specialist consultation, and peer support and feedback categories. Among the independent apps, the most frequently used was the science knowledge category, which all the applets offered. To a certain extent, this shows that such apps attach more importance to the popularization of scientific knowledge. Vaccination appointment management was considered very convenient by parents of young children because of the reduced waiting time [23], bearing in mind that low vaccination rates among young children were partly due to

parental indecision [24]. Studies have shown that educational interventions for vaccination-hesitant parents can increase vaccination coverage in children aged 6 months to 6 years [25], which explains the importance that developers place on providing scientific knowledge and that health interventions for users based on scientific evidence play a positive role in increasing immunization coverage. When the app ratings were analyzed in relation to the number of reviews, they were found to be moderately correlated, indicating that higher-rated apps were more popular among users. User feedback was used by developers to gain insight into the reality of app use and thus guide future development and updates.

User Experience

User evaluations of the apps expressed the real experience of using the apps. Users were concerned about five main issues: content, functionality, experience, privacy, and service attitude. Users who rated the privacy of the app were dissatisfied. App developers should focus on privacy aspects in future improvements and the development of high-quality apps. Additionally, compared with the platform-dependent applets, the user experience was better on the independent apps due to the higher security, the information being updated, and the strict review of the app stores.

Limitations

This study has several limitations. First, only the four most popular Android phone brands and related apps for iOS were evaluated, and only free Chinese apps from a specific period were included. Second, the researchers evaluated the apps based on short-term use, and some apps were excluded for reasons such as the inability to open or the need to provide an internal institutional registration code, so the findings may have been selectively biased. At present, versions of MARS have been developed and validated in Germany, Turkey, and Korea [26-28]. However, there were no scales or validation studies suitable for China. Last, given the current status of vaccination for COVID-19 in China, such apps were excluded due to the strong user or time-sensitive nature of ad hoc apps that provide only COVID-19 vaccination appointment services, which may also have had an impact on our results.

Conclusions

In this study, independent apps and nonindependent apps that rely on social or payment platforms (Alipay and WeChat applets) were included in the vaccination service category. The overall quality of such apps was considered acceptable, but the nonindependent apps were rated slightly lower, with room for improvement.

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Authors' Contributions

CZ was the first author and made significant contributions to the analysis and interpretation of the data as well as the conception and design of the paper. XG contributed to the conception and design of the paper. RZ contributed to the analysis of the data. WH and LW contributed to the conception and design of the paper. FW and LZ contributed to the design of the study and the analysis and interpretation of the data. DL was the corresponding author of the paper and contributed significantly to the conception and design of the paper as well as the acquisition and analysis of the data.

Conflicts of Interest

None declared.

Multimedia Appendix 1
App quality rating scale.
[DOCX File , 28 KB - ojphi_v16i1e50364_app1.docx]

Multimedia Appendix 2
Mobile Application Rating Scale scores for all apps.
[PDF File (Adobe PDF File), 86 KB - ojphi_v16i1e50364_app2.pdf]

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Abbreviations

MARS: Mobile Application Rating Scale

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Original Paper

Inferring Population HIV Viral Load From a Single HIV Clinic's Electronic Health Record: Simulation Study With a Real-World Example

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Abstract

Background: Population viral load (VL), the most comprehensive measure of the HIV transmission potential, cannot be directly measured due to lack of complete sampling of all people with HIV.

Objective: A given HIV clinic's electronic health record (EHR), a biased sample of this population, may be used to attempt to impute this measure.

Methods: We simulated a population of 10,000 individuals with VL calibrated to surveillance data with a geometric mean of 4449 copies/mL. We sampled 3 hypothetical EHRs from (A) the source population, (B) those diagnosed, and (C) those retained in care. Our analysis imputed population VL from each EHR using sampling weights followed by Bayesian adjustment. These methods were then tested using EHR data from an HIV clinic in Delaware.

Results: Following weighting, the estimates moved in the direction of the population value with correspondingly wider 95% intervals as follows: clinic A: 4364 (95% interval 1963-11,132) copies/mL; clinic B: 4420 (95% interval 1913-10,199) copies/mL; and clinic C: 242 (95% interval 113-563) copies/mL. Bayesian-adjusted weighting further improved the estimate.

Conclusions: These findings suggest that methodological adjustments are ineffective for estimating population VL from a single clinic's EHR without the resource-intensive elucidation of an informative prior.

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KEYWORDS

HIV; human immunodeficiency virus; viral load; population viral load; electronic health record; EHR; electronic health records; EHRs; electric medical record; EMR; electric medical records; EMRs; patient record; patient record; health record; health records; personal health record; PHR; selection weights; sampling; sampling bias; Bayes

Introduction

There has been increasing interest in using electronic health record (EHR) data as part of public health surveillance efforts [1]. In an interview conducted among local health departments, Comer et al [2] reported 23 such uses, including incidence or prevalence of infectious and chronic diseases, such as diabetes, hepatitis B and C, asthma, and depression, and uptake of disease prevention programs, including vaccination and HIV testing. Uptake of HIV testing is especially relevant and timely given the 2019 US Department of Health and Human Services' "Ending the HIV Epidemic: A Plan for America" initiative [3]. The plan calls for a 75% reduction in the number of new HIV diagnoses within 5 years and a 90% reduction within 10 years.

To realize this ambitious goal, health departments monitor data on HIV in their jurisdictions. There are a variety of metrics for

doing so, including incidence, prevalence, late diagnoses, and viral load (VL), a marker for the success of HIV testing programs and connection to care and treatment. Undetectable VL is the desired outcome in the HIV care continuum because an undetectable VL equates to zero transmission risk, the foundation of treatment as prevention [4]. A hierarchy of aggregated VL measures exist and relate to the natural sampling process that occurs from the source population when individuals are diagnosed (community VL), are connected to care (in-care VL), and have VL measures obtained (monitored VL) [5]. The broadest categorization, population VL, is the most comprehensive measure of the HIV transmission potential. However, population VL cannot be directly measured due to lack of complete sampling of the population of people living with HIV as well as lack of complete or recent VL data among those diagnosed [5]. Despite its utility and appeal, the measure has notable challenges, including population selection, varying definitions and calculations, and complete and accurate surveillance [6]. These issues may have led to the decline in its use following its introduction in 2009. Nevertheless, population VL—if quantifiable—is a useful latent measure of transmission potential and quality of HIV care and treatment in a specific geographic area. Even a biased measure can be useful if it can be calibrated to a less biased or an unbiased measure. For example, one contemporary paper using data from the 2010s investigated community VL and HIV incidence in South Carolina and found that community VL disparities mirrored disparities in HIV access to care for nonprioritized groups including women, rural populations, and heterosexual transmission [7].

Absent complete (or a representative random) sampling of a population of people living with HIV, one may turn to EHRs from various clinics to estimate population VL. A given health department might wish to know the distribution of VL among people living with HIV in its jurisdiction but only have a single HIV care program that serves the community. As such, the ability to estimate population VL from a single EHR may be of value. In fact, researchers have previously demonstrated how EHR data can improve the accuracy of HIV surveillance programs [8]. However, use of EHRs for these purposes faces methodological challenges, including ambiguous catchment [9]. A given EHR can be expected to over- or under-sample with respect to characteristics of people living with HIV (eg, health, income, race, age, distance to clinic). We sought to investigate the feasibility of imputing population VL from a single EHR and under what conditions this may be possible.

Methods

Creation of the Synthetic Data Set and Clinics

To establish the feasibility of recovering the true population VL from a single clinic's EHR, we would need both clinic-level VL EHR data as well as the VL from the source population, data which are difficult to obtain as this would require measuring VL among those unaware of their HIV status as well as those not engaged in care. In lieu of this, we created a hypothetical synthetic source population: This population can be considered a large urban area in the United States with a population size of 1,000,000 people and 1% HIV seropositivity, or 10,000 people living with HIV. We defined 3 demographic strata for the population, as follows: age: <35 years, 35-44 years, 45-54 years, >54 years; gender: male, female; race/ethnicity: non-Hispanic White, non-Hispanic Black or African American, Hispanic or Latino. These categories were not meant to be inclusive of all risk groups but rather commonly reported groups for calibrating VL.

The demography of people living with HIV was randomly sampled from a uniform distribution with probabilities informed from the Centers for Disease Control and Prevention (CDC) 2020 HIV Surveillance Report [10]. Specifically, approximately 75% of the population was set to male, and 25% was set to female. Age distributions were as follows: 18% <35 years, 19% 35-44 years, 24% 45-54 years, and 39% >54 years. Race/ethnicity distributions were as follows: 33% White, 45% Black or African American, and 23% Hispanic or Latino. VL was randomly sampled from a log-normal distribution with a $\log_{10}$ geometric mean of 3.65 (4449 copies/mL) and a $\log_{10}$ SD of 1.2. The mean was informed from the measured community VL from the San Francisco, CA HIV/AIDS Case Surveillance System for 2005-2008 [11], and the SD was informed from the CDC's guidance document on community VL [5]. VL was adjusted jointly across the demographic strata by multiplying the VL by a randomly sampled probability obtained from a normal distribution with the following means and accompanying SD of 10%: –1% male and +18% female; +21% <35 years, –10% 35-44 years, –26% 45-54 years, and –26% >54 years; –10% White, +13% Black or African American, and +15% Hispanic or Latino. These adjustments were informed from differences observed in VL in the San Francisco surveillance data [11].

To simulate the HIV care continuum from this source population, we set approximately 10% of the population as unaware of their HIV status. This group was more likely to be younger, male, and Black or African American based on a study of concurrent HIV and AIDS diagnosis in San Francisco [12]. Among those aware of their status, we created an "in care" group in which approximately 72% of those in care would be virally suppressed (<200 copies/mL), mirroring the 2021 San Francisco HIV epidemiology annual report [13], although we stress that our primary intention is not to replicate San Francisco surveillance data but rather create a hypothetical urban population. Sampling the "in care" group in this manner resulted in an average 20% of the aware group also being in care.

Finally, to isolate the effects of various sampling mechanisms, we created 3 HIV clinics with differing catchments. Clinic A was sampled directly from the source population, Clinic B was sampled from those aware of their HIV status, and Clinic C was sampled from those in care. Each clinic contained 250 active patients oversampled by male sex, White race, and age ≥45 years. The demographic composition of each clinic was set to reflect observed patterns of retention in HIV care [14] and to yield an EHR in which the mean VL differed from the source population. We created 1000 versions of each clinic to account for random variability.

Creation of the Catchment Sampling Weights and Weighted Analysis

Let *K* be the size of the source population, *V* be the number of people aware of their HIV status, *N* be the number of people in care, and *S* be the number of patients in care at a clinic. We can estimate the catchment sampling weight using equation 1:

$$W = 1 / Beta((S + 1), (N + 1 - S)) \textbf{ (1)}$$

In this equation, N arises from *Binomial*(*N*/*K*, *K*), where *N*/*K* is the prevalence of people living with HIV and in care in the source population. Weights are calculated per the demographic strata enumerated earlier that related to a clinic's catchment (ie, race, age, and gender) such that *V*, *N*, *S*, and *W* are all calculated separately for each stratum. The final sample weight is obtained for each person by multiplying the corresponding stratum-specific weights.

To allow for the possibility of weight misspecification when they are not estimated appropriately, for example due to an ambiguous catchment, we transformed *W* as outlined in equation 2:

$$P_{biased} = \log(P/(1-P)) + b*\log(VL) \textbf{ (2)}$$

In this equation, *P* is the inverse of *W*, that is, the individual selection probability of being in the clinic, and consequently, the inverse of P_{biased} is the misspecified (biased) weights. The coefficient "b" is the bias factor and was set to 0.1, a conservative starting point that would still meaningfully shift the weights. Under equation 2, a positive bias factor demonstrates the scenario whereby individuals with higher VLs are less likely to be sampled in the clinic, but, unbeknownst to the researchers, the catchment model does not identify them as such. Consequently, this bias factor down-weighted their contribution in the weighted analysis by a factor of 0.1, when they should have been up-weighted. Larger bias factors would create greater weight misspecification, albeit with the same conclusions.

We simulated 1000 of the unbiased and biased weights per participant, then calculated the population geometric mean (GM) VL for each clinic, where GM=exp(mean($\log_{10}$(VL))). We also calculated the unweighted GM and took the root mean squared error (RMSE) between the weighted and unweighted measures. The final calculations are thus based on the 1000 weights for each of the 1000 clinic As, 1000 clinic Bs, and 1000 clinic Cs. Our target estimand was the median and 95% interval of each clinic's GM distribution.

Postweighting Bayesian Adjustment

Following the weighted analysis, we conducted a Bayesian analysis with the expectation that this would further improve our ability to impute the population VL from a given clinic. This approach is analogous to that taken by others who treated weighted observations as "data" that enter the likelihood part of the Bayesian computation [15]. For this analysis, we assumed the true mean and variance were unknown and specified a Normal-Gamma conjugate prior, although, since our focus was only on the posterior mean, the calculations became simplified. The prior mean (μ_0) was informed by the San Francisco HIV/AIDS Case Surveillance System, namely $\log_{10}$ GM VL of 3.65. As a starting point for the prior sample size (n_0), we took the perspective of a clinic's population's VL measured at a previous time point (ie, available before the observed VL data used in the weighted analysis). For example, one might posit that such data were collected immediately upon diagnosis as opposed to routine monitoring during antiretroviral therapy. Following our weighted analysis, these observed measurements have a logarithmic mean of  and effective sample size, $n_w=\Sigma W$ for each of the 1000 clinic samples. The posterior logarithmic mean of the population VL (μ_n) conditional on posterior variance is specified in equation 3.

$$\mu_n = ((n_0 \times \mu_0) + n_w \times \text{  }) / (n_0 + n_w) \textbf{ (3)}$$

To examine the influence of the prior sample size, we operationalized n_0 in 3 ways: $0.25 \times n_w$, $0.5 \times n_w$, and $2 \times n_w$. Additionally, to reflect the earlier scenario of the prior data collected upon diagnosis, we conducted a final analysis for clinic C where μ_0 was informed from clinic B's weighted mean and the more conservative $n_0=0.25*n_w$. As before, these calculations were performed for each of the 1000 clinic weights for each of the 1000 clinics.

Real-World Clinic Data Set

As an applied demonstration of our methods, we obtained the most recently available VL on active patients retained in care for HIV at the Holloway Community Program at ChristianaCare (Wilmington, DE). Patients' age, race, and gender were coded using the same categories defined earlier for our synthetic population. Denominators needed for the catchment model were obtained from the US Census Bureau 2021 American Community Survey [16] population sizes for Delaware (the presumed catchment of the Holloway program) and the Delaware Integrated HIV Prevention and Care Plan for 2022-2026 that includes statewide surveillance data as of 2019 [17]. Using the procedures outlined earlier, we estimated the population VL from the clinic data; however, as we did not have access to historic unbiased estimates of VL for this jurisdiction, we used the prior as described in our synthetic analysis. To further acknowledge uncertainty in the prior mean (μ_0), we conducted a sensitivity analysis with μ_0 modified in 3 ways ($0.25 \times \mu_0$, $0.5 \times \mu_0$, and $2 \times \mu_0$) and repeated the Bayesian adjustment across the 3 prior sample sizes.

All analyses were performed in R version 3.6.3 (R Foundation for Statistical Computing). Analytic codes are available for download from [18]. HIV VL point estimates and 95% intervals are presented on a linear scale in the main text and a logarithmic scale in Multimedia Appendices 1-5.

Results

Synthetic Population and Clinics

Each clinic was approximately 93% male; 4% <35 years, 5% 35-44 years, 40% 45-54 years, and 51% >54 years; and 81% White, 13% Black or African American, and 6% Hispanic or Latino (Table 1).

Table 1. Characteristics of the synthetic population and clinics as well as the real-world cohort from the Holloway Community Program at ChristianaCare (Wilmington, DE).

Characteristic	Synthetic EHRs[a,b]				Real-world EHR
	Population[c] (n=10,000)	Clinic A[d] (n=250)	Clinic B[e] (n=250)	Clinic C[f] (n=250)	Holloway (n=1807)
Age (years), n (%)					
<35	1817 (18.2)	12 (4.8)	10 (4)	10 (4)	278 (15.4)
35-44	1819 (18.2)	12 (4.8)	12 (4.8)	15 (6)	299 (16.5)
45-54	2727 (27.3)	97 (38.8)	98 (38.2)	96 (38.4)	332 (18.4)
>54	3634 (36.3)	129 (51.6)	130 (52)	129 (51.6)	898 (49.7)
Gender, n (%)					
Female	2497 (25)	17 (6.8)	17 (6.8)	19 (7.6)	558 (30.9)
Male	7503 (75)	233 (93.2)	233 (93.2)	213 (92.4)	1249 (69.1)
Race/ethnicity, n (%)					
Non-Hispanic Black or African American	4446 (44.5)	30 (12)	27 (10.8)	32.5 (13)	1128 (62.4)
Non-Hispanic White	3332 (33.3)	205 (82)	207 (82.8)	200 (80)	514 (28.4)
Hispanic or Latino	2220 (22.2)	15 (6)	15 (6)	18 (7.2)	165 (9.1)
Viral load (copies/mL), geometric mean	3996	3147	3108	173	41
Viral load, $\log_{10}$ geometric mean	3.60	3.50	3.49	2.24	1.61

[a]EHR: electronic health record.

[b]The 3 synthetic clinic electronic health records (n=250 per clinic) were sampled from a source population of people living with HIV (n=10,000) and were oversampled by male sex, White race, and age ≥45 years.

[c]Synthetic population results given as the median values from 1000 hypothetical clinics.

[d]Sampled directly from the source population.

[e]Sampled from a subset of the source population based on diagnosed HIV.

[f]Sampled from a subset of the source population based on retention in care.

Figure 1 contrasts the observed, weighted, and Bayesian adjusted VLs comparing the clinics to the population (see Multimedia Appendix 1 for logarithmic results). Across the 1000 simulations, the median GM population VL was 3996 (95% interval 3780-4214) copies/mL. For each clinic A, B, and C, the median GM VL point estimates and 95% intervals were 3147 (95% interval 2294-4301), 3108 (95% interval 2216-4383), and 173 (95% interval 123-240) copies/mL, respectively. Following weighting, the estimates moved in the direction of the population value with correspondingly wider 95% intervals as follows: clinic A: 4364 (95% interval 1963-11,132) copies/mL; clinic B: 4420 (95% interval 1913-10,199) copies/mL; clinic C: 242 (95% interval 113-563) copies/mL. Bayesian adjustment resulted in a shrinking of intervals, depending on the prior sample size, where the large sample size resulted in tighter intervals, and clinic C had a notable shift in point estimates toward the population mean. With a 25% of the clinic prior sample size, the posterior estimates were 433 (95% interval 236-851) copies/mL; with a 50% of the clinic prior sample size, the posterior estimates were 639 (95% interval 384-1120) copies/mL; and with a 200% of the clinic prior sample size, the posterior estimates were 1685 (95% interval 1307-2231) copies/mL. When using the weighted clinic B estimates to inform the prior for clinic C, we also noted an improvement in estimating the population mean, with posterior estimates of 432 (95% interval 230-889) copies/mL.

Figure 1. Comparison of the distribution of the geometric mean HIV viral load for 3 clinic electronic health records (n=250 per clinic) sampled from a synthetic source population of people living with HIV (n=10,000), with results representing 1000 hypothetical clinicals each with 1000 sampling weight adjustments based on sampling from the source population (A) directly, (B) based on diagnosed HIV, or (C) based on retention in care (all 3 oversampled by male sex, White race, age ≥45 years). Bayesian 1: prior sample size of 25% of the weighted clinic sample size; Bayesian 2: prior sample size of 50% of the weighted clinic sample size; Bayesian 3: prior sample size of 200% of the weighted clinic sample size; Bayesian 4: prior mean informed from weighted clinic B estimates.

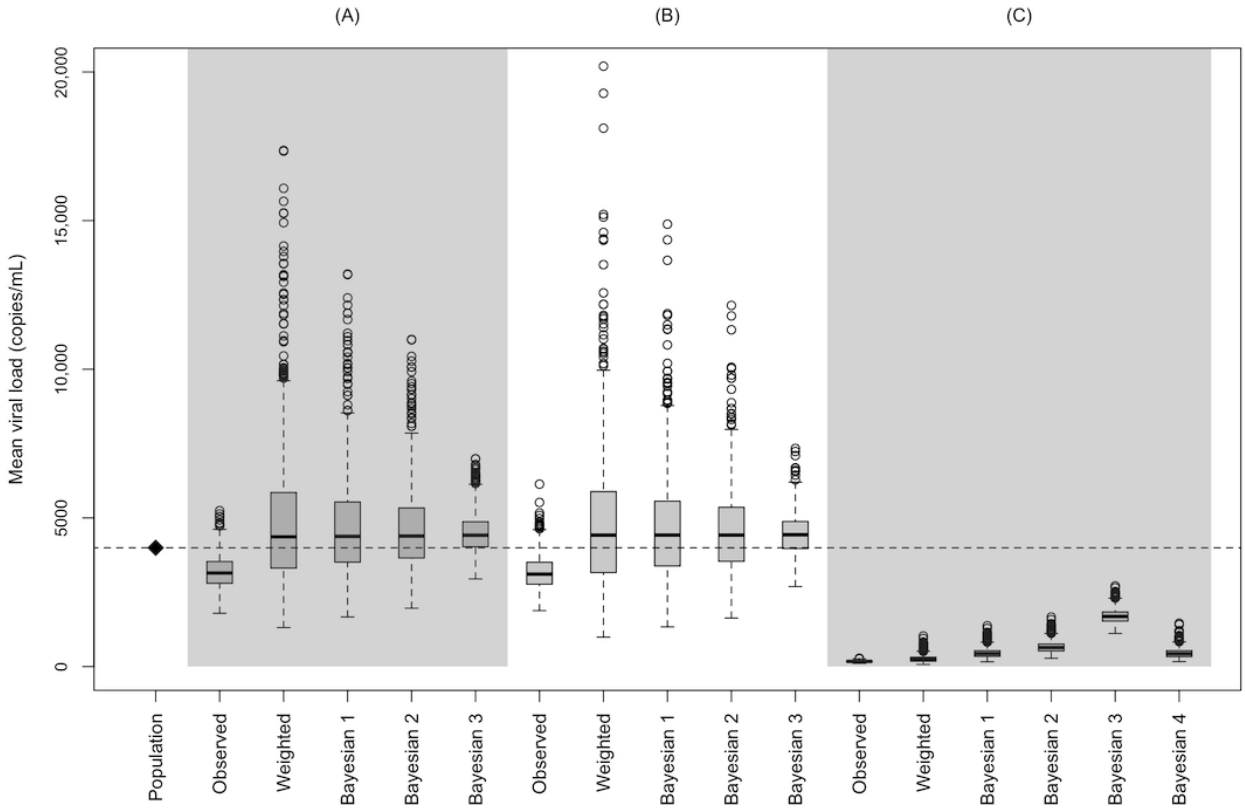


Figure 2 depicts the averaged RMSE for each clinic for each weighting strategy (see Multimedia Appendix 2 for logarithmic results). RMSE was greatest in the purely weighted analyses, with median errors and 95% intervals for each clinic as follows: clinic A: 1174 (95% interval 288-7261) copies/mL; clinic B: 1265 (95% interval 261-6369) copies/mL; and clinic C: 3745 (3385-4018) copies/mL. RMSE was lowest in the Bayesian analysis that followed weighting with the larger prior sample size, as follows: clinic A: 490 (95% interval 92-2026) copies/mL; clinic B: 528 (95% interval 96-1884) copies/mL; and clinic C: 2319 (95% interval 1773-2747) copies/mL. Figure 3 shows the impact of the weight misspecifications (see Multimedia Appendix 3 for logarithmic results). As expected, the biased weight systematically down-weighted higher VL individuals when they should have been up-weighted, as might occur based on an inaccurate catchment model where individuals with higher VLs were less likely to be sampled in the clinic.

Figure 2. Comparison of the root mean squared error (RMSE) of the geometric mean HIV viral load for 3 clinic electronic health records (n=250 per clinic) sampled from a synthetic source population of people living with HIV (n=10,000), with results representing 1000 hypothetical clinicals each with 1000 sampling weight adjustments based on sampling from the source population (A) directly, (B) based on diagnosed HIV, or (C) based on retention in care (all 3 oversampled by male sex, White race, age ≥45 years). Bayesian 1: prior sample size of 25% of the weighted clinic sample size; Bayesian 2: prior sample size of 50% of the weighted clinic sample size; Bayesian 3: prior sample size of 200% of the weighted clinic sample size; Bayesian 4: prior mean informed from weighted clinic B estimates.

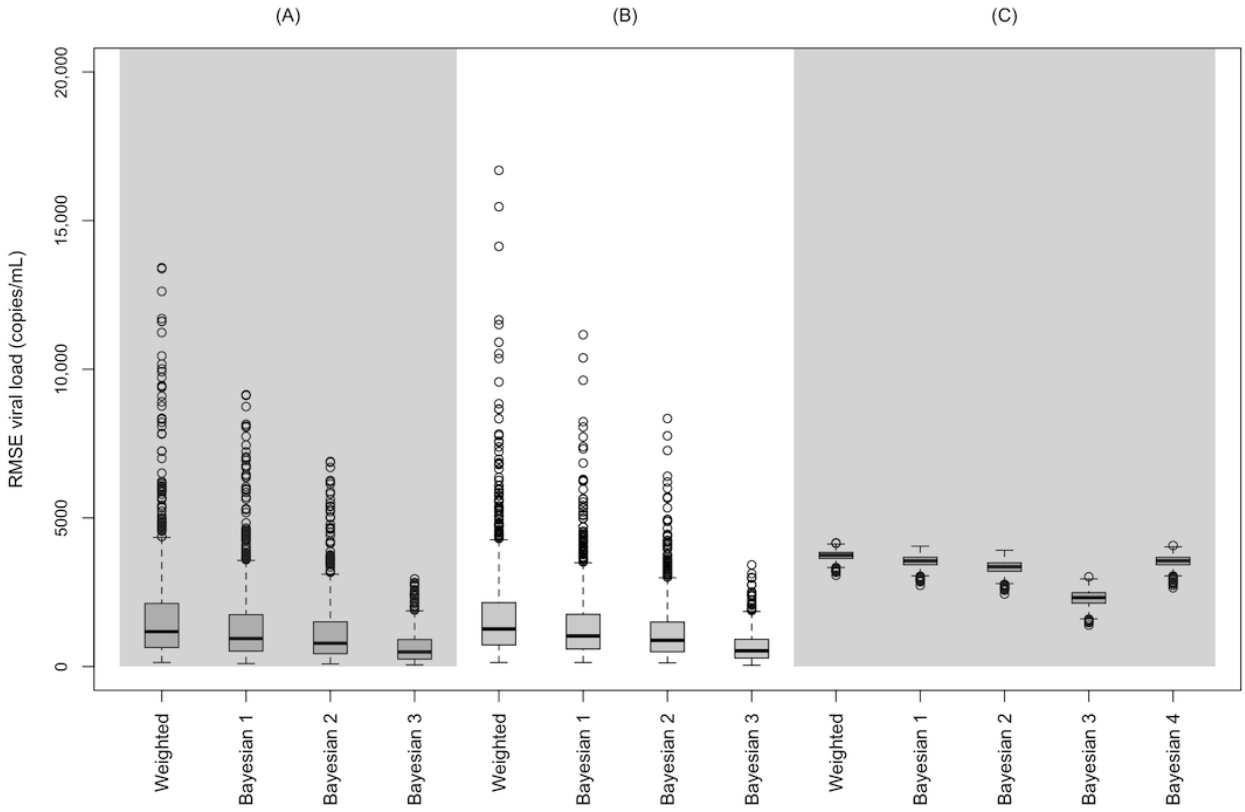
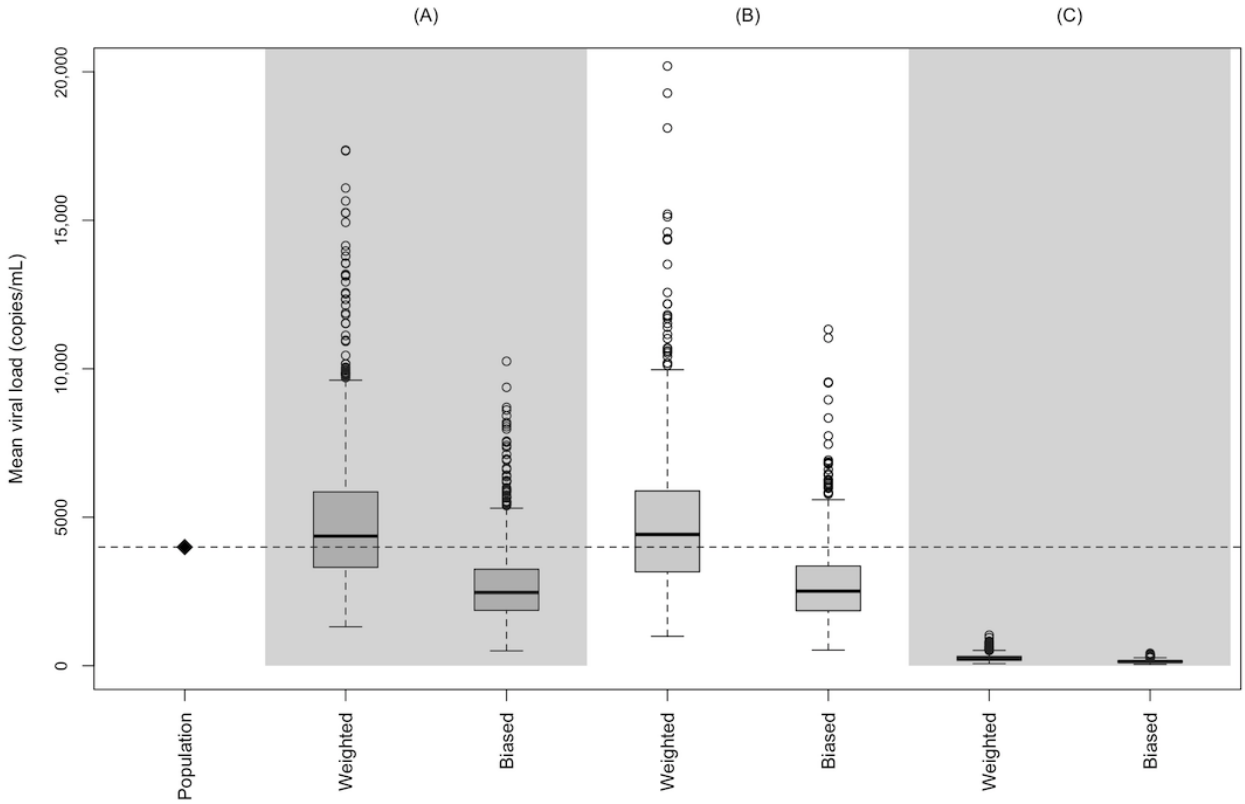


Figure 3. Comparison of weight misspecification in the weighted geometric mean HIV viral load for 3 clinic electronic health records (n=250 per clinic) sampled from a synthetic source population of people living with HIV (n=10,000), with results representing 1000 hypothetical clinicals each with 1000 sampling weight adjustments based on sampling from the source population (A) directly, (B) based on diagnosed HIV, or (C) based on retention in care (all 3 oversampled by male sex, White race, age ≥45 years).



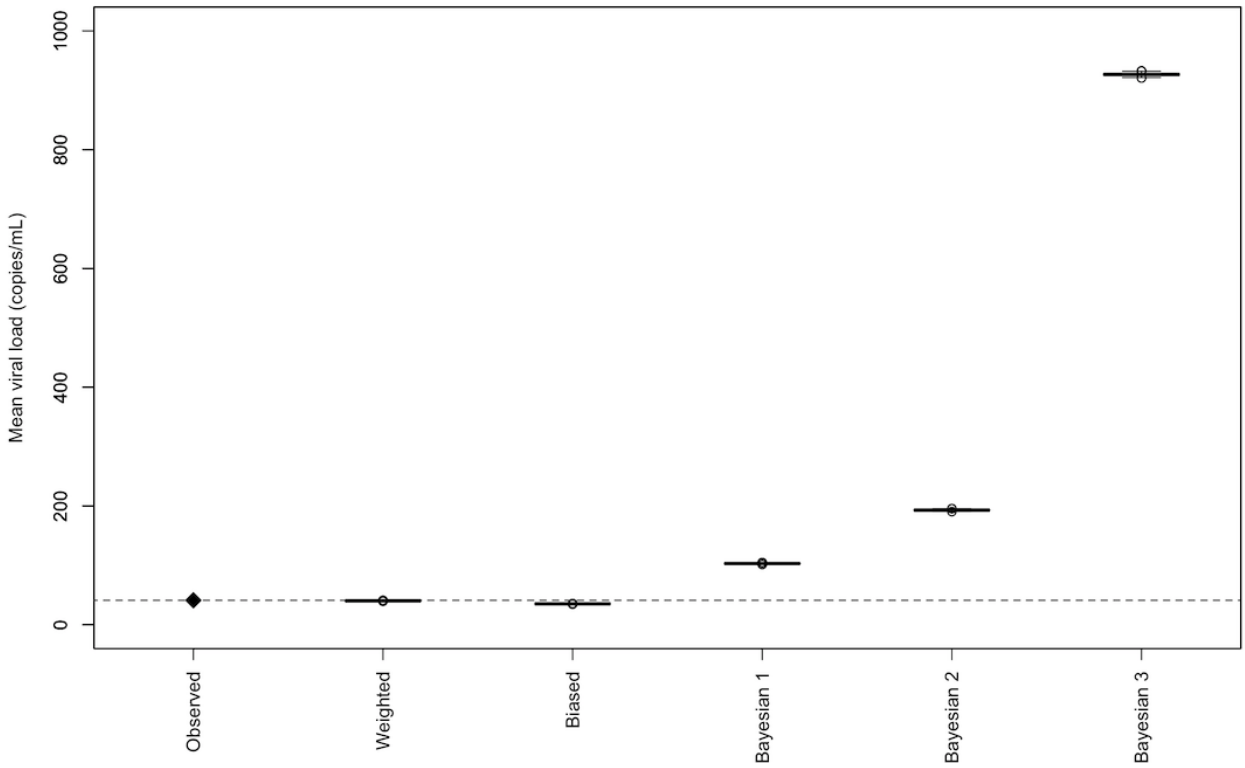
Holloway Community Program Clinic

The 2021 population in Delaware was 1,003,384. For each demographic stratum, the populations had the following characteristics: age (<35 years: 420,844; 35-44 years: 122,088; 45-54 years: 115,300; >54 years: 345,152), gender (male: 485,908; female: 517,476), and race/ethnicity (non-Hispanic White: 595,212; non-Hispanic Black or African American: 205,217; Hispanic or Latino: 101,213; other: 101,742). As of 2019, there were an estimated 3841 people living with HIV; 2984 were in care, and 857 were not in care. For each demographic stratum among those in care, the populations had the following characteristics: age (<35 years: 394; 35-44 years: 432; 45-54 years: 703; >54 years: 1455), gender (male: 2125; female: 859), and race/ethnicity (non-Hispanic White: 958; non-Hispanic Black or African American: 1725; Hispanic or Latino: 222; other: 79).

There were 1807 active patients in the Holloway Community Program with a resulted VL test as of the date of EHR data extraction. The GM VL of the clinic was 41, and the geometric SD was 190,261 copies/mL; 1656 of the 1807 (91.6%) patients were virally suppressed (<200 copies/mL). Additional characteristics may be found in Table 1.

Figure 4 presents the inferred population VL measure from the clinic's EHR (see Multimedia Appendix 4 for logarithmic results). The weighting-only adjustment had negligible impact compared with the unweighted estimate, while the biased weights shifted the estimates slightly lower to a median of 35 copies/mL. The biased weight systematically down-weighted higher VL individuals when they should have been up-weighted, as might occur based on an inaccurate catchment model where individuals with higher VLs were less likely to be sampled in the clinic. Meanwhile, the Bayesian adjustment moved the weighted estimate from 40 copies/mL to a median of 103 copies/mL with the 25% prior sample size, to 193 copies/mL with the 50% prior sample size, and to 926 copies/mL with the 200% prior sample size. Results were sensitive to the assumption about the informative prior's mean (Multimedia Appendix 5).

Figure 4. Inferred population geometric mean HIV viral load for Delaware based on active patients retained in care at the Holloway Community Program at ChristianaCare (Wilmington, DE), with results representing 1000 sampling weight adjustments. Bayesian 1: prior sample size of 25% of the weighted clinic sample size; Bayesian 2: prior sample size of 50% of the weighted clinic sample size; Bayesian 3: prior sample size of 200% of the weighted clinic sample size.



Discussion

Using a synthetic population, we observed that recovery of population VL from a single center's monitored VL was hampered when a historic measurement or informed guess at the prior population VL was unavailable. In other words, good VL data are preferred to methodological adjustments of incomplete data.

Community VL, calculated from individuals who have been diagnosed with HIV, has been used to generalize risk of HIV transmission and evaluate retention in care and viral suppression [6]. However, as mentioned in the Introduction, this measure has several shortcomings. First, it will almost always result in underestimated VL, as individuals who are unaware of their HIV status will likely have higher VLs. Relatedly, timing of the individual VL measure may also impact the community estimate, as VL will fluctuate over time (eg, acute vs chronic infection). Second, there may be issues with defining the specific geographic area of the community and whether this population is "closed." Although closed communities would allow for a more accurate community VL measurement, the applicability and feasibility are hindered in the real world by population migration. Third, sampling bias may be present when there is a high prevalence of undiagnosed people living with HIV [6]. In these situations, the use of the population VL may be more appropriate for reflecting transmission potential should we be able to impute data for those undiagnosed or not retained in care. To address these limitations, alternate metrics have been proposed, such as the prevalence of viremia based on viral suppression [19]. As such, researchers have adopted alternative community-level VL measures that reflect the prevalence of HIV in the community as well as distinguishing between those who are virally suppressed and those who have a high VL and are more likely to contribute to community spread [6,19]. The methods we have demonstrated can readily be adapted to other HIV measures where a weighted mean may be desired, such as CD4 cell counts among people living with HIV for a given jurisdiction. Regardless of the metric used, there is still risk of ecologic fallacy at the aggregate level wherein a higher population VL may not correspond to higher individual transmission risk when prophylaxis is common.

Others have acknowledged the important challenge of the use of EHR data for population inference when health care–seeking behavior and access to care impact representativeness. EHR-based studies are susceptible to issues of confounding, information bias, and selection bias [9]. Bower et al [20] demonstrated how selection into an EHR is not random and recommended techniques such as sampling (poststratification) weights and propensity scoring and inverse probability weighting (IPW) to adjust estimates, in their case, of cardiovascular disease risk. Flood et al [21] used EHR data to estimate childhood obesity and found that the application of sampling weights to their data allowed estimates to be comparable to a nationally representative survey. Goldstein et al [22] used IPW to adjust for presumed selection bias in a

single-center EHR-based study when exposure and outcome relate to catchment. It is worth delineating how these 2 complementary strategies—sampling/poststratification weighting versus propensity scoring/IPW—differ in EHR research.

The IPW approach requires specification of a probability model (ie, the propensity score) for selection into the EHR from the source population, conditioned on measured characteristics related to this process. However, this demands the EHR capture relevant details on the catchment process, or those data can be readily linked, and EHRs are well-known to lack data on epidemiological determinants [23]. On the other hand, using a sampling weight assumes we have access to the denominators from which the EHR data are sampled. One such source of data we have used are census estimates, which can be stratified by factors relating to catchment and tuned to the local environment. The challenge with this approach is that, in practice, we may not know all the characteristics defining catchment process, the census might not capture those characteristics, or there may be ambiguous geography. Indeed, catchment is a multifactorial and sometimes nebulous process related to health care availability, accessibility, affordability, accommodation, and acceptability [24]. One potential way to gain insight into catchment is to compare EHR data with census data to see which characteristics are over- or under-represented for a given geographic area defined by the clinic. If the census lacks data on catchment-relevant factors but the EHR captures these details (eg, sexual orientation), this may favor the IPW approach.

Another important limitation of our approach was our construction of the sampling weights. We assumed a simple random sample within each catchment stratum to calculate the sampling weights. In our synthetic population, this was known with certainty, although we blinded ourselves to this oracle view by not retaining the selection probabilities during the data generation process but rather relying on our catchment model. However, as exemplified in our biased weighted analysis and the real-world clinic data set, the catchment stratum may be uncertain and, in our case, presumably underestimated population VL. Many extensions exist to improve weighting approaches, such as raking, which we did not evaluate herein [25]. We also observed a decrease in precision—widening of intervals—when comparing the weighted versus unweighted results. This has been termed the bias-variance tradeoff, where improved accuracy may be accompanied by worsened precision [26].

A particular strength to our approach is the straightforward implementation and Bayesian adjustment that can be carried out with minimal programming ability. The included source code [18] can serve as a starting point. More complicated cluster survey designs may also benefit from Bayesian methods [27,28]. Bayesian analysis requires careful deliberation over which priors may be most appropriate. Informative priors are useful and straightforward, but obtaining unbiased estimates of VL can be prohibitively expensive for some jurisdictions, and measures obtained in one jurisdiction may not be exchangeable with another. Indeed, we observed that our real-world application was sensitive to the choice of prior. Nonetheless, even a small unbiased survey can dramatically reduce RMSE and thus may be justified. This would have to be done only once to seed Bayesian prospective surveillance of population VL. These methods can be adapted to other aggregated measures of disease prevalence, for both research and practice purposes, especially if an historic prior estimate is available.

Health departments have expressed interest in using EHR data for many community health measures that can help inform resource allocation and public health decision-making in different contexts. Comer et al [2] identified 23 of these; hepatitis B and C infection was a high priority measure and one in which previous surveys such as the National Health and Nutrition Examination Survey [29,30] can serve as an informative prior. If, for example, a focal outbreak of hepatitis C is detected from an EHR, this could suggest targeted treatment and prevention efforts to cure infection and reduce future transmission.

In short, we observed that methodological adjustments were ineffective to recover the true population VL in our data without prior knowledge of what this value may be. Further validation using real-world EHR data from diverse clinical settings is needed to confirm this finding. Should such prior data be available, then it may be possible to infer population characteristics from a biased clinic sample in the EHR. Moving forward, we encourage those with access to population-based surveys of community health metrics—especially at subnational levels—to continue to disseminate these data to enable epidemiologic methods such as ours.

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Authors' Contributions

The study was conceived by NDG and IB. NDG obtained the funding. NDG and IB conducted the analyses. All authors interpreted the findings, drafted the initial manuscript, and approved the final submission.

Conflicts of Interest

NDG consults for ChristianaCare, unrelated to this work. All other authors report no financial conflicts of interest.

Multimedia Appendix 1
Comparison of the distribution of the logarithmic geometric mean HIV viral load (VL) for three clinic electronic health records (n=250 per clinic) sampled from a synthetic source population of people living with HIV (n=10,000). Clinic A was sampled directly from the source population, whereas clinics B and C were sampled from a subset of the source population based on diagnosed HIV (clinic B) or retention in care (clinic C). All synthetic clinics oversampled by male sex, White race, and 45 years of age or older. Results represent 1,000 hypothetical clinics each with 1,000 sampling weight adjustments. 1 Prior sample size of 25% of the weighted clinic sample size. 2 Prior sample size of 50% of the weighted clinic sample size. 3 Prior sample size of 200% of the weighted clinic sample size. 4 Prior mean informed from weighted clinic B estimates.
[PNG File , 189 KB - ojphi_v16i1e58058_app1.png]

Multimedia Appendix 2
Comparison of the root mean squared error (RMSE) of the logarithmic geometric mean HIV viral load (VL) for three clinic electronic health records (n=250 per clinic) sampled from a synthetic source population of people living with HIV (n=10,000). Clinic A was sampled directly from the source population, whereas clinics B and C were sampled from a subset of the source population based on diagnosed HIV (clinic B) or retention in care (clinic C). All synthetic clinics oversampled by male sex, White race, and 45 years of age or older. Results represent 1,000 hypothetical clinics each with 1,000 sampling weight adjustments. 1 Prior sample size of 25% of the weighted clinic sample size. 2 Prior sample size of 50% of the weighted clinic sample size. 3 Prior sample size of 200% of the weighted clinic sample size. 4 Prior mean informed from weighted clinic B estimates.
[PNG File , 151 KB - ojphi_v16i1e58058_app2.png]

Multimedia Appendix 3
Comparison of weight misspecification in the weighted logarithmic geometric mean HIV viral load (VL) for three clinic electronic health records (n=250 per clinic) sampled from a synthetic source population of people living with HIV (n=10,000). Clinic A was sampled directly from the source population, whereas clinics B and C were sampled from a subset of the source population based on diagnosed HIV (clinic B) or retention in care (clinic C). All synthetic clinics oversampled by male sex, White race, and 45 years of age or older. Results represent 1,000 hypothetical clinics each with 1,000 sampling weight adjustments. The biased weight systematically down-weighted higher VL individuals when they should have been up-weighted, as might occur based on an inaccurate catchment model where individuals with higher VLs were less likely to be sampled in the clinic.
[PNG File , 147 KB - ojphi_v16i1e58058_app3.png]

Multimedia Appendix 4
Inferred population geometric mean HIV viral load (VL) for Delaware based on active patients retained in care at the Holloway Community Program at ChristianaCare (Wilmington, DE). Results represent 1,000 sampling weight adjustments. The biased weight systematically down-weighted higher VL individuals when they should have been up-weighted, as might occur based on an inaccurate catchment model where individuals with higher VLs were less likely to be sampled in the clinic. 1 Prior sample size of 25% of the weighted clinic sample size. 2 Prior sample size of 50% of the weighted clinic sample size. 3 Prior sample size of 200% of the weighted clinic sample size.
[PNG File , 110 KB - ojphi_v16i1e58058_app4.png]

Multimedia Appendix 5
Sensitivity analysis of inferred population geometric mean HIV viral load (VL) for Delaware based on active patients retained in care at the Holloway Community Program at ChristianaCare (Wilmington, DE). Results represent 1,000 Bayesian sampling weight adjustments. Sensitivity analysis compared three alternate specifications of the prior mean for VL: 25%, 50%, and 200% of the original specification (m0). Prior sample size was varied three ways: 25%, 50%, and 200% of the weighted clinic sample size.
[PNG File , 118 KB - ojphi_v16i1e58058_app5.png]

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Abbreviations

CDC: Centers for Disease Control and Prevention
EHR: electronic health record
GM: geometric mean
IPW: inverse probability weighting
PLWH: people living with HIV
RMSE: root mean squared error
VL: viral load

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Original Paper

Trends in the Ophthalmic Workforce and Eye Care Infrastructure in South India: Cross-Sectional Questionnaire Study

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Abstract

Background: This study is part of broad-based research to determine the impact of blindness control activities in general and with special reference to the Andhra Pradesh Right to Sight Society (APRTSS) activities in the southern Indian states of Andhra Pradesh and Telangana. As part of the global "VISION 2020: The Right to Sight" initiative, the APRTSS was established in the undivided state of Andhra Pradesh in 2002. Since then, the APRTSS has been actively implementing the strategies of VISION 2020 to reduce visual impairment and blindness in the state.

Objective: The availability and distribution of the eye care workforce are essential to reach the goals of VISION 2020: The Right to Sight, the global initiative to eliminate avoidable blindness. This study assessed the trends in the availability and distribution of eye health professionals and eye care infrastructure in 2 southern Indian states: Andhra Pradesh and Telangana.

Methods: This cross-sectional study used a pretested questionnaire to gather data for the year from 2012 to 2013. Data for 2002 to 2003 were collected from available historical records. The questionnaires were pretested in a pilot study conducted before the main survey. Pretested questionnaires were administered to all eye care professionals—ophthalmologists (n=1712) and midlevel ophthalmic personnel (MLOP; n=1250)—eye care facilities with ≥10 inpatient beds or performing ≥100 cataract surgeries per annum (n=640), local nongovernmental eye care organizations (n=182), and international eye care organizations (n=10). Data were collected for 2 different time periods: the baseline year of 2002 to 2003 and the target year of 2012 to 2013. Data analysis was conducted using SPSS version 19.0.

Results: The response rates were 81.1% (519/640) for eye care facilities, 96.1% (1645/1712) for ophthalmologists, and 67.6% (845/1250) for MLOP. From 2002-2003 to 2012-2013, there has been an increase in eye care facilities, from 234 to 519 (121.8%); ophthalmologists, from 935 to 1712 (83.1%); and MLOP, from 767 to 1250 (63%). The ophthalmologist:population ratio improved from 1:88,260 in 2002-2003 to 1:51,468 in 2012-2013. The MLOP:population ratio improved from 1:168,283 in 2002-2003 to 1:138,117 in 2012-2013 but still falls short of the ideal number.

Conclusions: Both southern Indian states are able to meet the requirements for ophthalmologists and eyecare infrastructure as per the goals of VISION 2020. However, the number of MLOP falls short of the ideal ratio for the population. This study has some limitations. For example, most of the data collected through questionnaires were based on self-report, which might introduce bias due to memory recall or over or under-reporting of certain information. However, this was addressed by cross-checking the collected data with information from supplementary sources.

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KEYWORDS

trends; human resources; infrastructure; eye care; South India

Introduction

Blindness and visual impairment represent a major public health problem in India [1-4]. The major causes of blindness and visual impairment in Andhra Pradesh and Telangana include cataract, refractive errors, retinal diseases, glaucoma, and corneal opacities, as reported in the Andhra Pradesh Eye Diseases study [5]. To tackle the problem of blindness and visual impairment, we need adequate human resources and sufficient infrastructure in eye care. Since the global "VISION 2020: the Right to Sight" initiative was launched in 1999, there has been a lot of progress in not only lessening the burden of blindness and visual impairment but also increasing the number of skilled eye care professionals and eye care infrastructure [6,7].

In line with the global Vision 2020 initiative, the undivided Andhra Pradesh state (the state was divided into Andhra Pradesh and Telangana states in 2014) established the Andhra Pradesh Right to Sight Society (APRTSS) in 2002 to work toward the VISION 2020 goals. Since its formation, the APRTSS has coordinated closely with major stakeholders in eye care such as those in the government, nongovernmental organization (NGO), and private sectors. Its activities include human resource development, infrastructural strengthening, disease control, and advocacy. To determine the impact of APRTSS VISION 2020 activities, we carried out a research project collecting information about the APRTSS activities from the baseline year of 2002 to 2003—the year in which the APRTSS was established—and the target year of 2012 to 2013—after a period of 10 years.

As part of the aforementioned research project, we carried out a survey about the ophthalmic workforce and infrastructure to identify the trends over a period of 10 years. An evidence base is essential to understand trends in human resources for health [8]. However, no regular mechanism exists in India to collect data on human resource trends in the provision of eye care services [9]. This study fills that gap by identifying trends in eye care. The results of the survey will be helpful to identify gaps, strengthen the eye care facilities, and overcome the maldistribution of human resources and infrastructure, in order to achieve the goals of VISION 2020. This study assessed trends in the availability and distribution of eye health professionals and eye care infrastructure in 2 southern Indian states: Andhra Pradesh and Telangana.

Methods

Study Design

This cross-sectional study used a pretested questionnaire for the year 2012 to 2013. The data for the 2002-2003 period were collected from available historical records.

We used questionnaires in both electronic and hard copy formats to collect the data. The questionnaires were developed based on the 6 building blocks of the universal health care system [10].

Ethical Considerations

This study was conducted as part of the research project on the "Impact of implementation of blindness control activities in the state of Andhra Pradesh," which was approved by the ethics committee of the LV Prasad Eye Institute (reference number: LEC 09-13-097) and conducted in accordance with the tenets of the Declaration of Helsinki.

Definitions

For the purpose of this study, an eye care facility was defined as any health care facility where ophthalmologist services are available. The eye care facilities were identified as secondary or tertiary eye care facilities. For the purpose of this study, secondary eye care was defined as any eye care facility having an ophthalmologist conducting cataract and basic minor surgical procedures. Tertiary eye care was defined as any eye care facility with secondary eye care services as well as at least one subspecialty such as cornea, glaucoma, retina, or oculoplasty. Eye care facilities were categorized as government eye care facilities if they were established and funded by the government or other public sources such as universities and public sector organizations. NGO eye care facilities functioned on a no-profit, no-loss basis. Eye care facilities with a profit motive, irrespective of whether owned by an individual or a group of people or agencies, were categorized as private eye care facilities.

Inclusion Criteria

All eye care facilities with ≥10 inpatient beds or performing ≥100 cataract surgeries per annum were eligible.

Questionnaire

The questionnaire had 4 sections. Each section was distributed to concerned eye care professionals both in electronic form and hard copy to obtain the data.

Section 1: Questionnaire for Eye Care Facilities

The questionnaire for eye care facilities (Multimedia Appendix 1) was distributed to the director, superintendent, administrator, or manager in charge of the care facility. It was completed to obtain information for both the baseline and target years. It contained questions ranging from the services available, human resources, infrastructure, training facilities for eye care professionals, and any other relevant data.

Section 2: Questionnaire for Ophthalmologists

The questionnaire for ophthalmologists (Multimedia Appendix 2) was sent to all ophthalmologists working in government, NGO, and private eye care facilities. It was intended to be completed both by email and in hard copies by surface mail. It contained questions about demographic details; whether the ophthalmologist performs surgeries; whether the ophthalmologist practices in any subspecialties such as anterior segment surgeries, glaucoma, or retina; the average number of cataract surgeries per month; the principal method followed during cataract surgeries; professional experience; academic activity; and any training undergone.

Section 3: Questionnaire for MLOP

The questionnaire for MLOP (Multimedia Appendix 3) was distributed to all optometrists, ophthalmic assistants, and nurses working in all government, NGO, and private eye care facilities. It contained questions to elicit information on knowledge, skills, experience, and special training undergone such as in contact lens practice, refresher training in retinoscopy methods, and biomedical training for equipment maintenance. We also collected information on how many refractions were conducted per month, how many pairs of spectacles were prescribed per month, any administrative work, and any research activities.

Section 4: Questionnaire for District Blindness Control Societies and NGOs in Eye Care

The questionnaire for district blindness control societies (DBCSs) and NGOs in eye care (Multimedia Appendix 4) was distributed to program managers to obtain information on the impact of the implementation of blindness control activities in the district. It contained 3 subsections: section A for program managers of DBCS, section B for NGOs in eye care, and section C for international NGOs in eye care who were active in the state.

Follow-Up

Follow-up mechanisms were instituted every 2 weeks after mailing the questionnaire to the various stakeholders, and reminders were sent at the 3rd month and again at the 6th month.

Additional Data Sources

In addition to the data collected through questionnaires, we gathered information from the following sources: (1) member directory for the All India Ophthalmological Society and its website, (2) directory of the Andhra Pradesh Ophthalmological Society and its website, (3) directory of the Telangana Ophthalmological Society and its website, (4) directory of the Andhra Pradesh Paramedical Board, and (5) websites of leading eye care institutions.

The information obtained from these sources helped us cross-check the data received through the questionnaires from eye care facilities, ophthalmologists, MLOP, and DBCSs. The data collected were entered in Excel sheets by 2 different data operators and cross-checked for any typographical errors. The data were analyzed using SPSS version 19.0 (IBM Corp) for Windows.

Results

Participants

As per the inclusion criteria, a total of 640 eye care facilities were identified, and a questionnaire was sent to the directors or those in charge of the facilities. Of the 640 facilities, responses were received from 519. Table 1 shows the number of questionnaires distributed to the various participants and the response rates. All the DBCSs responded to the questionnaire, whereas the lowest response rate was from MLOP.

Table 1. Response rates for eye care facilities, eye care professionals, and eye care organizations.

Questionnaire recipient	Questionnaires distributed, n	Response rate, n (%)
Eye care facilities	640	519 (81.1)
Ophthalmologists	1712	1645 (96.1)
Midlevel ophthalmic personnel	1250	845 (67.6)
Local NGOs[a]	182	165 (90.7)
International NGOs	10	9 (90)
DBCSs[b]	23	23 (100)

[a]NGOs: nongovernmental organizations.

[b]DBCSs: district blindness control societies.

Eye Care Facilities and Service Delivery

The number of eye care facilities in the undivided state increased from 234 in 2002-2003 to 519 in 2012-2013 (121.8% increase). From 2002-2003 to 2012-2013, there was a marginal increase in the number of eye care facilities in the government sector (44 to 58, 31.8%), there was a substantial increase in the NGO sector (105 to 165, 57.1%), and the highest increase was seen in the private sector (85 to 296, 248.2%; Table 2).

Table 2. Number of eye care facilities in the combined state of Andhra Pradesh in 2002-2003 and 2012-2013.

Type of facility	Facilities in 2002-2003, n	Facilities in 2012-2013, n
Government	44	58
NGO[a]	105	165
Private	85	296

[a]NGO: nongovernmental organization.

The number of eye care facilities delivering secondary eye care in the undivided state increased from 198 in 2002-2003 to 440 in 2012-2013 (122.2% increase), and the number of eye care facilities delivering tertiary care increased from 36 in 2002-2003

to 79 in 2012-2013 (119.4% increase). The secondary and tertiary eye care facilities experienced a large jump in number from 2002-2003 to 2012-2013, whereas there was no increase in the number of tertiary eye care facilities in the government sector for the same period (Table 3).

Of 519 eye care facilities, 455 facilities (87.7%) were offering patient care services exclusively. Only 17% (88/519) of eye care facilities offered training facilities for eye care professionals and eye bank services in addition to patient care.

Regarding the eye care workforce, there was a substantial increase in the number of ophthalmologists in both southern Indian states. There was an insufficient increase in MLOP to meet the need. There was a large jump in the number of eye care managers, mostly in NGO and private eye care facilities (Table 4).

Table 3. Increase in secondary and tertiary eye care facilities from 2002 to 2012 by sector.

Eye care facility sector	Facilities in 2002-2003, n	Facilities in 2012-2013, n	Increase, %	*P* value
Secondary				<.001
Government	34	48	41	
NGO[a]	88	139	58	
Private	76	253	233	
All secondary	198	440	122	
Tertiary				.009
Government	10	10	0	
NGO	17	26	53	
Private	9	43	378	
All tertiary	36	79	119	

[a]NGO: nongovernmental organization.

Table 4. Eye care workforce in the 2002-2012 period.

Job role	Andhra Pradesh, n		Telangana, n		Both states, n		Increase, %
	2002	2012	2002	2012	2002	2012	
Ophthalmologists							
Professor or senior consultant[a]	132	288	146	338	278	626	125
Assistant professor or junior consultant[b]	257	364	248	467	505	831	64
Ophthalmologists acting as superintendents or directors	69	148	83	107	152	255	67.8
All ophthalmologists	458	800	477	912	935	1712	83.1
Midlevel ophthalmic personnel (MLOP)							
Optometrists, refractionists, ophthalmic assistants, vision technicians	272	410	238	472	510	882	72.9
Ophthalmic nurses and general nurses working in eye care facilities	58	111	72	130	257	368	43.2
All MLOP	330	521	310	602	767	1250	63
Eye care managers	69	163	83	244	152	407	167.8

[a]Ophthalmologists with ≥10 years of experience.

[b]Ophthalmologists with ≤10 years of experience.

The ophthalmologist:population ratio ranged from 1:6309 in Hyderabad district, which is the capital area, to 1:193,822 in Nalgonda district (Table 5). This shows there was a maldistribution of ophthalmologists among the districts in the state. The ratio of optometrists and allied personnel to the population ranged from 1:66,209 in Ranga Reddy district to 1:221,173 in Guntur district. Overall, the ophthalmologist:population ratio in the state was 1:49,404, which appears to be optimal as per the VISION 2020 guidelines.

We looked at the number of eye care beds available for the population, and this improved from an average of 1:17,457 in 2002-2003 to an average of 1:13,877 in 2012-2013 (Table 6). There was also a lot of variation in the availability of eye care beds among the districts; for example, in Hyderabad district, 1 eye care bed was available for 3805 persons, compared with 1 eye care bed for 30,014 persons in Karimnagar. The total number of eye care beds increased from 4339 in 2002-2003 to 6103 in 2012-2013 (40.6% increase). On average, 1

ophthalmologist was available per 100,000 people/6 eye care beds in 2002-2003, which increased to an average of 2 ophthalmologists per 100,000 people/7 eye care beds in 2012-2013. A greater number of ophthalmologists per 100,000 population will improve the accessibility and availability of ophthalmologists to the public.

Table 5. Human resources in eye care in the districts of undivided Andhra Pradesh.

District name	Population, n		Ophthalmologists, n		Ophthalmologist:population ratio		MLOP[a], n		MLOP:population ratio	
	2002-2003[b]	2012-2013[c]	2002-2003	2012-2013	2002-2003	2012-2013	2002-2003	2012-2013	2002-2003	2012-2013
Adilabad	2,479,347	2,741,239	N/A[d]	22	N/A	1:124,601	N/A	24	N/A	1:114,218
Hyderabad	3,686,460	3,943,323	N/A	625	N/A	1:6309	N/A	12	N/A	1:328,610
Karim Nagar	3,477,079	3,776,269	N/A	42	N/A	1:89,911	N/A	31	N/A	1:121,815
Khammam	2,565,412	2,797,370	N/A	30	N/A	1:93,245	N/A	10	N/A	1:279,737
Mahbub Nagar	3,506,876	4,053,028	N/A	18	N/A	1:225,168	N/A	28	N/A	1:144,751
Medak	2,662,296	3,033,288	N/A	14	N/A	1:216,663	N/A	20	N/A	1:151,664
Nalgonda	3,238,449	3,488,809	N/A	18	N/A	1:193,822	N/A	27	N/A	1:129,215
Nizamabad	2,342,803	2,551,335	N/A	29	N/A	1:87,977	N/A	19	N/A	1:134,280
Ranga Reddy	3,506,670	5,296,741	N/A	99	N/A	1:53,502	N/A	80	N/A	1:66,209
Warangal	3,231,174	3,512,576	N/A	55	N/A	1:63,865	N/A	39	N/A	1:90,066
Anantapur	3,639,304	4,081,148	N/A	45	N/A	1:90,692	N/A	24	N/A	1:170,047
Chittoor	3,735,202	4,174,064	N/A	44	N/A	1:94,865	N/A	23	N/A	1:181,481
East Godavari	4,872,622	5,154,296	N/A	93	N/A	1:55,422	N/A	37	N/A	1:139,305
Guntur	4,405,521	4,887,813	N/A	41	N/A	1:119,214	N/A	22	N/A	1:222,173
Kadapa	2,573,481	2,882,469	N/A	23	N/A	1:125,324	N/A	20	N/A	1:144,123
Krishna	4,218,416	4,517,398	N/A	108	N/A	1:41,827	N/A	22	N/A	1:205,336
Kurnool	3,512,266	4,053,463	N/A	57	N/A	1:71,113	N/A	30	N/A	1:135,115
Nellore	2,659,661	2,963,557	N/A	58	N/A	1:51,095	N/A	22	N/A	1:134,707
Prakasam	3,054,941	3,397,448	N/A	47	N/A	1:72,286	N/A	34	N/A	1:99,924
Srikakulam	2,528,491	2,703,114	N/A	11	N/A	1:245,737	N/A	20	N/A	1:135,155
Visakhapatnam	3,789,823	4,290,589	N/A	171	N/A	1:25,091	N/A	23	N/A	1:186,547
Vizianagaram	3,789,823	2,344,474	N/A	15	N/A	1:156,298	N/A	23	N/A	1:101,933
West Godavari	3,796,144	3,936,966	N/A	47	N/A	1:83,765	N/A	23	N/A	1:171,172
All districts	7,572,7541	8,458,0777	858[e]	1712	1:88,260	1:49,404	450[e]	613	1:123,535	1:137,978

[a]MLOP: midlevel ophthalmic personnel.

