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Contents

Viewpoint

Review

Original Papers

The Pandemic, Infodemic, and People's Resilience in India: Viewpoint

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Abstract

The COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused widespread fear and stress. The pandemic has affected everyone, everywhere, and created systemic inequities, leaving no one behind. In India alone, more than 34,094,373 confirmed COVID-19 cases and 452,454 related deaths have been reported as of October 19, 2021. Around May 2021, the daily number of new COVID-19 cases crossed the 400,000 mark, seriously hampering the health care system. Despite the devastating situation, the public response was seen through their efforts to come forward with innovative ideas for potential ways to combat the pandemic, for instance, dealing with the shortage of oxygen cylinders and hospital bed availability. With increasing COVID-19 vaccination rates since September 2021, along with the diminishing number of daily new cases, the country is conducting preventive and preparatory measures for the third wave. In this article, we propose the pivotal role of public participation and digital solutions to re-establish our society and describe how Sustainable Development Goals (SDGs) can support eHealth initiatives and mitigate infodemics to tackle a postpandemic situation. This viewpoint reflects that the COVID-19 pandemic has featured a need to bring together research findings across disciplines, build greater coherence within the field, and be a driving force for multi-sectoral, cross-disciplinary collaboration. The article also highlights the various needs to develop digital solutions that can be applied to pandemic situations and be reprocessed to focus on other SDGs. Promoting the use of digital health care solutions to implement preventive measures can be enhanced by public empowerment and engagement. Wearable technologies can be efficiently used for remote monitoring or home-based care for patients with chronic conditions. Furthermore, the development and implementation of informational tools can aid the improvement of well-being and dissolve panic-ridden behaviors contributing toward infodemics. Thus, a call to action for an observatory of digital health initiatives on COVID-19 is required to share the main conclusions and lessons learned in terms of resilience, crisis mitigation, and preparedness.

Introduction

The rapid spread of COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in extensive panic among the public. The COVID-19 pandemic has impaired social values as well as the economy of the country, thereby creating systemic inequities [1]. In a highly populous country like India, the pandemic has pulled down the

economic progress attained in recent years by people belonging to lower and middle socioeconomic classes, and it has pushed 230 million people into poverty [2]. In India alone, there were more than 34,094,373 confirmed COVID-19 cases and 452,454 related deaths reported as of October 19, 2021 [3]. With most Indian cities reporting COVID-19 cases and a government restriction on operating hours for businesses, there has been a large exodus of workers from cities to rural areas. This raised a unique challenge for the health system, as rural areas lacked health infrastructure such as medical supplies and equipment required for testing and providing essential health care to people (see Multimedia Appendix 1). The dire snapshot of the COVID-19 crisis in India reflects underinvestment in both its health care and public health system. Moreover, misinformation circulating in social media has driven panic at a pace and scale never experienced before. A study surveyed panic levels, ranging from 0 (minimum) to 5 (maximum), among 1075 social media users, wherein higher panic levels were reported among Indian users [4].

Following the first case of COVID-19 reported in India, the government took a bold step to lock down the country of 1.3 billion people [5]. India was proactive in curbing the COVID-19 pandemic by taking steps to strengthen its health care system and infrastructure and by manufacturing personal protective equipment (PPE). A national task force was established by the Indian Council of Medical Research to initiate research studies and identify priorities for clinical research, epidemiology, surveillance, diagnostics, biomarkers, vaccines, and drug development [6]. As a result, India reported one of the lowest rates of COVID-19–related mortality in the early stages of the pandemic. Nonenforcement of policies by the Indian government to ensure public adherence to face masks, sanitation, hygiene, and social distancing likely caused silent widespread transmission of COVID-19 [7].

The second wave of COVID-19 had proven to be rampant and virulent (Figure 1 [8]). The new "double mutant variant" of coronavirus had been detected, which was considered a variant of concern due to its immune escape properties, and it was known to have high infectivity and transmission rates. Despite these variants of concern, other possible factors for the surge in cases likely include noncompliance of COVID-19–appropriate behavior by the citizens and the widespread reopening of economic activity. In addition, general elections in multiple Indian states and religious mass gatherings, such as the "Kumbh Mela" (from April 1 to 17, 2021), were considered as super-spreader events, as they resulted in thousands of COVID-19–positive cases (see Multimedia Appendix 1). As pilgrims continued their travels and returned home, they further spread the infection in cities across India.

One major challenge related to COVID-19 in India was the apparent lack of data access and availability for analysis or data modeling from the Indian Council of Medical Research [9,10]. The delayed access and the lack of testing and sequencing capacities led to the sequencing of less than 1% of total positive samples, compared to 4% in the United States and 8% in the United Kingdom [9]. Despite these delays and rising concerns, the general public carried out various measures to mitigate the infection spread by using emerging technologies and social media strategies. Through this viewpoint, we propose the pivotal role of digital solutions and public participation to re-establish our society and describe how Sustainable Development Goals (SDGs) can support eHealth initiatives. In the sections below, we describe the situation of overwhelming health systems, community resilience initiatives and their implications in health care delivery, and finally, how digital health solutions can help achieve SDGs and mitigate pandemics.

Figure 1. The trend of daily new cases and deaths in India from April 2020 to October 2021; adapted from the World Health Organization COVID-19 Explorer [8].
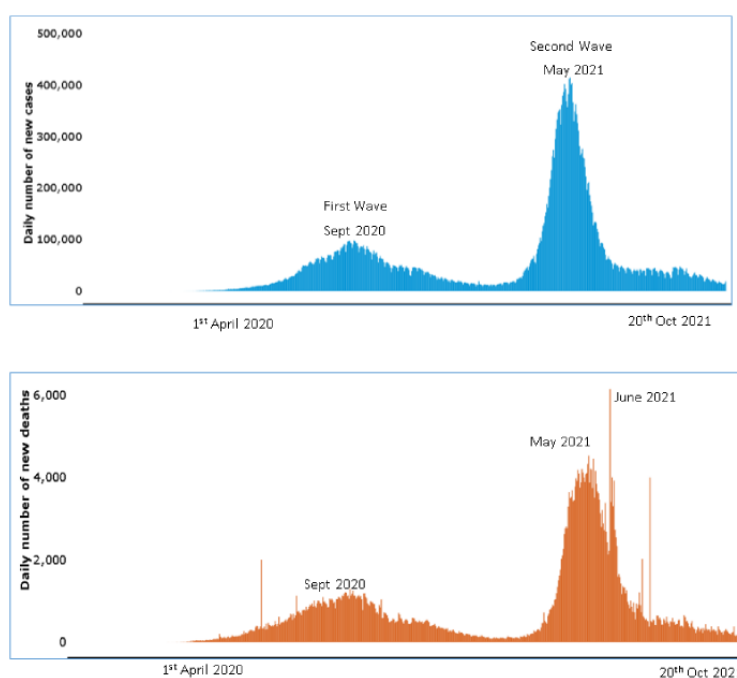
Overwhelming the Capacity of Health Systems

Despite the slow and gradual increase in the number of COVID-19 cases since January 2021, it was only on April 2, 2021, that the government raised alarm, labeling the situation as grim and serious. Although the evidence from other geographical territories showed that a rapid increase in COVID-19 cases could seriously disrupt health delivery systems, create stress in the health workforce, limit access to hospital services, and increase mortality, limited efforts were made to address this surge capacity. In May 2020, an analysis by National Institution for Transforming India (NITI) Aayog—India's nodal policy planning agency—identified the severe dearth of medical equipment, such as testing kits, PPE, masks, and ventilators. The agency also noted the long-running shortage of emergency health care and lack of professionals, with the ratio of doctors to patients recorded as 1:1445, that of hospital beds to people recorded as 0.7:1000, and that of ventilator to population recorded as 40,000 to 1.3 billion (1:130,000) [11]. Efforts to address these gaps comprehensively have been inadequate.

Community Resilience Initiatives and Their implications for Health Services Delivery Models

In the last few years, there has been an exponential growth in the use of digital technologies in the Indian population. Furthermore, there has been a rapid development of telehealth services through the web-based registration system in India that leverages the expanding health information technology infrastructure [12-15]. Moreover, India is one of the powerhouses for the development of mobile and web-based solutions. As such, one should not be surprised that many digital solutions are emerging, such as the development of groups and websites to assist people in finding crematoriums amidst the ongoing devastating crisis or locating hospitals with available beds [16,17]. Apart from the government, community-based initiatives such as the involvement of religious organizations, welfare groups such as the Rotary Club and Lions Club, as well as individuals and social influencers were at the frontline to spread awareness and provide support [18]. Digital reach has further empowered the urban community groups to catalyze their initiative from COVID-19 awareness to mitigation. All these initiatives had an impact on countless families and were often led by the community. This impact included ensuring proper information sharing and health communication, training of primary health care workers in identifying and deflating misinformation and providing simple and relevant sources of updated information [19,20]. These are prime examples of citizen science and participatory health [21].

Social media emerged as a glimmer of hope amid the ongoing COVID-19 crisis. With hospitals struggling to maintain enough medical supplies and preventing shortage of oxygen, several people have resorted to sending out SOS calls on social media. Most people publishing such posts on social media platforms have been seeking beds, oxygen, and convalescent plasma. Hospitals across India have also been regularly using social media hashtags, such as #Covid19IndiaHelp, #SOSDelhi, and #helpcovidindia, on Twitter to seek urgent help, specifically to circumvent oxygen shortages [22]. Several web-based resources have been a source of crucial information, for example, a data science platform was used to collate various resources, ranging from oxygen to intensive care unit (ICU) beds and essential medicines from different places across India [12,16,17]. Many of these resources provide a comprehensive dashboard for COVID-19 resources in Indian cities. Mobile apps were able to provide information on oxygen cylinders, ICU beds, medicines, and plasma availability. Twitter India launched a *COVID-19 Resources* page featuring SOS calls and tweets that offer help to patients who require services, such as ambulance, oxygen, medicines, and ICU beds. Volunteer-led platforms such as Project StepOne offered tele-triage and teleconsultations for individuals with COVID-19 symptoms and provided self-management support at home through remote monitoring. This platform has over 7000 impaneled doctors and is partnering with 16 state governments to address COVID-19 management through telemedicine solutions [23,24].

Digital Health and SDGs to Mitigate Infodemics

Misinformation is its own pandemic [25]. The uncertainties related to diagnosis and treatment of COVID-19 have led to a significant growth of health misinformation, transforming an infrastructure of health promotion into that of health conspiracy. Misinformation does not stop at national borders and requires the development and coordination of initiatives, with partners to promote and ensure healthy lives and well-being for people of all age groups. The COVID-19 pandemic has highlighted a need to bring together findings across disciplines, build greater coherence within the field, and serve as a driving force for multi-sectoral, cross-disciplinary collaboration. In the first few months of the COVID-19 pandemic, about 2300 reports on COVID-19–related misinformation were published in 25 different languages across 87 countries. Following the spread of misinformation, 5876 hospitalizations and 800 deaths were reported [26]. The United Nations SDGs are extremely relevant, as they help us understand the broad impacts of the COVID-19 crisis through an economic, social, and environmental lens and play an important role in ensuring that one crisis does not fuel the development of another. Disease and poverty may interact with each other, especially considering that over 736 million people in the world live in extreme poverty and are unduly affected by ill health, thus impacting SDG1 (no poverty) [20]. Furthermore, the COVID-19 crisis is expected to generate increasing food insecurity, especially among low-income groups. This can affect SDG 2 (zero hunger) and surge the need for food sources and public nutrition provision [20]. Published studies indicate that the SDG for good health and well-being (SDG3) will be difficult to achieve, as the COVID-19 pandemic has caused India to delve into poverty and inequality [27].

Disinformation works against the purpose of education and learning. Collective mobilization of knowledge to promote

quality education (SDG4) and lifelong learning provides the necessary tools to fight the tsunami of infodemic exacerbated by the COVID-19 pandemic through teaching (at the individual level) strategies to spot misinformation, verify the source of information, and educate the public about research bias. The transformative effects of digital knowledge, literacy, and skills can enable users to understand ethics and human rights to defend against the fabrication and dissemination of disinformation. Although this may help individuals discern authentic information, it may also undermine their trust in science and lead to disinterest [28].

According to reports, interventions supported via SDG4 may improve learning strategies to identify misinformation; however, they may not necessarily reduce sharing of misinformation [29]. Evidence from a 2020 study suggests that information overload and trust in information on the internet are strong predictors of unverified information sharing [30]. The path forward toward media literacy will need to include educational institutions adopting an evidence-based media literacy curriculum to enable individuals to discern fact from opinion. This has been practiced by many educational institutions around the world. Training provided by WhatsApp and the National Association of Software and Service Companies through in-person events in India and social media posts would be critical to identify misinformation [28]. Educational campaigns and the development of a toolkit to quarantine misinformation could potentially have long-lasting effects on the frequency and effectiveness of media accuracy in social contexts. Furthermore, apps could play a more proactive role by filtering content and increasing restrictions of what information can be freely forwarded. Thus, social media apps do act as a source of motivation for information propagation. In this context, Alvin Toffler rightly said that, in this information and communication technology era, the illiterate will not be those who cannot read and write, but those who cannot distinguish between reliable and misleading information available online [31].

Digital health ecosystems have the potential to fulfill the objectives of SDGs. For example, digital technologies can prevent digital isolation, boost connectivity, and provide access to tools and information, which can provide insightful information on populations to achieve health objectives. Digital health technologies have been at the forefront of the COVID-19 pandemic and have caused a shift toward telehealth (eg, virtual visits, care, and e-prescriptions), mobile apps (patient monitoring), and instant messaging applications (risk assessment and screening, triage, etc) [32-34].

Innovative technologies and smartphone apps can help manage the prevention of disease and treatment regimens. Although the benefits of digital health solutions lean toward SDG3, the connection between other SDGs may not be so direct and requires further exploration. These solutions call for a trained workforce, good governance, funding, and an interdisciplinary and intersectoral approach, bringing together all the main actors in the digital health ecosystem—governments, international organizations, health service institutions, academia, research centers, and the public and private industries [35].

The use of mobile apps has enabled health agencies to remotely provide data to the government on the number of cases, symptoms, and prevention measures during the early stages of COVID-19. For example, a World Health Organization (WHO) Health Alert delivers COVID-19 facts to billions via the WhatsApp mobile app [36]. Although apps using global positioning system (GPS) coordinates raise ethical questions on data privacy, some argue that these are essential to identify COVID-19 hotspots and install strong isolation and quarantine measures in certain locations [37]. The pandemic has demonstrated the usefulness of incorporating digital health solutions into our national health care systems. India launched a mobile app Aarogya Setu for exposure notification and contact tracing—it has been promoted as a digital tool to protect people from COVID-19. Despite being the world's most downloaded mobile app [38], lack of integration into health systems for effective public health responses has limited its usefulness in the pandemic response [39]. Although there is limited data on the acceptance of these tools, these reports highlight the need for greater participatory research and concerted action toward its holistic assessment and implementation. Taiwan has showcased how technologies can assist in the control of the COVID-19 pandemic. Taiwan has extensively used information and communication technologies and big data analytics [40]. Moreover, proactive public participation to using face masks and hand sanitizer has led to unintended benefits, such as reducing the risk of not only COVID-19 but also other infectious diseases [41].

Conclusions

The grim COVID-19 situation in India has highlighted the need for better coherence, investment, and public participation, in order to minimize the negative impacts of the pandemic. Although this pandemic has considerably hampered the health care system, it also has given us opportunities to re-establish and restructure its functioning. This is the right time to reorganize the system with new initiatives, such as insurance to cover home care solutions, new policy developments for technology usage, among others. Digital solutions can mitigate infodemics and plays a key role in re-establishing our society through the lens of SDGs. This viewpoint highlights the need to develop and apply digital solutions to pandemic situations and further reprocess to focus on SDGs. Proactive development of educational tools can promote well-being and help dissuade panic-ridden behaviors that lead to infodemics. Public empowerment and engagement are key to promote the use of digital health care solutions for implementing preventive measures. Wearable technologies can be efficiently used for remote monitoring of patients with chronic conditions. Furthermore, the development and implementation of informational tools can aid to improve well-being and dissipate panic-ridden behaviors contributing to infodemics. Thus, a call to action for an observatory of digital health initiatives on COVID-19 is required to share key findings and lessons learned in terms of resilience, crisis mitigation, and preparedness.

Authors' Contributions

SSA and MR conceptualized, designed, conducted the research, prepared the initial manuscript drafts, and assisted with manuscript revision. LFL was involved in content development and manuscript draft preparation. OJ performed data collection, content development, and revision of the manuscript. TP was involved in revision of the manuscript. BP was involved in content development and revision of the manuscript.

Conflicts of Interest

LFL is the Chief Scientific Officer at Adhera Health Inc, a digital health company. The other authors have none to declare.

Multimedia Appendix 1
Experiences from various parts of India demonstrating panic and resilience among the public during the COVID-19 pandemic.
[PDF File (Adobe PDF File), 2615 KB - publichealth_v7i12e31645_app1.pdf]

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Abbreviations

GPS: global positioning system

XSL•FO

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ICU: intensive care unit
NITI: National Institution for Transforming India
PPE: personal protective equipment
SDG: Sustainable Development Goal
WHO: World Health Organization

XSL•FO

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Review

Availability and Suitability of Digital Health Tools in Africa for Pandemic Control: Scoping Review and Cluster Analysis

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Abstract

Background: Gaining oversight into the rapidly growing number of mobile health tools for surveillance or outbreak management in Africa has become a challenge.

Objective: The aim of this study is to map the functional portfolio of mobile health tools used for surveillance or outbreak management of communicable diseases in Africa.

Methods: We conducted a scoping review by combining data from a systematic review of the literature and a telephone survey of experts. We applied the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines by searching for articles published between January 2010 and December 2020. In addition, we used the respondent-driven sampling method and conducted a telephone survey from October 2019 to February 2020 among representatives from national public health institutes from all African countries. We combined the findings and used a hierarchical clustering method to group the tools based on their functionalities (attributes).

Results: We identified 30 tools from 1914 publications and 45 responses from 52% (28/54) of African countries. Approximately 13% of the tools (4/30; Surveillance Outbreak Response Management and Analysis System, Go.Data, CommCare, and District Health Information Software 2) covered 93% (14/15) of the identified attributes. Of the 30 tools, 17 (59%) tools managed health event data, 20 (67%) managed case-based data, and 28 (97%) offered a dashboard. Clustering identified 2 exceptional attributes for outbreak management, namely *contact follow-up* (offered by 8/30, 27%, of the tools) and *transmission network visualization* (offered by Surveillance Outbreak Response Management and Analysis System and Go.Data).

Conclusions: There is a large range of tools in use; however, most of them do not offer a comprehensive set of attributes, resulting in the need for public health workers having to use multiple tools in parallel. Only 13% (4/30) of the tools cover most of the attributes, including those most relevant for response to the COVID-19 pandemic, such as laboratory interface, contact follow-up, and transmission network visualization.

KEYWORDS

Introduction

Background

In 1998, following the resolution of the 48th World Health Assembly, the African Region of the World Health Organization (WHO) approved Integrated Disease Surveillance and Response (IDSR) for all member states in Africa to adopt as the main strategy for strengthening national disease surveillance systems [1,2]. The IDSR system is a regular and continuous reporting of surveillance data for priority epidemic-prone diseases by the health facilities from the district to national or state levels of the health system using paper case forms [2]. The IDSR makes it possible for countries to be able to identify and contain disease outbreaks. Nonetheless, countries using the IDSR system face delays in transferring data from one level to another, are error-prone with low completeness, and face difficulty in updating data after it has been posted from one level to another [3].

The ubiquitous development of mobile health (mHealth) surveillance tools to alleviate the challenges faced by the paper-based IDSR has resulted in a large variety of tools in the field. Researchers have conducted studies to review the properties of and challenges faced by mHealth intervention programs [4-6]. However, a knowledge gap exists in the extent to which these tools are similar to each other and the relevant minimum set of attributes these tools share. Thus, assessing and mapping tools according to certain requirements and attributes will be of great importance to international organizations, public health stakeholders, and mHealth development teams.

Objective

The aim of this study is to map mHealth tools used in Africa for surveillance or outbreak management of communicable diseases to identify commonalities among tools, propose recommendations for further development of mHealth tools, and discuss countries' needs.

Methods

We established a 2-stage systematic scoping approach by combining data from an mHealth tool user telephone survey and a literature search (peer-reviewed or gray literature). To reduce bias and increase coverage of identified tools, we combined these approaches, as many mHealth tools may not be covered in scientific publications, and those that are covered may not be in use in any of the African countries [7].

Survey

In the first stage, we created a list of 15 relevant attributes by combining information from the following sources: (1) the Technical Guidelines for Integrated Disease Surveillance and Response in the African Region [8], (2) the WHO Ebola Virus Disease Consolidated Preparedness Checklist [9], and (3) authors' expert-based knowledge and experiences with communicable disease surveillance. The first 2 sources reflect contributions from >100 public health experts from the WHO, the Centers for Disease Control and Prevention, the United Nations Office for the Coordination of Humanitarian Affairs,

and ministries of health in African countries. Figure S2 in Multimedia Appendix 1 shows the flowchart of how we extracted the relevant attributes, whereas Table 1 and Multimedia Appendix 1, Table S2 present the definitions of the attributes included and excluded from the study, respectively. Furthermore, we used the respondent-driven sampling method and conducted a telephone survey on the relevant attributes of mHealth tools used in Africa [10].

To recruit the interviewees, we designed a short email questionnaire and sent it (through the Africa Centers for Disease Control and Prevention official email), in May 2019, to each surveillance focal point or state epidemiologist of all 54 member states of the African Union. The question in the email requested the (1) names of electronic tools used for disease surveillance or outbreak management in their respective countries, (2) contact details of relevant stakeholders who could participate in a telephone survey, and (3) websites of the tools if available. To the countries that did not respond to the initial questionnaire, we sent a reminder email 2 weeks later. Subsequently, we assembled the collective responses and developed a database comprising stakeholders and owners of the tools, whom we then contacted to take part in the telephone survey. We assessed 15 relevant attributes during a telephone survey conducted in English or French from stakeholders who were successfully contacted and willing to participate. Stakeholders who could not be contacted or refused to participate were dropped. Each telephone survey lasted 15 minutes on average. We requested interviewees to provide additional contact information of persons who might be able to provide more information on the respective tool or on other tools for which we had not yet conducted interviews. The respondent-driven sampling and subsequent telephone interviews were conducted by BCS from October 2019 to February 2020.

Literature Search

In the second stage, we searched for articles published from January 1, 2010, to December 24, 2020, on MEDLINE via the PubMed interface and Google Scholar using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines as a search strategy [11]. We included articles on digital apps designed for communicable disease surveillance used in Africa during the period from 2010 to 2020. We excluded articles on digital apps without a mobile component or those used solely for noncommunicable diseases, patient management, or laboratory management.

We developed the search strategy on PubMed by first identifying keywords corresponding to our inclusion criteria and subsequently performing a series of search tests using these terms and Boolean operators. We then identified the search with 100% sensitivity based on a predefined set of 10 articles on mHealth tools known to the authors. The exact query used on December 26, 2020 on PubMed was *((Mobile Applications)* OR *(Digital Applications)* OR *mHealth* OR *eHealth)* AND *((Public Health)* OR *(Communicable Diseases)* OR *Surveillance)* AND *Africa,* while that used on Google Scholar was *Africa* AND *surveillance* AND *(Mobile Applications)* OR *(digital applications)* AND *(Infectious diseases).*

After the deduplication of the records, BCS and JLZN independently screened the titles and abstracts and included only those articles that mentioned any electronic tool for communicable disease surveillance. We then extracted a set of unique tools from the collection of eligible articles. Subsequently, BCS and JLZN independently selected the tools that met the inclusion criteria using information from the respective publications and websites of these tools.

Data Extraction

The 2 authors then mapped the selected tools based on the list of 15 relevant attributes using the information found in the articles and on the websites of the tools. The literature search and subsequent mapping of the tools spanned from November 2020 to January 2021. Subsequently, we merged the findings from the survey with those from the literature review to construct the data for analysis. The data comprised 30 rows (tools) and 15 columns (attributes; Table 1). The value of each cell in the data was 1 (if the tool had the attribute), 0 (if the tool did not have the attribute), or blank (if missing). Figure 1 shows a flowchart of how we identified the tools included in this study.

Table 1. Number and proportion of 15 relevant attributes of 30 electronic tools for communicable diseases surveillance used in Africa from January 2010 to December 2020.

Attribute label and type	Attribute description	Number of tools with available data for attribute (N=30)	Number of tools having attribute, n (%)
Offline[a]			
Nonfunctional	The tool functions without a connection to the internet and synchronizes with the server when connectivity is available	30	29 (97)
Dashboard[b]			
Nonfunctional	The tool has a dashboard to display epidemiological indicators and charts	29	28 (97)
Synchronization[a]			
Nonfunctional	The tool can synchronize with the server using 3G, 4G, or WiFi	30	27 (90)
Aggregate[b]			
Functional	The tool can be used for monthly or weekly aggregate and zero reporting (tally tool)	29	25 (86)
Geolocation[b]			
Nonfunctional	The tool can document and display the exact geolocation of entities on a map (eg, cases, contacts, and events)	30	24 (80)
Open source[a]			
Nonfunctional	The source code of the tool is publicly available, and software can be used without license fees	26	22 (85)
Case - based[b, c]			
Functional	The tool can be used for case-based reporting (line listing tool)	30	20 (67)
Events[b, c]			
Functional	The tool can document data on disease events (ie, event-based surveillance)	29	17 (59)
Flexible form[a]			
Nonfunctional	The tool has a flexible form builder for users to design questions and the type of data to collect	27	13 (48)
Attributes that apply to case-based tools only[d]			
Symptom[b]			
Functional	The tool documents symptoms for cases	20	20 (100)
Exposure[b]			
Functional	The tool documents epidemiological data (eg, exposures to other cases, animal contacts, and travel history) for cases	20	19 (95)
Hospitalization[b]			
Functional	The tool documents hospitalization for cases	20	19 (95)
Laboratory[b, c]			
Functional	The tool has a laboratory interface to document samples and their test results	19	13 (68)
Contact follow-up[b, c]			
Functional	The tool can document and track chains of transmission by linking contacts to cases and document follow-up data (contact tracing)	20	8 (40)
Transmission network[a]			

Attribute label and type	Attribute description	Number of tools with available data for attribute (N=30)	Number of tools having attribute, n (%)
Nonfunctional	The tool has a feature for visualizing and exploring chains of transmission (disease transmission network)	19	2 (11)

[a]Identified through expert-based knowledge and experiences with communicable diseases surveillance.

[b]Identified from the World Health Organization's Technical Guidelines for Integrated Disease Surveillance and Response in the African Region [8].

[c]Identified from the World Health Organization's Ebola Virus Disease Consolidated Preparedness Checklist [9].

[d]N=20.