[b]Census 2001 [11].

[c]Census 2011 [12].

[d]N/A: not available.

[e]Approximate number from supplementary records.

Table 6. Population and number of eye care beds by district.

District name	Population, n		Eye care beds, n		Eye care bed:population ratio	
	2002-2003	2012-2013	2002-2003	2012-2013	2002-2003	2012-2013
Adilabad	2,479,347	2,737,738	207	265	1:11,978	1:10,331
Hyderabad	3,686,460	4,010,238	855	1054	1:4312	1:3805
Karimnagar	3,477,079	3,811,738	102	127	1:34,089	1:30,014
Khammam	2,565,412	2,798,214	97	187	1:26,448	1:14,964
Mahbub Nagar	3,506,876	4,042,191	144	184	1:24,353	1:21,968
Medak	2,662,296	3,031,877	87	87	1:30,601	1:34,849
Nalgonda	3,238,449	3,483,648	198	228	1:16,356	1:15,279
Nizamabad	2,342,803	2,552,073	142	197	1:16,499	1:12,955
Ranga Reddy	3,506,670	5,296,396	127	242	1:27,612	1:21,886
Warangal	3,231,174	3,934,842	242	367	1:13,352	1:10,722
Anantapur	3,639,304	4,083,315	182	262	1:19,996	1:15,585
Chittoor	3,735,202	4,170,468	123	144	1:30,367	1:28,962
East Godavari	4,872,622	5,151,549	192	372	1:25,378	1:13,848
Guntur	4,405,521	4,889,320	207	277	1:21,283	1:17,651
Kadapa	2,573,481	2,884,524	152	297	1:16,931	1:9712
Krishna	4,218,416	4,529,009	102	170	1:41,357	1:26,641
Kurnool	3,512,266	4,046,601	107	162	1:32,825	1:24,979
Nellore	2,659,661	2,966,082	93	112	1:28,599	1:26,483
Prakasam	3,054,941	3,392,764	220	223	1:13,886	1:15,214
Srikakulam	2,528,491	2,699,471	147	267	1:17,201	1:10,110
Visakhapatnam	3,789,823	4,288,113	205	330	1:18,487	1:12,994
Vizianagaram	3,789,823	2,342,868	132	217	1:28,711	1:10,797
West Godavari	3,796,144	3,934,782	276	331	1:13,754	1:11,888
All districts	75,727,541	84,665,533	4339	6103	1:17,457	1:13,877

Discussion

Principal Findings

Estimates indicate there are 4.95 million people who are blind (0.36% of the total population), 35 million people who are visually impaired (2.55%), and 0.24 million children who are blind in India [13]. Cataract and refractive errors remain the major causes of blindness and visual impairment, respectively, in India [13-16]. Cataract is responsible for nearly two-thirds of the blindness load in the older population in India [1-4], and one-fifth of blindness is due to uncorrected refractive errors [1-3]. There have been significant improvements in the field of blindness prevention, management, and control since the "VISION 2020: The Right to Sight" initiative [17]. In view of this background, India needs a pool of well-qualified, skilled, and optimal eye care professionals and sufficient infrastructure to eliminate avoidable and needless blindness and visual impairment.

The global advisory committee for VISION 2020 recommended a set of criteria for human resources and infrastructure based on expert consensus of the number of cataract procedures that could be performed by a surgeon per year under optimal conditions and the number of beds required for the same per 1 million population [9]. It was assumed that at least 50 procedures per bed per year could be optimally performed. Based on these assumptions, the following norms were recommended: 1 ophthalmologist per 50,000 population, 1 MLOP per 50,000 population, and 1 eye care bed per 20,000 population.

In this study, the ophthalmologist:population ratio in 2002-2003 was 1:88,822, and in 2012-2013, it reached 1:51,416. The state had almost reached the optimal ophthalmologist:population ratio. Previous data show that the national average ophthalmologist:population ratio is 1:107,000, ranging from 1:9000 in some regions to 1:608,000 in some areas [9]. There was a decrease in the percentage of ophthalmologists in the government sector and virtually no change in the percentage of ophthalmologists in the NGO sector. In addition, there was a substantial increase in the number of ophthalmologists in the private sector from 2002-2003 to 2012-2013. Some of the ophthalmologists, who were mainly working in the private sector, offered their services for a few hours a day or 1 to 2 days a week to NGO eye care facilities, either free or for a fee. As

per our study definition, these ophthalmologists who were providing their services part-time for the NGO eye care facilities were treated as working in the private sector only. Hence, the number of ophthalmologists working in the NGO sector appears to be under-reported when compared with that of other sectors.

As per VISION 2020, there should be 20 ophthalmologists and 50 beds per 1 million population [18]. The importance of the ophthalmologist:population ratio is that it can serve as a guide to forecast ophthalmic manpower requirements [19]. As per the norm, the number of available eye care beds is sufficient, and there is no need to increase the number of eye care beds; in addition, there is a shift toward day surgeries for cataract [8].

The distribution of ophthalmologists was skewed toward urban areas. Due to the lack of educational facilities for their children and other lifestyle-related infrastructure in underdeveloped areas, ophthalmologists and private eye care facilities tend to be established in developed urban areas. In the Telangana region, the majority of the ophthalmologists were practicing in Hyderabad City, whereas in coastal Andhra, many of the ophthalmologists were practicing in the urban areas of Visakhapatnam and Vijayawada. Compared with the coastal Andhra region, this phenomenon of ophthalmologists working in urban areas was more pronounced in the Telangana region. As urban areas became more crowded with ophthalmologists, there was a trend that some ophthalmologists started their practices in smaller towns in 2012-2013. In 2002-2003, ophthalmologists were mainly present in the district headquarters and major population areas. This trend changed in 2012-2013 when more eye care facilities were opened in less populated areas.

Murthy et al [20] reported that 69% of ophthalmologists worked in the private and NGO sectors, while 31% were working in the government sector. In this study, 88% of ophthalmologists were working in the private and NGO sectors, and the remaining 12% were working in the government sector. In this study, the majority of the ophthalmologists in the government sector were working in teaching institutions rather than in district and subdistrict hospitals similar to that reported by Murthy et al [20]. In this study, we found the average number of surgeries performed by surgeons in the NGO sector was significantly higher than that in other sectors in both the baseline and target years. After the ophthalmologists in the NGO sector, ophthalmologists in the government sector were performing more surgeries than those in the private sector.

Ophthalmologists with less than 10 years of experience were performing more cataract surgeries than those with more than 10 years of experience (P=.001). This may be because some of the senior ophthalmologists were involved in teaching and research. This finding corroborates the fact that nonteaching ophthalmologists were performing more cataract surgeries than their teaching counterparts.

The state should ideally have 1693 MLOP for its population of 84.6 million. The state needs 1080 more MLOP to reach this number. The majority of the MLOP either were not trained in streak retinoscopy or did not have access to streak retinoscopes. There is a need for a strategy to ensure that all MLOP can perform streak retinoscopy.

There were many reasons for the increase in the number of both secondary and tertiary eye care facilities in all 3 sectors—government, NGO, and private—from 2002-2003 to 2012-2013. The number of eye care facilities as well as the number of eye care professionals increased during this period. The highest increase in eye care facilities (248%) was seen in the private sector due to the establishment of many institutions for eye care professionals in both government and NGO sectors. People trained at these institutes either were absorbed into the private sector or started their own practice, because there was no recruitment in the government sector or minimal opportunities in the NGO sector. This is the reason why the number of secondary eye care facilities increased more than tertiary eye care facilities. Another reason was, compared with other fields in medical practice, it is easier to start a solo practice in eye care, as it does not depend on cooperation from other medical streams. For example, to start a general surgery or orthopedics practice, one requires the services of an anesthetist. To start a pediatric practice, good laboratory services are required. Of the 519 eye care facilities functioning in 2012-2013, 253 (48.7%) were from the private sector. This was similar to the findings reported by Murthy et al [1], in which more than one-half of the eye care facilities belonged to the private sector.

Limitations

This study has some limitations. Most of the data collected through questionnaires were based on self-report, which might introduce bias due to memory recall or over or under-reporting of certain information. However, this was addressed by cross-checking the collected data with information from the supplementary sources mentioned in the Methods section.

Conclusion

Regarding human resources, there was a substantial increase in the number of ophthalmologists, particularly in the private sector. In fact, the percentage of ophthalmologists in the government sector decreased from the baseline year to the target year, whereas in the NGO sector, it remained the same.

Though all 3 sectors—government, NGO, and private—showed an increase in the number of eye care facilities from the baseline year to the target year, substantial increases were seen in the private sector and, to some extent, in the NGO sector. Most of the eye care facilities offered patient care services only. The outpatient services and inpatient services were also higher in 2012-2013 in all 3 sectors, but the NGO sector contributed a major share, followed by the private sector. Regarding outreach activities, the NGO sector dominated the services, to the extent of 80%-97%. One NGO facility collected the majority of eyes for corneal transplantation, and the remaining eye care facilities in the government, NGO, or private sector showed very little improvement in their collection of eyes.

Regarding eye care infrastructure, there was a 41% increase in the number of beds available for eye care, and this increase was mainly due to the NGO sector, followed by the private sector. The average number of surgeries per surgeon per annum was highest in the NGO sector, followed by the government sector. There was a major shortage of MLOP in the state to attain the ideal ratio of 1 MLOP per 50,000 population. To attain the ideal

number of MLOP, there is an urgent need to increase the number of training facilities for MLOP. Overall, the functioning of the DBCSs for planning and supervising district eye care programs was satisfactory.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Questionnaire for eye care facilities.
[XLSX File (Microsoft Excel File), 658 KB - ojphi_v16i1e50921_app1.xlsx]

Multimedia Appendix 2
Questionnaire for ophthalmologists.
[XLSX File (Microsoft Excel File), 485 KB - ojphi_v16i1e50921_app2.xlsx]

Multimedia Appendix 3
Questionnaire for midlevel ophthalmic personnel.
[XLSX File (Microsoft Excel File), 494 KB - ojphi_v16i1e50921_app3.xlsx]

Multimedia Appendix 4
Questionnaire for district blindness control societies (DBCSs) and nongovernmental organizations (NGOs) in eye care.
[XLSX File (Microsoft Excel File), 463 KB - ojphi_v16i1e50921_app4.xlsx]

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Abbreviations

APRTSS: Andhra Pradesh Right to Sight Society
DBCS: district blindness control society
MLOP: midlevel ophthalmic personnel
NGO: nongovernmental organization

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Original Paper

Electronic Health Records for Population Health Management: Comparison of Electronic Health Record–Derived Hypertension Prevalence Measures Against Established Survey Data

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Abstract

Background: Hypertension is the most prevalent risk factor for mortality globally. Uncontrolled hypertension is associated with excess morbidity and mortality, and nearly one-half of individuals with hypertension do not have the condition under control. Data from electronic health record (EHR) systems may be useful for community hypertension surveillance, filling a gap in local public health departments' community health assessments and supporting the public health data modernization initiatives currently underway. To identify patients with hypertension, computable phenotypes are required. These phenotypes leverage available data elements—such as vitals measurements and medications—to identify patients diagnosed with hypertension. However, there are multiple methodologies for creating a phenotype, and the identification of which method most accurately reflects real-world prevalence rates is needed to support data modernization initiatives.

Objective: This study sought to assess the comparability of 6 different EHR-based hypertension prevalence estimates with estimates from a national survey. Each of the prevalence estimates was created using a different computable phenotype. The overarching goal is to identify which phenotypes most closely align with nationally accepted estimations.

Methods: Using the 6 different EHR-based computable phenotypes, we calculated hypertension prevalence estimates for Marion County, Indiana, for the period from 2014 to 2015. We extracted hypertension rates from the Behavioral Risk Factor Surveillance System (BRFSS) for the same period. We used the two 1-sided *t* test (TOST) to test equivalence between BRFSS- and EHR-based prevalence estimates. The TOST was performed at the overall level as well as stratified by age, gender, and race.

Results: Using both 80% and 90% CIs, the TOST analysis resulted in 2 computable phenotypes demonstrating rough equivalence to BRFSS estimates. Variation in performance was noted across phenotypes as well as demographics. TOST with 80% CIs demonstrated that the phenotypes had less variance compared to BRFSS estimates within subpopulations, particularly those related to racial categories. Overall, less variance occurred on phenotypes that included vitals measurements.

Conclusions: This study demonstrates that certain EHR-derived prevalence estimates may serve as rough substitutes for population-based survey estimates. These outcomes demonstrate the importance of critically assessing which data elements to include in EHR-based computer phenotypes. Using comprehensive data sources, containing complete clinical data as well as data representative of the population, are crucial to producing robust estimates of chronic disease. As public health departments look toward data modernization activities, the EHR may serve to assist in more timely, locally representative estimates for chronic disease prevalence.

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KEYWORDS

public health informatics; surveillance; chronic conditions; electronic health record; health management; hypertension; surveillance; public health; prevalence; population-based survey

Introduction

Hypertension is the most prevalent risk factor for mortality throughout the world [1]. The condition is characterized by elevated systolic blood pressure (>140 mm Hg) or diastolic blood pressure (>90 mm Hg) [2]. An estimated 1 out of 3 adults in the United States has been diagnosed with hypertension, which translates to almost 75 million Americans [2]. This results in substantial use of health care services and medications, as well as lost wages [3,4]. The estimated direct and indirect costs of hypertension exceed US $48 billion each year in the United States [5]. In concurrence with economic loss, uncontrolled hypertension is associated with excess morbidity and mortality, and nearly one-half of individuals with hypertension do not have the condition under control [2].

Uncontrolled hypertension is associated with an increased risk of coronary heart disease, stroke, and kidney disease, which are the 3 leading causes of death in the United States [5]. Hypertension is a comorbid condition for nearly 70% of individuals who have their first myocardial infarction and almost 80% of those who have their first stroke [6]. Additionally, hypertension is associated with an excess risk of severe COVID-19 illness with a risk of hospitalization more than double that of nonhypertensive individuals [7]. The association with increased morbidity and mortality is a critical public health concern given the high prevalence of the condition. To address this increasing public health concern, public health programs and policies aimed at reducing morbidity, mortality, and costs associated with hypertension are required. To create these policies, public health departments are reliant on timely, accurate, stable estimates of disease prevalence. This is required both for timely detection and effective evaluation.

Identifying the prevalence of hypertension as well as measuring hypertension control at the community level remains a challenge for local health departments. While clinical guidelines from the National Quality Forum and others (eg, Centers for Disease Control and Prevention and Healthcare Effectiveness Data and Information Set) exist [8], measurement happens at the level of a provider or health system as opposed to the community. Public health departments typically rely on surveys for measuring community-level estimates of hypertension. However, surveys have known limitations including cost and timeliness due to long gaps between data collection and when results are available. Additionally, the local samples are insufficiently small for precise estimates within communities and subpopulations (ie, wide CIs). Therefore, local health departments seek alternative methods for obtaining timely, complete, accurate, and precise information about the prevalence of chronic conditions such as hypertension and measures of control for individuals with chronic illness.

Since the passing of the Health Information Technology for Economic and Clinical Health Act of 2009, electronic health record (EHR) systems have become more common, representing a potential data source for chronic disease surveillance. As of 2016, over 70% of ambulatory providers use EHR systems [9]. As health care organizations increasingly capture data from routine health care visits in EHR systems, national initiatives, including the digital Learning Health System of the National Academy of Medicine [10] and the Robert Wood Johnson Foundation's data for health [11], aim to leverage such data to improve the delivery of health care and community health outcomes. The hope is that by leveraging existing digital data sources, public health agencies may access more timely and precise information to assess and improve health in their communities.

While there exists much optimism about EHR systems' ability to provide timely, complete, and accurate estimates for hypertension and other chronic diseases, evidence to date has been mixed. In a systematic review of the quality of data used for quality-of-care measurement, the completeness of data varied "substantially across studies," ranging from 0.1% to 51% for blood pressure and from 10% to 38% for smoking status [12]. Missing data ranged between 24% and 38% for cholesterol; 3% and 31% for blood pressure; and 5% and 23% for blood glucose (hemoglobin A_{1C}) [12].

Despite these challenges, EHR data may be useful for community health surveillance. More recent work by the New York City (NYC) Department of Mental Health and Hygiene shows promising results in using EHR data for measuring the prevalence and control of chronic diseases [13,14]. By querying EHR systems in primary care practices representing 15% of the city's population, the health department found prevalence rates were in line with community-based surveys for diabetes, obesity, hypertension, and smoking even when the survey respondents were limited to those who had received primary care in the prior year (NYC Health and Nutrition Examination Survey and the NYC Community Health Survey [15]). More recent studies give hope that EHR data could be used by health departments to improve the timeliness and precision of their community health assessments [16-18].

Given limited prior evidence, we sought to validate computable phenotypes for hypertension using EHR data available through a community-based health information exchange (HIE) network. The use of HIE data was selected to examine data representing a geographic community rather than the population of a single health system. Our goal is to identify methods that can be leveraged by health departments for the surveillance of chronic illnesses and the calculation of control measures.

Accordingly, the objective of this analysis was to analyze the equivalence of EHR-based methods for deriving the prevalence of hypertension compared to an established community survey. To facilitate this analysis, 6 distinct EHR-based phenotypes for hypertension were used to establish prevalence rates in 1 county. These rates were then tested for equivalency with the prevalence calculated by a national survey. We hypothesized that at least 1 of the selected phenotypes would produce equivalent estimates.

Methods

Data Sources

Indiana Network for Patient Care

The primary data source was the Indiana Network for Patient Care (INPC), a regional HIE with data covering emergency department visits, hospital admissions, and large outpatient health care clinics from across the state. Data were supplemented with direct extracts from 1 health system to provide additional vital measurements and medication data that were not currently shared with the INPC. For this study, the focus was Marion County, Indiana, which is the county containing the largest city, Indianapolis, and we leveraged 3 of the 5 major health systems. Using the 3 health systems ensures that approximately 780,000 (80%) of the population of Marion County was captured for this study. According to the 2010 census, Marion County had a resident population of 977,203 with a racial composition of 30% Black or African American, 11.6% Hispanic, and 61.9% White.

Data were extracted for all adults (at least aged 18 years as of January 1, 2014) living in Marion County who sought care (outpatient, inpatient, or emergency department encounters) at 1 of the 3 large integrated delivery networks that connect to the INPC between January 1, 2014, and December 31, 2015. We used 2 years of data to capture a representative number of clinical encounters since individual health care use may not occur annually. This period was used due to the availability of comprehensive data from 3 of the 5 major health systems in the area. Given the period covered in this data set, the data do not establish current prevalence rates for Marion County but rather serve as an example for the surveillance methodology deployed. The algorithms to detect hypertension in the community were implemented on the data set, which contained diagnosis codes, vital measurements, and medications.

Behavioral Risk Factor Surveillance System

For the gold standard comparison, we used the Behavioral Risk Factor Surveillance System (BRFSS)—the US national survey related to health-related behaviors, chronic health conditions, and the use of preventive services. The prevalence estimates produced by the BRFSS are carefully developed, validated, and weighted to minimize biases in response or coverage [19]. The BRFSS collects data in all 50 states, the District of Columbia, and territories. However, for small geographics (eg, county) or population subgroups, the BRFSS is imprecise with large CIs. For this study, the data related to the 2015 prevalence of hypertension in Marion County, Indiana, was used.

Measures

To facilitate analysis, BRFSS prevalence measures were compared to EHR-based measures extracted from the HIE. The 2015 BRFSS results include an overall hypertension prevalence rate as well as rates by age, race, and gender for Marion County. These measures were extracted from the US Centers for Disease Control and Prevention website [20].

The computable phenotypes used for this study were previously developed and reported separately [21]. Briefly, 6 phenotypes for hypertension were developed using algorithms (or rules) executed using 1 or more types of structured EHR data. These rules were validated using chart review to calculate sensitivity, specificity, and positive predictive value [21]. Defining multiple permutations allowed for evaluating the best-performing phenotype. The phenotypes are as follows:

- P1: clinical diagnostic codes only (in which an individual has either 1 inpatient or 1 outpatient encounter documenting a hypertension diagnosis)
- P2: vital statistics only (in which an individual has at least 1 blood pressure reading above the hypertension threshold)
- P3: vital statistics only (in which an individual has at least 2 blood pressure readings above the hypertension threshold)
- P4: clinical diagnosis and vital statistics (P1 and P2)
- P5: clinical diagnosis and vital statistics (P1 and P3)
- P6: Inclusive of P1-P5 and medications (P1, P2, or the use of hypertension medication)

Using the 6 different EHR-based computable phenotypes, we calculated hypertension prevalence estimates from data for residents of Marion County, Indiana, from the years 2014 and 2015. Prevalence was calculated as the number of persons with data satisfying the given phenotype divided by the number of persons with any HIE record for a health care encounter.

Ethical Considerations

Exempt approval for this study was received by the Indiana University Institutional Review Board (1701925087).

Statistical Analysis

Demographics for the INPC-derived cohort were calculated using P6, which is the broadest and most sensitive phenotype [21]. Using the estimates for Marion County outlined above, equivalency testing was performed. Equivalence testing examines whether 2 independent statistics are similar enough to be treated as though they are equivalent. The null hypothesis is that the statistics differ by at least a specified amount. If the test results in a P value <.05, then the null hypothesis is rejected with a conclusion that the 2 statistics differ by less than the specified amount. We used the two 1-sided *t* test (TOST) to test equivalence between BRFSS- and INPC-based prevalence estimates. The TOST was performed at the overall level as well as stratified by age, gender, and race. The TOST was performed with 80% and 90% CI. As with other large national surveys, BRFSS estimates have wide CIs. Accordingly, widening the TOST analysis threshold was considered to account for the wide CIs within the BRFSS data set compared to the small CIs associated with the larger INPC data set. The 95% CI of the BRFSS overall hypertension estimates for Marion County is 7-7.5 percentage points wide. The stratified BRFSS hypertension rates are slightly wider. Accordingly, our specified amounts align with the CIs for the BRFSS. This study used SAS (version 9.4; SAS Institute Inc) and Excel 365 (Microsoft) for analyses.

Results

The demographics for the BRFSS and INPC cohorts are presented in Table 1. The EHR-based phenotypes were calculated from INPC data for 548,232 patients, which was the number of adult patients with at least 1 clinical encounter during

the period. Overall, the cohort was 61.2% (n=335,548) women and 27% (n=148,117) Black or African American. Of the total INPC-derived cohort, 210,764 (38.4%) patients were identified as hypertensive by phenotype P6, which is the broadest—and most sensitive—definition of hypertension according to Valvi et al [21]. The INPC-derived hypertension cohort was 57.6% (121,307/210,764) women and 33.2% (70,060/210,764) Black or African American. The BRFSS-derived hypertensive cohort was 55.2% (197/357) women and 17.6% (63/357) Black or African American. The INPC cohort was more racially diverse than the BRFSS cohort overall. The BRFSS cohort had less representation of the younger population and overrepresentation of those aged 65 years and older.

Table 1. Cohort demographics[a].

Demographics	Overall population		Hypertensive population	
	BRFSS[b] (n=934), n (%)	INPC[c] (n=548,232), n (%)	BRFSS (n=357), n (%)	INPC (n=210,764), n (%)
Gender				
Women	524 (56.1)	335,548 (61.2)	197 (55.2)	121,307 (57.6)
Men	410 (43.9)	212,684 (38.8)	160 (44.8)	89,457 (42.4)
Race				
Black	152 (16.7)	148,117 (27)	63 (17.6)	70,060 (33.2)
White	702 (75.2)	308,213 (56.2)	273 (76.6)	120,832 (57.3)
Other	80 (8.6)	91,902 (16.8)	21 (5.9)	19,872 (9.4)
Age group (y)				
18-39	197 (21.1)	214,655 (39.2)	24 (6.7)	52,777 (25)
40-64	406 (43.5)	240,064 (43.8)	136 (38.1)	101,416 (48.1)
65+	331 (35.4)	93,513 (17)	197 (55.2)	56,571 (26.8)

[a]Table 1 contains gender, race, and age counts and percentages for each of the cohorts. The cohorts include the overall population for both BRFSS and INPC as well as the hypertensive population.

[b]BRFSS: Behavioral Risk Factor Surveillance System.

[c]INPC: Indiana Network for Patient Care.

The TOST analysis was undertaken at both the 90% and 80% CIs. The TOST analysis at the 90% CI resulted in 2 phenotypes (P2 and P5) having statistically significant results, indicating their equivalency to BRFSS estimates, or, more specifically, given the assumptions of this analysis, it is at least 90% likely that hypertension prevalence estimates from the BRFSS and phenotypes P2 and P5 will differ by no more than 5 percentage points. However, performance in the stratified groups was much poorer with statistical significance for women only in phenotypes P1 and P4. By the nature of TOST, the wider an estimate's CI, the less chance that the null hypothesis will be rejected; some stratified groups have CIs so wide that their TOSTs had zero power. The analysis at the 80% CI yielded statistically significant results across multiple phenotypes. At the 80% CI, phenotypes P2, P3, and P5 showed equivalency overall, with P2 and P5 also showing equivalence in 9 of the demographic subsets and P3 showing equivalence in 7 of those subsets. Tables 2-4 depict the full 80% CI analysis for P2, P3, and P5. All remaining analyses are included in the Multimedia Appendices 1 and 2.

Table 2. Full 80% CI analysis for phenotype 2, with overall ≥1 vitals indicated. This table depicts all analytical results for P2 at the 80% CI.

Characteristic	BRFSS[a,b], n/N (%)	INPC[c,d], n/N (%)	%Δ[e] (Δ80% CI)
Overall	235/934 (28.4)	159,330/548,298 (29.1)	0.7 (–1.8 to 3.1)[f]
Gender			
Men	127/410 (31)	66,758/212,684 (31.4)	0.4 (–10.6 to 11.4)
Women	137/524 (26.1)	92,570/335,548 (27.6)	1.5 (–6.6 to 9.6)[f]
Race			
Black or African American	54/152 (35.7)	57,026/148,120 (38.5)	2.8 (–3.3 to 8.9)[f]
White	187/702 (26.6)	89,205/308,224 (28.9)	2.3 (–0.3 to 5)[f]
Other	18/80 (22.6)	13,099/91,954 (14.2)	–8.4 (–15 to –1.7)
Age group (y)			
18-39	21/197 (10.8)	49,634/214,685 (23.1)	12.3 (9.2 to 15.4)
40-64	133/406 (32.8)	76,795/240,084 (32)	–0.8 (–4.5 to 2.9)[f]
65+	204/331 (61.6)	31,238/88,569 (35.3)	–26.3 (–30 to –22.6)
Men by race			
Black or African American	24/60 (40.6)	22,226/56,004 (39.7)	–0.9 (–7.1 to 5.2)[f]
White	91/314 (29.1)	38,832/120,672 (32.2)	3.1 (–1 to 7.2)[f]
Other	9/36 (24.1)	5,700/36,008 (15.8)	–8.3 (–18.1 to 1.6)
Women by race			
Black or African American	30/92 (32.2)	34,800/92,113 (37.8)	2.5 (–0.9 to 5.8)[f]
White	95/388 (24.4)	50,373/187,541 (26.9)	–7.6 (–16.3 to 1.1)
Other	9/44 (20.8)	7,379/55,894 (13.2)	5.6 (–2.4 to 13.5)
Men by age group (y)			
18-39	18/99 (18.5)	20,478/77,992 (26.3)	7.8 (2.3 to 13.3)
40-64	56/178 (31.2)	33,928/98,778 (34.3)	3.1 (–2.2 to 8.5)[f]
65+	90/133 (67.4)	11,957/34,606 (34.6)	–32.8 (–38.6 to –27.1)
Women by age group (y)			
18-39	3/98 (3.4)	29,155/136,663 (21.3)	11.5 (15.6 to 20.2)
40-64	78/228 (34.2)	42,866/141,286 (30.3)	–3.9 (–9.1 to 1.4)[f]
65+	114/198 (57.5)	19,281/53,954 (35.7)	–21.8 (–29.1 to –14.5)

[a]BRFSS: Behavioral Risk Factor Surveillance System.

[b]Sample size=934.

[c]Indiana Network for Patient Care.

[d]Sample size=548,298.

[e]Δ: mean difference.

[f]Behavioral Risk Factor Surveillance System and Indiana Network for Patient Care phenotypes were determined as statistically equivalent by the two 1-sided *t* test method.

Table 3. Phenotype 3, overall ≥2 vitals indicated. This table depicts the full analytical results for P3 at the 80% CI.

Characteristic	BRFSS[a,b], n/N (%)	INPC[c,d], n/N (%)	%Δ[e] (Δ80% CI)
Overall	235/934 (28.4)	122,051/548,298 (22.3)	–6.1 (–8.6 to –3.7)[f]
Gender			
Men	127/410 (31)	50,997/212,684 (24)	–7 (–18 to 4)
Women	137/524 (26.1)	71,053/335,548 (21.2)	–4.9 (–13 to 3.1)
Race			
Black or African American	54/152 (35.7)	45,513/148,120 (30.7)	–5 (–11.1 to 1.2)
White	187/702 (26.6)	67,594/308,224 (21.9)	–4.7 (–7.4 to –2)[f]
Other	18/80 (22.6)	8,944/91,954 (9.7)	–12.9 (–19.5 to –6.2)
Age group			
18-39	21/197 (10.8)	34,282/214,685 (16)	5.2 (2.1 to 8.2)[f]
40-64	133/406 (32.8)	60,657/240,084 (25.3)	–7.5 (–11.2 to –3.8)
65+	204/331 (61.6)	25,699/88,569 (29)	–32.6 (–36.3 to –28.9)
Men by race			
Black or African American	24/60 (40.6)	17,678/56,004 (31.6)	–9 (–15.2 to –2.9)
White	91/314 (29.1)	29,448/120,672 (24.4)	–4.7 (–8.8 to –0.6)[f]
Other	9/36 (24.1)	3,871/36,008 (10.8)	–13.3 (–23.2 to –3.5)
Women by race			
Black or African American	30/92 (32.2)	27,835/92,113 (20.3)	–4.1 (–7.4 to –0.7)[f]
White	95/388 (24.4)	38,146/187,541 (9.1)	–11.7 (–20.4 to –3)
Other	9/44 (20.8)	5,072/55,894 (30.2)	–2 (–9.9 to 6)[f]
Men by age group			
18-39	18/99 (18.5)	13,875/77,992 (17.8)	–0.7 (–6.2 to 4.8)[f]
40-64	56/178 (31.2)	27,100/98,778 (27.4)	–3.8 (–9.1 to 1.6)[f]
65+	90/133 (67.4)	9,694/34,606 (28)	–39.4 (–45.1 to –33.6)
Women by age group			
18-39	3/98 (3.4)	20,407/136,663 (14.9)	11.5 (9.2 to 13.8)
40-64	78/228 (34.2)	33,556/141,286 (23.8)	–10.4 (–15.7 to –5.2)
65+	114/198 (57.5)	16,005/53,954 (29.7)	–27.8 (–35.1 to –20.5)

[a]BRFSS: Behavioral Risk Factor Surveillance System.

[b]Sample size=934.

[c]Indiana Network for Patient Care.

[d]Sample size=548,298.

[e]Δ: mean difference.

[f]Behavioral Risk Factor Surveillance System and Indiana Network for Patient Care phenotypes were determined as statistically equivalent by the two 1-sided *t* test method.

Table 4. Phenotype 5, overall ≥1 clinical diagnosis or ≥1 vitals indicated. This table depicts the full analytical results for P5 at the 80% CI.

Characteristic	BRFSS[a,b], n/N (%)	INPC[c,d], n/N (%)	%Δ[e] (Δ80% CI)
Overall	235/934 (28.4)	151,645/548,298 (27.7)	–0.7 (–3.2 to 1.7)[f]
Gender			
Men	127/410 (31)	63,992/212,684 (30.1)	–0.9 (–11.9 to 10.1)
Women	137/524 (26.1)	87,652/335,548 (26.1)	0 (–8 to 8.1)[f]
Race			
Black or African American	54/152 (35.7)	71,464/148,120 (48.2)	12.5 (6.4 to 18.7)
White	187/702 (26.6)	137,674/308,224 (44.7)	18.1 (15.4 to 20.8)
Other	18/80 (22.6)	31,158/91,954 (33.9)	11.3 (4.6 to 17.9)
Age group (y)			
18-39	21/197 (10.8)	36,157/214,685 (16.8)	6 (3 to 9.1)[f]
40-64	133/406 (32.8)	74,864/240,084 (31.2)	–1.6 (–5.3 to 2.1)[f]
65+	204/331 (61.6)	38,356/88,569 (43.3)	–18.3 (–22 to –14.6)
Men by race			
Black or African American	24/60 (40.6)	21,091/56,004 (37.7)	–2.9 (–9.1 to 3.2)[f]
White	91/314 (29.1)	37,622/120,672 (31.2)	2.1 (–2 to 6.2)[f]
Other	9/36 (24.1)	5,268/36,008 (14.6)	–9.5 (–19.3 to 0.4)
Women by race			
Black or African American	30/92 (32.2)	30,285/88,868 (34.1)	1.9 (–5.1 to 1.6)[f]
White	95/388 (24.4)	41,094/181,412 (22.7)	–1.7 (–6.1 to 9.8)[f]
Other	9/44 (20.8)	5,959/54,954 (10.8)	–10 (–18.7 to –1.3)
Men by age group (y)			
18-39	18/99 (18.5)	14,819/77,992 (19)	0.5 (–5 to 6)[f]
40-64	56/178 (31.2)	33,567/98,778 (34)	2.8 (–2.6 to 8.2)[f]
65+	90/133 (67.4)	15,011/34,606 (43.4)	–24 (–29.8 to –18.3)
Women by age group (y)			
18-39	3/98 (3.4)	21,331/136,663 (15.6)	12.2 (9.9 to 14.5)
40-64	78/228 (34.2)	41,296/141,286 (29.2)	–5 (–10.2 to 0.3)
65+	114/198 (57.5)	23,345/53,954 (43.3)	–14.2 (–21.5 to –6.9)

[a]BRFSS: Behavioral Risk Factor Surveillance System.

[b]Sample size=934.

[c]Indiana Network for Patient Care.

[d]Sample size=548,298.

[e]Δ: mean difference.

[f]Behavioral Risk Factor Surveillance System and Indiana Network for Patient Care phenotypes were determined as statistically equivalent by the two 1-sided *t* test method.

Discussion

Principal Findings

Our study examined the prevalence estimates of 6 distinct EHR-based phenotypes to ascertain whether EHR-derived estimates are equivalent to estimates produced by survey methods. The 2 clinical phenotypes (P2 and P5) relying primarily on vital statistics data showed the closest equivalence to BRFSS hypertension prevalence estimates. This suggests that clinical variables, such as blood pressure readings, are important in classifying hypertension cases when compared to national survey data. However, clinical measurements are often missing from national surveys (eg, BRFSS). When clinical measurements are present (eg, the National Health and Nutrition Examination Survey), the survey possesses an even smaller

sample size and is frequently more costly. Establishing robust local prevalence estimates may require local health departments to capture blood pressure measurements, which is cost prohibitive. EHR data may provide a more economical approach to the collection of clinical measurements. Additionally, EHRs can supply these measurements regularly forgoing the need for additional, specific public health data collection efforts.

Interestingly, phenotypes that relied on diagnosis code data performed less robustly. Previous studies have demonstrated the underreporting of conditions when relying on diagnostic codes alone [22-24]. Accordingly, it is possible that diagnostic codes themselves are not sensitive enough for identification of hypertension. Further, 1 possible reason for this is the type of encounter for which an individual is seen. For example, if the patient is being seen primarily in emergency or inpatient settings, a diagnosis of hypertension may not be coded, but the vital measurements would be available.

In our results, P6, which is the broadest and most sensitive definition of hypertension [21], did not align with the BRFSS at the overall population level. The hypertension BRFSS instrument item asks "has a doctor told you that you have hypertension?" [20]. This allows for variability in interpretation and may include individuals with a single elevated blood pressure incident or someone who is prehypertensive. Accordingly, it is logical that a computable phenotype using a combination of clinical data elements would be more sensitive to a diagnosis of hypertension but not to the broad question posed by the BRFSS. However, the phenotypes using a variety of clinical measurements may be a more robust measurement of hypertension for local health departments to deploy.

The results showcase the importance of the inclusion of vital statistics, which proved more sensitive for overall comparison and certain subpopulations when the CI threshold was lower. The results of P6 being associated with lower CIs were not surprising given the smaller sample sizes inherent in analyses of subpopulations. Compared to estimates from survey data, more numerous records available in the HIE or multiple EHR systems would allow for smaller CIs in estimates about subpopulations.

While not all algorithms demonstrated equivalency, 2 of the phenotypes demonstrated the potential for EHR data to provide prevalence estimates that are likely to be within 10 percentage points of BRFSS estimates. Accordingly, the use of EHR data may be a better option to estimate disease burden than costly community health surveys. EHR data have several benefits. First, EHR-derived prevalence estimates are timelier. This methodology can be implemented regularly (eg, quarterly and semiannually) to address the needs of the community compared to national surveys. National surveys are typically conducted annually and require time for postprocessing for data. These conditions result in delayed estimates, making the data untimely for certain population health questions. For certain conditions and interventions, this may prove useful for the identification of community needs as well as the timely assessment of community-level interventions. For example, we are using these methods to estimate changes in childhood obesity in multiple urban neighborhoods that received community-level interventions to address childhood obesity [25].

Second, the EHR-derived measures can be tailored to the specific needs of local health departments. Working in coordination with health care systems or HIE networks, local health departments may arrange to receive the data most relevant to their specific question rather than using proxy constructs from national data. Additionally, the EHR-based measures were manually validated and demonstrated to be of high quality, showing strong specificity and positive predictive values [21]. As reported in the results, the computable phenotypes identified a higher prevalence for the Black or African American community. Some of this variation could be attributed to the overrepresentation of inner-city health system patients within the County. However, the demographic analysis supports the premise that the BRFSS may be underrepresentative of the Black or African American population. This argument may be bolstered by the higher prevalence of subpopulations represented within the INPC demographics, both the overall cohort and the hypertension cohort. High-quality estimates, partnered with customization to local needs, will ultimately provide more robust measures for the local health departments.

Further, 1 limitation in the broader use of this methodology is most public health agencies' lack of legal authority to require reporting of data about chronic conditions. Currently, hospitals are not required to report clinical measurements or metrics related to chronic diseases, such as hypertension, to public health authorities beyond discharge data. Discharge data primarily consist of diagnostic codes, which may not reliably capture chronic disease burden as discussed above. Currently, the reporting of these data is voluntary and, therefore, unlikely to occur given the resources, human, and technological requirements to do so on the part of providers. However, HIE networks (such as INPC) have existing infrastructures that can be leveraged to address community surveillance needs. Data are already aggregated across health care systems and providers within the community, addressing a large amount of the work required to implement surveillance of chronic conditions. This analysis suggests support for leveraging HIE networks in the community for chronic disease surveillance.

The widening use of the Fast Healthcare Interoperability Resources standard and the Trusted Exchange Framework and Common Agreement for health data exchange may also increase public health agencies' opportunity to access EHR data [26,27]. There are still barriers to the full adoption of HIE networks into the public health environment, such as infrastructure [28] and data quality [29]. However, the COVID-19 pandemic revealed the role HIE could play in support of public health needs [17]. This is increasingly becoming important given the burden of post–COVID-19 conditions [30] and the potential increase in chronic conditions after the pandemic. Surveillance of chronic conditions is critical to public health practice. The efforts to modernize the nation's public health infrastructure, which are currently underway, should consider the important role HIE networks can play in support of chronic disease surveillance. Admittedly, future work will involve the implementation of HIE networks in those areas of the United States where they are not currently present.

A second limitation is the inconsistent and imprecise equivalency we have demonstrated between the HIE and BRFSS estimates. The BRFSS estimates themselves are fairly imprecise even for a population of about 1 million, as in Marion County, and so make a weak "gold standard," especially for subpopulations. Conversely, EHR data only reflect persons with health care encounters, and persons with frequent visits are more likely to have enough EHR data to satisfy some phenotype definition. With health care use varying by health status, race, age, employment, and other factors, EHR data would need adjustment for systematic biases before being interpreted as representative of the general community or subpopulations of interest. Further research would reveal what adjustments can improve how well EHR-based estimates approximate population health statistics. This study is subject to limitations related to the quantity and type of available data. Equivalence may be improved by a more complete capture of an area's health care providers, especially in ambulatory and primary care settings. Improved data capture would increase the EHR-based prevalence estimates. Data might be weighted according to patient characteristics, such as race, age, gender, or type of health insurance, allowing estimates to be adjusted to be more representative of the general population.

As noted above, this study is subject to limitations related to data availability, namely the period for which comprehensive data was available. There have been advancements in EHR adoption and use in the period from 2014 to now. EHR and HIE adoption will continue to be advanced by data modernization activities, which have in turn been spurred by gaps identified in the COVID-19 pandemic. The data availability of important measurements such as vitals, medications, and diagnoses will likely become routinely captured and shared as part of these activities. This suggests, and more recent literature suggests, that the accuracy of computable phenotypes may improve with these advancements [31,32].

Conclusions

This study demonstrates the feasibility of using EHR-derived prevalence estimates as rough substitutes for population-based survey estimates at the community level. It highlights the importance of critically assessing which data elements to include when deriving the EHR-based estimates. Using comprehensive data sources, containing complete clinical data as well as data representative of the population, may enhance local estimates. The number of people represented in EHR data versus survey data may allow for locally accurate EHR-based measurements of subpopulations. This is critical when considering health disparities as more robust measurements for subpopulations may enable targeted public health interventions.

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Data Availability

The data sets generated or analyzed during this study are not publicly available due to privacy and governance concerns but are available from the corresponding author upon reasonable request and with the completion of appropriate governance.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Two 1-sided *t* test analyses at 80% CI.
[DOCX File , 35 KB - ojphi_v16i1e48300_app1.docx]

Multimedia Appendix 2
Two 1-sided *t* test analyses at 90% CI.
[DOCX File , 30 KB - ojphi_v16i1e48300_app2.docx]

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Abbreviations

BRFSS: Behavioral Risk Factor Surveillance System
EHR: electronic health record
HIE: health information exchange
INPC: Indiana Network for Patient Care
NYC: New York City
TOST: two 1-sided *t* test

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Original Paper

Effect of Long-Distance Domestic Travel Ban Policies in Japan on COVID-19 Outbreak Dynamics During Dominance of the Ancestral Strain: Ex Post Facto Retrospective Observation Study

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Abstract

Background: In Japan, long-distance domestic travel was banned while the ancestral SARS-CoV-2 strain was dominant under the first declared state of emergency from March 2020 until the end of May 2020. Subsequently, the "Go To Travel" campaign travel subsidy policy was activated, allowing long-distance domestic travel, until the second state of emergency as of January 7, 2021. The effects of this long-distance domestic travel ban on SARS-CoV-2 infectivity have not been adequately evaluated.

Objective: We evaluated the effects of the long-distance domestic travel ban in Japan on SARS-CoV-2 infectivity, considering climate conditions, mobility, and countermeasures such as the "Go To Travel" campaign and emergency status.

Methods: We calculated the effective reproduction number R(t), representing infectivity, using the epidemic curve in Kagoshima prefecture based on the empirical distribution of the incubation period and procedurally delayed reporting from an earlier study. Kagoshima prefecture, in southern Japan, has several resorts, with an airport commonly used for transportation to Tokyo or Osaka. We regressed R(t) on the number of long-distance domestic travelers (based on the number of airport limousine bus users provided by the operating company), temperature, humidity, mobility, and countermeasures such as state of emergency declarations and the "Go To Travel" campaign in Kagoshima. The study period was June 20, 2020, through February 2021, before variant strains became dominant. A second state of emergency was not declared in Kagoshima prefecture but was declared in major cities such as Tokyo and Osaka.

Results: Estimation results indicated a pattern of declining infectivity with reduced long-distance domestic travel volumes as measured by the number of airport limousine bus users. Moreover, infectivity was lower during the "Go To Travel" campaign and the second state of emergency. Regarding mobility, going to restaurants, shopping malls, and amusement venues was associated with increased infectivity. However, going to grocery stores and pharmacies was associated with decreased infectivity. Climate conditions showed no significant association with infectivity patterns.

Conclusions: The results of this retrospective analysis suggest that the volume of long-distance domestic travel might reduce SARS-CoV-2 infectivity. Infectivity was lower during the "Go To Travel" campaign period, during which long-distance domestic travel was promoted, compared to that outside this campaign period. These findings suggest that policies banning long-distance domestic travel had little legitimacy or rationale. Long-distance domestic travel with appropriate infection control measures might not increase SARS-CoV-2 infectivity in tourist areas. Even though this analysis was performed much later than the study period, if we had performed this study focusing on the period of April or May 2021, it would likely yield the same results. These findings might be helpful for government decision-making in considering restarting a "Go To Travel" campaign in light of evidence-based policy.

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KEYWORDS

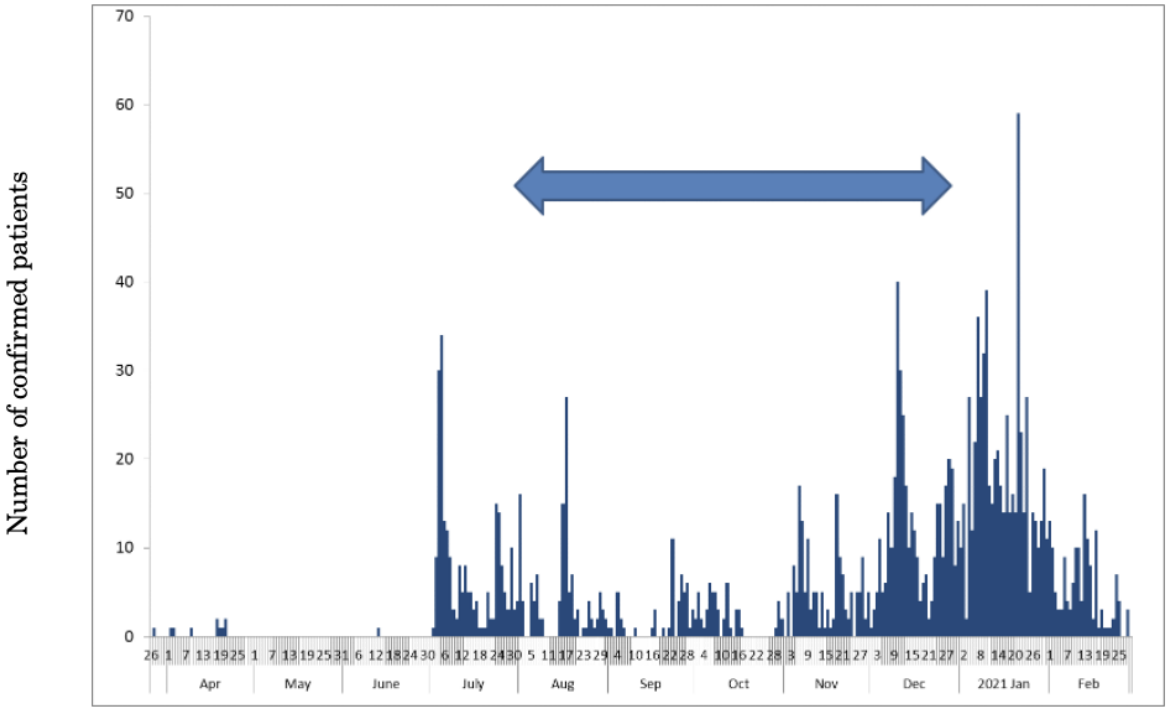
airport users; COVID-19; effective reproduction number; Go To Travel campaign; hotel visitors; mobility; long-distance travel; infection control; lockdown; travelling; travel; pandemic

Introduction

Important features of countermeasures against the COVID-19 outbreak in Japan were restrictions such as staying at home, wearing a mask, holding virtual meetings at organizations, and conducting contact tracing. All these measures were implemented on a voluntary basis; that is, the government strongly recommended such measures but none was required as a matter for law enforcement. Therefore, lockdowns such as those that occurred in the United States or some European countries, entailing enforced laws, never occurred in Japan. Even though these countermeasures were recommended by the government without enforced laws, aside from laws implemented at border controls and for quarantines, most Japanese people cooperated with the recommendations voluntarily.

At the beginning of the COVID-19 outbreak in Japan, school closures and voluntary event cancellations were required from February 27 through March of 2020. Large commercial events were also cancelled. Subsequently, a state of emergency was declared from April 7 through May 25, with voluntary restrictions against leaving the home and requiring the shutting down of businesses serving customers. During this period, the first peak in the outbreak was reached on April 3, 2020. Another peak then emerged on July 29, as shown in Figure 1. The so-called “Go To Travel” campaign (GTTC) started on July 22, 2020, with 50% subsidized travel and coupons issued for shopping at tourist destinations. The policy was aimed at reinforcing sightseeing businesses, even though such a measure entailed the possibility of expanding the outbreak. Thereafter, the GTTC continued through December 2020, by which time a third wave of infections had emerged, which was larger than either of the prior two waves. Therefore, the GTTC was implicated as the main underlying reason for the third wave [1].

Figure 1. Numbers of newly confirmed COVID-19 cases in Kagoshima prefecture, Japan, from March 26, 2020, to the end of February 2021. Bars represent the epidemic curve showing the numbers of patients by onset date. The arrow indicates the period during which the "Go To Travel" campaign was in effect.



Although results were mixed, some studies suggested that the spread of COVID-19 was associated with climate conditions in China [2-4]. However, other research based on cross-sectional international comparisons in European countries found no association between climate conditions and COVID-19 outbreak surge dates [5]. In Japan, high temperatures, humidity, and sunlight exposure were associated with reduced infectivity according to analyses of cross-sectional data [6]. One review [7] indicated an association of outbreaks with temperature, whereas no association was confirmed with humidity, rainfall, or even air pollution. Another cross-sectional analysis conducted in Italy [8] showed an association of COVID-19 outbreaks with air pollution. If such an association was valid for Japan, then the GTTC might not in fact be the main contributor to the occurrence of the third wave of infections in the winter of 2020-2021.

Indeed, mobility was presumed to be the main driver of outbreak dynamics, at least for the first wave in Japan [9] as well as globally [10]. In a study conducted early in the pandemic, up to April 2020, Flaxman et al [11] demonstrated that

nonpharmaceutical interventions, including lockdowns, strongly reduced transmission in at least 11 European countries. However, another study including 131 countries found that the introduction and relaxation of lockdowns or movement restrictions had only limited the effects on infectiousness, except for public event bans, although their data were limited to the end of July 2021 [12]. Another study indicated that strict movement restrictions in Argentina imposed as of March 2020 were effective at reducing mobility, but not for mitigating the outbreak [13]. These mixed results suggest that such countermeasures might not have significantly affected the infectivity of SARS-CoV-2.

By contrast, there is abundant evidence demonstrating the effects of international travel and restrictive policies on pandemic dynamics, mainly focusing on the effects of long-distance domestic travel [14-17]. However, despite a report indicating that 80% of patients with COVID-19 on an island in Canada had acquired a travel-related infection from July 1, 2020, to May 31, 2021 [18], in Japan, only 12% of patients had a recent history of international travel in the very early phase of the pandemic from January 13 to March 31, 2020 [19].

Some studies have emphasized associations among international trade and outbreak sizes [20,21]. Although the traded goods are likely not the source of infectiousness, international trade volumes might be related to outbreak size, as this volume can reflect the movements of business representatives accompanying international trade. Unfortunately, these two studies were based on cross-sectional analyses and therefore it was not possible to isolate the effects of the number of travelers from the effects of high population densities or air pollution discharged by manufacturing industries. Therefore, these studies did not provide sufficient evidence to confirm that travelers were mainly responsible for expanding the outbreak. Moreover, immediately after the pandemic was declared, most international borders had been closed in principle and almost all planned face-to-face meetings related to international trade were held as virtual meetings [22].

Countermeasures against the spread of COVID-19 differed considerably with respect to international and domestic travel, as the former involves border controls and restrictive quarantines, which might be more effective at reducing transmission [23-26]. By contrast, domestic travel recommendations might be limited to voluntary restrictions against going out and long-distance domestic travel. Even in the case of a long-distance domestic travel ban, a chain of short-distance trips to a neighboring city, including commuting to a school, workplace, or shopping center, might ultimately act to transmit viruses over long distances, given some delay. In this sense, experience and evidence related to international travel might not be directly applicable to long-distance domestic travel.

To our knowledge, no study has examined the impact of long-distance domestic travel on outbreak situations in rural areas. One might expect that such information might be less available for epidemiological analysis. Although annual or monthly data related to travelling or sightseeing might be generally available, such records are generally not widely available. Moreover, these data would be quite aggregated, and the number of data points would likely be too small to support sufficient power for statistical analyses considering short time periods of less than 1 year. Fortunately, epidemiologists, statisticians, and companies managing resort hotels and buses to airports in rural areas can provide travel-related data collaboratively. In fact, daily data of bus users from airports and visitors to these hotels are available for many areas in Japan. Therefore, the hypothesis that sightseeing visitors and long-distance domestic travelers were largely responsible for spreading the virus and contributed to COVID-19 outbreaks in rural areas can be tested directly. This hypothesis served as the rationale for ceasing the GTTC and for banning long-distance domestic travel during the first and second states of emergency in Japan. Nevertheless, this rationale has neither been analyzed nor confirmed to date.

Therefore, the objective of this study was to directly examine the hypothesis that long-distance domestic travel was responsible for expanding the COVID-19 outbreak, supporting the rationale and legitimacy of the policy followed in Kagoshima prefecture, Japan. This area was selected given that Kagoshima, located north of Okinawa but in southern Japan (Figure 2), has one airport that is used for commuting to more urban areas of the country, such as Tokyo and Osaka. Moreover, collaborative data obtained from epidemiologists and from leading tourist industry companies were available for Kagoshima, offering a valuable resource for this analysis that can contribute to more insightful consideration and policy evaluation.

Figure 2. Map of Japan with Kagoshima prefecture indicated in the red circle and the airport routes to the main tourism cities for long-distance domestic travel marked.

Methods

Sample and Data

Data reflecting the daily numbers of Kagoshima airport limousine bus users were provided by Iwasaki Industrial Corp, Ltd, of Kagoshima. However, the information does not completely reflect the traffic to and from the airport, as some airport users commuted to or from the airport by taxi, private car, or rental car. Moreover, some tourists visited Kagoshima without using an airline, such as by train, car, bus, or ship. Nevertheless, most tourists from Tokyo, Osaka, or other urban areas typically use airlines to visit Kagoshima. Therefore, although the extent of domestic travel could not be verified completely, we infer that the available information accurately reflects the general picture of movement during this time.

The study period was defined as June 20, 2020, through February 2021. Before this period, COVID-19 cases had been confirmed only sporadically. Therefore, the effective reproduction number R(t) could not be stably estimated. However, after this period, the Alpha variant strain emerged and dominated up to 35% of all cases throughout Japan by the end of March 2021 [27]. The infectiousness of the Alpha variant was estimated to be 35%-90% higher than that of the ancestral strain [28-31]. Such a large difference in virus characteristics could affect the estimations related to our study objectives. Therefore, we limited the study period to the time prior to the emergence of the Alpha variant strain.

Variables

Climate variables considered were average temperature (measured in degrees Celsius) and relative humidity data for Kagoshima during the day; these data were obtained from the Japan Meteorological Agency [32].

We also used mobility data provided by Google, which includes data for six types of locations: restaurants, shopping malls or amusement centers, grocery stores or pharmacies, parks, transition areas, workplaces, and homes [33]. These data show mobility comparisons according to a base day; a value of 100 was assigned if the number of people recorded for a given type of place was the same as that recorded on the base day.

Additionally, we considered the impact of major countermeasures against the pandemic implemented in Japan: two emergency state declarations, the GTTC, and school closure and voluntary event cancellation. The latter measure extended from February 27 through March in 2020, requiring school closure and cancellation of voluntary events, along with cancellation of private meetings. The first state of emergency was declared on April 7, 2020, which ceased at the end of May. This involved required school closures, shutting down of some businesses, and voluntary restrictions against going out. For Kagoshima prefecture, the state of emergency spanned from April 16 to May 14, 2020. To subsidize travel and shopping at tourist destinations, the GTTC started on July 22, 2020, and was halted at the end of December 2020.

The second state of emergency was declared on January 7, 2021, and continued until March 21, 2021, for the 11 most-affected prefectures in Japan. This countermeasure required restaurant closure at 8 PM, along with voluntary restrictions against going out, but it did not require school closure. During the study period, the GTTC and the second state of emergency were in effect. Although this second state of emergency was not declared for Kagoshima prefecture, it was implemented in major cities, including Tokyo and Osaka.

Models and Data Analysis

The numbers of newly confirmed COVID-19 cases each day were reported by the Kagoshima Prefecture Office from May 13, 2020, through February 2021 [34]. The effective reproduction number R(t) was estimated according to a previous study [35]. We first estimated the onset date of patients for whom onset dates were not reported. Letting $f(k)$ represent the empirical distribution of the incubation period and letting N_t denote the number of patients for whom onset dates were not available as published at date t, the number of patients for whom the onset date was known is designated t-1. The number of patients with onset date t-1 for whom onset dates were not available was estimated as $f(1)N_t$. Similarly, patients with onset date t-2 and for whom onset dates were not available were estimated as $f(2)N_t$. Therefore, the total number of patients for whom the onset date was not available, given an onset date of s, was estimated as $\Sigma_{k=1}f(k)N_s+k$ for the long duration extending from s.

Moreover, the reporting delay for published data from the Ministry of Health, Labour and Welfare of Japan might be considerable. In other words, if $s+k$ is larger than that in the current period t, then $s+k$ represents the future for period t. Consequently, N_{s+k} is not observable. Such a reporting delay engenders underestimation of the number of patients. Therefore, the formula must be adjusted to $\Sigma_{k=1}^{t-s}f(k)N_s+k$ /$\Sigma_{k=1}^{t-s}f(k)$. Similarly, patients for whom the onset dates were available are expected to be affected by the reporting delay. Therefore, the formula $M_s|_t$ /$\Sigma_{k=1}^{t-s}f(k)$ was used, where $M_s|_t$ represents the reported number of patients for whom the onset date was period s as of the current period t.

We defined R(t) as the number of infected patients on day t divided by the number of patients who were presumed to be infectious. The number of infected patients was calculated from the epidemic curve by the onset date using an empirical distribution of the incubation period, which is $\Sigma_{k=1}f(k)E_{t+k}$, where E_t denotes the number of patients for whom the onset date was period t. The distribution of infectiousness in symptomatic and asymptomatic cases $g(k)$ was assumed to be 30% on the onset day, 20% on the following day, and 10% for the subsequent 5 days [36]. Therefore, the number of infectious patients was calculated as $\Sigma_{k=1}g(k)E_{t-k}$ and R(t) was defined as $\Sigma_{k=1}f(k)E_{t+k}/\Sigma_{k=1}g(k)E_{t-k}$. The empirical distributions of f and g based on actual data in Japan were obtained from an earlier report [35].

The bootstrapping procedure was applied to calculate the 95% CIs of R(t). We used fully replicated bootstrapping for a constant number of cases in this study period. There were L patients in the actual data of this study period, with numbering of the patients from the initial case to the last case. Initially, no patient was on the bootstrapped epidemic curve. If a random variable drawn from a uniform distribution of (0,1) was included in the interval [i/(L–1), (i+1)/(L–1)], then we added 1 to the onset date of the i+1th patient to the bootstrapped epidemic curve. We replicated this procedure L–1 times. Thereby, we obtained the bootstrapped epidemic curve with L–1 patients. We calculated R(t) based on the bootstrapped epidemic curve. We denote R(t) based on the jth bootstrapped epidemic curve as $R(t)^j$. We repeated these processes 10,000 times to obtain $R(t)^j$ (j=1–10,000). We reordered superscripts in each t from $\min_j\{R(t)^j\}$ to $\max_j\{R(t)^j\}$ and denoted the reordered $R(t)^j$ as $R(t)^{*k}$ (k=1–10,000). The estimated R(t) was then taken as the median of $R(t)^j$, denoted $R(t)^{*5000}$, and its 95% CI is $R(t)^{*250}$–$R(t)^{*9750}$.

To clarify associations among R(t) and the GTTC or other variables in addition to climate, mobility, and countermeasures, we used ordinary least-squares regression to regress the daily R(t) on daily dummy variables for the GTTC (G(t)); daily data of airport limousine bus users and visitors at the resort hotels (L(t)); as well as dummy variables for daily climate ($H_1(t)$ for temperature and $H_2(t)$ for humidity), mobility ($M_i(t)$ (i=1-6)), and the second state of emergency as follows:

$$R(t) = \alpha + \beta G(t) + \gamma L(t) + \delta_1 H_1(t) + \delta_2 H_2(t) + \Sigma\eta_i M_i(t) + \theta P(t) + \varepsilon(t)$$

The start of the study period was June 20, 2020. Therefore, school closure and voluntary event cancellation and the first state of emergency had ceased; accordingly, we are unable to estimate their effects on R(t).

We anticipated the following influence of the explanatory variables: airport limousine bus users and visitors at the resort hotels or part of the GTTC would contribute to increased infectivity if the policy banning long-distance domestic travel was rational, and countermeasures such as the emergency state or school closure and voluntary event cancellation were presumed to decrease infectivity. We adopted 5% as the significance level and performed all statistical analyses using Stata SE 17.0 software (Stata Corp).

Ethical Considerations

Information about the number of patients used for this study was collected under the Law of Infection Control, Japan, published by the Kagoshima Prefectural Office [34]. Iwasaki Industrial Corp Ltd provided the number of airport limousine bus user data from their business records. Both data sets only provided the number of persons, and thus did not include private or privacy information. There were therefore no ethical issues related to this study.

Results

Figure 1 shows the numbers of newly confirmed cases of COVID-19, including asymptomatic cases, in Kagoshima from March 26, 2020, to February 28, 2021. The initial case was

detected in Kagoshima on March 26. However, data were sporadic in the initial phase. From June 2020, cases were reported continuously.