Figure 1. Flowchart to identify electronic tools for communicable disease surveillance used in Africa from January 2010 to December 2020.
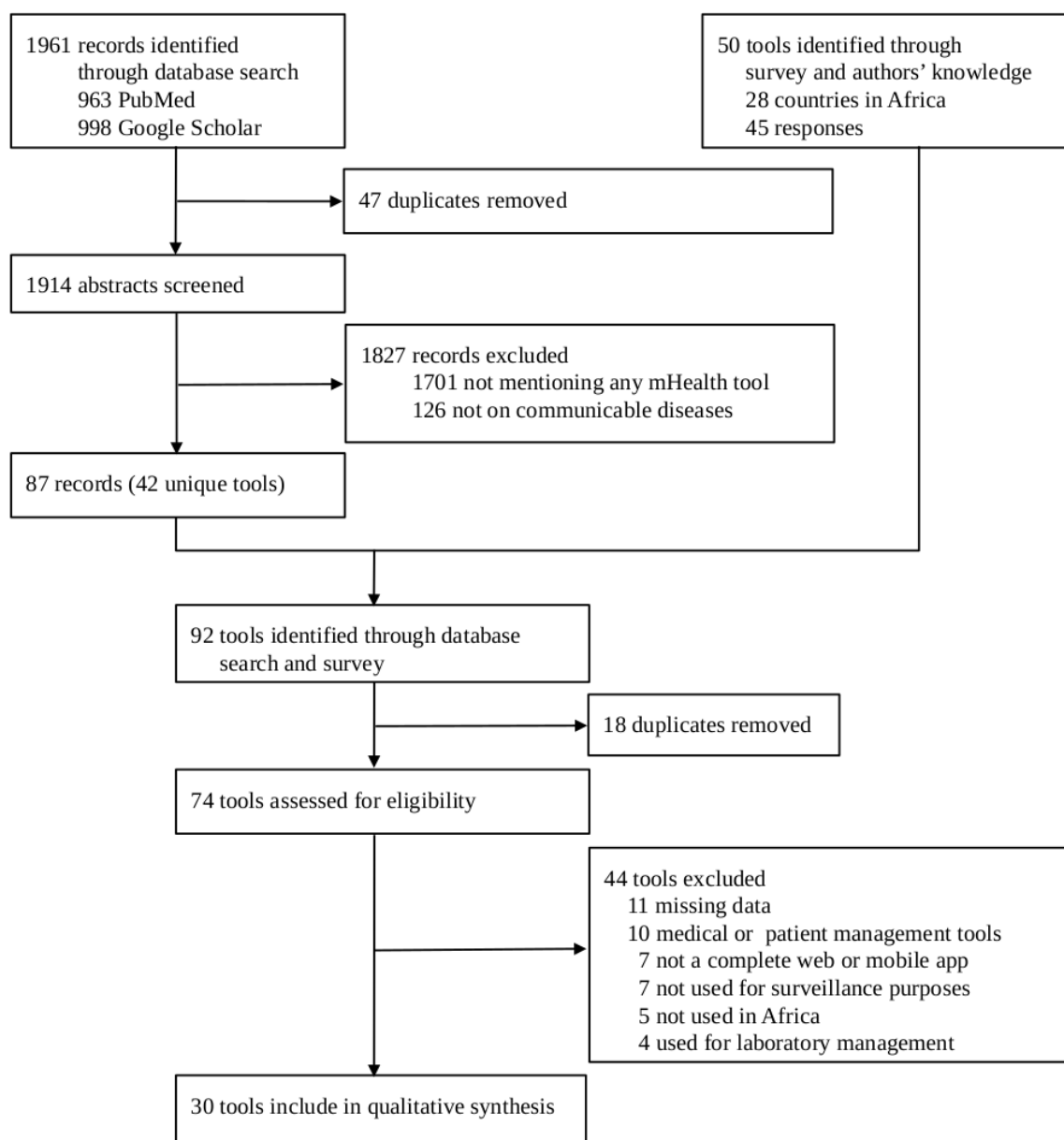
Data Analysis

To explore the similarities among the tools in terms of the relevant attributes, we visualized the data using hierarchical clustering [12]. As the data comprised binary variables only, we adopted the Jaccard similarity measure and complete linkage method to construct the dendrogram [13]. We used the constant-height tree cut method with a minimum cluster side of 1 to group the branches of the dendrogram [14]. To visualize the tools and attributes in the same figure, we used a heat map and clustered the data in such a manner that similar tools and attributes were assembled together [15]. We also calculated the proportion of tools that shared each attribute. From the responses obtained from the survey, we derived categories with frequencies for the challenges and needs to sustain mHealth programs in these countries. We used R (R Core Team) and the ComplexHeatmap package in this analysis [15].

Results

Tools and Associated Attributes

The telephone survey had 45 full responses from 28 countries. Table S1 in Multimedia Appendix 1 shows the countries that responded to the telephone survey and their corresponding number of responses. The number of respondents per country ranged from 1 to 3 (Table S1 in Multimedia Appendix 1). Of the 28 countries, 26 (93%) countries used specific electronic tools for surveillance, and 2 (7%) countries did not have a specific electronic tool but used telephone calls, email, and WhatsApp to transfer surveillance data from one level to another.

We evaluated 15 relevant attributes from 30 tools identified through a literature search (from 1914 records) and a survey (Figure 1). Surveillance tools most frequently used in >1 country based on the results of the telephone survey were District Health Information Software 2 (DHIS2; used by 23/26, 88% of the countries), Early Warning, Alert, and Response System (6/26, 23% countries), Auto-Visual Acute flaccid paralysis Detection And Reporting (5/26, 19% countries), Epi Info (4/26, 15% countries), Surveillance Outbreak Response Management and Analysis System (SORMAS; 2/26, 8% countries), and electronic IDSR (2/26, 8% countries). Of the 30 tools, 3 (10%) were developed and used only in 1 country each: Notifiable Medical Conditions Surveillance System in South Africa, Meningitis Platform in Morocco, and District Health Information Management System in Ghana. In addition, 10% (3/30) of the tools were designed to manage only 1 disease: Coconut Surveillance for malaria, Meningitis Platform for meningitis, and Auto-Visual Acute flaccid paralysis Detection And Reporting for acute flaccid paralysis. Regarding the broadly implemented DHIS2, the participating countries used it for different purposes, namely aggregate surveillance, case-based surveillance, or as a data warehouse or data storage for vaccination campaigns and infrastructural data. On the basis of available data, the number of tools covering each specific attribute ranged from 2 to 29 (Table 1). Offline mode and dashboard were the attributes covered by 97% (28/30) tools, whereas contact follow-up and transmission network were included in 11% (2/30) of the tools (Table 1). The number of attributes for each of the 30 identified tools ranged from 3 to 14 (Table 2).

Table 2. Description of 30 electronic tools for communicable diseases surveillance used in Africa from January 2010 to December 2020.

Name of tool and description[a]	Society affiliation	Attributes[b] (N=15), n (%)
DHIS2[c] [16]		
DHIS is an open-source software platform for the reporting, analysis, and dissemination of data for all health programs. DHIS2 is typically used as a national health information system for data management and analysis purposes, for health program monitoring and evaluation, as facility registries and service availability mapping, and for logistics management, and for mobile tracking of pregnant mothers in rural communities.	The Health Information Systems Program at the University of Oslo	14 (93)
SORMAS[d] [17-20]		
SORMAS is an open-source mobile eHealth system that processes disease control and outbreak management procedures in addition to surveillance and early detection of outbreaks through real-time digital surveillance, including peripheral health care facilities and laboratories. SORMAS adheres to data standards and enhances technical and contextual interoperability with other systems.	Helmholtz Centre for Infection Research, Braunschweig, Germany	14 (93)
Go.Data [21]		
Go.Data is an outbreak investigation tool for field data collection during public health emergencies. The tool includes functionality for case investigation, contact follow-up, and visualization of chains of transmission, including secure data exchange, and is designed for flexibility in the field to adapt to the wide range of outbreak scenarios. The tool is targeted at any outbreak responder.	World Health Organization	14 (93)
CommCare [22]		
CommCare is an open-source mobile platform designed for data collection, client management, decision support, and behavior change communication. It is used by client-facing community health workers during visits as a data collection and educational tool and includes optional audio, image, and video prompts.	Dimagi, Inc Mobile Solutions for International Development	14 (93)
Epi Info [23]		
Epi Info is a public-domain suite of interoperable software tools designed for the global community of public health practitioners and researchers. It provides easy data entry forms and database construction, a customized data entry experience, and data analyses with epidemiological statistics, maps, and graphs for public health professionals who may lack an information technology background.	Centers for Disease Control and Prevention (CDC)	13 (87)
eIDSR[e] [24]		
eIDSR is an electronic disease surveillance and response system using mobile technology and interactive voice response. eIDSR was developed by leveraging the expertise of DHIS2 to customize a comprehensive eIDSR module on the platform.	The Ministry of Health Rwanda Biomedical Center and USAID's Rwanda Health Systems Strengthening Project led by Management Sciences for Health	13 (87)
KoBoToolbox [25]		
KoBoToolbox is a free and open-source suite of tools for data collection and analysis in humanitarian emergencies and other challenging environments. Most users are people working in humanitarian crises, aid professionals and researchers working in low-income countries.	Harvard Humanitarian Initiative	13 (87)
Voozanoo [26]		
The Voozanoo platform is used for research (cohorts, epidemiological, or clinical studies), epidemiological surveillance, alert and response to epidemics, and prevention, screening, or coordination of care (computerized patient record and medical databases).	Epiconcept	13 (87)
Epicollect5 [27]		
Epicollect5 is a mobile and web-based application for free and easy data collection. It provides modules for the generation of forms and freely hosted project websites. Data are collected (including GPS and media) using multiple devices, and all data can be viewed on a central server (via maps, tables, and charts).	Centre for Genomic Pathogen Surveillance	13 (87)
ODK[f] [28]		

Name of tool and description[a]	Society affiliation	Attributes[b] (N=15), n (%)
ODK lets you build powerful offline forms to collect the data you need wherever it is. It supports geolocations, images, audio clips, video clips, and bar codes, as well as numerical and textual answers. ODK can evaluate complex logic to control the display prompts and impose constraints on their responses; it also supports groups of repetitive questions and data collection in multiple languages.	ODK Collect data anywhere	13 (87)
EWARS[g] [29,30]		
EWARS is designed to improve disease outbreak detection in emergency settings, such as in countries in conflict or following a natural disaster. It is a simple and cost-effective way to rapidly set up a disease surveillance system.	World Health Organization	12 (80)
SurveyCTO [31]		
SurveyCTO is a reliable, secure, and scalable mobile data collection platform for researchers and professionals working in offline settings.	Dobility	12 (80)
Afyadata [32]		
Afyadata is an open-source tool for collecting and submitting data from health facilities to the main server and receiving feedback from the main server. The tool provides a graphical user interface for involved health stakeholders to analyze and visualize data. It is a customized version of ODK, which has the best form management modules.	The Southern African Centre for Infectious Disease Surveillance Foundation for One Health	12 (80)
REDCap[h] [33]		
REDCap is a tool for data collectors needing to capture data offline. Data can be collected on an iPhone, iPad, Android phone, or tablet.	Vanderbilt University Medical Center	12 (80)
Magpi [34]		
Magpi can be used to create forms that are responsive and look great on Android and iOS mobile and tablets in any language. It captures better data using GPS, near-field communication, signatures, bar codes, photographs, and other form responses.	Magpi	11 (73)
Incident Tracker [35]		
Incident Tracker is a comprehensive way to report, track, and trend incidents. It works directly with numerous health care agencies. Incident Tracker uses the Microsoft Azure platform for the industry's highest security and data protection levels.	McKula Inc	10 (67)
Meningitis platform		
Meningitis Platform is used in Morocco for the surveillance of meningitis cases. It was developed in-country and is commonly known as meningitis platform. We identified this tool through the telephone survey, and it has no official website.	Ministry of Health (Morocco)	9 (60)
Coconut plus (coconut surveillance) [36]		
Coconut Surveillance is a free and open-source software designed for malaria elimination. There are no licensing fees, and it is available at no cost. It includes an interactive SMS text messaging for case notification, a mobile software app designed to guide mobile case workers, and an analytics software app designed for surveillance and response program managers.	Research Triangle Institute International in collaboration with the President's Malaria Initiative the Zanzibar Malaria Elimination Program.	9 (60)
NMCSS[i] [37]		
NMCSS is a tool for reporting notifiable medical conditions by all health professionals (nurses, doctors, and pathologists). The app allows for real-time reporting of infectious diseases at the point of diagnosis to local, district, provincial, and national health authorities, facilitating timely communication among all CDC personnel at various health levels.	National Institute for Communicable Diseases on behalf of the National Department of Health, South Africa	9 (60)
Sense Followup [38]		
Sense Followup is a hybrid mobile app built for Android phones or tablets. It provides a simple interface that guides health workers through the processes of registering a contact and performing a follow-up.	eHealth Africa	7 (47)
AVADAR[j] [39,40]		

Name of tool and description[a]	Society affiliation	Attributes[b] (N=15), n (%)
AVADAR is a mobile SMS text messaging–based software app designed to improve the quality and sensitivity of acute flaccid paralysis surveillance. Health care workers and key informants within hospital facilities and local communities uses AVADAR.	eHealth Africa	6 (40)
EWORS[k] [41]		
EWORS uses advanced surveillance mechanisms to detect disease outbreaks earlier than possible. EWORS allows for the electronic collection and analysis of routine clinical and nonclinical data to identify the likelihood of occurrence of a disease outbreak in a given region.	InStrat Global Health solutions	6 (40)
mAlert		
The mAlert system is used for reporting notifiable diseases. It integrates health surveillance data into a single platform for analysis. We identified this tool through the telephone survey, and it has no official website.	Mozambique National Institute of Health	6 (40)
DHIMS2[l] [42]		
DHIMS2 is a customization of DHIS2 for Ghana. It is used for the management of health data at all administrative levels on Ghana.	Ghana Health Service	5 (33)
SIS-MA (Health Information System for Monitoring and Evaluation) [43]		
The National Health Information System for Monitoring and Evaluation aims to support the collection, analysis, interpretation, and dissemination of health data that is used to plan public health services across Mozambique from all districts to the capital through the provinces according to the hierarchical organizational structure of the Ministry of Health.	Mozambican Open Architecture Standards and Information Systems and Jembi health systems	5 (33)
mSERS[m]		
mSERS is an SMS text messaging–based tool used in Nigeria for aggregate reporting of health data. We identified this tool through the telephone survey, and it has no official website.	CDC	5 (33)
ARGUS [44]		
ARGUS was designed to make the best use of limited human and financial resources for public health surveillance. It is open-source, easy to configure, and multilingual.	World Health Organization	5 (33)
RapidSMS [45]		
RapidSMS is a free and open-source framework for building interactive SMS text messaging apps, which integrates tightly with Django to provide a rich reporting interface.	Innovation Team at the United Nations Children's Fund and the RapidSMS Team	4 (27)
mTrac [46]		
The mTrac system was designed for the real-time data collection, verification, accountability, and analysis of aggregate data and community engagement for the improvement of health care service delivery. mTrac is powered by RapidSMS.	Ministry of Health of Uganda	4 (27)
FrontlineSMS [47]		

Name of tool and description[a]	Society affiliation	Attributes[b] (N=15), n (%)
FrontlineSMS is a free and open-source software used by a variety of organizations to distribute and collect information via SMS text messaging. The software works without an internet connection and with a cell phone and computer.	Frontline	3 (20)

[a]Description retrieved from the official website for tools having a website.

[b]Number of attributes supported by tools based on available data.

[c]DHIS2: District Health Information Software 2.

[d]SORMAS: Surveillance Outbreak Response Management and Analysis System.

[e]eIDSR: electronic Integrated Disease Surveillance and Response.

[f]ODK: Open Data Kit.

[g]EWARS: Early Warning, Alert, and Response System.

[h]REDCap: Research Electronic Data Capture.

[i]NMCSS: Notifiable Medical Conditions Surveillance System.

[j]AVADAR: Auto-Visual Acute flaccid paralysis Detection And Reporting.

[k]EWORS: Early Warning Outbreak Response System.

[l]DHIMS2: District Health Information Management System 2.

[m]mSERS: mobile Strengthening Epidemic Response System.

Clustering of Tools

We plotted the 30 electronic tools identified from 28 countries in a dendrogram. (Figure 2). Cutting the dendrogram at a height of 0.46, we grouped the tools into 5 main clusters (Figure 2). The largest cluster (in black) has 57% (17/30) of the tools that share the following attributes: case based, symptoms, hospitalization, exposures, events, aggregate, geolocation, synchronization, and dashboard. The second-largest cluster (in turquoise with 6/30, 20% of the tools) contains tools used to manage aggregate data but cannot manage case-based data. In addition, they share the following attributes: geolocation, synchronization, and dashboard. The third-largest cluster (in red with 4/30, 13% of the tools) comprises tools used to manage aggregate data but cannot manage case-based data. They also lack geolocation, synchronization, or a dashboard attribute. The smallest cluster (in green) comprises only the Sense Followup tool. It is characterized by case-based and contact follow-up attributes but lacks the following functional attributes: hospitalization, exposure, events, laboratory, and aggregate. To identify the single functional attribute that can be used to cluster the tools into 2 distinct groups, we performed a subclustering of the tools based on the 8 functional attributes only. Case-based was the most distinguishable functional attribute among the tools (Figure S1 in Multimedia Appendix 1). Figure 3 presents the clustering of the tools (horizontal dendrogram) and their attributes (vertical dendrogram) using a heat map. The 2 most distinguishable attribute clusters comprise 1 attribute only: transmission network (offered by SORMAS and Go.Data) and contact follow-up (offered by 8/30, 27% of the tools).

Figure 2. Dendrogram of 30 electronic tools for communicable disease surveillance used in 28 African countries from May 2019 to December 2020. AVADAR: Auto-Visual Acute flaccid paralysis Detection And Reporting; DHIMS2: District Health Information Management System 2; DHIS2: District Health Information Software 2; eIDSR: electronic Integrated Disease Surveillance and Response; EWARS: Early Warning, Alert, and Response System; EWORS: Early Warning Outbreak Response System; mSERS: mobile Strengthening Epidemic Response System; NMCSS: Notifiable Medical Conditions Surveillance System; ODK: Open Data Kit; REDCap: Research Electronic Data Capture; SORMAS: Surveillance Outbreak Response Management and Analysis System.

Figure 3. Heatmap of 30 electronic tools for communicable disease surveillance used in 28 African countries from May 2019 to December 2020. AVADAR: Auto-Visual Acute flaccid paralysis Detection And Reporting; DHIMS2: District Health Information Management System 2; DHIS2: District Health Information Software 2; eIDSR: electronic Integrated Disease Surveillance and Response; EWARS: Early Warning, Alert, and Response System; EWORS: Early Warning Outbreak Response System; mSERS: mobile Strengthening Epidemic Response System; NMCSS: Notifiable Medical Conditions Surveillance System; ODK: Open Data Kit; REDCap: Research Electronic Data Capture; SORMAS: Surveillance Outbreak Response Management and Analysis System.
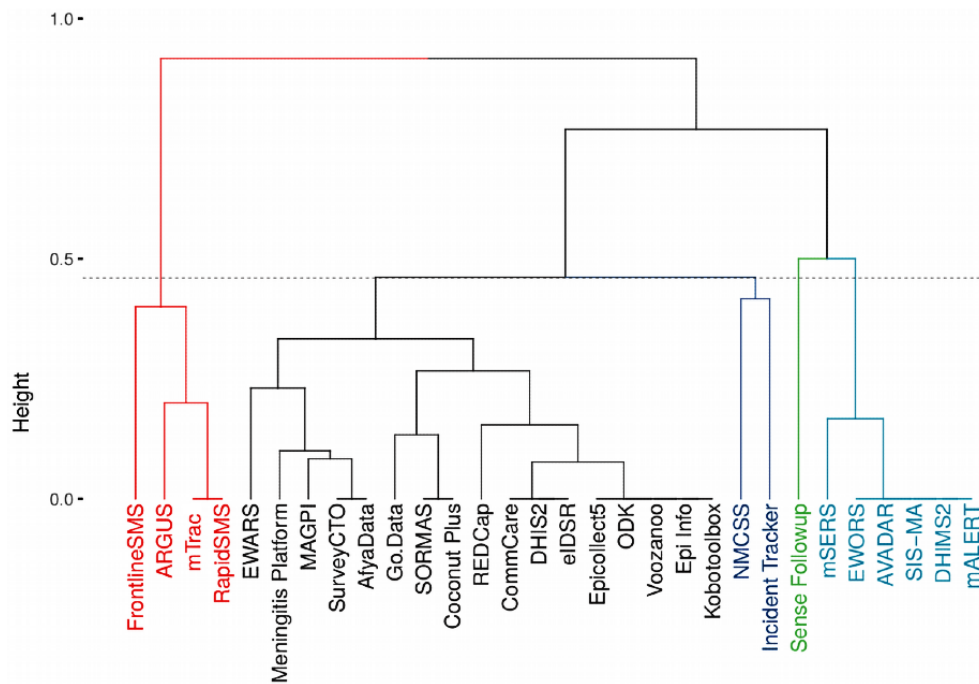
Challenges to Sustain mHealth Programs

In the survey, challenges and needs to sustain mHealth programs in countries were expressed as (1) the lack of integration among the different apps used for managing health data in the country (7/27, 26% responders), (2) the need to improve the skills—comprising documenting complete and accurate data and data analysis using statistical software—of public health workers at district and regional levels through training programs within or between the different countries in Africa (6/27, 22% responders), (3) the lack of stable internet connectivity to synchronize data between mobile devices and the server (2/27, 7% responders), and (4) the lack of sustainability for continuous use of a tool after its initial piloting phase (2/27, 7% responders).

Discussion

Principal Results

We identified 30 digital tools for surveillance or outbreak management of communicable diseases used in Africa and a comprehensive set of 15 attributes. However, none of the 30 tools included all 15 attributes. The tools that supported 14 of the attributes were SORMAS, Go.Data, CommCare, and DHIS2. Unlike CommCare, which is a generic multipurpose tool for collecting data in a variety of fields such as research, agriculture, and international development, the other tools were developed mainly for public health use. This may explain why they supported most of the relevant attributes. On the basis of our finding from clustering, the single functional attribute that distinguished the tools into 2 main groups is the possibility for case-based reporting. Case-based surveillance has epidemiological benefits over aggregate surveillance, such as facilitating the assessment of risk factors, routes of transmission, and data quality; it also allows for immediate reporting upstream, continuous updating, and addition and correction of information, whereas for aggregate reporting, this is not possible or only possible to a very limited extent. Some of the tools supported disease-specific attributes that were not among the list of the 15 attributes evaluated. For example, DHIS2 has a module for the supply chain management of medicine. SORMAS integrates disease-specific surveillance and case management features. These include disease control measures and the management of prescriptions, treatments, and clinical courses. AfyaData, on the other hand, offers functionalities for both human and animal surveillance.

Experts considered 2 important functions as essential for responding to outbreaks: contact follow-up and visualization of chains of transmission. These functions were properly represented in 2 tools only, SORMAS and Go.Data. When isolation is enforced, contact follow-up can reduce the number of secondary cases caused by each case [48]. As contact data are usually large and complex, functionalities to visualize, filter, and compute indicators from the transmission network data may help public health officials identify superspreading events of cross-border transmission chains, thus prioritizing intervention measures. The attributes present in most tools are the ability to function offline and a dashboard for epidemiological indicators. The study participants perceived the ability of tools to work offline and synchronize with the server whenever internet connectivity is available as an important feature of the tools. This may reflect the fact that digital communication infrastructure in public health services in many areas of Africa is not reliable and continuous enough to rely solely on continuous web-based services. Furthermore, a real-time dashboard is an efficient feature to assist response coordination teams in deciding and monitoring intervention measures, especially in an outbreak situation where a delay of just 1 day can significantly reduce the effect of certain control measures.

Limitations

Although we received responses only from 52% (28/54) of African countries for our survey, our literature review was not limited to those. Therefore, we believe that it is unlikely to have systematically missed any kind of tools, which would have resulted in a substantially different conclusion. For some tools, neither the interviewee nor any other available source of information could confirm the absence or presence of a specific attribute. As this was only the case for <3% (12/450) of tool-attribute combinations, the impact on the overall findings appears small. For tools that we identified and mapped with the information obtained from literature search only (ARGUS, Voozanoo, Epicollect5, Incident Tracker, and REDCap [Research Electronic Data Capture]), we were unable to validate whether they were in actual use in any African country. It should also be mentioned that the field of mHealth has been undergoing accelerated change since 2015; thus, it is to be expected that the findings of this study may change in the medium to long term.

Systematic Assessments of Digital Tools for COVID-19 Response

Since the beginning of the COVID-19 outbreak, researchers and organizations have conducted systematic assessments of digital tools that can be used for COVID-19 outbreak response [49-51]. Some of the complementary features covered by these assessments, in addition to the general surveillance attributes assessed in this review, are remote monitoring of symptoms whereby patients or contacts can self-notify their symptoms during the follow-up period [52,53] and electronic immunization registries to plan and manage COVID-19 vaccine delivery and immunization programs [54]. The increased availability of these features in response to COVID-19 may indicate the demand for these attributes to be covered by or integrated into digital surveillance for other communicable or vaccine-preventable diseases.

Recommendations for Future Research

Future research on mHealth could investigate other attributes necessary for mHealth programs that we did not consider in this study, such as the 2 features identified in the assessments of digital tools for COVID-19 response, financial cost for implementation and maintenance of a tool, data protection standards, data security audits, and multiple indicators of the global goods maturity matrix developed by Digital Square [55,56]. Factors associated with the challenges in sustaining mHealth programs identified in this study, such as data quality, sustainability, and integration, could be investigated in future studies.

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Conclusions

However, at the moment, our findings can support public health institutions in choosing the most appropriate existing tools that suit their needs, or assist developers in including relevant attributes into future tools, by highlighting some key attributes to be considered. From the challenges identified by both the systematic review and the survey, we would like to emphasize the following measures to sustain mHealth programs: improving internet connectivity for mobile devices, improving integration between tools or apps to facilitate data sharing, consistent supervision of users in the field to ensure data quality, and measures (such as maintenance, user support, and funding) to ensure sustainable use of tools or apps after the initial piloting phase. Among the large number of tools identified, only a few offer a comprehensive set of attributes as identified during our review and survey. This challenges users by being restricted to a limited set of functions per tool and having to use multiple tools in parallel to cover a larger scope of functional and nonfunctional attributes. Only 4 tools (SORMAS, Go.Data, CommCare, and DHIS2) cover a sufficiently complete set of attributes to offer an integrated and comprehensive digital support for epidemic control as in the current COVID-19 pandemic. To have a digital solution covering all the attributes evaluated in this study, any of the 4 aforementioned tools could be further developed with minimal resources compared with the others.

Authors' Contributions

GK conceived and designed the study. BCS was responsible for data collection, data analysis, and writing the original draft. BL, JD, AZ, and KS contributed to the scientific analysis, supervision, and interpretation of the results. JLZN contributed to data collection and data curation. All authors contributed to writing the final version of the manuscript.

Conflicts of Interest

BCS, JD, and GK contributed to the design and implementation of the Surveillance Outbreak Response Management and Analysis System. Apart from this, all authors declare no conflicts of interest.

Multimedia Appendix 1
Names of countries that responded to the telephone survey, dendrogram of the tools clustered based on 8 functional attributes, flow chart of identified relevant attributes, and description of attributes excluded from the study.
[PDF File (Adobe PDF File), 176 KB - publichealth_v7i12e30106_app1.pdf]

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Abbreviations

DHIS2: District Health Information Software 2
IDSR: Integrated Disease Surveillance and Response
mHealth: mobile health
SORMAS: Surveillance Outbreak Response Management and Analysis System
WHO: World Health Organization

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<u>Original Paper</u>

Predicting the Number of Suicides in Japan Using Internet Search Queries: Vector Autoregression Time Series Model

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Abstract

Background: The number of suicides in Japan increased during the COVID-19 pandemic. Predicting the number of suicides is important to take timely preventive measures.

Objective: This study aims to clarify whether the number of suicides can be predicted by suicide-related search queries used before searching for the keyword "suicide."

Methods: This study uses the infoveillance approach for suicide in Japan by search trends in search engines. The monthly number of suicides by gender, collected and published by the National Police Agency, was used as an outcome variable. The number of searches by gender with queries associated with "suicide" on "Yahoo! JAPAN Search" from January 2016 to December 2020 was used as a predictive variable. The following five phrases highly relevant to suicide were used as search terms before searching for the keyword "suicide" and extracted and used for analyses: "abuse"; "work, don't want to go"; "company, want to quit"; "divorce"; and "no money." The augmented Dickey-Fuller and Johansen tests were performed for the original series and to verify the existence of unit roots and cointegration for each variable, respectively. The vector autoregression model was applied to predict the number of suicides. The Breusch-Godfrey Lagrangian multiplier (BG-LM) test, autoregressive conditional heteroskedasticity Lagrangian multiplier (ARCH-LM) test, and Jarque-Bera (JB) test were used to confirm model convergence. In addition, a Granger causality test was performed for each predictive variable.

Results: In the original series, unit roots were found in the trend model, whereas in the first-order difference series, both men (minimum tau 3: −9.24; max tau 3: −5.38) and women (minimum tau 3: −9.24; max tau 3: −5.38) had no unit roots for all variables. In the Johansen test, a cointegration relationship was observed among several variables. The queries used in the converged models were "divorce" for men (BG-LM test: P=.55; ARCH-LM test: P=.63; JB test: P=.66) and "no money" for women (BG-LM test: P=.17; ARCH-LM test: P=.15; JB test: P=.10). In the Granger causality test for each variable, "divorce" was significant for both men (F_{104}=3.29; P=.04) and women (F_{104}=3.23; P=.04).

Conclusions: The number of suicides can be predicted by search queries related to the keyword "suicide." Previous studies have reported that financial poverty and divorce are associated with suicide. The results of this study, in which search queries on "no money" and "divorce" predicted suicide, support the findings of previous studies. Further research on the economic poverty of women and those with complex problems is necessary.

KEYWORDS

suicide; internet search engine; infoveillance; query; time series analysis; vector autoregression model; COVID-19; suicide-related terms; internet; information seeking; time series; model; loneliness; mental health; prediction; Japan; behavior; trend

Introduction

COVID-19, which was first detected in December 2019 and was declared a pandemic by the World Health Organization in March 2020, has rapidly spread worldwide [1]. In Japan, the number of COVID-19 infections has fluctuated ever since the first person was confirmed positive in January 2020. Although the vaccination rate has been increasing, the emergence of virus variants with greater transmissibility and virulence has prolonged the pandemic [2]. The Japanese government has declared a state of emergency several times, requesting citizens to refrain from venturing out and asking restaurants and large-scale commercial facilities to close.

The limited economic activities resulting from COVID-19 restrictions have raised concerns about significant economic losses and a resultant increase in suicides [3,4]. The number of suicides in Japan, which has been decreasing since 2010, has increased rapidly since October 2020 amid the COVID-19 outbreak, especially among women [5]. Several studies have reported that employment status and economic factors are associated with suicide [6,7], which may have increased because of the impact of the pandemic on the labor market. Unlike the Lehman Brothers shock, which had a major impact on the manufacturing industry and the male labor market, the influence of COVID-19 has had a strong adverse impact on the female labor market and has been referred to as "she-cessions" [8]. Furthermore, women in Japan are likely to be at higher risk than men because they have often lagged in terms of educational standards and working conditions and have been severely affected by the pandemic [9]. In addition, increased domestic violence has been reported because of staying at home amid the COVID-19 pandemic [10].

Before the outbreak of the pandemic, the public health department of the government adopted several measures to reduce suicides. However, similar support may not be possible in the current circumstances because a large share of the human resources is earmarked for preventing COVID-19 infections. In addition, as suicide statistics can only be collated after suicide occurs and requires time for compilation, the official statistics are published only after a time lag. The cause of suicide in the official statistics is also determined based on the results of a postincident investigation by a third party such as the police; hence, official statistics cannot be used for preventive intervention. Lennon [11] demonstrated a strong correlation between unintentional injury mortality (nonsuicidal) and suicide rates, and argued that the suicide rate may be underestimated, depending on the judgment of the third party as to whether the act leading to the injury was suicidal or nonsuicidal. Therefore, preventive intervention against suicide is an important issue because it is likely that there are also potential suicides that are not captured by official statistics.

Internet search behavior has been reported to be negatively correlated with the suicide rate in the general population but positively correlated with both intentional self-harm and completed suicide in young people [12]. In Japan, internet searches for specific suicide-related terms have also been reported to be associated with the incidence of suicide among individuals aged between 20 and 30 years [13]. The negative effects of the internet on suicide generally tend to be emphasized, reflected in the term "cybersuicide" [14] originating from the phenomenon whereby suicide is encouraged when people contemplating suicide meet online. However, the internet may also help prevent suicide; for example, when suicide-related searches are performed on search engines, information on consultation desks is presented at the top of the search results, thereby helping prevent suicides [15-17].

Most previous research on suicide and queries used in internet search engines have used correlation analysis [18-22] or regression analysis [23-28]. In a correlation analysis study, Gunn and Lester [21] reported a positive correlation between suicide rates and the search terms such as "commit suicide," "how to suicide," and "suicide prevention," while Sueki [20] reported a significant correlation only for "depression" and no correlation with "suicide" or "how to suicide." Jimenez et al [19] also analyzed the correlation between 57 suicide-related words and suicide rates, and found that words such as "allergy," "antidepressant," "alcohol absence," and "relationship breakdown" were significantly correlated. The studies using regression analysis also used the number of searches for words such as "suicide," "how to commit suicide," or "depression" to predict suicide rates. Internet search trends were reported to be associated with suicide rates for "suicide," "depression," and "divorce," while Page et al [28] reported that queries such as "how to commit suicide" and "ways to kill yourself" are not straightforward indicators. In the few studies that used time series analysis, predictions were made based on direct queries such as "suicide" and "suicide methods" [29,30], and did not consider suicide-related queries or timing of searches. To prevent suicide, it is necessary to detect suicidal intent; it may be too late to do this by considering searches specifically for "suicide." Furthermore, previous studies were published before the COVID-19 pandemic and did not generate predictions of suicide based on search queries.

A novel aspect of this study is that we construct a model to predict suicide by extracting suicide-related search words, rather than searches explicitly for the term "suicide." Additionally, we use a vector autoregressive (VAR) model, namely, multivariate time series analysis, to examine whether the volume of search words can predict the trend toward an increasing number of suicides in Japan due to the influence of COVID-19. The results of this study will make it easier to determine the number of suicides in advance and to consider preventive measures.

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Methods

This study used the infoveillance approach for suicide in Japan by search trends in search engines.

Measures

The monthly number of suicides collected by the National Police Agency was used as an outcome variable [5]. The data used in this study were obtained for January 2016 to March 2021 (latest available) period.

As a predictive variable, we used the number of queries associated with "suicide" from the search query log of "Yahoo! JAPAN Search," one of the major search engines in Japan. To select queries for analysis, we first calculated the degree of association between the query "suicide" and the queries searched together with "suicide" based on the following formula for calculating a relevance score between word A and word B:

The five phrases that were used as search queries before searching for "suicide" and were highly relevant to "suicide" were extracted. These phrases were "abuse"; "work, don't want to go"; "company, want to quit"; "divorce"; ›and "no money." The search queries before "suicide" were used for analysis to detect trends before suicide occurrence. Monthly data from January 2016 to December 2020 were used to obtain the number of searches for the five extracted queries; this period matched that for which suicide statistics were obtained. In addition, these search numbers were tabulated by gender, and a correction was applied to adjust for the sex ratio in the Japanese population, as follows:

Statistical Analysis

The augmented Dickey-Fuller (ADF) test, a unit root test, was performed to verify the stationarity of each variable used in the analysis. ADF tests were conducted in the trend model, which assumed a time trend term and constant term, and the drift model, which assumed only a constant term. As the time series data with unit roots becomes steady in many cases by taking a difference, the ADF test is performed on the difference variable. The lag order was selected by checking the convergence of the model while making decisions based on Akaike information criterion.

Johansen test was performed to verify the existence of cointegration (a relationship in which the linear sum of two unit-root processes becomes a stationary process) between each variable. The variables in this study were confirmed to have cointegration, and all series of the first-order differences resulted in stationary processes; therefore, we used VAR models with first-difference processes. The VAR model is a multivariate time series analysis, developed based on the philosophy of "let the data speak for themselves (i.e. measurement without theory)." It has high prediction accuracy and has been widely recognized in the field of macroeconomic models [31]. The VAR model is most suitable for this study as a method for multivariate time series analysis with high prediction accuracy using search data of search engines selected without theoretical background. Confirming the VAR model convergence necessitates confirming whether it satisfies the following three standard assumptions for the disturbance term (residual): (1) does not have serial correlation (autocorrelation), (2) has a uniform dispersion, and (3) has a normal distribution. We performed the Breusch-Godfrey Lagrangian multiplier (BG-LM) test (null hypothesis [H0]: no serial correlation), the autoregressive conditional heteroskedasticity Lagrangian multiplier (ARCH-LM) test (H0: uniform dispersion), and the Jarque-Bera (JB) test (H0: normal distribution) to confirm serial noncorrelation, uniform dispersion, and normal distribution of the disturbance term, respectively. All analyses in this study were performed using R version 3.6.2 (R Foundation for Statistical Computing). This study involved secondary analysis of public statistics and anonymized existing data; therefore, ethical approval by an ethics committee was not required.

Results

Confirmation of Unit Root and Cointegration Relationship

According to the ADF test, the null hypothesis of unit root existence for the variables "suicide" and "company, want to quit" in men and "suicide"; "divorce"; "no money"; and "company, want to quit" in women could not be rejected in the original series. In the first-order difference series, the null hypothesis was rejected for all variables for both men and women (Tables 1 and 2). In the Johansen test, "divorce" and "company, want to quit" were adopted for both men and women as the null hypothesis of r=0 (no cointegration) based on 10% of the critical values, but other variables were rejected. When r=1 (cointegration rank 1), the null hypothesis was adopted for all the variables (Table 3).

Table 1. Results of the augmented Dickey-Fuller test (original series).

	Male				Female			
	Trend		Drift		Trend		Drift	
	Lag	Tau3	Lag	Tau2	Lag	Tau 3	Lag	Tau 2
The number of suicides	1	−3.29[a]	1	−2.74[b]	1	−2.34	1	−2.38
Search number of								
"Abuse"	1	−5.80[c]	1	−5.86[d]	1	−5.98[c]	1	−5.94[d]
"Divorce"	1	−2.34	1	−2.62[b]	1	−2.96	1	−3.02[e]
"No money"	1	−4.29[c]	1	−3.16[e]	1	−3.34[a]	1	−2.32
"Work, don't want to go"	1	−3.92[f]	1	−3.82[d]	1	−3.65[c]	1	−3.25[e]
"Company, want to quit"	1	−4.53[c]	1	−2.35	1	−4.46[c]	1	−1.85

[a]Trend model critical value 10%=−3.15.
[b]Drift model critical value 10%=−2.58.
[c]Trend model critical value 1%=−4.04.
[d]Drift model critical value 1%=−3.51.
[e]Drift model critical value 5%=−2.89.
[f]Trend model critical value 5%=−3.45.

Table 2. Results of the augmented Dickey-Fuller test (first-order difference series).

	Male				Female			
	Trend		Drift		Trend		Drift	
	Lag	Tau3	Lag	Tau2	Lag	Tau 3	Lag	Tau 2
The number of suicides	1	−5.91[a]	1	−5.94[b]	1	−3.81[c]	1	−3.90[b]
Search number of								
"Abuse"	1	−9.24[a]	1	−9.33[b]	1	−9.42[a]	1	−9.50[b]
"Divorce"	1	−5.38[a]	1	−5.28[b]	1	−5.87[a]	1	−5.82[b]
"No money"	1	−7.73[a]	1	−7.80[b]	1	−6.72[a]	1	−6.77[b]
"Work, don't want to go"	1	−7.64[a]	1	−7.60[b]	1	−7.01[a]	1	−6.96[b]
"Company, want to quit"	1	−7.12[a]	1	−7.19[b]	1	−7.71[a]	1	−7.71[b]

[a]Trend model critical value 1%=−4.04.
[b]Drift model critical value 1%=−3.51.
[c]Trend model critical value 5%=−3.45.

Table 3. Results of Johansen (cointegration) tests, including the trend term and a seasonal dummy variable, between the number of suicides and each search query.

Variables and H_0	Lags	Test statistics	Critical values		
			10%	5%	1%
Male					
Search number of "Abuse"	2				
r≤1		10.82[a]	10.49	12.25	16.26
r=0		41.21[b]	22.76	25.32	30.45
Search number of "Divorce"	3				
r≤1		4.65	10.49	12.25	16.26
r=0		26.01[c]	22.76	25.32	30.45
Search number of "No money"	5				
r≤1		5.99	10.49	12.25	16.26
r=0		34.66[b]	22.76	25.32	30.45
Search number of "Work, don't want to go"	5				
r≤1		12.52[c]	10.49	12.25	16.26
r=0		35.49[b]	22.76	25.32	30.45
Search number of "Company, want to quit"	2				
r≤1		12.08[a]	10.49	12.25	16.26
r=0		29.45[c]	22.76	25.32	30.45
Female					
Search number of "Abuse"	3				
r≤1		15.63[c]	10.49	12.25	16.26
r=0		36.50[b]	22.76	25.32	30.45
Search number of "Divorce"	3				
r≤1		4.23	10.49	12.25	16.26
r=0		25.09[c]	22.76	25.32	30.45
Search number of "No money"	5				
r≤1		3.07	10.49	12.25	16.26
r=0		32.00[b]	22.76	25.32	30.45
Search number of "Work, don't want to go"	5				
r≤1		9.72	10.49	12.25	16.26
r=0		35.27[b]	22.76	25.32	30.45
Search number of "Company, want to quit"	3				
r≤1		12.99[c]	10.49	12.25	16.26
r=0		30.35[c]	22.76	25.32	30.45

[a]>1%.

[b]>10%

[c]>5%.

Prediction of the Number of Suicides by the VAR Model and Granger Causality Test

From the aforementioned results, as all first-order difference series were standing waves and there were variables with a first-order cointegration relationship, a VAR model using the first-order difference series was designed for each gender. Figures 1 and 2 plot a VAR model constructed using data from January 2016 to December 2020 and the number of suicides from January 2021 to March 2021 predicted by the model for men and women, respectively.

Figure 1. Changes in the number of suicides and predicted values of vector autoregression models using each search query (men). ARCH-LM: autoregressive conditional heteroscedasticity Lagrangian multiplier.

Abuse

Breush-Godfrey test: $\chi^2 = 51.86$, P = .63
ARCH-LM test: $\chi^2 = 57.93$, P = .09
Jarque-Bera test: $\chi^2 = 302.32$, P = 2.2e-16

Divorce

Breush-Godfrey test: $\chi^2 = 53.99$, P = .55
ARCH-LM test: $\chi^2 = 41.27$, P = .63
Jarque-Bera test: $\chi^2 = 24.27$, P = .66

No money

Breush-Godfrey test: $\chi^2 = 58.87$ P = .52
ARCH-LM test: $\chi^2 = 46.92$, P = .39
Jarque-Bera test: $\chi^2 = 11.01$, P = .01

Work, don't want to go

Breush-Godfrey test: $\chi^2 = 38.35$, P = .36
ARCH-LM test: $\chi^2 = 41.27$, P = .63
Jarque-Bera test: $\chi^2 = 16.74$, P = .02

Company, want to quit

Breush-Godfrey test: $\chi^2 = 58.73$, P = .52
ARCH-LM test: $\chi^2 = 67.05$, P = .02
Jarque-Bera test: $\chi^2 = 10.51$, P = .03

Observed curve
Fitted curve
Predict curve

Figure 2. Changes in the number of suicides and predicted values of vector autoregressive models using each search query (women). ARCH-LM: autoregressive conditional heteroscedasticity Lagrangian multiplier.
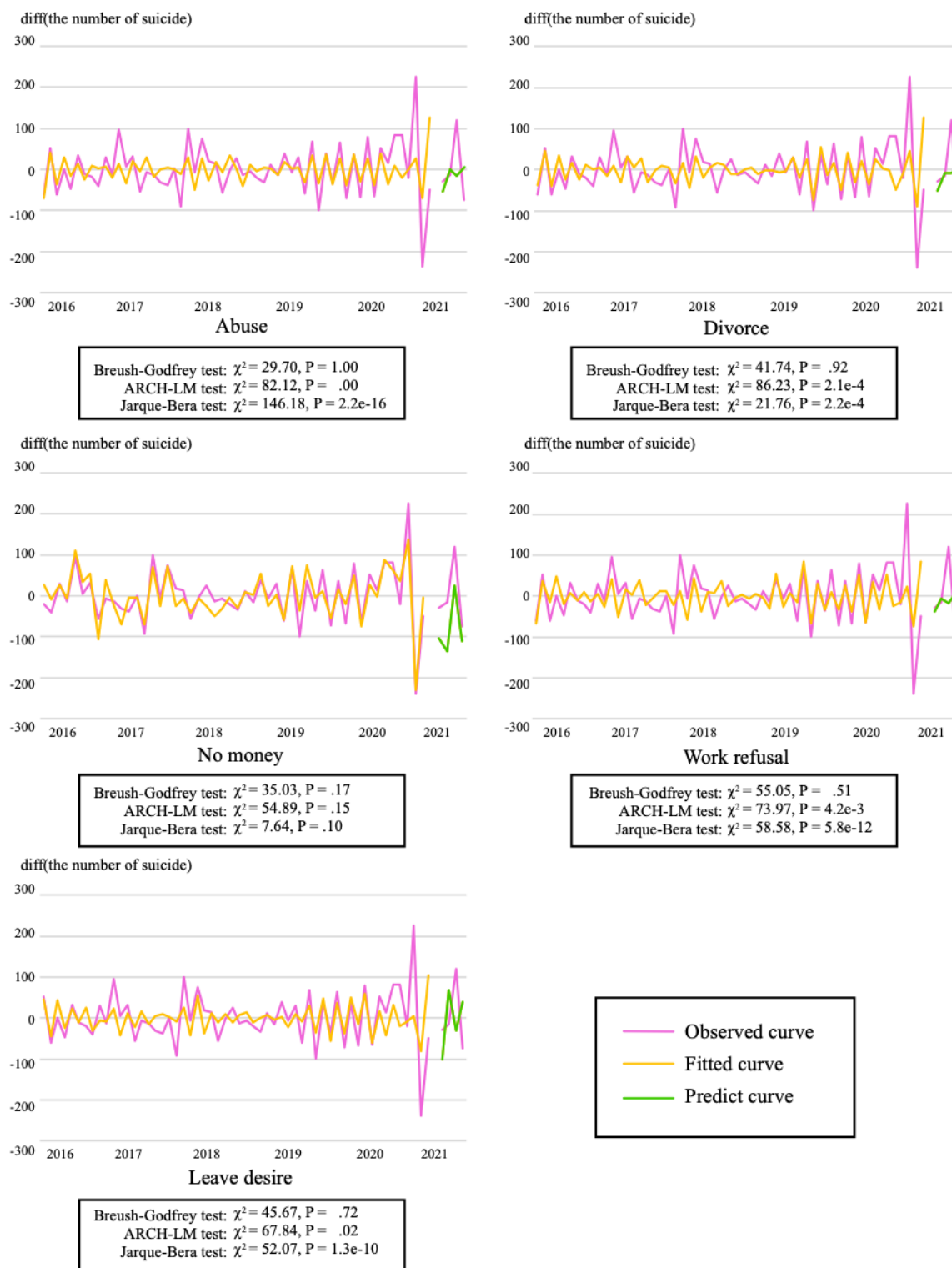
For the BG-LM, ARCH-LM, and JB tests performed to confirm whether the model converged, the variables that converged at the 5% level were "divorce" for men (BG-LM: χ^2_{20}=53.99, P=.55; ARCH-LM: χ^2_{45}=41.27, P=.63; JB: χ^2_2=24.27, P=.66) and "no money" for women (BG-LM: χ^2_{20}=35.03, P=.17; ARCH-LM: χ^2_{45}=54.89, P=.15; JB: χ^2_2=7.64, P=.10). Furthermore, at the 1% level, the model for men converged for

"no money" (BG-LM: χ^2_{20}=58.87, P=.52; ARCH-LM: χ^2_{45}=46.92, P=.39; JB: χ^2_2=11.01, P=.01); "work, don't want to go" (BG-LM: χ^2_{20}=38.35, P=.36; ARCH-LM: χ^2_{45}=41.27, P=.63; JB: χ^2_2=16.74, P=.02); and "company, want to quit" (BG-LM: χ^2_{20}=58.73, P=.52; ARCH-LM: χ^2_{45}=67.05, P=.02; JB: χ^2_2=10.51, P=.03), but only "no money" converged for

women—a result that is the same as that at the 5% level. In the Granger causality test for each variable (Table 4), "divorce" was significant at the 5% level for both men ($F_{104}=3.29$; $P=.04$) and women ($F_{104}=3.23$; $P=.04$).

Table 4. Result of Granger causality test of each search query for the number of suicides.

	Male		Female	
	F test (df)	P value	F test (df)	P value
Search number of				
"Abuse"	0.238 (102)	.79	0.237 (104)	.76
"Divorce"	3.290 (104)	.04[a]	3.229 (104)	.04[a]
"No money"	0.752 (110)	.39	0.736 (62)	.68
"Work, don't want to go"	0.840 (74)	.56	1.641 (104)	.20
"Company, want to quit"	3.760 (110)	.06	1.028 (98)	.38

[a]$P<.05$.

Discussion

Principal Results

The models using the number of searches for the term "divorce" for men and "no money" for women converged best among the search queries used in this study to predict the number of suicides. In Figures 1 and 2, in the convergent model, both the VAR model and the predicted value using the model fit well the measured value. This result indicates that the model, based not only on the search query "suicide" but also on the queries related to "suicide," was effective at predicting the number of suicides.

Further, the model with the query "no money" converged best for women, with an increasing number of suicides during the COVID-19 pandemic. In recent years, "invisible" poverty has been reported to have become more severe among the younger generation, especially among single-mother households in Japan [32-34]. Furthermore, compared to the economic downturn caused by the Lehman Brothers shock, which had a large impact on males in the manufacturing industry, the economic downturn caused by the COVID-19 pandemic has had a large impact on females and is sometimes referred to as she-cession [8,35]. A decrease of 700,000 female workers against 390,000 male workers has occurred in Japan since the COVID-19 pandemic began. The reason is that more than half of the female employees are nonregular employees who are engaged in industries that have been severely impacted by the pandemic—food service, life-related service, entertainment, and retail industries [35,36]. The increase in suicide among women in Japan may be attributed to the potential economic problems of disadvantaged women. For the same reason, although the variation in suicide projections was smaller for men than for women, given the good convergence test results, the influence of COVID-19 is smaller on men than on women, and a future gradual increase in suicides may be observed among men.

By contrast, "Analysis of Suicides in Coronavirus (Emergency Report)" [37] published by the Japan Suicide Countermeasures Promotion Center indicated that the number of suicides among "women with housemates" and "unemployed women" increased substantially. In addition, the report also suggests that various problems such as domestic violence, childcare concerns, mental illness, nursing care fatigue, and the Werther effect—an increase in the number of suicides because of reports of famous people committing suicide—as contributing factors. Regarding the query "no money" (which was a good predictor of women's suicide in this study), namely, economic poverty, the background of the poverty and the problems associated with poverty were not considered, which is a topic that requires further research.

Regarding future work, it is desirable to conduct a study of the effectiveness of long-term forecasts and to consider economic indicators other than those related to search queries (eg, searches for "poverty" and "unemployment"). This would enable a practical prediction model to be developed that would be useful for policy decision-making.

Limitations

This study has several limitations. First, the age at which people commit suicide versus the age at which they search for suicide-related information may differ. However, the number of searches used in this study included searches using personal computers, tablets, and smartphones. Considering that the smartphone and personal computer penetration rates in Japan in 2020 were 86.8% and 68.1%, respectively [38], most of the searches by each age group can be considered to have been covered. Second, the Metropolitan Police Department's suicide statistics used in the study include provisional figures and are compiled based on the address of the place where the person committed suicide, not the place where the person lived. Bias might therefore exist, as the number of suicides is relatively high in areas where mass suicides occur or in locations famous for suicides. Amid the COVID-19 pandemic, the impact of economic shocks on suicide may be moderate because the government has been providing financial support and enforcing behavioral restrictions on its citizens. The economic impact could be even stronger if government support changes or if COVID-19's impact persists in the future. The predictions in this study do not consider government support during the pandemic and may overstate the actual number.

Comparison With Prior Work

The results of this study support the results of previous studies related to suicide but are novel in that they were demonstrated

using search behavior on the internet. For men, search queries such as "no money"; "work, don't want to go"; and "company, want to quit" were also significant at the 1% level, consistent with previous studies in which economic indicators and employment status were associated with suicide [6,7]. In Japan, the employment rate of men is higher than that of women culturally, and the suicide rate is also higher for men. Since the early 1980s, the word "Karoshi," which means a permanent inability to work or death because of acute ischemic heart disease caused by excessive work overload and suicides because of mental disorders caused by overwork, has been created and reported in Japan [39,40]. Therefore, the fact that the search queries related to employment were associated with men may represent a characteristic of Japan.

In the Granger causality test, the query "divorce" was significant for both genders. In Western countries such as the United States and Canada, divorce has been reported to be a risk factor for suicide, particularly among men [41,42]. However, the same tendency reportedly cannot be replicated in Japan. Although the prediction model for the number of suicides did not converge well, divorce may also be an important factor associated with suicide in Japan [43] and requires further investigation.

Conclusions

In this study, we found that the trend in the number of suicides could be predicted using search queries related to suicide that occurred before searching for the keyword "suicide." The queries that converged in the prediction model for the number of suicides were "divorce" for men and "no money" for women. As of September 2021, the pandemic situation in Japan and the world persists because of the emergence of variants of concern and adverse economic effects, and an increase in the number of suicides is predicted. Further research on the situation of women living in economic poverty and having complex problems and considering mechanisms to support them amid the COVID-19 pandemic—which has severely impacted them—is necessary.

Conflicts of Interest

SF is an employee of Yahoo Japan Corporation, a Japanese internet service company that provides the "Yahoo! JAPAN Search" services analyzed in this study.

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Abbreviations

ADF: augmented Dickey-Fuller
ARCH-LM: autoregressive conditional heteroskedasticity Lagrangian multiplier
BG-LM: Breusch-Godfrey Lagrangian multiplier
JB: Jarque-Bera
VAR: vector autoregressive

Original Paper

Factors Driving the Popularity and Virality of COVID-19 Vaccine Discourse on Twitter: Text Mining and Data Visualization Study

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Abstract

Background: COVID-19 vaccination is considered a critical prevention measure to help end the pandemic. Social media platforms such as Twitter have played an important role in the public discussion about COVID-19 vaccines.

Objective: The aim of this study was to investigate message-level drivers of the popularity and virality of tweets about COVID-19 vaccines using machine-based text-mining techniques. We further aimed to examine the topic communities of the most liked and most retweeted tweets using network analysis and visualization.

Methods: We collected US-based English-language public tweets about COVID-19 vaccines from January 1, 2020, to April 30, 2021 (N=501,531). Topic modeling and sentiment analysis were used to identify latent topics and valence, which together with autoextracted information about media presence, linguistic features, and account verification were used in regression models to predict likes and retweets. Among the 2500 most liked tweets and 2500 most retweeted tweets, network analysis and visualization were used to detect topic communities and present the relationship between the topics and the tweets.

Results: Topic modeling yielded 12 topics. The regression analyses showed that 8 topics positively predicted likes and 7 topics positively predicted retweets, among which the topic of vaccine development and people's views and that of vaccine efficacy and rollout had relatively larger effects. Network analysis and visualization revealed that the 2500 most liked and most retweeted retweets clustered around the topics of vaccine access, vaccine efficacy and rollout, vaccine development and people's views, and vaccination status. The overall valence of the tweets was positive. Positive valence increased likes, but valence did not affect retweets. Media (photo, video, gif) presence and account verification increased likes and retweets. Linguistic features had mixed effects on likes and retweets.

Conclusions: This study suggests the public interest in and demand for information about vaccine development and people's views, and about vaccine efficacy and rollout. These topics, along with the use of media and verified accounts, have enhanced the popularity and virality of tweets. These topics could be addressed in vaccine campaigns to help the diffusion of content on Twitter.