Figure 3 presents the estimated R(*t*) and 95% CI for the study period. Before June 2020, the R(*t*) was large and volatile because very few cases were reported. After June 2020, because new cases were reported almost daily, the R(*t*) became smaller and exhibited less volatility. The largest peak was in November 2020 while the GTTC was in effect.

Figure 4 portrays the number of the airport limousine bus users during the study period. The main peak of airport limousine bus users occurred before the outbreak emergence. During April and May of 2020, when the first state of emergency was declared, this number decreased considerably, reaching 0 in September 2020 when the airport was closed because a typhoon struck the area.

Table 1 presents the estimation results (adjusted R^2=0.2772; n=273 observations) from the regression model. Climate conditions, including temperature and humidity, did not show any significant associations with R(*t*). In addition, there was no association of specific places with R(*t*) over the shorter period, except for restaurants and grocery stores. One can infer that going to a restaurant increased infectivity, whereas going to a grocery store, perhaps as a reflection of "staying home," reduced infectivity. This result might indicate that a "stay-at-home" policy, including a lockdown or voluntary ban against going out as practiced in Japan, was legitimate. However, staying at "home" itself and going to a "workplace" were not found to be significant factors influencing R(*t*), even though they had negative coefficients. The first and second states of emergency and the GTTC had negative and significant effects on R(*t*). In particular, the estimated coefficients of these variables were quite large. The second state of emergency, which was not applied to Kagoshima, also showed an association with reduced infectivity.

Figure 3. Effective reproduction number (black line) with 95% CIs (gray lines) of COVID-19 in Kagoshima prefecture, Japan, from June 20, 2020, to the end of February, 2021.

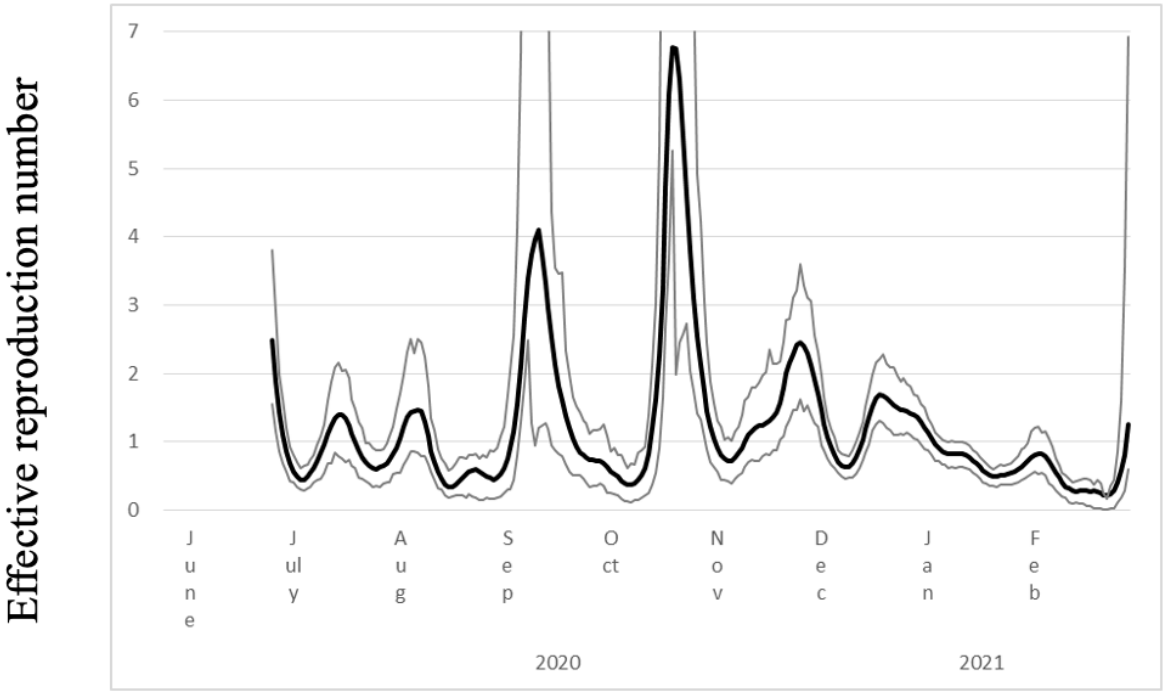


Figure 4. Number of airport limousine bus users at Kagoshima airport from the beginning of 2020 to the end of 2021.

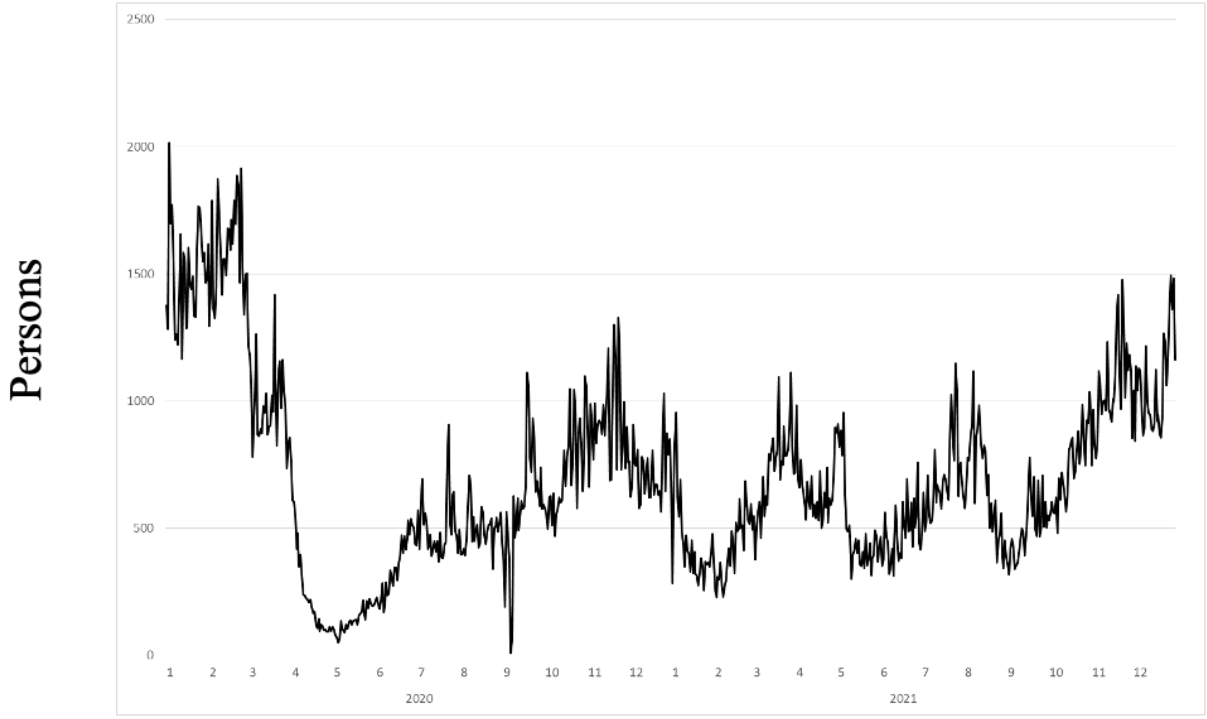


Table 1. Estimated effects of various factors on infectivity (effective SARS-CoV-2 reproductive number) obtained using data from June 20, 2020, to the end of February 2021 In Kagoshima prefecture, Japan.

Explanatory variable	Estimated coefficient	*P* value
Airport limousine bus users	–0.003	.02
Temperature	0.013	.76
Humidity	0.003	.89
Places		
Restaurant, shopping mall, or amusement center	0.094	.03
Grocery store or pharmacy	–0.095	.03
Park	–0.038	.08
Transition	0.028	.52
Workplace	–0.035	.44
Home	–0.303	.09
Second state of emergency	–3.774	<.001
GTTC[a]	–3.040	<.001
Constant	7.646	<.001
F value (*df*=11, 261)[b]	10.48	<.001

[a]GTTC: “Go To Travel” campaign.

[b]The *F* test was used to evaluate the null hypothesis that all coefficients except for constant terms are 0.

Discussion

Principal Findings

Estimation results for the GTTC and the number of airport limousine bus users indicate that the promotion of long-distance domestic travel might decrease SARS-CoV-2 infectiousness. This finding thus appears to be inconsistent with a legitimate policy banning long-distance domestic travel, including cessation of the GTTC. Our findings suggest that during sightseeing or long-distance domestic travel, tourists/visitors and hosts might be much more conscientious about infection control and might therefore be less likely to infect others than when they are in their hometown. These phenomena were also indicated through a psychographical study and market research

[37,38]. In other words, people in their hometown might exhibit less conscientious behaviors and might therefore be more likely to become infected. Therefore, discouraging long-distance domestic travel might actually engender worse infection rates overall within a local area.

This finding is consistent with earlier studies [35,39]. One study showed that the GTTC reduced infectiousness, whereas the other study found that events with an audience might not raise infectiousness compared to events without an audience.

Another study [40] using two types of patient data (onset date and the date of testing positive) found much higher travel-associated COVID-19 incidence during the period of July 22-26, when the GTTC was initiated, than during either an earlier period of June 22 to July 21, July 15-19, or June 22 to July 21 in terms of the incidence rate ratio (IRR). The same study also compared the period of August 8-31.

Some notable points can be identified from this previous study [40]. First, the proportion of people with a travel history during the GTTC period was comparable to that during the two prior periods. In particular, the proportion of people with a travel history among patients with COVID-19 who had an available onset date was smaller for the GTTC period than during the prior period of July 15-19. However, the authors found a significantly higher COVID-19 incidence at the beginning of the GTTC. These findings might merely reflect the fact that the total number of patents in the GTTC period was higher than that during the prior period. In other words, they did not control for the underlying outbreak situation and therefore found an incorrect association. Use of the IRR would be valid if the underlying outbreak situation other than the examining point was the same in the two considered periods. Therefore, application of the IRR might be inappropriate for addressing this issue. At the very least, controlling for the potential differences in the outbreak situation is considered to be necessary. The underlying outbreak situation, unrelated to the GTTC, was reflected in the number of patients without a travel history or any sightseeing. One potential approach to control for the underlying outbreak situation is to consider the share of patients with a travel history or sightseeing. However, that share did not increase markedly during the initial stage of the GTTC. This lack of a marked increase indicates that the authors' results and conclusions are misleading.

Second, Anzai and Nishiura [40] referred to the period of August 8-31, 2020, when the GTTC was still in effect. The proportion of patients with a travel history was much smaller than that during the period of July 22-26 when the GTTC started or in the prior period. Although the authors did not compare the COVID-19 incidence in August with that of either the prior period or July 22-26 when the GTTC started, the rate of incidence in August 2020 was likely lower than that in other periods. In fact, some patients with active COVID-19 infections traveling under the GTTC might have been included in the study period, August 2020, as described above. Their inclusion might be inconsistent with the authors' conclusion.

Third, we observed the peak of newly infected persons on July 23, 2020, which was the start date of the GTTC, for the entirety of Japan. Therefore, we infer that the GTTC might have reduced infectiousness. We also considered the potential effect of climate conditions on the variation in infectivity. At around the end of July, the rainy season in Japan ends and summer begins, accompanied by high temperatures. Therefore, the GTTC might have been insufficient to increase the number of COVID-19 patients and cancel out the benefits from the improved climate conditions. Taken together, these points suggest that the GTTC might not have been the main factor determining the course of the COVID-19 outbreak.

Moreover, if the GTTC did have a strong effect on the outbreak dynamics, then there would be an increase in the number of patients with no travel history. For example, one can consider a patient traveling under the GTTC on July 22 and 23, with disease onset occurring on July 24. Although this patient had a travel history in the GTTC period, they would not be included in a group of patients with a travel history whose onset date corresponds to the initial GTTC period of July 27-31. Nevertheless, presymptomatic patients are well known to become infectious during the symptomatic period [36]. In the above scenario, this patient might infect staff members of hotels or other individuals encountered in the visiting areas. However, if their onset dates were July 27 and 28, they would be included in the group of patients without a travel history in the GTTC start period of July 27-31. Therefore, the GTTC certainly increased the number of patients without a travel history but did not increase the number of patients with a travel history in this case. Consequently, when considering the effects of the GTTC, it is important to account for the total number of patients with COVID-19, irrespective of their travel history.

Finally, it is noteworthy that this study could have been performed in the middle or end of March 2021, if we had analyzed those data at that time. We found the same results as those found from this study. In fact, this analysis was performed in 2022, although similar research without the valuable data used for this study was posted to the medRxiv preprint server on January 4, 2021, and we obtained the same results for the GTTC [35]. In general, an ex ante policy evaluation is necessary, although it was very difficult to estimate its effects precisely. By contrast, an ex post evaluation performed as soon as possible could have been possible if such preparation had been arranged before policy activation. If such preparation had been done, then the policy banning long-distance domestic travel with no legitimate rationale could have been prevented in 2021 and thereafter.

Another study in Japan [41] showed that the GTTC was responsible for the introduction of an emerging sublineage of SARS-CoV-2 in October 2020 to Hokkaido, Japan's second largest island. The ratio of the number of travelers at Hokkaido to that on the same month in the prior year was the largest in October 2020. However, this might not necessarily imply that the outbreak was accelerated by the GTTC or the number of travelers.

For this study, because daily airport user data were not available, we used the number of daily airport limousine bus users as a proxy of daily airport users, including those who did not use limousine buses. However, monthly airport user data have since been published [42]. Therefore, we further evaluated the

representativeness of airport limousine bus users for airport users on a monthly basis. The correlation coefficient between monthly airport limousine bus users and airport users during 2020 and 2021 was 0.9881 (P<.001). Therefore, we can infer that airport limousine bus users constitute a good proxy of overall airport users. Moreover, even though bullet-train or bus services were available as a means of transportation to Kagoshima from neighboring or nearby prefectures, airlines are the only means of transportation to Kagoshima from areas with large populations in Japan, such as Osaka and Tokyo. Therefore, we can infer that airport limousine bus users are a good proxy of long-distance domestic travel volumes for Kagoshima.

This study excluded some variables suggested by earlier studies, such as vaccination, contact tracing, or mass gathering events, which potentially affect infectivity. Vaccination for COVID-19 started in March 2021 in Japan for health care workers. Therefore, there was no vaccination performed during our study period [43-45].

Moreover, contact tracing had been performed with the same intensity during the study period in Japan and was continued until the Omicron variant strain emerged. The public health center could not be traced with the same intensity. Contact tracing might be effective, at least in the very early stage, when the number of cases was limited to a few patients per public health center [46]. However, even in the very early stage of the pandemic in Japan, 80% of the infection sources were unknown. Therefore, contact tracing should not be expected to be effective in most cases in Japan [47]. Nevertheless, we were not able to estimate the effects or intensity of contact tracing for this study because it did not vary during the study period.

Mass gathering events such as the Olympic and Paralympic Games were also excluded from our analyses because of the study period. Even though international visitors seeking to see the games were refused because many players and officers were already crowded in a small area, an outbreak in the players' village had been expected [48].

Limitations

This study has some limitations. First, this study specifically assessed data from Kagoshima. Therefore, it remains unclear whether the same results would hold for other regions or for the entirety of Japan.

Second, we particularly examined the ancestral strain of SARS-CoV-2, which might be less infective than the Alpha variant strain [28-31] and the subsequent dominant Delta and Omicron variant strains [29,30,49,50]. Thus, the effects of a policy banning long-distance domestic travel might have been different under a scenario of the dominance of these variant strains.

Third, if complete daily information about long-distance domestic travel to Kagoshima prefecture were available, obviating the use of data particularly addressing only some travel, then the implications might differ from those obtained with this analysis. We consider that our data do reflect complete and precise travel information, although it is not possible to prove this at present.

Fourth, regression analyses such as that used for this study cannot demonstrate causality. Although we interpreted the number of airport limousine bus users as showing decreased infectivity, lower infectivity pushed up the number of airport limousine bus users. Therefore, the results need to be interpreted cautiously.

Conclusion

We demonstrated that the GTTC or the increase of tourists and long-distance domestic travel visitors might not contribute to increasing COVID-19 infectiousness. Therefore, the policy banning long-distance domestic travel, including cessation of the GTTC, was neither fair nor rationally justified. Even though this analysis was performed much later than the study period of focus, the same results would be obtained considering the periods of April or May 2021 if we had performed this study at that time. The findings might have been helpful at that time for more rational decision-making when the government was considering whether to restart the GTTC. If so, then evidence-based policy might be suggested and operated. This perspective is in line with that of an earlier study [51].

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Data Availability

The data of airport limousine buses are not publicly available because they are sales data of the private company. However, the data are available from the corresponding author on reasonable request. Other data used for this study are available from the corresponding author.

Authors' Contributions

JK was responsible for the coordination of the study and analyzed the data. YI collected and prepared the data for analysis. Both authors contributed to the writing and review of the final manuscript.

Conflicts of Interest

None declared.

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Abbreviations

GTTC: “Go To Travel” campaign
IRR: incidence rate ratio
R(*t*): effective reproduction number

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Original Paper

Vaccine Hesitancy in Taiwan: Temporal, Multilayer Network Study of Echo Chambers Shaped by Influential Users

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Abstract

Background: Vaccine hesitancy is a growing global health threat that is increasingly studied through the monitoring and analysis of social media platforms. One understudied area is the impact of echo chambers and influential users on disseminating vaccine information in social networks. Assessing the temporal development of echo chambers and the influence of key users on their growth provides valuable insights into effective communication strategies to prevent increases in vaccine hesitancy. This also aligns with the World Health Organization's (WHO) infodemiology research agenda, which aims to propose new methods for social listening.

Objective: Using data from a Taiwanese forum, this study aims to examine how engagement patterns of influential users, both within and across different COVID-19 stances, contribute to the formation of echo chambers over time.

Methods: Data for this study come from a Taiwanese forum called PTT. All vaccine-related posts on the "Gossiping" subforum were scraped from January 2021 to December 2022 using the keyword "vaccine." A multilayer network model was constructed to assess the existence of echo chambers. Each layer represents either provaccination, vaccine hesitant, or antivaccination posts based on specific criteria. Layer-level metrics, such as average diversity and Spearman rank correlations, were used to measure chambering. To understand the behavior of influential users—or key nodes—in the network, the activity of high-diversity and hardliner nodes was analyzed.

Results: Overall, the provaccination and antivaccination layers are strongly polarized. This trend is temporal and becomes more apparent after November 2021. Diverse nodes primarily participate in discussions related to provaccination topics, both receiving comments and contributing to them. Interactions with the antivaccination layer are comparatively minimal, likely due to its smaller size, suggesting that the forum is a "healthy community." Overall, diverse nodes exhibit cross-cutting engagement. By contrast, hardliners in the vaccine hesitant and antivaccination layers are more active in commenting within their own communities. This trend is temporal, showing an increase during the Omicron outbreak. Hardliner activity potentially reinforces their stances over time. Thus, there are opposing forces of chambering and cross-cutting.

Conclusions: Efforts should be made to moderate hardliner and influential nodes in the antivaccination layer and to support provaccination users engaged in cross-cutting exchanges. There are several limitations to this study. One is the bias of the platform used, and another is the lack of a comprehensive definition of "influence." To address these issues, comparative studies across different platforms can be conducted, and various metrics of influence should be explored. Additionally, examining the impact of influential users on network structure and chambering through network simulations and regression analysis provides more robust insights. The study also lacks an explanation for the reasons behind chambering trends. Conducting content analysis can

help to understand the nature of engagement and inform interventions to address echo chambers. These approaches align with and further the WHO infodemic research agenda.

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KEYWORDS

network analysis; infodemiology; vaccine hesitancy; Taiwan; multiplex network; echo chambers; influential users; information dissemination; health communication; Taiwanese data set; multilayer network model; vaccine hesitant; antivaccination; infoveillance; disease surveillance; public health

Introduction

Vaccine Hesitancy and Infodemiology

Vaccine hesitancy, as defined by the World Health Organization's (WHO) Strategic Advisory Group of Experts, refers to the reluctance or refusal to vaccinate despite the availability of vaccinations. While straightforward in definition, vaccine hesitancy encompasses a spectrum of attitudes [1]. This spectrum arises from complex interactions involving health attitudes, decision-making processes, cultural contexts, and health infrastructure. These factors contribute to varying degrees of vaccine confidence, vaccine complacency, and accessibility to vaccination services [2]. Theories borrowed from the health behavior literature underscore the complexity of vaccination intentions. For instance, the Health Belief Model posits that individuals assess the perceived severity of a disease (perceived susceptibility and severity) alongside the perceived benefits and barriers of treatment before making a decision [3]. These theories emphasize that the decision to vaccinate is influenced by a multifaceted interplay of factors. The implications of vaccine hesitancy are significant, as evidenced by the resurgence of diseases such as measles, with studies showing that even a small drop in vaccination rates can lead to substantial increases in disease outbreaks and cost health care systems millions [4,5]. Consequently, the WHO identified vaccine hesitancy as one of the top 10 global health threats in 2019 [6].

Implicit in the definition of vaccine hesitancy is its dynamic nature across a spectrum, indicating that attitudes toward vaccination can evolve over time. Monitoring this phenomenon necessitates a flexible, dynamic approach to complement traditional epidemiological methods. Social media has become increasingly utilized for this purpose due to its widespread adoption and the real-time nature of the data it offers. This enables prompt detection of changes in public sentiment. Furthermore, social media plays an increasingly influential role in shaping public perceptions of vaccination. This influence was particularly pronounced during the COVID-19 pandemic, where misinformation proliferated alongside scientific communication, complicating public health responses [7,8]. The pandemic brought renewed focus on vaccine hesitancy studies, especially with the development and scrutiny of COVID-19 vaccines. This prompted the WHO to increase investment in infodemiology research.

The WHO outlined a comprehensive research agenda for managing infodemics, which represents a situation in which an excess of information, including false or misleading content, spreads in both digital and physical spaces during outbreaks [9,10]. This framework is organized into five 5 streams, each targeting various aspects of infodemic management. The first stream focuses on measuring and monitoring the evolution of infodemics, utilizing various metrics and tools to track information flow. A subtheme within this stream involves triangulating data from multiple sources and standardizing taxonomies and classifications. The second stream aims to detect the origin, evolution, and spread of information across various platforms, with a specific emphasis on the influence of key actors in disseminating this information. The third and fourth streams focus on deploying and evaluating interventions that mitigate the effects of infodemics, thereby enhancing community resilience. The overarching goal of the research agenda, encapsulated in the final stream, is to integrate these tools into broader epidemic management strategies, promoting a paradigm shift in epidemic management that incorporates infodemic control.

In the vaccine hesitancy infodemic space, the majority of studies have primarily concentrated on the first and second streams. A review by Yin [11] provides a summary of the most commonly used big data methods and key research topics in vaccine hesitancy. However, several gaps remain in this area. One significant gap is the need for more comprehensive tracking of vaccine sentiment. While many studies focus on identifying either pro- or anti-vaccination sentiment [11,12], there is a notable lack of attention given to the gray area of vaccine "hesitancy," which represents a potentially vast spectrum. Another gap is the predominance of studies focusing on English, possibly influenced by its global linguistic dominance as a *lingua franca* and the availability of tools for English-language analysis. Analyzing diverse contexts and languages enriches the vaccine hesitancy discourse by triangulating global trends with context-specific insights. A third gap lies in the exploration of thematic areas that remain underexplored. Many studies use sentiment analysis and topic modeling as relatively straightforward tools for tracking vaccine sentiment. However, these methods have limitations in identifying how sentiments cluster and the key actors responsible for such clustering. Another frequently neglected thematic area is the temporal aspect of sentiment change. Given that vaccine hesitancy is a dynamic state, tracking these changes over time is crucial for comprehensive understanding. For these reasons, this study focuses on vaccine hesitancy in Taiwan during the COVID-19 pandemic using social network analysis. The choice of methods, the case study of Taiwan, and the emphasis on influencers aim to contribute to the WHO's infodemiology efforts by proposing new surveillance methods, providing insights from a distinct context for triangulating broader trends, and exploring the understudied area of vaccine hesitancy (influencing). The following sections delve into the literature on echo chambers

and influential users in vaccine hesitancy, offering conceptual clarifications, a task aligned with the WHO's infodemic research agenda.

Echo Chambers, Influential Users, and Information Transmission

Overview

Social networks exert a growing influence on decision-making processes. Grounded in Social Network Theory, individuals leverage personal networks to access relevant information and support from peers [13]. These networks enable individuals to gather social cues from others with similar experiences, fostering a sense of belonging and aiding in identity formation [14-16]. As a result, integrating health communication into these contexts can potentially facilitate behavior change across various health issues. This change is facilitated by modifying the mediators of health decision-making, particularly by reinforcing perceived efficacy and self-efficacy through social networks [15]. Consequently, social networks are well-suited for health promotion, leveraging their mass scale and interpersonal properties.

While social networks foster a sense of identity and belonging, this characteristic can also pose a potential pitfall. Homophilous communities, also known as echo chambers, perpetuate and reinforce specific ideas or beliefs, potentially distorting perception and normalizing ideologies that diverge from the mainstream. This polarization solidifies individuals in their own viewpoints, restricting exposure to diverse perspectives [17-19]. In public health, when these entrenched views contradict best practice recommendations, the implications for health behavior and outcomes can be substantial. This phenomenon is particularly evident in the context of vaccine hesitancy [20], where polarization and echo chambers have fueled the persistence and expansion of hesitant narratives, thereby impeding vaccination efforts. It is crucial to identify when and by whom this occurs to effectively guide health communication strategies aimed at mitigating these effects.

Echo Chambers

Echo chambers have garnered renewed attention, largely due to significant shifts in technology, media, and communication over the past decade. Originally a metaphor from acoustic environments where sounds reverberate in enclosed spaces, "echo chambers" now refer to the phenomenon of amplifying and reinforcing ideologies within closed, like-minded communities.

The phenomenon can largely be broken down into 2 processes: chambering and echoing. Chambering occurs as individuals naturally segregate into groups with like-minded preferences, beliefs, and attitudes. Echoing ensues when those within the chamber influence others in a nonrational manner with their beliefs. These processes are interconnected and often coevolve, sometimes sequentially. For instance, many users primarily seek out content that is relevant or interesting to them [21]. This behavior is amplified by social media algorithms that prioritize content similar to what users have previously engaged with [22]. Consequently, users are more likely to connect with others who share similar tastes and preferences. Additionally, individuals may actively avoid information that contradicts their worldview [23]. Chambering, where individuals segregate based on shared beliefs, is a prerequisite for the echoing effect.

In the context of vaccines and vaccine hesitancy, online echo chambers have primarily been studied to identify their existence, despite the frequent use of the term "echo chamber." Chambers are often operationalized by demonstrating polarization or homophily to illustrate clustering. The consensus in current research leans toward confirming the presence of chambering. Several large-scale studies conducted on Twitter have indeed confirmed the presence of a chambering effect. For instance, Cossard et al [24] found that skeptics and advocates for vaccination tend to reside in separate homophilous clusters, with skeptics forming a tighter cluster and advocates distributed across several smaller clusters. Johnson et al [25] partially corroborate this finding, noting that antivaccination communities often engage more with undecided communities than with provaccination communities. Crupi et al [26], in their study on COVID-19 networks in Italy, observed that while there is convergence on certain topics of discussion, smaller communities focused on antivaccination issues, such as conspiracy theories or concerns about vaccination passports, persist. Mønsted and Lehmann [27] found similar dynamics globally on Twitter/X, where subgroups exhibit preferential attachment—a measure of homophily—resulting in what they term "epistemic echo chambers." Moreover, this phenomenon extends to platforms of different natures. Schmidt et al [28] discovered that the consumption of vaccine-related content on Facebook is characterized by an "echo chamber effect," with polarization intensifying over time. Van Raemdonck [29] also observed that chambering occurs differently based on platform structure. Using Facebook and Reddit as examples, they found that Facebook uses "groups" to shield users from outside ideologies, while Reddit naturally forms chambers through reinforcement against external challenges. Meyer et al [30] found that polarization also exists on web forums for the Canadian Broadcasting Corporation, particularly in debates surrounding flu vaccinations.

Less researched is the association between chambering and echoing, particularly in the context of vaccine hesitancy. However, only a few studies have explored this because of the challenges in linking online behavior to beliefs and actions. Research in this area has typically relied on survey data, modeling, or experimental methods. For instance, Jennings et al [31] found that individuals who primarily rely on platforms such as YouTube for information are more likely to encounter misinformation, believe in conspiracies, and exhibit a lower willingness to vaccinate. This study, however, did not directly measure online echo chambering but rather indirectly assessed it through a questionnaire that identifies users who engage with a limited subset of online media, linking this behavior to beliefs. In modeling approaches, Müller et al [32] investigated how the emergence of echo chambers around measles contributed to the occurrence and persistence of antivaccination opinions, suggesting a significant chambering effect. Phillips and Bauch [33] argued that echo chambers serve as early warning signs of vaccine hesitancy and can thereby influence infection dynamics. The study by Giese et al [34] on flu found that individuals tend

to find incoming information more convincing if it aligns with their existing attitudes.

Although measuring echoing, particularly its direct connection to behaviors or beliefs, is challenging, its association with chambering makes the latter a suitable starting point to analyze potential impacts on behavior (ie, true "echo chambering"). Measuring chambering across different platforms and contexts contributes to this body of knowledge, which is a primary aim of this study. Additionally, the evolution and changes over time in these dynamics are understudied but essential for understanding temporal intervention points. Lastly, in addition to measuring the macroscopic phenomenon of chambering, understanding the individuals who contribute to this phenomenon sheds light on the echo chambering process. This understanding is crucial for targeted promotion efforts aimed at vaccination.

Influential Users

Katz's [35] 2-step flow of communication hypothesis, proposed in 1957, suggests that mass media messages reach the public through the mediating role of opinion leaders [6]. (Often, there is a distinction between opinion leaders [sometimes referred to as key opinion leaders] and influencers. This manuscript uses the words interchangeably.) These opinion leaders, often characterized by qualities that resonate with a group's interests or circumstances, wield significant influence over group opinions on relevant issues [7]. Before the internet, professional groups such as doctors and nurses commonly played the role of opinion leaders in health, enjoying significant trust from their patients. Nonprofessionals, such as individuals in high schools, could also serve as opinion leaders influencing their peers' health decisions [8,9]. In both scenarios, trust was a crucial trait for exerting influence. In the social media era, influence is decentralized, giving rise to online influencers.

Identifying influencers and understanding the extent of their influence are crucial for research in this area. Influencers can be identified through their real-world identity (eg, the US Centers for Disease Control and Prevention [CDC] on platforms such as Twitter/X as a health influencer). They can also be recognized by their potential for message diffusion [36], their opinions and stances on topics, or their tone (eg, individuals with high message dissemination potential or those advocating for vaccination being provaccination). Network measures such as centrality or community detection, known as topological measures, can also be used (eg, connectedness within a network as a proxy for influence). To comprehend their sphere of influence and potential reach, Bamakan et al [37] offer a valuable framework. In their review of marketing influencers, they propose 4 aspects through which opinion leaders can exert influence [7]. One aspect is breadth, indicating their local or global influence over domestic or international markets. The second aspect is the diversity of topics, indicating their degree of specialization, ranging from single-topic specialists to diverse, multitopic experts. The third aspect is polarity, whether they promote positive or destructive messaging (eg, antivaccination). The fourth aspect is temporality, indicating their short- or long-term influence on their community. This framework will be crucial in delineating the scope of the overall study.

In health literature, online influencers are frequently leveraged to promote evidence-based public health behaviors and accelerate the diffusion of health innovations and promotions [10,11]. Regarding vaccines, studies have explored the role of online influencers in both promoting and discouraging vaccination. For instance, in the context of the human papillomavirus vaccine, "mommy bloggers" with trusted reputations in new-mother forums successfully promoted human papillomavirus vaccination [5,12]. Online medical expert celebrities, utilizing increased interactivity and promotional content, successfully promoted COVID-19 vaccination in China [21]. However, these promotional efforts were often countered by the actions of other types of influencers. Whereas health experts promoted vaccination, politicians used their platforms to express dissent, fostering distrust and posing threats to vaccination campaigns [22,23]. Analyzing who the influencers are and understanding their role in the network is crucial for the dual effort of increasing vaccine promotion messages and reducing antivaccination content.

Less studied, however, is the role of influencers in driving the chambering effect. While chambers represent a macro-network phenomenon, they are fueled by individual users—micro-network contributors—whose activity within the network may contribute to chamber formation. These users' connectivity serves as an indicator of their engagement within the overall network, also acting as a proxy for their ability to disseminate information. The capacity to spread messages is crucial due to its implications on the nature and effectiveness of message dissemination. For proponents of vaccines, wide-reaching messages are essential to promote a provaccination stance. Conversely, within antivaccination communities, messages that fail to spread circulate among insulated groups, reinforcing the antivaccination sentiment. Focusing on the upstream factor of opinion leaders' role in echo chamber formation helps understand their ability to catalyze or deter vaccination efforts.

However, studying the influencer's role in driving echo chambers requires clarity on its scope. Although measuring influence on behavior is challenging in an infodemic study, examining communication dynamics within a network to understand chambering is more feasible. Additionally, using the 4 aspects mentioned—locality, diversity, polarity, and temporality—can aid in refining measures and delineating the study's scope. This study investigates the formation of chambers within a local forum regarding varying stances on vaccines over time. Initially, the study takes a macroscopic view and then shifts focus to examine the role of influencers. By concentrating on the upstream factor of chambering, the study aims to evaluate its potential impact on promoting or discouraging vaccination efforts.

This study utilizes data from a Taiwanese forum to investigate the following question: How do engagement patterns within and across COVID-19 stances contribute to the formation of chambers over time? This exploration begins by examining the layer level (macro-network), followed by an analysis at the node level (micro-network). At the macro level, the study explores pairwise connectivity between layers over time. At the micro level, it identifies highly connected nodes (opinion leaders) and

evaluates their engagement behavior within the multilayer network to assess their role in chambering.

Methods

Data and Approach

PTT is a terminal-based bulletin board system (BBS) in Taiwan developed by Yi-Chin Tu (杜奕瑾) and other students from National Taiwan University in 1995 [38]. It serves as a free and open forum where users can discuss a wide range of topics including politics, culture, entertainment, and current affairs. Often referred to as Taiwan's "Reddit," PTT is one of the most active forums in Taiwan. From July 2022 to July 2023, the average number of users per day was 56,000 [39]. The user base includes adolescents to young adults, predominantly male, and the forum can host politically charged and radical opinions, similar to Reddit.

The empirical strategy involves evaluating chambering at the network level, identifying opinion leaders based on their network connectivity, and documenting how their behavior influences chambering dynamics over time.

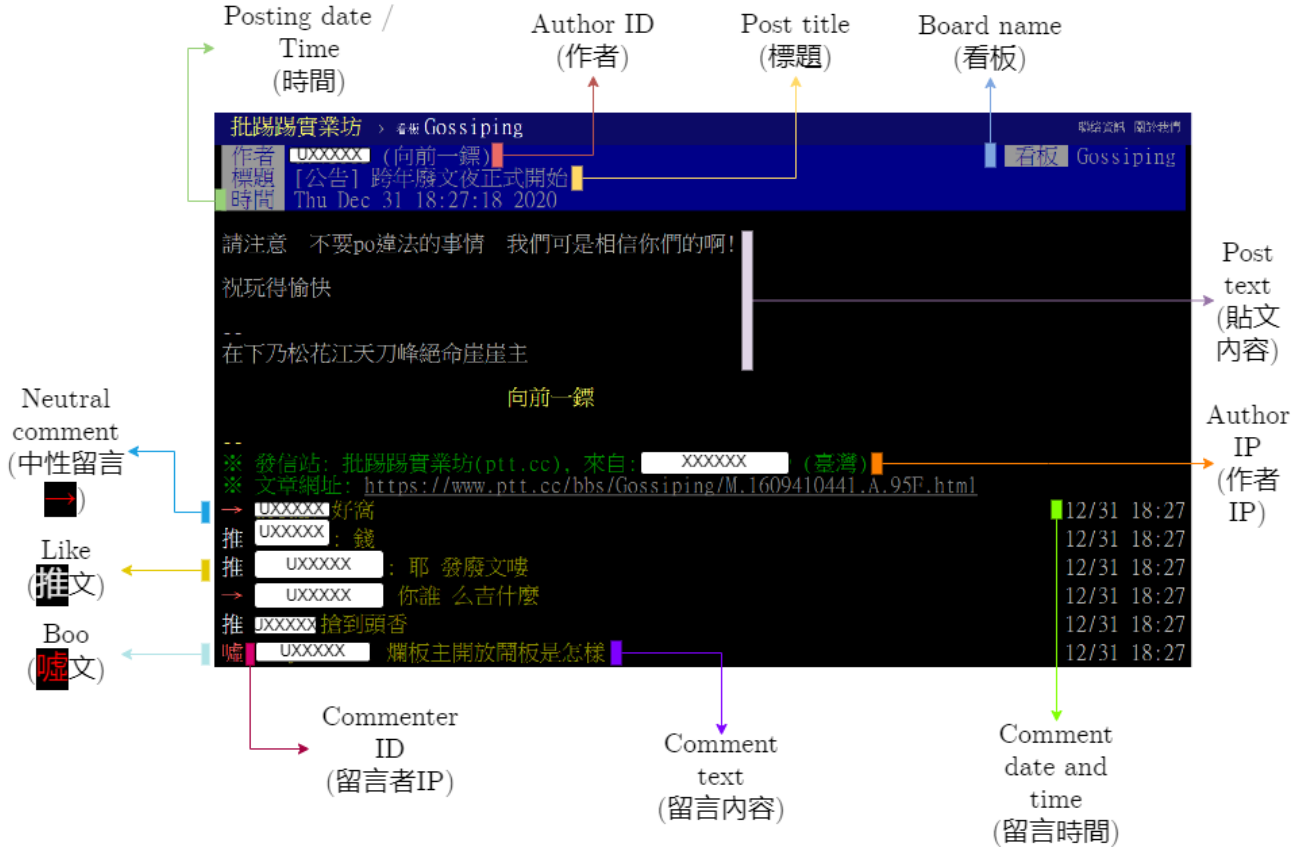
I argue initially that the locality and diversity—the first 2 aspects of influencers—are confined to the forum and its topics. Extracting all vaccine-related discussion boards on PTT focuses the discussion on a case study specific to Taiwan. Next, to analyze polarity, I categorize these boards into 3 sentiments—provaccination, vaccine hesitant, and antivaccination—within vaccine-related discussions. These stances form a conceptual multilayer network, where each layer represents a sentiment toward vaccination. Subsequently, various layer-level analyses are conducted both at the macro and micro levels over time, taking into account the fourth aspect, temporality, for influencers.

Network Representation

Structure of PTT

The web-based version of PTT is structured with terminology in both English and Chinese. The bulletin consists of boards (看板) and board masters (版主), which correspond to subject areas and administrators on any forum. Posts within each board can be made in 2 ways: by creating a new post (PO文 or 貼文) or by replying to a post (回應文). Within each post, users have the option to leave a follow-up comment that expresses sentiment: they can like (推), boo (噓) (equivalent to a "hiss" or "shh" sound), or leave a neutral reaction (→). These reactions are denoted by corresponding Chinese characters in the comment section, or simply an arrow for neutral reactions. Comments are limited to 39 characters per line. Each post includes user information such as posting time (時間), author ID (作者), title (標題), and IP address (作者IP). Additionally, information on commenters' posting dates, times, and IPs is provided. All of these are captured in Figure 1.

Figure 1. Chinese and English labelling of 1 thread of the PTT forum to show its structure. Usernames omitted for protecting individual identity.



The raw corpus comprises all posts from the "Gossiping" board on PTT spanning from January 1, 2021, to December 1, 2022. "Gossiping" is the largest and most active board on PTT, covering a wide range of topics. The start date coincides broadly with the initiation of a government vaccination campaign, while the end date marks Taiwan's reopening to tourists. This time

frame captures significant vaccine-related events in Taiwan, including vaccine procurement, outbreaks, domestic vaccine development, discovery of COVID-19 variants, and changes in vaccination policy, among others. All posts were collected using a web-crawler (ptt-web-crawler) developed by GitHub user "jwlin."

To identify vaccine-related message boards, the filter term "vaccine" (疫苗) was used to search through the raw corpus and extract relevant boards. Each discussion board was independently labeled by 2 assessors as "provaccine," "vaccine hesitant," or "antivaccine" according to Table 1. These criteria have been predefined after consulting the literature on the scope and definitions of vaccine hesitancy [1,2,40], with a particular focus on efficacy appraisals as defined by the Health Belief Model [41]. It is important to note that hesitancy encompasses a broad spectrum, and the categories are designed to encompass various forms of "hesitancy," including those who have "refused" vaccination due to lack of access or other reasons. As the filter using "vaccine" is nonspecific, we anticipated that there may be 2 irrelevant categories of classifications. The first category is "neutral," which includes reposts of vaccine-related statistics (often related to stocks or vaccination coverage) intended without expressing an opinion on uptake. These news items are distinct from other articles that may include a stance or reason for sharing (eg, sharing news on the drawbacks of vaccination). The second category is "irrelevant" vaccination, which may tangentially mention vaccines without direct relevance to the discussion. These categories were excluded from the final network and not included in the analysis. The target interrater agreement goal was set at 85% or higher, with any discrepancies resolved by the main author. The final agreement reached 83% (4829/5818 boards), with the remaining decisions made by the main author.

Table 1. Provaccination, vaccine hesitant, and antivaccination board classification criteria.

COVID-19 vaccine layer	Example
Provaccination	• Claim will get vaccinated once available. • Discussing vaccine efficacy or safety with the intention of promoting vaccination. • Announcing that one has been vaccinated. • Supporting any part of the vaccine approval process. • Advocating for getting vaccinated.
Vaccine hesitant—doubting efficacy	• Saying they will wait and see if the vaccine is safe or effective. • Doubtful or worried about the quick approval process of the vaccine. • Indifferent to get vaccines as a result of perceived low risk of getting diseases. • Suspicious of vaccine side effects. • Mentioning that they have side effects after vaccination.
Vaccine hesitant—barriers to access	• Claiming no opportunities to get vaccinated (cannot book an appointment). • Discuss the excessive time and energy needed to find/book an appointment
Antivaccination	• Religious or philosophical objection or refusal. • The belief that vaccination interferes with natural immunity. • Criticizing the vaccine industry. • The belief that vaccination is dangerous and would not take it. • The belief that vaccination is against human rights/is infringing on individual rights. • Not choosing to vaccinate for reasons related to the government.
Neutral	• Vaccine-related news with no opinion on the uptake (eg, vaccination rates, economic, insurance, stock news). • Listing vaccination rates, or COVID-19 case rates. • If news points in the direction of any category 1-4, put it in the corresponding category.
Irrelevant to vaccination	• Discussion of other vaccines that are not related to the COVID-19 vaccine. • Mentions "vaccine" but does not elaborate on opinion.

The classifications of "provaccine," "vaccine hesitant," and "antivaccination" represent the 3 layers (or stances) of the multilayer network, used interchangeably. To obtain network data, each row was "flattened" such that 1 row represented a directional author-commenter pair. For each row, several steps were taken. First, depending on the direction of the comment, I assigned provaccine, vaccine hesitant, or antivaccination labels based on their alignment with the sentiment of the original labeled post. For example, individuals who "like" a provaccination thread were categorized into the provaccination layer, and neutral comments were also classified as provaccination. Commenters who "boo" a thread were assigned to the opposing camp (eg, those who "boo" provaccination boards were placed in the antivaccination camp). In cases where a comment could reasonably fit into 2 categories (such as "booing" an antivaccination post, which could indicate vaccine hesitancy or provaccination), a random assignment was made. Additionally, each row was assigned a weight based on the sentiment of the comment: "likes" were assigned a weight of 2, "neutral" a weight of 1, and "boo" was weighted as 0.2. These weights were chosen to reflect varying degrees of affinity between nodes; however, they do not indicate a linear increase in weight. Negative weights were avoided in this structure due

to complications in establishing shortest paths when negative weights are used in network construction.

Temporal Multilayer Framework

A multilayer network graph M consists of 3 layers $M = \{G^P, G^H, G^A\}$, with each layer being a directed, weighted graph that represents the aggregate connections between commenters and authors for vaccine sentiments provaccination (P), vaccine hesitant (H), and antivaccination (A). Each layer $l \in M$ of graph G consists of all interactions of the set of nodes V^l and set of edges E^l and is represented as $G^l = (V^l, E^l)$, with each node being a user and each edge being a comment on that user's post. This multilayer structure allows users to participate on multiple layers (ie, the equivalent of saying they may express various sentiments on vaccination). Constructing the network in such a way allows for the comparison across different sentiment layers on various network metrics. This is the static representation.

For the evolving network, assume that we observe the network over a finite time T, with starting point t_s=0 and ending point t_e=T. Each layer in M is defined as $G^l_{0,T} = (V,E_{0,T})$ on a time interval [0, T] which consists of a set of nodes or vertices V and a set of temporal edges $E_{0,T}$. The evolving multilayer network is thus $M_{0,T} = \{G^P_{0,T}, G^H_{0,T}, G^A_{0,T}\}$. This multilayer, temporal network is observed at discrete time points $t_1, t_2, \ldots, t_{n-1}, t_n$. At any time point t_n, an instantiation of the multilayer, M_n, is observed, whereby each G^l_n contains the set of temporal edges E^l_n such that  with edges between nodes u, v contained within the period  such that  (ie, the instantiation time is between the start time t_s and end time t_e, and the end time t_e is later than the start t_s). The graphs, being directed, are also nonmirrored such that $(u, v) \neq (v, u)$.

Statistical Analysis

Degree Growth

Influential accounts are those that are very interactive in or across networks. They generally have 2 characteristics: they receive many comments from different users (opinion leaders) and give many comments to different users (engagers). We measure the first characteristic as *indegree* and the second as *outdegree*. Together, the 2 measures for each node indicate an account's activity, and consequently its influence within the network. In addition, as an extension, because the discussion network is multilayer, we use 3 new metrics from Nguyen et al [42] to account for cross-layer interactions, termed *cross-layer metrics*. Correspondingly, we have *cross-indegree* and *cross-outdegree* [42]. These are derivatives from the larger literature of cross-layer measures for multiplex networks [43].

Indegree

The indegree d^l_{in} of node v in layer l measures the number of edges pointing inward to v. If the number of in-neighbors of node v in layer l is $N^l_{in}(v) = \{(u, v) \in E^l\}$, where E^l is the set of edges and u is any other neighbor, the indegree is calculated as $d^l_{in}(v) = |N^l_{in}(v)|$. Any account with a high indegree means that the user has received a lot of attention from other users in the same layer l.

Diversity: Cross-Indegree

The cross-indegree d^M_{in} of node v in the multilayer network M measures the number of edges pointing inward to v across all layers. If the number of unique in-neighbors across the different layers of the network for node v in multilayer network M is the union across layers  , the cross-indegree is calculated as (this calculation is the same as counting the number of unique in-neighbors across the entire network). The higher the cross-indegree, the more that an author attracts attention from users in other layers, or across the network (high engagement across the 3 vaccine sentiments).

Outdegree

The outdegree d^l_{out} of node v in layer l measures the number of edges pointing outward from v. If the number of in-neighbors of node v in layer l is $N^l_{out}(v) = \{(v,u) \in E^l\}$, where E^l is the set of edges and u is any other neighbor, the outdegree is calculated as $d^l_{out}(v) = |N^l_{out}(v)|$. Any account with a high outdegree means that the user has commented on many other users in the same layer l.

Diversity: Cross-Outdegree

The cross-indegree d^M_{out} of node v in the multilayer network M measures the number of edges pointing outward of v across all layers. If the number of unique out-neighbors across the different layers of the network for node v in multilayer network M is the union across layers  , the cross-outdegree is calculated as  . The higher the cross-outdegree, the more that an author engages from users in other layers, or across the network per similar reasoning (indicating commenting across the 3 vaccine sentiments).

Engagement Growth

Spearman Rank

The activity of certain nodes differs across different layers in the multilayer network. To verify whether the active users differ across different layers of the network, I conducted a Spearman rank correlation to measure the similarity between nodes in common for each pairwise combination of layers. This is done for indegree and outdegree because it is a directed network, and measures different aspects of nodes in a network. Correlations run between –1 and 1, with the former indicating a negative correlation between ranks and the latter indicating a positive correlation. Spearman ranks were conducted at each time t_n for temporal visualization, with the total at time T representing the entire Spearman across the entire network. A descriptive metric of the number of overlapping nodes in each pairwise layer was also done to see how nodes generally participate across sentiment layers, both in total and over time.

Temporal Diversity (Macro)

To understand temporal interactions between layers, 2 different levels of analysis were performed. One is the macroscopic network level, assessing how average cross-indegree and

cross-outdegree change over time for layers. The second is at the microscopic network level, focusing on how nodes in each layer interact across the 3 layers, and how this changes over time.

For the macro-level, the cross-indegree of a node v in the multilayer network M, d^M_{in}, is the union of inward edges across the entire network. Similarly, the cross-outdegree of a node v in the multilayer network M, d^M_{out}, is the union of edges pointing outward from v, and is a measure of commenting activity into the multilayer network. These 2 equations account for the number of comments received and given, respectively, for each *node* for each layer. To aggregate either measure up to the layer level l, we sum these values across all nodes in the layer to get the layer cross-indegree, l^M_{in}, and layer cross-outdegree, l^M_{out}:

where $v \in V^l$ indicates all possible nodes in the given layer, and then averaged across all nodes in the layer. The values are computed at each time point t_n and plotted over the interval [0, T] to see how receiving and commenting activities happen temporally. An overall estimate was also made of the multilayer network by taking the value at time T, assuming the network at that time represents the entire network of connections until the right censoring time.

Temporal Degrees (Micro)

For the micro level, I looked at how select nodes (influential nodes) in each layer branched across the 3 layers over time. This was done for 2 types of users: highly diverse nodes and hardliners. The results of these gave an idea of how much different node types contribute to the echo chambering effect. The former compares the participation sites (ie, layers) of nodes that are highly engaging on the forum to see where they are engaging. The latter compares the participation of individuals that only exist within their layer to drive conversation within their layer, entrenching the echo chamber. For highly diverse nodes, the top 50 nodes were taken and their indegrees and outdegrees were measured across each layer for comparison.

For the latter, an entropy constant was used to determine the distribution of connections across the 3 layers. For each node v, $p(l)_v$ was calculated, which is the probability of a connection extending from node v being in layer l. For this purpose, the number of connections any node v has in a layer l is divided by the node in all other layers. The entropy for that node in that layer, $H_{v,l}$, is then computed as follows:

with higher values indicating more equal distribution. To identify the hardliners, the 30 lowest values of entropy within each layer were identified, and their indegree and outdegrees were compared in each layer (across layers).

Overlapping Nodes

A descriptive metric of the number of overlapping nodes in each pairwise layer was done to see how nodes generally participate across sentiment layers, both in total and over time.

Validation: Bootstrapping

Layer classification was performed by 2 independent raters following predefined criteria for stance identification. Although these criteria were developed based on existing literature, there remains a possibility that classifications and resulting statistics could occur by chance. To assess this variability, I conducted all measurements using averages derived from a bootstrap sample (n=1000) as a benchmark for statistical estimates.

Ethical Considerations

All data from PTT are open and publicly available. All data from PTT in its raw form include usernames.These usernames are deidentified and anonymised during the research process to ensure they cannot be traced back to individuals. To do this, a 6 digit alphanumeric temporary username is generated for each unique user. Data is available upon request.

Results

Network Description

From a total of 48,288 scraped boards, 2992 were selected for analysis after categorization: 1283 were provaccination, 1322 were vaccine hesitant, and 387 were antivaccination (Table 2). Boards classified as neutral and irrelevant (n=2826) were excluded from the analysis. The number of nodes and edges in the network correspond to users and comments, respectively. The discussions on the vaccine hesitant layer are the most active with most nodes (v=14,037) and edges (e=33,520), followed by the provaccine layer (v=11,087, e=23,504). Average degrees mirrored this trend, with the vaccine hesitant layer showing the highest degrees and the antivaccination layer the lowest.

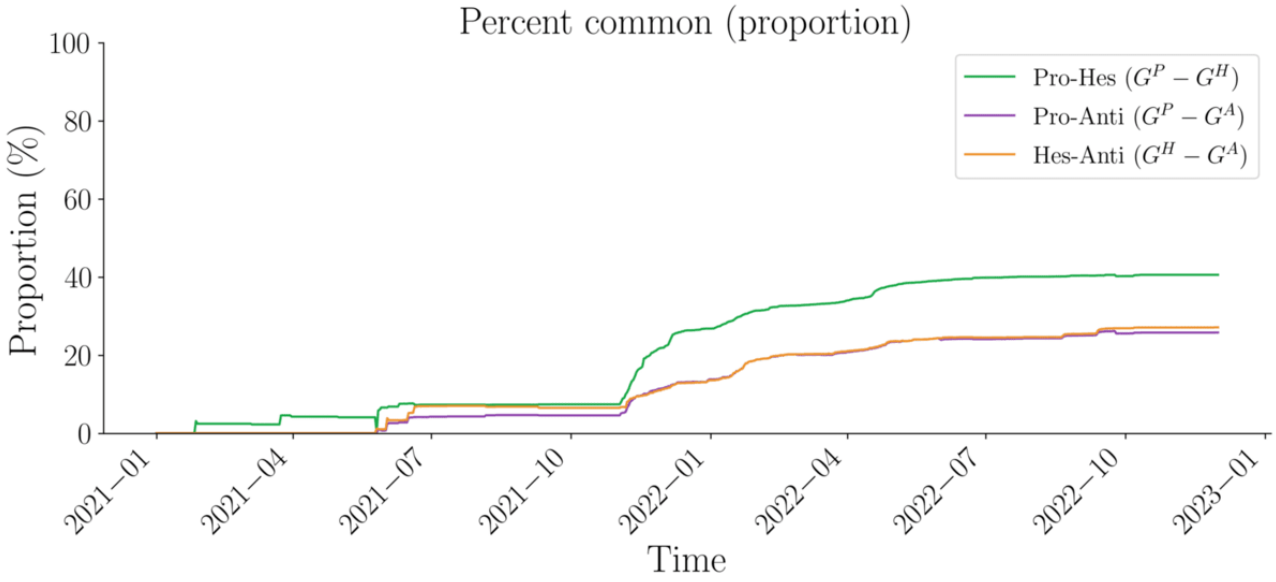
Table 2. Properties of the multilayer network by layer (for average degree, bootstrap n=1000).

Layer	Number of posts, n	Nodes (v; average)	Edges (e; average)	Average degree
G^P	1283	11,087	23,504	4.24 (4.21-4.27)
G^H	1322	14,037	33,520	4.77 (4.75-4.80)
G^A	387	5477	8696	3.18 (3.15-3.20)

Based on the node overlap results across layers, it appears that a significant portion of nodes engaging in provaccination topics also participated in vaccine hesitant discussions (Figure 2). This pattern persists consistently over time, indicating ongoing

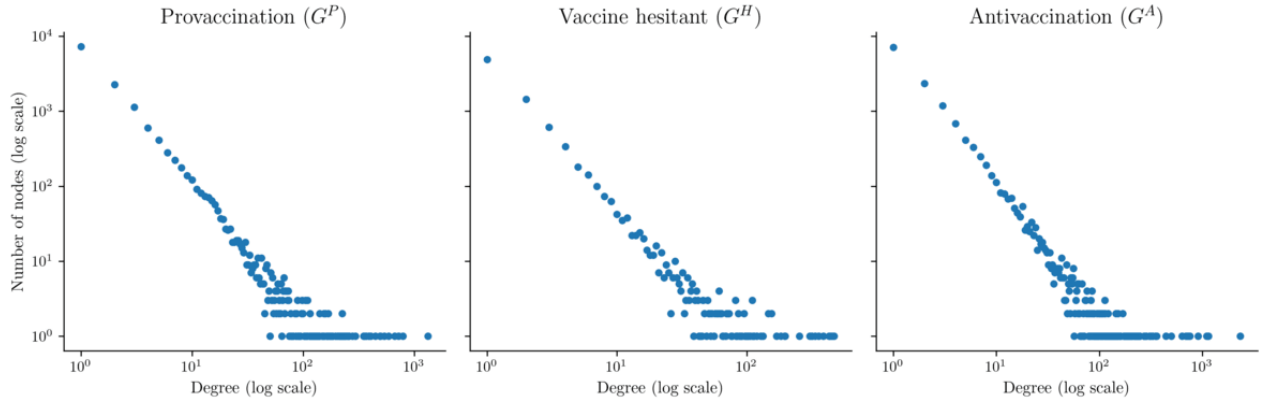
engagement in both topics. A notable sharp increase is observed around November 2021, reflected in the steepening slope of the overlapping curve between provaccination and vaccine hesitant discussions. This trend could be attributed to heightened discussions following the Omicron outbreak. The overlap proportion of nodes engaging in antivaccination topics appears lower for both, indicating that these discussions occur on a smaller scale and are more isolated within the overall network.

Figure 2. Percentage of overlapping nodes in each sentiment layer over time. anti: antivaccination; Hes: hesitant; pro: provaccination.



In network studies, a common analysis involves examining whether networks exhibit power-law distributions, characterized by a connection pattern where a few nodes have many connections and most nodes have few. Figure 3 shows histograms of node degree distributions on a logarithmic scale, visually illustrating a power-law distribution with a heavy tail. The sigma, an exponential parameter of the power-law distribution, was estimated for each layer. Layers that adhere to power-law networks exhibit probability distributions of degree d, $p(d)$, following a power-law relationship $p(d)\ d^{\delta}$, where $\delta \geq 1$ is an exponential parameter (typically with a value around 2). Upon estimating sigma for the power-law parameter, it was found that all 3 layers have sigma values of around 2. For the significance test, where significant P values (ie, $P \leq .05$) indicate a deviation from the power-law value $\delta \approx 2$, all layers exhibited a power-law network (G^P: δ=2.2, P=.067; G^H: δ=2.3, P=.068; G^A: δ=2.3, P=.09). This suggests that all 3 layers are characterized by a distribution where a few nodes have many connections. A previous study on PTT also identified a similar power-law structure on the platform [42].

Figure 3. Log-log plots of number of nodes by degrees to determine power-law structure.



Macro-Network Echo Chambering

Table 3 presents Spearman rank correlations for the entire network. It shows that, on average, the ranking based on indegree is higher than that based on outdegree. This implies that individuals who receive many comments within 1 layer also tend to do so in other layers. Particularly notable is the strong correlation between the provaccination and hesitant layers, indicating a significant overlap in nodes between these 2 layers as a partial explanation for this trend. The hesitant-antipair also shows a comparable trend, with high rankings in indegree suggesting that similar users receive comments across these layers, despite their smaller overlap in node percentage. In terms of commenting activity, overall correlations weakened, indicating that users tend to comment on sentiment boards aligned with their stance, possibly

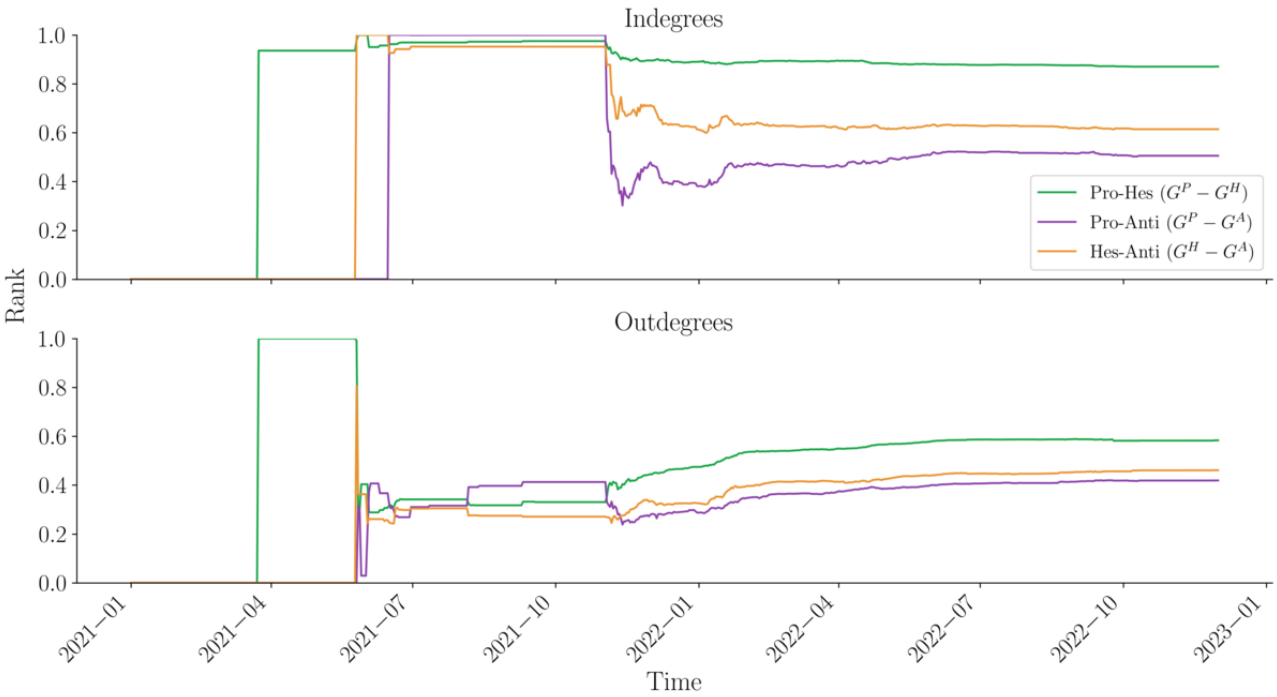
indicating an echo chamber effect. Across all pairwise comparisons of layers, the provaccination and antivaccination layers exhibited the least correlation in indegree and outdegree rankings, suggesting polarization within the network. The low overlap in node percentage further supports this observation.

Table 3. Pairwise Spearman ranks by indegree and outdegree metric by pairwise layer comparison (overall, bootstrap n=1000).

Layer	Indegree, mean (CI)	Outdegree, mean (CI)
(G^P, G^H)	0.8698 (0.8693-0.8703)	0.5831 (0.5825-0.5838)
(G^P, G^A)	0.5035 (0.5025-0.5044)	0.4212 (0.4200-0.4224)
(G^H, G^A)	0.6138 (0.6129-0.6146)	0.46130 (0.4602-0.4623)

These trends vary slightly over time (Figure 4). From the initial period to November 2021, we observe a high correlation in users receiving comments across different layers, indicating a small group of key users generating boards of interest. However, in terms of commenting activity, the correlation between provaccination and antivaccination sentiments is highest, suggesting some disruption in the observed echo chamber effect. Simultaneously, the overall percentage of overlapping nodes remains low (considering that Spearman ranks are compared only among similar nodes). As the network expands and the percentage of common nodes increases between the provaccination and hesitant sentiment networks, we also observe a sharp decline in users receiving and giving comments across the provaccination and antivaccination layers, suggesting a temporal polarization effect. This trend becomes particularly noticeable around November 2021.