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Introduction

Background

Since the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic in March 2020 [1], the United States has seen the highest number of confirmed cases and deaths [2]. Many health organizations, including the WHO [3] and the US Centers for Disease Control and Prevention (CDC) [4], consider vaccination as a critical prevention measure to help end the pandemic and restore society to its normal status. Owing to remarkable advances in vaccinology, scientists developed COVID-19 vaccines within an unprecedented short time. In December 2021, less than 1 year after the virus was identified, the first two vaccines were approved for emergency use in the United States: the Pfizer-BioNTech vaccine and the Moderna vaccine [5]. Both of these vaccines use messenger RNA (mRNA)-based technology, which had not been approved previously for general use in humans [5]. Johnson & Johnson's Janssen vaccine, which is based on a slightly more mature technology of a viral vector, became the third vaccine approved for emergency use in the United States in February 2020 [6]. Owing to their novelty, COVID-19 vaccines had potential to fuel the existing vaccine debate, including arguments over vaccine safety and effectiveness, which had received notable attention in recent years before the pandemic [7]. In addition, political polarization, reaffirmed in the 2020 presidential election, was manifested in a wide range of issues, including responses to the COVID-19 pandemic [8] and vaccines [9]. Generally, Democrats had more favorable attitudes toward COVID-19 vaccines than Republicans [9]. These political fissures further had potential to propel the vaccine debate. Amidst the heated discussion of COVID-19 vaccines, the United States has been rolling out the most massive vaccination campaign in its history to fight against the pandemic [10].

Investigating public discourse about COVID-19 vaccines will shed light on people's perception and attitudes. As a major social media platform and a vital source for text-based public discourse, Twitter has been studied to understand public discourse about vaccines in general [11-14] and about specific vaccines, including COVID-19 vaccines [15,16]. Text-mining techniques have been increasingly used in recent research to investigate tweets about the COVID-19 pandemic (eg, [17-21]) and about COVID-19 vaccines [15,16]. These studies have employed machine learning algorithms to automatically analyze massive amounts of tweets and capture latent textual information such as topics, sentiment, and trends.

Although text mining is clearly an effective way to identify underlying textual clusters and patterns from vast amounts of tweets, less is known about how such information can help to understand the diffusion of information and opinions on Twitter. The aim of this study was to investigate message-level drivers of the popularity and virality of tweets about COVID-19 vaccines using text-mining techniques. Specifically, the objective of the study was to investigate how text-mined topics and valence, together with social media message features affect likes and retweets. Another aim of the study was to examine the topic communities of the most liked and most retweeted tweets using network analysis and visualization. These findings have implications for the direction of vaccine campaigns.

Literature Review

The extent to which a message results in optimal diffusion on social media can be assessed by users' favorable responses such as clicking "like" and "share" buttons to overtly indicate individual interest and support [22,23]. On Twitter, users can click on the "Like" icon to show appreciation for a tweet or on the "Retweet" icon to share it publicly with their followers [24]. Prior research has considered the like count of a tweet as an indicator of its popularity and the retweet count of a tweet as an indicator of its virality [23,25]. Drawing on these studies [23,25], we assessed the popularity of a tweet by the number of likes and assessed the virality of a tweet by the number of retweets. Compared with liking, retweeting is a more social behavior [26]. For both responses, the bandwagon effect postulates that the adoption of trends increases more with respect to the number of people who have already done so [22].

This study investigated three categories of message-level factors that, according to prior research, can drive the diffusion of media content online: information, emotion, and social media message features. As Twitter is a major source of text-based information, we drew on the literature related to the social transmission of online text information, including news articles and tweets. Past research on the virality of online news has suggested two categories of determinants: informational and emotional. From the informational perspective, information utility, as gauged by overall content usefulness, was found to prompt social media sharing of general news articles [27]. In the health context, a content attribute that taps into information utility is the presence of efficacy information [26], which provides ways to promote health or overcome a health risk [28]. Research has shown that overall content usefulness and presence of efficacy information both facilitate viewing and sharing of health news articles on social media [26]. In the situation of the COVID-19 pandemic, gaps in knowledge about the new coronavirus was evident in the United States early on [29] and demand for information of practical value was expected [25,30]. In addition, according to the uncertainty reduction theory, to alleviate risks in crises, people intend to engage in uncertainty reduction efforts by collecting credible information and sharing with others [25]. Nanath and Joy's [25] text mining study revealed that the optimism and solution topic as well as the mental health topic were positive predictors of retweet counts of COVID-19–related tweets. In addition to information utility, novel content in health news has been found to increase sharing [26]. COVID-19 vaccines were newly developed to help fight off the new coronavirus; thus, content related to aspects such as development and efficacy had the intrinsic feature of novelty and could potentially help to close the knowledge gaps.

Past research has generally shown that there were more positive than negative tweets on Twitter about vaccines in general [11-13] and about COVID-19 vaccines in particular [15,16]. Although positive content has been found to increase likes on social media [22,23], the findings are mixed regarding the impact of valence on the virality of online content. Berger and Milkman [27] found that positive sentiment increased social

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media sharing of general news. A plausible explanation is that positive sharing reflects the positivity of the sender [26], which may enhance self-presentation [31] and identity communication [27]. However, Nanath and Joy [25] found that negative emotions increased the social transmission of COVID-19–related tweets. Moreover, Blankenship et al [11] revealed that antivaccine tweets were retweeted more than provaccine tweets. In comparison, Kim [26] revealed that content valence was unrelated to the virality of health news on social media.

In addition to content topic and valence, social media message features, including media presence, linguistic features, and account verification, could impact the popularity and virality of online content. Media presence and linguistic features can affect content processing fluency and further affect favorable online responses such as liking and retweeting. Content on social media may be of any mode such as text, photos, and videos. Past research has shown that a tweet with embedded media (ie, a photo or a video) stimulates likes and retweets [23]. It is postulated that the cognitive processing of photos is more fluent than that of words as it is faster to activate the semantic meaning of photos than that of words [32,33]. Therefore, tweets featuring embedded media are more likely to trigger favorable online responses.

In comparison, past research has revealed that linguistic features such as the number of hashtags, mentions, and external links decrease likes [23] and retweets [23,25]. It is suggested that these features increase content processing disfluency in two aspects. First, compared to the black color adopted by text, the blue color adopted by hashtags, mentions, and external links decreases the font-background contrast and causes visual perpetual disfluency [23,34]. Second, the nonalphanumeric symbols used by hashtags, mentions, and external links (ie, #, @, ://) create orthographical disfluency [23,35]. The content disfluency requires more cognitive effort to process the message and hence decreases favorable responses [23].

Finally, account features could potentially affect likes and retweets. In the face of information explosion in the digital age, account authenticity could be of particular importance in the diffusion of information. On Twitter, verified accounts have a blue badge next to the profile name to let users know that it is authentic. Twitter paused public submissions for account verification in 2017 and reopened the gate using a new application process in May 2021 [36]. The end date of our data retrieval was April 30, 2021, and therefore the data did not reflect the newly verified accounts. In addition, it is noteworthy that the tweets posted by verified accounts may not be verified.

Research Model and Questions

This study contributes to the literature by providing a conceptual model to understand the combined effects of the three above-mentioned categories of factors—content topics, content valance, and social media message features, including media presence, linguistic features, and account verification—on the popularity and virality of tweets about COVID-19 vaccines. We employed topic modeling to identify latent topics of tweets. We employed sentiment analysis to assess the valence of tweets. Automated extraction generated data about social media

features. Therefore, we put forward the following research questions:

> *Research question 1 (RQ1): How do content topics, content valence, and social media message features affect the popularity of tweets about COVID-19 vaccines?*
>
> *Research question 2 (RQ2): How do content topics, content valence, and social media message features affect the virality of tweets about COVID-19 vaccines?*

In addition, among the 2500 most liked and most retweeted tweets, respectively, we used network analysis and visualization to detect topic communities and present the relationship between the topics and the tweets. We had the following research questions:

> *Research question 3 (RQ3): What are the salient topics of the most liked tweets?*
>
> *Research question 4 (RQ4): What are the salient topics of the most retweeted tweets?*

This study can help to advance knowledge on complex drivers of the popularity and virality of tweets about COVID-19 vaccines using machine-based text mining and network visualization in the context of a heated vaccine debate in the United States. These findings offer practical implications for health practitioners to employ more effective social media content.

Methods

Data Source

We collected publicly available original tweets about COVID-19 vaccines from January 1, 2020, to April 30, 2021, using snscrape [37], which were further filtered according to user profile data to include only English-language tweets and those from US-based users. This approach resulted in 501,531 tweets recorded in the final dataset.

Drawing on prior social media studies on vaccines [38,39], we developed keywords by balancing the general COVID-19 vaccine information with brand-specific information. As of April 30, 2021, which was our data retrieval end date, Pfizer-BioNTech, Moderna, and Johnson & Johnson/Janssen vaccines were authorized for emergency use in the United States [40]. At that time, the three vaccines, together with the AstraZeneca vaccine, had conditional marketing authorizations in European Union countries [41]. Although the AstraZeneca vaccine was not used in the United States, it garnered media and public attention in the United States, and therefore we also included this brand in the search. In addition, as COVID-19 vaccines varied in terms of the underlying technology, we considered technology-specific information. Pfizer-BioNTech and Moderna used mRNA technology, and Johnson & Johnson and AstraZeneca-Oxford used viral vector technology. Moreover, we checked government Twitter accounts such as the US CDC and Food and Drug Administration accounts to explore hashtags. Finally, the following strategy was used to scrape Twitter data. A tweet had to contain the keyword

(case-insensitive unless otherwise specified) "vaccine," together with one of the keywords "COVID," "COVID19," "COVID-19," "Pfizer," "Pfizer-BioNTech," "Moderna," "Johnson & Johnson," "Janssen," "AstraZeneca," and "Oxford-AstraZeneca"; or contain the keyword "vaccine" together with one of the following combinations: "mRNA" and "COVID," "viral vector" and "COVID," and "adenovirus" and "COVID"; or contain either of the two hashtags "#covid19vaccine" and "#covidvaccine."

Data Processing

The final dataset was preprocessed via genism [42] for topic modeling and sentiment analysis. We tokenized each tweet as a list of words [43], and removed high-frequency stop words such as "https" and "covid," in addition to the standard nltk stop words library [44], which were not expected to contribute to the uniqueness of each topic. The text corpus was then trained to recognize frequent bigrams such as "New York," using a gensim bigram model [42]. Next, all words were lemmatized to their dictionary form [43] to reduce redundancy in the bag of words (BOW) encoding. Finally, these lemmatized single words (ie, unigrams) and bigrams recognized by the bigram model were used to build the BOW representation for our latent Dirichlet allocation (LDA) model. That is, the corpus was encoded as a vector space, with each vector component representing a lemma.

Measures

Like Count

The like count of each tweet, which is the number of likes a tweet gets, was captured in the data set. As a small number of tweets generated a great number of likes, the distribution was right-skewed. To reduce right skewness, we used the natural logarithm of like counts in statistical analyses, as in past research [23].

Retweet Count

The retweet count of each tweet, which is the number of retweets a tweet gets, was captured in the data set. Similar to like counts, retweet counts had a right-skewed distribution. To reduce right skewness, we used the natural logarithm of retweet counts in statistical analyses, as in past research [23,25].

Content Topic

The tweets were subjected to topic modeling using the LDA model [45]. Topic modeling is a commonly used unsupervised learning method that generates a probabilistic model for the corpus of text data [46]. As one of the two main topic models [46], LDA is increasingly being used to analyze textual data [47], including tweets (eg, [16-18,20,25]).

LDA depends on two matrices to define the latent topical structure: the word-topic matrix and the document-topic matrix [47]. In our study, a document was a tweet. The general idea is that a tweet is represented by a Dirichlet distribution of latent topics, where each latent topic is represented by a Dirichlet distribution of words [46].

The word-topic matrix reveals the conditional probability with which a word is likely to occur in a topic. The word-topic matrix

is used to interpret the topics. A topic can be interpreted by examining a list of the most probable words ranked solely by their frequency to occur in that topic, using 3 to 30 words [48]. To aid topic interpretation, we also considered the ranking of the most probable topic-specific words by both frequency and relevance, as suggested by Sievert and Shirley [48]. The relevance for ranking words within a topic is indexed by a weight parameter, λ, with a value ranging from 0 to 1. A value closer to 0 highlights rare but exclusive words for the topic and a value closer to 1 highlights frequent but not necessarily exclusive words for the topic [48]. We adopted the recommended λ of 0.6 [48]. Lastly, we reviewed sample tweets with the highest topic-specific loadings to finalize topic interpretations.

The document-topic matrix reveals the conditional probability with which a topic is likely to occur in a tweet. In other words, it reveals the topic loadings for each tweet. The information was used in the regression models for prediction as well as in network analysis and visualization. The topic loading value ranges from 0 to 1, with a value closer to 1 indicating the higher topic loading of a tweet.

Content Valence

We used TextBlob [49], an open-source python library, to generate the valence score of each tweet. The range of the valence score is from –1 to 1, with the value of –1 indicating the most negative and the value of 1 indicating the most positive valence.

Media Presence

Data on whether a tweet had a photo, gif, or video were extracted, respectively.

Linguistic Features

The numbers of hashtags, mentions, and hyperlinks were extracted, respectively.

Account Verification

For each tweet, whether the account that posted it was verified or not was extracted.

Data Analysis

We performed linear regression analyses to examine the predictors of likes and retweets. Since the purpose of the study was to investigate the factors that affected the popularity and virality of tweets as indexed by like counts and retweet counts, we only considered the tweets that were liked and retweeted, as in past research [23,25]. In the models, the log-transformed like counts and retweet counts were respectively regressed on 12 topic loadings extracted from topic modeling, the valence score generated from sentiment analysis, three variables of media presence, three variables of linguistic features, and account verification.

Network Analysis and Visualization

We used two-mode visualization to present the relationship between topics and the 2500 most liked tweets and the 2500 most retweeted tweets, respectively. To prepare data for rendering each relationship network, we created a node list

consisting of topic and tweet nodes, and an edge list consisting of tweet IDs, the topics each tweet was connected to, and an edge weight representing the topic loading of each tweet. Each topic node with its name was sized in proportion to the sum of topic loadings of all tweets. To assist the viewer in discerning topics, we used a community detection algorithm built in Gephi [50], which is based on the Louvain modularity method that has been used in prior research [12]. Community detection algorithms [51] identify cohesive groups in the network [52,53]. In the network visualization, node color reflected topic community membership.

Results

Content Topics

We trained a topic model using LDA, with a search space on topic numbers from 3 to 21. Using a uniform search grid on Dirichlet concentration parameters, the model parameters were trained to optimize the coherence score C_v [54], which is a likelihood measure of word cooccurrence in the same topics. The best model was achieved at 12 topics with C_v=0.42. Table 1 summarizes the 12 topics. Interpretation of each topic was based on the top 10 probable words ranked solely by frequency and jointly by frequency and relevance, as well as review of sample tweets with high topic-specific loadings.

Table 1. Summary of topics and valence.

Topic number	Topic label	Top 10 words by frequency (λ=1)	Top 10 words by frequency and relevance (λ=0.6)	Valence
1	Vaccine access	vaccine, community, health, help, access, need, work, pandemic, country, support	vaccine, community, health, access, help, support, effort, global, distribution, ensure	0.137
2	Vaccine efficacy and rollout	vaccine, case, new, variant, show, death, test, risk, virus, report	case, vaccine, variant, show, new, test, death, study, pause, report	0.147
3	Vaccine development and people's views	vaccine, people, take, say, would, do, want, think, give, woman	vaccine, would, take, woman, people, think, enough, do, say, try	0.158
4	Vaccination status	get, vaccine, vaccinate, shot, people, shoot, vaccinated, first, fully, wait	get, vaccinate, shot, shoot, people, vaccinated, fully, family, wait, die	0.143
5	Feeling and side effect	get, vaccine, feel, go, good, day, side effect, make, work, arm	feel, get, side effect, good, go, arm, day, fact, science, normal	0.117
6	Vaccine appointment	vaccine, appointment, today, site, schedule, open, visit, call, clinic, vaccination	appointment, site, vaccine, open, schedule, visit, clinic, join, register, call	0.133
7	Vaccine availability	vaccine, available, week, say, year, question, old, last, next, come	available, question, old, year, week, say, last, next, answer, month	0.149
8	Vaccination eligibility and administration	dose, vaccine, receive, today, first, second, eligible, administer, day, start	dose, receive, second, eligible, today, first, administer, vaccine, day, begin	0.354
9	Age and issues	age, vaccine, offer, people, group, encourage, read, rollout, issue, concern	age, offer, group, encourage, rollout, reason, article, issue, explain, doctor	0.107
10	Preventive measures	safe, mask, keep, spread, stop, stay, wear, still, continue, passport	safe, mask, keep, spread, stop, stay, wear, passport, place, home	0.089
11	Student and county	retweet, check, student, event, walk, turn, county, staff, please, team	retweet, check, student, event, walk, turn, county, staff, please, team	0.093
12	Trust and communication	share, trust, watch, video, speak, play, minute, fall, head, availability	share, trust, video, speak, play, minute, watch, fall, head, availability	0.089

Content Valence

The overall valence was positive, with a score of 0.145. The range of the valence score is from –1 to 1, with –1 indicating the most negative and 1 indicating the most positive valence. As shown in Table 1, all 12 topics were associated with positive valence.

Determinants of Like Counts

Table 2 reveals the effects of the four categories of independent variables on the log-transformed like counts. The regression model was significant at P<.001 (adjusted R^2=0.151). RQ1 was related to the determinants of likes. Out of the 12 latent topics identified by topic modeling, Topics 1 to 8 had weak but significant effects on likes. The valence also had a weak but significant effect on likes. Positive tweets increased likes. Media (photo, gif, or video) presence increased likes. Among linguistic features, the number of hashtags and that of external links decreased likes, whereas the number of mentions increased likes. Account verification increased likes.

Table 2. Linear regression models on predictors of popularity and virality of tweets.

Variables	Ln (like count)[a] (n=286,657)		Ln (retweet count)[a] (n=168,961)	
	β	P value	β	P value
Topics				
T1: Vaccine access	.029	.048	.062	<.001
T2: Vaccine efficacy and rollout	.049	<.001	.077	<.001
T3: Vaccine development and people's views	.055	<.001	.078	<.001
T4: Vaccination status	.048	<.001	.068	<.001
T5: Feeling and side effect	.040	<.001	.052	<.001
T6: Vaccine appointment	.027	<.001	.033	<.001
T7: Vaccine availability	.018	<.001	.019	<.001
T8: Vaccination eligibility	.011	<.001	.006	.08
T9: Age and issues	.009	.13	.009	.10
T10: Preventive measures	−.030	.26	−.037	.25
T11: Student and county	.076	.14	−.080	.14
T12: Trust and communication	−.079	.11	−.072	.21
Emotion (valence)	.059	<.001	.0003	.93
Media presence				
Has photo	.188	<.001	.088	<.001
Has gif	.019	<.001	.001	.64
Has video	.100	<.001	.084	<.001
Linguistic features				
Number of hashtags	−.072	<.001	−.059	<.001
Number of mentions	.007	.005	−.002	.45
Number of external links	−.126	<.001	.003	.18
Verified account	.452	<.001	.378	<.001

[a]To account for the right skewness of the data distribution, the natural log–transformed like counts and retweet counts were used in the analyses.

Determinants of Retweet Counts

Table 2 also reveals the effects of the four categories of independent variables on the log-transformed retweet counts. The regression model was significant at $P<.001$ (adjusted R^2=0.130). RQ2 focused on the determinants of retweets. Out of the 12 latent topics identified by topic modeling, Topics 1 to 7 had weak but significant effects on retweets. The valence had no effect on retweets. Media presence of a photo or video increased retweets. Among linguistic features, the number of hashtags decreased retweets. Account verification increased retweets.

Topic and Tweet Relationship Networks

RQ3 focused on salient topics among the most liked tweets. As shown in Figure 1, among the 2500 most liked tweets, Louvain clustering identified 4 out of the 12 topics. The tweets were clustered around vaccine access (Topic 1), followed closely by vaccine efficacy and rollout (Topic 2) and then vaccine development and people's views (Topic 3). The other topics

were not salient and presented as one remaining cluster. Each topic community was represented by one color.

Table 3 summarizes the top 10 liked paraphrased tweets, like counts, dominant topics, and topic loadings. The first most liked tweet, which was posted in July 2020 and had 91,163 likes as of April 30, 2021, was clustered around vaccine access (Topic 1). It called for Medicare for All along with free COVID testing, treatment, and vaccines.

RQ4 focused on salient topics of the most retweeted tweets. As shown in Figure 2, among the top 2500 most retweeted tweets, Louvain clustering identified 5 out of the 12 topics the LDA identified in the total tweets. The top retweeted tweets mostly clustered around vaccine efficacy and rollout (Topic 2), closely followed by access to vaccine (Topic 1), and then vaccine development and people's views (Topic 3) and vaccination status (Topic 5). The other topics were not salient and presented as one remaining cluster. Each topic community was represented by one color.

Figure 1. Topic communities of the 2500 most liked tweets. Two-mode visualization was used to present the relationship between topics and the 2500 most liked tweets. The topics and the tweets are connected by edges weighted by topic loadings of each tweet. Each topic node with its name is sized in proportion to the sum of topic loadings of all tweets. Colors indicate topic communities as partitioned by the Louvain algorithm.
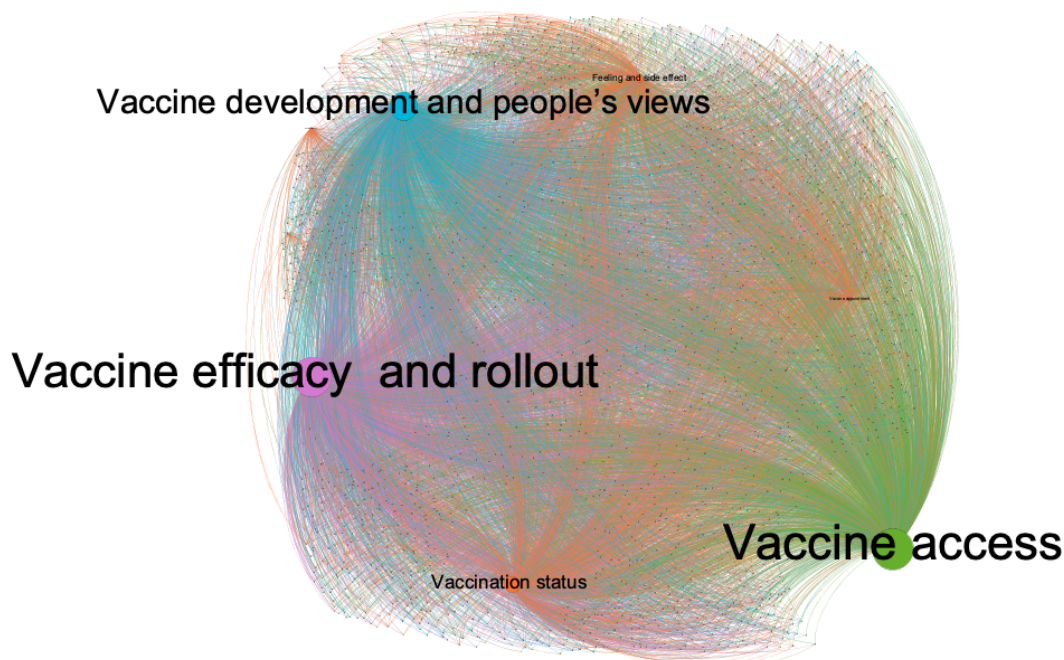
Table 3. Top 10 liked paraphrased tweets.

Like rank	Like count	Tweet	Dominant topic number and label	Dominant topic loading
1	91,163	Medicare for All along with free COVID testing, treatment, and vaccines are necessities of a decent society (July 2020).[a]	Topic 1: Vaccine access	0.518
2	90,177	Trump's attempt to deny vaccines to New York is playing politics with people's lives (November 2020).[a]	Topic 2: Vaccine efficacy and rollout	0.578
3	63,681	I participated in Moderna experiments to see if its vaccine and booster were safe and effective (April 2021)	Topic 3: Vaccine development and people's views	0.373
4	55,223	President Biden took credit for the vaccine from President Trump (March 2021)[a]	Topic 1: Vaccine access	0.964
5	48,631	The number of vaccine doses administered outnumbered that of new cases at a 10-to-1 ratio (February 2021)	Topic 2: Vaccine efficacy and rollout	0.514
6	46,997	I had ended my support for Trump and started taking COVID seriously. I got vaccinated, thanks to Biden and health workers (March 2021)	Topic 4: Vaccination status	0.578
7	36,753	Like with smallpox, vaccinations along with surveillance and contact tracing are essential to COVID's elimination (April 2020)[a]	Topic 2: Vaccine efficacy and rollout	0.547
8	36,250	Pfizer's mRNA vaccine candidate showed initial evidence of efficacy (November 2020)[a]	Topic 3: Vaccine development and people's views	0.844
9	35,604	President Trump delivered on his goal of having a safe and effective COVID vaccine by the end of the year (May 2020)	Topic 3: Vaccine development and people's views	0.533
10	35,514	The current vaccination pace will take 10 years to reach herd immunity. We need to speed this up (December 2020)[a]	Topic 2: Vaccine efficacy and rollout	0.385

[a]Tweet was among the top 10 liked and concurrently one of the top 10 retweeted tweets.

Figure 2. Topic communities of the 2500 most retweeted tweets. Two-mode visualization was used to present the relationship between topics and the 2500 most retweeted tweets. The topics and the tweets are connected by edges weighted by topic loadings of each tweet. Each topic node with its name is sized in proportion to the sum of topic loadings of all tweets. Colors indicate topic communities as partitioned by the Louvain algorithm.
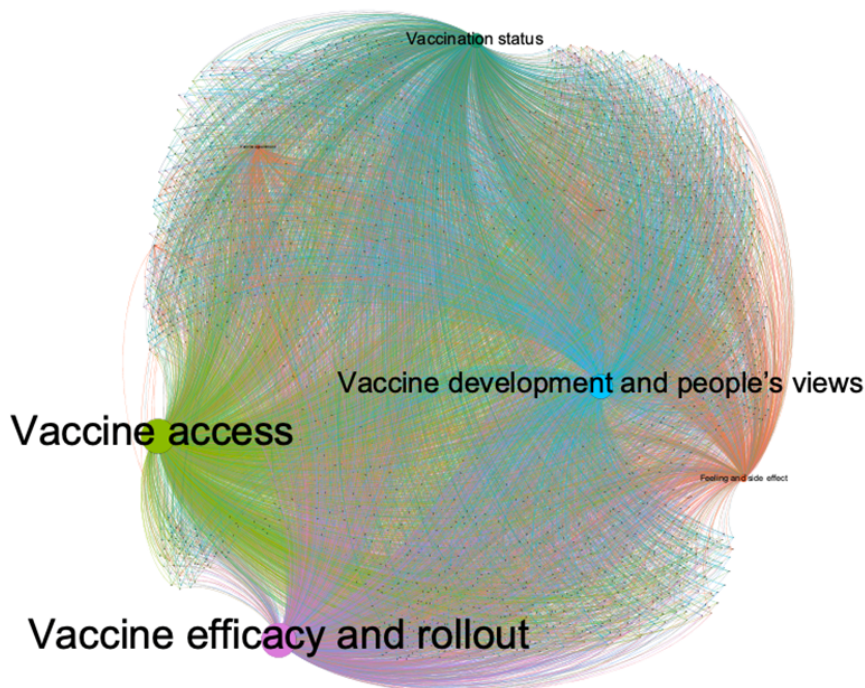

Table 4 summarizes the top 10 retweeted paraphrased tweets, their retweet counts, and dominant topics. The first most retweeted tweet, which was posted in December 2020 and garnered 17,427 retweets through April 2021, clustered around vaccine efficacy and rollout (Topic 2). This emphasized the long time needed to reach herd immunity based on the vaccination pace at that time.

Table 4. Top 10 retweeted paraphrased tweets.

Retweet rank	Retweet count	Tweet	Dominant topic number and label	Dominant topic loading
1	17,427	The current vaccination pace will take 10 years to reach herd immunity. We need to speed this up (December 2020)[a]	Topic 2: Vaccine efficacy and rollout	0.385
2	16,288	Medicare for All along with free COVID testing, treatment, and vaccines are necessities of a decent society (July 2020)[a]	Topic 1: Vaccine access	0.518
3	15,575	Trump's attempt to deny vaccines to New York is playing politics with people's lives (November 2020)[a]	Topic 2: Vaccine efficacy and rollout	0.578
4	14,536	The FDA[b] and CDC[c] recommend a pause in the use of the Johnson & Johnson COVID19 vaccine (April 2021)	Topic 1: Vaccine access	0.417
5	12,473	Pfizer's mRNA vaccine candidate showed initial evidence of efficacy (November 2020)[a]	Topic 3: Vaccine development and people's views	0.844
6	11,684	President Biden took credit for the vaccine from President Trump (March 2021)[a]	Topic 1: Vaccine access	0.964
7	11,046	Russian vaccine trial shows high efficacy (February 2021)	Topic 2: Vaccine efficacy and rollout	0.618
8	10,151	UK's vaccine is safe and induces an immune reaction (July 2020)	Topic 2: Vaccine efficacy and rollout	0.844
9	8586	Like with smallpox, vaccinations along with surveillance and contact tracing are essential to COVID's elimination (April 2020)[a]	Topic 2: Vaccine efficacy and rollout	0.547
10	8282	Why we need two doses of mRNA vaccines (April 2021)	Topic 1: Vaccine access	0.488

[a]Tweet was among the top 10 retweeted and concurrently one of the top 10 liked tweets.

[b]FDA: Food and Drug Administration.

[c]CDC: Centers for Disease Control and Prevention.

Discussion

Principal Results

This study investigated the combined effects of the three categories of message-level factors on the popularity and virality of tweets about COVID-19 vaccines using text-mining techniques. We also examined the topic communities of the most liked and most retweeted tweets using network analysis and visualization. In this section, we first discuss how text-mined topics and valence, together with autoextracted information about social media message features affected likes and retweets. We further discuss limitations and implications for the directions of vaccine campaigns.

Out of the 12 latent topics identified by topic modeling, Topics 1-8 increased likes and Topics 1-7 increased retweets. Vaccine development and people's views (Topic 3) had the largest positive impact on likes and retweets, as reflected by β coefficients. The intrinsic novelty feature of COVID-19 vaccines could provide plausible explanations. The vaccines were newly developed to help fight off the new coronavirus, and two out of the four brands examined in the study used mRNA, a technology that had not been approved previously for general use in humans [5]. Therefore, information about vaccine development and technology was more popular and viral. Relatedly, 3 out of the top 10 liked tweets reflected Topic 3, two of which were about mRNA vaccines. One out of the top 10 retweeted tweets reflected Topic 3, which was about mRNA vaccines. The findings were consistent with those in past

research that suggested the impact of novel content in the social transmission of health news [26].

Vaccine efficacy and rollout (Topic 2) had the second largest positive impact on likes and retweets, as indicated by β coefficients. Prior research revealed the impact of efficacy information on the virality of online health news [26] and in tweets about the COVID-19 pandemic [25]. This study also underscores the importance of efficacy information on the virality of tweets about COVID-19 vaccines.

The findings suggest that tweets focusing on the topic of vaccine development and people's views, and the topic of vaccine efficacy and rollout highly meet the public's needs for information during the COVID-19 pandemic, and therefore tend to become popular and viral on Twitter. It is plausible that these tweets provide useful and novel information that help to reduce uncertainty in a health crisis. Vaccine campaigns could provide more information about these topics to help the diffusion of information on social media.

It is notable that polarized political information such as that supporting a political party could be intertwined with different topics. Polarized political information was contained in 5 out of the top 10 liked tweets and in 3 out of the top 10 retweeted tweets. As political stance may play a role in the vaccine debate in the United States [9], it would be interesting for future studies to investigate its impact in addition to other factors.

This study showed that the overall valence of the tweets was positive. This was consistent with findings in prior research on

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tweets about vaccines in general [11-13] and about COVID-19 vaccines in particular, regardless of country [15,16]. The results showed that positive valence increased likes. This is in alignment with findings in prior research [22,23]. In comparison, the results showed no impact of valence on retweets. Past research revealed mixed findings regarding the effects of valence on retweets [11,25-27]. The explanation may rest in the complex cognitive sources underlying retweeting behavior. Compared with liking, retweeting is a more social behavior that may involve expected reactions from recipients about the content and/or the sender [26].

Regarding social media message features, account verification had the largest positive impact on likes and retweets among all factors, as reflected by β coefficients. This finding underscores the importance of account authentication in the popularity and virality of tweets in the face of massive amounts of information. Credible information is vital to reduce uncertainty in a crisis according to the uncertainty reduction theory [25,55]. However, it is notable that account authentication does not always mean content authentication. Accordingly, misinformation spread by verified accounts could pose greater challenges to vaccine campaigns. Vaccine campaigns could try to use and motivate different verified accounts, including institutional and individual accounts, to share credible information for wider reach and to prevent the spread of misinformation.

Furthermore, in alignment with the literature [32,33], the presence of a photo or video enhanced likes and retweets. The presence of a gif increased likes but did not affect retweets. In addition, consistent with the literature [23,34,35], the number of hashtags decreased likes and retweets. The number of external links decreased likes, but did not affect retweets. Inconsistent with the literature [23,25], the number of mentions facilitated likes, but did not affect retweets.

The results revealed that among the examined factors, more could impact likes than retweets. Eight topics predicted likes, whereas seven predicted retweets. Valence predicted likes but did not predict retweets. The presence of a gif, the number of mentions, and the number of external links predicted likes but not retweets. A comparison between like counts of the top 10 liked tweets and retweet counts of the top 10 retweeted tweets also suggested that a tweet was much more likely to be liked than to be retweeted. The number of likes for the highest liked tweet was more than five times the number of retweets for the highest retweeted tweet. These findings indicate more challenges to make a tweet viral than popular.

Limitations

This study has several limitations. We used machine-based text mining to identify the underlying topics and valence in the vast amounts of tweets about COVID-19 vaccines. We then included the text-mined topics and valence, together with autoextracted information of social media message features in the regression models for prediction of the popularity and virality of tweets. Although this approach reduced manual coding, the results were mostly limited to autoidentified and autoextracted factors. Our manual reviews of sample tweets in each topic as well as the top 10 liked and retweeted tweets provided clues that politically polarized information could be intertwined with different topics. It would be interesting for future research to investigate how this may affect the popularity and virality of tweets. For instance, retweeting could derive from complex cognitive sources such as self-presentation [31] and identity communication [27]. A question arises whether consistency in the political stance between the sender and the recipients impact retweets.

Furthermore, the findings were limited to US-based public discourse about COVID-19 vaccines on Twitter. Social media platforms have played an important role in disseminating information and opinions during the COVID-19 pandemic [56]. It would be interesting for future research to compare Twitter with other social media platforms. For instance, the relative significance of examined factors in predicting popularity and virality may vary depending on the social media platform analyzed, as each has its own features.

Finally, the results revealed message-level drivers of the popularity and virality of tweets about COVID-19 vaccines. We included account verification as an independent variable in the regression models and the results showed that it had a positive impact on likes and retweets. However, we did not identify social bots in the massive amounts of tweets. It would be interesting for future studies to investigate the impact of social bots.

Conclusions

This study suggests the public interest in and demand for information about vaccine development and people's views, as well as vaccine efficacy and rollout during the COVID-19 pandemic. These topics, along with the use of media and verified accounts, enhance the popularity and virality of tweets. These issues could be addressed in vaccine campaigns to help the diffusion of content on Twitter.

Conflicts of Interest

None declared.

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Abbreviations

BOW: bag of words
CDC: Centers for Disease Control and Prevention
LDA: latent Dirichlet allocation
mRNA: messenger RNA
WHO: World Health Organization

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Analyzing Citizens' and Health Care Professionals' Searches for Smell/Taste Disorders and Coronavirus in Finland During the COVID-19 Pandemic: Infodemiological Approach Using Database Logs

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Abstract

Background: The COVID-19 pandemic has prevailed over a year, and log and register data on coronavirus have been utilized to establish models for detecting the pandemic. However, many sources contain unreliable health information on COVID-19 and its symptoms, and platforms cannot characterize the users performing searches. Prior studies have assessed symptom searches from general search engines (Google/Google Trends). Little is known about how modeling log data on smell/taste disorders and coronavirus from the dedicated internet databases used by citizens and health care professionals (HCPs) could enhance disease surveillance. Our material and method provide a novel approach to analyze web-based information seeking to detect infectious disease outbreaks.

Objective: The aim of this study was (1) to assess whether citizens' and professionals' searches for smell/taste disorders and coronavirus relate to epidemiological data on COVID-19 cases, and (2) to test our negative binomial regression modeling (ie, whether the inclusion of the case count could improve the model).

Methods: We collected weekly log data on searches related to COVID-19 (smell/taste disorders, coronavirus) between December 30, 2019, and November 30, 2020 (49 weeks). Two major medical internet databases in Finland were used: Health Library (HL), a free portal aimed at citizens, and Physician's Database (PD), a database widely used among HCPs. Log data from databases were combined with register data on the numbers of COVID-19 cases reported in the Finnish National Infectious Diseases Register. We used negative binomial regression modeling to assess whether the case numbers could explain some of the dynamics of searches when plotting database logs.

Results: We found that coronavirus searches drastically increased in HL (0 to 744,113) and PD (4 to 5375) prior to the first wave of COVID-19 cases between December 2019 and March 2020. Searches for smell disorders in HL doubled from the end of December 2019 to the end of March 2020 (2148 to 4195), and searches for taste disorders in HL increased from mid-May to the end of November (0 to 1980). Case numbers were significantly associated with smell disorders ($P<.001$) and taste disorders

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(P<.001) in HL, and with coronavirus searches (P<.001) in PD. We could not identify any other associations between case numbers and searches in either database.

Conclusions: Novel infodemiological approaches could be used in analyzing database logs. Modeling log data from web-based sources was seen to improve the model only occasionally. However, search behaviors among citizens and professionals could be used as a supplementary source of information for infectious disease surveillance. Further research is needed to apply statistical models to log data of the dedicated medical databases.

Introduction

COVID-19 is a contagious respiratory illness caused by the novel coronavirus (SARS-CoV-2). It has been prevailing worldwide since the beginning of 2020 [1]. Various symptoms may be related to COVID-19, such as smell and taste disorders [2]. Loss of smell was a new COVID-19 symptom first reported by the British Rhinology Society in March 2020 [3], and a high prevalence of smell and taste dysfunction among patients with COVID-19 has been found [2]. Internet users seek information on COVID-19 during the pandemic. Infodemiology is an area of science research that scans the internet for user-contributed health-related content [4], with the goal of improving public health [5]. It offers digital data (internet, social media) that can be collected and analyzed in real time, to understand how and why people search for health information and how it affects the data [5]. In terms of disease surveillance, search queries on health-related information may serve as early predictors of population health compared with traditional epidemiology [6]. Besides, the combination of internet surveillance data (online searches) and traditional surveillance data (such as laboratories and physicians' diagnoses) has been shown to provide additional information for alerting and informing the public, as well as better targeting public health policies [7]. However, predicting the course of the pandemic may be difficult due to a variety of factors that have been found to contribute to an infectious disease outbreak [5,8]. Previously, data from search engines have generated high hopes for contributing to outbreak surveillance [7,9-11]. For example, for influenza outbreaks, Google Trends and Google Flu Trends have been used as models for predicting incidences of the disease [10,11]. In China, an increase in internet searches on coronavirus was observed 5-10 days before the disease outbreak and was found to predict an increase in suspected and laboratory-confirmed COVID-19 cases [8]. Strong positive correlations were also found between initial symptoms of COVID-19 and Google search interests [12]. Refining the data signal by reducing surrounding noise remains a big challenge in the field of infodemiology [6]. One of the problems is that general search engines and other internet platforms cannot characterize the users performing the searches, including both citizens and health care professionals (HCPs). Citizens' searches may be more easily influenced by epidemiologically irrelevant factors such as publicity. However, previous studies have shown that focusing research on the dedicated databases used by HCPs provides reliable data for the surveillance of infectious diseases [13,14].

Infodemiology has been acknowledged by public health organizations and the World Health Organization (WHO) as an important emerging scientific field of practice during the pandemic [15], and plays an important role in health informatics research [4]. Infodemiology can be applied to web-based sources of COVID-19–related smell and taste disorders. Many studies on COVID-19–related searches for loss of smell and taste have analyzed information seeking from Google and Google Trends [16-18]. Strong correlations have been found between COVID-19 cases and Google searches on loss of smell and coronavirus information in several countries [16,18]. However, some studies have shown no correlation between Google searches for loss of smell/taste and COVID-19, and their usability as a web-based surveillance method has also been criticized [17]. Novel infodemiological approaches are needed to analyze searches for COVID-19 symptoms from internet databases. Little data exist on how statistical modeling of website log data on smell/taste disorders and coronavirus from the dedicated evidence-based medicine (EBM) sources used by citizens and professionals could enhance disease surveillance and outbreak detection during the COVID-19 pandemic.

In Finland, Health Library (HL) is by far the most frequently used general public health portal on the internet. More than 50 million articles are opened per year by a population of 5.3 million in Finland. The service is free of charge with no advertising, and is provided by the Finnish Medical Society Duodecim, which is a 140-year-old scientific organization with over 24,000 physician members (>90% of the Finnish physicians). Physician's Database (PD), an online source, provides medical information for HCPs. The articles in HL have been written and updated by the same physicians that are authors of the PD aimed at HCPs. Recommendations and evidence summaries are published in PD and are referenced in HL articles for the general public. Most of the HL articles are accessed via Google searches by the general public, with more than 80% using mobile devices. The remaining users (approximately 20%) access the service directly via the web address [19]. When producing the medical articles (>10,000 in total) in HL, the quality criteria of Health On the Net [20] are met.

Previous studies [13,14] on these databases have showed that HCPs' searches in PD on Lyme borreliosis and influenza precede the trends shown by current outbreak surveillance data (public primary care diagnoses and laboratory findings). Therefore, we hypothesized that PD searches could be used as a supplementary source of information for examining COVID-19

spread. In addition, citizens' searching behavior of web-based health information during epidemics may closely follow those of HCPs [21]. Therefore, we also hypothesized that HL information seeking among citizens could be used as a supplementary source of information for disease surveillance [21]. Lyme borreliosis and influenza show seasonal patterns of cases and searches [13,14,21], while COVID-19 may not show seasonal patterns so clearly. Of note, the log data on COVID-19 in HL and PD have previously not been analyzed using statistical models. Here we hypothesized that our models would provide a novel approach to analyze web-based seeking behaviors among citizens and professionals. The aim of this study was (1) to assess whether citizens' and HCPs' searches for smell disorders, taste disorders, and coronavirus relate to epidemiological data on COVID-19, and (2) to test our negative binomial regression modeling (ie, whether the inclusion of the case count could improve the model).

Methods

Databases and Register

We collected weekly coronavirus log data from HL and PD (December 30, 2019 to November 30, 2020) in Finland [22]. We used the number of searches (ie, article links opened by clicking on the entries within the database) from the 3 HL articles ("Smell disorders," "Taste disorders," and "New Coronavirus") and PD articles ("Smell disorders," "Taste disorders," and "Coronavirus"). The taste disorder article was published on the HL platform in mid-May 2020. These database logs were combined with the register data on the number of COVID-19–positive test results (cases) from the Finnish National Infectious Diseases Register of the Finnish Institute for Health and Welfare [23]. The time scale (49 weeks) included the first and second waves of COVID-19 cases. The first wave started in Week 5 (first COVID-19 case) but a clear increase in cases appeared in Week 11, and the wave ended in Week 26. The second wave occurred between Weeks 27 and 49.

Descriptive Statistical Analysis

First, we plotted the searches for all 3 indicators (smell disorders, taste disorders, and coronavirus) over the last 10 years (2010-2020) in both databases (HL and PD) on a weekly basis to see if there were any visual trends in patterns. Second, we assessed weekly searches for the 3 indicators in HL and PD, as well as COVID-19 cases during December 30, 2019, and November 30, 2020 (49 weeks), to compare if they preceded or appeared at the same time (peaked) in patterns.

Time-Series Analysis

Third, we ran time-series analyses using negative binomial regression models of the number of searches explained by time (week) and weekly cases of COVID-19. For each model, we determined if the case count was a significant predictor. We assumed statistical significance at $P<.05$. We also performed likelihood ratio tests (LRTs) using analysis of variance (ANOVA) and Akaike information criterion (AIC) to assess model fit. Time-series analyses were conducted in R (R version 4.0.5; packages "zoo" and "MASS") using RStudio (R Foundation for Statistical Computing) [24]. Log data were analyzed anonymously using internet protocol addresses of the purchasers of the PD, not the personal internet protocol addresses of the professionals. Thus, no individual HCP performing the searches can be identified. No ethical statements were needed.

Results

Descriptive Statistical Analysis

When plotting the searches for smell disorders, taste disorders, and coronavirus over the last 10 years (2010-2020) in HL and PD, we found that time lag was unlikely upon visual inspection, seasonality was not assessable due to COVID-19 waves, and nothing indicative appeared in pre-2020 data (Figure 1). Between December 30, 2019, and November 30, 2020 (Figures 2 and 3), coronavirus searches drastically increased in HL (from 0 to 744,113 in Weeks 1-11) and PD (from 4 to 5375 in Weeks 1-13), prior to the first wave of COVID-19 cases (starting in Week 11). Citizens' searches for smell disorders in HL doubled (from 2148 to 4195) from the end of December 2019 (Week 1) to the end of March 2020 (Week 13). Citizens' searches for taste disorders in HL increased (from 0 to 1980) from mid-May (Week 21) to the end of November 2020 (Week 49). Professionals' searches for smell and taste disorders in PD showed uneven patterns (Figure 3). The maximum and minimum months and weeks, as well as the total number of searches and cases are shown in Table 1.

Figure 1. Health Library and Physician's Database weekly searches for smell disorders, taste disorders, and coronavirus in Finland during 2010-2020.
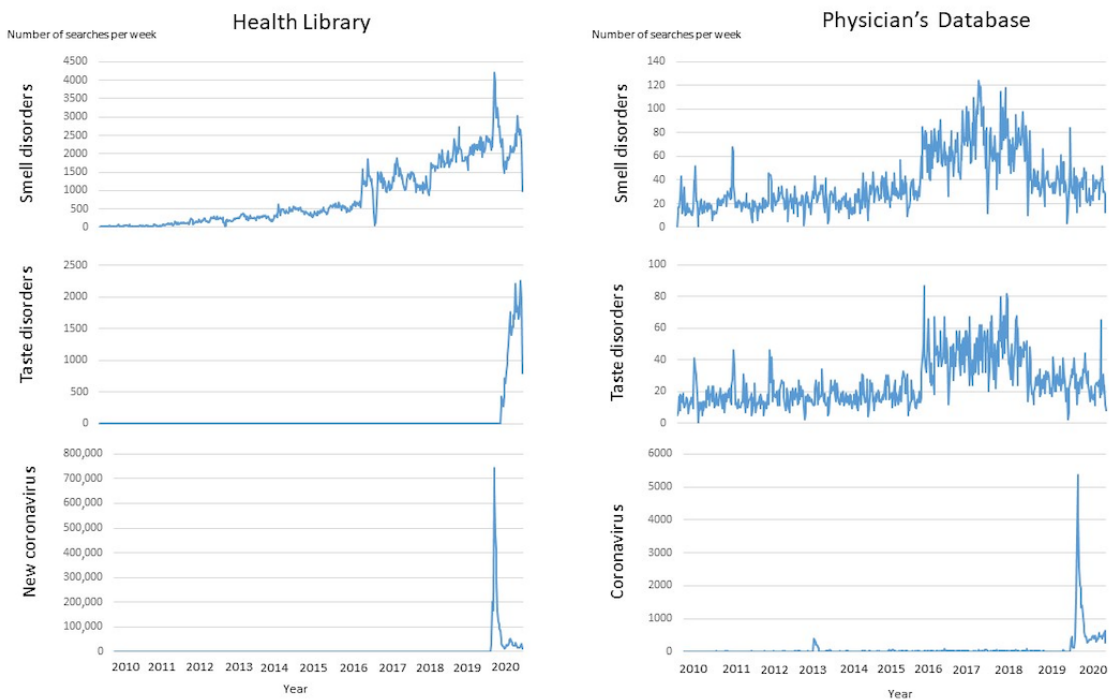
Figure 2. COVID-19 cases and Health Library searches for smell disorders, taste disorders, and new coronavirus in Finland between December 30, 2019, and November 30, 2020.
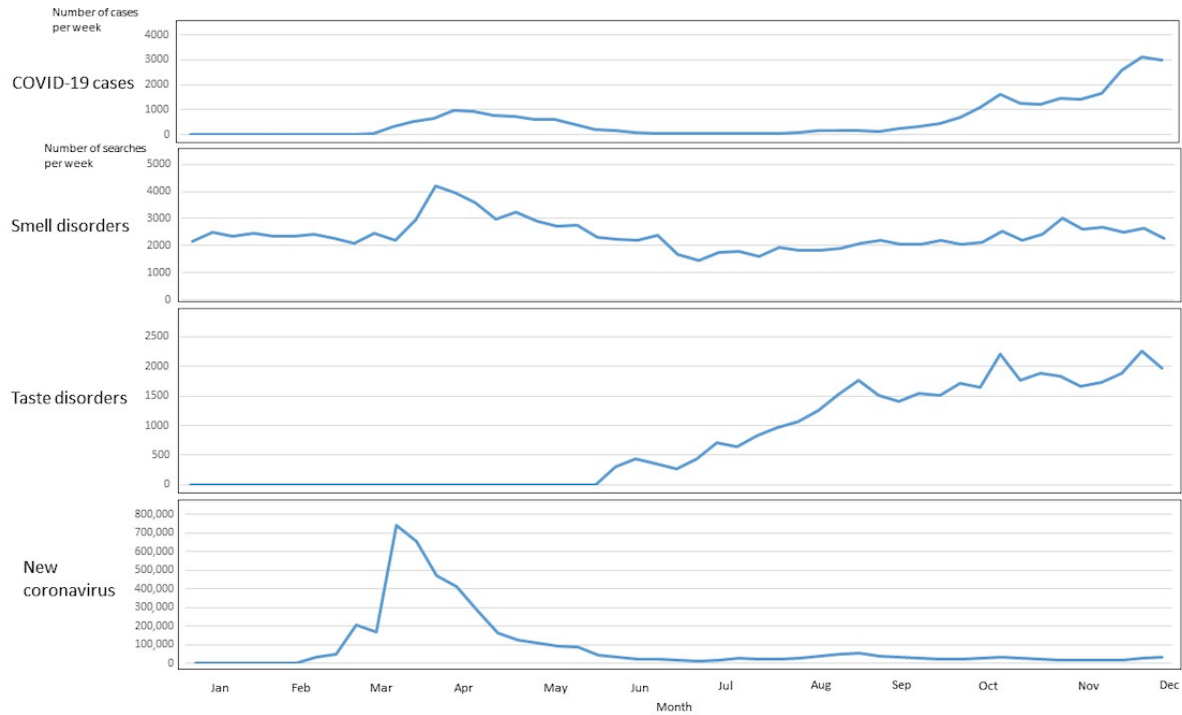
Figure 3. COVID-19 cases and Physician's Database searches for smell disorders, taste disorders, and coronavirus in Finland between December 30, 2019, and November 30, 2020.
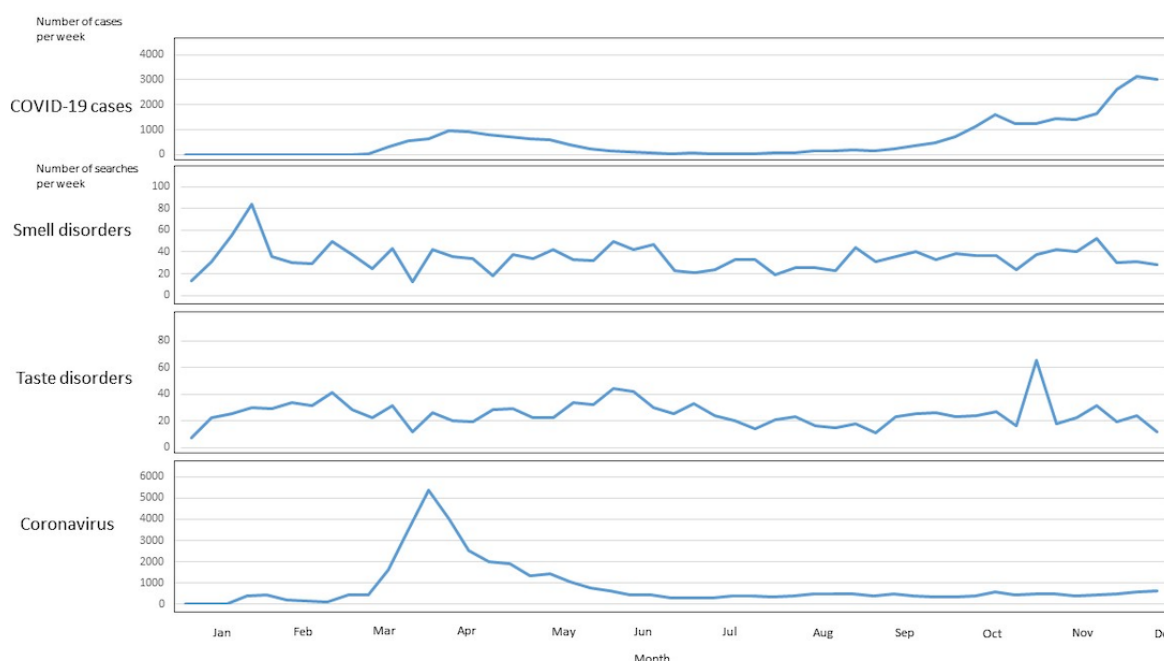
Table 1. The maximum and minimum months and weeks of searches and cases, and the total number of Health Library and Physician's Database searches for smell disorders, taste disorders, and coronavirus, as well as COVID-19 cases in Finland between December 30, 2019, and November 30, 2020.

Database	Maximum number of searches or cases (peaks)		Minimum number of searches or cases		Total number of searches or cases (cumulative)
	Month (week)	Searches in maximum week	Month (week)	Searches in minimum week	
Health Library					
Searches for smell disorders	March (13)	4195	June (26)	1468	117,477
Searches for taste disorders	November (48)	2262	December to May (1-21)	0	37,114
Searches for new coronavirus	March (11)	744,113	December to February (1-6)	0	4,395,898
Physician's Database					
Searches for smell disorders	January (4)	84	March (12)	13	1706
Searches for taste disorders	October (43)	65	December (1)	7	1235
Searches for coronavirus	March (13)	5375	December (1)	4	39,779
COVID-19 cases	November (48)	3134	December to February (1-4)	0	28,385

Time-Series Analysis

Smell disorder searches in HL were significantly associated with case numbers in the time-series analysis ($P<.001$; Figure 4A). Including the case numbers in the model of smell disorders did significantly improve the model (LRT ANOVA $P<.001$, AIC reduced from 752.71 to 725.58). While case numbers were associated with taste disorders in HL ($P<.001$), the model was statistically significant improved (LRT ANOVA $P<.001$, AIC reduced from 10,464.04 to 5524.93) but not performing adequately based on visualization (Figure 4B). Even after including case numbers and new coronavirus searches in HL, the model did not improve (LRT ANOVA $P>.99$, AIC increased from 1141.26 to 5,642,226.89; Figure 4C). When plotting PD

searches for coronavirus and COVID-19 case numbers, the model improved (LRT ANOVA *P*=.001, AIC reduced from 754.74 to 745.94; Figure 5C). For smell and taste disorders, there was no improvement in the model (Figure 5A and Figure 5B). The results of LRT ANOVA and AIC are presented in Table 2.

Figure 4. Health Library weekly searches (gray line) with fitted trends (green line) for smell disorders (A), taste disorders (B), and new coronavirus (C) in Finland between December 30, 2019, and November 30, 2020. Fitted trends took into account time and COVID-19 cases.