Figure 4. Pairwise Spearman ranks by indegree and outdegree metric by pairwise-layer comparison (temporal). anti: antivaccination; Hes: hesitant; pro: provaccincation.



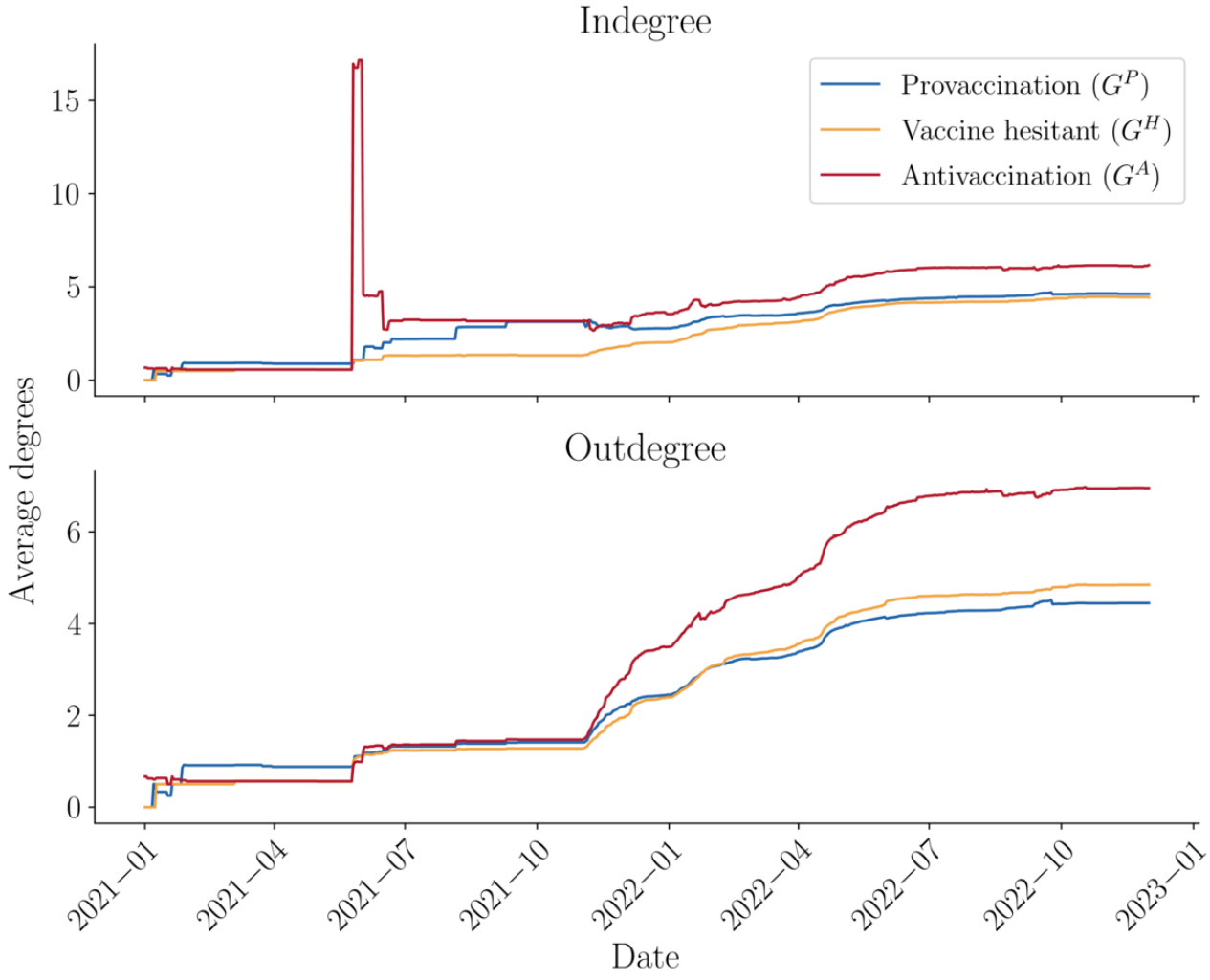
When comparing across layers, the antivaccination layer exhibits the highest average indegree and outdegree diversity overall (Table 4). To elucidate this trend, it is important to note that while the Spearman rank only considers nodes appearing in multiple layers (indicating engagement across different vaccine sentiments), the layer average encompasses all nodes, whether they participate in multiple layers or only 1. Therefore, while common nodes may suggest some attenuation of chambering in receiving comments and polarization in giving comments, there are also unique nodes that span multiple layers. This trend is most pronounced for the antivaccination layer, indicating that it is the least chambered among the layers based on the activity of its constituent nodes, despite its relatively smaller size.

Table 4. Average indegree and outdegree diversity by layer (total).

Layer	Indegree diversity, mean (CI)	Outdegree diversity, mean (CI)
G^P	4.62 (4.59-4.64)	4.44 (4.43-4.45)
G^H	4.43 (4.41-4.48)	4.84 (4.83-4.85)
G^A	6.16 (6.05-6.27)	6.95 (6.89-7.00)

Temporally, these trends are generally consistent, with a few notable exceptions. Figure 5 tracks the average indegree and outdegree diversity by layer over time. Before November 2021, there is a notable peak in the average indegree for the antivaccination layer. This spike likely corresponds to a post that received significant attention, despite the antivaccination layer being relatively small at that time. Otherwise, the antivaccination layer maintains a higher average indegree consistently until December 2022. Regarding outdegree, all 3 layers show similar values until November 2021, after which the antivaccination layer exhibits a sharp increase followed by a gradual decline. This increase suggests intensified commenting behavior within the layer, potentially indicating a break in the echo chamber effect compared with the other 2 layers.

Figure 5. Average indegree and outdegree diversity by layer (temporal).



Micro-Network Echo Chambering

The findings in the previous section indicate a push-and-pull effect between chambering and nonchambering dynamics. Although nodes common to both layers may exhibit some chambering tendencies, the antivaccination layer as a whole includes more nodes that extend across multiple layers. This section further explores the chambering trend by examining the contributions of 2 user types, high-diversity nodes and hardliners, within the multilayer network.

Comparing indegrees and outdegrees of highly diverse nodes across each layer reveals their polarized engagement, contributing to sentiment echo chambers. The results indicate that nodes with the most diverse participation predominantly receive and give comments on provaccination topics (Table 5). This trend is particularly substantial for indegrees, where most

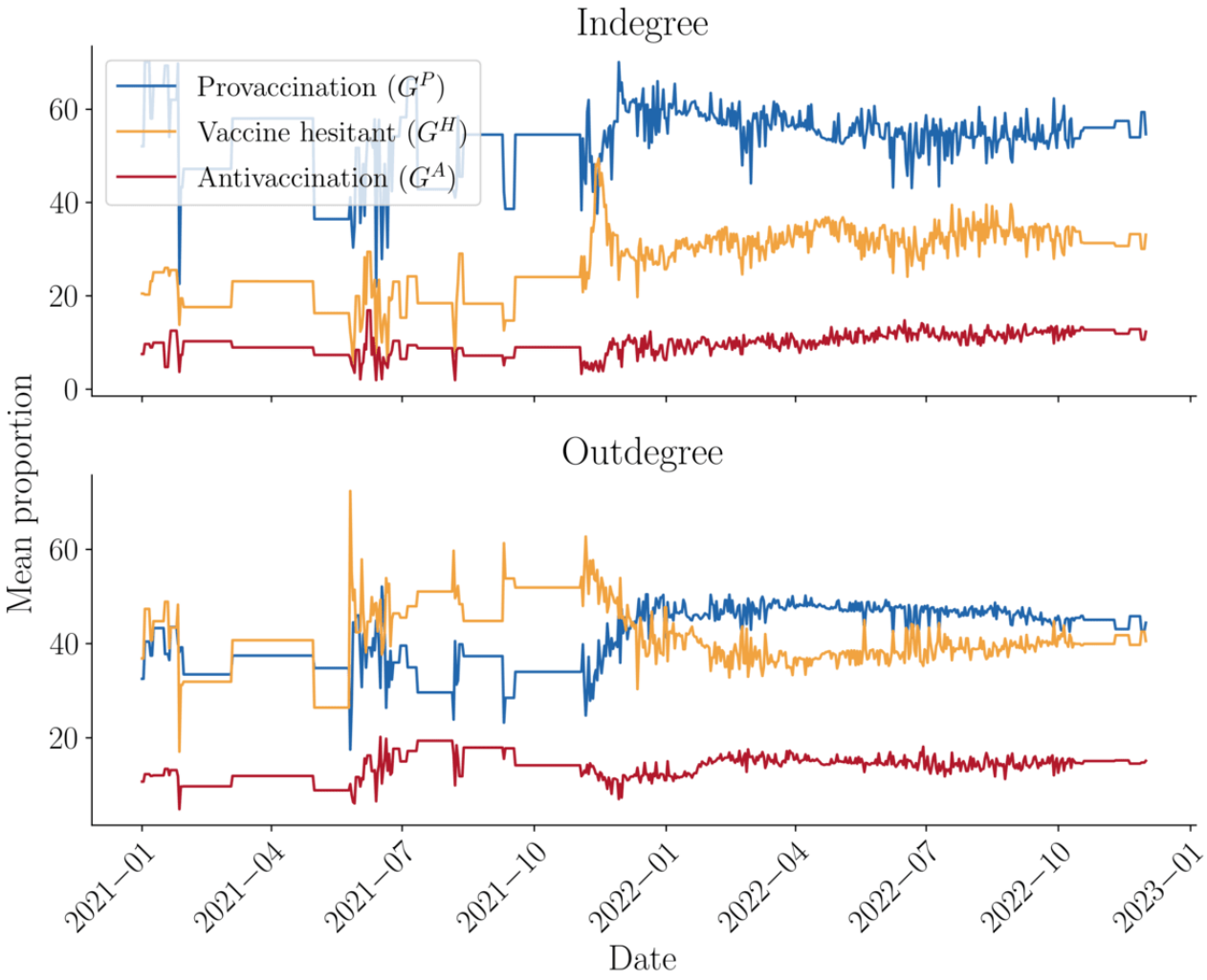
comments are received on the provaccination layer. For outdegree, there is no difference between the provaccination and hesitant layers, indicating that diverse nodes comment similarly on both topics and potentially disrupt the chambering effect. However, considering the larger size of the vaccine hesitant layer, this could imply that diverse nodes receive more comments from the provaccination layer, reinforcing chambering. Compared with the provaccination and hesitant layers, the antivaccination layer shows the least interaction from diverse nodes in terms of both giving and receiving comments. This trend is anticipated due to the smaller size of the antivaccination layer, and the proportion of connections aligns with its relative size compared with the other layers. These findings suggest that the forum as a whole may exhibit a preference for engaging with provaccination messaging, indicating a form of chambering, albeit in a protective manner. Diverse nodes are then spanners through the network.

Table 5. The proportion of connections into each vaccine topic layer by the top 50 diverse nodes (total).

Layer	G^P		G^H		G^A	
	Indegree, mean (CI)	Outdegree, mean (CI)	Indegree, mean (CI)	Outdegree, mean (CI)	Indegree, mean (CI)	Outdegree, mean (CI)
Proportion of connections	54.63 (43.42-60.84)	44.40 (42.41-46.39)	33.07 (26.70-39.43)	40.51 (37.70-43.34)	12.30 (7.62-16.99)	15.09 (13.62-16.54)

Temporally, these trends largely hold, with a notable exception in the outdegree for the vaccine hesitant layer (Figure 6). Initially, commenting from diverse nodes was predominantly directed at the vaccine hesitant layer, but by November 2021, there was a notable shift toward engagement with the provaccination layer. This shift may indicate a trend toward forming a “health community” facilitated by network spanners. Further reinforcing this point is that the gap between the provaccination and hesitant layers diminishes from July 2022 until the end of the period under study, indicating another shift in the chambering effect. This breaking of chambering is also evident in the indegree for the antivaccination layer, which shows a slight overall increase starting from November 2021. This suggests that the antivaccination layer is increasingly engaging with diverse nodes.

Figure 6. Proportion of connections into each vaccine topic layer by top-50 diverse nodes (temporal).



Hardliners (ie, those who predominantly engage within their own layer) are compared across layers to assess how they drive echo chambering within their respective layers. The results indicate that antivaccination hardliners are more active in commenting on antivaccination boards compared with the other 2 layers (Table 6). This trend remains consistent over time and shows a slight sharp increase in February 2022 during the Omicron outbreak in Taiwan (Figure 7, upper panel). However, this does not imply that the vaccine hesitant layer is entirely inactive within itself. The high indegrees suggest significant commenting within the layer, possibly indicating that a few nodes are responsible for disseminating information received by others. This trend gradually intensifies over time, with spikes observed during early vaccine procurement and the announcement of relaxed antiepidemic measures in late 2022 (Figure 7, bottom panel). Antivaccination hardliners predominantly receive information within their own group, particularly surging during the Omicron outbreak and continuing steadily thereafter. This engagement suggests that hardliners in the vaccine hesitant and antivaccination layers contribute to the entrenched ideologies within their respective groups over time.

Figure 7. Temporal and cumulative outdegree and indegree growth among hardliners for each layer (temporal).

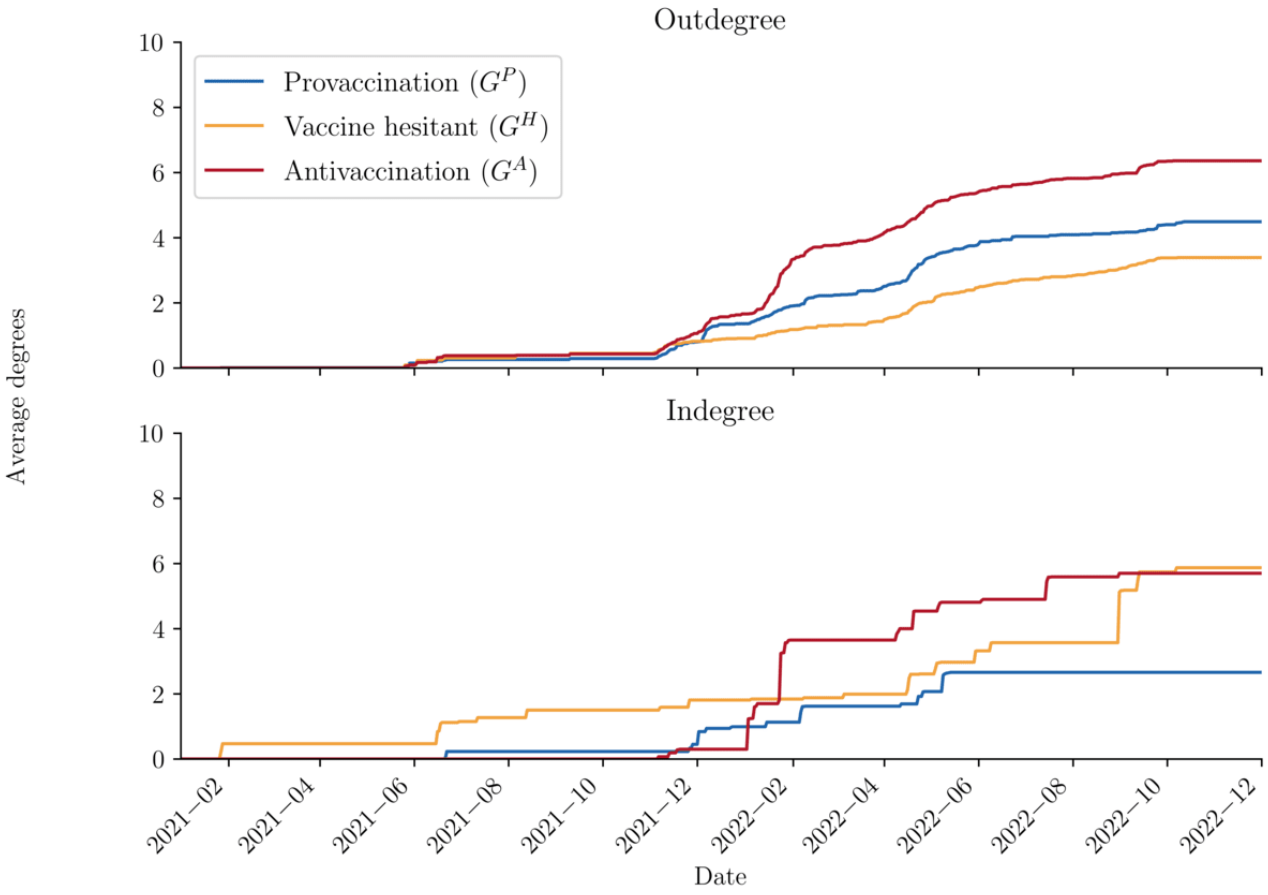


Table 6. Total standardized outdegree and indegrees for hardliners within their own layer (total).

Layer	Outdegrees, mean (CI)	Indegrees, mean (CI)
G^P	2.84 (2.81-2.88)	1.70 (1.62-1.77)
G^H	2.15 (2.11-2.19)	3.71 (3.47-3.96)
G^A	4.03 (3.97-4.10)	3.58 (3.38-3.78)

Discussion

Principal Findings

This study examined temporal chambering at the macro-network layer level and assessed the role of influential users in this process. Overall, the layers demonstrated chambering in their commenting behaviors, particularly evident in the strong polarization between the provaccination and anti-vaccination stances. Diverse nodes showed significant cross-layer engagement, particularly in the provaccination and vaccine hesitant layers. This contrasts with hardliners, who show more activity within the vaccine hesitant and antivaccination layers. These findings suggest strategies for information management moving forward and contribute to the evolving field of infodemic management.

Despite attempts to definitively assess the existence or absence of echo chambers, it is apparent that multiple chambering and nonchambering processes likely occur. For instance, analysis of similar nodes through Spearman ranks indicates varying degrees of chambering across layers and measurement criteria. The provaccination and antivaccination layers appear to exhibit the highest polarization on both measures, while the provaccination and vaccine hesitant layers show the least polarization. These findings align with previous network studies that have identified echo chambers in social media discussions on vaccines, particularly along the provaccine and antivaccine lines [24,26,29]. Additionally, the trend for receiving comments (indegree) shows less overall polarization compared with the trend in commenting (outdegree), suggesting that users may actively engage by expressing their own sentiment preferences.

Another significant factor contributing to chambering is the activity of specific nodes. Hardliners show significantly higher activity within the antivaccination layer compared with the other 2, indicating a stronger entrenchment effect (chambering). Strategies to mitigate this effect could include flagging or tagging posts from antivaccination hardliners [44]. Flagging represents an effort to balance the protection of an open, democratic forum while countering harmful messaging, akin to Singapore's Protection from Online Falsehoods and

Manipulation Act (POFMA) [45]. Additionally, involving moderators in content management [46,47] aimed at antivaccination hardliners could mitigate their impact on chambering [48]. Highly diverse nodes also allocate fewer comments proportionally to the antivaccination layer, with their engagement primarily centered around the provaccination layer, contributing to their diversity. These provaccination users can serve as valuable resources for disseminating promotional messages, given their demonstrated willingness to engage. Using these multipronged strategies concurrently aligns with common approaches to countering antivaccination movements [49].

Conversely, certain nodes engage in activities that disrupt chambering. The antivaccination layer exhibits the highest average indegree and outdegree compared with the other layers. This indicates that, apart from the nodes common to the Spearman calculations, a significant portion of this layer actively participates in both receiving and giving comments across the entire network. These findings contribute to the broader discourse on "structural hole spanners" within networks [50]. These individuals often act as bridges across diverse topics, engaging with users who hold cross-cutting attitudes toward vaccination [51]. These findings also support earlier research indicating that the vaccine hesitant group serves as a "battleground" where pro- and antivaccination narratives compete [25]. The intermediate Spearman rank values between the hesitant layer and the other 2 layers in both indegree and outdegree reinforce this idea, suggesting that the hesitant layer exhibits closer overlap with both groups.

Temporally, there are several active periods where trends shift. In the initial period from January to June 2021, the presence of a few boards makes each layer more responsive to new threads and comments, resulting in stepped patterns and high fluctuations. Surprisingly, despite Taiwan's slow vaccine procurement and its first "large" outbreak (approximately 300 daily cases), which would typically attract more attention, the forum remains relatively silent on COVID-19 vaccine issues. Around June 2021, as vaccines become more readily available, several trends become more pronounced. The most significant changes occur in November 2021: cross-cutting users comment more on the provaccination layer, antivaccination hardliners become more insular, and polarization intensifies between the provaccine and antivaccine layers. During this period, various booster policies, the Delta outbreak, and the impending Omicron outbreak likely contributed to increased dialog around vaccines.

Limitations and Next Steps

There are several limitations to this study and avenues for exploration, particularly in relation to the WHO's infodemiology research agenda.

The first concern pertains to the data set. Social media platforms often attract specific user demographics and ideological stances. Additionally, the amount of data accessible through application programming interfaces may restrict the availability of scraped data, affecting the representativeness of the general population, a key goal in epidemiological studies. These inherent biases in social media data can internally skew the results. Despite PTT's loose moderation and nonprofit nature, it is not immune to these limitations. To better contextualize the study, it is crucial to acknowledge its limitations stemming from these factors. To mitigate this bias, several approaches can be considered. First, conducting a comparative study—either on another topic within the same forum or across different platforms—would be beneficial. For instance, conducting similar analyses on DCard, an X-style platform known for attracting a younger demographic, could provide cross-validation of findings across different generations and platform types. This approach can also be extended to more international platforms such as X or Instagram. Another method is to validate the findings by comparing them with sentiment data from epidemiological sources. Conducting such comparative studies can enhance the reliability of these findings, ensuring that observed differences are not merely artifacts of platform or network size variations. These methods align well with the infodemic research agenda, emphasizing the triangulation of diverse data types to better integrate epidemiological and infodemiology insights.

Another limitation is that the definition of "influence" is not exhaustive in this study. The study identifies influential users using indicators such as diversity and hardliners, but these metrics are not comprehensive. The choice of indicators is often constrained by the platform's structure and available data. For instance, follower count could be a measure of influence on platforms such as X, but PTT lacks such indicators. Despite these limitations specific to PTT, a broader array of metrics for measuring influence remains possible. Indeed, measuring the percentage of positive or negative engagement based on sentiment markers of user posts, as well as their active time spent on the forum, could provide additional dimensions to assess influence. Exploring a spectrum of influence metrics across comparative studies could further enrich our understanding of user dynamics within different platforms.

To better gauge the actual impact of "influential users" on chambering and network structure, conducting network simulations could be highly beneficial. These simulations could help bridge the gap between identifying influential users based on various metrics and understanding how their behaviors contribute to the overall network dynamics and chambering phenomena. Exploring these methods would indeed advance the understanding of chambering dynamics in online discussions about vaccination. Conducting network simulations where influential nodes are systematically removed can reveal how their presence or absence affects the clustering and cohesion of different sentiment layers. Additionally, performing regressions at the user level to analyze factors influencing their engagement across provaccine, vaccine hesitant, and antivaccine stances could provide insights into the drivers of polarization and chambering within the network. These approaches align well with the goals of infodemic management during epidemics, as outlined in the WHO research agenda.

Understanding the underlying reasons behind chambering trends in online discussions about vaccination is crucial for preparing and responding to future infodemics effectively. Identifying whether these trends are triggered by outbreaks, policy changes, or other factors unrelated to outbreaks can provide insights into the temporal dynamics of chambering. This knowledge aids in tracking infodemics and vaccine sentiment on social media platforms. Integrating this narrative with analyses of clustering

and network dynamics helps illustrate the cause-effect chains driving chambering and their broader impacts on public discourse and health communication strategies. This comprehensive distillation of pathways represents a critical step in the broader paradigm shift toward integrating epidemic studies with infodemic studies, rather than treating them as separate entities.

The importance of overlapping across the layers is underemphasized in this study and carries implications for construct validity. The current framework assumes that each layer encapsulates all sentiments related to a specific vaccine stance, essentially forming a "discussion sphere" or "space" around that stance. Users can comment in multiple layers because they hold diverse vaccine sentiments, thereby blurring the exclusivity of layers and indicating cross-cutting behavior, which breaks the chambering effect. A clearer illustration of how users comment across layers over time would help distinguish true chambering from typical forum behavior where users engage across multiple boards.

The final major limitation is the absence of content analysis. Although layer- and node-level metrics serve as proxies for cross-layer communication, the specific direction and nature of engagement, such as the content exchanged, are unclear without detailed content analysis. Understanding the content aspect would provide further insights into how engagement occurs between these layers and users. This also partially addresses the issue of overlapping, shifting from engagement across layers as a measure of chambering to engagement with similar vaccine sentiments. Further along the infodemic management agenda, understanding content also informs how interventions should be designed. For instance, engagement with pro- and antivaccination content could lead to either constructive or destructive discussions. Focusing on specific content types, such as misinformation, further illustrates the existence or formation of echo chambers. This approach also aligns with the WHO's research agenda on infodemics, linking echo chambering to unhealthy behaviors and potentially serving as a focal point for public health interventions.

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Data Availability

Data from PTT are publicly available. Data used for this analysis are available upon reasonable requests made to the author of this paper.

Conflicts of Interest

None declared.

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Abbreviations

BBS: bulletin board system
CDC: Centers for Disease Control and Prevention
POFMA: Protection from Online Falsehoods and Manipulation Act
WHO: World Health Organization

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Original Paper

Google Trends Assessment of Keywords Related to Smoking and Smoking Cessation During the COVID-19 Pandemic in 4 European Countries: Retrospective Analysis

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Abstract

Background: Smoking is a modifiable risk factor for SARS-CoV-2 infection. Evidence of smoking behavior during the pandemic is ambiguous. Most investigations report an increase in smoking. In this context, Google Trends data monitor real-time public information–seeking behavior and are therefore useful to characterize smoking-related interest over the trajectory of the pandemic.

Objective: This study aimed to use Google Trends data to evaluate the effect of the pandemic on public interest in smoking-related topics with a focus on lockdowns, vaccination campaigns, and incidence.

Methods: The weekly relative search volume was retrieved from Google Trends for England, Germany, Italy, and Spain from December 31, 2017, to April 18, 2021. Data were collected for keywords concerning consumption, cessation, and treatment. The relative search volume before and during the pandemic was compared, and general trends were evaluated using the Wilcoxon rank-sum test. Short-term changes and hereby temporal clusters linked to lockdowns or vaccination campaigns were addressed by the flexible spatial scan statistics proposed by Takahashi and colleagues. Subsequently, the numbers of clusters after the onset of the pandemic were compared by chi-square test.

Results: Country-wise minor differences were observed while 3 overarching trends prevailed. First, regarding cessation, the statistical comparison revealed a significant decline in interest for 58% (7/12) of related keywords, and fewer clusters were present during the pandemic. Second, concerning consumption, significantly reduced relative search volume was observed for 58% (7/12) of keywords, while treatment-related keywords exhibited heterogeneous trends. Third, substantial clusters of increased interest were sparsely linked to lockdowns, vaccination campaigns, or incidence.

Conclusions: This study reports a substantial decline in overall relative search volume and clusters for cessation interest. These results underline the importance of intensifying cessation aid during times of crisis. Lockdowns, vaccination, and incidence had less impact on information-seeking behavior. Other public measures that positively affect smoking behavior remain to be determined.

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KEYWORDS

internet; coronavirus; COVID-19; SARS-CoV-2; pandemics; public health; smoking cessation; tobacco products; Google Trends; relative search volume; Europe; online; search; smoking; addiction; quit; cessation; trend; cluster; public interest; lockdown; vaccination; spread; incidence

Introduction

COVID-19 Pandemic in Europe

The SARS-CoV-2 (COVID-19) pandemic posed unprecedented challenges to global health care and public health. SARS-CoV-2, the virus responsible for COVID-19 infection, initially surfaced in Wuhan, China, in December 2019 and quickly spread worldwide [1]. The first cases in Europe were reported in January 2020, shortly after it was declared a global pandemic by the World Health Organization (WHO) [2].

Smoking is a COVID-19 Risk Factor

European countries exhibited disparate patterns of incidence and mortality rates during the pandemic that triggered national governments to pass varying public restrictions, for example, the shutdown of public institutions, curfews, quarantine, and the use of face masks in public spaces [3,4]. The predominant manifestation of COVID-19 infections is characterized by the clinical triad of cough, fever, and symptoms resembling those of influenza [5]. In the initial stages of the pandemic, there ensued a discourse regarding putative protective attributes associated with smoking, as a study showed a lower incidence of COVID-19 infection among smokers [6]. These studies received a lot of media attention. However, as cumulative data have been assimilated, smoking is currently discerned as a substantial risk factor for potentially life-threatening consequences following infection [5,7-11]. Also, the authors of the mentioned studies had severe nondeclared conflicts of interest with the tobacco industry [12]. Hence, in light of the ongoing COVID-19 pandemic, smoking as a modifiable risk factor has re-emerged as a focal point within public health concerns.

Changes in Smoking Behavior During the Pandemic

Many studies addressed smoking behavior during the COVID-19 pandemic in different locations, during diverging periods, and using varying methods [13-19]. A large meta-analysis points to an increase in smoking [15]. Still, no general conclusion can be drawn from the presented evidence regarding changes in consumption and cessation. Smoking cessation can be categorized into 2 groups. One is commercially available substitutes, such as nicotine patches and e-cigarettes. The latter are advertised as less harmful cessation aids. Despite that, the current evidence is ambiguous and their role during the COVID-19 pandemic is understudied [17]. In addition, expert guidance is available for smoking cessation. Yet during the pandemic and due to associated restrictions regarding mobility and face-to-face meetings, availability might have been a challenge for patients [20]. In a previous study, our group shed light on the quitting behavior of smokers and ex-smokers in England, Germany, Spain, and Italy during the pandemic [21]. Despite psychological distress about the severe outcomes of COVID-19 infection, no higher rates of smoking cessation attempts were observed. Individuals may react both ways and augment their consumption patterns as a mechanism for stress mitigation or demonstrate an increased interest in cessation programs or the adoption of alternative nicotine replacement products due to a fear of severe outcomes [21-24].

Methodological Introduction to Google Trends Data

This follow-up study further investigates the aforementioned countries. Google Trends data were retrieved to monitor public interest in smoking, cessation, and treatment. Google Trends data reflect interest for keywords on a scale from 0 to 100 (relative search volume [RSV]) relative to all search inquiries in a given period and location. Google Trends data have been proven a valid tool in medical research and have been applied throughout various fields of medicine, for example, evaluating the effects of interventions or forecasting future trends to prepare health care providers [25,26]. In smoking-related research, different tobacco control measures have been evaluated using RSV [27-30]. Furthermore, a study by Cavazos-Rehg et al [31] linked the information-seeking behavior on Google with real-life use of tobacco products. Google Trends data have the advantage of being easily accessible, objective, and always up-to-date. These properties are especially useful in the dynamic event of a pandemic [32,33]. Furthermore, during the COVID-19 pandemic, people turned to the internet for guidance on health-related topics [34]. Previous publications displayed an increase in RSV for selected mental health–related keywords [32,35]. As cited above, psychological distress also seems to play a major role in motivation for cessation [21-23]. In line, studies at the intersection of Google Trends data and smoking research during the pandemic are limited but showed stable or decreased interest in cessation [16,19,36].

Hypothesis, Study Design, and Implications

Based on previous research, we hypothesized that major events during the pandemic caused substantial changes in public interest for smoking-related topics concerning consumption, cessation, and treatment [15,16,36]. Among these major events, it was assumed that lockdowns, vaccination campaigns, and rising incidence would induce the greatest echo in Google Trends data [33]. From the results of available survey studies, we expected the RSV to mirror the trend of increased interest in consumption and a decrease in cessation and treatment [15].

For investigation, a reasonable period was selected from December 31, 2017, to April 4, 2021, capturing the dynamics of the transition into the pandemic state and comprising multiple waves of infection. Changes in RSV were evaluated in 3 separate ways. First, the overall RSV for the abovementioned domains after the start of the pandemic were compared. Second, short-term changes in RSV were addressed. Cluster analysis was conducted to discern the lockdown measures, the start of vaccination, and changing incidence rates that evoked the greatest levels of interest, in terms of RSV. Third, the general occurrence of clusters was compared between the before and during the pandemic state.

Identification of optimal timing and kind of intervention is essential to protect vulnerable groups during a public health crisis. Currently, evidence in the field of smoking cessation during the pandemic is mainly reliant on survey-generated data and is heterogeneous. RSV data are a cost-effective and instantaneous tool to monitor public interest and might effectively supplement the survey data. By screening various keywords, appropriate interventions might be determined. These insights could guide policy makers and health care providers:

first, if intensification of public campaigns for cessation aid and information about treatment is necessary in times of pandemics and second, to follow up on possible detrimental effects on smoking behavior due to political measurements such as lockdowns.

Methods

Data Collection

Google Trends query was carried out based on methodological suggestions by Nuti et al [25]. The weekly RSV was retrieved from Google Trends on July 1, 2023, for each country during the period from December 31, 2017, to April 18, 2021, to investigate a reasonable time preceding the pandemic to identify changes [37]. The preceding period had to be long enough to serve as a comparison mirroring long-term trends and patterns. The observed period after the onset of the pandemic spanned approximately the first 3 waves of infections according to the Robert Koch Institute and hereby sufficiently reflects dynamics at the beginning of the pandemic [38]. Major events during the pandemic were lockdowns and vaccinations. The dates of these events are country-wise depicted in Table 1. Data were collected for the indicated keywords, as listed in Table 2. All query categories were searched, no quotation marks were used, and locations were set according to the 4 countries. To examine alterations in the search behavior surrounding smoking-related keywords, our study targeted 3 specific domains: cessation, treatment, and consumption. A comprehensive translation of the relevant keywords into all 4 designated languages was conducted. Word selection was carried out based on expert consensus and literature review. Most common tobacco products and treatment options were filtered [39-44]. For terms regarding cessation, previous research concerning RSV data in the context of cessation was searched [16,28-30,36]. However, choices were restricted by the overlapping availability of Google Trends data for each country. Otherwise, keywords were chosen to display a broad spectrum of each abovementioned domain. Noteworthy Champix (trade name for varenicline) was chosen over varenicline as varenicline showed higher variability in RSV over time, increasing the susceptibility of this keyword to outliers. In the following text, the English term is used for cases of subsumption.

Table 1. Dates of major events by country. Since there is high heterogeneity of lockdown measures between the investigated countries, the listing of specific bans was omitted. However, shared characteristics of lockdowns were the closure of public cultural facilities, curfew, the ban on assembly, and restriction of mobility.

	England	Germany	Italy	Spain
Start of lockdowns	• March 23, 2020 • November 5, 2020 • January 6, 2021	• March 22, 2020 • November 1, 2020	• March 10, 2020 • October 26, 2020 • March 15, 2021	• March 14, 2020 • October 25, 2020
Start of vaccination	• December 8, 2020	• December 27, 2020	• December 27, 2020	• December 27, 2020

Table 2. Keywords by country and domain.

Domain	England	Germany	Italy	Spain
Consumption	• Cigarette • Cigar • Tobacco	• Zigarette • Zigarre • Tabak	• Sigaretta • Sigaro • Tabacco	• Cigarrillo • Cigaro • Tabaco
Cessation	• Smoking cessation • Smoke free • Stop smoking	• Raucherentwöhnung • Rauchfrei • Rauchen aufhören	• Smettere di fumare • Anti fumo • Non fumatore	• Deshabituatión tabaquita • Libre de humo • Dejar de fumar
Treatment	• Nicotine patch • e-cigarette • Champix	• Nikotinpflaster • E-Zigarette • Champix	• Cerotti alla nicotina • Sigaretta electtronica • Champix	• Parche de nicotina • Cigarillo electrónico • Champix

RSV serves as a temporally resolved representation of search behavior concerning a designated keyword. The term “relative” refers to the quantitative assessment of search queries associated with the keyword relative to the total search query volume prevalent at a given point in time in a specified location. To facilitate meaningful comparisons and emphasize variations in search term popularity over time, the time point at which this ratio reaches its maximum is conventionally designated as having an RSV of 100. All other values within the examined period are subsequently expressed regarding this maximum.

Data concerning the COVID-19 pandemic incidence were retrieved from the UK Health Security Agency data dashboard for England [45] and from Our World in Data COVID-19 Data set for Germany, Italy, and Spain [4]. Lockdown measurements and the start of vaccination were selected and gathered from the media.

Statistical Analysis

For statistical analysis of time series, 3 different approaches were used. First, for overall trends, the Wilcoxon rank-sum test was applied to compare the entire RSV by keywords before and during the pandemic. A similar approach was previously presented by Cunningham et al [36]. The onset was defined as January 24, 2020, with the first reported cases in Europe [2].

To verify that the date chosen for the division of the time series was appropriate, we confirmed by checking the RSV of common search terms linked to the pandemic (exemplary for Germany: "COVID-19," "Coronavirus," and "Pandemie"). The week of the first reported case in Europe coincided with the emerging interest in the indicated terms as RSV started to rise (Multimedia Appendix 1). These dynamics were also presented by Effenberger et al [46]. *P* values were adjusted using the Benjamini-Hochberg procedure to control for false discovery rate [47]. This approach only compares RSV before and during the pandemic, therefore fluctuations within the pandemic are beyond the scope of this kind of analysis. A higher temporal resolution is necessary to reveal changes in RSV within the time of the pandemic.

Hence, for short-term changes in RSV possibly linked to COVID-19–related events, a cluster detection test was used. This flexible scan statistics was introduced by Takahashi et al [48] and is a common approach in epidemiologic research and has been previously used in the context of RSV data [27]. For events evoking the greatest interest in a population, we anticipated lockdown measurements, vaccination campaigns, and steep rises in incidence, based on expert consensus and previous research [33]. R programming language (R Core Team) was used to apply the *FleXScan* package [49]. The settings for the algorithm were adapted from Tabuchi et al [27] and are (1) the prespecified significance level for the restriction $\alpha 1=.2$, (2) the significance level of the test $\alpha=.05$, (3) replications of the Monte Carlo hypothesis testing 999, (4) maximum length of a cluster 17 weeks, and (5) minimum length of a cluster 2 weeks. For the baseline of expected RSV at an indicated date, the median RSV of the period 26 weeks flanking the corresponding date was used. This ensured that temporal clusters could be identified irrespective of long-term trends.

Third, a chi-square test was performed to compare the number of weeks that were part of clusters before and during the pandemic. Clusters were aggregated by domains. This was done to verify if the accumulation of periods with heightened interest was randomly distributed before and after the onset of the pandemic. $P<.05$ were considered statistically significant. Tabular data were handled in .xlsx format. R Studio and R programming language were used for all calculations and generation of plots [50,51].

Ethical Considerations

The use of publicly available data and nonpersonally identifiable information within this research obviates the necessity for an ethics review process.

Results

Visual Inspection

RSV for keywords of smoking consumption, cessation, and treatment from December 31, 2017, to April 4, 2021, are depicted in Figure 1. Visual inspection revealed 3 aspects. First, there are large differences in the variability of the RSV for the keywords examined. High variability is characterized by trends on the x-axis and isolated spikes with high RSV. Keywords in the consumption group appeared to be less variable, while terms in the cessation and treatment groups showed higher variability, especially in Italy and Spain (Figure 1). Second, overarching trend lines seem to decline within all domains and countries, with few exceptions that are later presented. Third, there seems to be no accumulation of substantial clusters after the start of the pandemic, again with few exceptions (Figure 1).

Figure 1. Relative search volume data and new cases per million over time. Dashed lines illustrate long-term trends in relative search volume calculated as linear regression. The vertical dotted line indicates the defined start of the pandemic in Europe with the first confirmed case on January 24, 2020. The vertical solid lines mark the start of lockdowns. The gray dashed lines mark the start of the vaccination campaigns. The color-coded solid lines below the x-axis mark the clusters. Countries are separated by quadrants: upper-left England (ENG), upper-right quadrant Germany (DEU), lower-left Italy (ITA), and lower-right Spain (ESP). RSV: relative search volume.

Consumption

For the general effects of the pandemic, a comparison of the entire RSV was conducted before and after the start. Hereafter, a short-term relationship between lockdown measures and the start of vaccination and RSV data was established. Observations were made to ascertain whether clusters initiate or exhibit an abrupt termination with the commencement of lockdown measures.

For consumption, we saw an overarching trend of decline in RSV after the start of the pandemic. For 7 (58%) out of 12

consumption-related keywords, a significantly reduced RSV was observed. However, there were exceptions. “Cigar” had more RSV during the pandemic than before in England (P=.04). Besides, in Germany and Spain, we saw an increase in informational demand for “tobacco” (P<.001 and P=.03; Table 3). In short-term dynamics, long-lasting clusters for “tobacco” at the beginning of the pandemic for the aforementioned countries were observed. A second “tabaco” cluster emerged in Spain at the beginning of the second wave. Around the time of the start of the vaccination campaign, short-lasting clusters for cigar were observed in all countries except Spain (Figure 1). Overall, clusters regarding consumption during the pandemic only occurred significantly more frequently in Germany (P=.01). Otherwise, numbers remained stable (Table 4).

Table 3. Comparison of relative search volume before and during the COVID-19 pandemic using the Wilcoxon rank-sum test. *P* values were adjusted using the Benjamini-Hochberg procedure.

	Before the COVID-19 pandemic, median (IQR)	During the COVID-19 pandemic, median (IQR)	Trend during pandemic	Adjusted *P* value
England				
Cigarette	80 (76-83)	71 (68-74)	↓[a]	<.001
Tobacco	52 (50-56)	47 (44-53)	↓	<.001
Cigar	59 (54-65)	63 (55-69)	↑[b]	.04
Smoking cessation	51 (43-62)	45 (34-54)	↓	<.001
Smoke free	37 (33-41)	35 (31-38)	↓	.03
Stop smoking	57 (52-62)	55 (50-60)	=[c]	.16
e-Cigarette	36 (23-47)	28 (17-37)	↓	<.01
Nicotine patch	31 (22-38)	38 (28-43)	↑	.01
Champix	61 (52-71)	60 (53-68)	=	.62
Germany				
Zigarette	70 (65-75)	43 (41-45)	↓	<.001
Tabak	51 (46-58)	72 (64-81)	↑	<.001
Zigarre	48 (41-56)	50 (42-60)	=	.40
Raucherentwöhnung	66 (57-78)	48 (42-57)	↓	<.001
Rauchfrei	38 (34-43)	27 (25-31)	↓	<.001
Rauchen aufhören	46 (42-53)	39 (36-43)	↓	<.001
E-Zigarette	59 (48-67)	36 (33-41)	↓	<.001
Nikotinpflaster	33 (24-38)	34 (29-41)	=	.15
Champix	51 (38-67)	47 (37-55)	=	.07
Italy				
Sigaretta	67 (61-73)	51 (45-57)	↓	<.001
Tabacco	81 (77-85)	81 (77-86)	=	.95
Sigaro	38 (35-42)	35 (30-40)	↓	<.01
Anti fumo	18 (0-27)	12 (0-21)	=	.31
Non fumatore	0 (0-24)	14 (0-21)	=	.18
Smettere di fumare	71 (62-79)	53 (48-60)	↓	<.001
Sigaretta elettronica	61 (54-68)	38 (32-43)	↓	<.001
Cerotti alla nicotina	0 (0-0)	0 (0-0)	=	.08
Champix	25 (0-37)	13 (0-29)	↓	.01
Spain				
Cigarrillo	52 (41-62)	29 (24-35)	↓	<.001
Tabaco	61 (59-65)	64 (59-72)	↑	.03
Cigarro	67 (59-73)	52 (47-56)	↓	<.001
Deshabituación tabaquica	0 (0-0)	0 (0-0)	=	.65
Dejar de fumar	39 (33-44)	31 (27-34)	↓	<.001
Libre de humo	0 (0-22)	0 (0-0)	=	.52
Cigarrillo electrónico	25 (14-33)	15 (0-25)	↓	<.001
Parche de nicotina	0 (0-0)	0 (0-0)	=	.63
Champix	8 (7-11)	12 (10-14)	↑	<.001

[a]↓: significant decline.

[b]↑: significant incline.

[c]=: no significant changes corrected.

Table 4. Comparison of cluster weeks before and during the COVID-19 pandemic by chi-square test.

Country and period	Consumption			Cessation			Treatment		
	Cluster	No cluster	*P* value	Cluster	No cluster	*P* value	Cluster	No cluster	*P* value
England			>.99			.04			.81
Before the COVID-19 pandemic	6	321		29	298		24	303	
During the COVID-19 pandemic	3	189		7	185		16	176	
Germany			.01			.07			.01
Before the COVID-19 pandemic	10	317		22	305		29	298	
During the COVID-19 pandemic	17	175		5	187		5	187	
Italy			.24			<.001			.82
Before the COVID-19 pandemic	10	317		53	274		44	283	
During the COVID-19 pandemic	2	190		10	182		28	164	
Spain			.60			.22			.08
Before the COVID-19 pandemic	24	303		36	291		19	308	
During the COVID-19 pandemic	11	181		14	178		20	172	

Cessation

As for consumption, a decrease in interest in cessation was noticeable across all countries for nearly all keywords, with 7 (58%) out of 12 keywords showing a significant decline. Keywords with nonsignificant changes were frequently affected by high variability in RSV, for example, “libre de humo” (*P*=.52) or “non fumatore” (*P*=.18). No keyword showed significantly increased RSV during the pandemic (Table 3). In temporal evaluation, no relation between the occurrence of clusters and incidence, lockdowns, or vaccination could be established. Interestingly, England, Italy, and Spain showed an accumulation of clusters around the new year before the pandemic. Such clusters were missed in these countries during the pandemic (Figure 1). Generally, clusters for cessation were less frequent during the pandemic in all countries, especially in England and Italy, and significant differences were observed (*P*=.04 and *P*<.001; Table 4).

Treatment

Treatment showed a heterogeneous picture. The comparison of the RSV did not yield uniform results. The only consistent finding across all countries was a decline in interest in “e-cigarette” (England *P*<.01; Germany, Italy, and Spain *P*<.001). Interest in “Champix” has risen in Spain (*P*<.001), whereas it has fallen in Italy (*P*<.01; Table 3). The cluster analysis revealed a long cluster for “Champix” in Spain, which began before the pandemic. Otherwise, there was a longer cluster for Italy concerning “sigaretta elettronica,” occurring between the second and third waves and ending with the start of the third lockdown. No other temporal correlations could be established (Figure 1). During the pandemic, only Germany showed a significantly shorter duration of clusters for treatment (*P*=.01). Here, similar to the effects noticed for cessation, before the pandemic, clusters of treatment around the turn of the year were present. These were absent during the pandemic (Table 4).

Generally, across all countries, the collected data point to less interest in the domain cessation during the COVID-19 pandemic. But also, the domain consumption was overall of less interest while the number of clusters remained mostly the same. Treatment-related keywords behaved less uniformly. Here, only e-cigarettes showed a country-spanning decline.

Discussion

Principal Findings

In this study, the effect of the COVID-19 pandemic on internet search query data concerning smoking-related keywords was investigated. Despite some differences in country-specific manner, overarching trends are displayed. This study comprises 3 main findings. First, through analysis of overall RSV before and during the pandemic, a substantial drop in interest in the domains of cessation, and second, consumption was observed.

Treatment showed heterogeneous trends in a country-dependent manner. Third, in short-term analysis, a sparse relationship of substantial clusters to lockdown measurements or the start of vaccination campaigns could be established as discussed in the following paragraphs concerning consumption, cessation, and treatment. These events seem to have little influence on search queries. Clusters are preferably evoked by other incidents. However, as seen in the overall RSV comparison, a trend toward lower interest in cessation during the pandemic was presented with fewer cluster weeks. For consumption, the number of cluster weeks remained stable during the pandemic despite a decrease in overall RSV for this domain, possibly pointing to events beyond the scope of this study triggering spikes of interest despite a decline in overall interest.

Research on the interplay between the COVID-19 pandemic and smoking exhibits multifaceted outcomes. Initially, smokers may have perceived smoking cessation as unnecessary due to emerging reports suggesting nicotine's potential protective role against severe COVID-19 infection [6,13,52]. However, in the short term, mounting evidence underscored the deleterious impact of smoking on the disease trajectory [7-9,11]. Intuitively, one might hypothesize that this phenomenon prompted numerous smokers to limit their smoking habits, albeit temporarily [53]. However, diverging from this expectation, the majority of empirical studies conducted during the pandemic across diverse global regions present contradictory findings. The meta-analysis conducted by Bakaloudi et al [15] elucidates a prevailing pattern of escalated or maintained smoking behavior across most studies. A plausible explanation for the observed phenomenon is the characterization of the COVID-19 pandemic as a stressor, rendering smoking cessation more challenging [54]. Research demonstrating a positive correlation between elevated stress levels and smoking behavior is noteworthy. [14,22,55,56]. Smoking is construed as a coping mechanism to manage psychosocial stressors associated with lockdown scenarios [23,24,57-59].

Consumption

As opposed to the study by Bakaloudi et al [15] mentioned in the *Introduction* section that investigated worldwide trends, our investigation revealed a decline in consumption-associated RSV. There might be two possible explanations: (1) there is a plethora of studies that account for regional differences and (2) some also report a decline in smoking during the pandemic [23,53]. In Spain, smokers decreasing their consumption seem to outnumber users with increased consumption [60]. Interestingly, the same study reports a decline in sales for cigarettes and cigars during the pandemic with a substantial rise in tobacco sales that resamples our findings from RSV analysis. Besides, before the onset of the pandemic, a discernible trend emerged across the European Union marked by a general decrease in smokers [61]. England, for example, implemented the campaign "Smokefree 2030" in 2019, so interest might have been exhausted [62]. Perhaps as a consequence of the campaign or the pandemic, England saw a diminishing number of smokers in 2020 [63]. Furthermore, less social interaction and heightened awareness of severe health risks might have resulted in the coincidence of fewer new smokers during the pandemic. Notably, studies regarding the initiation of smoking habits during the pandemic are missing. Regular users even with increased consumption might not significantly contribute to search volume because of satisfied informational demand. Matching this hypothesis, a study from Italy presents a decrease in smoking prevalence while overall cigarette consumption increased, attributed to regular users [64].

Second, there is a methodological shortcoming of RSV data. These data are a relative indicator of interest compared with general interest in all searched keywords. As other keywords rise, the shares of interest for the investigated keywords decline, even if the absolute number of search queries remains stable. Especially during the COVID-19 pandemic, this might introduce a bias as COVID-19–related keywords rose exponentially [46]. To account for this shortcoming, we used a moving median approach in our analysis as laid out in the Methods section. This way, clusters were evaluated relative to a period of 1 year, and long-term trends were less influential on cluster evaluation. Accordingly, when looking into cluster accumulation during COVID-19 pandemic, stable numbers were observed as opposed to the comparison of plain RSV.

In the context of cluster detection, attribution to events beyond the scope of this study must be considered. Here, 2 clusters are striking. In Germany, interest in "Tabak" peaked from April to July 2020, which was most likely caused by COVID-19–related import restrictions. Cheap imported cigarettes were not available, so customers shifted their consumption behavior [41]. Also, the pattern of repetitive short-lasting interest in cigar at the time of the start of the vaccination campaign should be carefully interpreted as this might coincide with behavior during festivities. Still, it sticks out that during the pandemic, these clusters were absent. We hypothesize that due to reduced social gatherings around the holidays, people shifted their interest, and especially occasional cigar consumption was thus limited.

Cessation

Interest for cessation leveled during the pandemic across all countries, seen in overall RSV and number of clusters. Specific keywords where significance was missed should be interpreted with caution due to high variability in search volume. Regarding cessation during the pandemic, most identified survey studies point toward increased interest in cessation, mainly due to a fear of the disease [20,21,24,65]. However, these studies are frequently victim to effects like social desirability [66]. Also, cohort selections mark a large confounder.

Studies on RSV data are in line with our findings and indicate constant or decline in cessation interest [16,19,36]. However, 2 of these investigations solely entailed a visual assessment of the Google search data without using statistical methodologies. Few keywords were analyzed, and the scope was limited to either a single country or the global RSV data. This approach, given the globally diverse trajectory of the pandemic, appears lacking in specificity. On the contrary, the presented approach provides more objective data analysis. Furthermore, recent publications indicate that an increased level of stress hinders smokers from abstinence, and cessation programs switched to disadvantageous remote settings or were discontinued [20,22,56,57,64].

Treatment

For treatment, we saw diverse developments. There was a decline in e-cigarettes throughout. This trend was evident in other studies, especially in a young population and at the beginning of the pandemic [67-69]. However, a cross-sectional study by Gallus et al [70] reveals that the effect is probably cohort-dependent. Mostly, adolescents decreased consumption, attributed to harder access because of fewer social gatherings [70,71]. In line with this, we observed a lasting cluster for "sigaretta elettronica" in Italy from January to March 2021, and during this time, the incidence declined and restrictions were less harsh, implying an increase in social gatherings. The cluster showed an abrupt end with the start of the third lockdown [72]. RSV data are anonymized, and no conclusion about subgroups can be drawn. Previous studies elaborated on the disparities of internet use for health-related topics in different age groups [73,74]. As this is a limitation of the method that might account for further differences between the presented results and results from cohort studies. Hence, studies investigating internet use for cessation-related topics among different age groups are needed.

The categorization of e-cigarettes within the category of treatment is debatable. In some instances, e-cigarettes solely serve recreational purposes, particularly among the younger demographic [75,76]. The analysis of RSV revealed a notable similarity between e-cigarettes and keywords of consumption, with a decline in both cases. The classification of e-cigarettes within the treatment category stems from comprehensive meta-analyses, demonstrating their efficacy as treatment products [39]. Furthermore, the National Health Service recommendations explicitly advise against the use of e-cigarettes by nonsmokers [77]. Motivational factors influencing e-cigarette usage have been investigated, with prevailing evidence suggesting a large proportion of users use e-cigarettes as aids for smoking cessation or reduction [75,78,79]. Especially, these goal-oriented users continued consumption [80]. Consequently, the categorization of e-cigarettes within treatment aligns with the observed patterns described in previous studies.

Temporal analysis revealed a peaking interest in "Champix" in Spain starting before the pandemic. This is most likely confounded by the coverage of Champix cost by the Spanish health insurance at the beginning of 2020 [81]. Another season-dependent effect was seen in England, Italy, and Spain, with repetitive clusters for treatment around New Year before the pandemic but not during the pandemic. We argue that people shifted their New Year's resolutions during the health crisis.

Limitations

Alongside the previously mentioned shortcomings of RSV data, further limitations shall be discussed. First, changes in lockdown policies were passed by the day and hence any cluster detected during the pandemic could have been attributed to one of these changes or diverse non–COVID-19-related occurrences. However, to ensure compatibility across countries, we had to limit the investigated events to major lockdowns, rises in incidence, and vaccinations as we anticipated these would create drastic changes in RSV.

Second, keyword selection poses a bottleneck for Google Trends studies as the selection is mostly reliant on expert consensus, and literature review and is limited by the data provided by Google Trends. Here, relevant terms might be missed or might be searched in a divergent context. By choosing the reference terms based on criteria described in the *Methods* section with only minor changes between countries introduced by translation or availability of keywords provided by Google Trends, we aimed to be as objective as possible. Furthermore, 3 groups of consumption, cessation, and treatment display various aspects of smoking behavior and 3 reference terms per group should suffice to mirror products and word usage prevalent in society.

Third, only 1 search engine and hereby internet-based source was used for data acquisition. Although Google dominates the market concerning search engines, further research might encompass other valuable internet-based resources, such as social media platforms and news forums, to estimate population response to public health crises [82-84].

Furthermore, Google Trends data retrieved for an entire country are low in regional resolution, especially under consideration of disparate incidence rates in national regions information might be lost.

Implications of the Presented Results

For optimal allocation of resources, it is crucial to evaluate the impact of a health crisis on a vulnerable population. During the COVID-19 pandemic, smokers were among this population [7]. The optimal timing of public health intervention often remains elusive. Survey studies in this setting are disadvantageous. Google Trends studies, in contrast, mirror real-time effects, investigate a large share of the population, and are cost effective. By screening a plethora of keywords, appropriate interventions might be determined. Here, Ayers et al [85] demonstrated an interesting approach to identify search terms and behavioral shifts upon tax increases on cigarettes.

In this study, the decline in cessation interest could have justified policy makers' efforts to intensify campaigns informing about cessation programs during the pandemic. A more detailed analysis of terms associated with cessation, such as quitlines and local support groups, would be required in further studies to filter optimal interventions. Besides, interest in treatment options seemed to stagnate. Here health care providers could have increased their efforts to educate people about therapy strategies.

Finally, RSV data have provided useful insights for various research in medicine [16,26,28-30,32,36]. Future studies in the context of smoking and health crises could use these data to predict smoking trends early to expand cessation programs and also to monitor the potentially unexpected detrimental effects of other public health measures on smokers. However, there is a need for the following studies to develop methods to deal with shortcomings in keyword selection, regional resolution, and subgroup analysis.

Conclusion

Trends were comparable across all countries with minor differences. A decline in interest in consumption and cessation

was observed. Besides, treatment terms showed heterogeneous dynamics, while specifically, e-cigarettes displayed a markedly decreased RSV. Temporal clusters of peaked RSV were only sparsely linked to lockdown measures and changes in incidence. The flexible scan statistics proved as a valid tool for cluster detection. The resulting clusters corresponded with visual inspection and could partially be linked to events other than lockdown measures or vaccination campaigns. This study underlines the importance of intensifying cessation aid considering the decreased interest during the pandemic. Measures that positively affect smoking behavior in times of health crisis remain to be determined.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Exemplary screenshots of relative search volume (RSV) data from Google Trends for German search terms commonly linked to the pandemic. Starting in the week of the first reported case in Europe, there is an emerging interest in the indicated terms.
[DOCX File , 134 KB - ojphi_v16i1e57718_app1.docx]

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Abbreviations

RSV: relative search volume
WHO: World Health Organization

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Original Paper

Evaluation of Drug and Herbal Medicinal Promotions on Social Media During the COVID-19 Pandemic in Relation to World Health Organization Ethical Criteria and South African Health Products Regulatory Authority Guidelines in South Africa: Cross-Sectional Content Analysis

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Abstract

Background: Consideration of ethics in the promotion of medications is essential to safeguard the health of consumers, particularly during health crises. The World Health Organization (WHO) and the South African Health Products Regulatory Authority (SAHPRA) have established stringent standards to ensure the integrity of pharmaceutical promotions and safeguard public health, including advertisements on the internet and social media platforms. However, the dynamic nature of online advertising poses challenges for monitoring and enforcing ethical standards.

Objective: The study aimed (1) to examine the COVID-19 drug and medicinal promotions across online platforms and social media from 2020 to 2022 in South Africa and (2) to ensure that drug promotions adhere to ethical guidelines outlined by the WHO and SAPHRA.

Methods: A cross-sectional content analysis was conducted to assess drug and medicinal advertisements across various internet and social media platforms. A systematic approach was used to identify and analyze promotional content, focusing on adherence to ethical guidelines outlined by WHO and SAPHRA. Data were collected and analyzed to determine the extent of compliance and identify any potential violations or areas for improvement.

Results: A total of 14 online drug advertisements were included in this analysis. Our findings show that most of the drugs advertised did not meet the regulations and guidelines provided by WHO and SAHPRA. There were omissions about active ingredients, proprietary names, adverse drug responses, precautions, and overdosage and adverse drug reactions. Traditional medicines were not fully consistent with the approved WHO ethical criteria data sheet.

Conclusions: Our analysis highlights the critical importance of ensuring compliance with ethical guidelines in drug promotions on the internet and social media platforms. There is a need for continued vigilance and enforcement efforts to uphold ethical standards and protect the health of the public. Ongoing monitoring and collaboration between national drug regulatory agencies, pharmaceutical companies, and online platforms will be essential for promoting responsible advertising. In addition, safety monitoring and pharmacovigilance systems for herbal medicinal products are yet to be established.

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KEYWORDS

drug advertising; internet; social media; ethical guidelines; traditional medicine; COVID-19

Introduction

Background

During the COVID-19 pandemic, there was intense interest in finding potential treatments for the SARS-CoV-2 infection among existing drugs. Several existing medications were publicized as potential treatments for COVID-19 on the internet [1]. Social media and social networks significantly impact communities, and this technology is increasingly becoming an integral part of daily life in modern society [2]. Rapid innovations in information technology are consistently being introduced through various social media and networking websites for communication, information sharing, and entertainment. This increasing dependence on social media and web-based media has been shown to significantly influence behaviors and promote educational learning [2-4].

Faced with a pandemic with no known or approved medications, different untested treatments were advertised and promoted on the internet to the public [5]. In addition, many people were wary of visiting hospitals and relied heavily on social media to obtain information regarding the management of the COVID-19 pandemic [6]. Misinformation spread rapidly from the early days of the COVID-19 outbreak, including falsified information on drug use [7]. Millions of people were exposed to misleading promotions of drugs and services during the pandemic claiming to prevent and cure COVID-19 [7].

Ethics in the promotion of drugs is a critical aspect of the pharmaceutical and health care industries to ensure that the marketing of drugs is conducted in a responsible, transparent, and ethical manner to protect public health, maintain trust, and uphold the integrity of health care systems [8,9]. According to the World Health Organization (WHO), medicinal drug promotion is defined as “all informational and persuasive activities by manufactures and distributors, the effect of which is to induce the prescription, supply, purchase, and/or use of medicinal drugs” [10].

The WHO has laid down ethical criteria for medicinal drug promotion or rational use and has recommended pharmaceutical companies to implement these guidelines, ensuring that advertisements should at least contain a summary of scientific information. Furthermore, WHO indicates that promotional claims for drugs should be truthful, reliable, and not contain misleading or important omissions that may compromise public health [10].

The South African Health Products Regulatory Authority (SAHPRA) ensures that all medicines are registered and advertised in compliance with the Medicines Act. It recognizes that inappropriate promotion and advertisement of medicines contribute to irrational use that potentially brings harm to users [11]. The regulatory body ensures the safety, efficacy, quality, and proper distribution of pharmaceuticals and medical products. SAHPRA evaluates and approves new drugs and medical products for marketing, which involves reviewing extensive data from pharmaceutical companies, including preclinical and clinical trial results, to determine if the product is safe and effective for its intended use [11].

In South Africa, SAHPRA, a statutory body, monitors and regulates the control of medicines in accordance with the Medicines and Related Substances Act 101 of 1965, as amended. Under Regulation 42 for advertising and marketing, an “advertisement” according to the Medicines and Related Substances Act refers to “...any written, pictorial, visual, or other descriptive matter or verbal statement or reference that (a) appears in any newspaper, magazine, pamphlet, or other publication; (b) is distributed to members of the public; or (c) brought to the notice of members of the public in any manner whatsoever, which is intended to promote the sale of that medicine...” [11,12].