Figure 5. Physician Database weekly searches (gray line) with fitted trends (green line) for smell disorders (A), taste disorders (B), and coronavirus (C) in Finland between December 30, 2019, and November 30, 2020. Fitted trends took into account time and COVID-19 cases.

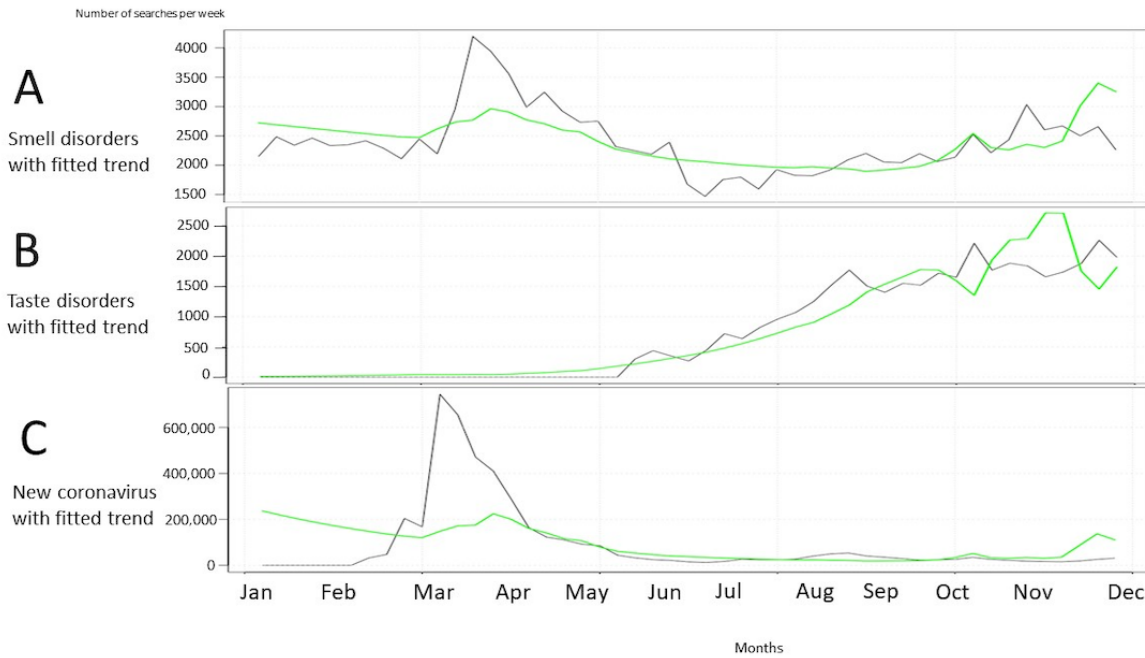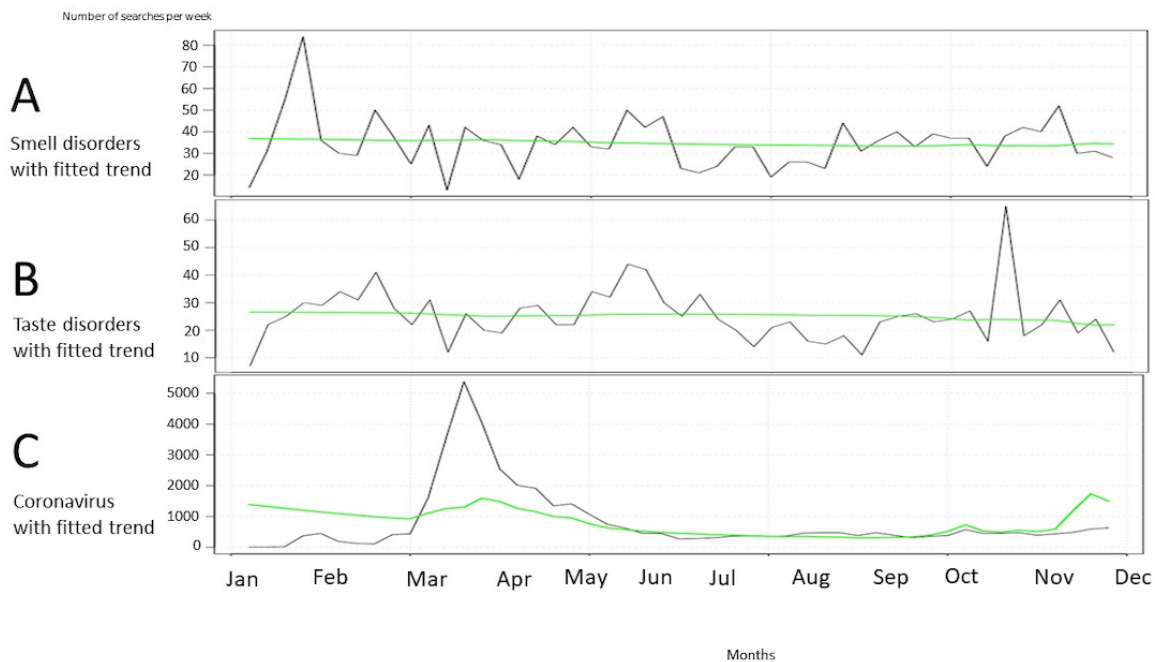**Table 2.** Health Library and Physician's Database searches for smell disorders, taste disorders, and coronavirus fitted with a trend of COVID-19 cases, including P values of cases in model, LRT[a], ANOVA[b], and AIC[c], and model improvement information.

Database	P value of cases in model	LRT ANOVA, P value	AIC	Model improvement
Health Library				
Searches for smell disorders	<.001	<.001	From 752.71 to 725.58 (Reduced)	Improved
Searches for taste disorders	<.001	<.001	From 10,464.04 to 5524.93 (Reduced)	Improved
Searches for new coronavirus	<.001	>.99	From 1141.26 to 5,642,226.89 (Increased)	Not improved
Physician's Database				
Searches for smell disorders	.76	.77	From 380.26 to 382.17 (Increased)	Not improved
Searches for taste disorders	>.99	.63	From 358.68 to 360.46 (Increased)	Not improved
Searches for coronavirus	<.001	.001	From 754.74 to 745.94 (Reduced)	Improved

[a]LRT: likelihood ratio test.

[b]ANOVA: analysis of variance.

[c]AIC: Akaike information criterion.

Discussion

Principal Findings

In our study, we were able to characterize the searching behaviors of citizens and HCPs during the COVID-19 epidemic in Finland 2020. We found that information seeking on coronavirus preceded the cases in the first wave, but not in the second one. Searches for smell and taste disorders showed a visually clear pattern in citizens' searching, while HCPs' searches remained uneven throughout the months. A clear model improvement was found when fitting the model of case numbers and plotting citizens' smell and taste disorder searches and professionals' coronavirus searches, respectively.

Citizens' HL Searches

For smell disorders, when we plotted HL searches and fitted a model that took into account time and COVID-19 case numbers in Finland, the case numbers could explain some of the dynamics of the search. This means that the model has improved from a statistical point of view. However, a visual pattern was not performing well. For taste disorders, when we plotted HL searches and fitted a model that took into account time and COVID-19 cases, the case numbers could again explain the dynamics of searches. This indicated that compared with a model that would only include time, there is an improvement when the COVID-19 incidence is added to the model. However, this model was also not performing very well visually, showing deviation at the end of the year. When plotting new coronavirus searches in HL and fitting a model taking into account time and COVID-19 cases, the case numbers could not explain the dynamics of the search. This means that inclusion of COVID-19 cases does not improve the model statistically. New coronavirus searches and COVID-19 cases seemed to coincide in this model, indicating that with more cases, more users read up on coronavirus and associated symptoms from internet sources. However, it could also mean that for the smell and taste disorders, more people get these symptoms because of COVID-19, and therefore look them up from internet sources. It is not possible to determine this interpretation from the data, but as the searches for coronavirus follow the same pattern, the plausible explanation is that citizens seek web-based information on new coronavirus and its associated symptoms (smell and taste disorders).

Professionals' PD Searches

When plotting PD searches for coronavirus and fitting a model that took into account time and COVID-19 case numbers in Finland, the case numbers could explain some of the dynamics of the search. These results show that the model has improved. However, improvement appears only when the cases are up and professionals search more for information. For smell and taste disorders, there is no improvement in the models, possibly because there were seen simply as symptoms of COVID-19, thus not warranting investigation as individual disorders. In PD searches for smell and taste disorders, a temporary increase was seen in patterns during 2017-2019, caused by changes in logs on the platform. However, it did not affect our results. Our findings showed that modeling professionals' seeking behavior on COVID-19 did not perform as well as we had hypothesized.

Comparison With Prior Work

Prior studies have assessed the searches for coronavirus and smell/taste disorders related to COVID-19 from Google and Google Trends [16-18]. The usability of web-based surveillance methods has also been criticized [17]. In infodemiology, refining the data signal by reducing surrounding noise remains a big challenge [6]. General search engines and the results they provide may yield unreliable health information for HCPs and citizens, and engines cannot distinguish the users, possibly resulting in poorer detection of infectious diseases based on internet searches. In Finland, PD is aimed at HCPs, thus we are able to assess the searches performed by HCPs. Prior studies have found that PD searches for Lyme borreliosis [13] and influenza [14] preceded the trends shown by current outbreak surveillance data (public primary care diagnoses and laboratory findings). We concluded that PD searches could be used as a supplementary source of information for disease surveillance. Besides, a prior study [21] has found that citizens' searches in HL followed epidemiological data on Lyme borreliosis. Both

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HL and PD are built upon EBM sources. General search engines may yield unreliable results that will lead searchers to the online sources of misinformation on COVID-19 [25]. Our study has demonstrated the difference between citizens' and HCPs' database search behaviors on coronavirus, as well as smell and taste disorders and their relation to COVID-19 cases with statistical model testing during the COVID-19 epidemic in Finland 2020. Our results strengthen prior findings of using the searches in HL and PD as a supplementary source of information for infectious disease surveillance.

Strengths and Limitations

The strengths of our study were representativeness (HCPs using PD) and timeliness (real-time internet databases), as well as reliable medical internet sources (citizens and HCPs using EBM databases). Some limitations of this study should be taken into consideration. Coronavirus searches in HL and PD began to increase prior to the outbreak and continued rising during the first wave, and then decreased. However, the increasing pattern was not seen during the second wave. A possible reason may be that the second wave appeared very soon after the first one, thus making the disease more familiar to HCPs who needed less information on the virus. In addition, daily news and media publications on COVID-19 may have had a huge impact on both citizens' and HCPs' information seeking behavior on the internet and from web-based sources. Initial curiosity in the novel disease resulted in an increased searching pattern. However, citizens and HCPs may have been later fatigued by overwhelming media coverage of COVID-19 or they went to other sources, resulting in a rapid decrease in searches, although confirmed cases remained high during the course of the pandemic. Patients with COVID-19 may be asymptomatic or presymptomatic [26], thus they may not be eager to seek internet information on COVID-19. This may also decrease searches in the databases. A previous study [17] has suggested that the decrease in Google searches for taste and smell loss after the first months of the pandemic can be explained by news on digital media. Besides, genuine interest on self-symptoms before they become broadly known to the general public may have faded [17]. Prior studies have found that Google searches for smell and taste loss varied between countries [27] but remained at a higher level after the beginning of the pandemic [27,28]. In our study, searches for smell and taste disorders showed visually better prediction among citizens than HCPs, possibly indicating that loss of smell or taste may have been the only concerning symptom of mild COVID-19 cases. Therefore, citizens may have searched for information from web-based sources about these symptoms rather than visiting a doctor. We also found that HCPs' PD searches for smell and taste disorders showed no improvement in models due to the small number of searches. There were no citizens' HL searches for taste disorders from the end of December 2019 to mid-May 2020, since the first article was published in mid-May and searching started to increase. We cannot distinguish if the increase in searches resulted from citizens' interest in a novel article or in COVID-19–related symptoms. However, we assume the increase may include both.

Conclusions

Our study has visually shown how much and how fast citizens and HCPs began to seek health information from web-based sources at the start of the COVID-19 outbreak and how this searching has carried on during the pandemic in Finland 2020. Modeling log data statistically improved the model only occasionally. However, citizens' and professionals' search behaviors could be used as an additional source of information for infectious disease surveillance. Further research is needed to apply statistical models to log and register data of the dedicated reliable medical sources, as well as to assess predictive values of smell and taste disorder searches on the internet. Novel infodemiological approaches provide an understanding of citizens' and professionals' information seeking behaviors on COVID-19 from web-based databases. Results could be used in decision making, planning, and research, in collaboration with experts working in various fields of public health medicine and health informatics.

Authors' Contributions

MM, SP, CH, PM, VJ, HP, MK, and OH designed the study concept. MM, SP, and OH performed the literature search. MM, SP, CH, PM, VJ, and OH gathered the study data. MM, SP, CH, and VJ carried out the data analyses and interpretation. MM, SP, CH, PM, VJ, HP, MK, and OH reviewed the final version of the manuscript. MM and SP drafted the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Conflicts of Interest

MK has held various trustee positions in the Finnish Medical Society Duodecim since the late 1990s. OH has held various trustee positions in the Finnish Medical Society Duodecim and Duodecim Medical Publications Ltd since 2009. The other authors have no conflicts of interest.

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Abbreviations

AIC: Akaike information criterion
ANOVA: analysis of variance
EBM: evidence-based medicine
HCPs: health care professionals
HL: Health Library
LRT: likelihood ratio test
PD: Physician's Database

Original Paper

Smokers' Likelihood to Engage With Information and Misinformation on Twitter About the Relative Harms of e-Cigarette Use: Results From a Randomized Controlled Trial

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Abstract

Background: Information and misinformation on the internet about e-cigarette harms may increase smokers' misperceptions of e-cigarettes. There is limited research on smokers' engagement with information and misinformation about e-cigarettes on social media.

Objective: This study assessed smokers' likelihood to engage with—defined as replying, retweeting, liking, and sharing—tweets that contain information and misinformation and uncertainty about the harms of e-cigarettes.

Methods: We conducted a web-based randomized controlled trial among 2400 UK and US adult smokers who did not vape in the past 30 days. Participants were randomly assigned to view four tweets in one of four conditions: (1) e-cigarettes are as harmful or more harmful than smoking, (2) e-cigarettes are completely harmless, (3) uncertainty about e-cigarette harms, or (4) control (physical activity). The outcome measure was participants' likelihood of engaging with tweets, which comprised the sum of whether they would reply, retweet, like, and share each tweet. We fitted Poisson regression models to predict the likelihood of engagement with tweets among 974 Twitter users and 1287 non-Twitter social media users, adjusting for covariates and stratified by UK and US participants.

Results: Among Twitter users, participants were more likely to engage with tweets in condition 1 (e-cigarettes are as harmful or more harmful than smoking) than in condition 2 (e-cigarettes are completely harmless). Among other social media users, participants were more likely to likely to engage with tweets in condition 1 than in conditions 2 and 3 (e-cigarettes are completely harmless and uncertainty about e-cigarette harms).

Conclusions: Tweets stating information and misinformation that e-cigarettes were as harmful or more harmful than smoking regular cigarettes may receive higher engagement than tweets indicating e-cigarettes were completely harmless.

Trial Registration: International Standard Randomized Controlled Trial Number (ISRCTN) 16082420; https://doi.org/10.1186/ISRCTN16082420

KEYWORDS

e-cigarettes; misinformation; Twitter; social media

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Introduction

e-Cigarette use is associated with potentially health risks owing to exposure to particulate matter, metals, and other constituents [1]. However, there is growing evidence that the short-term health risks of vaping nicotine are considerably lower than smoking regular cigarettes [1,2]. Recent studies among current smokers reported misperceptions that e-cigarettes are as harmful or more harmful than smoking are increasing in both the United Kingdom and the United States [3]. Misperceptions about the relative harms of e-cigarettes compared with smoking may deter smokers from considering switching to e-cigarettes to reduce their harm from continuing to smoke combustible cigarettes [4,5].

While recent research has described e-cigarette marketing and information on various social media platforms [6-10], there is limited knowledge on the types and sources of e-cigarette–related information and misinformation on social media and how such information and misinformation influences public misperceptions about e-cigarette harms. Misinformation can be defined as information that is incorrect or misleading [11], which differs from misperceptions, defined as false or inaccurate beliefs of the individual. Some examples of misinformation about e-cigarettes include e-cigarettes as being as or more harmful than combustible cigarettes, or that e-cigarettes are completely harmless. Specifically, there is a knowledge gap in assessing smokers' engagement with information and misinformation about the relative harms of e-cigarettes compared with smoking. Measuring audiences' engagement with health information and misinformation on social media, such as Twitter, can provide important insights as to how misinformation spreads and potentially impact users' vaping behavior. The theory of planned behavior posits that intentions are strong predictors of behavior [12]; thus, the likelihood of engagement can be a predictor for actual engagement with information and misinformation.

Moreover, research shows that health rumors and health information and misinformation can undermine public health efforts because misinformation is disseminated more quickly and widely than accurate information on the internet [13]. Perceived message importance can mediate the sharing of information and misinformation on the internet [13]. There have been some studies on engagement done on other platforms but not many focus on Twitter, which is a popular social media platform that many people frequent to discover news and information. Other studies that explore information and misinformation data on Twitter are more descriptive or focus on the content of Twitter posts [14-16], or look at tobacco use as the outcome rather than engagement as the outcome [17]. There is a need for more scientific evidence looking at engagement with misinformation on social media to better develop public health interventions [18].

To address this research gap, we analyzed data from a larger web-based randomized controlled experiment to compare smokers' likelihood to engage with various forms of information and misinformation on Twitter related to e-cigarette harms. We looked at and compared the United States and the United Kingdom specifically, since regulations and public perceptions of e-cigarettes differ in these 2 countries, and we wanted to examine the relationships across these contexts. Information and misinformation about e-cigarettes on social media are prevalent, and this exploratory study on one social media platform, Twitter, helps examine whether exposure to information and misinformation about e-cigarettes impacts the likelihood of engagement. These findings will inform future work to replicate studies across additional social media platforms and research to measure actual engagement with information and misinformation.

Methods

Methods Overview

Data for this analysis was obtained from a web-based experiment among 1200 US and 1200 UK adult smokers. The study's primary objective was to examine the effects of exposure to information and misinformation on e-cigarette harms on Twitter on smokers' intentions to quit smoking and use e-cigarettes [19]. This analysis focuses on the measures of likelihood to engage with misinformation on e-cigarette harms on Twitter, which were collected as part of the overall study. Participants were enrolled through the web-based consumer research panel Prodege, recruited via internet sources, such as email invitations, telephone alerts, banners and messaging on websites, and online communities (CONSORT [Consolidated Standards of Reporting Trials] diagram in Figure 1). Eligible participants were aged 18 years and older, smoked cigarettes in the past 30 days, and had not used e-cigarettes in the past 30 days.

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) flow diagram.
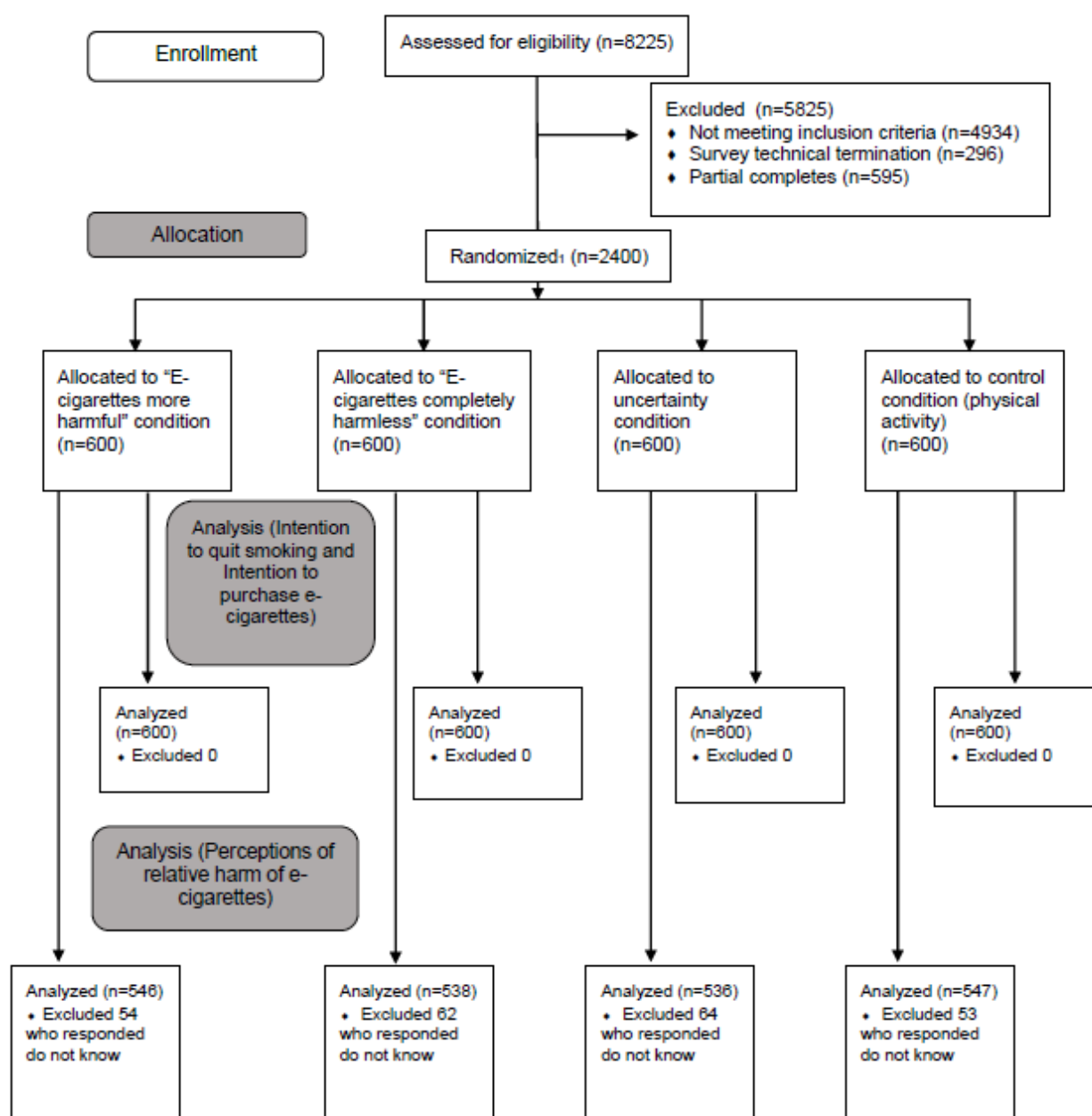
1. *Survey recruitment used a least-fill approach; as a respondent came in, they were assigned to the exposure with the lowest complete count.*

Participants first completed baseline measures of their intentions to quit smoking and use e-cigarettes. Next, participants were randomly assigned through the built-in least-fill randomizer function on the Prodege survey platform to view four tweets within one of the following four experimental conditions in a 1:1:1:1 ratio: (1) e-cigarettes are as harmful or more harmful than smoking, (2) e-cigarettes are completely harmless, (3) uncertainty, or (4) control (physical activity). Based on the current state of the science of e-cigarette harms [1,2], conditions 1 and 2 represented the misinformation tweets, and condition 3 represented comments of media discourse on Twitter often claiming the evidence on e-cigarette harms is uncertain or questioned scientific claims.

The tweets shown to participants were captured through a validated machine learning algorithm developed by the study team [20,21]. We chose to use real tweets rather than artificially created ones to allow for a more realistic representation of what participants would potentially encounter on social media, and this would provide more external validity for the study's results. Using the random sample function in SPSS, 499 tweets were identified from a larger corpus of over 700,000 tweets about e-cigarette harms, which was then narrowed down to 20 tweets per experimental condition by the study team. Inclusion criteria for the tweets were the following: (1) explicit statement that e-cigarettes were either as or more harmful than smoking, completely harmless, or uncertain; (2) no mention of children or young people; (3) no mention of specific diseases; (4) no profanities; (5) had multiple "likes" or "retweets"; (6) no

advertising; (7) no pictures; and (8) was available publicly (ie, not deleted). We then selected four representative tweets for each of the experimental conditions. Tweets for the control condition comprised 4 physical activity tweets to reduce bias and avoid topics related to e-cigarettes and substance use. Within each condition, participants viewed 4 tweets in the same order. Multimedia Appendix 1 displays the tweets that comprised each condition.

In this study, we focused narrowly on the topic of e-cigarette relative harms versus short-term harms of smoking cigarettes and relied on the state of the science that was contemporaneous to the occurrence of tweets and when the study was conducted [1,2]. In the United Kingdom, e-cigarettes are tightly regulated and have been endorsed as a harm reduction strategy for smokers [22]. The conclusions from these reports are reflected in public health agencies' health messaging in the United States and the United Kingdom that e-cigarettes are 95% less harmful than continuing to smoke cigarettes [23,24]. In addition, the most recent Public Health England report concluded that the relative risk of adverse health effects from e-cigarette use are expected to be substantially lower than conventional cigarette smoking [25]. This provided the rationale for categorizing tweets to the contrary as misinformation in this study. However, we recognized evidence of absolute health effects from e-cigarette use and therefore categorized tweets that indicated e-cigarette use being completely harmless as misinformation.

Following each tweet, participants were shown a brief description of what it means to reply, retweet, like, and share a message on Twitter. They were then asked to indicate whether they are likely to reply, retweet, like, or share the tweet they just viewed. Before answering these questions, participants were also provided with a link to Twitter's official definitions of each form of engagement (Multimedia Appendix 2). They were then asked to complete posttest measures of intentions to quit smoking and use e-cigarettes, followed by questions regarding demographics and tobacco use. Participants were asked how often they visited or used eight different social media platforms (Twitter, Instagram, Facebook, Snapchat, YouTube, WhatsApp, Pinterest, and LinkedIn) on a 6-point scale ranging from several times a day to never. We ran a randomization check and confirmed randomization was successful because baseline characteristics did not differ across the 4 conditions. The University of Bristol's institutional review board approved this study.

Measures

Outcome Measure: Likelihood of Engagement With Tweets

We operationalized the likelihood of engagement with tweets as the likelihood of replying, liking, retweeting, or sharing such information based on prior research on engagement with news and health information on Twitter [26]. These forms of engagement represent the 4 options that Twitter users can choose to interact with every tweet within the Twitter platform. After reading each of the 4 tweets in their assigned experimental condition, participants were asked 4 questions, which included "Are you likely to Reply/Retweet/Like/Share this message?"

Response options were "yes (1)" or "no (0)." Multimedia Appendix 3 summarizes the mean (SD) values of the four distinct engagement variables by condition. The Kuder-Richardson coefficient (KR-20) across the 16 engagement items was 0.93, indicating high internal consistency. We created a combined likelihood of engagement index by summing the responses to the 16 engagement questions (range 0-16).

Covariates

We obtained participants' characteristics including sex (male or female), country (the United Kingdom or the United States), race (White or non-White), education (high/secondary school or below; some college/further education college; college/university degree or higher), age (in years), social media use (daily use of 8 different social media platforms; eg, Twitter, Facebook, Instagram, and YouTube), daily internet use (hours per day), past e-cigarette use (never or ever), and baseline perceived relative harm of e-cigarettes compared to combustible cigarettes (Likert scale of much less harmful to much more harmful).

Statistical Analysis

The analytic sample comprised participants who reported using any of the social media platforms at least once a month—974 used Twitter at least once a month and 1287 participants never used Twitter but had used other social media platforms at least once a month. We excluded 139 participants who reported that they never used any of the 8 social media platforms as the questions on likelihood of engagement (reply, retweet, like, and share a tweet) may not be meaningful for these participants. Although the experimental stimuli were presented in the specific context of a tweet, we included both Twitter users and those who used other social media in our analysis because we expected that those who used other social media would be familiar with the concept of engaging with tweets.