However, it should be noted that in South Africa, medications are categorized or scheduled, and as per legal requirements, manufacturing details can be omitted based on the schedule assigned to the medication [11]. Medicine schedules are numbers given to pharmaceutical products based on their benefits and risks. The lower the risk of the product, the lower the scheduled number. Unscheduled medicine on the other hand can be purchased at a pharmacy and this medicine has a schedule of 0. Over-the-counter medicine can be purchased at a pharmacy without a prescription, and this medicine has a schedule of 0, 1, or 2. Prescription-only, controlled substances and strictly controlled substances range from schedule 3 to 8 [13].

Given this background, in this paper, we present an analysis of the ways pharmaceutical drugs were advertised and promoted to treat mild-to-moderate symptoms during the COVID-19 pandemic in South Africa. The research question for this study is: How did the promotion of drugs and medicinal products on online platforms and social media in South Africa between 2020 and 2022 adhere to the ethical guidelines established by the WHO and SAHPRA? The study aims to conduct a thorough analysis of these promotions and assess their compliance with the ethical standards established by WHO and SAHPRA.

The study assessed whether the information provided to the public on drug safety and efficacy was adequate to encourage the rational use of medicinal products. This analysis fills a critical gap in understanding the regulatory compliance and the ethical reliability of drug promotions in a public health crisis. [14]. By evaluating adherence to WHO and SAHPRA ethical guidelines, the study introduces a framework for assessing regulatory compliance in online drug advertising, which is crucial for maintaining ethical standards in social media drug promotions. By integrating both WHO and SAHPRA guidelines, the study provides a dual-perspective analysis that can be used as a model for other regions and regulatory environments. The findings will assist policymakers, regulators, and pharmaceutical

companies to improve the ethical standards and effectiveness of drug promotions on web-based platforms.

Theoretical Framework

In this study, we used the regulation and ethical compliance framework to analyze drug advertisements on social media and their adherence to established ethical and regulatory standards. Regulatory and ethical compliance frameworks have been used in cross-sectional studies to assess health practice adherence to ethical standards [15,16]. Using regulatory frameworks guided by WHO and SAHPRA emphasized accuracy, transparency, ethical considerations, and regulatory compliance. We analyzed data based on these components of the framework. By emphasizing ethical and regulatory compliance in drug promotions, we identified areas that need improvement to protect consumers from harm, promote transparency and accountability in marketing practices, and uphold the integrity of the pharmaceutical industry.

Methods

Ethical Considerations

No ethics approval was applied for because according to the Biomedical Research Ethics guidance, certain research projects qualify for exemption from ethics review for example studies on information/data that is already fully in the public domain.

Study Design

A cross-sectional content analysis was conducted for drug and medicinal promotions on the internet and social media platforms to address whether drugs aligned with the ethical guidelines established by the WHO and SAPHRA. A cross-sectional content analysis provided a snapshot of drug promotional practices on social media, allowing for the assessment of adherence to WHO and SAHPRA ethical guidelines at that specific point in time as done in other studies, such as Vivek et al [17] and Boeson et al [18]. In this analysis, this method was used to assess the ethical and regulatory compliance of drug promotions during the COVID-19 pandemic. Given the dynamic nature of the COVID-19 pandemic and the swift changes in public health communication, a cross-sectional content analysis provided timely insights that could inform immediate regulatory adjustments and public health strategies.

Study Screening

Drug advertisements were searched for on South African pharmacy websites and social media platforms, such as Facebook (Meta) and Twitter (rebranded as X). Drug and traditional medicine advertisements circulating on WhatsApp (Meta) were also considered. Key search terms included the phrases “COVID-19 treatments in South Africa,” “medications promoted in South African pharmacies during COVID-19,” and “traditional medicines used during the COVID-19 pandemic in South Africa.” Inclusion and exclusion criteria were later used (Textbox 1).

Textbox 1. Inclusion and exclusion criteria.

Inclusion criteria

- Pharmaceutical drugs and substances
- Traditional and herbal-based medicines
- COVID-19 pandemic related
- Promoted in South Africa
- Available from December 2019 to December 2020

Exclusion criteria

- Not COVID-19 pandemic related
- Advertisements that were not South Africa based
- Advertisements that had internet and web restrictions placed on them

Data Charting Process

A total of 14 drug advertisements were extracted to Microsoft Excel and were assessed as per the WHO and SAHPRA guidelines. The WHO ethical criteria [10] used for assessment are listed in Textbox 2.

We used a Microsoft Excel spreadsheet to summarize the data including the source of the advertisements as illustrated in Multimedia Appendix 1.

Textbox 2. World Health Organization ethical criteria for assessment.

- The names of the active ingredients using either international nonproprietary names or the approved generic names of the drug
- Propriety name of such medicine
- Active ingredient per dosage form or regimen
- Name of other ingredients known to cause problems
- Mention the approved therapeutic uses of the drug
- Side effects and major adverse drug reaction
- Precautions, contraindications, and warnings
- Name and address of the manufacturer or distributor

Results

A total of 14 drug advertisements were extracted covering the first year of the COVID-19 pandemic. Two authors, RSC and JN, independently assessed the advertisements.

Promotional Drug Advertisements as Per the Standard Criteria for WHO Ethical Considerations

Most advertisements did not provide full product information. In total, 8 (57%) out of 14 advertisements had no adverse effects mentioned in the wording or illustration. Overall, 10 (71%) out of 14 advertisements did not indicate major adverse reactions that could result from taking the drug. Promotional advertisements omitted the names of the active ingredients, international proprietary names or the approved generic names of the drug, the brand names, and the name and address of the manufacturer or distributors. A total of 13 social media drug promotions did not adhere to ethical guidelines.

Names of the Active Ingredients Using Either International Nonproprietary Names or the Approved Generic Names of the Drug

Drug advertisements on hydroxychloroquine, lopinavir, *Lippia javanica* (umsuzwane), and aspirin did not indicate the names of the active ingredients. The other drugs had generic names listed as outlined in Multimedia Appendix 1.

Name of Other Ingredients Known to Cause Problems

All the drug advertisements did not provide comprehensive and accurate information about all ingredients. Therefore, there was no indication of drugs that had the potential to cause adverse reactions or interactions.

Adverse Effects and Major Drug Reactions

Vitamin C, zinc, rivaroxaban, ivermectin, lopinavir or ritonavir, *Artemisia afra* (umhlonyane), eucalyptus or gum tree extract, and *L javanica* (umsuzwane) did not outline both adverse effects and drug reactions on their promotional advertisements. Favipiravir had adverse effects stated, but no adverse drug reactions.

Name and Address of the Manufacturer or Distributor

Five promotional advertisements, namely favipiravir, ivermectin, lopinavir or ritonavir, statins, and aspirin, clearly stated the manufacturer and distributor of the drugs. The rest of the drug advertisements did not specify this detail.

Traditional Medicine Promoted as Per the Standard Criteria for WHO Ethical Considerations

The wording and illustrations in advertisements for *A afra* (umhlonyane), eucalyptus or gum tree extract, and *L javanica* (umsuzwane) were not fully consistent with the approved WHO ethical criteria data sheet. The text on the traditional medicine advertisements was not fully legible. All 3 substances lacked information on the names of ingredients that may cause problems. The advertisements had no mention of the adverse effects that arise from the use of this traditional medicine. It was observed that major adverse reactions were not mentioned in all 3 advertisements. Warnings were however mentioned for the eucalyptus or gum tree extract, with an indication that it should be used under precaution as directed by a pharmacist

Promotional Drug Advertisements as per SAHPRA Guidelines for Marketing According to the Medicines and Related Substances Act, 1965

The Medicines and Related Substances Act of 1965 states that drug advertisements should clear proprietary names, the approved name, and the quantity of each active ingredient. According to these guidelines, the drug advertisements that were analyzed lacked sufficient detail. All the drugs, except aspirin, had no proprietary names and active ingredients mentioned in their advertisements. We note that SAHPRA had no guidelines at the time of this study specified for traditional and complementary medicines (Multimedia Appendix 2).

Discussion

Principal Findings

Our findings show that most of the drugs advertised did not meet the regulations and ethical guidelines provided by WHO and SAHPRA. The individuals most likely to be aware of WHO, SAHPRA, and South African government regulations are registered pharmaceutical companies, pharmacists, and health care professionals like doctors and nurses who have completed dispensing courses. Influencers and public figures may not be knowledgeable about whether the information they share on their platforms meets legal standards.

The COVID-19 pandemic changed marketing through extensive use of web-based technology. Studies have shown that valuable marketing strategies have been gained during this pandemic, and they can be adopted in the post–COVID-19 pandemic era.

A systematic review done on marketing during the COVID-19 pandemic revealed that social media marketing improved the interaction between retailers and consumers [19]. The learnings can be adopted after the COVID-19 pandemic. In this analysis, addressing a key gap in understanding how well drug promotions on social media follow regulations and provide quality information during a health crisis can be adopted for future pandemic crises.

An effective pharmacovigilance system that aligns with WHO, SAHPRA, and national drug policies in South Africa is essential for monitoring and communicating drug safety information to the public. Pharmacovigilance, aimed at minimizing risks and maximizing the benefits of medicinal products, is an important public health tool, as observed in other studies [20,21]. Regulatory bodies should be a crucial part of the national health system, working within the guidelines of clear pharmaceutical policies and legal frameworks [22]. A systematic review of pharmacovigilance systems in resource-limited countries, using the WHO pharmacovigilance indicators, highlighted that strengthening these systems is required with resource and research data consolidation [23]

From this analysis, the most common deviations from the marketing guidelines resulted in the unethical promotion of unapproved or unregistered medicine. There were omissions about active ingredients, proprietary names, adverse drug responses, precautions, and overdosage. Lack of sufficient information about adverse drug reactions may lead to improper use of medications, potentially resulting in harm to patients [24-26]. Furthermore, not knowing about potential drug interactions can lead to dangerous combinations of medications [5].

Complete disclosure is imperative for consumers to make informed decisions about their health care [27]. Being completely transparent ensures that individuals have a clear understanding of the risks involved, helping them make responsible choices for their well-being [28]. Failure to disclose risks and adverse effects, which goes against the WHO ethics guidelines and SAHPRA's advertising guidelines, involves providing incomplete information about a medicine's potential adverse effects.

The role of pharmacists in medication management needs to be emphasized and acknowledged. Their vital contribution in assisting individuals in making informed decisions, particularly in the purchase of specific medications, can be improved during health crises. Potential risks arise when there is a lack of health professional guidance when people buy medication. In addition, our findings reveal the lack of regulation of herbal and traditional medicine, multivitamin, and drug supplements in advertising and promotion. With the absence of clear guidelines in South Africa, there is no oversight to verify the accuracy of the information, including ingredients and claims displayed on product containers. Safety monitoring and pharmacovigilance systems for herbal medicinal products are yet to be established [18].

Policy Recommendations

Based on our findings, we recommend strengthening existing ethical guidelines and regulations established by WHO and SAHPRA to address specific challenges related to web-based and social media drug promotions. This should include updating regulations to cover new digital marketing practices and ensuring that these guidelines are comprehensive and applicable to various online platforms. Furthermore, regulatory frameworks can implement more digitally advanced monitoring systems to regularly review drug promotions on social media and other online platforms for adherence to ethical guidelines. The use of advanced technologies, such as artificial intelligence, to automate the detection of noncompliant content can be useful. Public awareness campaigns to educate consumers about the importance of ethical drug advertising can be created to inform the public on how to identify misleading advertisements and report noncompliant drug promotions. Promoting digital literacy to help consumers critically evaluate online health information and make informed decisions can also be introduced.

Finally, drug and medication regulatory bodies need to be able to enforce stringent guidelines and regulations regarding the inclusion of adverse reaction information in drug advertisements and promotional materials [29]. These regulations should require comprehensive and balanced reporting of these reactions. Disclosing all ingredients, especially those known to cause problems, is essential for patient safety and informed decision-making. Regulatory enforcement, transparency, and education efforts can help ensure that this information is consistently and accurately communicated in drug advertisements and other medication-related materials. Health care providers can also be encouraged to engage in patient-centered care by discussing potential adverse reactions with their patients during medication consultations. This helps patients become active participants in their health care.

Conclusion

Our cross-sectional content analysis of drug and medicinal advertisements on the internet and social media platforms highlights the critical importance of adhering to ethical guidelines established by the WHO and SAHPRA. This study has shown that continuous monitoring and adherence to these guidelines safeguard public health and ensure the integrity of promotional activities within the pharmaceutical industry, especially during health crises such as the COVID-19 pandemic.

Our analysis, structured around these regulatory frameworks, has uncovered significant gaps in compliance that stress the necessity for more rigorous enforcement of ethical standards. These gaps can lead to the dissemination of misleading or incomplete information, which can have severe consequences for public health.

Concerted efforts from regulatory bodies, pharmaceutical industry, public health organizations, and researchers are needed to ensure that advertising practices are transparent, accurate, and prioritize the well-being of consumers. Further research is needed to explore the underlying factors contributing to noncompliance and to develop effective strategies for improving adherence to ethical regulations. This research should also focus

on the impact of digital and web-based marketing practices on public health and evaluate the efficacy of current regulatory frameworks in the digital age. Strengthening these efforts will be vital in maintaining public trust and promoting the rational use of medicinal products.

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Authors' Contributions

All authors directly participated in this study. RSC handled conceptualization, formal analysis, and writing—original draft. JN managed data collection and preliminary analysis. LTM and KB performed writing—review and editing. JS contributed to supervision and writing—review and editing

Conflicts of Interest

None declared.

Multimedia Appendix 1
Analysis of drug advertisements according to the World Health Organization ethical criteria, 2019-2020.
[DOCX File , 28 KB - ojphi_v16i1e58378_app1.docx]

Multimedia Appendix 2
Summary of promotional drugs according to South African Health Products Regulatory Authority Guidelines, 2019-2020.
[DOCX File , 125 KB - ojphi_v16i1e58378_app2.docx]

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Abbreviations

SAHPRA: South African Health Products Regulatory Authority
WHO: World Health Organization

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Original Paper

Machine Learning for Prediction of Tuberculosis Detection: Case Study of Trained African Giant Pouched Rats

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Abstract

Background: Technological advancement has led to the growth and rapid increase of tuberculosis (TB) medical data generated from different health care areas, including diagnosis. Prioritizing better adoption and acceptance of innovative diagnostic technology to reduce the spread of TB significantly benefits developing countries. Trained TB-detection rats are used in Tanzania and Ethiopia for operational research to complement other TB diagnostic tools. This technology has increased new TB case detection owing to its speed, cost-effectiveness, and sensitivity.

Objective: During the TB detection process, rats produce vast amounts of data, providing an opportunity to identify interesting patterns that influence TB detection performance. This study aimed to develop models that predict if the rat will hit (indicate the presence of TB within) the sample or not using machine learning (ML) techniques. The goal was to improve the diagnostic accuracy and performance of TB detection involving rats.

Methods: APOPO (Anti-Persoonsmijnen Ontmijnende Product Ontwikkeling) Center in Morogoro provided data for this study from 2012 to 2019, and 366,441 observations were used to build predictive models using ML techniques, including decision tree, random forest, naïve Bayes, support vector machine, and k-nearest neighbor, by incorporating a variety of variables, such as the diagnostic results from partner health clinics using methods endorsed by the World Health Organization (WHO).

Results: The support vector machine technique yielded the highest accuracy of 83.39% for prediction compared to other ML techniques used. Furthermore, this study found that the inclusion of variables related to whether the sample contained TB or not increased the performance accuracy of the predictive model.

Conclusions: The inclusion of variables related to the diagnostic results of TB samples may improve the detection performance of the trained rats. The study results may be of importance to TB-detection rat trainers and TB decision-makers as the results may prompt them to take action to maintain the usefulness of the technology and increase the TB detection performance of trained rats.

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KEYWORDS

machine learning; African giant pouched rat; diagnosis; tuberculosis; health care

Introduction

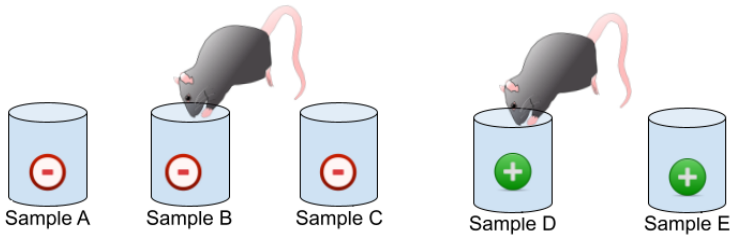
Background

African giant pouched rats (*Cricetomys ansorgei*) are native to sub-Saharan Africa, making them resistant to local parasites and diseases [1]. The term "pouched rat" refers to their large cheek pouches that are used for carrying food back to their burrows, where the food is either eaten or stored. These rats are nocturnal and omnivorous, eating various insects, fruits, and vegetables. They are large (adult males and females weigh about 1.3 kg and 1.2 kg, respectively) and are long-lived, averaging 8 years in captivity. Moreover, they have a highly developed olfactory capacity, enabling them to do specific detection tasks with training [2]. As such, in 1997, APOPO (Anti-Persoonsmijnen Ontmijnende Product Ontwikkeling or "Anti-Personnel Landmines Detection Product Development" in English) started researching how to train these rats for scent detection. APOPO is a Belgian nongovernmental organization whose mission is to protect people and the planet using scent detection animals [3]. Rat pups born at APOPO's breeding facility are weaned from their mother at 10 weeks old. Rats begin training in a custom-engineered line cage immediately after they are weaned. Training for tuberculosis (TB) detection takes place in this apparatus, which requires upwards of 9 months to master. Each rat's home cage is outfitted with a clay nest pot to simulate the rat's natural underground burrow, a wood shaving substrate, and unlimited access to water that is routinely infused with a multivitamin and electrolyte supplement. The majority of the diet of the rats is provided during training sessions in the form of crushed commercial rodent chow pellets mixed with mashed bananas and avocados, which serves as appetitive reinforcement for the operant conditioning procedures. This diet is supplemented with a variety of fresh fruits, vegetables, and grains [3].

While APOPO began with training rats to detect landmines in former conflict zones, the demonstrated success influenced the 2001 idea to also train the rats to detect the presence of Mycobacterium tuberculosis in human sputum samples [4]. Data reported annually to the World Health Organization (WHO) by countries show that TB is one of the major causes of ill health and death worldwide. TB is a life-threatening infectious disease that attacks the lungs and can also harm other parts of the body. The transmission occurs from one person to another when a person with TB talks, sneezes, or coughs. The development of novel, accurate, robust, and rapid diagnostic capabilities will result in improved case detection, disease surveillance, health care delivery, and quality of future research [5]. In 2004, APOPO and Sokoine University of Agriculture (SUA) partnered with the Tanzanian National Institute of Medical Research (NIMR) and the Tanzanian National Tuberculosis and Leprosy Program (NTLP) to develop a scent-detection technology for diagnosing human TB in resource-poor areas [6]. While microscopy is the most commonly used method to detect TB in developing countries, its effectiveness remains a problem [3]. In Tanzania, the Ministry of Health, Community Development, Gender, Elders, and Children (MOHCDGEC) permitted APOPO to conduct research using rats to detect TB bacteria in sputum samples [7].

Figure 1 illustrates the concept of rat scent detection of TB. Sputum samples collected from partner DOTS (directly-observed treatment, short-course) clinics are heat inactivated (autoclaved) and then loaded into aluminum bars, which are positioned beneath holes in the floor of the line cage apparatus [4]. The rat sniffs each sample in succession as it walks from one side of the apparatus to the other. The rats are trained to pause over TB-positive samples for about 3 seconds but to quickly move past TB-negative samples [1]. During operational research, rats are rewarded with food for correctly pausing over (or "indicating") samples that the DOTS clinic has determined to be TB positive. Samples which the DOTS clinic determines to be TB negative but which the rat indicates as TB positive (by pausing for 3 seconds) are flagged as suspect and subjected to additional confirmatory diagnostics in APOPO's laboratory, using WHO-endorsed methods (typically, concentrated smear microscopy). During routine operational research, APOPO's scent detection rats evaluate upwards of 100 samples (averaging 10% TB positive) from DOTS clinics within each 20-minute session. Referencing sample and patient information within a secure database allows APOPO to immediately notify the DOTS clinic of new cases so the patient can be contacted and can begin treatment. This procedure has effectively identified more than 29,000 TB patients who had a missed diagnosis prior to evaluation by TB-detection rats [4].

Figure 1. Tuberculosis (TB) testing and detection using trained rats. The rats test and detect TB-negative and TB-positive samples.



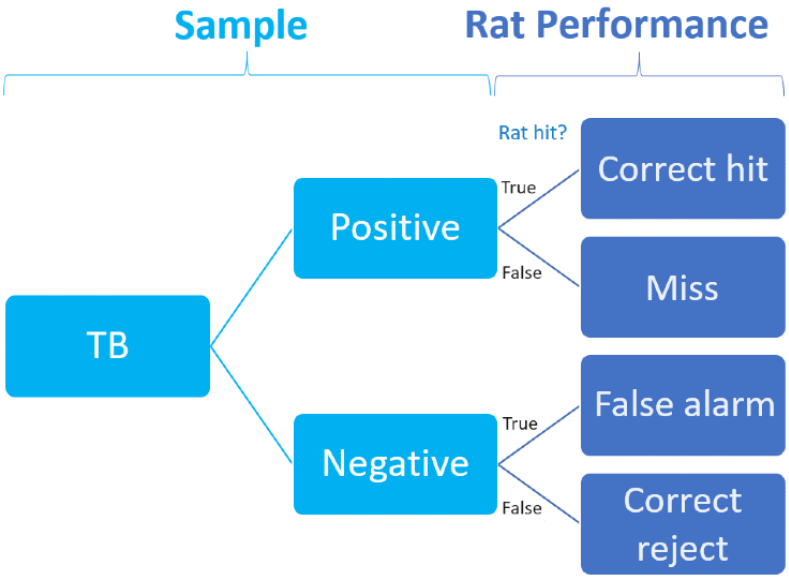
Conceptual Framework

The theoretical concepts and empirical framework of this study are based on Signal Detection Theory (SDT). SDT describes how features of the stimulus and detector factors affect performance on stimulus detection tasks [8]. SDT helps to distinguish between the sensitivity of a detector and the underlying signal. In medical diagnosis, this translates to the efficacy of a diagnostic tool to accurately detect the presence of a pathogen or other signal with medical significance [9], that is, the diagnostic "sensitivity." However, in rats, determining diagnostic accuracy depends on the rat's training and the diagnostic results from partner health clinics using WHO-endorsed methods. During training, the behavior of each

rat is recorded, including indication responses committed in response to samples known to either contain or not contain TB (TB positive or TB negative). These data allow trainers to accurately track each rat's discrimination learning [4]. There are numerous independent variables related to each rat evaluation session, including the rat's identity (name), age, sex, and bodyweight, as well as the characteristics of the sample itself, including DOTS clinic diagnostic results (ID_BL_DOTS) and results of any applicable confirmatory diagnosis within APOPO's laboratory (ID_BL_APOPO), which are combined to form another independent variable called TB_Status.

In this study, one of the primary dependent variables was captured as hit, which refers to whether or not (true or false) the rat provided an indication (continuously sniffed the sample for at least 3 seconds, as estimated by the rat handler). Combining the hit variable with WHO-endorsed diagnostic results (ID_BL_DOTS and ID_BL_APOPO) provided 4 possible outcomes termed rat performance for each sample evaluated (Figure 2), including correct hit, miss, false alarm, and correct reject, which are used in determining the diagnostic accuracy of each rat. Correct hit refers to samples that the rat indicated and were confirmed to contain TB; false alarm (or suspect) refers to samples that the rat indicated but which could not be confirmed to contain TB. Additionally, miss (sample confirmed to be TB positive) and correct reject (no TB mycobacterium confirmed) refer to samples that the rat failed to indicate (sniff for 3 seconds) [3]. In other words, the rat's sensitivity represents the percentage of correct hits out of the sum of total correct hits and total misses (all confirmed TB-positive samples evaluated by the rat). Similarly, the rat's specificity represents the percentage of correct rejects out of the sum of correct rejects and false alarms (all samples found to be TB negative) [10]. By this logic, sensitivity refers to the rat's ability to accurately find true positive (TP) cases, while specificity measures its ability to accurately reject negative cases. Hence, sensitivity (correct hit) and specificity (correct reject) together comprise overall diagnostic accuracy.

Figure 2. Relationship among the status of tuberculosis (TB), hit, and the performance of the rat. Hit refers to whether or not (true or false) the rat provided an indication.



From Figure 2, if the TB status was already known to be positive at the time of the rat evaluation and hit was true, the rat's behavior was categorized as "correct hit." Conversely, if the TB status was positive and hit was false, the rat's behavior was categorized as "miss." On the other hand, if the TB status was determined to be negative at the time of the rat evaluation and hit was true, the rat's behavior was categorized as "false alarm" or suspect. Finally, if the TB status was negative and hit was false, the rat's behavior was categorized as "correct reject."

Hence, contrary to the study by Jonathan et al [10], this study considered the status of TB in the sample the rat was evaluating. In that study, the modeling methods only used the dichotomous variable of hit as true or false (ie, did the rat sniff the sample for ≥3 seconds) without regard for what the rat was sniffing. Within the data set analyzed, about 78.8% of samples were not hit (hit=false), somewhat reflecting the estimated underlying prevalence of TB across the samples. However, assuming this distribution reflected that the most common outcome (hit=false) served as the desired or correct outcome in all instances when modeling rat performance, the models predicted when a trained rat would fail to detect TB (ie, miss a TB-positive sample or correctly reject a TB-negative sample) rather than detect it. Furthermore, the predictive power of the models did not take into account what the rats were smelling, since the rats were trained to perform differently (hit true or false) depending on the presence of TB within the sample. Therefore, the aim of this study was to replicate the procedures of the study by Jonathan et al [10] but with the inclusion of variables related to the detection of TB and with expansion of modeling to include 2 additional machine learning (ML) algorithms.

Objectives of the Study

This study applied the same data set from APOPO's TB-detection rat training and research center in Morogoro, Tanzania, as used by Jonathan et al [10] but with the inclusion of WHO-endorsed diagnostic results, including those provided by partner DOTS clinics (smear microscopy, ID_BL_DOTS)

and, where applicable, those performed by APOPO (either concentrated smear microscopy, ID_BL_FM, or fluorescent microscopy, ID_BL_APOPO) to confirm samples flagged suspect by the rats. As with Jonathan et al [10], this study used the decision tree, random forest, and naïve Bayes algorithms and included support vector machine (SVM) and k-nearest neighbor (kNN) ML techniques to improve the accuracy of the predictive models. Furthermore, it provides extensive simulations using real data to determine if ML techniques can accurately predict the performance of rat TB detection. Additionally, this paper compares the classification accuracy performance of the 5 ML predictive models. The rest of this paper is organized as follows: the Related Work subsection provides details of related literature focusing on African giant pouched rat TB detection, including the current status and its implications, along with the application of ML in diagnosing and detecting TB; the Methods section presents the methodology of this study; the Results section provides a description of the performance results and performance measurements of the predictive models; and the Discussion section discusses the findings, provides conclusions, and mentions the scope for future work.

Related Work

Diagnosis of TB by African Giant Pouched Rats: Current Status and its Implications

African giant pouched rats cost-efficiently complement other TB diagnostic tools through second-line screening via scent detection to increase TB case detection. Patient samples are provided by partner DOTS clinics that perform initial screening. The rats can test up to 100 samples in 20 minutes or less, while a laboratory technician requires about 4 days to accomplish the same task using microscopy [11]. Samples that the clinic deems TB negative but which the rats indicate are TB positive are then retested using WHO-endorsed methods, such as concentrated smear microscopy or GeneXpert. Samples that are confirmed positive are communicated to the respective DOTS clinic, effectively providing 24-hour result turnaround and improved linkage to care [6]. Applying this method since 2007 has enabled TB-detection rats to identify more than 29,000 patients who had a missed diagnosis during initial screening [4]. Thus, rat scent detection technology is of great importance to the community and public health hospitals because it increases case detection, enables treatment, and curbs the spread of the disease [3].

Application of ML and Big Data Analytics in Diagnosing and Detecting TB

Technology advancement has allowed access to data from multidimensional sources with high throughput velocity. The term used to describe this kind of data is “big data,” which is difficult to analyze for interesting patterns or inefficiencies without ML technologies [12]. The application of ML in health care is important to improve human health, and ML and big data analytic technologies have brought advancements in TB health care services owing to the increase of health care data and the availability of analytics to solve health problems [13]. ML is a technology that enables a machine to learn from past data and predict the outcome. Thus, in health care, ML contains sophisticated algorithms that help to learn features from a large volume of health care data and then use the obtained insights to assist clinical practices [14]. Big data analytics is the use of advanced analytic techniques on vast amounts of data in different formats, such as structured, semistructured, and unstructured data, from different sources. Big data analytics can help to discover useful information that facilitates decision-making and health care outcome prediction. Therefore, ML and big data analytics can assist physicians by providing up-to-date medical information from clinical practices for proper patient care. As such, the application of ML and big data analytics can help to reduce diagnostic and human errors in the outcomes of clinical practices [15].

ML in health care depends on different techniques, which include classification, clustering, and association, for its operation. These techniques help to learn past data and detect knowledge patterns [16]. Classification techniques are used to develop models that predict future events from the manipulated data and offer solutions to real-world health problems such as diagnosis and treatment of diseases [16]. Classification is the ML technique that operates by building predictive models that categorize and assign labels to manipulated and newly encountered instances [16]. These predictive models help solve multiclassification problems through prediction and analysis. Moreover, the models are used as decision-support tools that help medical professionals interpret diagnosis results [17]. For example, Abdar et al [18] used the boosted C5.0 and CHAID classification algorithms to build a decision tree model for the early diagnosis and prediction of liver disease. In addition, ML technologies were used in the diagnosis of TB to categorize and find relationships among the manipulated variables [19]. This study developed an efficient and reliable framework for automatic TB bacilli detection based on deep learning and ML algorithms. The study also suggested that a classification model can be used to discriminate between positive and negative samples [19].

The classification algorithms recently used in the diagnosis of TB include decision tree, random forest, naïve Bayes, SVM, and kNN [20]. These algorithms are suggested as an alternative for health care professionals to improve the diagnosis of TB. The decision tree algorithm C4.5 was used to build a model to predict the presence of TB bacteria. The results showed that the decision tree had a prediction accuracy of 99% [21]. The decision tree generates rules that are simple and easy to understand and interpret for a decision maker [16].

Moreover, a random forest classification algorithm was used to discriminate the TB bacilli with a sensitivity and specificity of above 89.34% and 62.89%, respectively. Furthermore, it is proposed that the naïve Bayes algorithm can be used for the diagnosis of TB [22]. Additionally, SVM is known as a useful model to identify abnormalities in the lungs for the diagnosis of TB [23]. Following this, algorithm comparison is of great importance to find a reliable algorithm in the given data [24].

Methods

ML Algorithms

In this study, the ML algorithms used are decision tree, random forest, naïve Bayes, SVM, and kNN to build predictive models that categorize data and assign a label to manipulated and newly encountered data. The purpose of involving different algorithms is to compare and improve the prediction accuracy of rats for TB detection.

Real Data Sets

This paper used 2 data sets provided by APOPO: detection rats data set and RAT_WEIGHT data set, which were combined to form the final data set, as shown in Table 1. The detection rats data set contained 471,133 observations from 2011 to 2019 and involved 18 variables (17 independent and 1 dependent). The RAT_WEIGHT data set contained 1438 records collected from 2012 to 2019 and involved 4 independent variables. Moreover, these data contained 5 female rats with IDs 56, 72, 80, 85, and 96. However, the fifth rat with ID 96 from the RAT_WEIGHT data set was eliminated in the analysis because it lacked the necessary detection performance variables in the detection rats data set. Therefore, 4 female rats were used in this study. The 2 data sets and corresponding variables are displayed in Table 1.

Table 1. Rats data set description.

Data set and number	Variable name	Data type	Description	Variable type
Detection rats data set				
1	DOTS_NAME	String	Name of the DOTS[a] center	Independent
2	DOTS_PATIENTS_NUMBER	Integer	Number of patients from the DOTS center	Independent
3	ENTRY_YEAR	Integer	Year when the patient attended the DOTS center	Independent
4	ID_SAMPLE	Integer	Identification of the sample	Independent
5	ID_BL_DOTS	Integer	Identification of the bacteria level from the DOTS center	Independent
6	HIT	Boolean	TB[b] detection rat performance (categorical variable)	Dependent
7	ID_BL_APOPO	Integer	Identification of the bacteria level from the APOPO[c] center	Independent
8	ID_CONFIGURATION	Integer	Identification of the cage during training	Independent
9	ID_BL_FM	Integer	Identification of the bacteria level by fluorescence microscopy	Independent
10	ID_EVALUATION_SESSION	Integer	Identification of the evaluation session	Independent
11	SESSION_DATE	Date	Date when a session was performed	Independent
12	ID_RAT	Integer	Identification of the rat	Independent
13	RAT_NAME	String	Name of the rat	Independent
14	GENDER	String	Sex of the rat	Independent
15	AGE	Integer	Age of the rat	Independent
16	START_TIME	DateTime	Date and time when the detection task started	Independent
17	END_TIME	DateTime	Date and time when the detection task ended	Independent
18	DOB	Date	Date when the rat was born	Independent
RAT_WEIGHT data set				
1	ID_RAT	Integer	Identification of the rat	Independent
2	RAT_NAME	String	Name of the rat	Independent
3	WEIGHT_DATE	Date	Date when the weight of the rat was measured	Independent
4	WEIGHT	Integer	Weight of the rat	Independent

[a]DOTS: directly-observed treatment, short-course.

[b]TB: tuberculosis.

[c]APOPO: Anti-Persoonsmijnen Ontmijnende Product Ontwikkeling.

Applied Variables

The data underwent initial preprocessing to obtain the required variables for developing the predictive models. All data preparation was implemented by Python owing to its large number of libraries for scientific computing and the development of ML predictive models [24]. The sample (either TB negative or the bacterial concentration of TB positivity provided by the partner DOTS clinic, ID_BL_DOTS) was compared to APOPO's confirmatory diagnosis (where applicable) using concentrated smear microscopy (ID_BL_APOPO) to create a variable termed Definitive_Status. This variable reflected the APOPO result when one was provided; otherwise, it indicated the DOTS clinic result. The Definitive_Status was then transformed into the dichotomous variables of TB_Status to reflect the final status of the sample as either positive or negative for TB (collapsing across bacterial concentrations for positive samples). Then, TB_Status was compared to hit to compute the dependent variable of Rat_Performance, which consists of 4 categories: correct hit, miss, false alarm, and correct reject (Figure 2).

After the data preparation, 4 variables for the detection performance of the rats, including TB_Status, age, weight, and hit, as shown in Table 2, were used to build the predictive model. Moreover, this study used 366,441 observations for analysis after removing the null rows from the rats data set to prevent noises, outliers, and inconsistencies in the data. The sklearn model selection library through a train-test split class was used to partition the data (366,441 observations) into 256,508 observations (70%) in the training data and 109,933 observations (30%) in the test data. It is important to mention that, due to the binary nature of many variables and the underlying prevalence of TB infections, the data used in this study lack a normal distribution, as shown in Multimedia Appendix 1.

Categorical variables were used to build predictive models, and 256,508 observations (70%) were used for training the models. The TB_Status variable consisted of 10.90% (27,950/256,508) positive samples and 89.10% (228,558/256,508) negative samples. The hit variable consisted of 21.33% (54,719/256,508) true values and 78.67% (201,789/256,508) false values.

Table 3 shows a statistical summary of the distribution of continuous variable data before and after the random data split. Despite most of the distributions being the same, the mean of age and weight variables showed a difference of 0.01. Moreover, the SD of ID_RAT and weight differed by 0.01.

Table 2. Description of the dependent and independent variables used to build predictive models.

Variable	Description	Data type	Variable type	Value
TB_Status	Final diagnosis of the sample as either TB[a] positive or TB negative. Combines the diagnostic results of both DOTS[b] and APOPO[c] (lab confirmation, when applicable) wherein APOPO status (results) overrides DOTS.	Object	Independent/categorical	True or false
Age	Age of the rat in years at the time when the rat evaluated the patient sample in question	Object	Independent	Age ranges from 0.79 to 7.95 years
Weight	Average rat body weight (in grams) per year because most of DetectionRats-Data describes the daily detection tasks and misses their corresponding weights since the weight of the rats from the RAT_WEIGHT data set was measured every week.	Object	Independent	Average rat body weight ranges from 843.67 to 1054.83 grams
Hit[d]	Defined as a continuous sniff (nose insertion into the cage hole) for ≥3 seconds. True means the rat "indicated" that the sample contained TB (held its nose in the hole for at least 3 seconds). False means the rat rejected the sample (did not hold its nose for at least 3 seconds).	Object	Dependent/categorical	True or false

[a]TB: tuberculosis.

[b]DOTS: directly-observed treatment, short-course.

[c]APOPO: Anti-Persoonsmijnen Ontmijnende Product Ontwikkeling.

[d]Hit refers to whether or not (true or false) the rat provided an indication.

Table 3. Descriptive statistics of the continuous variables used to build predictive models before and after random data split.

Data split status and variable	Age (years)	Weight (g)
Before random data split (n=366,441, 100%)		
Mean	3.83	899.40
SD	1.72	84.37
IQR	3.71	866.80
Minimum	0.79	843.67
Maximum	7.95	1054.83
After random data split (n=256,508, 70%)		
Mean	3.84	899.41
SD	1.72	84.36
IQR	3.71	866.80
Minimum	0.79	843.67
Maximum	7.95	1054.83

Model Building

The predictive model in this study was developed using 5 different ML techniques: decision tree, random forest, naïve Bayes, SVM, and kNN. This study used Python libraries for data preprocessing, matrix processing, mathematical functions, visualization, and classification. These are Pandas, Numpy, Matplotlib, and Scikit-learn [25]. The repetitive approach was used to generate a decision tree by dividing the training data. The data were divided recursively until the same class of variables, depending on conditions, using roughly 15,000 samples per leaf, were distributed among each division to create the decision tree. After that, each node in the decision tree used a split point to test the altered variables and choose how to divide the data. The split decision was concerned with the information gain and entropy of a computed variable. The variable that had the greatest information gain and the least entropy was therefore divided and put to the test. The choice regarding the data split and decision tree building was made based on information gain and entropy [16]. This study used pruning to maintain control over the parameters being used to remedy expansion.

During the training procedure, many decision trees were randomly constructed using the random forest technique. Based on the provided manipulated variables, the algorithm's ultimate decision was based on the selection of the majority of the trees. There was a connection between the outcome and the number of trees in the forest. The outcome was therefore more accurate with an increase in the number of trees. As a result, the technique handled 500 trees in the ensemble, and it calculated the error rate using the training set of information. In the random forest approach, the training data were used to generate random splits for the root node and variable node. Since there was no parameter control during training, the connection between trees remained strong. Additionally, the frequency and values of the adjusted variables from the provided data were counted to generate the classification model using the naïve Bayes method. This method determined the dependent variable's a priori probabilities as well as the conditional probabilities for each independent variable based on the altered data. The naïve Bayes technique has been specifically utilized to contrast its prediction performance with the outcomes produced by other ML techniques. It does not display the weights of each variable included in the classification.

SVM is one of the most common supervised ML algorithms owing to its greater predictive power. SVM analyzes data, recognizes patterns, and produces input-output functions from a set of labeled training data. It works by classifying a response variable by drawing a decision boundary line or hyperplane to separate 2 classes. Then, the maximum margin hyperplanes are constructed to optimally separate the output classes from each other in the training data. The goal is to find the optimal separating hyperplane where the separating margin is maximized. The linear kernel was used to allow flexibility and loss functions. The kNN algorithm is a supervised ML algorithm that works by identifying a set of k-nearest observations to the test point and calculating mainly the Euclidean distance between an observation and its kNN in training data. The k in kNN refers to the number of nearest neighbors the classifier will retrieve and use to make its prediction. The chosen k in kNN was 1, as it is suggested to provide the best test prediction.

Performance Measurements

This study used accuracy, specificity, sensitivity, and F1 score as metrics to evaluate the performance of the generated predictive models and compare classification performances. These measurements were supported in the *scikit-learn* library through the classification report class.

Accuracy

The classification accuracy was calculated based on the confusion matrix, which accurately categorized the actual class labels of the test data and the class labels of the predicted models. It was also obtained by dividing the number of truly classified instances by the number of instances in the test phase. Accuracy considers TP, true negative (TN), false positive (FP), and false negative (FN). The classification accuracy for the data set was measured according to the following formula:

Accuracy = (TP + TN) / (TP + FP + TN + FN) **(1)**

Sensitivity

Sensitivity is defined as the number of TP cases over the number of TP cases plus the number of FN cases. Sensitivity identifies the correct positive predictions relative to the total actual positive cases. It is sometimes called a recall metric. The formula of sensitivity is as follows:

Sensitivity = TP / (TP + FN) **(2)**

Specificity

Specificity is the ratio between TN cases and all negative cases. In this study, the precision measure identified the correct positive predictions relative to total positive predictions. For diagnostic tools, this could be termed positive predictive value (PPV) or precision. It essentially provides confidence that any given positive response reflects a truly positive condition [25]. The formula of specificity is as follows:

Specificity = TN / (TN + FP) **(3)**

F1 Score

The F1 score is the harmonic mean of specificity and sensitivity. Basically, it is the weighted average of specificity and sensitivity. The F1 score was calculated from the specificity and sensitivity of the test data set [25]. The formula of the F1 score is as follows:

F1 score = 2 ([Precision × Sensitivity] / [Precision + Sensitivity]) **(4)**

It is important to mention that specificity and sensitivity are similar to precision and recall, respectively.

Restrictions of the Study

This study ran the predictive models on a computer with a Core i5-5300U CPU at 2.30 GHz (2301 MHz, 2 cores, 4 logical processors) and 8 GB of RAM. The sample size, on the other hand, was small, with only 4 rats and a gender imbalance. Moreover, the hit variable consisted of fewer true values (21.26%) than false values (78.74%).

Ethical Considerations

The study was approved by the SUA (DPRTC/R/142/vol.01/104) and Medical Research Coordinating Committee of Tanzania (NIMR/HQ/R.8a/Vol.1X/3905). The use of African giant pouched rats as a potential tool for TB diagnosis has received ethics clearance from the Tanzanian Medical Research Coordinating Committee [26]. The Office of Laboratory Animal Welfare has approved APOPO's Animal Welfare Assurance (OLAW; Assurance Identification Number A5720-01).

Results

Comparing Classification Performance Measurements of the Predictive Models

This study used different ML techniques to build the predictive models following the methodology presented in Figure 3. Moreover, this study employed several metrics, including accuracy, sensitivity, specificity, and F1 score, to measure the classification performance of the predictive models based on test data. Figure 4 shows the confusion matrices of the SVM and random forest classifiers, while Table 4 summarizes the performance of all 5 ML techniques used to build the predictive models. The accuracy classification performance of the kNN technique was low at about 81.25%, while the best performing algorithm was SVM. As it can be seen from Table 4, validation showed that the SVM classifier based on the 4 variables shown in Table 2 achieved an accuracy of 83.39%, but it also reported that SVM had better ability to recognize the status of TB as either positive or negative in a given sample.

Figure 3. Process flow of machine learning–based prediction models of rat tuberculosis detection performance. The rectangle symbols represent data, while the histogram entails model evaluation metrics. DT: decision tree; kNN: k-nearest neighbor; NB: naïve Bayes; RF: random forest; SVM: support vector machine.

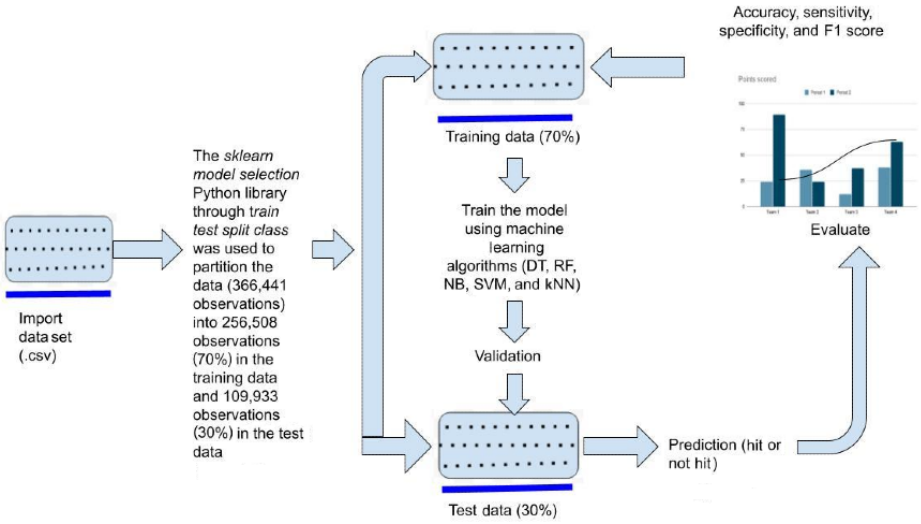


Figure 4. Confusion matrices of the predictive models. (A) Support vector machine classifier; (B) Random forest classifier.

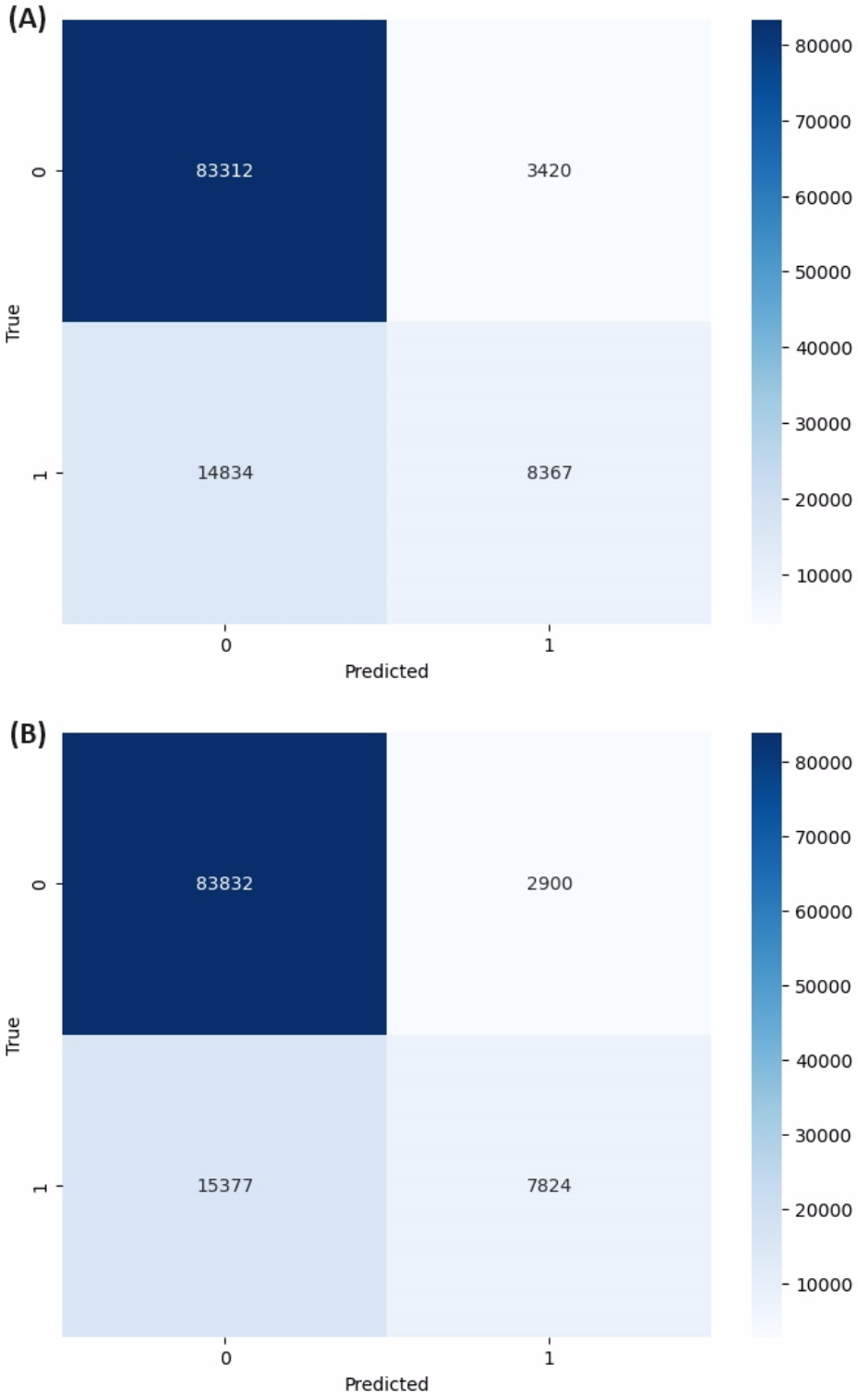


Table 4. Comparing the classification performance of classifiers of rat tuberculosis detection.

Classification performance measurement	Predictive model				
	Decision tree	Random forest	Naïve Bayes	Support vector machine	K-nearest neighbor
Accuracy, %	83.32	83.38	82.56	83.39	81.25
Sensitivity, %	65.00	65.00	63.00	66.00	64.05
Specificity, %	79.00	79.00	77.00	78.00	72.05
F1 score, %	67.00	67.00	66.00	69.00	66.05
Correctly classified observations (true positive), n	91,602	91,602	90,370	91,602	89,326
Incorrectly classified observations (false negative), n	18,331	18,331	19,163	18,331	20,607

Important Variables Influencing the TB Detection Performance of the Rats

This study used the random forest variable importance function to output the predictor variables based on the mean decrease in Gini (impurity). Random forest showed high performance in the feature ranking. The mean decrease in the Gini value is the average (mean) of a variable's total decrease in the likelihood of incorrect classification of a new instance of a random variable from the data set. Multimedia Appendix 2 shows the predicted variable importance based on the mean decrease in the Gini value using the random forest algorithm.

From Table 5, higher (0.817152) and lower (0.026657) mean decreases in the Gini value result in greater and less variable importance, respectively. In other words, TB_Status and weight were the most and least significant variables, respectively, for predicting rat TB detection accuracy. However, for easy interpretation and visualization of these results, the variable importance function of the random forest algorithm sorted and displayed the variables as reported in Multimedia Appendix 2 based on the prediction importance. As such, the variable that contributed most to the prediction had the highest mean decrease in Gini values, followed by the variables with less importance.

Table 5. Random forest variable importance based on the mean decrease in the Gini value.

Variable	Variable name	Mean decrease in the Gini value
0	TB_Status	0.817152
1	Age	0.156190
2	Weight	0.026657

Algorithm for the Prediction of Rat TB Detection Performance

The study also employed a prediction algorithm for TB detection as illustrated in Textbox 1.

Textbox 1 shows the algorithm that predicts if the rat will hit the sample or not. First, data were imported and normalized to acquire the required data format. Then, the statistical summary of the independent variables used to build predictive models was described. Considering Figure 3, the train_test_split library was used to divide the data set into training data (70%) for developing the models and test data (30%) for validating the models. The predictive models were trained based on the decision tree, random forest, naïve Bayes, SVM, and kNN classifiers, using the train data. Meanwhile, the validation of the models was performed using the test data. Then, accuracy, sensitivity, specificity, and F1 score were used to measure the classification performance of each classifier, as reported in Table 4. Furthermore, the input variables TB_Status, age, and weight were entered for prediction. Following the prediction, models were validated using the test data. Hence, data visualization was performed using the Matplotlib library for proper interpretation of the results. On the other hand, if the constraints were not met, the algorithm could be terminated.

In addition to the above algorithm for the prediction of rat TB detection performance, Figure 3 indicates the process flow of ML models and their predictions using *Python* libraries. The TB input data set was imported as a .csv file. After preprocessing the data, the *sklearn model selection* library was used to partition the data into training data (70%) and test data (30%) by using a simple random split method. The training data were used to build a predictive model using decision tree, random forest, naïve Bayes, SVM, and kNN classifiers. After building the predictive model, the inputs, including TB_Status, age, and weight, were computed to predict if the rat would hit the sample or not. Thereafter, the predictive models were evaluated for their prediction performance using accuracy, sensitivity, specificity, and recall metrics.

Textbox 1. Algorithm for the prediction of rat tuberculosis detection performance.

I. Import and normalize the dataset (.csv)

II. Calculate IQR, mean, SD, minimum, and maximum

III. Perform splitting of the data set

1. if splitting is successful and not any constraints then

- train the model

2. Perform machine learning (ML) modeling based on decision tree, random forest, naïve Bayes, support vector machine, and k-nearest neighbor

3. Perform validation of the ML modeling

4. Perform ML model prediction

5. Validate the prediction model by calculating *accuracy*, *sensitivity*, *specificity*, and *F1 score*

6. if *accuracy and other parameters are good* then

- input: *TB_Status*, *age*, *weight*

7. Perform ML model prediction if the rat would hit the sample or not

8. Update the predicted value of new data for reporting

9. Make data visualization in Python

10. else

11. Perform termination check

12. else

13. End

Discussion

Principal Findings

The aim of this study was to build on the prior work of Jonathan et al [10] to develop models that predict if a trained TB-detection rat would hit (indicate the presence of TB within) a patient sample or not using ML techniques by incorporating variables related to the diagnostic results of the TB samples. This study used decision tree, random forest, naïve Bayes, SVM, and kNN ML techniques to build predictive models. The ML techniques successfully categorized the data by assigning a label to each computed data point. The results revealed that for the 5 different algorithms used, the classification accuracy was the greatest for SVM, suggesting its superiority to the decision tree, random forest, naïve Bayes, and kNN classifiers. The SVM classifier outperformed by yielding a classification accuracy of about 83.39% for predicting if the rat would hit the sample or not. This level of accuracy surpasses the 78.82% accuracy found with decision tree and naïve Bayes by Jonathan et al [10], suggesting that the inclusion of sample information serves as a valuable variable that influences the performance of TB-detection rats and improves the accuracy of the prediction models. Moreover, Jonathan et al [10] employed a small amount of data compared to the data used in this study. In fact, TB_Status was found to be the most significant variable in predicting rat TB detection performance. However, there was an insignificant accuracy difference between the constructed models and those created by Jonathan et al [10], which could be due to the characteristics of the data [16]. Therefore, the additional variables are likely to influence rat behavior, and the true status of patient samples can only be determined by available diagnostics.

Conclusion

This study has shown the usefulness of ML techniques to identify factors that influence TB detection performance of rats. The techniques used were decision tree, random forest, naïve Bayes, SVM, and kNN to develop models that predict if the rat would hit the sample or not by incorporating valuable variables related to TB detection performance of rats. The performance of the predictive models was measured by accuracy, sensitivity, specificity, and F1 score metrics. The results showed that the SVM predictive model outperformed in the classification and prediction of the performance of rats in TB detection by yielding the highest accuracy of 83.39%. Furthermore, the obtained results suggest that the inclusion of variables related to the diagnostic results of TB samples improves the performance of the predictive models. Therefore, the results might benefit TB-detection rat trainers and TB decision-makers in improving the diagnostic accuracy of rats by predicting if a trained TB-detection rat would hit a patient sample or not. They can adopt several measures, including ensuring that all hit samples are confirmed within APOPO's laboratory (ID_BL_APOPO). Furthermore, taking into consideration that the age of the rat at hit and clinic diagnostic results are predictors of detection performance.

Acknowledgments

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Distribution of continuous independent variables.
[PNG File , 20 KB - ojphi_v16i1e50771_app1.png]

Multimedia Appendix 2
Random forest variable importance plot.
[PNG File , 16 KB - ojphi_v16i1e50771_app2.png]

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Abbreviations

APOPO: Anti-Persoonsmijnen Ontmijnende Product Ontwikkeling
DOTS: directly-observed treatment, short-course
FN: false negative
FP: false positive
kNN: k-nearest neighbor
ML: machine learning
SDT: Signal Detection Theory
SUA: Sokoine University of Agriculture
SVM: support vector machine
TB: tuberculosis
TN: true negative
TP: true positive
WHO: World Health Organization

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Original Paper

Geospatial Imprecision With Constraints for Precision Public Health: Algorithm Development and Validation

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Abstract

Background: Location and environmental social determinants of health are increasingly important factors in both an individual's health and the monitoring of community-level public health issues.

Objective: We aimed to measure the extent to which location obfuscation techniques, designed to protect an individual's privacy, can unintentionally shift geographical coordinates into neighborhoods with significantly different socioeconomic demographics, which limits the precision of findings for public health stakeholders.

Methods: Point obfuscation techniques intentionally blur geographic coordinates to conceal the original location. The pinwheel obfuscation method is an existing technique in which a point is moved along a pinwheel-like path given a randomly chosen angle and a maximum radius; we evaluate the impact of this technique using 2 data sets by comparing the demographics of the original point and the resulting shifted point by cross-referencing data from the United States Census Bureau.

Results: Using poverty measures showed that points from regions of low poverty may be shifted to regions of high poverty; similarly, points in regions with high poverty may be shifted into regions of low poverty. We varied the maximum allowable obfuscation radius; the mean difference in poverty rate before and after obfuscation ranged from 6.5% to 11.7%. Additionally, obfuscation inadvertently caused false hot spots for deaths by suicide in Cook County, Illinois.

Conclusions: Privacy concerns require patient locations to be imprecise to protect against risk of identification; precision public health requires accuracy. We propose a modified obfuscation technique that is constrained to generate a new point within a specified census-designated region to preserve both privacy and analytical accuracy by avoiding demographic shifts.

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KEYWORDS

social determinants of health; geocoding; privacy; poverty; obfuscation; security; confidentiality; low income; geography; geographic; location; locations; spatial; geospatial; precision

Introduction

Geographic information systems (GISs) are increasingly important for public health research and policy makers and are instrumental in measuring socioeconomic equity in health care [1,2]. Social determinants of health are the conditions in which individuals are born, live, work, and age; mesolevel determinants are from the physical environment and encompass items such as geographic location and access to resources [3]. Location-based exposures tied to geographic location are a pivotal element to one's health [4-6]; ongoing research suggests that zip code is on par with genetic code in influencing individual health [7-10]. Even greater research utility lies in more precisely geolocating patients beyond the zip code level, yet privacy regulations often prevent high-resolution patient residential address data from being shared for research purposes

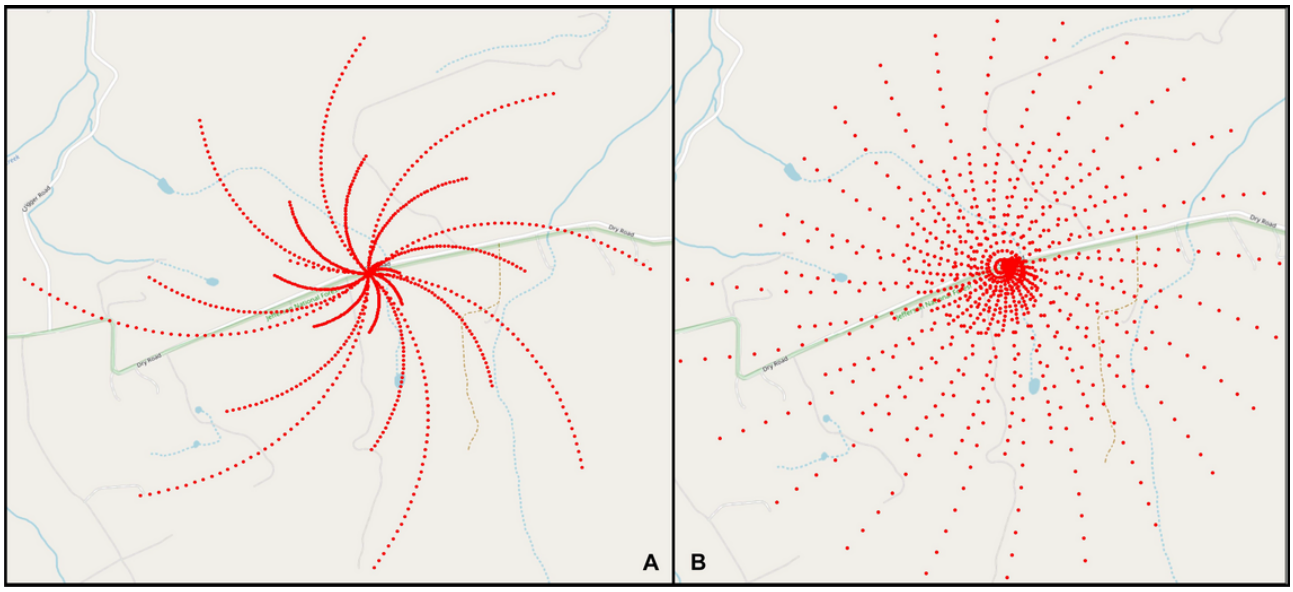
[11]. Privacy is paramount when working with health care data and access is regulated at different levels through both institutional policies and government-mandated legal protections [12]. The Health Insurance Portability and Accountability Act (HIPAA) mandates privacy protections of personal health information in the United States; it outlines which data elements are considered private, including patient addresses needed for geospatial analysis for place-based epidemiology.

Although institutional review boards may grant researchers and other agencies access to identified data that pose minimal risk to the patient, there may exist institutional hesitancy to disclose this data due to the inherent privacy and sensitivity of residential addresses. As a current example, this tension is apparent between state and federal public health and safety agencies using the Overdose Detection Mapping Application Program (ODMAP), which maps in real time the exact locations of suspected drug overdoses, often occurring in residential locations [13,14]. Geocoding a patient's address (ie, converting to geographic coordinates) is often an intermediate step in secondary data analyses; it is either used to link the patient to external geographic units (eg, census tracts to obtain neighborhood socioeconomic status from the United States Census Bureau) or to calculate distance from other entities, such as health care providers and facilities. For example, accessibility of buprenorphine, a medication for opioid use disorder, may be determined using addresses of health care providers that are authorized to prescribe the medication [15]. In these examples, imprecise locations may be sufficient for confident linkage to administrative units or approximate distance measures and preferred for research to preserve privacy. In these scenarios, thoughtful and controlled techniques designed to generate inexact data are needed to reduce precision [12,16].

To this end, geospatial or location-based privacy methods seek to maintain an appropriate level of confidentiality for a given task, service, or application while balancing the utility that these offer [17-19]. For example, users of location-based services on a cellular phone expect some level of privacy when sending personal data, and different strategies exist that anonymize pools of people by anonymizing data at point of collection. Location-based *k*-anonymity provides a method where one's data and location are indistinguishable from *k*–1 other people [20]. Other methods, such as geographic masking, alter coordinates systematically to limit the risk of reidentification when releasing data [21]; no universally accepted method exists for protecting geospatial privacy [16].

Point obfuscation refers to the deliberate degrading of the resolution of coordinate information with the goal of protecting the privacy of the individual represented by the point [22]; this may be referred to as geographic masking, geomasking, jittering, or dithering and relies upon transformations or perturbations using randomness or artificial noise [22]. The *N-RAND* algorithm generates *N* candidate points in a given area and selects the furthest point [23]; *theta-RAND* limits candidate points to a specific area defined by a chosen angle [24]. We introduce modifications to the pinwheel obfuscation method which shifts points along pinwheel-like paths for a randomly chosen angle [25]; examples are shown in Figure 1. The noise added by this method is asymmetrical and highly variable, making it less open to privacy attacks designed to eliminate uniform and predictable noise [25]. However, the limitation of any point obfuscation technique is that coordinate shifts may change real-world locations and distort the linked health-related metrics. For example, a study defining a participant's rurality based on administrative units may be impacted if obfuscated coordinates move the participant across boundaries into an urban area.

Figure 1. Pinwheel obfuscation at theta 45 degrees (A) and 15 degrees (B).



Address *correction* positively impacts the accuracy of assigning a patient to a geographic area [26]. On the other hand, the goal of point obfuscation is to *intentionally generate an incorrect* address to preserve patient privacy without compromising analytical conclusions. Our paper demonstrates that indiscriminate point obfuscation impacts studies linking points to neighborhood-level socioeconomic demographics and subsequently provides new methods needed to constrain

pinwheel obfuscation to yield results confined in specific census-designated regions, such as blocks, block groups, or tracts. The constraint reduces concerns that neighborhood-level measures are inappropriately assigned at the patient level, leading to misclassification bias. We use poverty status as an example of data recorded by the United States Census Bureau to explore the potential impact of unintentional administrative boundary shift. Also, we demonstrate how indiscriminate point obfuscation impacts hot spot analysis at the census tract level. The role of this work is to provide evidence that point obfuscation techniques may substantially alter neighborhood-level socioeconomic demographics and that the intentional imprecision in these techniques must be constrained to support precision public health.

Methods

Overview

We implemented our methods using PostGIS, an open-source project that adds geospatial objects and procedures to the PostgreSQL database. We previously demonstrated PostGIS as a capable environment for geospatial privacy research [27,28]. We make our custom PostGIS functions available as open-source software [29]. The pinwheel technique was originally designed because other point obfuscation methods could be reversed by methods designed to filter uniform noise; the randomness of the pinwheel has been shown to maintain high variability, making it less susceptible to privacy attack [25]. Our geographically constrained pinwheel algorithm leverages the same concept as the original pinwheel algorithm and improves its research utility by adding constraint checking that controls how the new obfuscated point is selected. There is a function, *PINWHEEL*, that obfuscates a single point given a specific *theta*, maximum radius *r*, and a calculated random degree *a*; these are used to calculate a projection distance that can leverage PostGIS's projection function, *ST_PROJECT*, to calculate the resulting obfuscated point.

The left-hand side of Figure 1 shows 1000 candidate points for a given seed point using a 45-degree angle; we sequentially varied the maximum radius while keeping *theta* constant at 45 degrees. Similarly, the right-hand side of Figure 1 shows the same simulation but with 15-degree angles; this demonstrates that *theta* controls the width of the pinwheel layers and that small angles naturally yield closer layers. In practice, a random degree may be used to further obfuscate the results.

Census Bureau geometries are input as reference data. The smallest census-based geographic boundary, the census block, is contained in the block group; a census block group typically represents between 600 and 3000 people. Block groups are organized into census tracts, which typically contain between 1200 and 8000 people and have an optimum size of 4000 people [30]. The United States Census Bureau publishes and updates files containing the geometries for these regions; these geometries are used in point intersection calculations to assign a region to a given point.

To obfuscate, points from the original list, *P1*, are fed into the *PINWHEEL* function and saved into *P2*. To constrain obfuscation, our method recalculates the pinwheel candidate for any generated candidates falling outside a specific region associated with the original point; we can constrain to standard administrative units: state, county, tract, block group, and block geometry. Furthermore, we can constrain obfuscation to custom geometries, such as buffer zones or other areas that may be relevant for research projects. The region of the points can be calculated with PostGIS's *ST_CONTAINS* function, which tests the intersection of the points with the Census Bureau geometries. The regions are compared for every matching pair of existing and new points in *P1* and *P2*. If the regions are dissimilar, *PINWHEEL* is rerun on the existing point. This continues until all points in *P1* have a matching obfuscated point in *P2* where *P1* regions align with *P2* regions.

We tested our methods with 2 different data sets, with geographic coverage ranging from multiple states to a single large urban area. Our first data set contained 1,000,000 records formatted in the Observational Medical Outcomes Partnership (OMOP) common data model [31]; we previously leveraged this data for geospatial research on open data and privacy [27]. Our second data set contains 58,102 case records from the Medical Examiner Case Archive from Cook County, Illinois, which contains the city of Chicago; we previously used this open data for research on geographic clustering of fatal overdoses [32] and to create an open data pipeline for spatial analyses on substance use disorders [33]. This open data set was released by the Cook County Medical Examiner's Office (CCMEO) and offers details on all deaths recorded by the CCMEO from August 2014 to April 2022, including the address where the incident occurred and the address of the death. Deaths by suicide recorded in the CCMEO data set were also used for our hot spot analysis example.

Ethical Considerations

This study was exempt from ethical review since no private health data were used and no human subjects were involved.

Results

As expected, the pinwheel obfuscation method initially resulted in points shifting into different geographic regions; the frequency of these region shifts is summarized in Table 1 for our OMOP and CCMEO data. We categorized these shifts by census-designated regions by increasing population size (block, block group, tract, county, and state). Shifts were proportional to the maximum radius allowed; a radius of 1000 meters was the largest distance tested and naturally generated the most region shifts. Blocks are the smallest geographic unit and experienced the most change: 747,934 of 1,000,000 (74.8%) of the OMOP points and 53,415 of 58,102 (91.9%) of the CCMEO points were moved to different census blocks after obfuscation up to 1000 meters away. This empirically indicates that smaller geographical regions are more likely to shift when using any significant distance in the obfuscation method. Blocks are the smallest of the census-designated administrative boundaries. There is no maximum size for a census block; minimum block size is 30,000 square feet (2787.1 m^2) for polygons bounded by roads or 40,000 square feet (3716.1 m^2) otherwise, which is

smaller than the largest obfuscation distance selected for our testing [34].

Additionally, the results demonstrate that even with very small distances unintentional consequences may occur; even moving the point using a radius of 1 meter resulted in misclassification. Although relatively rare, point obfuscation 1 meter away could change a point's county in 0.0007% of the OMOP data (7/1,000,000) or a point's census tract in 0.09% of the CCMEO data (58/58,102). There are no universally accepted best practices for point obfuscation, and the most effective allowed distance may vary with study area and application [16]. Due to the inclusion of the city of Chicago in the Cook County data, the census-designated regions in the CCMEO data are geographically smaller than those in our OMOP data, which cover multiple states; census tracts generally contain between 1200 and 8000 residents, meaning urban census tracts are geographically smaller than rural census tracts. This can be seen in our results, where a radius of 100 meters or larger yielded a higher percentage of shifts in our CCMEO data than our OMOP data.

Our results demonstrate that indiscriminate point obfuscation can shift a point into different census-designated geographical regions; this is a natural and expected consequence of moving a point. However, we now discuss and quantify the potential impact of shifting to linked administrative units (ie, neighborhoods) by comparing census demographics before and after obfuscation. The United States Census Bureau conducts large-scale surveys, such as the decennial census and the American Community Survey (ACS). The yearly ACS samples approximately 250,000 household units monthly. From the ACS, we picked the estimated number of "individuals with income in the past 12 months below poverty level" as an example demographic; these data are publicly available at the census tract level. We chose poverty status due to its saliency in health outcomes research [35,36].

We give a high-level overview of the obfuscation impact on poverty status measurement in Table 2 to justify the need for a geographically constrained obfuscation technique when assigning points to a population-based rate of individuals living under the poverty line (as a percentage of the total population). In our OMOP data, a pinwheel distance of 1000 meters resulted in 22.4% (n=224,065) of records with a different poverty rate after obfuscation where those changes were, on average, a mean 7.3% (SD 7.4%) away from the original rate (median 5%, range 91.9% to –78.6%). We also show the magnitude of the difference between the original and obfuscated address by showing minimum and maximum differences of rates. Negative differences imply the obfuscated record had a lower assigned poverty rate while positive differences imply the obfuscated record had a higher assigned poverty rate. For completeness and to complement Table 1, we include small distances of 10 and 1 meters in Table 2, although we did not anticipate such small distances would impact poverty rate assignments.

Table 1. The number of records shifted into a different region varied per obfuscation radius (in meters) and size of region.

Data set and radius (meters)	Records, n×1000 (%)				
	Block	Block group	Tract	County	State
Observational Medical Outcomes Partnership (n=1,000,000)					
1000	747 (75)	367 (37)	226 (22)	16 (1.6)	1.1 (0.11)
500	616 (62)	210 (21)	114 (12)	8 (0.8)	0.479 (0.049)
100	236 (24)	35 (3.5)	16 (1.6)	1.3 (0.13)	0.071 (0.007)
1	3.2 (0.34)	0.359 (0.03)	0.194 (0.02)	0.08 (0.008)	0.004 (0.0004)
1	0.304 (0.03)	0.044 (0.004)	0.018 (0.001)	0.007 (0.0007)	0 (0)
Cook County Medical Examiner's Office (n=58,102)					
1000	53 (91.9)	40 (70.4)	31 (53.3)	0.161 (0.27)	0.034 (0.05)
500	49 (85.4)	29 (50.7)	19 (33)	0.082 (0.14)	0.01 (0.02)
100	27 (47.7)	7.8 (13.4)	4.5 (7.8)	0.012 (0.02)	0.001 (0.002)
10	1.2 (2.22)	0.495 (0.85)	0.343 (0.59)	0.001 (0.002)	0 (0)
1	0.187 (.032)	0.082 (0.14)	0.058 (0.09)	0 (0)	0 (0)

Table 2. Poverty rates are substantially different before and after obfuscation.

Data set and distance (meters)	Records with changed poverty rate, n (%)	Difference in rate (%), mean (SD)	Difference in rate (%), median (maximum to minimum)
Observational Medical Outcomes Partnership (n=1,000,000)			
1000	224,065 (22.4)	7.3 (7.4)	5 (91.9 to –78.6)
500	113,682 (11.3)	7.3 (7.5)	5 (91.9 to –78.6)
100	16,121 (1.6)	7.4 (7.7)	5.1 (78.6 to –78.6)
10	193 (0.01)	6.5 (6.4)	4.2 (35.9 to –32.6)
1	18 (0)	11.7 (8.1)	10.5 (38.8 to –12)
Cook County Medical Examiner's Office (n=58,102)			
1000	30,843 (53.1)	8.3 (7.7)	6 (61.7 to –69)
500	19,139 (32.9	8.2 (7.6)	5.9 (58.4 to –61.7)
100	4506 (7.8)	8.2 (7.5)	6 (58.4 to –58.4)
10	343 (0.6)	8.1 (7.3)	6.2 (33.2 to –55.4)
1	58 (0.1)	6.8 (6.5)	4.4 (31 to –18.2)

A larger percentage of records in the CCMEO data experienced rate changes in comparison to our OMOP data. With a distance of 1000 meters, 53.1% (n=30,843) of records were assigned into a region with a different poverty rate where those changes were a mean 8.3% (SD 7.7%) away from the original rate (median 6%, range 61.7% to –69%). The magnitude of changes was not substantially different from our OMOP data (averages of 7.3% vs 8.3% and medians of 5% vs 6%, respectively, for 1000 meters); yet the frequency of these changes was notably higher (22.4% vs 53.1%, respectively, for 1000 meters).

Figure 2 shows an example census tract (17031031100) in Cook County, Illinois; 33 deaths were recorded in this area. Figure 2A shows an example simulation using pinwheel obfuscation with a 1000-meter radius; Figure 2B shows the results of our geographically constrained pinwheel obfuscation. The original point is orange, and the obfuscated point is blue; the census tracts are colored according to quintile of our poverty measure, where lightly colored areas have the lowest poverty rates. For this example, pinwheel obfuscation resulted in 22 of 33 (66%) of the points shifting census tracts; 12 of 33 (36%) of these were shifted into areas of higher poverty, while 10 of 33 (33%) were shifted into areas of lower poverty. Of those positive shifts, 4 of 12 were pushed to the highest category (33%) while the other 8 were moved into the second-highest poverty quintile. This example shows how obfuscation may move points from one extreme to another.

Hot spot analysis is known to be an effective tool for understanding how health outcomes and social determinants of health concentrate and cluster together [37-39]. We explored the impact of indiscriminate point obfuscation on a hot spot analysis of deaths by suicide from our CCMEO data; suicides were identified by the manner of death field in the CCMEO data and span the time period August 2014 to April 2022. Figure 3 shows the results of hot spot analyses using ArcGIS Pro [40] on the original data (Figure 3A) and data obfuscated with the pinwheel method using an unconstrained 1000-meter radius (Figure 3B). The obfuscation naturally blurred the correct hot spots, but (unexpectedly) new hot spots emerged, as identified by the pink boxes in Figure 3B. Most notably, a hot spot (95% confidence) spills into the neighboring and uninhabited Lake Michigan (census tract 17031990000). Highlighted in green are regions of interest with substantial change; the upper green box demonstrates the disappearance of a hot spot (99% confidence), and the lower green box demonstrates how indiscriminate obfuscation can bridge 2 hot spots together and weaken the signal that distinct clusters exist. By definition, the hot spots corresponding to the geographically constrained pinwheel method are identical to the true clusters in Figure 3A because of the confinement to the point's original census tract. When linked to an administrative boundary such as census tract, results are consistent before and after obfuscation when the pinwheel method is constrained; only distance-based results would be impacted by moving the original point. By constraining the pinwheel process to a specific geographic region, the results of any method depending upon aggregation within those regions will not be impacted by our method.

Figure 2. Poverty and point obfuscation of original points (orange) to obfuscated points (blue) using a pinwheel (A) and a geographically constrained pinwheel (B).

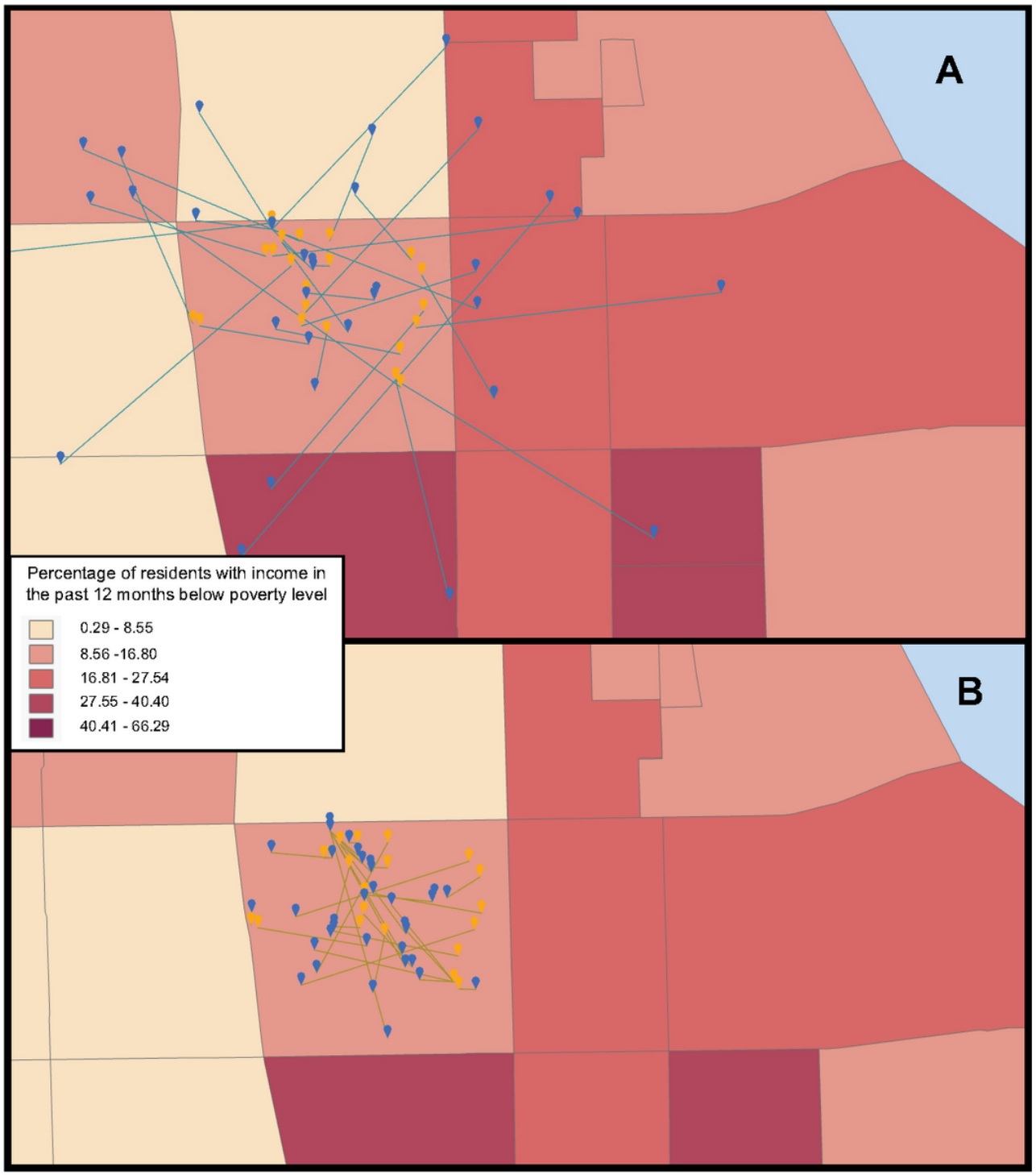
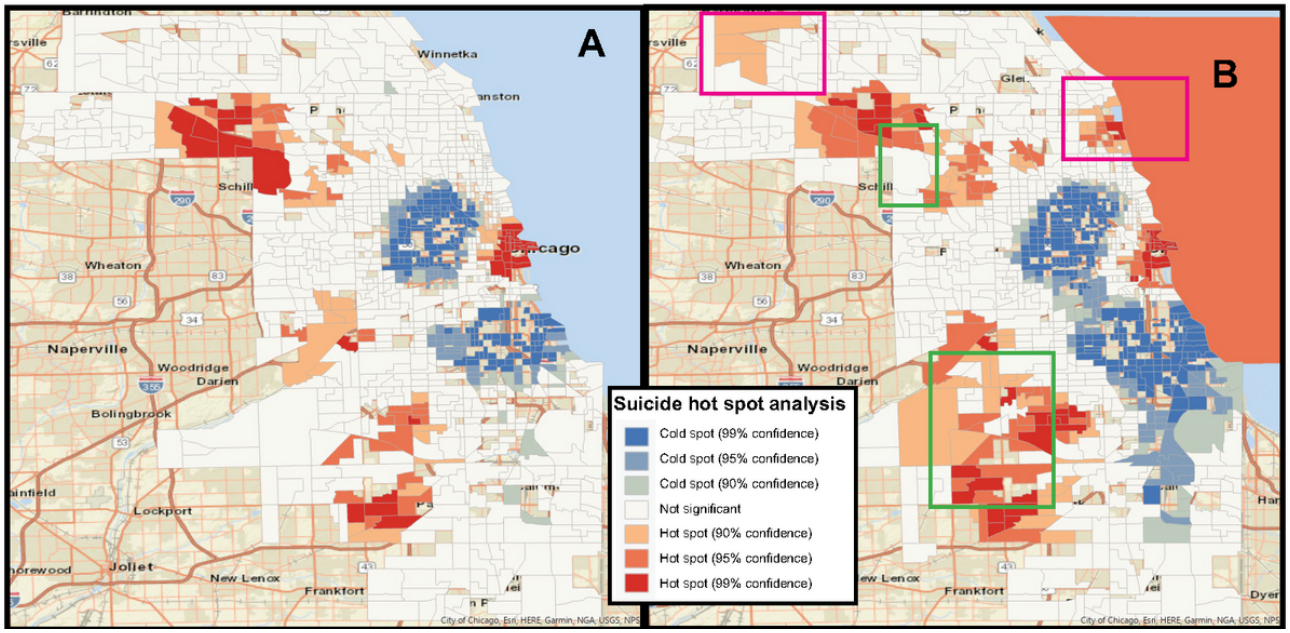


Figure 3. Hot spot analysis of suicides using original data (A) and obfuscated data (B).



Discussion

Principal Findings

We demonstrated that imprecise point obfuscation results in shifts across geographic regions and showed that these shifts do result in points geolocating in regions with vastly different socioeconomic contexts. This justifies the need for more precise point obfuscation techniques; our method constrains the candidate points into a specific region, which guarantees identical regional demographics after privacy protection is applied. The official poverty rate for the United States was 11.5% in 2022, and in the state of Kentucky, it was 16.5%, which places it 46th in a ranking of poverty rates in the United States [41]. For comparison, New Hampshire was ranked first and has the lowest poverty rate of 7.2% [41]. These example rates for the United States indicate areas experiencing differences of 5% to 7% in poverty rate, such as those reported in Table 2, represent vastly different socioeconomic dynamics. The extreme of this is illustrated in Table 2, where the largest difference between rates before and after obfuscation was 91.9% when records having relatively low poverty rates were assigned into areas having extreme poverty rates of 100% after obfuscation. The frequency of rate differences was substantially higher in the CCMEO data, which represents only Cook County, Illinois, and is home to Chicago, the third-largest urban area in the United States. In the 1990s, there were notable declines in the concentration of poverty in Chicago [42]. This decline, mixed with concerns regarding how gentrification has impacted the socioeconomic dynamics of Chicago, may explain why changes in poverty rate would occur at a higher frequency than in our larger OMOP data [43]. The impact of these shifts is important to understand when working with sensitive, protected health information and social determinants of health to correctly identify associations between place and health. As an example of poverty and health, women in high-poverty places are at greatest risk of being diagnosed with late-stage breast cancer [44]. Furthermore, different research studies may require different definitions of "neighborhood" when accessing socioeconomic statuses; for example, a person with multiple economic disadvantages may have a much narrower spatial range and limited social mobility.

We included small distances in our analysis to show that shifts occur even at very small distances. In obfuscation practice, small distances, such as 1 meter, would likely not be used due to the shifted point being too close to the original point and therefore not providing privacy; the balance between protecting privacy and protecting utility is context sensitive [21].

Limitations

Different analytical applications may be variably sensitive to shifts in demographics; our method eliminates analytical concerns by avoiding shifts altogether. The caveat to our method is that constraining inherently limits the maximum distance a point can travel, which may not be suitable for all applications in terms of privacy requirements. For example, in Figure 2, pinwheel obfuscation moved points on average 482 meters away, while our geographically constrained pinwheel algorithm moved points on average 217 meters away. Some applications may not be suitable for point obfuscation; for example, research studies requiring distance to be preserved between subjects and waypoints such as hospitals or clinics may not tolerate any shifting of geographic coordinates.

Public Health Impact

A previous evaluation of the pinwheel obfuscation method indicated that it had no major impact on geospatial analyses such as heat maps and hot spots [45]. However, we demonstrated that erroneous hot spots may be generated when analyzing deaths by suicide in Cook County, Illinois, including hot spots in uninhabitable areas. The issue presented in this paper is not a deficiency of the pinwheel technique, but a deficiency of data linkage using obfuscated points generated from any technique; if the variable that data linkage depends upon changes during obfuscation, then utility is harmed. We contend that any point

obfuscation technique may be constrained to specific geographies.

An alternative solution could be that socioeconomic demographics are calculated using the real address data before data release, but data owners, especially state and local health agencies, have varying degrees of technical sophistication and may not be able to compute demographics. Our research group geocodes electronic health records on behalf of our local health care enterprise on campus, and we make the data available to any university researcher using our local data warehouse. Mobile applications, networking, and research with Internet of Things technology have explored privacy at different levels; our work is a step closer to context-aware point obfuscation within the epidemiology domain.

Conclusions

A growing number of publicly available data sets are including precision geographic data for analysis. Our own work has explored decedent data published from open data portals for use in precision public health [14,33]. Point obfuscation can naturally shift a point into a different census-designated region; the regional differences before and after shifting highlight significantly different socioeconomic demographics. This is a natural consequence of moving a point and is not a weakness of the techniques themselves. We chose poverty as an example demographic due to its popularity in public health research; we also wish to explore the results of linking other census-level demographics. As future work, we will evaluate other techniques of point obfuscation and explore how these techniques may differ from those presented here. We show that it is possible to enhance point obfuscation by constraining where the new point may be placed; this ensures that the original point is obfuscated in a way that will not impact analyses depending upon the linkage to external region-based data.

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Conflicts of Interest

None declared.

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Abbreviations

ACS: American Community Survey
CCMEO: Cook County Medical Examiner's Office
GIS: geographic information system
HIPAA: Health Insurance Portability and Accountability Act
ODMAP: Overdose Detection Mapping Application Program
OMOP: Observational Medical Outcomes Partnership

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Original Paper

Deriving Treatment Decision Support From Dutch Electronic Health Records by Exploring the Applicability of a Precision Cohort–Based Procedure for Patients With Type 2 Diabetes Mellitus: Precision Cohort Study

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Abstract

Background: The rapidly increasing availability of medical data in electronic health records (EHRs) may contribute to the concept of learning health systems, allowing for better personalized care. Type 2 diabetes mellitus was chosen as the use case in this study.

Objective: This study aims to explore the applicability of a recently developed patient similarity–based analytics approach based on EHRs as a candidate data analytical decision support tool.

Methods: A previously published precision cohort analytics workflow was adapted for the Dutch primary care setting using EHR data from the Nivel Primary Care Database. The workflow consisted of extracting patient data from the Nivel Primary Care Database to retrospectively generate decision points for treatment change, training a similarity model, generating a precision cohort of the most similar patients, and analyzing treatment options. This analysis showed the treatment options that led to a better outcome for the precision cohort in terms of clinical readouts for glycemic control.

Results: Data from 11,490 registered patients diagnosed with type 2 diabetes mellitus were extracted from the database. Treatment-specific filter cohorts of patient groups were generated, and the effect of past treatment choices in these cohorts was assessed separately for glycated hemoglobin and fasting glucose as clinical outcome variables. Precision cohorts were generated for several individual patients from the filter cohorts. Treatment options and outcome analyses were technically well feasible but in general had a lack of statistical power to demonstrate statistical significance for treatment options with better outcomes.

Conclusions: The precision cohort analytics workflow was successfully adapted for the Dutch primary care setting, proving its potential for use as a learning health system component. Although the approach proved technically well feasible, data size limitations need to be overcome before application for clinical decision support becomes realistically possible.

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KEYWORDS

personalized care; electronic health records; EHRs; machine learning; type 2 diabetes mellitus; T2DM; decision-making

Introduction

The concept of learning health systems (LHSs) is an approach to health care that emphasizes continuous learning and improvement through the use of data and analytics [1]. Realizing that the US health care system was continuing to fall far short of its potential of delivering the best care at a lower cost, LHS was introduced in 2012 by the Institute of Medicine Committee on the Learning Health Care System in America as a “vision of what is possible if the nation applies the resources and tools at hand by marshaling science, information technology, incentives, and care culture to transform the effectiveness and efficiency

of care - to produce high-quality health care that continuously learns to be better." in their report *Best Care at Lower Cost: The Path to Continuously Learning Health Care in America* [2]. The underlying concept of the LHS is to harness the power of data and analytics to learn from every patient and feed the knowledge of *what works best* back to clinicians, public health professionals, patients, and other stakeholders to create rapid cycles of continuous improvement, which should allow to derive full benefits from leveraging data, systems, and human interconnectedness on an ever-increasing scale as is also seen in other sectors of the economy [3].

To help in deriving recommendations for implementation and evaluation criteria, LHSs have been conceptualized in frameworks from various perspectives, for example, impact on quality of health care [4], health care system evolution [5], and value creation [6].

The implementation of an LHS in practice requires the transition of a complex system of multiple stakeholders, processes, and technical (information) systems, irrespective of scale: local, regional, national, or international [7]. McDonald et al [8] recently identified the following as key enablers and actions required to enact LHSs: promotion of patient engagement, ensuring availability and access to data that are fit for purpose, keeping a focus on generating and implementing knowledge, creating organizational readiness, and stimulation of learning systems at different scales.

The diversity of factors identified illustrates the broadness of scope needed in assessing progress in the relatively novel field of LHSs. To date, very few reviews on the subject exist. Somerville et al [9] in a systematic review identified key implementation strategies, potential outcome measures, and components of functioning LHSs but stressed that further research is needed to better understand the impact of LHSs on patient, provider, and population outcomes and health system costs.

As is evident from this short overview of literature on LHSs, the use of data to create knowledge is one aspect of LHSs; however, it is a central one. Focusing specifically on the impact of the use of electronic health records (EHRs) on delivery or outcomes of health care, only 5 (12%) out of 43 eligible studies in a single available review study were found to document a medium-to-high level of evidence for impact [10]. This observation underlines the need for ongoing efforts to implement and evaluate the incorporation of EHR data analytics–driven knowledge generation in LHSs.

EHRs are electronic systems used to collect and store medical information of patients longitudinally over time and to collect and store information relevant to managing clinical workflows. As such, EHR data can be of a diverse nature. These data can be used for evaluation in various ways to extract knowledge [11]. Although traditionally done via statistical analyses, recent advances in machine learning techniques and applications have allowed the development and deployment of integrative algorithms that relate health care outcomes to multiple diverse sources of information present in EHRs. These algorithms can analyze large volumes of data to identify patterns and correlations and perform predictions. Approaches based on patient similarity are a typical recent example of this. A patient similarity approach tries to derive knowledge that is relevant to a given patient of interest who is presenting to the health care professional by analyzing information that is pertinent to clinically similar patients identified by a machine learning algorithm.

This study focuses on knowledge generation from EHRs in the Dutch primary health care setting based on a patient similarity approach. From a data analytics perspective, it seems appropriate to start exploring such an approach for a disease with substantial prevalence and incidence, that is, large volumes of data present in EHRs.

In 2013, approximately half of the Dutch population reported having at least 1 chronic disorder. One of the most common chronic disorders with a high disease burden is diabetes mellitus (DM). In 2021, approximately 4.9% of the Dutch population reported to have diabetes, of whom 90% (4.2%) had type 2 DM (T2DM) and the remaining had type 1 DM [12]. Therefore, T2DM was used as an example disease to explore the feasibility of an LHS approach in the Dutch primary care setting from a data analytical viewpoint.

In T2DM, a diminished insulin response in combination with insulin resistance results in hyperglycemia. Although T2DM is more common in participants aged >45 years, the numbers are increasing for younger individuals owing to a rise in obesity, sedentary lifestyle, and the intake of energy-dense diets [13]. Diabetes can be diagnosed and glycemic control can be monitored by measuring the glycated hemoglobin (HbA1c) levels or measuring the plasma glucose concentration. Diagnosis thresholds for HbA1c and plasma glucose concentration are >7% (53 mmol/mol) and >126 mg/dL (7 mmol/L), respectively [14]. Testing for HbA1c is convenient, fast, and standardized, but it is more costly and comes with a lower sensitivity than testing for plasma glucose. As a result, it has become a standard practice to use more frequent glucose measurements for regular monitoring and HbA1c measurements only at longer intervals or in special cases to assess the disease state and judge the necessity for treatment change. The initial steps in treating and managing T2DM involve lifestyle modifications, such as adopting a healthy diet, engaging in regular exercise, and quitting smoking. In the second step, when lifestyle modifications fail to achieve an adequate glycemic level, an antidiabetic medication is administered following national care standards. In the Netherlands, the first line of medication is metformin for non–high-risk patients and sodium-glucose transport protein 2 (SGLT-2) inhibitors for high-risk patients. There are various follow-up therapies, such as sulfonylureas, dipeptidyl peptidase 4 inhibitors, glucagon-like peptide-1 receptor agonists, SGLT-2 inhibitors, α-glucosidase inhibitors, and insulin [15].

In the Netherlands, general practitioners (GPs) are often the first point of contact for patients diagnosed with T2DM and act as gatekeepers to secondary care. Therefore, they play an important role in the diagnosis and treatment of these patients. To make treatment choices for individual patients with diabetes, physicians consider treatment guidelines and their own knowledge and experience, also—implicitly or

explicitly—considering the patient's perspective. Following the LHS approach, the decision-making may be supported by the on-demand availability of more objective information based on larger groups of comparable patients, such that the physician can see the actual data on improvements obtained after changing treatment in similar patients. This requires integration and sharing of data between physicians and health institutes. However, in practice, in Dutch primary health care settings, medical data sharing is still mostly limited to local or small regional settings, thus hampering the implementation of an LHS. The Netherlands Institute for Health Services Research (Nivel) hosts the Nivel Primary Care Database (PCD), in which routinely recorded data from EHRs from primary health care providers are collected and used to monitor health and use of health services in a representative sample of the Dutch population. Therefore, the Nivel-PCD was an appropriate database to study data analytical aspects for an LHS approach for patients with T2DM in the Dutch primary care setting.

This study aims to explore the applicability of a recently developed precision cohort analytics approach based on EHRs [16] as a candidate data analytical decision support tool focusing on data analytical aspects.

Methods

Overview

Our approach resides in patient matching and uses the precision cohort analytics methods developed by Ng et al [16]. In brief, there are different studies focused on building and applying matching methods. There is also evidence that patient similarity–based modeling outperforms population-based predictive methods [17]. Methods that can learn a disease-specific similarity metric by developing a locally supervised metric learning are very valuable to identify clinically similar patients. Similarity-based modeling algorithms can make use of different sources of data formats: textual data, numerical measurements, recorded signals, images, and vital signs. The algorithms used commonly are neighborhood-based algorithms, distance-based similarity metrics, correlation-based similarity metrics, cosine-similarity metrics, and cluster-based algorithms [17]. A clinical decision support (CDS) system that is intended to improve health care by improving medical decisions with clinical knowledge, patient information, and other health information intelligently filtered or presented at appropriate times [18] can for example include the following:

1. Mapping of clinical data from a patient to a specific point in a clinical pathway to advise treatment
2. Prediction of an individual's responsiveness to different treatments based on the respective gene expression profiles
3. Identifying a patient as a candidate for a specific treatment based on a set of clinical characteristics with an associated desired treatment
4. Generating a patient trajectory graph from clinical data, capturing conditions, outcomes, interventions, and suggestions from medical guidelines at different patient group levels

The precision cohort treatment options approach used in this work is based on the abovementioned CDS approaches with the following adjustments:

1. Identification and extraction of relevant clinical treatment decision points (DPs) from the longitudinal patient data to use as events of interest for modeling and analysis
2. Selection and generation of features to determine patient similarity from different sources of information, such as guidelines, clinical measurements, prescriptions, consultations, and comorbidities
3. For a given patient of interest, creation of a precision cohort of patient events that are similar to the given clinical state
4. Demonstration of the available treatment options and statistics based on a retrospective analysis of the generated precision cohort

When a new patient presents with a need for a treatment decision, the approach can be used to create a precision cohort of the most clinically similar participants in the database and provide statistics on the past outcomes of different treatment decisions taken for these patients. This information can be used to support the health professional in their treatment choice. In this study, the published precision cohort analytics approach was adapted to the guidelines and EHR characteristics of the Dutch care setting. Results are compared with those of Ng et al [16], and their relevance for the Dutch setting is discussed. The outcomes may provide a further stimulus to ongoing initiatives to establish primary care medical data sharing at the national level in the Netherlands.

The major steps of this workflow are (1) EHR data extraction and preprocessing, (2) DPs identification and extraction (3), patient similarity model training, (4) precision cohort identification, and (5) treatment options and outcomes analysis.

EHR Data Extraction and Preprocessing

The data were extracted from the Nivel-PCD [19]. Using an algorithm developed in prior research within Nivel-PCD [20], a total of 11,490 registered patients were identified as diagnosed with T2DM between 2012 and 2014, having at least 6 months of prior history in the database. The follow-up period was limited to a period of 5 years. Patients with incomplete data in this 5-year period were also included. The identification of patients with morbidities was done using an algorithm developed by Nielen et al [21] to construct episodes of illness based on routinely recorded EHRs. For the data extraction, only GP practices that permitted to use the data for scientific research were selected. Patient ID and GP practice ID are unique for these data and cannot be linked to other data sets to reduce the risk of tracking individual patients. For the selected 11,490 patients with T2DM, several tables were provided containing clinical information on 625,641 prescriptions (date, International Classification of Primary Care [ICPC] code, and ICPC description); 402,602 consultations (date and [Dutch] CTG code); 3,360,555 measurements (date, [Dutch GP association] Netherlands Huisartsen Genootschap code, and result or value); and 228,810 comorbidities (ICPC code and start and end date [based on the episodes of illness construct mentioned above] and type of comorbidity episode: 4 weeks, 8 weeks, 16 weeks, long-lasting, or chronic [21]).

To allow for a more explicit interpretation and analysis of the data, all clinical codes were replaced by the respective descriptions (Textbox 1), and dates were rewritten to a standard format, across all the tables.

Textbox 1. List of clinical codes and source of descriptions used.

Clinical measurement

- Netherlands Huisartsen Genootschap [22]

Prescription

- Anatomical Therapeutic Chemical Classification System [23]

Comorbidity code type

- International Classification of Primary Care (International Classification of Primary Care codes were processed using a table provided by Nivel)

Consultation code type

- CTG [24]

Decision Points

Identification and Extraction

From the several tables, points in time were extracted to serve as events of interest for the analysis and the modeling processes. These points are named DPs, and they are defined as points in time from the longitudinal data, of each patient, after the diagnosis date, where the disease is considered as being not under control either because HbA1c>7% or fasting glucose>7 mmol/L. These DPs thus represent opportunities to initiate a change in the treatment plan. This point must have another matching HbA1c or fasting glucose test in the follow-up period that classifies the outcome of the treatment decision, either as not under control (an HbA1c test>7% or a fasting glucose test>7 mmol/L) or as under control (an HbA1c test<7% or a fasting glucose test<7 mmol/L). Over time during longitudinal follow-up, a patient can have multiple DPs as long as the abovementioned criteria are fulfilled. A DP is composed of the following:

1. An index date:
   - Date of an HbA1c or fasting glucose test that indicates a disease-uncontrolled situation along with the new treatment decision taken at this point.
2. A baseline period preceding the DP index date that represents the disease condition and the active treatment status, featuring the following:
   - The treatment that was in effect
   - The applicable clinical guidelines
   - Data characterizing the condition of the patient
   - All available clinical history until the DP index date. In case of multiple information available for the same field, the most recent was taken.
3. An observation period that follows the DP date, featuring the following:
   - The new treatment
   - The treatment outcome: either disease controlled or disease uncontrolled, during a period of 90 to 365 days after the index date

Target Outcome Variables

As described in the *Introduction* section, alternatively to using HbA1c International Federation of Clinical Chemistry and Laboratory Medicine as a target outcome variable, in this study, we also used fasting glucose, venous (laboratory) as a target outcome variable following the same procedure to extract DPs, but with a threshold of 7 mmol/L (Table 1). As mentioned in the *Introduction* section, these 2 clinical measurements are the most widely used tests for diagnosing T2DM. Although we have no information for both these metrics for all the patients, having 2 possible outcome judgment options allowed us to make wider use of the Nivel-PCD data available for each participant.

Table 1. Percentage of patients with measurements and those without and total number of decision points (DPs) that are controlled and uncontrolled for both glycated hemoglobin (HbA1c) and fasting glucose as target outcome variables (n=11,490).

	Target outcome variable	
	HbA1c	Fasting glucose
Patients with measurements, n (%)	10,375 (90.3)	10,824 (94.2)
Number of DPs with outcomes		
Controlled	9,683	8,522
Uncontrolled	7,645	32,492
Patients without any measurements, n (%)	1115 (9.7)	666 (5.8)

Treatments Considered

Many different prescriptions occur in the Nivel-PCD data set. To reduce the complexity of the analysis, we considered only medication-based treatments that specifically targeted T2DM (pharmacologic treatments), and we merged 3 different forms of healthy lifestyle advice encountered in the records (ie, "follow dietary advice," "advice healthy food given," and "advice physical activity given") into a single nonpharmacological treatment, henceforth called "healthy lifestyle." To select medications specifically targeting T2DM, treatment options present in the Nivel-PCD were compared against the Pharmaceutical Compass [25], containing independent pharmaceutical information for medical professionals, published by the Dutch National Healthcare Institute. Textbox 2 shows the resulting list of individual medications targeting DM that were considered in this study. Treatment options that combine multiple medications were also considered, for example, metformin and gliclazide (denoted as metformin_gliclazide).

As the dosage information was not available in the data sample used for this study, changes in drug dose were not captured and were interpreted as "no change" treatments.

For each DP, we assigned an active treatment (baseline period) and a new treatment (observation period). For assessing the active treatment of each DP, the medical history of the patient's measurements was queried, and we applied the following reasoning: if neither pharmacologic nor lifestyle advice was found, then the DP was given a "no treatment" type of active treatment; if both pharmacologic and nonpharmacologic treatments were available, the 2 were merged (eg, metformin+healthy lifestyle). For assessing the new treatment, the same reasoning was applied; however, if the new treatment was the same as the active treatment, it was denoted as "no change."

Textbox 2. List of medications targeting type 2 diabetes mellitus considered in this study.

Treatment options

- Metformin
- Sitagliptin
- Insulin aspart
- Insulin degludec
- Insulin detemir
- Insulin glargine
- Insulin (human)
- Repaglinide
- Glimepiride
- Tolbutamide
- Gliclazide

Guidelines

Treatment decisions were made by the physicians based on clinical guidelines together with their personal past experience and considering the history and condition of the patient. The aim of using the guidelines is to improve the appropriateness of medical practice by leading to a better patient outcome while reducing costs, to aid authorities in deciding on the approval of drugs and devices, and to identify areas that need further research [26]. The guidelines for T2DM, published by the Dutch College of General Practitioners, including recommendations for the diagnosis, treatment, and management of patients, were incorporated in this study [27]. The relevant criteria for this study were derived from the guidelines to recommend medications and confirmed in a discussion with a GP:

1. Aged >70 years
2. Disease duration >10 years
3. BMI <25 kg/m^2

Patient Condition

The clinical condition of patients was assessed using clinical measurements (which included data on, eg, BMI, diastolic blood pressure, and low-density lipoprotein), comorbidities, and consultation codes (Textbox 1). In addition, 2 patient condition criteria (mobility and mental state) were added based on the discussion with a GP, who emphasized that these are crucial aspects to consider when deciding which treatment is most appropriate.

Patients with mobility limitations are unlikely to perform physical exercise; therefore, even adhering to a restrictive healthy diet may not sufficiently control diabetes, necessitating medication sooner compared to patients without impaired mobility.

To assess the mobility state of the patient, we looked at comorbidities and measurements that indicated any possible obstacle to the ability to move. The list of comorbidities and measurements considered is represented in Table 2. We discriminated between the chronic and temporary duration of each comorbidity as used in the episodes of illness construct

[21]. It has to be emphasized that the operationalization of reduced patient mobility as evident from Table 2 is a highly subjective choice made by the authors based on their intuitive understanding. It serves only for initial exploration of the feasibility of introducing additional GP considerations beyond the standard clinical guidelines.

Similarly, the mental state of the patient is also very important when deciding the appropriate treatment option. Patients who are going through events that alter their emotional state, affecting their concentration, positiveness, or willingness to adhere to treatment, may need a stricter treatment regime.

To assess the emotional state of the patient, we made an equally subjective choice of the different comorbidities that might be affecting their emotional state (Table 3).

Table 2. List of comorbidity and measurement types considered to assess the mobility state of patients. The upper part of the table shows the comorbidity International Classification of Primary Care (ICPC) code, description, and type of duration. At the bottom, it shows additional variables that were considered relevant to reflect mobility impairments, that is, the measurement type, Netherlands Huisartsen Genootschap (NHG) code description, and the duration.

Code	Code description	Duration
ICPC		
L15	Knee symptoms or complaints	Temporary
L95	Osteoporosis	Chronic
L90	Osteoarthritis of the knee	Chronic
N17	Vertigo or dizziness (excluding H82)	Chronic
L14	Leg or thigh symptoms or complaints	Chronic
K90	Stroke or cerebrovascular accident	Chronic
L73	Fracture: tibia or fibula	Temporary
L03	Low back symptoms or complaints without radiation (excluding L86)	Chronic
L89	Osteoarthritis of the hip	Chronic
L76	Fracture: other	Temporary
R96	Asthma	Chronic
L79	Sprain or strain of other joints	Temporary
L74	Fracture: hand or foot bone	Temporary
L16	Ankle symptoms or complaints	Chronic
L97	Chronic internal knee derangement	Chronic
N18	Paralysis or weakness (excluding A04)	Chronic
L84	Osteoarthritis of the spine	Chronic
L77	Sprain or strain of the ankle	Temporary
L75	Fracture: femur	Temporary
L70	Infections musculoskeletal system	Temporary
L78	Sprain or strain of the knee	Temporary
NHG		
K93	Left foot amputation	Chronic
K94	Right foot amputation	Chronic

Table 3. List of comorbidity types considered to assess the emotional state of patients. The table shows the comorbidity International Classification of Primary Care (ICPC) code, description, and type of duration.

ICPC code	Description	Duration
P01	Feeling anxious, nervous, tense, or inadequate	Temporary
P02	Acute stress or transient situational disturbance	Temporary
P20	Disturbances of memory, concentration, or orientation	Chronic
P74	Anxiety disorder or anxiety state	Chronic
Z18	Illness problem with a child	Temporary
Z19	Loss or death of a child	Chronic
P06	Disturbances of sleep or insomnia	Temporary
Z15	Loss or death of a partner	Temporary
A80	Accident or injury NOS[a]	Temporary
P03	Feeling depressed	Temporary
P99	Other mental or psychological disorder	Chronic
P72	Schizophrenia	Chronic
P76	Depressive disorder	Chronic
P73	Affective psychosis	Chronic
Z25	Problems resulting from assaults or harmful events	Temporary
P04	Feeling or behaving irritable or angry	Temporary
P77	Suicide attempt	Chronic
P98	Other or unspecified psychoses	Chronic
P70	Dementia (including senile and Alzheimer)	Chronic

[a]NOS: not otherwise specified.

Patient Similarity Modeling

Feature Selection

Patient similarity was evaluated firstly based on the characteristics captured with the DP, that is, active treatment, applicable guidelines, and patient condition (including clinical history). In addition, to enrich the patient's clinical information, more features were engineered. For instance, a Boolean feature named *has_chronic_comorbidity* was created to represent if the patient had or did not have a chronic comorbidity recorded at the time of interest in the medical history. In addition, the number of prescriptions, number of clinical measurements, number of consultations, and number of comorbidities from the disease diagnosis date until the DP date were added as candidates to the similarity features set.

As some algorithms cannot work directly with categorical data, one-hot encoding was applied to the variable *new_treatment*, converting this single column into N new columns, with N being the total number of different treatments (including combinations) observed in the data set. The same was done for the *active_treatment* variable.

The final data frame of DPs extracted and processed from the Nivel data set was composed of multiple feature types: identifiers, dates, and categorical and numerical data.

The resulting DPs data frame had a large amount of missing data. As a first selection step, only features that had at least 80% nonmissing values were retained [28].

Thereafter, the remaining missing values were imputed using the k-nearest neighbors (KNN)–based KNNImputer method from the *scikit-learn* library [29], with the following parameters: 2 nearest neighbors and a uniform weighting of all points in the neighborhood. The result of this step was a data frame of DPs without any missing values.

A further selection of the most salient features associated with disease control was done using the approach by Ng et al [16]. A total of 200 different L1-regularized logistic regression models (also known as the least absolute shrinkage and selection operator [LASSO] models) for predicting disease outcomes were created. LASSO is a linear regression technique that incorporates a penalty term to the sum of squared errors to shrink the coefficients toward 0 and perform feature selection. The penalty term is determined by the α parameter. Each model used a randomly selected subset (75%) of the data. The features selected by at least 150 of the 200 models were considered stable, and the remaining features were discarded. To find the best α parameter for the LASSO model, a grid search approach was applied. Different values of α were tested (100, 20, 10, 2, 1.67, 1.43, 1.25, 1.11, and 1), and the value corresponding to the highest F_1-score was selected.

As the 2 target outcome variables were unbalanced, we used the F_1 score [30], rather than accuracy, as a metric of prediction performance.

It is important to note that 2 different data frames were built, and separate similarity models were built, for the 2 outcome variables HbA1c and fasting glucose. Each of the data frames was split into 2 sets: a training set that was used to train the patient similarity model and a scoring set used as a repository of clinical events and to create multiple precision cohorts.

Similarity Model Training

The similarity model used the set of stable features obtained from the previous steps to calculate patient similarity. This model learns a T2DM distance measure that is a modified version of the Mahalanobis distance (MD). The MD measures the distance relative to a centroid or central point, in which all means from all variables intersect; the larger the MD, the further away from the centroid the data point is. The MD can also be used to calculate the distance between 2 points, or in this case, 2 patients (x_i and x_j) using the covariance matrix. Here, a modified version of the MD formula was used, with the covariance matrix replaced by a weight matrix W, which is learned from the training data.

(1)

The similarity model sets the weight matrix to maximize the target class discriminability (disease control state) by adjusting the weights of every feature. This was done by locally separating points from different classes while keeping together points that belong to the same class, using a large margin nearest neighbor (LMNN) [31] machine learning algorithm.

The number of points to consider for the calculations is defined by the number of neighbors parameter (K). Different values of K were tested: 2, 3, 4, 5, 6, and 7.

To assess the effect of the LMNN algorithm, we compared the performance of a KNN classification model [29] on the raw data and the data transformed by the similarity model [32]. For the KNN algorithm, a grid search approach was used to find the best set of parameters:

1. Number of neighbors (N): (3, 4, 5, ..., or 30)
2. Weight function: uniform (all points in each neighborhood weighted equally) or distance (closer neighbors of a query point will have a greater influence than neighbors that are further away).

The learned similarity weights for each variable for T2DM separately for HbA1c and fasting glucose as target outcome variables are shown in Multimedia Appendices 1 and 2.

Precision Cohort Construction

Precision cohort construction consists of selecting the most clinically similar patient DPs based on the characteristics of the patient of interest at the time of the consultation. The process of generating precision cohorts needs to ensure that the baseline confounders are adjusted so that the effect analysis is valid (ie, a good covariate balance is achieved). The selection was done in a 2-step procedure: a filtering step and a similarity rating.

To filter the patients who are more similar to the patient of interest, filter variables were generated. These filter variables were composed of guidelines plus the active treatment. For instance, if the patient was aged 80 years and was currently taking metformin, the filter variable was age_above_70y+metformin. By using this filter variable, it was ensured that only patients aged >70 years and who were taking metformin were selected for the precision cohort. It is important to mention that only data from the "baseline period" of the DP were used for the filtering process, which means that the treatment decision at the time of the DP (index date) was not considered, as we want to analyze the entire pool of new treatments in the precision cohort. Combining the set of guidelines with the set of active treatments resulted in a very large number of filter cohorts of widely varying sizes. Considering that it is difficult to recommend treatment options for patients with clinically odd profiles as this method requires a large patient pool to recommend statistically significant treatment options, we focused only on the most representative cohorts, that is, those with >200 DPs.

For the second step (similarity rating), the similarity model explained in the *Similarity Modeling* section was used to calculate the similarity scores for the filtered DPs. The similarity score is a distance metric; thus, smaller scores indicate a higher similarity between a patient's DP and the DP of the patient of interest. The similarity score was converted to a normalized distance using a minimum-maximum normalization method to allow an easier interpretation of these scores.

Thereafter, the final precision cohort was generated by retaining only the "most similar" patients. However, reducing the cohort size may compromise the cofactor balance. Therefore, the covariate balance of the precision cohort with varying sizes was calculated to assess bias and matching validity by comparing the "no treatment change" (new treatment is the same as the active treatment) with the "treatment change" (new treatment different from the active treatment) groups. Covariate balance was calculated as the difference in the means of each covariate between the 2 groups divided by the SD of the treated group [33]. The closer this value was to 0, the better balance we had between the groups.

To have a trade-off between the covariate balance value and the number of DPs in the precision cohort, a normalized distance value of 2 was defined as a cutoff. This value was chosen after visual inspection of several covariate balance plots for different precision cohorts. Some studies agreed that covariate balance values <0.1 were satisfactory [34], although another study suggested that a value of 0.25 was good enough [35]. With a normalized distance cutoff value of 2, a covariate balance of 0.1 was achieved for most of the precision cohorts.

In summary, the precision cohort construction process involved the following:

1. Filtering DPs with the same filter variables as the patient of interest
2. Calculating the similarity scores for the filtered DPs

3. Ranking DPs based on similarity scores (normalized distance)
4. Retaining only the DPs with a normalized distance <2

Treatment Options and Outcomes Analysis

Treatment outcomes analyses were performed both from a global perspective (ie, across all filter cohorts) and a personalized perspective (ie, in the precision cohorts). The latter can be used as a retrospective analysis to generate personalized treatment options for a given patient of interest.

The set of DPs in the precision cohort was grouped by treatment decision. For each of these treatment groups, we computed the following:

1. The number of DPs
2. The percentage of DPs that have a controlled outcome
3. The difference in the respective outcome compared with the "no treatment" change option
4. A statistical significance assessment using a Bonferroni corrected χ^2P value of 0.5 to adjust for multiple comparisons

To better visualize the difference between the different treatments for each precision cohort, the results were presented in a Sankey diagram [36].

To reduce the number of treatment options with a low number of DPs, we decided to only include those with at least 1% of the total DPs in the precision cohort, with a minimum of 10 DPs. For instance, if the precision cohort had 2000 DPs, we only included treatment options with at least 20 DPs.

Ethical Considerations

This study was approved according to the governance code of Nivel-PCD (NZR-00320.048). The use of EHRs for research purposes is allowed under certain conditions. When these conditions are fulfilled, neither obtaining informed consent from patients nor approval by a medical ethics committee are obligatory for this type of observational study containing no directly identifiable data (Art. 24 General Data Protection Regulation Implementation Act jo art. 9.2 sub j General Data Protection Regulation).

Results

Separate analyses were conducted for HbA1c and fasting glucose as target outcome variables.

HbA1c Outcome Scenario

Decision Points

For the HbA1c scenario, we found 17,328 DPs across the available longitudinal data from the 11,490 patients with T2DM.

Although seemingly large, this was still 10-fold lower compared with previous work by Ng et al [16], who retrieved >171,000 DPs for 24,373 patients with T2DM from their data set, for HbA1c as an outcome.

The processed HbA1c set was split into 5199 DPs for the training set and 12,129 DPs for the scoring set. As the class (disease control) was unbalanced, we had to ensure that we had the same proportion of each class for both training and scoring sets. For this case, of the 17,328 DPs, we had 9704 (56%) uncontrolled DPs and 7624 (44%) controlled DPs. This same proportion was maintained for the training set: there were 2905 uncontrolled DPs and 2294 controlled DPs in the training set and 6793 uncontrolled DPs and 5336 controlled DPs in the scoring set.

Patient Similarity Modeling

The methods of feature generation, missing data imputation, and feature selection explained in the *Methods* section were applied to this subset. The LASSO model α value used was 1.43, with an F_1-score of 0.613.

The training set was used to construct a similarity model. The optimal k value for the LMNN algorithm was 3. Both the raw data and the data transformed with the similarity model were subjected to the KNN algorithm. The most optimal parameter combination for the KNN algorithm was determined to be N=6 neighbors and a weight function based on distance (data not shown).

Next, the tuned version of the KNN algorithm was used to evaluate the LMNN algorithm performance (refer to the *Methods* section). The F_1-score was 0.606 for raw data versus 0.613 for transformed data. Thus, indeed, the LMNN algorithm resulted in improved classification performance.

The learned similarity weights for each variable for HbA1c as the target outcome variable are shown in Multimedia Appendix 1. These weights are disease specific for T2DM. A total of 26 features were retained for the similarity model. Interestingly, there was rather limited variation in size: similarity weights were all of comparable value (typically ranging between 0.4 and 0.6), except for features "#comorbidities" and "Systolic BP."

Precision Cohort Construction

The largest observed filter cohorts for HbA1c are shown in Figure 1. These 25 cohorts covered approximately 75% of all the DPs in the scoring set. Of these 25 cohorts, 20 (80%) had >100 DPs. Only 10 cohorts had >200 DPs, considered potentially useful for constructing precision cohorts. As expected, the cohorts containing metformin were the largest ones as it is the first line of medication for the treatment of T2DM. The cohort "healthy lifestyle_metformin" was the largest cohort for the HbA1c outcome scenario. The cohort "all_guidelines_variables_false" also contained a large number of DPs. In this cohort of patients, who were aged ≤70 years, were not mobility or mentally impaired, and had a BMI of ≥25 kg/m^2, no antidiabetic treatment (medication or healthy lifestyle advice) was administered or the information was not registered. Furthermore, of the 25 largest cohorts, 17 (68%) had "healthy lifestyle," 16 (64%) had "metformin," 11 (44%) had "mobility impaired," 7 (28%) had "age_above_70y," and 3 (12%) had "mental impaired." No other pharmacological treatments than metformin and gliclazide (6 occurrences) were represented in the 25 largest cohorts.

Following the procedures explained in the *Precision Cohort Construction* section, precision cohorts were generated for a

number of randomly chosen patients from various filter cohorts. Figure 2 shows a covariate balance plot for 1 randomly chosen patient in the metformin filter cohort as an example. As can be appreciated from the figure, the best cofactor balance was achieved for normalized distance 2.0.

Figure 1. The 25 largest cohorts for glycated hemoglobin (HbA1c) as a target outcome variable based on the filter variables. The blue bars represent the number of decision points (DPs) on a logarithmic scale (left vertical axis), and the orange line shows the cumulative coverage on a linear percentage scale (right vertical axis).

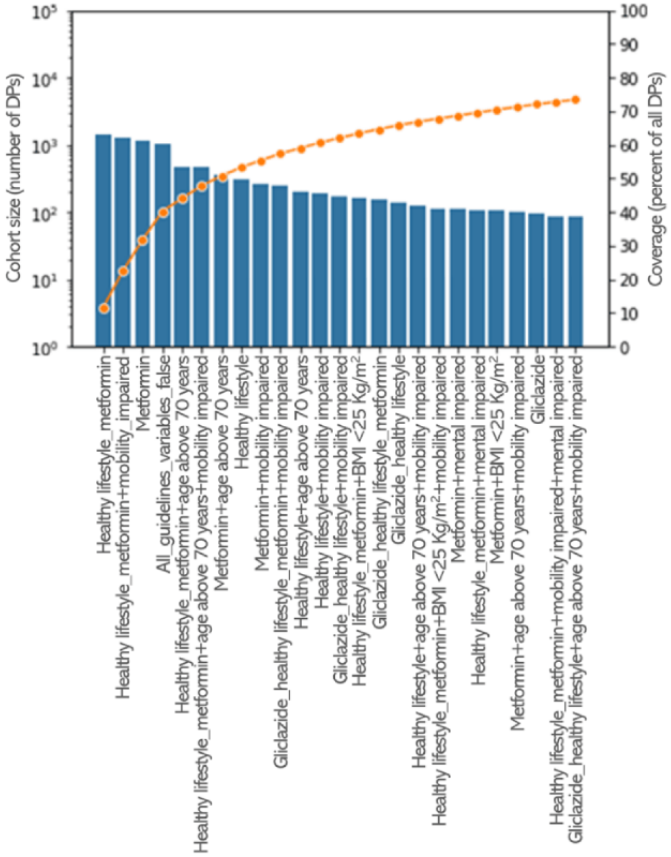
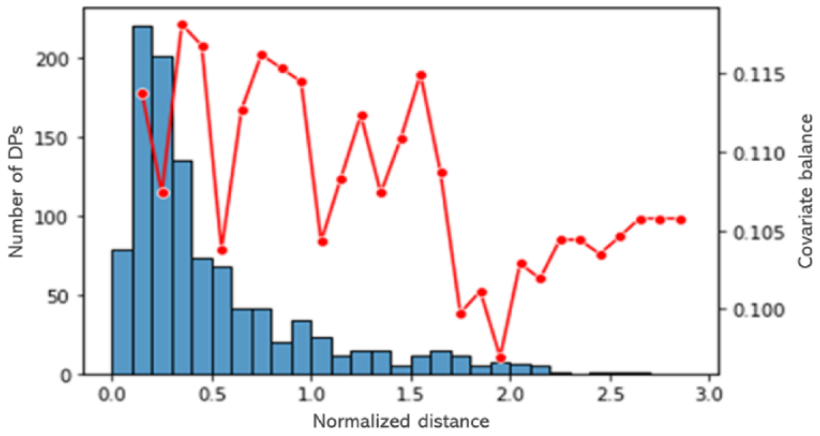


Figure 2. Illustration of the metformin precision cohort generation for the glycated hemoglobin (HbA1c) outcome target. The decision points (DPs) in the subset were grouped by normalized distance (similarity score) to the patient of interest. The blue bars represent the number of DPs per bar or grouped DPs (left vertical axis), and the red dotted line shows the cumulative covariate balance values for the different bars or grouped DPs (right vertical axis).



Treatment Options and Outcomes Analysis

Table 4 shows the overall percent controlled of the 20 most representative treatment options on a global scale, that is, across the cohorts based on the filter variables. In >47% of cases, the GP decided to continue the current treatment despite the HbA1c levels being classified as uncontrolled. Despite no change, >44% of patients had their HbA1c levels subsequently "controlled" during the follow-up. Some alternatives, however, had much better outcomes. For instance, the option of stopping the "no treatment" option and starting taking metformin, that is, the first line of medication treatment according to the guidelines, resulted in 57.6% (213/370) of DPs with HbA1c controlled, whereas starting treatment with healthy lifestyle advice resulted in >64%

(63/98) controlled outcomes. Despite this difference, starting treatment with metformin was chosen almost 4 times more often than starting with healthy lifestyle treatment (370 vs 98 cases). The combination of metformin and lifestyle advice was beneficial over continuing each of these treatments as a single treatment. This list is relevant for analyzing the global picture of the available treatment options and the corresponding outcomes. However, for individual patients, the treatment option analysis might differ from the overall picture depending on the precision cohort that more closely reflects the clinical scenario for the particular patient. As an example of such a case-specific analysis, Figure 3 uses a Sankey diagram to represent the different treatment options for a given patient that belongs to the cohort "Metformin."

In Table 4, it can be noticed that adding healthy lifestyle advice to the metformin prescription was a treatment option with a statistically significant better-associated outcome (210/324, 64.8%), whereas changing from metformin to only healthy lifestyle advice alone led to a worse disease outcome in the precision cohort for this particular patient. Changing the treatment to gliclazide or tolbutamide, or adding gliclazide to metformin, also resulted in better outcomes; however, the differences were not statistically significant because of the low number of cases involved. We can also see that from the most similar patients who kept taking only metformin, 45.69% (605/1324) of the patients improved their disease condition. For the remaining 54.31% (719/1324) of the patients, the outcome was "uncontrolled" in the follow-up.