We used the R software for coding and analysis of the data. We first conducted descriptive analyses of the individual likelihood of engagement variables (reply, retweet, like, and share) and the combined likelihood of engagement measure stratified by condition. Next, we performed a bivariate Poisson regression of likelihood of engagement as the outcome, treating the overall combined engagement variable as a positive count variable, and condition as a categorical predictor. Condition 1 (tweets that e-cigarettes are as harmful or more harmful than smoking) was used as the referent condition to allow for comparison to the condition portraying e-cigarettes most negatively. We then fitted a Poisson regression of likelihood of engagement as the outcome, adjusting for covariates among Twitter users and those who used other social media.

We stratified the bivariate and multiple regression models by country to analyze the association between condition and engagement among US and UK samples with Twitter users and other social media users. Nagelkerke R^2 and Akaike information criterion values were calculated for each regression model to determine the overall goodness of fit, accounting for the number of parameters in the model. There were no missing values for the engagement variable as well as covariates. To compare engagement in conditions 1, 2, and 3 versus that in condition 4

(control), we repeated the above analyses using condition 4 as the referent condition for both samples (Multimedia Appendices 4 and 5).

Results

Participant Characteristics

Table 1 summarizes the participant characteristics by country among Twitter users and other social media users. Compared to UK participants, US participants tended to be older, more educated, and more racially diverse. We found that the participant characteristics among Twitter and other social media users were similar (refer to Table 1 for more details).

Figure 2 summarizes the means of the counts of the specific types of engagement as well as overall engagement, by condition.

Table 1. Study sample characteristics among Twitter users and other social media users.

Characteristics	Twitter users		Other social media users	
	United States (n=449)	United Kingdom (n=525)	United Kingdom (n=676)	United Kingdom (n=611)
Age (years), mean (SD)	47.7 (13.2)	40.2 (13.4)	50.7 (13.8)	45.3 (14.5)
Females, %	51.0	43.1	51.9	46.0
Non-White, %	32.3	6.9	28.0	6.9
Education, %				
High/secondary school or below	25.2	34.5	34.3	46.8
Some college/further education college	40.5	36.6	37.7	36.0
College/university degree or higher	34.3	29.0	28.0	17.2
Never vaped/used an e-cigarette, %	47.7	43.2	48.8	46.8
Social media use, mean (SD; range[a])	2.6 (1.7; 0-8)	3.0 (1.8; 0-8)	1.4 (1.1; 0-7)	1.7 (1.3; 0-7)
Daily internet use, mean (SD; range)	7.2 (4.8; 0-24)	6.1 (4.1; 0-24)	6.3 (4.4; 0-24)	5.3 (3.6; 0-24)

Figure 2. Mean values of the counts of the specific types of engagement as well as overall engagement, by condition.
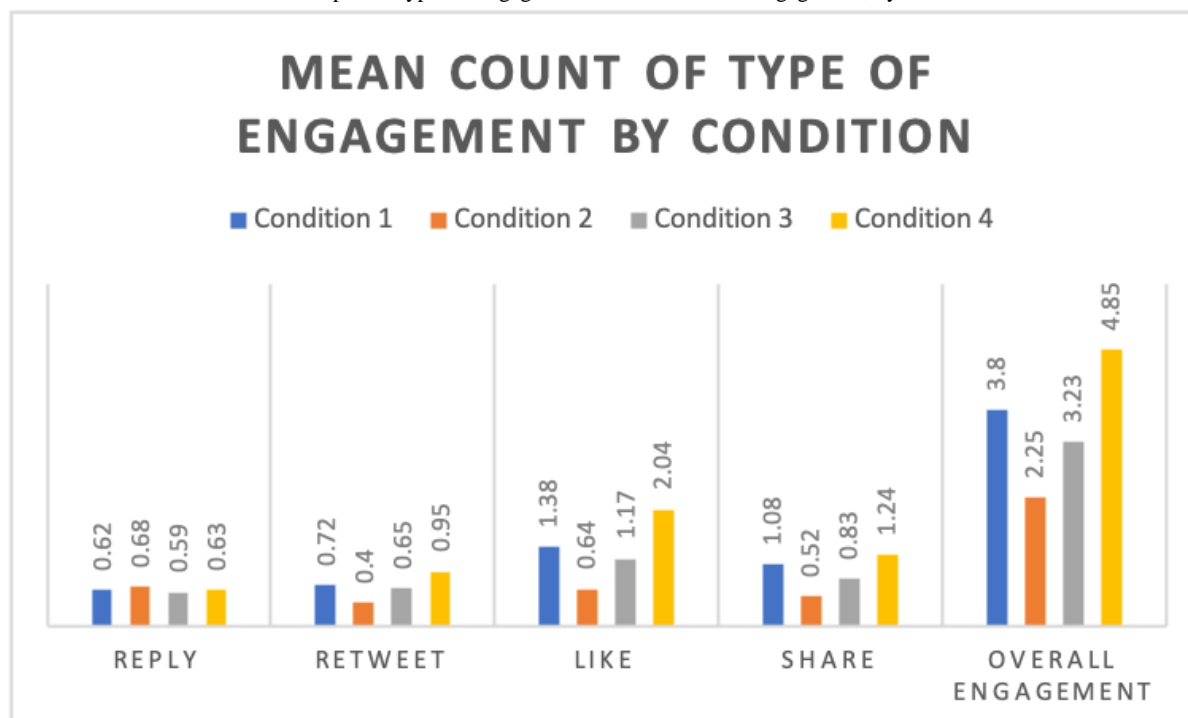
Predictors of Likelihood of Engagement Among Twitter Users

Multimedia Appendix 6 summarizes the regression analyses of the association between the condition and the combined engagement measure among Twitter users and stratified by US and UK participants. Among Twitter users, participants were more likely to engage with tweets in condition 1 (e-cigarettes are as harmful or more harmful than smoking) than in condition 2 (e-cigarettes are completely harmless). Across the various

models, we found that country, age, race, education, increased social media use, and baseline perceived harm that e-cigarettes are more harmful than combustible cigarettes were associated with increased likelihood of engagement (Multimedia Appendix 6).

These findings were substantively similar in stratified analyses among US and UK participants, except for condition 3 (uncertainty about e-cigarette harms). In the overall sample, participants were not significantly more likely to engage with tweets in condition 1 (e-cigarettes are as harmful or more harmful than smoking) than in condition 3 (uncertainty about e-cigarette harms). However, after stratifying by country, US participants were less likely to engage with tweets in condition 3 than in condition 1, and UK participants were more likely to engage with tweets in condition 3 than in condition 1.

Predictors of Likelihood of Engagement Among Other Social Media Users

Multimedia Appendix 7 summarizes the regression analyses of the association between condition and the combined engagement measure for the overall study sample and stratified by US and UK participants. In the overall sample of other social media users, participants were more likely to likely to engage with tweets in condition 1 (e-cigarettes are as harmful or more harmful than smoking) than in conditions 2 (e-cigarettes are completely harmless) and 3 (uncertainty about e-cigarette harms). Across the models, country, age, race, education, social media use, and daily internet use were associated with an increased likelihood of engagement (Multimedia Appendix 7). In the UK stratified sample, social media users were not significantly more likely to engage with condition 4 (the control condition) than with condition 1 (e-cigarettes are as harmful or more harmful than smoking).

Discussion

Principal Findings

To our knowledge, this is one of the first studies to examine differences between Twitter and social media users' likelihood of engagement with web-based health-related information among US and UK smokers who are not currently using e-cigarettes. Utilizing a randomized controlled experiment for a web-based sample of US and UK adult smokers, we found that participants were more likely to engage with tweets that stated e-cigarettes were as harmful or more harmful than smoking—specifically retweets, likes, and shares—compared with tweets indicating e-cigarettes were completely harmless. Among Twitter users, there were differences in the US versus the UK sample in the likelihood of engagement with tweets in the uncertainty condition compared with tweets that e-cigarettes were as or more harmful. Although the overall likelihood of engagement was modest across the conditions, these findings indicate meaningful differences between potential engagement with tweets displaying misinformation of e-cigarettes' relative harm versus smoking and tweets on information and misinformation of e-cigarettes being harmless among smokers.

In the context of increasing trends of misperceptions that e-cigarettes are as harmful or more harmful than smoking among

US adult smokers [4], our findings indicate the need for further investigation of public health implications of the increased likelihood of engagement with misinformation that e-cigarettes are as harmful or more harmful as smoking and the underlying reasons. Knowledge of the impact of misinformation is important to inform the development of corrective approaches or media literacy interventions to ensure that smokers have accurate perceptions of the relative harms of e-cigarettes and to help smokers make informed decisions for reducing harm [13,27]. Research is also needed to understand the underlying cognitive and affective mechanisms that motivate smokers' likelihood to engage with information on social media about e-cigarettes' relative harm versus smoking. The influence of the internet on population health is continuing to expand, and there is a need to better understand how people are increasingly engaging with "health social media" [28,29]. Prior content analyses of Twitter posts support the importance of incorporating social media into tobacco-related interventions [30,31], and research supports the potential of using Twitter as a means to engage the public in health promotion [32,33].

Our differing findings of Twitter and non-Twitter social media users as it relates to engaging with uncertain information on the internet presents preliminary evidence that we cannot generalize these findings to all social media users. The next steps leading from this research would be to replicate this study to examine information and misinformation about e-cigarette harms, especially in the context of being exposed to uncertain information on other social media platforms, such as Facebook and Instagram, and among users of those specific platforms. Knowledge of the impact of misinformation could also be used to advocate for the use of emerging approaches, such as infodemiology [34-36], to further research the phenomena in the population and to inform public health and public policy. Uncertainty may be perceived differently depending on the social media platform and their users from different countries. However, our mostly similar results comparing Twitter and non-Twitter social media users show how social media users of other platforms can still provide insight into what forms of e-cigarette information are more likely to spread on the internet.

Limitations

This study was limited by the measurement of participants' likelihood of engagement with information and misinformation on Twitter in the setting of a web-based study. Study participants were part of an opt-in panel and were not representative of US and UK smokers. In addition, in the interest of presenting actual tweets and not experimentally manipulated tweets, the selected tweets in within the 4 conditions differed in various aspects (eg, names and credentials of the users posting the tweet, length of the tweet, and the number of likes or retweets) in addition to differences in the content regarding e-cigarette harms. The rationale for using actual tweets was to retain the original content of the tweets occurring in the real world. Future research may consider replicating this study using experimentally manipulated tweets to keep other message characteristics constant across conditions. This study did not address nuances in potential absolute harms arising from e-cigarette use, such as youth use and abuse liability, higher dose of nicotine delivery, and individuals creating their own mixtures of e-liquids. Our

approach does not address youth e-cigarette use because it was beyond the scope for our initial research questions. We acknowledged the potential harms and therefore categorized tweets that mention e-cigarettes as harmless to be misinformation. Future research is needed to better assess how the public engages with information and misinformation on social media, which describes harms associated with e-cigarette use.

Conclusions

Despite the limitations, this study provides preliminary evidence that brief exposure to information regarding e-cigarettes being as harmful or more harmful than smoking on social media may be associated with increased levels of engagement compared to information that e-cigarettes are harmless, and this was consistent across Twitter and other social media users and across US and UK participants. But when compared to uncertain information, the pattern of findings was more nuanced and differed between Twitter and other social media users. This requires further investigation, and future research may consider exploring how length of engagement, as well as individual characteristics of the social media post itself such as source of information, content, number of replies, retweets, likes, or shares

on the post, and other characteristics may influence the likelihood of engagement with misinformation. Efforts to examine the impact of engagement with such misinformation on smokers' beliefs and attitudes of relative harms of e-cigarettes and intentions to use e-cigarettes to reduce harm are needed, as a previous study has found that youth exposure to misinformation on YouTube can influence attitudes toward tobacco products [37]. The influence of the internet on population health is continuing to expand, and there is a need to better understand how people are increasingly engaging with "health social media" [18,38,39]. Evidence from this study is critical to inform future corrective interventions to address misperceptions and provide accurate information to smokers about relative harms of e-cigarettes [40,41]. Tools to mitigate misinformation, which have been used in other areas of public health that could be applied to e-cigarette–related information and misinformation may be through accuracy nudges, impactful hashtags, and web-based health communities [42-44]. Our findings can inform how information spreads on social media, and how future public health efforts and interventions can better understand likelihood of engagement on social media to combat the misinformation that exists on the internet.

Authors' Contributions

ASLT, CW, OE, JD, and JB contributed to conceptualizing the study and obtained the funding. JL conducted the data analysis. JL and ASLT drafted the initial manuscript. All authors contributed to drafting the manuscript, and reviewed and approved the final manuscript for publication. ASLT is responsible for the overall content as guarantor.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Message stimuli with each condition.
[PDF File (Adobe PDF File), 3391 KB - publichealth_v7i12e27183_app1.pdf]

Multimedia Appendix 2
Twitter engagement definitions provided in survey.
[PDF File (Adobe PDF File), 9 KB - publichealth_v7i12e27183_app2.pdf]

Multimedia Appendix 3
Descriptive Table of Mean (Standard Deviation) Values of 4 Engagement Behaviors by Condition.
[PDF File (Adobe PDF File), 36 KB - publichealth_v7i12e27183_app3.pdf]

Multimedia Appendix 4
Predictors of Likelihood of Engagement of Tweets among Twitter Users with Control Condition as Referent Group.
[PDF File (Adobe PDF File), 73 KB - publichealth_v7i12e27183_app4.pdf]

Multimedia Appendix 5
Predictors of Likelihood of Engagement of Tweets among Other Social Media Users with Control Condition as Referent Group.
[PDF File (Adobe PDF File), 59 KB - publichealth_v7i12e27183_app5.pdf]

Multimedia Appendix 6
Predictors of Likelihood of Engagement of Tweets Among Twitter users.
[PDF File (Adobe PDF File), 77 KB - publichealth_v7i12e27183_app6.pdf]

Multimedia Appendix 7
Predictors of Likelihood of Engagement of Tweets Among Other Social Media Users.
[PDF File (Adobe PDF File), 83 KB - publichealth_v7i12e27183_app7.pdf]

Multimedia Appendix 8
CONSORT-eHEALTH checklist (V 1.6.1).
[PDF File (Adobe PDF File), 314 KB - publichealth_v7i12e27183_app8.pdf]

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Abbreviations

CONSORT: Consolidated Standards of Reporting Trials
FDA: Food and Drug Administration
KR-20: Kuder-Richardson coefficient
NIH: National Institutes of Health

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<u>Original Paper</u>

The Spread of COVID-19 Crisis Communication by German Public Authorities and Experts on Twitter: Quantitative Content Analysis

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Abstract

Background: The COVID-19 pandemic led to the necessity of immediate crisis communication by public health authorities. In Germany, as in many other countries, people choose social media, including Twitter, to obtain real-time information and understanding of the pandemic and its consequences. Next to authorities, experts such as virologists and science communicators were very prominent at the beginning of German Twitter COVID-19 crisis communication.

Objective: The aim of this study was to detect similarities and differences between public authorities and individual experts in COVID-19 crisis communication on Twitter during the first year of the pandemic.

Methods: Descriptive analysis and quantitative content analysis were carried out on 8251 original tweets posted from January 1, 2020, to January 15, 2021. COVID-19–related tweets of 21 authorities and 18 experts were categorized into structural, content, and style components. Negative binomial regressions were performed to evaluate tweet spread measured by the retweet and like counts of COVID-19–related tweets.

Results: Descriptive statistics revealed that authorities and experts increasingly tweeted about COVID-19 over the period under study. Two experts and one authority were responsible for 70.26% (544,418/774,865) of all retweets, thus representing COVID-19 influencers. Altogether, COVID-19 tweets by experts reached a 7-fold higher rate of retweeting ($t_{8,249}$=26.94, P<.001) and 13.9 times the like rate ($t_{8,249}$=31.27, P<.001) compared with those of authorities. Tweets by authorities were much more designed than those by experts, with more structural and content components; for example, 91.99% (4997/5432) of tweets by authorities used hashtags in contrast to only 19.01% (536/2819) of experts' COVID-19 tweets. Multivariate analysis revealed that such structural elements reduce the spread of the tweets, and the incidence rate of retweets for authorities' tweets using hashtags was approximately 0.64 that of tweets without hashtags (Z=–6.92, P<.001). For experts, the effect of hashtags on retweets was insignificant (Z=1.56, P=.12).

Conclusions: Twitter data are a powerful information source and suitable for crisis communication in Germany. COVID-19 tweet activity mirrors the development of COVID-19 cases in Germany. Twitter users retweet and like communications regarding COVID-19 by experts more than those delivered by authorities. Tweets have higher coverage for both authorities and experts when they are plain and for authorities when they directly address people. For authorities, it appears that it was difficult to win recognition during COVID-19. For all stakeholders studied, the association between number of followers and number of retweets was highly significantly positive (authorities Z=28.74, P<.001; experts Z=25.99, P<.001). Updated standards might be required for successful crisis communication by authorities.

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Introduction

Background

The occurrence of the SARS-CoV-2 virus and the ongoing COVID-19 pandemic have made crisis communication inevitable. Across countries, people use social media as their source of information about development of the pandemic [1]. Consequently, public authorities use different social media channels to deliver information about various aspects of the virus, such as incidence rates, information about its spread, and the efficacy of measures or regulatory decisions. The COVID-19 pandemic hit Germany at the beginning of 2020. General information in Germany has been delivered on Twitter, with authorities, and particularly other experts such as scientists, science communicators, politicians, and journalists, distributing COVID-19–related tweets [2] and content on the German Twitter network. Both authorities and COVID-19 experts use Twitter to directly share their own insights and opinions with the Twitter community in an unfiltered manner independent of traditional media.

Prior Work

The number of scientific publications regarding COVID-19 is enormous, including several studies that investigated COVID-19 crisis communication on social media platforms such as Twitter. Crisis communication via Twitter was also studied before the COVID-19 pandemic. For example, surveys investigated Twitter data in regard to crisis communication with a focus on health crises [3], natural disasters [4-7], terrorist attacks [8], or nuclear disasters [9]. Twitter communication during the COVID-19 pandemic has been studied with respect to the following topics: conspiracy theories [10], misinformation and fake news [11,12], stigmatization [13,14], public opinions [15-17], sentiments [18-22], sources of information [23,24], and social networks [25,26]. Likewise, country comparisons [27,28] have been performed. Although previous studies showed that the power of social media, especially Twitter, in crisis communication is very high [29], the Twitter communication behavior of different stakeholder groups has been relatively less studied.

COVID-19 Twitter crisis communication studies have shown that different stakeholders such as scientists, governmental authorities, and politicians, as well as health care professionals tweeted more during COVID-19 [30]. Other studies observed that science-oriented Twitter users contributed to the spread of scientific publications to a great extent [31]. The background of the tweeter has a great impact on the spread of tweets. Existing differences in the popularity of stakeholder groups during COVID-19 have already been documented. Scientists, especially virologists, are now more popular on Twitter than governmental sources [32]. An Italian study analyzed Twitter mentions as a proxy of trust in scientists and reported a loss of trust in science, which was explained by increasing frustration with the COVID-19–induced situations [33].

In the aftermath of the Japan earthquake in 2011, the crisis communication and leadership of the government were neither clear nor apparent on Twitter [34]. Thus, crisis communication by authorities is seen as fundamental during COVID-19 [35] and authorities publish a disproportionally large number of scientifically correct tweets [36]. Previous studies have also shown that during COVID-19, tweets published by authorities are rarely among the most successful tweets [37,38]. This summary of previous studies on the role of authorities and experts indicates that while some findings about the role of different stakeholders exist, direct comparison of communication between authorities and experts against the background of COVID-19 has not yet been addressed.

Approach

Given this context, the aim of this study was to describe and analyze COVID-19–related tweets by authorities and experts in Germany. This seems to be a necessary task, as COVID-19 is the first health crisis digitally explained and discussed directly by experts, and as such, it competes with the official crisis communication of authorities for attention and coverage. Tweet spread, as our variable of interest, was measured by retweet and like counts. To compare the content of stakeholder tweets and to explain the spread of tweets, the intrinsic message features of "structure," "content," and "style" of COVID-19 tweets were compared. Variables related to structure are those capturing whether tweets consist of hashtags, images, URLs, and mentions. With regard to the content features of tweets, Vos et al [3] distinguished four different content categories based on prior work on Twitter risk communication against the background of an infectious disease, hazard content, and fear appeals: severity, susceptibility, efficacy, and technical information. This study builds on this work and further expands the content variables with social, politics, and other categories to best capture COVID-19–specific content and to study similarities and differences in crisis communication. Variables related to style are those using first- or second-person words. Negative binomial regressions were performed to evaluate the spread of tweets, focusing mainly on the number of retweets but also on the number of likes of COVID-19 tweets, and to describe the differences in spread in crisis communication based on 39 German authorities and experts.

Methods

Tweet Collection and Data Cleaning

The data set consisted of tweets from 39 German public authorities and experts. The selection of the 39 German authorities and experts was informed by the importance of authorities and experts during the COVID-19 crisis and their visibility in the German discussion. Additionally, these public authorities and experts are active users on Twitter. These stakeholders included 21 authorities and 18 experts. The Federal Ministry of Health and The Robert Koch Institute (RKI) in Berlin were included among the authorities. The expert group

consisted of virologists, science communicators, physicians, and other scientists. Multimedia Appendix 1 shows a list of all 39 accounts included in this study.

Tweets of the 39 Twitter accounts were retrieved with a Twitter application programming interface (API) account of the authors. Using tokens, timelines of all stakeholders were retrieved on January 15, 2021. Data analysis was carried out using RStudio (version 1.31093 for Windows) and additional code packages as well as Excel for Microsoft 365 MSO. When creating a

Twitter account, users confirm that their tweets are public and can be analyzed by third parties [39]. Using Twitter data for crisis communication analysis is a standard procedure and has been carried out in the context of previous crisis situations, as indicated in the Introduction.

Data retrieval led to 81,455 tweets from authorities and experts. This first data set of 81,455 tweets needed further adjustments. Figure 1 shows the process of data adjustments, including the first step of data retrieval over the Twitter API.

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram of Twitter data adjustment steps. API: application programming interface.
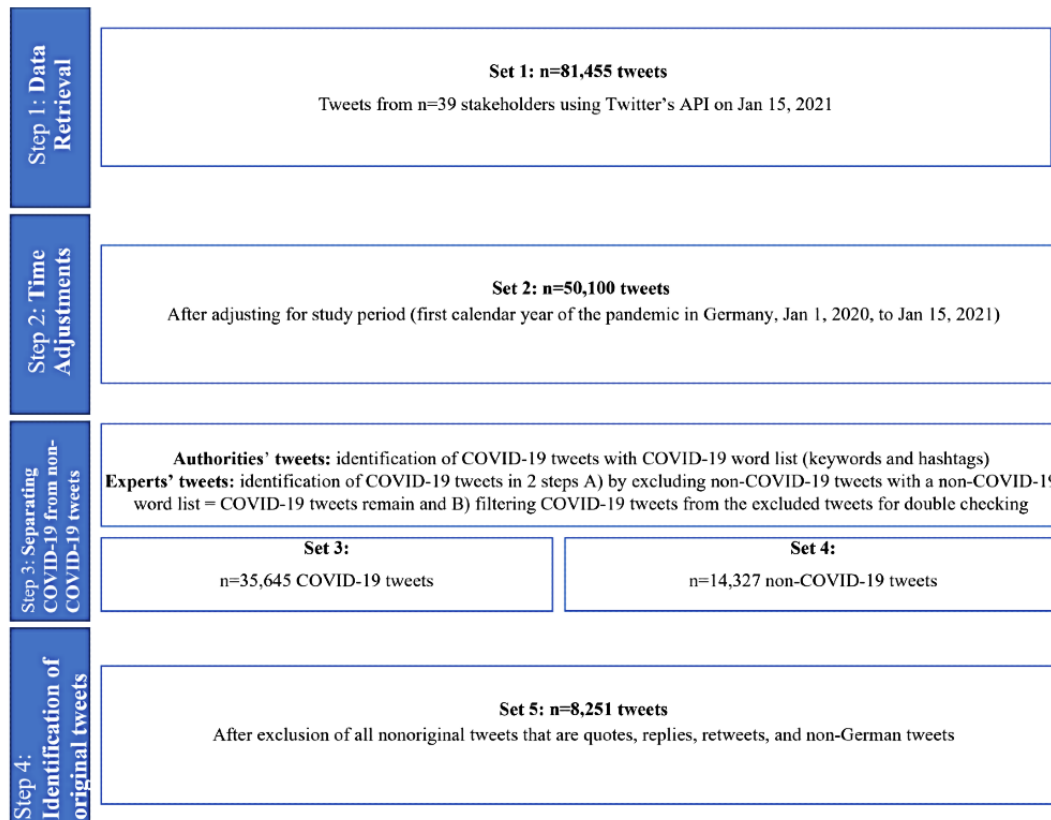
The time frame of tweet analysis was set from January 1, 2020, to January 15, 2021, to capture the first calendar year of the pandemic. However, as vaccinations had just started in Germany at the end of December 2020, and discussions about vaccinations were at a high, the time frame was expanded to January 15. Therefore, as a second step, the data set was adjusted by time so that only tweets from January 1, 2020, to January 15, 2021, were included for the analysis of COVID-19 crisis communication within the first year of the pandemic, leaving 50,100 tweets.

Next, it was necessary to filter COVID-19–related tweets and exclude tweets with other content. To achieve this, COVID-19–related tweets were identified with filter words based on COVID-19 keywords and hashtags. At first glance, tweets of authorities and experts appeared to be very different, and therefore a different filter strategy was used for the two groups. As authorities' tweets were characterized by the use of hashtags and keywords, COVID-19 tweets were filtered in one step. A COVID-19 word and hashtag list was compiled with 1282 words and hashtags. This list contains a wide spectrum of

COVID-19–related words, including different spellings (eg, "corona case," "corona cases").

Comparatively, few of the experts' tweets used hashtags and keywords. As the group of experts' main expertise is COVID-19, it was assumed that most of these tweets were related to the pandemic; therefore, COVID-19 tweets were identified in two filter steps. In the first filter step, non-COVID-19 tweets were filtered with a non-COVID-19 list of words and hashtags, containing 5789 non-COVID-19–related words (eg, "Navalny," "Neanderthals"). In this way, most of the COVID-19 experts' tweets remained in the sample. In the second filter step, the excluded experts' tweets were filtered again using the COVID-19 filter to capture the experts' tweets dealing with non-COVID-19 and COVID-19–related topics in one tweet (eg, cancer and COVID-19). Overall, 35,645 COVID-19–related tweets were obtained, 14,624 of which were published by authorities and 21,021 of which came from experts. Authorities tweeted more about non-COVID-19 topics with 13,100 tweets compared to 1157 non-COVID-19 tweets from experts. The

complete COVID-19 and non-COVID-19 word lists to separate the tweets are available in Multimedia Appendix 2.

For the content analysis, this study focused on original tweets only. These were tweets written and posted directly from the stakeholders, which excluded replies, retweets, and quotes, as well as tweets in the English language. Thus, COVID-19 tweets were subsequently reduced by quotes, retweets, and replies, leaving 8251 original COVID-19 tweets for content analysis. Of these original COVID-19 tweets, 5432 were from authorities and 2819 were from experts. This last filter step of reducing the data to original tweets illustrated that experts were extremely involved in the COVID-19 discussion on Twitter, with a high share of replies, quotes, and retweets in the broader data set.

Descriptive Analysis

Based on the text corpus of all COVID-19 tweets by authorities and experts published within the time frame, we first analyzed descriptive statistics of the tweets (eg, their retweets and likes). Content analysis was then performed. German tweets of authorities and experts were used in text form. For regressions explaining the spread of tweets, retweet and like counts were used as dependent variables.

Some of the explanatory model variables to explain the number of retweets and likes were generated following a previous study [3]. Variables related to structure were those capturing whether tweets feature hashtags, images, URLs, and mentions (see [1]). Four dummy variables indicate whether a tweet contained either a hashtag, an image, a URL, or a mention, respectively.