Table 4. The 20 largest observed global treatment option groups for glycated hemoglobin as the target outcome variable. The list shows the size of each group and the associated percentage controlled during follow-up (n=12,129).

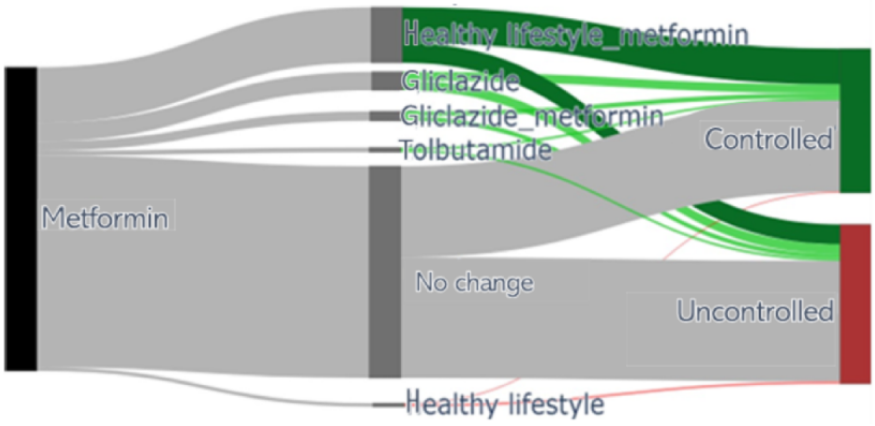
Treatment option	Frequency, n (%)	DPs[a] controlled, n (%)
No change	5747 (47.38)	2541 (44.21)
Metformin_new+healthy lifestyle_metformin_stop[b]	1324 (10.92)	605 (45.69)
Healthy lifestyle_new+healthy lifestyle_metformin_stop[c]	402 (3.31)	170 (42.29)
Metformin_new+no treatment_stop[b]	370 (3.05)	213 (57.57)
Healthy lifestyle_metformin_new+metformin_stop[b]	324 (2.67)	210 (64.81)
Healthy lifestyle_metformin_new+healthy lifestyle_stop[b]	246 (2.03)	165 (67.07)
Healthy lifestyle_metformin_new+no treatment_stop[b]	222 (1.83)	138 (62.16)
Gliclazide_healthy lifestyle_new+healthy lifestyle_metformin_STOP[c]	217 (1.79)	86 (39.63)
Metformin_new+healthy lifestyle_STOP[b]	169 (1.39)	91 (53.85)
Gliclazide_new+healthy lifestyle_metformin_stop[c]	151 (1.24)	65 (43.05)
Gliclazide_new+metformin_stop[b]	148 (1.22)	80 (54.05)
Gliclazide_metformin_new+gliclazide_healthy lifestyle_metformin_stop[c]	147 (1.21)	38 (25.85)
Gliclazide_new+gliclazide_healthy lifestyle_stop[c]	123 (1.01)	41 (33.33)
Healthy lifestyle_new+no treatment_stop[b]	98 (0.81)	63 (64.29)
Gliclazide_healthy lifestyle_metformin_new+healthy lifestyle_metformin_stop[b]	68 (0.56)	32 (47.06)
Gliclazide_metformin_new+metformin_stop[c]	59 (0.49)	30 (50.85)
Metformin_new+gliclazide_healthy lifestyle_stop[b]	59 (0.49)	16 (27.12)
Gliclazide_healthy lifestyle_new+gliclazide_healthy lifestyle_metformin_stop[c]	58 (0.48)	17 (29.31)
Healthy lifestyle_metformin_new+gliclazide_healthy lifestyle_stop[c]	58 (0.48)	12 (20.69)
Healthy lifestyle_metformin_new+gliclazide_healthy lifestyle_metformin_stop[c]	57 (0.47)	21 (36.84)

[a]DP: decision point.

[b]Treatment options with a controlled percentage higher than the "no change" treatment option.

[c]Treatment options with a lower percentage than the "no change" treatment option.

Figure 3. Personalized treatment options observed in the precision cohort for a given patient belonging to the filter cohort "Metformin," using glycated hemoglobin (HbA1c) as the target outcome variable. The initial node, in black, includes all the DPs in the precision cohort for the particular patient of interest. This patient has all the guidelines variables as "False" and is currently on a metformin prescription. Each pathway from the initial node is a different treatment decision observed in the data. The thickness of the pathway is proportional to the number of DPs, and it is assigned with a label that represents the new medication, and the percentage of DPs controlled in the follow-up. The "no change" treatment option is colored in gray, and it is considered the baseline treatment option. The terminal nodes represent the outcome; the nodes in green denote the DPs that achieved control, whereas those in red indicate the uncontrolled ones. Treatment options with better control than the baseline option are colored in green, whereas those with a worse control are colored in red. Treatment options with a statistical significance are colored dark green or dark red.



Fasting Glucose Scenario

Decision Points

For the fasting glucose target outcome variable, we found 41,014 DPs across the available longitudinal data, that is, approximately 2.5 times more than for the HbA1c scenario.

The processed data set was split into 12,304 DPs for the training set and 28,710 for the scoring set. Again, the disease control target outcome variable was not balanced; thus, the proportions were kept the same for both training and scoring sets. In this case, we had 79% (32,401/41,014) uncontrolled DPs and 21% (8613/41,014) controlled DPs. Accordingly, the same proportion was kept for both the training and the testing sets.

Patient Similarity Modeling

Similarly to the HbA1c scenario, the methods of feature generation, missing data imputation, and feature selection explained in the Methods section were applied for the fasting glucose scenario. The LASSO model α value used was 1.67, with an F_1-score of 0.691. The training set was used to train the similarity model. The optimal k value for the LMNN algorithm was 5. The KNN algorithm was applied to the raw data and the transformed data. The best combination of parameters was N=6 and weight function=distance, that is, the same as that for the HbA1c scenario (data not shown).

Next, the tuned version of the KNN algorithm was used to evaluate the LMNN algorithm performance. The F_1-score was 0.849 for raw data and 0.856 for transformed data. Thus, only a small improvement in classification performance was achieved by the LMNN algorithm.

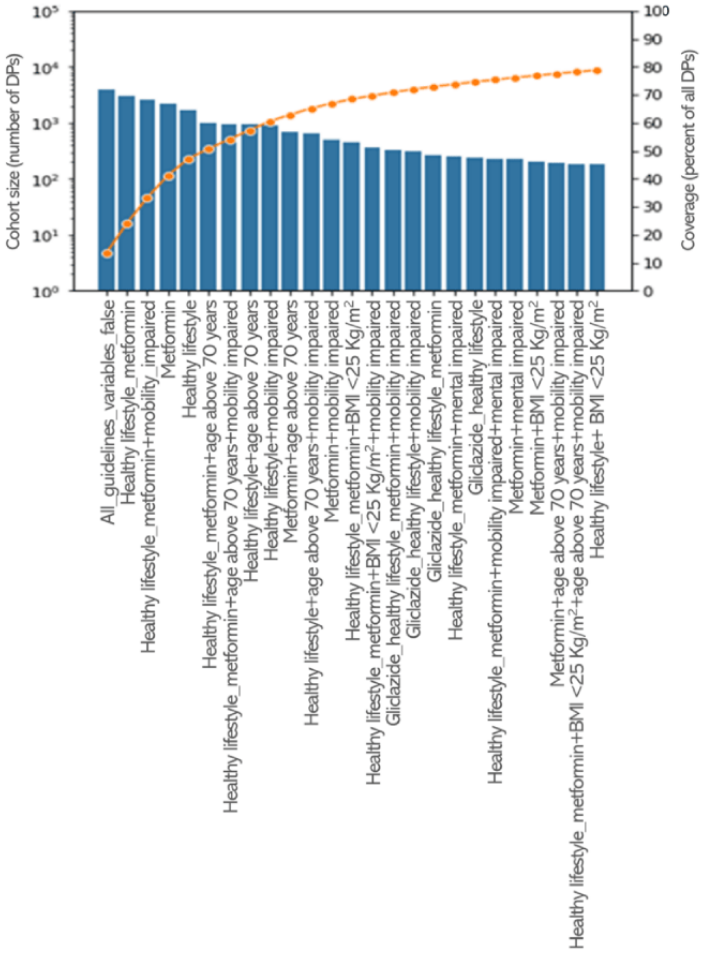
The learned similarity weights for each variable for fasting glucose as target outcome variable are shown in Multimedia Appendix 2. These weights are disease specific for T2DM. A total of 48 features were retained for the similarity model, 22 more than that for HbA1c. In total, 25 features were of the "active _treatment_"-type, whereas for HbA1c, only 5 features were of this type. This indicates that the active treatment was much more predictive of disease outcome than in the HbA1c scenario. With approximately half of weight values between 0.4 and 0.65, and half between 0.7 and 1.15, there was much more variation in the size of weights compared with the HbA1c scenario. Similar to the HbA1c scenario, the feature "Systolic BP" had a low weight, probably because it had little discriminating power.

Precision Cohort Construction

In Figure 4, the 25 largest observed filter cohorts for fasting glucose are represented. Together, these covered approximately 80% of DPs in the data set. In line with the much larger number of DPs compared with the HbA1c scenario, 20 of the largest filter cohorts had >200 DPs. Contrary to the HbA1c scenario, here the largest cohort was the "all_guidelines_variables_false," followed by the "healthy lifestyle_metformin cohort," which is in accordance with what we expected as the fasting glucose values are used more frequently to diagnose T2DM and most patients do not start medication immediately. Furthermore, of the 25 largest cohorts, 17 (68%) had "healthy lifestyle," 16 (64%) had "metformin," 11 (44%) had "mobility impaired," 7 (28%) had "age_above_70y," and 3 (12%) had "mental impaired," all identical to the HbA1c scenario. Moreover, 23 (92%) of the 25 largest cohorts for the fasting glucose scenario were also in the list of the 25 largest cohorts for the HbA1c scenario, and the ranking in size was similar (≤3 positions difference). No other pharmacological treatments than metformin and gliclazide (4 occurrences) were represented in the 25 largest cohorts.

Various precision cohorts for randomly selected patients were constructed to verify that the chosen normalized distance threshold of 2.0 indeed resulted in optimal cofactor balance overall (data not shown) for the fasting glucose outcome scenario as well.

Figure 4. The 25 largest cohorts for fasting glucose as target outcome variable based on the filter variables. The blue bars represent the number of decision points (DPs) on a logarithmic scale (left vertical axis), and the orange line shows the cumulative coverage on a linear percentage scale (right vertical axis).



Treatment Options and Outcomes Analysis

Table 5 shows the overall controlled percentage of the 20 most representative treatment options, that is, across all filter cohorts. In >57.4% (16,480/28,709) of the cases, the existing treatment was continued, and in only 23.29% (3839/16,480) of the cases, this led to patients becoming "controlled" as judged by the fasting glucose value. Interestingly, in this scenario, the option of starting to take metformin and stopping the "no treatment" resulted in a lower success percentage when compared with the "no change" option. More differences are apparent when comparing with the HbA1c scenario; overall, the percentages of a "controlled" outcome seem more than 2-fold lower and never >37%, thereby seemingly indicating a much more pessimistic perspective.

Figure 5 represents the different treatment options observed in a precision cohort for a given patient that belongs to the cohort "Metformin with mobility impairments" using a Sankey diagram.

Analyzing the Sankey diagram in Figure 5, we can notice that for patients with mobility impairments who were taking metformin, only a small proportion of those who were kept on the same prescription met with an improved disease control outcome. The ones who changed from metformin to gliclazide showed an improvement, although the number of DPs for these 2 options was not very large, and the result was not statistically significant as a consequence. These results showed that the set of patients, similar to the patient of interest, had difficulties in having the fasting glucose controlled and might need more attention from the health care professionals. Many other cohorts could be included; we chose 2 examples that had a decent number of patients to show how this approach works in practice.

Table 5. The 20 largest observed global treatment option groups for fasting glucose as the target outcome variable. The list shows the size of each group and the associated percentage controlled during follow-up (n=28,710).

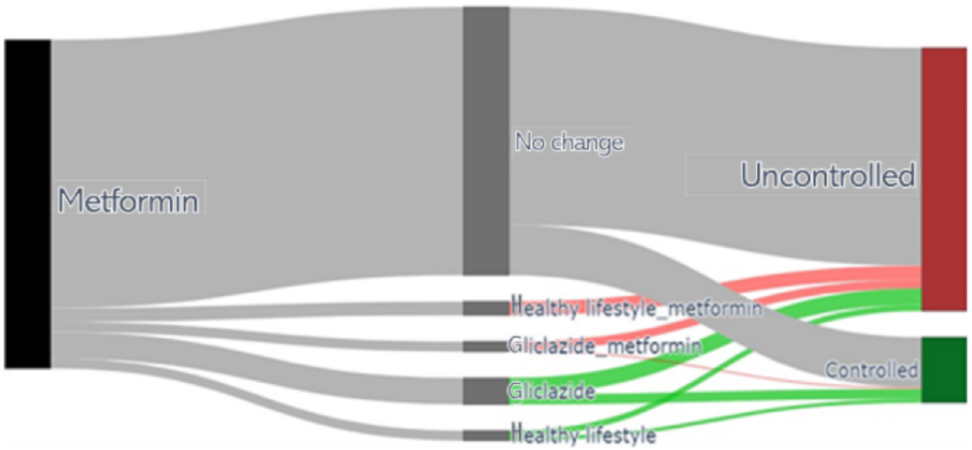
Treatment option	Frequency, n (%)	DPs[a] controlled, n (%)
No change	16,480 (57.4)	3839 (23.29)
Metformin_new+healthy lifestyle_metformin_stop[b]	3130 (10.9)	586 (18.72)
Healthy lifestyle_new+healthy lifestyle_metformin_stop[b]	1011 (3.52)	201 (19.88)
Metformin_new+no treatment_stop[b]	639 (2.23)	110 (17.21)
Healthy lifestyle_new+no treatment_stop[c]	638 (2.22)	203 (31.82)
Healthy lifestyle_metformin_new+metformin_stop[b]	612 (2.13)	59 (9.64)
Healthy lifestyle_metformin_new+healthy lifestyle_stop[c]	429 (1.49)	157 (36.6)
Healthy lifestyle_metformin_new+no treatment_stop[b]	399 (1.39)	69 (17.29)
Gliclazide_metformin_new+gliclazide_healthy lifestyle_metformin_stop[b]	284 (0.99)	28 (9.86)
Metformin_new+healthy lifestyle_stop[c]	265 (0.92)	97 (36.6)
Gliclazide_healthy lifestyle_new+healthy lifestyle_metformin_stop[b]	259 (0.9)	32 (12.36)
Gliclazide_new+gliclazide_healthy lifestyle_stop[b]	223 (0.78)	39 (17.49)
Gliclazide_new+healthy lifestyle_metformin_stop[c]	204 (0.71)	54 (26.47)
Gliclazide_new+metformin_stop[b]	165 (0.57)	22 (13.33)
Gliclazide_healthy lifestyle_metformin_new+healthy lifestyle_metformin_stop[b]	105 (0.37)	5 (4.76)
Healthy lifestyle_new+metformin_stop[b]	102 (0.36)	15 (14.71)
Metformin_new+gliclazide_healthy lifestyle_stop[b]	102 (0.36)	13 (12.75)
Gliclazide_metformin_new+gliclazide_healthy lifestyle_stop[b]	98 (0.34)	8 (8.16)
Healthy lifestyle_metformin_new+gliclazide_healthy lifestyle_stop[b]	93 (0.32)	6 (6.45)
Metformin_tolbutamide_new+healthy lifestyle_metformin_tolbutamide_stop[b]	91 (0.32)	2 (2.2)

[a]DP: decision point.

[b]Treatment options with a controlled percentage lower than the “no change” treatment option.

[c]Treatment options with a controlled percentage higher than the “no change” treatment option.

Figure 5. Personalized treatment options observed in a precision cohort for a given patient belonging to the filter cohort "Metformin with mobility impairments," using fasting glucose as target outcome variable. The initial node, in black, includes all the decision points (DPs) in the precision cohort for the particular patient of interest. This patient has all the guidelines variables as "False," except the mobility impairment as "True," and is currently on a metformin prescription. Each pathway from the initial node is a different treatment decision observed in the data. The thickness of the pathway is proportional to the number of DPs, and it is assigned with a label that represents the new medication, and the percentage of DPs controlled in the follow-up. The "no change" treatment option is colored in gray, and it is considered the baseline treatment option. The terminal nodes represent the outcome; the nodes in green denote the DPs that achieved control, whereas those in red indicate the uncontrolled ones. Treatment options with better control than the baseline option are colored in green, whereas those with a worse control are colored in red. No treatment options with statistical significance were found in the precision cohort for this patient.



Discussion

Principal Findings

This contribution evaluated the feasibility of using a precision cohort treatment options approach to generate personalized treatment options for patients with T2DM in the Dutch primary care setting. The approach involves the identification of relevant clinical treatment DPs from the longitudinal patient data to use as events of interest for modeling and analysis, patient similarity modeling for precision cohort construction, and treatment options and outcomes analysis as main elements. All procedures functioned well from a technical viewpoint; however, data size limitations proved challenging for reaching statistical significance for differences in outcomes of multiple treatment options.

Decision Points

Key information considered with the DPs included outcomes, clinical information (treatments and guidelines), and patient condition (measurements and comorbidities).

Outcomes

Two target outcome variables for T2DM were considered in this study, independently, to make the best use of the available data, as both HbA1c and fasting glucose are clinical measurements that can provide information about the T2DM state of the patient. The use of the 2 different outcome variables in separate scenarios enables a comparison between them and, in our perspective, offers the physician an opportunity to choose the one more relevant for a given clinical situation. In comparing the results for both scenarios, it is important to consider their different use in clinical practice. According to the guidelines, fasting glucose is used for diagnosis and primarily for making decisions about changing the dose of the prescribed medication. As the medication dose was not available from the data set, increasing the dose was considered to be a "no change" choice in this analysis. This probably explains that the percentage of "no change" cases for the glucose scenario was more than a factor of 1.2 higher than for the HbA1c scenario. According to the guidelines, only once the dosing is considered maximal, an uncontrolled fasting glucose value may be used to initiate the next progressive step in the treatment plan (ie, a different medication). Contrastingly, HbA1c, which reflects the patient's glycemic status over the past 8 to 12 weeks, is specifically used to decide whether to initiate a treatment change to a different medication. From the data it appears that when a treatment change is based on fasting glucose, the status during follow-up is judged as "controlled" only approximately half as often as when the treatment change is based on HbA1c. This difference remains unexplained; however, the case might be that a fasting glucose cutoff of 7 mmol/L is a more stringent criterion than the HbA1c cutoff of 7%.

To mimic the situation in practice where measurements of HbA1c and fasting glucose are intermittently made in the same patient to follow disease status, we also tried to analyze a "mixed case" scenario in which both HbA1c and fasting glucose measurements were used to build the DPs (eg, use HbA1c to identify a noncontrolled situation, then use fasting glucose to evaluate the treatment follow-up). This approach, however, did not result in the expected increase in the number of DPs extracted from the data, so it was not pursued further. The observed discrepancy in results for the different target variables makes clear that for the implementation of the precision cohort analytics approach in practice in the future, a unified definition of when the disease is to be considered "controlled," and a common decision on what metric is to be used to assess it, needs to be made.

Treatments and Guidelines

The data extraction retrieved all the usual medications used to treat T2DM, except for SGLT-2 inhibitors. Since 2021, the recommendations for high-risk patients include SGLT-2

inhibitors as medication. The absence of this treatment in the data set seemingly might indicate that the current Dutch guidelines for patients with T2DM were not followed in the study population. However, this can be explained not only by the fact that the data used here are from before 2021 but also by the fact that patients considered high risk are more likely to be referred to a specialist in secondary care, whereas the Nivel-PCD is concerned with primary care.

In the Netherlands, T2DM treatment over time has focused increasingly on lifestyle adjustments where possible, especially in the early stage of treatment where lifestyle improvement is the first treatment of choice except for high-risk cases [37]. This is, for example, reflected in a recent analysis of patients with T2DM diagnosed between 2015 and 2019, which showed that half of these patients did not receive antidiabetic medication prescriptions within 1 year of the diagnosis data [38]. Thus, lifestyle advices are probably often given; however, the fact that the "all_guidelines_variables_false" cohort was the fourth largest cohort for the HbA1c scenario seems to indicate that lifestyle adjustment is not integrally registered in the data fields within the Nivel-PCD (it is hardly imaginable that patients diagnosed with T2DM would receive no treatment at all). Incomplete registration of lifestyle treatment might have occurred because it is a default standard choice, or possibly because it is registered in the text fields of the patient dossiers that GPs use to make notes and are not collected in the Nivel-PCD. This will likely have led to an underestimation of the "healthy lifestyle advice" treatment group and likely to some misclassification, especially of patients in cohorts that involved "no treatment_stop" in this analysis.

Moreover, the merging of the nonpharmacologic treatments such as diet and exercise (registered as separate treatments in the Nivel-PCD) into a single "healthy lifestyle advice" as done in this study did not allow us to assess the individual contribution of each of the separate lifestyle interventions. However, this analysis still offers a way to evaluate the importance of lifestyle interventions for the patient's health. Future studies could explore the efficacy of individual lifestyle adjustments as a first line of therapy for patients with T2DM, provided they are adequately registered.

The absence of medication dosage information in the available data set means that the current approach cannot be used to inform decisions regarding dosage changes. Similarly, the influence of medications that are not directly targeting diabetes, for example, the ones targeting blood pressure, was not considered in this retrospective analysis. Nevertheless, information on prescriptions of these other medications is available in the data set, and as drugs may have interactions, future studies might explore the possibility of including a larger spectrum of medications for a deeper analysis, leading to more refined models and decision-making tools.

Patient Condition

The idea to use both mobility and emotional states complementary to standard clinical measurements such as blood pressure, blood lipids, and creatinine came as a suggestion from a GP consulted for the study. We took care to also include the aspect that such impairment may be temporal instead of chronic, for example, in the case of a broken leg. As mentioned, for this exploratory analysis, we made subjective, intuitive choices to operationalize these conditions, which were not validated by independent experts. Therefore, they remain subject to debate. However, the fact that 11 (44%) of the 25 largest cohorts included "mobility impaired" suggests that it is indeed relevant to include a mobility assessment as a filter variable for defining the precision cohorts. The same holds for emotional state; however, with inclusion in only 3 (12%) of the 25 largest cohorts, the importance seems lower than for mobility impairment.

The patient condition characteristics used in this analysis are necessarily limited to the information available in the Nivel-PCD. Information about social behavior, ethnicity, socioeconomic status, medication adherence, and many other factors was not included, which might have a major impact on the disease outcome. This fact points to a world beyond what was analyzed in this study.

Patient Similarity Modeling and Precision Cohort Construction

The selection of precision cohorts was done in a 2-step procedure, first a filtering step and then a similarity rating. The filtering step was based on guidelines, mobility, and mental state. The vast majority of the largest filter cohorts involved metformin and lifestyle advice as treatments, reflecting the importance of these as the first line of treatments according to the clinical guidelines. Patient similarity modeling and precision cohort construction were technically well feasible. However, data size limitations became apparent for the HbA1c scenario, where only 10 filter cohorts were considered sufficiently large (>200 DPs) to allow the construction of precision cohorts. This contrasts with the analysis of Ng et al [16] of the US EHR data, where the 75 largest T2DM cohorts based on filter variables had >200 DPs.

Treatment Options and Outcomes Analysis

The technical feasibility of treatment options and outcome analysis was also well established. For the HbA1c target outcome, approximately half of the global treatment options resulted in better outcomes than the "no change" option. For fasting glucose as the target outcome, this was the case for only very few treatment options, suggesting that the use of fasting glucose as the target outcome needs careful consideration. The few examples of precision cohort–based treatment options and outcomes analysis clearly illustrated the lack of statistical power available with the current data set. This further underlines that the method has high data availability requirements. Because a correction for multiple testing has to be applied, reaching statistical significance for differences in outcomes of multiple treatment options proved challenging, even for filter cohorts with 1000 DPs, as demonstrated in Figures 3 and 5. It is estimated that to overcome this limitation, the data set size should be at least an order of magnitude larger.

Future Perspectives

The method developed and applied for the Dutch primary care situation in this study aims to create precision cohorts that include a set of patients who are more similar to the patient of

interest in different attributes, from classic clinical measurements to assessments of mobility state and even mental state. This would allow the physician to selectively consider a group of patients that were in a very similar situation to the patient of interest and view statistics on past outcomes of available treatment options. Over time, with the increase in the available patient information and developments in computational methods, the ability to thus incorporate past clinical experience to generate more personalized treatment options for individual patients is enhanced, thereby potentially contributing to better treatment outcomes.

In this study, we took a highly reductionist approach to defining treatment outcome, that is, an HbA1c or fasting glucose clinical test result that falls below a predetermined threshold. As such it is of a highly reductionist nature.

Although we recognize that a patient's perspective and experience are crucial factors both in decision-making and in evaluating treatment efficacy, our data-driven approach was as yet unable to account for those aspects. Still, the technique can support shared decision-making by practitioner and patient because the information on expected treatment outcomes is more personalized toward the individual patient and therefore more relevant in the discussion when balancing risks and expected outcomes with patient preferences and values. Although this study did not explore the actual use of the precision cohort approach for shared decision-making in practice, it offers valuable insight into the potential use from a data availability perspective.

It is important to mention that this approach does not aim to replace or lessen the actions of the physicians but to provide refined tools to support them in the medical decision-making process.

The workflow elaborated in this study was applied to the T2DM case but can be applied to any other disease or health disorder for which rich data and guidelines are available. Indeed, Ng et al [16] applied their approach to hypertension and hyperlipidemia as well as T2DM. However, applying the approach to different diseases requires rerunning all the steps of the workflow to adapt for the different diseases, including patient selection, choice of target outcome variables, incorporation of applicable clinical guidelines, selection of salient features, and tuning of the similarity model.

In this study, data availability was identified to be a principally limiting factor for feasibility. Considering that further personalization will lead to yet smaller cohorts, it is evident that increasing the pool of data for the precision cohort approach is essential to achieve a more meaningful and more robust analysis. Given that approximately 1 million patients have T2DM in the Netherlands, there is a realistic perspective for this; however, it will require combining health data from different EHR sources nationwide, which is a challenge in itself. This problem is aggravated for diseases for which the amount of data (ie, patients) is much smaller or the spectrum of treatment choices is larger.

Although methods to reduce the presence of bias in the data were applied, having more data available offers a possibility to improve the workflow, especially with respect to better selection of the confounder variables. This may lead to a better generalization, improving the performance of the workflow as a whole.

Conclusions

This study explored the feasibility of applying a patient similarity–based precision cohort approach to derive personalized treatment options for patients with T2DM treated in primary health care in the Netherlands using the Nivel-PCD. A previously published data analysis and modeling workflow for US EHR data was successfully adapted for this Dutch primary care setting, proving its potential for use in an LHS context. Although the approach proved technically well feasible, data size limitations need to be overcome before application for CDS purposes becomes realistically possible.

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Data Availability

The data sets generated during and analyzed during this study are not publicly available. The Data from the Nivel Primary Care Database are available for research by other organizations upon approved data use request.

Authors' Contributions

XP was involved in co-designing and executing the study and writing the manuscript. AdG was involved in conceptualizing, obtaining funding, co-designing the study, and writing the manuscript. WM was involved in conceptualizing the study, accomplishing study data access, and reviewing the manuscript. XP performed all data analytics work. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Features used for the similarity model for glycated hemoglobin. For each variable, the name, the use (filter or similarity), the type of feature (numerical, Boolean, etc), and the similarity weight (influence on the model) are shown.
[PNG File , 193 KB - ojphi_v16i1e51092_app1.png]

Multimedia Appendix 2
Features used for the similarity model for fasting glucose. For each variable, the name, the use (filter or similarity), the type of feature (numerical, Boolean, etc), and the similarity weight (influence on the model) are shown.
[PNG File , 350 KB - ojphi_v16i1e51092_app2.png]

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Abbreviations

CDS: clinical decision support
DM: diabetes mellitus
DP: decision point
EHR: electronic health record
GP: general practitioner
HbA1c: glycated hemoglobin
ICPC: International Classification of Primary Care
KNN: k-nearest neighbors
LASSO: least absolute shrinkage and selection operator
LHS: learning health system
LMNN: large margin nearest neighbor
MD: Mahalanobis distance
Nivel: The Netherlands Institute for Health Services Research

PCD: Primary Care Database
SGLT-2: sodium-glucose transport protein 2
T2DM: type 2 diabetes mellitus

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Original Paper

Analyzing Google COVID-19 Vaccine Intent Search Trends and Vaccine Readiness in the United States: Panel Data Study

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Abstract

Background: Factors such as anxiety, worry, and perceptions of insufficient knowledge about a topic motivate individuals to seek web-based health information to guide their health-related decision-making. These factors converged during the COVID-19 pandemic and were linked to COVID-19 vaccination decision-making. While research shows that web-based search relevant to COVID-19 was associated with subsequent vaccine uptake, less is known about COVID-19 vaccine intent search (which assesses vaccine availability, accessibility, and eligibility) as a signal of vaccine readiness.

Objective: To increase knowledge about vaccine intent search as a signal of vaccine readiness, we investigated the relationship between COVID-19 vaccine readiness and COVID-19 vaccine intent relative search volume on Google.

Methods: We compiled panel data from several data sources in all US counties between January 2021 and April 2023, a time during which those with primary COVID-19 vaccinations increased from <57,000 to >230 million adults. We estimated a random effects generalized least squares regression model with time-fixed effects to assess the relationship between county-level COVID-19 vaccine readiness and COVID-19 vaccine intent relative search volume. We controlled for health care capacity, per capita COVID-19 cases and vaccination doses administered, and sociodemographic indicators.

Results: The county-level proportions of unvaccinated adults who reported that they would wait and see before getting a COVID-19 vaccine were positively associated with COVID-19 vaccine intent relative search volume (β=9.123; *Z*=3.59; *P*<.001). The county-level proportions of vaccine-enthusiast adults, adults who indicated they were either already vaccinated with a primary COVID-19 vaccine series or planned to complete the vaccine series soon, were negatively associated with COVID-19 vaccine intent relative search volume (β=–10.232; *Z*=–7.94; *P*<.001). However, vaccine intent search was higher in counties with high proportions of people who decided to wait and see and lower in counties with high proportions of vaccine enthusiasts.

Conclusions: During this period of steep increase in COVID-19 vaccination, web-based search may have signaled differences in county-level COVID-19 vaccine readiness. More vaccine intent searches occurred in high wait-and-see counties, whereas fewer vaccine intent searches occurred in high vaccine-enthusiast counties. Considering previous research that identified a relationship between vaccine intent search and subsequent vaccine uptake, these findings suggest that vaccine intent search aligned with people's transition from the wait-and-see stage to the vaccine-enthusiast stage. The findings also suggest that web-based search trends may signal localized changes in information seeking and decision-making antecedent to vaccine uptake. Changes in web-based search trends illuminate opportunities for governments and other organizations to strategically allocate resources to increase vaccine uptake. Resource use is part of the larger public policy decisions that influence vaccine uptake, such as efforts to educate the public during evolving public health crises, including future pandemics.

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KEYWORDS

information-seeking behavior; COVID-19; internet use; vaccination; vaccine hesitancy

Introduction

Background

Individuals regularly seek health information to guide their health-related decision-making about varied topics, including cancer screening [1], electronic cigarette use [2], vaccination against human papillomavirus [3], and COVID-19 [4]. People acquire this information from many sources, including their medical providers [5]; traditional media sources such as broadcast television and radio [6]; and digital media sources such as apps, websites, and streaming video and audio [7]. Many people search for web-based health-related information [7,8] using search engines such as Google (Google LLC), which has >90% of the web-based search market share in the United States [9,10]. Individuals are more likely to seek knowledge on the web when they perceive online information to be available, high quality, trustworthy, useful, and credible [11,12].

People search for information when they have insufficient knowledge about a topic or perceive a knowledge gap [13]. In addition, worry and anxiety are associated with higher levels of health information seeking [14,15]. These conditions can lead to hesitancy in making health decisions because people perceive limitations in their knowledge, hampering their ability to successfully mitigate risks [16-18]. Health information seeking–related worry, anxiety, and perceived limitations in knowledge converged when the COVID-19 pandemic began in 2020, as the public initially knew little about SARS-CoV-2 (the virus that causes COVID-19) [19,20]. High levels of anxiety and worry about COVID-19 extended to COVID-19 vaccination decision-making [13], with a substantial proportion of the public initially hesitant about whether (or when) to get a COVID-19 vaccine [21,22]. High levels of COVID-19 anxiety and increases in depressive symptoms and stress were also present among health care workers [23].

In response to COVID-19 and COVID-19–related mortality, countries used several public policy responses during the pandemic emergency period, including increasing health care spending [24], strengthening early warning systems and adding robust contact tracing systems [25], and supporting research to develop COVID-19 vaccines and treat COVID-19 [25]. Once COVID-19 vaccines were created and approved, many high-income countries could vaccinate their populations more quickly [26], which reduced COVID-19 mortality [27]. Conversely, countries with fewer resources and lower access to COVID-19 vaccines could not vaccinate their populations as quickly [28].

As countries implemented public policy responses during the early stages of the COVID-19 pandemic, researchers observed surges in web-based COVID-19–related content [29,30] and an increase in COVID-19–related searches [31]. Using data from Google Trends (Google LLC), which quantifies relative interest in a search topic, researchers identified spikes in the number of new COVID-19 cases that coincided with increases in relative COVID-19 search activity [4,32]. COVID-19-related searches included general searches about COVID-19 as well as specific search queries, such as those about the safety and efficacy of COVID-19 vaccines, unfounded concerns regarding ethylmercury content in vaccine preservatives (there are no preservatives in COVID-19 vaccines [33]), and unfounded links [34] between vaccination and autism (this claim has been proven false [4,35]). Moreover, from March to June 2020 (in the early stages of the pandemic), high levels of anxiety and depression in the population were associated with increases in COVID-19 vaccine searches in the United States [20].

COVID-19–related searches also increased with the announcement and publication of scientific advancements in COVID-19 vaccine development [4,36]. One study used a machine learning methodology to show that people who were clustered into a group that was more likely to gather information on the web from multiple sources had longer life expectancies, were college educated, had higher per capita incomes, lived in metropolitan areas, and were less likely to be vaccine hesitant [37], suggesting that web-based searches related to COVID-19 may have influenced individuals' COVID-19 vaccination decisions. Studies using Google Trends data found a positive association between the amount of peer-reviewed scientific research about Pfizer and Moderna COVID-19 vaccines and information-seeking searches about these vaccines [36] and an association between the December 2020 US emergency use authorization and an immediate increase in Google search volume about the unfounded link [38] between side effects of the vaccine and fertility [39,40].

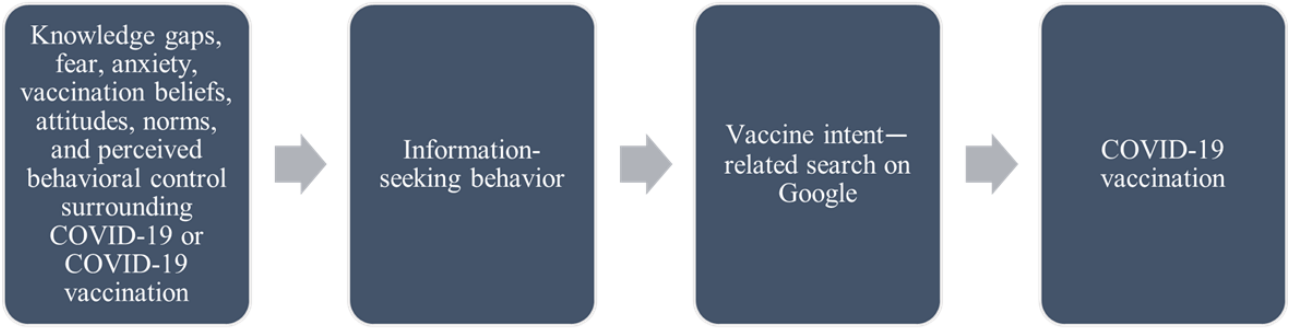
Moreover, insights gathered from Google COVID-19 vaccination search index trend data demonstrated that increased interest in this topic was associated with the number of new COVID-19 vaccinations administered over the subsequent 3 weeks and with vaccination rates observed months later [41]. The Google COVID-19 vaccination search index trend data were processed in a more specified manner than data available from Google Trends to make them more usable for researchers and practitioners. We used Google COVID-19 vaccination search index trend data in this analysis and not data from Google Trends.

To better understand the relationship between COVID-19-related web-based search and COVID-19 vaccination intentions and uptake, we investigated the potential association between COVID-19 vaccine readiness and the volume of COVID-19 vaccine intent–related searches on Google between January 2021 and April 2023. During this time frame, the number of adults with primary COVID-19 vaccinations increased from <57,000 to >230 million [42]. Vaccine readiness is a composite measure of vaccine intention and behavior. Vaccine intent–related searches included those on the accessibility, availability, and eligibility of for COVID-19 vaccines and those on topics such as "COVID-19 vaccine near me" [43]. Vaccine intent–related searches represent what could be the first step after making a decision to get vaccinated (Figure 1), as individuals seek information on how to get their COVID-19 vaccination. Evidence indicates that increased vaccine intent searches preceded higher COVID-19 vaccination rates [41].

Researchers have developed theories and models to explain health behavior uptake that have empirical support to elaborate the conditions under which people are more likely to seek information. The theory of planned behavior (TPB) posits that

the decision to engage in a volitional behavior is primarily influenced by behavioral intention, which is shaped by a combination of factors such as attitudes, social norms, and perceived behavioral control [44]. The Planned Risk Information Seeking Model (PRISM) builds upon the TPB by focusing on individuals who perceive limitations in their knowledge that can help them mitigate risks [16-18]. More specifically, PRISM suggests that people who perceive limitations in their knowledge are more likely to seek information to increase their knowledge and address perceived knowledge insufficiency [16].

Figure 1. Information-seeking process for COVID-19 vaccination.



Altogether, these theories suggest that people move through an information-seeking process, as outlined in Figure 1. This figure illustrates the process by which individuals moved from deciding to seek additional information about COVID-19 or COVID-19 vaccination to getting a COVID-19 vaccine.

In the first stage, multiple factors drove individuals' information-seeking behavior to address COVID-19 vaccination knowledge gaps, including fear and anxiety about COVID-19 or COVID-19 vaccination [13]; vaccination beliefs [45]; and, more broadly, their relevant attitudes, norms, and perceived behavioral control [16]. As vaccine-hesitant individuals gained more information through web-based searches to fill perceived or actual knowledge gaps and moved from being vaccine hesitant to vaccine ready, these theories suggest that individuals were more likely to perform vaccine intent–related searches as the final step of a decision-making and information-seeking process that culminated in getting a COVID-19 vaccine to mitigate the risk of COVID-19–related harm to their health.

Objectives

This study investigated the following research question: Is there an association between COVID-19 vaccine readiness and the volume of COVID-19 vaccine intent–related searches on Google?

Google searches related to vaccine intent excluded searches for COVID-19 vaccine safety and general searches about the COVID-19 vaccine [46]. We examined county-level proportions of 3 groups of adults based on vaccine readiness: vaccine enthusiasts, those who wanted to wait and see, and those who had no intention to get vaccinated.

We expected that vaccine enthusiasts, people who had already gotten their primary COVID-19 vaccination or intended to get vaccinated soon, would be less likely to search for COVID-19 vaccine intent information on the web because they had already made or enacted an affirmative COVID-19 vaccination decision for themselves. Accordingly, we hypothesized a negative relationship between the county-level proportion of adults who were vaccine enthusiasts and the county-level relative COVID-19 vaccine intent search volume on Google (hypothesis 1).

Conversely, we expected that individuals in the wait-and-see group initially lacked the information they needed to make a vaccination decision and, therefore, would be more likely to search for COVID-19 vaccine information on the web to facilitate decision-making. As these individuals became vaccine ready, we expected that they would be more likely to perform COVID-19 vaccine intent searches as a final step in a decision-making and information-seeking process. That process concluded when they got a COVID-19 vaccine. Accordingly, we hypothesized a positive relationship between the county-level proportion of adults who were in the wait-and-see group and the county-level relative COVID-19 vaccine intent search volume on Google (hypothesis 2).

Methods

Ethical Considerations

Institutional review board approval for this research was not required because it did not meet the US Department of Health and Human Services' (HHS) definition of human subjects research. All data for this study came from deidentified, publicly available sources.

Data

Data were drawn from several publicly available sources, including Google vaccine search insights data [43], the HHS Monthly Outcome Survey (MOS) [47], the US Centers for Disease Control and Prevention's (CDC's) Weekly United States COVID-19 Cases and Deaths by County database [48], the HHS Area Health Resources Files (AHRFs) [49], the US Federal Communications Commission's (FCC's) Form 477 County Data on Internet Access Services [50], and the Subnational Ideology and Presidential Election Estimates data set [51,52].

COVID-19 vaccine intent search data were derived from Google's weekly vaccine search insights data by county. These data provided insights on topics related to COVID-19 vaccine availability, accessibility, and eligibility [43]. Hereafter, we refer to these searches as the COVID-19 vaccine intent relative

search volume. The MOS provided data on the proportions of the population who were in each vaccine readiness group: vaccine enthusiasts, wait and see, and no intent to get vaccinated [47]. These groups are more defined in detail in the *Measures of Variables* section. The CDC data contained the number of COVID-19 cases per capita and the number of COVID-19 vaccination doses per capita [48]. The HHS AHRFs contained county-level public health infrastructure and demographic data [49]. The publicly available FCC data reflected the rates of internet access in each US county [50]. Finally, data from the American Ideology Project provided county-level political context measures (for 2016 and 2020) [51,52].

We used these data to investigate the link between COVID-19 vaccine readiness and COVID-19 vaccine intent relative search volume. The data were recorded or aggregated for each month and each county, so the unit of analysis was the county-month.

Measures of Variables

The dependent variable was the monthly county-level COVID-19 vaccine intent relative search volume from January 4, 2021, to April 24, 2023, in the United States. Google weekly vaccine search insights data provided weekly vaccination intent–related searches conducted by individuals at the zip code level. These searches included those related to the availability, accessibility, and eligibility of COVID-19 vaccines [43]. These data were normalized with a minimum value of 0 to indicate no relative interest. We aggregated these data using the median relative intent search index indicator by county and month. We used median values instead of mean values because they were less subject to being skewed by outliers. More information about this measure is provided in the *Data Sources and Analytic Method* section of Multimedia Appendix 1 [53-58] and on Google's COVID-19 Vaccination Search Insights page [43,59].

Our independent variables were 2 monthly, county-level measures of the proportions of people in each of the 2 COVID-19 vaccine readiness categories: vaccine enthusiasts and wait and see. Vaccine enthusiasts indicated that they were "already vaccinated or reported that they will get a vaccine as soon as they can" [47]. The wait-and-see group [47] reported "that they will wait to get a primary series vaccination for one or more reasons" [47]. Our reference category (the no-intent-to-get-vaccinated group) was the proportion of people who were unvaccinated and reported that they would never get a COVID-19 vaccine [47]. These measures were constructed using small area estimates that were based on covariates in the MOS. More information on the construction of these measures and the underlying MOS data sets is provided in the *Data Sources and Analytic Method* section of Multimedia Appendix 1 and on the HHS health database [47].

Internet access is not distributed equally across the United States because this distribution is largely driven by differences in affordability and density [60]. Although rural areas have less access and lower broadband wired speeds than urban areas, more people without broadband access live in urban areas than in rural areas [60-62]. To consider the potential influence of county-level variation in internet access on COVID-19 vaccine intent relative search volume, we aggregated fixed and broadband internet coverage rates by county using the most recent FCC data from 2021 [50] to calculate mean internet access.

A community's capacity to provide health care services to its constituents could influence an individual's perceived access to COVID-19 treatment and thereby influence their intention to get (or the uptake of) a COVID-19 vaccine [63,64]. To account for the potential influence of county-level health care capacity on COVID-19 vaccine readiness, our analyses controlled for 3 measures relevant to health care capacity in each county, as provided by the HHS AHRFs: the number of public health research facilities per county; the number of staffed intensive care unit hospital beds per 100,000 people; and the number of primary care physicians per county square mile [49]. Public health research facilities included the number of public health research centers, facilities, hospitals, universities, and similar institutions [49]. Through their research and outreach activities in their local area, public health research centers provide offline health information, may facilitate an environment that encourages access to vaccination, or may even have qualified staff who devote time to delivering COVID-19 vaccines. Primary care physicians included family medicine, general practitioners, and internists [49]. We expected that people would have better access to offline health information and perceive better access to COVID-19 vaccines as the numbers of public health research centers, intensive care unit beds, and primary care physicians per county increase.

To account for the potential influence of COVID-19 cases and vaccinations on COVID-19 vaccine intent relative search volume, we gathered weekly county-level CDC COVID-19 case and vaccination administration data [48]. We then normalized aggregated numbers of cases and vaccinations by computing per capita (100,000 people) measures. We calculated the differences in each of these quantities between the current month and the previous month and lagged each difference by 1 month, with the expectation that changes in COVID-19 cases and vaccinations in the previous month could be associated with subsequent changes in COVID-19 vaccine intent relative search volume. More specifically, a higher number of COVID-19 cases likely increased personal risk perception for getting COVID-19 and motivated information seeking about COVID-19 prevention behavior such as vaccinations. A higher number of COVID-19 vaccinations was likely to positively influence perceived social norms of getting vaccinated, which, in turn, would have affected vaccination information seeking.

Previous research has shown that attitudes and beliefs about COVID-19 vaccination and COVID-19 vaccine uptake differ based on sociodemographic characteristics, including race or ethnicity, income, and political ideology [21,22,37]. To account for the potential influence of sociodemographic characteristics on COVID-19 vaccine readiness, we gathered data from the HHS AHRFs on the county-level proportions of people who reported that they identified with the following racial or ethnic groups in the 2020 Census: non-Hispanic Black, Hispanic, non-Hispanic Asian and Pacific Islander, and non-Hispanic American Indian and Alaska Native. We also gathered HHS AHRF data on the per capita income of each county in 2021.

The models included 2 indicators that captured political context, developed from the American Ideology Project [51,52]. First, we created a measure for being an electoral pivot county, in which we examined the change in the US presidential election results between the 2016 and 2020 elections. The electoral pivot measure was a dichotomous variable coded as 1 for counties that contained a plurality of the population who voted for the Republican presidential candidate in the 2016 general election but voted for the Democratic presidential candidate in the 2020 general election and coded as 0 for those counties that did not meet this condition. Second, we included a measure that captured the change in county-level political ideology from 2016 to 2020. This measure was scaled such that higher values indicated more conservative counties in 2020 compared to 2016. More details about both measures are provided in the *Data Sources and Analytic Method* section of Multimedia Appendix 1.

Models and Data Analysis Procedure

To assess the relationship between COVID-19 vaccine readiness and COVID-19 vaccine intent relative search volume, we estimated a random effects generalized least squares regression model with time-fixed effects and clustered robust SEs by county. This methodology allowed us to model longitudinal data in which the dependent variable, county-level COVID-19 vaccine intent relative search volume, has a lower bound (0) but no theoretical upper bound. Using fixed effects allowed us to disentangle any relationships between independent and dependent variables while controlling for the effects of time. The SEs were clustered to adjust for uneven variance in COVID-19 vaccine intent relative search volume across counties [65]. We used the natural logs of mean internet access, public health research facilities, access to primary care physicians, monthly change in COVID-19 cases per capita, monthly change in COVID-19 vaccination doses per capita, and income per capita because they were not normally distributed in their raw forms.

After estimating the statistical model, we performed predictive margins tests to estimate the substantive impact of both COVID-19 vaccine readiness variables (monthly change in vaccine enthusiasts and monthly change in the wait-and-see group) more precisely on the COVID-19 vaccine intent relative search volume. More details about our analytic method and the predictive margins tests are available in the *Data Sources and Analytic Method* section of Multimedia Appendix 1.

We used a stepwise approach to arrive at the model, which provided an internal consistency check on the primary expectations with respect to control variable inclusion or exclusion. More details about how we implemented this approach and arrived at the model that we reported are available in the *Stepwise Regression Results* section of Multimedia Appendix 1. We conducted the analyses using Stata (version 17; StataCorp) [66].

Results

Descriptive Analyses

Figure 2 illustrates monthly changes in the percentage of US adults who were vaccine enthusiasts between February 2021 and April 2023 [67]. The figure indicates that the percentage of adults who became vaccine enthusiasts increased to varying degrees throughout 2021 in most months. From February to April 2021, for example, vaccine enthusiasts may have performed many vaccine intent searches on Google because it was difficult to find vaccines for them or their families during this period. Thus, it makes sense that there was a strong positive relationship during this period for vaccine enthusiasts but a negative relationship after they got vaccinated.

In addition, this visual shows changes in COVID-19 vaccine intent relative search on Google in 2021 that corresponded with changes in the proportion of adults who became vaccine ready. This suggests that vaccine intent searches could be associated with the first step people made in the vaccination information–seeking process to move from the wait-and-see stage to the vaccine-enthusiast stage. In this respect, vaccine intent searches may serve as a proxy for incident vaccine-ready cases.

Table 1 provides summary statistics for each variable included in the models. For example, in our sample, the mean of the monthly median COVID-19 vaccine intent relative search volume was 7.35 (SD 10.70; range 0.18-111.26); the mean monthly change in vaccine enthusiasts was 0.01 (SD 0.03; range –0.30 to 0.23); and the mean monthly change in the wait-and-see group was –0.01 (SD 0.02; range –0.24 to 0.39). More details about the model covariates are provided in the Data Sources and Analytic Method section of Multimedia Appendix 1.

Figure 2. COVID-19 vaccination intent searches and vaccine enthusiasts in the United States (January 2021 to April 2023). The change in the percentage of US adults who were vaccine enthusiasts came from the Monthly Outcome Survey (MOS). Data for the change in the median relative COVID-19 vaccination intent search came from Google's Vaccination Search Insights index.

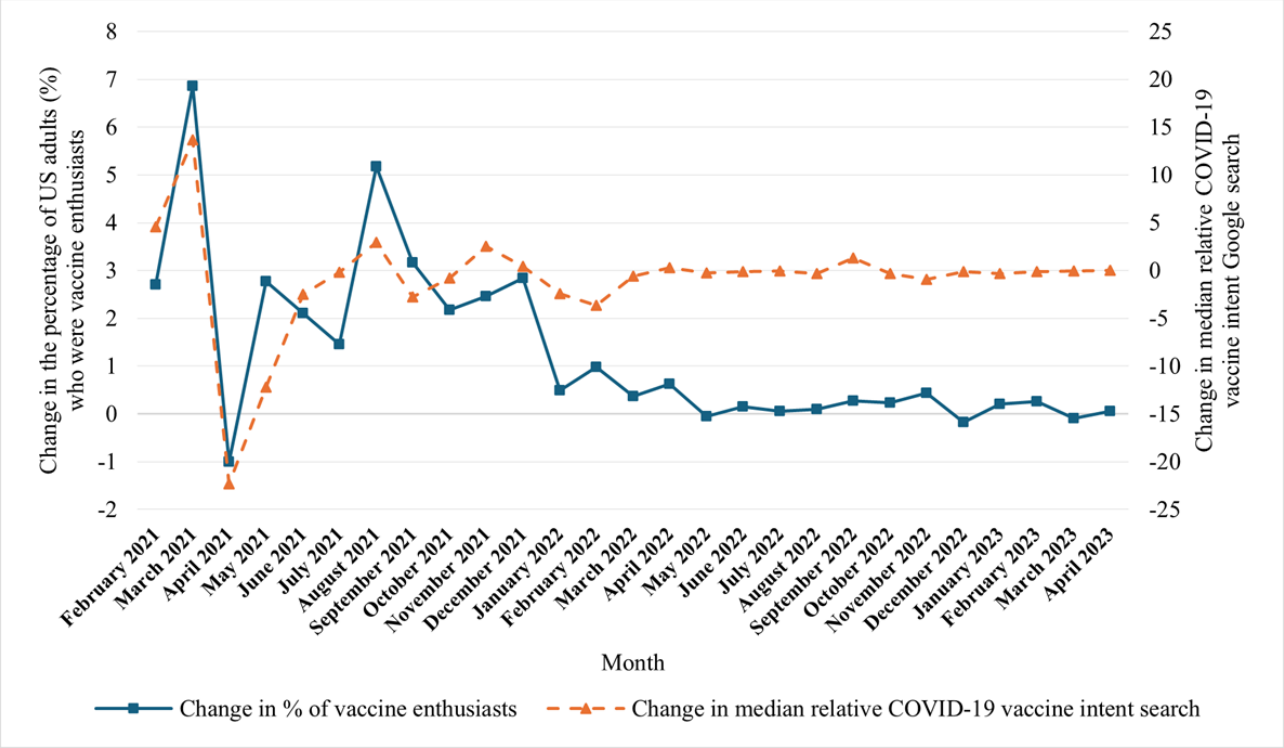


Table 1. Descriptive statistics of the analytic variables in the United States, January 2021 to April 2023.

Variable	Values, n	Values, mean (SD; range)
Dependent variable		
Monthly median COVID-19 vaccine intent relative search volume	14,087	7.350 (10.697; 0.182 to 111.261)
Independent variables		
Monthly change in vaccine enthusiasts	13,496	0.012 (0.033; –0.304 to 0.231)
Monthly change in the wait-and-see group	13,496	–0.011 (0.023; –0.240 to 0.388)
Monthly change in the no-intention-to-get-vaccinated group (reference)	13,496	–0.0003 (0.026; –0.201 to 0.217)
Health care capacity, internet access, and COVID-19 variables		
Mean internet access (raw)	14,087	0.811 (0.125; 0.102 to 1.000)
Mean internet access (natural log)	14,087	0.591 (0.076; 0.097 to 0.693)
Public health research facilities (raw)	14,087	0.232 (0.879; 0.000 to 11.000)
Public health research facilities (natural log)	14,087	0.117 (0.345; 0.000 to 2.485)
Access to primary care physicians (raw)	14,087	1.287 (6.033; 0.003 to 124.749)
Access to primary care physicians (natural log)	14,087	0.504 (0.559; 0.003 to 4.834)
Monthly change in COVID-19 cases per capita$_{t-1}$ (raw)	13,496	0.009 (0.012; 0.000 to 0.128)
Monthly change in COVID-19 cases per capita$_{t-1}$ (natural log)	13,496	0.008 (0.010; 0.000 to 0.095)
Monthly change in COVID-19 vaccination doses per capita$_{t-1}$ (raw)	13,166	0.030 (0.051; –0.373 to 0.871)
Monthly change in COVID-19 vaccination doses per capita$_{t-1}$ (natural log)	13,166	0.021 (0.040; –0.168 to 0.626)
Demographics		
Income per capita (raw)	14,087	58,032 (16,603; 31,153 to 191,220)
Income per capita (natural log)	14,087	10.937 (0.238; 10.347 to 12.161)
Change in ideology	14,087	–0.073 (0.053; –0.254 to 0.109)
Electoral pivot county	14,087	0.066 (0.248; 0.000 to 1.000)
Proportion of non-Hispanic White people (reference)	14,087	0.637 (0.184; 0.036 to 0.920)
Proportion of non-Hispanic Black people	14,087	0.111 (0.114; 0.003 to 0.691)
Proportion of Hispanic people	14,087	0.150 (0.145; 0.012 to 0.952)
Proportion of non-Hispanic Asian American and Pacific Islander people	14,087	0.048 (0.058; 0.004 to 0.559)
Proportion of non-Hispanic American Indian and Alaska Native people	14,087	0.007 (0.028; 0.001 to 0.436)

Regression Modeling

Table 2 provides the results from the regression model that evaluates the relationship between county-level changes in COVID-19 vaccine readiness and the COVID-19 vaccine intent relative search volume. This model generally performed well, as the overall R^2 value was 0.752. When accounting for variance within the panel, the R^2 value was 0.771, whereas the R^2 value when considering variance between counties was 0.310.

Table 2. Effect of county-level COVID-19 vaccine readiness on the COVID-19 vaccine intent relative search volume in the United States (January 2021 to April 2023).[a,b,c]

Variables	Model value (SE)	*P* value
Independent variables		
Monthly change in vaccine enthusiasts	–10.232 (1.289)	<.001
Monthly change in the wait-and-see group	9.123 (2.540)	<.001
Health care capacity, internet access, and COVID-19 variables		
Mean internet access (natural log)	–2.504 (1.110)	.02
Public health research facilities (natural log)	0.415 (0.236)	.08
Access to primary care physicians (natural log)[d]	0.859 (0.263)	.001
Monthly change in COVID-19 cases per capita$_{t-1}$ (natural log)	124.106 (11.621)	<.001
Monthly change in COVID-19 vaccination doses per capita$_{t-1}$ (natural log)	25.288 (3.315)	<.001
Demographics		
Income per capita (natural log)	4.856 (0.559)	<.001
Change in ideology	4.210 (1.473)	.004
Electoral pivot county	0.553 (0.263)	.04
Proportion of non-Hispanic Black people	–4.889 (0.796)	<.001
Proportion of Hispanic people	–1.115 (0.573)	.052
Proportion of non-Hispanic Asian American and Pacific Islander people	2.210 (2.164)	.31
Proportion of non-Hispanic American Indian and Alaska Native people	–5.504 (2.334)	.02
Intercept	–26.945 (6.225)	<.001
Model statistics		
N	13,166	—[e]
N (counties)	587	—
R^2 (between)	0.310	—
R^2 (within)	0.771	—
R^2 (overall)	0.752	—
Wald chi-square	20,835.93	<.001

[a]SEs in parentheses are clustered robust SEs.

[b]Coefficients were computed by using a generalized least squares panel regression with time-fixed effects.

[c]Binaries for fixed effects were excluded from this table.

[d]Staffed intensive care beds were perfectly colinear with the number of primary care physicians. Therefore, these 2 variables appeared in separate models.

[e]Not applicable.

The model indicates a negative association between COVID-19 vaccine readiness and the COVID-19 vaccine intent relative search volume: counties with a higher proportion of vaccine enthusiasts relative to other counties were associated with decreased COVID-19 vaccine intent relative search volume across all models (β=–10.232; *Z*=–7.94; *P*<.001). Moreover, counties with a higher proportion of people in the wait-and-see group relative to other counties were associated with increased COVID-19 vaccine intent relative search volume across all models (β=9.123; *Z*=3.59; *P*<.001). The results support our hypotheses of a negative relationship between counties with a higher proportion of vaccine enthusiasts relative to other counties and the COVID-19 vaccine intent relative search volume (hypothesis 1) and a positive relationship between counties with a higher proportion of individuals in the wait-and-see group compared to other counties and the COVID-19 vaccine intent relative search volume compared to other counties (hypothesis 2).

The results demonstrated that several covariates relevant to health care capacity, internet access, and COVID-19 were significantly associated with COVID-19 vaccine intent relative search volume. We found a negative, statistically significant association between internet access and the COVID-19 vaccine intent relative search volume (β=–2.504; *Z*=–2.26; *P*=.02). However, this result was likely an artifact, capturing the effect of population density and economic development on access to

COVID-19 pandemic response resources. In the *Robustness Checks Using Varied Operationalizations of the Explanatory Variables* section of Multimedia Appendix 1, we report results from analyses in which we disaggregated mean internet rate by fixed and mobile broadband accesses to elaborate on this effect.

Monthly changes in COVID-19 cases (β=124.106; *Z*=10.68; *P*<.001) and COVID-19 vaccinations administered (β=25.288; *Z*=7.63; *P*<.001) were positively and significantly associated with increased COVID-19 vaccine intent relative search volume. In addition, an increase in access to primary care physicians in a county was associated with increased COVID-19 vaccine intent relative search volume (β=0.859; *Z*=3.27; *P*=.001).

The results reported in Table 2 indicated significant associations between several demographic variables and the COVID-19 vaccine intent relative search volume. Wealthier counties were associated with higher COVID-19 vaccine intent relative search volume (β=4.856; *Z*=8.68; *P*<.001). Counties that became more ideologically conservative (β=4.210; *Z*=2.86; *P*=.004) and electoral pivot counties (β=0.553; *Z*=2.10; *P*=.04) were associated with higher COVID-19 vaccine intent relative search volume. Counties that comprised higher proportions of historically underserved populations, particularly non-Hispanic Black people (β=–4.889; *Z*=–6.14; *P*<.001) and non-Hispanic American Indian and Alaska Native people (β=–5.504; *Z*=2.36; *P*=.02) compared with non-Hispanic White people, were associated with lower COVID-19 vaccine intent relative search volume.

Results From Predictive Margins Tests

Figures 3 and 4 graphically illustrate the results from the predictive margins tests of county-level vaccine readiness and vaccine intent Google searches in the United States. Figure 3 denotes the predicted COVID-19 vaccine intent search volume that corresponds with county-level changes in the proportion of wait-and-see individuals, whereas Figure 4 represents the predicted COVID-19 vaccine intent search volume that corresponds with county-level changes in the proportion of vaccine enthusiasts.

Figure 3. Predicted COVID-19 vaccine intent search volume and the county-level change in the proportion of people in the wait-and-see group with 95% CIs in the United States (January 2021 to April 2023). The vertical reference line represents counties for which there was no change in their wait-and-see proportion between study waves.

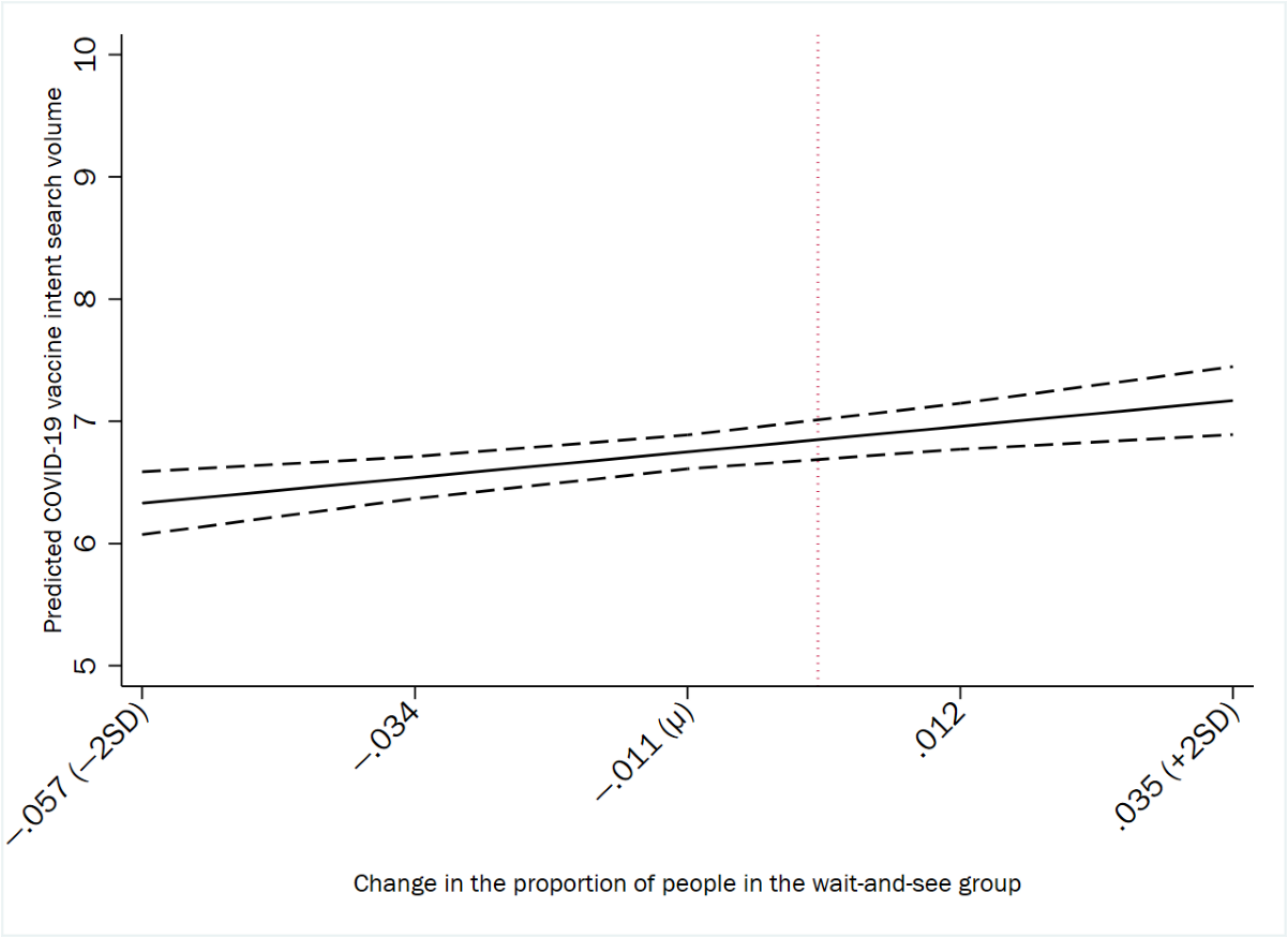
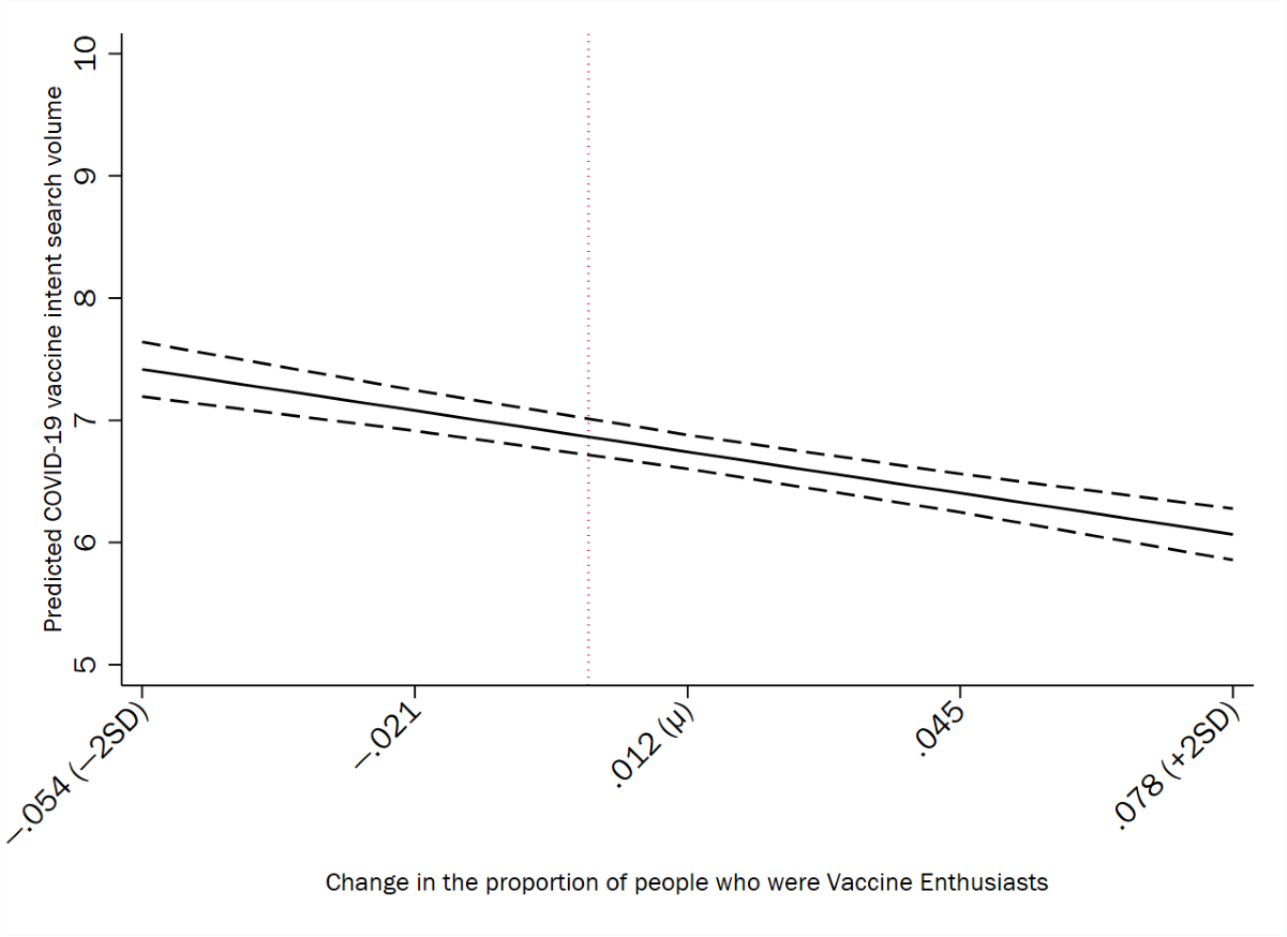


Figure 4. Predicted COVID-19 vaccine intent search volume and the county-level change in the proportion of people who were vaccine enthusiasts with 95% CIs in the United States (January 2021 to April 2023). The vertical reference line represents counties for which there was no change in their vaccine enthusiasm proportion between study waves.



At the county level, the results from predictive margins tests indicate that changes in the proportion of individuals in the wait-and-see group were positively associated with the COVID-19 vaccine intent relative search volume. Specifically, when the change in the county-level wait-and-see proportion moved from 0 (ie, unchanged counties) to a mean of –0.011 (SD 0.023), this difference was associated with a 1.47% decrease in the predicted county-level COVID-19 vaccine intent relative search volume. An increase in the change in the county-level wait-and-see proportion from 0 to 2 SDs above the mean of 0.035 was associated with a predicted county-level COVID-19 vaccine intent relative search volume of 7.169, reflecting a 4.66% increase from unchanged counties. Finally, when the change in the county-level wait-and-see proportion decreased from 0 to 2 SDs below the mean of –0.057, this difference was associated with a predicted COVID-19 vaccine intent relative search volume of 6.330, reflecting a 7.59% decrease from unchanged counties.

Changes in the county-level vaccine enthusiasm were negatively associated with the COVID-19 vaccine intent relative search volume. Specifically, an increase in the county-level vaccine-enthusiast proportion from 0 to a mean of 0.012 (SD 0.033) was associated with a 1.79% decrease in the predicted county-level COVID-19 vaccine intent relative search volume. An increase in the county-level vaccine-enthusiast proportion from 0 to 2 SDs above the mean of 0.078 was associated with a predicted county-level COVID-19 vaccine intent relative search volume of 6.067, reflecting an 11.63% decrease from unchanged counties. A decrease in the change in the county-level vaccine-enthusiast proportion from 0 to 2 SDs below the mean of –0.054 was associated with a predicted COVID-19 vaccine intent relative search volume of 7.417, reflecting an 8.05% increase from unchanged counties.

Robustness Checks

We performed several robustness checks to verify whether the observed results were products of the way in which we operationalized our variables. To check whether our results were a consequence of our choice of dependent variable, we used separate models in which we replaced our dependent variable with the mean COVID-19 vaccine intent relative search volume, minimum COVID-19 vaccine intent relative search volume, maximum COVID-19 vaccine intent relative search volume, aggregate COVID-19 vaccine search volumes, and COVID-19 vaccine safety search volumes. To verify whether our results were a consequence of how we operationalized our control variables, we used separate models in which we disaggregated internet access into 2 components, the natural logs of mobile and fixed internet access rates, and included the natural log of the total number of hospitals per county, the natural log of the number of total hospital staff per capita in each county, substituted naturally logged COVID-19 deaths per capita for naturally logged COVID-19 cases per capita, and 2

operationalizations of the CDC Agency for Toxic Substances and Disease Registry social vulnerability index. In general, these robustness checks did not result in substantive differences in the main findings. These checks provided evidence that the modeling was robust to alternative specifications of the dependent and control variables. More details about the robustness checks are available in Multimedia Appendix 1.

Discussion

Main Findings

This study examined the relationship between COVID-19 vaccine readiness and the COVID-19 vaccine intent relative search volume on Google. High-level findings are summarized in Table 3. Relative to other counties, counties with higher proportions of vaccine enthusiasts were associated with decreases in county-level COVID-19 vaccine intent relative search volume, and counties with higher proportions of individuals in the wait-and-see group were associated with increases in county-level COVID-19 vaccine intent relative search volume.

Table 3. Summary of statistical findings on COVID-19 vaccine intent relative search volume on Google.

Variable	Statistically significant	Direction of effect
Monthly change in vaccine enthusiasts	✓ (*P*<.001)	–
Monthly change in the wait-and-see group	✓ (*P*<.001)	+

Relative to other counties, counties with a higher proportion of people in the wait-and-see group may have had more individuals who perceived an information gap and used web-based searches to fill this gap, leading to observed increases in vaccine intent searches. This proposed explanation aligns with other research showing that information gaps and vaccine hesitancy were associated with increased information-seeking activity, especially during the time frame of the COVID-19 pandemic that we investigated [13,19,20,37,41]. These results suggest that individuals who were hesitant to receive COVID-19 vaccinations sought information on how to get their COVID-19 vaccination once they made the decision to get vaccinated. When these individuals performed intent-related searches, they likely became vaccine enthusiasts (ie, individuals who were ready to get vaccinated or got a COVID-19 vaccine). In aggregate, their decision to become vaccine enthusiasts helped lower fatality rates from COVID-19. Countries that vaccinated >26 million people substantially decreased their COVID-19 fatality rates from an average of 13% to 1% [27].

Our results further showed that several health care capacity and COVID-19 indicators were associated with higher levels of COVID-19 vaccine intent relative search volume. These increases align with research that has linked changes in COVID-19 cases and vaccinations to subsequent rises in COVID-19 vaccine search [4,41]. Results pertaining to health care capacity suggest that there were differences between access to health care information and access to health care resources as they related to COVID-19 vaccine search.

Our main findings remained statistically significant after accounting for county-level sociodemographic characteristics, indicators of county-level public health infrastructure, COVID-19 cases per capita, and COVID-19 vaccination doses per capita and were robust to alternative specifications of the dependent and independent variables. Consistent with the TPB and PRISM as well as prior research on the association between Google searches and COVID-19 vaccine hesitancy [4,37,41], counties that had a high proportion of vaccine enthusiasts had a smaller proportion of people who perceived limitations in their knowledge. This may explain the observed lower levels of vaccine intent searches in these counties.

In line with the TPB and PRISM and previous research on the relationship between Google search and COVID-19 vaccine hesitancy [4,37,41], it is feasible that increases in the proportion of individuals in the wait-and-see group corresponded with greater perceived limitations in their knowledge about mitigating risks related to COVID-19; these individuals may have sought to address these limitations by performing COVID-19 vaccine searches on Google. Once individuals in the wait-and-see group filled their perceived knowledge gap through vaccine searches, there was a corresponding shift from the decision to wait and see toward vaccine enthusiasm. The information acquired through those earlier searches and exposure to more information on COVID-19 vaccines may have influenced individuals' beliefs and attitudes toward vaccination. This shift and belief change may have influenced individuals' decisions to perform vaccine intent searches on Google to gain information about the availability, accessibility, and eligibility of COVID-19 vaccines.

In addition, the internet can act as a valuable information source for supporting health decision-making and other health behaviors. Our study results highlight the importance of having available, actionable, clear, and credible information about health behaviors, as people are more likely to seek health information from the internet when this information is available, clear, actionable, and credible [11,12]. Public health researchers and practitioners may benefit from additional research that queries the extent to which the decision-making processes that we have modeled operate when examining other vaccine-preventable diseases such as influenza and Mpox.

Our findings complement existing research on the effects of information seeking on public health, as we found that a higher county-level proportion of individuals in the wait-and-see group was associated with increases in county-level search volume for COVID-19 vaccine intent. These findings build upon other research that finds a negative association between searches for both "COVID anxiety" and "COVID depression" and the total number of vaccinations between August 2020 and November

2021 [32]. Similarly, there was an initial spike in searches related to the unfounded link between infertility and receiving a COVID-19 vaccine right after the emergency use authorization [38,39], followed by a marked decrease in the volume of these searches as people received COVID-19 vaccinations [40]. As more members of the wait-and-see group became vaccinated in the United States, their decision to become vaccinated helped lower fatality rates from COVID-19 [27]. Thus, increases in county-level proportions of people who became vaccine enthusiasts were associated with decreased county-level search volumes for COVID-19 vaccine intent, COVID anxiety, COVID depression, and infertility as a result of receiving a COVID-19 vaccine.

Moreover, our results suggest that some of the people who most needed access to this information to reduce perceived knowledge gaps about COVID-19 vaccination sought higher volumes of this information than vaccine enthusiasts or members of the no-intention-to-get-vaccinated group. Finally, this research underscores the potential for the use of Google and other web search data as early indicators of or proxies for subsequent health-related behaviors, making them valuable tools for public health efforts or interventions that seek to understand and promote vaccination and other health-related behaviors. Public health interventions or efforts can also use web search data to inform their public education efforts during evolving public health crises in a way that furnishes the information that the public needs to make health decisions.

Limitations

Although the findings from this research present compelling insights, we acknowledge several study limitations. First, Google's reporting of its search metrics was not uniform across data points. Specifically, artificial noise was intentionally added to data points to safeguard user privacy [43,59]. Although the presence of artificial noise in these data introduced some bias, this bias is nonsystematic in nature [59]. Nonsystematic measurement error could influence the certainty of our conclusions, but it did not introduce any systematic bias into the findings [68].

Second, it is possible that our model estimates did not sufficiently consider uneven variance in the COVID-19 vaccine intent relative search volume across counties. To account for uneven variance, we clustered the SEs by county [65]. However, this is a conservative approach to estimating SEs, as any remaining bias in statistical significance tests is likely against obtaining statistically significant findings, as the SEs may be too large [65]. Other approaches to estimating SEs may more effectively account for this uneven variance.

Third, the hypotheses that we tested were specific to the time frame that we examined. At the beginning of this time frame, COVID-19 vaccines were newly introduced to the population and becoming more widely available in the United States. Fourth, there are several limitations to this study related to the MOS small area estimates. These estimates relied on self-reported data from respondents with respect to vaccine readiness. Consequently, this measure may be subject to issues such as recall bias, selective recall, respondent bias, and social desirability bias [69]. In addition, those who solely or primarily speak languages other than English or Spanish are likely underrepresented in these estimates, as the MOS surveys were administered only in English or Spanish.

Fifth, there are 2 limitations related to web-based search. Google search does not represent all web-based searches. Although unlikely, given Google's dominant market share in the United States, it is possible that people varied their search behavior by platform, using some platforms for selected searches while others for different searches. In a similar vein, web-based search is not the only form of information seeking, as people seek health information from many sources, including medical providers [5] and traditional media sources such as broadcast television and radio [6].

Conclusions

Internet-based intent search presents an important signal for vaccine readiness change. During this period of steep increase in the uptake of primary COVID-19 vaccine series [42], the volume of vaccine intent searches was high in high wait-and-see counties and less in counties with high levels of vaccine enthusiasts. Considering that previous findings identified a relationship between vaccine intent search and subsequent vaccine uptake, these findings may indicate that vaccine intent searches aligned with people's transition from the wait-and-see stage to the vaccine-enthusiast stage [41]. Our findings build upon a growing body of literature and indicate an association between changes in COVID-19 vaccine readiness among adults and increased COVID-19 vaccine intent relative search volume. These results reinforce the promise of using search data as a signal, an early measure, or a proxy for subsequent health behaviors and navigate methods to jointly use search and survey data, using web-based search as a proxy for information seeking and decision-making to assess the association of these behavioral precursors and readiness *with* offline health behavior.

Because Google search plays an important role for those in the planning phase before they commit to or act upon health-related behaviors, these results have implications for public health campaign interventions. Google search data can be used to measure public health intervention or effort effectiveness and track the spread of misinformation or hesitancy about health-related behaviors [40,70]. As search trends can often be identified more quickly than self-reported behaviors or beliefs in surveys, this provides an opportunity for more timely strategic pivots by public health interventions or efforts. Thus, Google search data can be used to optimize the use of campaign resources such as paid media advertising and distribution.

Those who undertake public health interventions may provide additional, tailored information to educate the public in the areas in which there may be a higher proportion of those who are hesitant (ie, wait and see) but open to performing a particular positive health behavior (eg, vaccination), as this information can catalyze their decision-making and information-seeking processes toward that behavior. Public health education interventions can also include employer-based vaccine promotion outreach, as evidence indicates that working in organizations with higher perceived COVID-19 safety climates was associated with subsequent increases in vaccine readiness [71].

Similarly, public health interventions can allocate specific, tailored resources to promote positive health behaviors, including establishing additional clinics in selected locales and enhancing local internet infrastructure. To encourage vaccination, especially for children, these resources should be widely accessible with the least possible financial burden on individuals, families, and communities [72]. These resources can make it easier for people to perform health behavior intent searches and follow through with those positive health behaviors as soon as possible.

These results also have implications for public policy and public policy makers because vaccinations are a necessary, but by themselves insufficient, public policy solution to pandemics [25,26,73-76]. Vaccinations are one piece of the broader health policy landscape because there is an upper limit of a population that is vaccinable without encountering vaccine hesitancy [74,75]. While it is possible that vaccination can lead to decreased risk perception, which is postulated in the Peltzman effect [75,77], other literature shows that those who were COVID-19 vaccinated in the United States were also more likely to engage in other COVID-19 prevention behaviors such as mask wearing and social distancing [78]. It is important to use a holistic approach to assess the effectiveness of individual-level measures to modify behavior.

Beyond vaccination distribution and promotion, other country-level measures are associated with improved public health outcomes during pandemics [74]. These include having better early detection systems tracking disease cases [73], improved medical recordkeeping [25], and more resources and support for rapid vaccine development and dissemination [73]. More broadly, countries that had a higher gross domestic product per capita [74], high average levels of health care expenses overall [24], lower levels of air pollution [75], and more effective public governance structures [76] were associated with higher COVID-19 vaccination uptake and fewer negative effects from the COVID-19 pandemic. During pandemics, countries that carefully monitor vaccine intent search data can use data-centric strategies to their benefit. We found a positive association between the county-level proportion of unvaccinated adults who indicated that they would wait and see before getting a COVID-19 vaccine and COVID-19 vaccine intent relative search volume.

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Data Availability

The data sets generated during and analyzed during this study are available from several sources including Google's COVID-19 Vaccination Search Insights database [43], the US Department of Health and Human Services' (HHS) health database [47], the US Centers for Disease Control and Prevention's Weekly United States COVID-19 Cases and Deaths by County database [48], the HHS Area Health Resources Files [49], the US Federal Communications Commission's Form 477 County Data on Internet Access Services [50], and Warshaw and Tausanovitch's [51] Harvard Dataverse for the American Ideology Project.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Additional analyses and description of our analytic procedures.
[DOCX File , 98 KB - ojphi_v16i1e55422_app1.docx]

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Abbreviations

AHRF: Area Health Resources File
CDC: Centers for Disease Control and Prevention
FCC: Federal Communications Commission
HHS: Department of Health and Human Services
MOS: Monthly Outcome Survey
PRISM: Planned Risk Information Seeking Model
TPB: theory of planned behavior

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Improving Vaccine Clinic Efficiency Through the CANImmunize Platform

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Abstract

Our objective was to evaluate the CANImmunize digital solution and measure the impact on workflow and appointment booking at Bruyère Hospital.

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KEYWORDS

digital solutions; vaccine; CANImmunize platform; CANImmunize; platform; Canada; Canadian; workflow; booking; health care; digital health; hospital; patient; personnel

Introduction

Running immunization clinics in any organization or health system requires detailed planning, coordination, and collaboration. Barriers such as long wait times, misinformation about vaccination benefits, operating hours and locations of clinics, and inconsistent methods to record vaccination status contribute to lower vaccination rates [1,2].

CANImmunize Inc is a Canadian technology company that created a digital solution for end-to-end digital vaccine management that permitted centralized web-based booking across multiple clinics; digital preconsent; clinic management; and provision of proof of vaccination records, including integration with provincial registries and supported adverse event reporting systems.

Vaccine clinics are typically paper based, which requires significant human resources. Paper-based data collection is time-consuming, limiting the number of vaccinations that can be administered and making it difficult to track vaccination rates [3]. Our objective was to evaluate the CANImmunize product and measure the impact on workflow and appointment booking.

Methods

Setting and Participants

We implemented CANImmunize between November 2020 and April 2021 at Bruyère Hospital in Ottawa, Ontario. We offered vaccination appointments to staff, their families, and Bruyère Academic Family Health Team primary care clinic patients. All staff and patients were sent information about how to download the app, create an account, and sign up for an appointment.

Digital Solution

CANImmunize software consists of three components—the CANImmunize web portal, ClinicFlow, and the CANImmunize app. The web portal allows patients to book their appointment, complete COVID-19 screening, provide consent for the flu vaccine, and subsequently upload the vaccine receipt into Bruyère's Occupational Health and Safety System. ClinicFlow allows immunizers to handle appointment scheduling by tracking appointments, cycle times, wait times, and the total number of appointments per day. The CANImmunize app provides a permanent record of all patients' immunizations.

Outcomes

During ClinicFlow implementation, we measured the number of vaccinations, appointments, and staff subscriptions to the CANImmunize app and the time spent per appointment. To determine changes in the number of staff vaccine appointments and time spent by immunization clinic staff per appointment, we used data from the year before ClinicFlow was implemented. We used staff hourly rates to calculate the cost savings per vaccination.

Ethical Considerations

Our study qualifies as quality improvement because we report aggregate-level data from an implementation where the primary

purpose was to monitor, evaluate, or improve the quality of services delivered. Therefore, our study was not reviewed by a research ethics board.

Results

Over the study period, 1286 appointments were booked, and 2213 vaccines were administered to staff and their families. Appointments could have ≥1 person; for example, 1 staff member and their 2 children would be 1 appointment that results in 3 vaccines being administered. Each vaccine administrator reported a reduction in the time required for vaccination administration, decreasing from 15 minutes with the paper-based format to 10 minutes with the digital platform, resulting in total time savings of 107.2 hours (1286 appointments × 5 min).

Vaccine clinic staff reported a reduction in the clerical time required to upload staff vaccine data to the database, decreasing from 5 minutes per staff to 0 minutes, resulting in clerical time savings of 79.3 hours (952 staff × 5 min = 4760 min). In total, 952 Bruyère staff were vaccinated, with 174 individuals signing up for CANImmunize after their immunization appointment.

Discussion

Principal Findings

Productivity improved with time and cost savings after CANImmunize implementation. Booking through the app, completing consent forms before visits, easy patient registration, and automatic vaccination record uploading saved staff time and money. Automated record uploading improved the accuracy of vaccination rate tracking.

Consistent with our results, the World Health Organization described digital health as a safe and cost-effective way to use IT to improve health care access [4]. During the COVID-19 pandemic, several booking systems launched globally, becoming increasingly important as the complexities of the vaccine schedule increased due to the need for multiple doses and boosters. Moving forward, digital solutions to health problems will become increasingly important [5,6]. Vaccines will continually be promoted and administered to older populations where uptake has been historically low [7-9]. Therefore, well-developed software that can facilitate vaccine administration is essential.

Key lessons learned during our pilot included the importance of scheduling and family bubbles for improving throughput efficiency while maintaining social distancing, as well as the importance of ease of use among non–technically proficient individuals. These elements were incorporated into the broader population-wide release of the platform and contributed to its relative success.

Conclusions

Digital vaccine clinic booking in a health care facility improved efficiency while facilitating accurate and comprehensive recordkeeping.

Acknowledgments

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Conflicts of Interest

KW is a cofounder and chief scientific officer of CANImmunize Inc.

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Original Paper

Characterization of Post–COVID-19 Definitions and Clinical Coding Practices: Longitudinal Study

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Abstract

Background: Post–COVID-19 condition (colloquially known as “long COVID-19”) characterized as postacute sequelae of SARS-CoV-2 has no universal clinical case definition. Recent efforts have focused on understanding long COVID-19 symptoms, and electronic health record (EHR) data provide a unique resource for understanding this condition. The introduction of the *International Classification of Diseases, Tenth Revision* (*ICD-10*) code U09.9 for “Post COVID-19 condition, unspecified” to identify patients with long COVID-19 has provided a method of evaluating this condition in EHRs; however, the accuracy of this code is unclear.

Objective: This study aimed to characterize the utility and accuracy of the U09.9 code across 3 health care systems—the Veterans Health Administration, the Beth Israel Deaconess Medical Center, and the University of Pittsburgh Medical Center—against patients identified with long COVID-19 via a chart review by operationalizing the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) definitions.

Methods: Patients who were COVID-19 positive with either a U07.1 ICD-10 code or positive polymerase chain reaction test within these health care systems were identified for chart review. Among this cohort, we sampled patients based on two approaches: (1) with a U09.9 code and (2) without a U09.9 code but with a new onset long COVID-19–related ICD-10 code, which allows us to assess the sensitivity of the U09.9 code. To operationalize the long COVID-19 definition based on health agency guidelines, symptoms were grouped into a “core” cluster of 11 commonly reported symptoms among patients with long COVID-19 and an extended cluster that captured all other symptoms by disease domain. Patients having ≥2 symptoms persisting for ≥60 days that were new onset after their COVID-19 infection, with ≥1 symptom in the core cluster, were labeled as having long COVID-19 per chart review. The code’s performance was compared across 3 health care systems and across different time periods of the pandemic.

Results: Overall, 900 patient charts were reviewed across 3 health care systems. The prevalence of long COVID-19 among the cohort with the U09.9 ICD-10 code based on the operationalized WHO definition was between 23.2% and 62.4% across these health care systems. We also evaluated a less stringent version of the WHO definition and the CDC definition and observed an increase in the prevalence of long COVID-19 at all 3 health care systems.

Conclusions: This is one of the first studies to evaluate the U09.9 code against a clinical case definition for long COVID-19, as well as the first to apply this definition to EHR data using a chart review approach on a nationwide cohort across multiple health care systems. This chart review approach can be implemented at other EHR systems to further evaluate the utility and performance of the U09.9 code.

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KEYWORDS

veterans; long COVID-19; postacute sequelae of SARS-CoV-2; PASC; International Classification of Diseases; U09.9 ICD-10 code; algorithm validation; chart review; electronic health records; COVID-19

Introduction

Characterizing the public health burden of postacute sequelae of SARS-CoV-2, also known as post–COVID-19 condition or colloquially as long COVID-19, has been difficult, given that multiple clinical case definitions have been proposed by various international health agencies [1-3]. While the exact components of these definitions vary, they share some common underlying features such as the development of symptoms that are new onset after a COVID-19 infection and the persistence of new onset symptoms for a duration of time after acute infection period. Electronic health records (EHRs) provide a uniquely rich resource for studying this condition at scale, and there have been multiple efforts to describe long COVID-19 symptoms and estimate prevalence in various EHR systems [4-9].

Specifically, the introduction of the *International Classification of Diseases, Tenth Revision* (*ICD-10*) code U09.9 for "Post COVID-19 condition, unspecified" has provided an alternative method of evaluating this condition in EHRs, and its use has been described in various health care systems [10-13]. However, there is no universal diagnostic guideline for defining long COVID-19, and thus, there is no standard guideline for assigning U09.9. The use of the U09.9 code and its accuracy in identifying long COVID-19 have not yet been evaluated against any existing clinical case definitions in a multicenter setting. Clinical coding of long COVID-19 has the potential for misclassification, given the heterogeneity and ambiguity around the definition of long COVID-19 [14].

This study aims (1) to characterize the use of *ICD-10* code U09.9 across 3 health care systems and (2) to evaluate the accuracy of the U09.9 code against patients identified with long COVID-19 via chart review.

Methods

Data Sources and Study Cohort

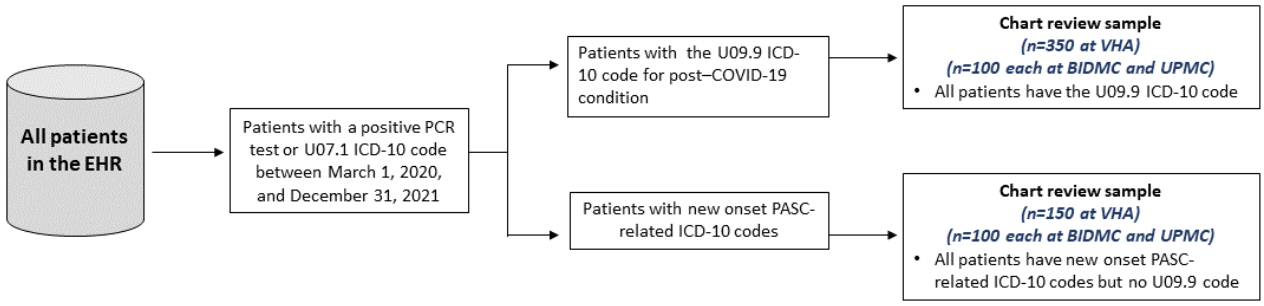
The Consortium for Clinical Characterization of COVID-19 by EHR (4CE) is an international consortium for data-driven studies on the COVID-19 pandemic [15]. Three health care systems from the 4CE contributed chart review results for this study, namely, the national Veterans Health Administration (VHA), the Beth Israel Deaconess Medical Center (BIDMC), and the University of Pittsburgh Medical Center (UPMC). Over 15 million patients are collectively provided care across all 3 health care systems [16-18]. The VHA is the largest integrated health care system in the United States with 171 medical centers throughout the country [16]. The BIDMC is an academic medical center that is part of Beth Israel Lahey health care system located in Boston, and the UPMC is a Pittsburgh-based health care system with 40 hospitals across Pennsylvania [17,18].

EHR data from the 3 health care systems were used to identify patients who were COVID-19 positive, define patient characteristics, and obtain clinical notes for chart review. The sampling strategy for our chart review is described in Figure 1. Patients who had their first incidence of COVID-19 diagnosis reported within the participating health care systems' EHR with either a U07.1 ICD-10 code for "COVID-19" or a positive polymerase chain reaction test performed between March 1, 2020, and December 31, 2021, were identified for chart review. From this COVID-19–positive cohort, we then sampled patients based on two approaches: (1) the presence of the U09.9 ICD-10 code, which was first introduced in the United States in October 2021, or (2) the presence of at least 1 new onset long COVID-19–related ICD-10 code if the patient did not have a U09.9 code. These long COVID-19–related ICD-10 codes were selected to enrich the chart review sample for patients who may potentially have long COVID-19. At the VHA, we further sampled patients from 2 time periods: those who were COVID-19 positive before September 1, 2021 (pre-U09.9 period), and those who were COVID-19 positive after this date (post-U09.9 period).

The presence of long COVID-19–related ICD-10 codes was identified via a data-driven process using EHR data from 10 health care systems at the 4CE [19]. Initial steps consisted of extracting longitudinal codified features such as ICD-10 codes and mapping these codified features to phecodes for new onset of conditions after COVID-19 infection. Phecodes are a curated grouping of ICD-10 codes used to analyze EHR data characterizing specific clinical symptoms or diagnoses [20]. New onset conditions were defined as those that were not present before the initial COVID-19 infection. The conditions were selected such that patients with COVID-19 are associated with a higher risk of a new onset of the condition after adjusting for baseline confounders such as age, sex, self-reported race,

and health care use. Marginal testing using a logistic regression framework was then performed to identify associated new onset conditions emerging 3 months after the initial infection. Conditions that passed marginal testing were then subject to conditional randomization analyses via distillation to robustly test whether a condition's new onset is conditionally dependent on prior COVID-19 infection [19]. The Benjamini-Hochberg procedure was used to adjust for multiple comparisons [21]. Multimedia Appendix 1 [19,20] presents a list of the phecodes identified.

Figure 1. Patient sampling strategy for chart review. BIDMC: Beth Israel Deaconess Medical Center; EHR: electronic health record; ICD-10: International Classification of Diseases, Tenth Revision; PASC: postacute sequelae SARS-CoV-2; PCR: polymerase chain reaction; UPMC: University of Pittsburg Medical Center; VHA: Veterans Health Administration.



Ethical Considerations

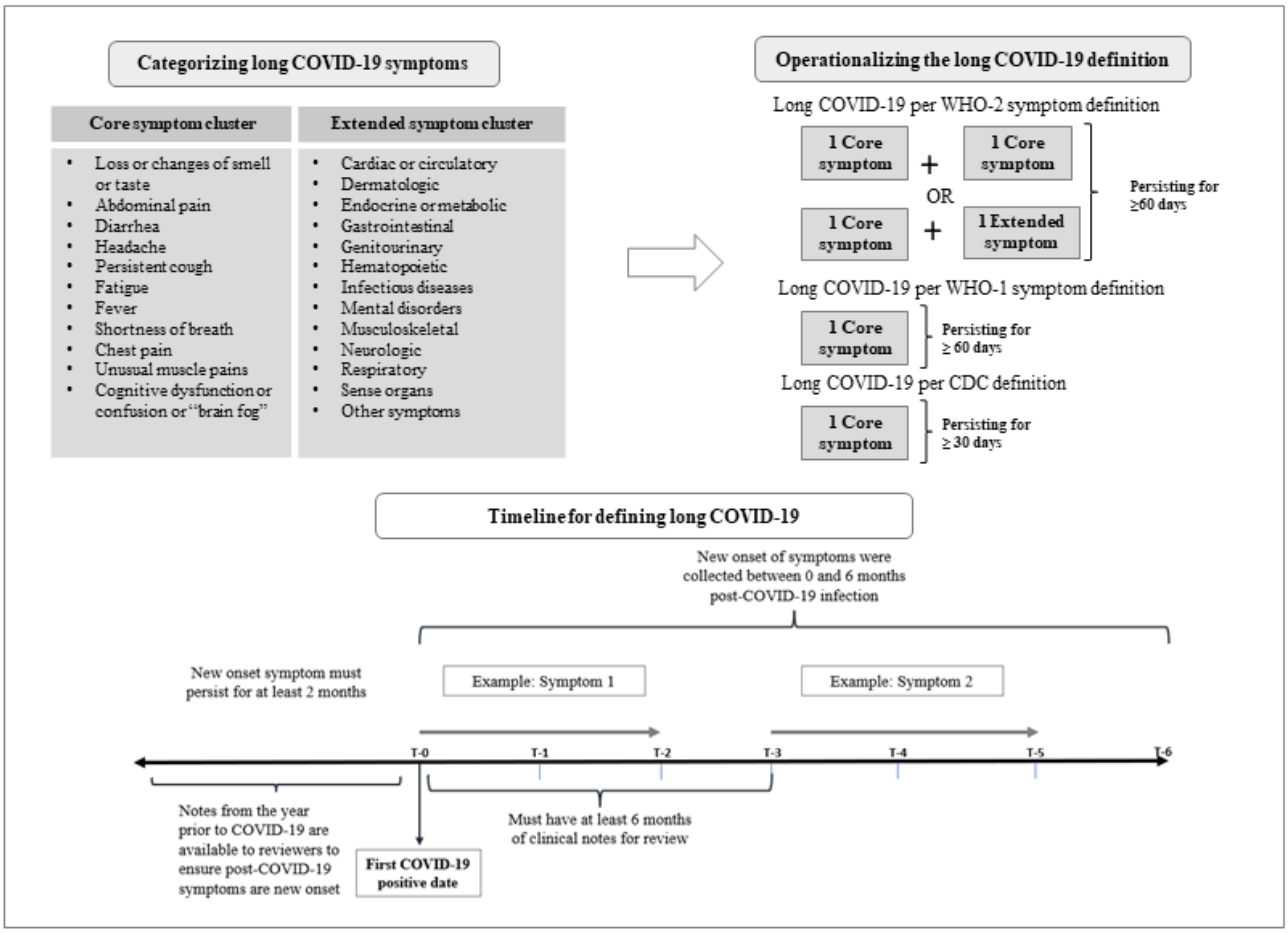
Exempt approval for this study was received by the Central Institutional Review Board at Veterans Affairs Boston Healthcare System (MVP000), BIDMC (2020P000565), and UPMC (STUDY20070095).

Chart Review Approach

The primary aim of our chart review was to operationalize the clinical case definition for long COVID-19 by the World Health Organization (WHO), with secondary aims to compare against a less stringent WHO definition and the Centers for Disease Control and Prevention (CDC) definition [3,22]. The chart review protocol (Multimedia Appendix 2) was developed at the VHA with guidance from 4CE subject matter experts to operationalize the WHO and CDC clinical case definitions. Long COVID-19 symptoms were identified from the WHO definition as well as through a literature review, and 11 commonly occurring symptoms among patients with long COVID-19 were classified into a "core" symptom cluster [23-26]. All other symptoms were classified into an "extended" symptom cluster based on their disease domain, which included cardiovascular, neurological, dermatological, musculoskeletal, digestive, and respiratory domains. For patients to be labeled as having long COVID-19 per the WHO definition during the chart review (reported here as "WHO-2"), at least 2 new onset symptoms after their COVID-19 infection were required (Figure 2). These could be either (1) two "core" symptoms or (2) one "core" and 1 "extended" cluster symptom, each of which must have persisted for 60 days or longer. All sampled patient charts had at least 6 months of clinical notes for review after the incident COVID-19 infection to allow appropriate assessment of symptoms. During chart review, all symptoms were collected based on their onset and duration of persistence for either 30 or 60 days (Multimedia Appendix 2) to allow evaluation against multiple long COVID-19 definitions. The less stringent WHO definition (reported here as "WHO-1") was defined as a patient having just 1 core symptom persisting for at least 60 days or longer, and the CDC definition was defined as a patient having just 1 core symptom persisting for at least 30 days.

Reviewers had access to all clinical notes 1 year prior to the incident COVID-19 infection to determine baseline symptoms and conditions. Any symptoms present at the time of the incident COVID-19 infection or exacerbations of existing conditions were not considered new onset and thus not captured in the review. Chart reviewers were instructed to look for consistent mention or documentation of COVID-19-related symptoms in the notes and mark the duration of persistence (30 or 60 days). However, symptoms that waxed and waned over time were captured. At the VHA, a total of 500 patient charts were reviewed, and 200 patient charts were reviewed at each of the other 2 sites—BIDMC and UPMC.

Figure 2. Chart review approach. CDC: Centers for Disease Control; WHO: World Health Organization.



Characterizing the U09.9 ICD-10 Code

To characterize the use of the U09.9 ICD-10 code in clinical practice, the following three metrics were investigated: (1) the frequency of the U09.9 code used over time from October 2021 to September 2022, (2) the frequency of the U09.9 code used across Veterans Integrated Service Networks (VISNs; which are regional systems of care at the VHA), and (3) the time elapsed between COVID-19 diagnosis and U09.9 code assignment.

Results

Characteristics of Study Cohort

Demographics and cohort sizes across the health care systems varied; notably, patients in VHA who had a COVID-19 diagnosis between March 1, 2020, and December 31, 2021, were generally White and male veterans. Among those who were assigned a U09.9 code, the demographics were generally similar with a few notable exceptions (Table 1). At the BIDMC and UPMC, however, the demographics were different, with a higher proportion of female patients who were assigned the U09.9 code. We also observed across all 3 health care systems that a higher proportion of those assigned a U09.9 code had received at least 1 dose of a COVID-19 vaccine compared to the general population of patients who were COVID-19 positive.

We observed a substantial variation in the use of the U09.9 code to diagnose long COVID-19 over time and region. Figures 3 and 4 show the results of our characterizations of the U09.9 code use 12 months following its introduction in the United States on October 1, 2021. Figure 3 shows the frequency of the U09.9 code diagnosis per 10,000 new COVID-19 cases that occurred in the last 12 months from when they received the code. Results from the 3 health care systems were anonymized so as to provide an unbiased interpretation. The frequency of the U09.9 code used to diagnose long COVID-19 was highest from January to March 2022 at health care system 1, from February to March 2022 at health care system 2, and from December 2021 to January 2022 at health care system 3.

There were also large regional differences in the use of the U09.9 code across VHA health care system VISNs (Figure 4). VISN17 assigned the U09.9 code to 28.4% (6304/22,196) of all patients who received this code at the VHA, while VISN1 assigned the U09.9 code to just 2.4% (533/22,196) of all patients who received the code at the VHA.

Table 1. Patient demographics.

Demographics	Patient cohort and health care system								
	All patients who were COVID-19 positive[a] from March 1, 2020, to December 31, 2021			All patients who were COVID-19 positive[a] with a U09.9 ICD-10[b] code			All patients who were COVID-19 positive[a] with a new onset long COVID-19 feature		
	VHA[c] (n=307,909)	BIDMC[d] (n=30,294)	UPMC[e] (n=147,653)	VHA (n=22,196)	BIDMC (n=164)	UPMC (n=6057)	VHA (n=294,302)	BIDMC (n=7245)	UPMC (n=92,120)
Age at incident COVID-19 diagnosis (years), mean (SD)	59.2 (16.1)	47.5 (20.5)	45.7 (23.8)	61.7 (15.1)	54.7 (13.9)	55.1 (17.2)	61.2 (15.7)	54.6 (18.4)	47.5 (24.1)
Sex, n (%)									
Male	272,957 (88.7)	16,579 (54.7)	63,421 (43)	19,275 (86.8)	58 (35.4)	2219 (36.6)	260,055 (88.4)	2947 (40.67)	38,348 (41.6)
Female	34,898 (11.3)	13,715 (45.3)	84,232 (57)	2921 (13.2)	106 (64.6)	3838 (63.4)	34,214 (11.6)	4298 (59.3)	53,772 (58.4)
Race, n (%)									
American Indian or Alaska Native	3521 (1.1)	31 (0.1)	704 (0.5)	273 (1.2)	1 (0.6)	0 (0)	3282 (1.1)	8 (0.1)	493 (0.5)
Asian	3326 (1.1)	1200 (4)	1303 (0.9)	249 (1.1)	4 (2.4)	70 (1.2)	3360 (1.1)	270 (3.7)	986 (1.1)
Black or African American	69,067 (22.4)	5074 (16.7)	14,966 (10.1)	3621 (16.3)	29 (17.7)	880 (14.5)	69,037 (26.5)	1730 (23.9)	10,564 (11.5)
Native Hawaiian or Pacific Islander	3189 (1)	21 (0.07)	35 (0.02)	239 (1.1)	0 (0)	0 (0)	3018 (1)	9 (0.1)	0 (0)
White	208,457 (67.7)	8983 (29.7)	125,503 (85)	16,102 (72.5)	105 (64)	4965 (82)	197,237 (67)	3096 (42.7)	77,471 (84.1)
Not reported	0 (0)	14,985 (49.5)	5141 (3.5)	0 (0)	25 (15.2)	142 (2.3)	0 (0)	2132 (29.4)	2606 (2.8)
Vaccination status, n (%)									
Received at least 1 dose of COVID-19 vaccine	199,235 (64.7)	9649 (31.9)	58,244 (39.4)	15,295 (68.9)	112 (68.3)	3521 (58.1)	203,569 (69.2)	4470 (61.7)	41,271 (44.8)
Did not receive at least 1 dose of COVID-19 vaccine	104,907 (34.1)	20,645 (68.1)	89,409 (60.6)	6684 (30.9)	52 (31.7)	2536 (41.9)	87,569 (29.8)	2775 (38.3)	50,849 (55.2)

[a]COVID-19 positive is defined as a patient having either a U07.1 ICD-10 code or a documented positive polymerase chain reaction test.

[b]ICD-10: International Classification of Diseases, Tenth Revision.

[c]VHA: Veterans Health Administration.

[d]BIDMC: Beth Israel Deaconess Medical Center.

[e]UPMC: University of Pittsburgh Medical Center.

Figure 3. Frequency of a new U09.9 ICD-10 code assignment per 10,000 new COVID-19 cases in the last 12 months, not including the month of U09.9 diagnosis. HS: health care system; ICD-10: International Classification of Diseases, Tenth Revision.

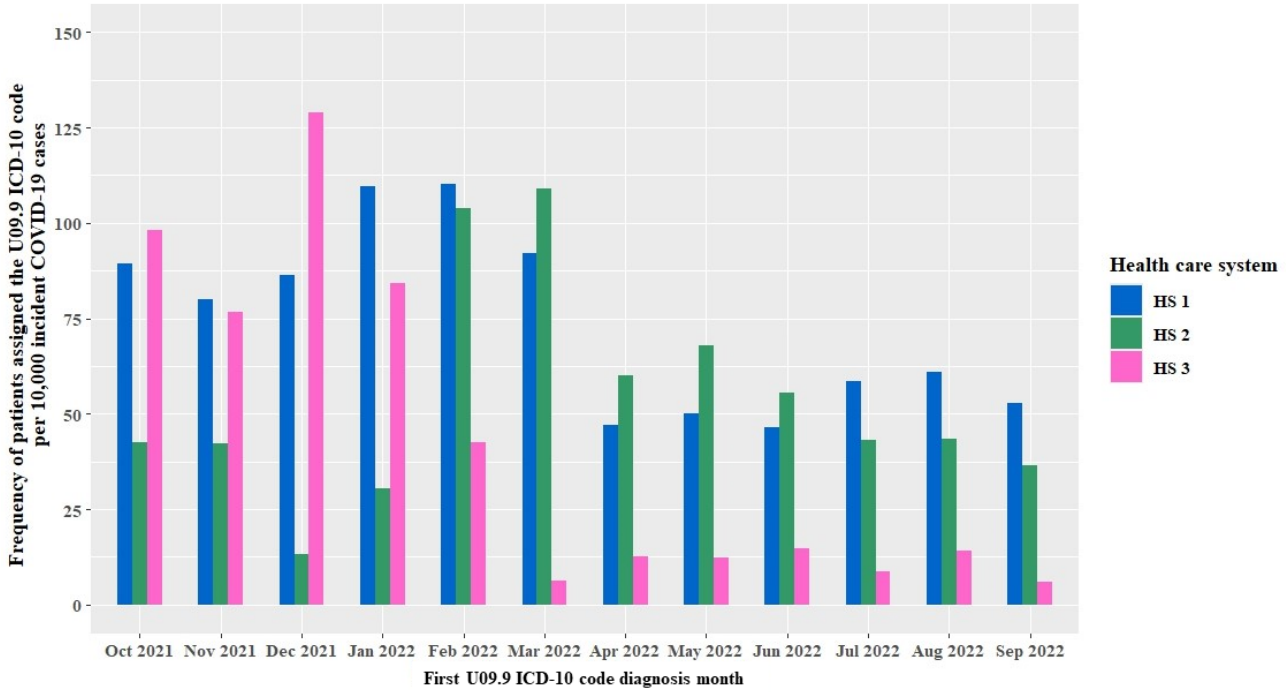
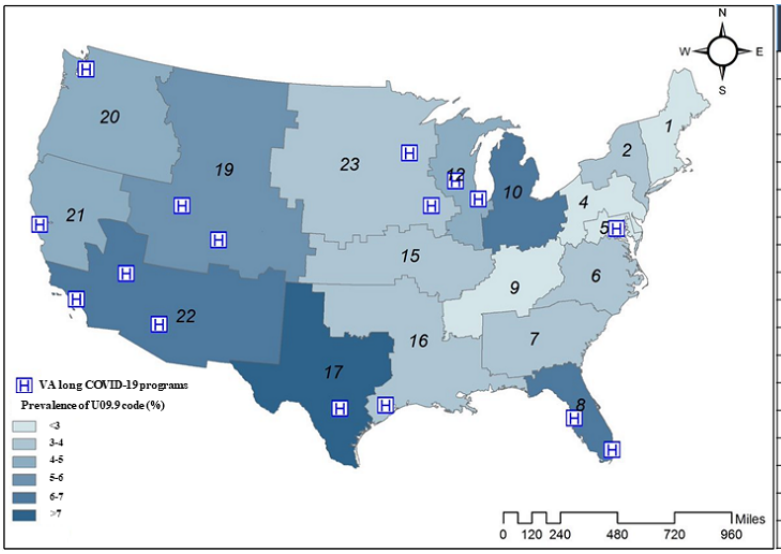


Figure 4. Prevalence of the U09.9 ICD-10 code by region. ICD-10: International Classification of Diseases, Tenth Revision; VA: Veterans Affairs; VISN: Veterans Integrated Service Networks.



VISN	Prevalence of U09.9 code (%)	Location
1	2.40	VA New England Healthcare System
2	3.50	New York or New Jersey VA Healthcare Network
4	3	VA Healthcare
5	3	VA Capitol Health Care Network
6	4	VA Mid-Atlantic Health Care Network
7	3.5	VA Southeast Network
8	7	VA Sunshine Healthcare Network
9	2.7	VA MidSouth Healthcare Network
10	6.4	VA Healthcare System
12	4.7	VA Great Lakes Health Care System
15	3.4	VA Heartland Network
16	3.8	South Central VA Health Care Network
17	28.4	VA Heart of Texas Health Care Network
19	5.4	Rocky Mountain Network
20	4.2	Northwest Network
21	4.5	Sierra Pacific Network
22	6.4	Desert Pacific Healthcare Network
23	3.9	VA Midwest Health Care Network

Chart Review Results

Chart review at the VHA was conducted by 2 clinical reviewers (M Maripuri and JH) with a 1% overlap and an interrater reliability of 80%. At the BIDMC and UPMC, a chart review was conducted by 1 clinical reviewer (BB-J and MJS, respectively). The most common symptoms identified during chart review among patients with long COVID-19 as per the WHO-2 definition were shortness of breath, fatigue, cough, and loss of smell or taste from the core symptom cluster. Among the extended symptom clusters, we most commonly saw symptoms across the cardiovascular, gastrointestinal, neurological, and respiratory disease domains.

Chart review was performed on a total of 900 patients infected with COVID-19 across 3 health care systems. These 3 institutions were anonymized to provide an unbiased interpretation of the results. The performance of the U09.9 code was evaluated by calculating the positive predictive value (PPV) or the probability of having long COVID-19 (as defined by chart review classification) among the patients who had the U09.9 code. When using the WHO-2 definition to define long COVID-19, the PPV was 29.8% at health care system 1 and 62.4% and 23.2% at health care systems 2 and 3, respectively (Figure 5). However, when we consider the WHO-1 and the CDC definitions, the PPV of long COVID-19 was higher at all 3 health care systems, but at health care system 2, the PPV was slightly higher for the WHO-1 definition and remained the same for the CDC definition (Figure 5).

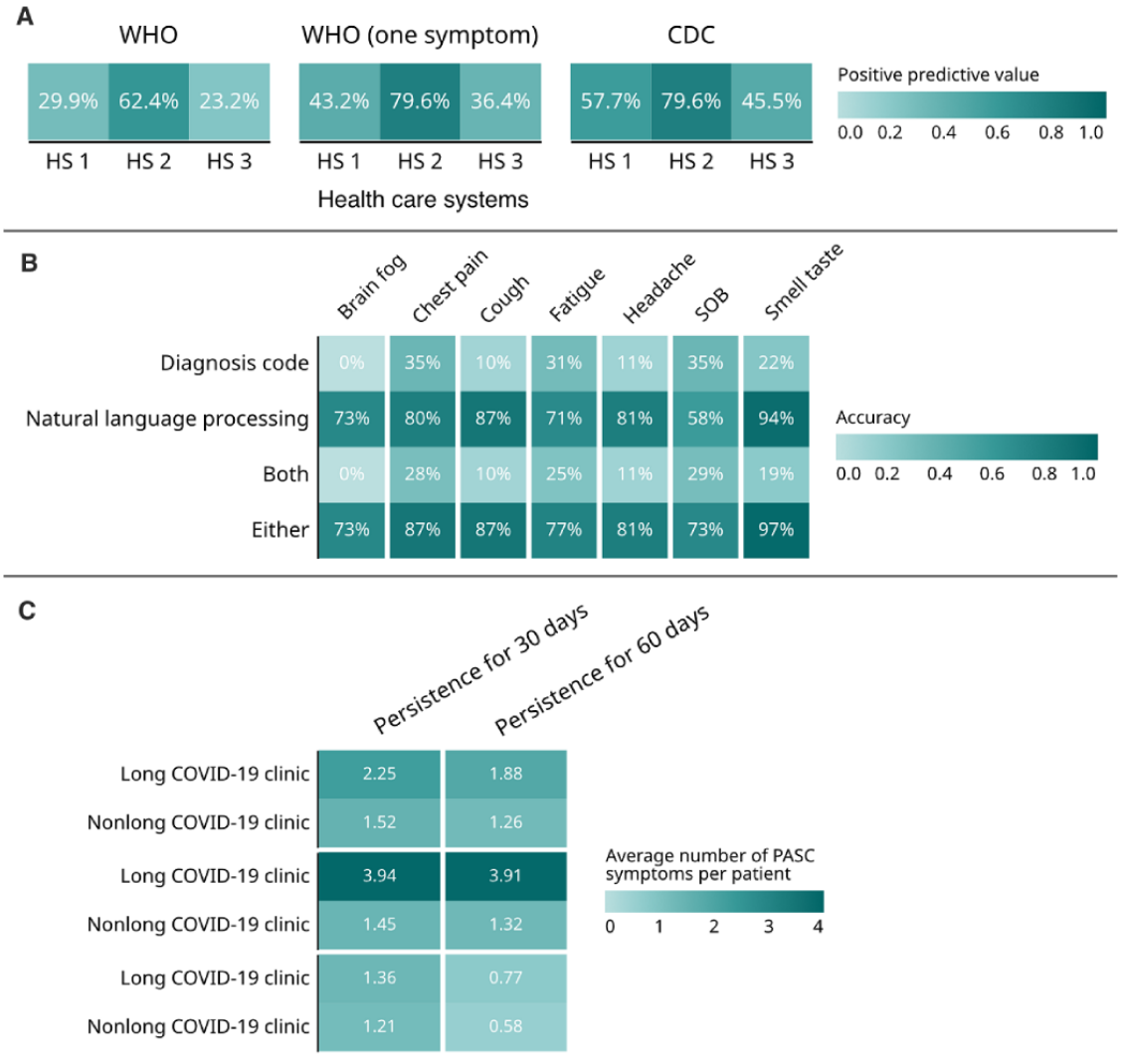
We also evaluated PPV in the sample of patients with new onset long COVID-19 features. Using the WHO-2 definition, the PPV was 7% at health care system 1 and 6.7% and 3% at health care systems 2 and 3, respectively.

Weighted sensitivity calculations were used due to the nonrandom nature of our labeled set in relation to the overall cohort. Our approach involved a random sampling of patients with the U09.9 code, while those without this code were intentionally downsampled. Applying standard sensitivity calculations to such a biased labeled set could lead to misleading results. To counteract this, weighted sensitivity was used, which assigns a specific sampling weight to each case in our labeled data set. This weight is calculated to be inversely proportional to the likelihood of a case's inclusion in the sample. By integrating this weighting system, we ensure that each case's contribution to the sensitivity analysis accurately mirrors its representation in the full cohort, thereby yielding more representative and reliable results. The overall performance of the U09.9 code based on the WHO-2 definition resulted in a weighted sensitivity of 15% at health care system 1 and 4.9% and 19.1% at health care systems 2 and 3, respectively.

Additionally, at the VHA, we looked at the prevalence of long COVID-19 among patients with the U09.9 ICD-10 code across different time periods based on their first COVID-19 infection date. From the chart reviewed cohort, 44.6% (50/112) had long COVID-19 from the pre-U09.9 period and 22.7% (53/233) from the post-U09.9 period at the VHA. The PPV of patients with long COVID-19 in the pre-U09.9 period is higher, as many of these patients were backcoded.

Through our chart review, we observed that patients were given the U09.9 code over a wide range of time from fewer than 29 days to over 365 days following their initial COVID-19 infection. Most patients did not have persisting symptoms after acute infection, and waxing and waning of symptoms were frequently observed.

Figure 5. Comparison of results among all sites. (A) Predictive values of ICD-10 U09.9 code for various clinical definitions of long COVID-19. (B) Capture of PASC symptoms using diagnosis codes and natural language processing data. (C) Average number of new onset PASC symptoms in long COVID-19 clinic patients. CDC: Centers for Disease Control; HS: health care system; ICD-10: International Classification of Diseases, Tenth Revision; PASC: postacute sequelae of SARS-CoV-2; SOB: shortness of breath; WHO: World Health Organization.



Discussion

Principal Results

This study provides a comprehensive, multicenter evaluation of the U09.9 code against proposed clinical case definitions for long COVID-19. It is also one of the first studies to apply a clinical case definition to EHR data using a chart review approach. The use of EHR data allowed evaluation of the U09.9 code across multiple health care systems nationwide. The availability of ample clinical notes enabled reviewers to ascertain whether observed symptoms after COVID-19 infection were truly new onset and to evaluate the duration of new symptoms, which are critical components of case definitions for long COVID-19. Another strength of this study was that we evaluated both the WHO and CDC clinical case definitions for long COVID-19 since one universal definition is not currently available. Our symptom collection approach (Multimedia Appendix 2) captured discrete symptoms by the duration of 30 or 60 days, which allowed for multiple case definitions to be applied.

There were large variations in the accuracy of the use of the U09.9 code for long COVID-19. We observed that 1 center had a much higher predictive value for patients with long COVID-19 among the U09.9 cohort across all definitions than the other 2 health care systems. This health care system also had the highest average number of new onset symptoms among patients seen in long COVID-19 clinics. The U09.9 code assignment at this health care system could have been more accurate due to a higher proportion of patients being seen at long COVID-19 clinics.

In a recent publication on this work, we also evaluated the capture of long COVID-19 symptoms using ICD-10 codes and natural language processing (NLP) data [14]. The Narrative Information Linear Extraction NLP tool was used to extract relevant concept unique identifiers that were manually mapped to each of the long COVID-19 symptoms we studied [27]. Among the chart-reviewed patients with the U09.9 code, we then identified the ones who had the various symptoms through the chart review. We then assessed what proportion of them with the symptom (ie, brain fog) had a corresponding ICD-10 or concept unique identifier mention of the concept and calculated the proportion of patients with the NLP or codified data capture. We shared the findings from this evaluation in Figure 5B. The performance of NLP was significantly better for all the commonly occurring long COVID-19 symptoms. The accuracy of using either a diagnosis code or NLP had the best results with 97% accuracy for loss of smell or taste and 87% accuracy for chest pain and cough.

Limitations

There were several limitations to this study. The cohort at the VHA had a higher proportion of male patients who were generally older and predominantly White. Incident COVID-19 infection was required for inclusion in the chart review, and it is possible that patients had an infection outside of the health care systems that was not recorded in the EHR. Patients may have also had symptoms that were not reported at health care system visits. The variation in the number of long COVID-19 clinics across regions may have led to a differential capture of symptoms for those patients who were seen at long COVID-19 clinics versus those who were seen by their primary care providers. We observed that symptoms among these patients were well documented as most long COVID-19 clinics have a specific template for evaluating and capturing COVID-19 symptoms [28]. In some instances, it was difficult to assess whether a symptom was truly new onset due to COVID-19 infection or a result of underlying health conditions noted at baseline. While the WHO definition has been in use since 2021, long COVID-19 is still an evolving disease, and the case definition may change over time as the condition is further characterized. We also faced some challenges in optimizing a heterogenous and sparse data capture within the EHR systems.

Comparison With Prior Work

The use of the U09.9 code has been described in several cohorts. The National Institutes of Health's National COVID Cohort Collaborative (N3C) reported on the growing use of U09.9 from October 2021 through January 2022 in a nationwide cohort of 21,072 patients with the code [10]. However, the N3C did not require patients in the cohort to have a positive COVID-19 test to evaluate the use of the U09.9 code, and 37.2% (n=12,550) of patients did not have a COVID-19 index date. McGrath et al [12] also reported increasing use of the U09.9 code in the months following its release in the nationwide HealthVerity cohort of 56,143 patients with a U09.9 code that included children younger than 18 years of age. Similar to the N3C, this cohort did not require a COVID-19 positive test for evaluation of the U09.9 code, and only 70.4% (n=8879) had a documented COVID-19 infection. Of the patients who were COVID-19 positive with U09.9, the median time from infection to U09.9 diagnosis was 56 (21-200) days. A study in Sweden by Bygdell et al [11] reported 10,196 patients with the U09.9 code. They also found that 2% of the population who were COVID-19 positive in the 2 largest regions of Sweden had U09.9 at least 28 days after infection.

Conclusions

Our findings suggest that the U09.9 code should be used judiciously in EHR-based studies of long COVID-19. Given the low PPV of the U09.9 code, its use as a proxy for long COVID-19 is not recommended. However, the sensitivity of the code makes it useful for identifying patients who may have long COVID-19 and thus require further clinical evaluation.

This was one of the initial efforts toward validating long COVID-19 against a clinical case definition and the U09.9 code through a chart review on a nationwide cohort. The chart review approach developed at the VHA can be implemented at other EHR systems to further evaluate the utility and performance of the U09.9 code. Further efforts to develop a more refined and reproducible phenotyping algorithm for long COVID-19 using NLP are underway, using the chart review labels from our study for algorithm training and development.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Selected postacute sequelae of SARS-CoV-2 feature phecodes.
[DOCX File , 25 KB - ojphi_v16i1e53445_app1.docx]

Multimedia Appendix 2
Chart review protocol.
[DOCX File , 27 KB - ojphi_v16i1e53445_app2.docx]

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Abbreviations

4CE: Consortium for Clinical Characterization of COVID-19 by Electronic Health Record
BIDMC: Beth Israel Deaconess Medical Center
CDC: Centers for Disease Control and Prevention
EHR: electronic health record
ICD-10: International Classification of Diseases, Tenth Revision
N3C: National COVID Cohort Collaborative
NLP: natural language processing
PPV: positive predictive value
UPMC: University of Pittsburg Medical Center
VHA: Veterans Health Administration
VISN: Veterans Integrated Service Networks
WHO: World Health Organization

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