The four content categories of severity, efficacy, susceptibility, and technical information from a previous study [3] were adjusted and extended to seven categories so as to capture the specific aspects of COVID-19 in this study. The dummy variable severity indicates tweets containing information about the severity of the COVID-19 illness, its seriousness, and symptoms, as well as the spread of the virus without a specific location. The dummy variable susceptibility indicates whether a tweet features region-specific information (eg, about incidences and about high-risk subpopulations). Efficacy refers to tweets that give information to help people cope with the disease, for example by applying preventative measures such as washing hands, social distancing, and vaccination. The variable technical information indicates tweets containing biological-technical information related to the technical spreading mechanism of the virus and/or referring to research organizations, research(ers), and COVID-19 studies. The next dummy variable was social, which was used for tweets containing information about the social consequences of the pandemic, such as home schooling or COVID-19 deniers. Politics was the sixth content variable that captured tweets containing information about political consequences such as short-term allowance or regulations. The last category, "other," was for all other COVID-19–related tweets that could not be attributed to one of the six previous categories.

Tweets were assigned to specific content categories by comparing single words in the tweets with word lists reflecting specific content. Whether or not a tweet contained information about severity was established by comparing tweet words with

a list of 521 specific severity words and hashtags. The list to detect susceptibility tweets contained 99 typical words and hashtags in the context of COVID-19 susceptibility. The efficacy word and hashtag list included 451 typical words. Technical information tweets were generated based on a list of 173 COVID-19 technical information words and hashtags. The word list for politics had 124 words and hashtags. Due to the nature of the word lists, tweets could simultaneously be categorized into different categories. The word lists for all categories are provided in Multimedia Appendix 2. Prior to categorization, tweets were adjusted by removing German stop words that did not contain relevant information themselves (eg, "or"). Two coders independently defined the word lists for the seven categories based on the positive COVID-19 filter. After initial coding of 70.50% of the words and consultation with the project initiator, the coding was completed. Coding of the tweets into categories was performed with an R markdown written specifically for the seven categories. Based on the occurrence of words, seven content dummy variables were created.

For the style intrinsic tweet feature, we again followed Vos et al [3] considering whether the tweet was written in the first or second person. Accordingly, dummy variables were created whenever a tweet was written in the first or second person, respectively. Vos et al [3] also considered whether the tweet used a retweet request. The COVID-19 tweets under study only rarely used this style element; thus, this element was neglected.

As it can be expected that retweets and likes would be higher for users with many followers, the followers count was included as another explanatory variable.

Negative Binomial Regression Analysis

Negative binomial regressions were used to explain the spread of a tweet. Negative binomial regressions are suitable when the dependent variable is a count variable with many zero observations. Tweet spread (ie, the dependent variable) was measured by either the retweet or like count. These counts were retrieved together with the tweets. In the context of this study, a retweet meant that a follower of the 39 stakeholders republished the stakeholder's tweet. The tweet content was therefore distributed by all users who retweeted that tweet. The more the retweets, the more the original tweet was spread. The like count was the second indicator used to measure the spread of tweets. Likes are an indicator of popularity. It is argued that retweets reflect more engagement as they indicate more interaction compared to likes. A retweet means that the user is sharing the stakeholder's content with the possibility to comment. This is not the case for likes. Overall, four different regressions were executed: four negative binomial regressions to explain the number of retweets (and likes), separated by authorities and experts. For the retweet and like counts, the dependent variables did not follow a normal distribution and the variance exceeded the mean. The data can be regarded as overdispersed, and therefore the negative binomial regression was the best choice to explain the count variables.

Results

Descriptive Analysis

A list of the Twitter stakeholders analyzed and descriptive statistics for their numbers of followings and followers are given in Multimedia Appendix 1. The development of the COVID-19 crisis communication of the 39 experts and authorities is shown in Figure 2.

Figure 2. Number of original COVID-19 tweets over time (January 1, 2020, to January 15, 2021) in Germany (N=8251).
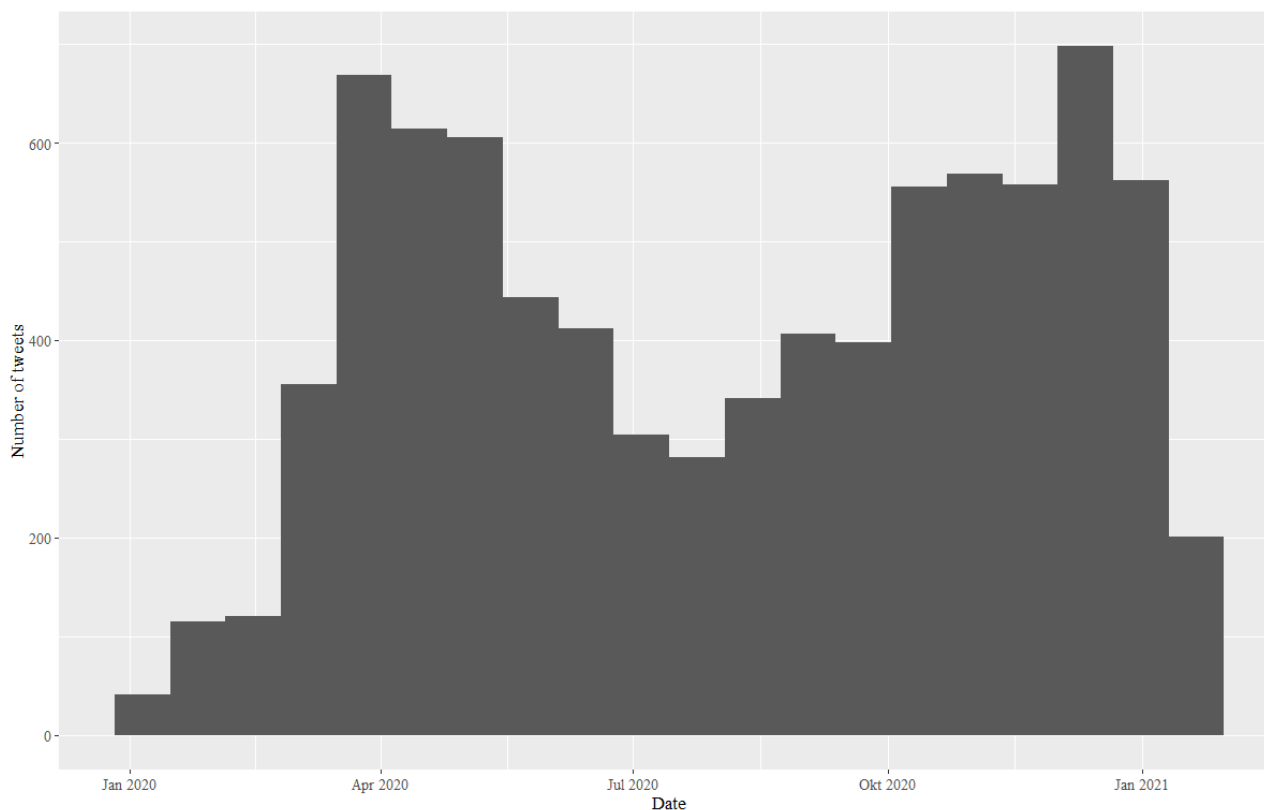
Strikingly, the number of COVID-19 tweets from January 1, 2020, to January 15, 2021, paralleled the development of COVID-19 cases in Germany, including the first two waves (March/April and beginning of October) during the sample period. The time of lower COVID-19 cases was also mirrored in the number of tweets, with a smaller number of tweets in the summer of 2020. This effect, namely the parallelism of tweet activity and (COVID-19) incidences, has already been documented elsewhere [28,40]. Moreover, both authorities and experts increasingly tweeted about COVID-19 when considering the number of tweets.

Table 1 shows the descriptive statistics for the dependent and independent variables in the regression models.

The descriptive statistics in Table 1 revealed strong differences in COVID-19 crisis communication between authorities and experts in Germany during the first year of the pandemic. We further focus on the differences in numbers of followings, followers, retweets, and likes as proxies of the distribution of COVID-19 communication.

On average, experts had 814 followings, representing 1.21 times the number of followings compared with that of authorities, with an average of 671. Although these numbers show that experts had a bigger network, the mean of followings did not differ significantly between the two groups ($t_{37}=0.54$, $P=.60$). The number of followings shows that stakeholders were willing to communicate with others. Among the authorities, the Helmholtz Association of German Research Centres (@HelmholtzG) had the highest number of followings (see Multimedia Appendix 1). In the group of experts, expert E9 had the highest number of followings, with more than 3200 followings. The regional office of the World Health Organization in Europe (@WHO_DE) had the lowest number of followings in the group of authorities and expert E11 had the lowest number in the expert group with only 2 followings.

The number of followers exceeded the number of followings to a great extent. Among the authorities, RKI had the highest number of followers, with more than 430,000. In the group of experts as well as overall, expert E8 had the biggest follower network, with more than 650,000 followers (as of January 15, 2021). Less than 1000 followers had the Max Planck Institute for Infection Biology in the group of authorities. In the experts' group, expert E1 had the lowest number of followers (1270). On average, experts had 99,059 followers, representing 1.31 times the number of followers for authorities with an average of 75,817 followers. However, this differences in mean followers was also insignificant ($t_{37}=0.52$, $P=.60$).

Experts were considerably more frequently retweeted with 7-fold (7.03) more retweets than authorities. On average, a tweet by authorities was retweeted 30.7 times, whereas tweets originating from COVID-19 experts were retweeted 215.7 times. This difference in mean retweets by stakeholder group was

statistically significant ($t_{8,249}$=26.94, P<.001). The dominance of experts became even more obvious when comparing mean likes: authorities' tweets were liked 90.8 times and the experts' tweets reached an average of 1257 likes, representing a 13.9 times increase for the experts' tweets. The difference in mean likes between authorities and experts was highly significant ($t_{8,249}$=31.27, P<.001).

Table 1. Descriptive statistics for variables used in the *t* tests and regression models (N=8251 tweets).

Variable	Description	Authorities (n=5432), mean (minimum, maximum)	Experts (n=2819), mean (minimum, maximum)
Retweet count	Metric variable for the number of retweets (dependent variable in negative binomial regression)	30.70 (0, 9982)	215.70 (0, 8457)
Like count	Metric variable for number of likes (dependent variable in negative binomial regression)	90.80 (0, 44,274)	1257 (0, 63,002)
Hashtag	Structural dummy variable that is 1 if a tweet has a hashtag	0.92 (0, 1)	0.19 (0, 1)
Images	Structural dummy variable that is 1 if a tweet uses images	0.69 (0, 1)	0.17 (0, 1)
URL	Structural dummy variable that is 1 if a tweet uses a URL	0.71 (0, 1)	0.71 (0, 1)
Mention	Structural dummy variable that is 1 if a tweet carries a mention	0.40 (0, 1)	0.24 (0, 1)
Severity	Content dummy variable that is 1 if a tweet contains words describing COVID-19 severity	0.75 (0, 1)	0.52 (0, 1)
Susceptibility	Content dummy variable that is 1 if a tweet contains words describing susceptibility to COVID-19	0.22 (0, 1)	0.05 (0, 1)
Efficacy	Content dummy variable that is 1 if a tweet contains words describing efficacy measures	0.35 (0, 1)	0.28 (0, 1)
Technical information	Content dummy variable that is 1 if a tweet contains a word related to technical virus information	0.04 (0, 1)	0.07 (0, 1)
Social	Content dummy variable that is 1 if a tweet contains words describing the social consequences of COVID-19	0.13 (0, 1)	0.08 (0, 1)
Politics	Content dummy variable that is 1 if a tweet contains words describing the political consequences of COVID-19	0.11 (0, 1)	0.04 (0, 1)
Other	Content dummy variable that is 1 if a tweet contains a word that cannot be attributed to other content variables	0.03 (0, 1)	0.31 (0, 1)
First person	Style dummy variable that is 1 if a tweet uses first-person words	0.27 (0, 1)	0.44 (0, 1)
Second person	Style dummy variable that is 1 if a tweet uses second-person words	0.04 (0, 1)	0.06 (0, 1)
Followers count	Metric variable as the number of followers per Twitter user	75,817 (971, 435,392)	99,059 (1270, 657,292)
Followings count	Metric variable as the number of followings per Twitter user	671 (38, 3424)	813.90 (2, 3293)

Considering the top users in crisis communication, previous studies evaluated the concentration of retweets among single users. For COVID-19 in Germany, two experts and the Federal Ministry of Health were responsible for 70.26% (544,418/774,865) of all retweets, and as such were the COVID-19 influencers in Germany on Twitter.

As seen in Table 1, the composition of COVID-19 tweets (N=8251) differed largely between authorities (n=5432 tweets) and experts (n=2819 tweets). Authorities strongly used structural content elements such as hashtags, images, URLs, and mentions, and clearly followed the common rules of general successful social media communication. It can be suggested that this is due to fact that authorities' tweets are published by their own social media departments who follow the rules of social media designs. Out of the 5432 tweets by authorities, 91.64% (n=4978) and 69.04% (n=3750) used hashtags or images, respectively, whereas only 19.44% (n=548) and 16.89% (n=476) of the 2819

experts' tweets used these elements. The proportion of tweets containing URLs was equal for authorities and experts. Mentions were included in 39.62% (n=2152) of the tweets by authorities' and in 24.26% (n=684) of the tweets by experts. Overall, the experts' use of structural elements was much lower than that of authorities. Experts clearly published their tweets on their personal accounts and did not spend time structuring the tweets in the same way as the official social media divisions of authorities.

There were also differences between the stakeholders under study with regard to the content of the tweets, with the strongest difference observed for severity. Overall, 75.00% (n=4074) of authorities' tweets referred to the severity of COVID-19, such as with reference to symptoms, whereas only 51.47% (n=1451) of experts' tweets were categorized into severity. In 22.22% (n=1207) of the authorities' tweets, there were words referring to susceptibility and regional information related to COVID-19,

whereas this was the case in only 4.68% (n=132) of the experts' tweets. With regard to efficacy information, the tweets of experts and authorities were similar with 34.70% (n=1885) and 27.49% (n=775) of tweets including this content, respectively. Tweets bearing technical information of the spread of the virus and references to scientific findings were more frequent for experts (n=188, 6.66%) than for authorities (n=224, 4.12%).

More of the authorities' tweets referred to the social consequences (n=719, 13.24%) and political consequences (n=617, 11.36%) of COVID-19 than the experts' tweets (n=225, 7.98% and n=104, 3.68%, respectively). The content category "other," which refers to words in the tweets that cannot be categorized by any of the category word lists, explains the differences observed: 31.80% (n=896) of experts' tweets and only 3.73% (n=203) of authorities' tweets were related to content that was not captured by the previous categories. Thus, the tweets of the experts were much simpler and did not use that many clearly detectable keywords, favoring more colloquialisms than authorities. An example is the tweet of a German expert "Sehr gut" ("very good") with additional links to external information. Categorization of these tweets by quantitative text analysis was impossible. Taken together, the findings from analysis of the structural variables show that authorities were much better in using structure, hashtags, and keywords.

The tweets of experts and authorities also differed with regard to the style variables: 26.82% (n=1457) of authorities' tweets and 43.70% (n=1332) of experts' tweets used first-person words, whereas 3.73% (203) of authorities' tweets and 5.57% (n=157) of experts' tweets used second-person words. The fact that experts used the second person slightly more often than authorities indicates that they interacted more with other Twitter users.

Negative Binomial Regression Analysis

Table 2 shows the results of the negative binomial regressions for authorities and experts on the retweet count of COVID-19 tweets.

The results for the like count regressions were similar, which are shown in Multimedia Appendix 3.

Table 2 provides the estimation results (incidence rate ratios [IRRs], Z values, and P values) separately for experts and authorities. IRRs were calculated from the estimated parameters of the negative binomial regression. They are easier to interpret than estimated values for negative binomial regressions. The IRR compares the impact of a (dummy) variable relative to the reference category, given that all other model variables are held constant. When the Z value from the negative binomial regression is positive, the direction of the effect is positive, whereas when the Z value is negative, the direction is negative.

Table 2. Negative binomial regression to explain the retweet count of COVID-19 tweets for authorities and experts (N=8251 tweets).

Variables	Authorities[a]			Experts[b]		
	IRR[c]	Z	P value	IRR	Z	P value
Model variable: constant	16.69	30.57	<.001	71.95	61.37	<.001
Structural variables						
Hashtag	0.64	−6.92	<.001	1.11	1.56	.12
Images	1.06	1.32	.19	1.06	0.87	.38
URL	0.82	−4.81	<.001	0.76	−4.27	<.001
Mentions	0.81	−5.45	<.001	0.73	−5.27	<.001
Content variables						
Severity	1.40	8.09	<.001	1.18	3.34	<.001
Susceptibility	1.02	0.46	.65	1.15	1.21	.23
Efficacy	1.34	8.63	<.001	1.10	1.71	.09
Technical information	1.45	4.23	<.001	1.00	0.06	.95
Social	1.24	4.05	<.001	1.27	2.69	.01
Political	0.71	−6.12	<.001	0.87	−1.12	.26
Style variables						
First person	0.93	−1.80	.07	1.10	0.02	.99
Second person	1.88	6.96	<.001	1.03	0.23	.82
Other: followers count	1.00	28.74	<.001	1.00	25.99	<.001

[a]Authorities: −2 log-likelihood=−44365.18; Akaike information criterion=44,395; null model logistic regression χ^2=1854.8 (P<.001); McFadden pseudo R^2=0.04.

[b]Experts: −2 log-likelihood=−33,752.49; Akaike information criterion=33,782; null model logistic regression χ^2=956,66 (P<.001); McFadden pseudo R^2=0.03.

[c]IRR: incidence rate ratio.

The regression constant for both authorities and experts was significant and positive. The first set of explanatory variables included four dummy variables that recorded whether a tweet used a hashtag, image, URL, or a mention, and as such captured structural elements of intrinsic message features. The number of retweets for authorities' COVID-19 tweets that used a hashtag was 0.64 the number of retweets for tweets that did not carry a hashtag, indicating a negative impact of hashtags. This result was highly significant ($P<.001$). For experts, the number of retweets was not significantly affected by hashtags ($P=.12$).

When both authorities' and experts' tweets had images, the retweet count was not significantly different compared with tweets without an image. Using URLs in an authority's tweet reduced the success of the tweet with respect to retweet counts: the number of retweets was approximately 0.82 that for authorities compared to tweets without URLs ($P<.001$). Likewise, experts' tweets using URLs led to a lower number of retweets, with an approximately 0.76 reduction compared to experts' tweets without URLs ($P<.001$). The usage of mentions reduced the success of retweets for authorities and experts alike. The number of retweets of authorities' tweets was approximately 0.81 that of authorities' tweets without mentions ($P<.001$). For experts, the number of retweets was also lower when a mention was present in the tweet, by a factor of 0.73, compared to experts' COVID-19 tweets without mentions ($P<.001$).

As a second category of intrinsic message features, the effect of different content and themes of tweets was analyzed, considering six content variables: tweets containing words referring to the severity of COVID-19, susceptibility, efficacy, tweets containing technical information about the spread of the virus, as well as tweets containing words referring to social and political consequences of the COVID-19 pandemic. As for the structural categories, there were fundamental differences in the success of COVID-19 crisis communication between authorities and experts. The first content category considered was severity. Authorities' tweets containing words referring to the severity of COVID-19 were associated with 1.40 more retweets than those of authorities' tweets that did not refer to severity ($P<.001$). Similarly, for experts, there was a positive and significant effect of severity content on the retweet count, which was approximately 1.18 times that of experts' tweets not referring to severity ($P<.001$).

The retweet count of authorities' COVID-19 tweets that contained informative words about susceptibility (eg, regarding SARS-Cov2 at-risk groups) was not significantly different from that of tweets without this information. For experts, there also was no significant impact of susceptibility content on the retweet count. Tweets with efficacy information increased the tweet success for authorities: the retweet count of authorities' tweets with efficacy content was approximately 1.34 times that of tweets without this content (holding all other model variables constant). This effect was highly significant ($P<.001$). For experts' tweets with efficacy content, there was no significant difference in the retweet count compared to that of tweets with no efficacy content.

For authorities, tweets with technical information about the spread of the virus and other scientific findings were positively

associated with retweet count. For authorities, the retweet count was approximately 1.45 that of tweets without this information ($P<.001$). For experts, the retweet count was not significantly different for this content category ($P=.95$).

Tweets that contained words referring to social consequences (eg, lockdown) led to a retweet count for authorities that was approximately 1.24 times ($P<.001$) that of tweets without this information. When experts tweeted about social consequences, the retweet count was approximately 1.27 times ($P=.01$) that of experts' tweets that did not refer to social consequences. If an authority's tweet contained references to the political consequences of the pandemic, the retweet count was 0.71 times ($P<.001$) that of tweets without political content. However, there was no significant impact of political words in experts' tweets on the retweet count ($P=.26$).

The third category of explanatory variables considered the impact of style elements of COVID-19 tweets on the retweet count. COVID-19 tweets written in first-person language had no impact on the retweet count for experts or authorities. However, when authorities' tweets used second-person language, the retweet count was approximately 1.88 times that of tweets that did not use it ($P<.001$). When experts used second-person words, their retweet count was not significantly different compared to that of tweets not using these words ($P=.82$).

The followers count, as an independent variable, had a highly significant impact on the spread of tweets for both authorities and experts ($P<.001$). Thus, spread of tweets is higher for stakeholders with a larger network.

These results reveal that there are differences and similarities in the determinants of the retweet success of COVID-19 tweets between authorities and experts.

Discussion

Main Findings

Overall, this study indicated strong differences between authorities and experts as to what increases the retweet rate of crisis communication regarding COVID-19 on Twitter.

Over the timeframe studied, authorities and experts tweeted increasingly about COVID-19 when considering the number of tweets (see Figure 2). However, authorities tweeted much more frequently about other non–COVID-19–related topics after filtering all tweets of the 39 stakeholders under study for COVID-19 and non–COVID-19 tweets (step 3 in Figure 1). The tweets of experts, with specific knowledge, were much more focused on COVID-19 during the first year of the pandemic in Germany. This focus on COVID-19 might be the reason why experts were perceived as more credible information sources (eg, in terms of numbers of followers) than authorities and received much higher spread on Twitter. Results regarding the types of tweets indicate that experts are much more involved in exchanging information with other Twitter users, as a great number of tweets are replies, retweets, and quotes.

The results of the negative binomial regression validated the descriptive analysis in that fundamental differences in crisis

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communication were observed between authorities and experts in Germany. These can be traced back to intrinsic message features such as the structural, content, and style features of tweets [3]. Structural elements in COVID-19 tweets, similar to URLs and mentions, were negatively correlated with the number of retweets for both authorities and experts. In addition, authorities' tweets with hashtags were less retweeted compared to tweets without hashtags. COVID-19 tweets of authorities clearly follow the common rules of successful social media communication. With a higher share of structural elements, crisis communication does need different social media communication standards to make authorities' crisis communication more successful. Crisis communication must be more immediate, direct, and fast to reach the public and should not be hidden behind those elements. The effect of a direct mention of other Twitter users indicates that the general community of Twitter users was excluded from that specific communication.

Referring to the content of COVID-19 tweets, for authorities, the content categories were mostly positively associated with the retweet count. Content covering susceptibility did not significantly affect spread, whereas information about severity, efficacy, technical information, and tweets about social consequences led to a higher retweet count for authorities.

Content about political consequences of the pandemic led to a lower number of retweets compared to tweets without political information, again for authorities only. This result seems remarkable, especially against the background of crisis communication, because political information is the core element of authorities' communication. Moreover, tweets referring to technical information about the spread of the virus and research results (eg, regarding vaccine development) led to a higher retweet count for authorities than tweets without these references.

Looking at the COVID-19 tweets of experts, it must be noted that fewer content variables were significant in explaining the retweet count. Only two content variables were significantly and positively correlated with the number of retweets. These were tweets dealing with the severity and social consequences of COVID-19. It is within these categories that the experts' knowledge was valued by Twitter users.

In contrast to the results regarding the structure of COVID-19 tweets, authorities' and experts' tweets using severity information were retweeted more often. For both groups, content about susceptibility was not associated with the retweet count. Information about efficacy and technical information increased the retweet count only for authorities' tweets. Tweets with content about social consequences led to a higher retweet count for both groups of stakeholders. Strikingly, political content in authorities' tweets was associated with a lower spread of corresponding tweets.

Style elements in COVID-19 tweets considered first- and second-person–specific words. Authorities should consider increasing tweets written in the second person to directly address users, as the relationship with the retweet count was positive. Style variables were not related to significant differences in retweets of experts. Overall, looking at intrinsic message

features of COVID-19 tweets reveals that authorities' tweets appear to be more designed with the strong use of structural elements such as hashtags and URLs compared with the COVID-19 tweet of experts.

Further, the larger the network of the stakeholders, the larger the retweet count. This indicates that stakeholders need to make great efforts in expanding and maintaining a large network to disseminate their crisis communication messages.

Comparing the results of this study with previous studies on crisis communication prior to the pandemic such as that of Vos et al [3], this study also shows that COVID-19 retweets depend on structural, content, and style variables; the account sending the message; as well as the network of the account (with a significant positive impact of the number of followers on retweet count). Regarding the content of the tweets, Vos et al [3] indicated that tweets dealing with severity of the Zika virus increase how often messages are shared. The same holds true for COVID-19, as this study shows that for both groups of stakeholders, tweets that deal with severity of COVID-19 are retweeted more often compared to tweets not referring to severity. As indicated by Vos et al [3], the Zika virus led to a situation of high ambiguity where little was known about the virus and the information need of the public was high. Accordingly, recommendation by authorities changed as more became known about the virus. The same holds true for COVID-19, especially during the first year of the pandemic.

There are also similarities to the swine flu crisis in 2009, which was studied by Kostkova et al [41], who showed that the number of swine flu cases was linked to the corresponding Twitter activity. We found the same relationship for COVID-19 cases and Twitter activity. Thus, Twitter communication can act as a rapid alert system, and it is possible to observe risk perceptions of the public by analyzing tweets.

Overall, confirming previous studies, there was a strong concentration of retweets in COVID-19 crisis communication. Two experts and the Federal Ministry of Health were responsible for 70.26% (544,418/774,865) of all retweets, and as such were COVID-19 influencers in Germany on Twitter. A study on the nuclear crisis of Fukushima [9] showed that 80.30% of retweets originated from only 2.00% of users.

This study also confirms previous Twitter-specific crisis communication studies in showing that all stakeholders tweeted more about COVID-19 over the course of time [30]. Caro [32] stated that virologists are very famous on Twitter. For Germany, we can confirm this finding as there is one virologist with by far the highest number of followers who belonged to the group of COVID-19 influencers identified in this study. The result that authorities are not very popular and that experts are the preferred information source over authorities has been documented elsewhere [32,37]. This study confirms this pattern for COVID-19 based on the significantly higher number of followers for experts indicating higher popularity. Rao et al [38] showed that alarming tweets of US health authorities were retweeted less often compared to reassuring tweets. Although this study did not compare alarming vs reassuring tweets, we found that tweets of authorities and experts dealing with the severity of COVID-19 are retweeted more often, whereas there

was no significant effect of susceptibility tweets on retweets in Germany.

Implications

Overall, there are several differences in crisis communication between authorities and experts regarding COVID-19 in Germany: experts have a larger network of followings and followers, receive a much higher spread via retweets and likes, and engage to a larger extent more directly with Twitter users about COVID-19 themes compared to authorities (which became more obvious after filtering out quotes, replies, retweets, and non-German tweets). Regarding intrinsic message features, the fact that experts use fewer structural and style elements in tweets than authorities and exceed them by far in spread indicates that other aspects such as sympathy, reputation, publicity, reliability, general media presence, and directness/speed in communication are more important for crisis communication on Twitter.

Both groups should tweet more about specific COVID-19–related topics. Tweets with content about the severity of COVID-19 had more retweets compared with tweets that did not make severity references. However, it seems advisable to prevent alarmism in the public. More research is needed to determine how the results can be translated one by one to authorities' crisis communication, such as when it comes to directness in crisis communication versus preventing alarmism.

Limitations

It must be noted that Twitter users are not representative of the overall German population. By contrast, only few, albeit more educated, people use Twitter in Germany [42]. Considering the two groups under study, authorities and experts, there were a few stakeholders who hardly contributed to COVID-19 crisis communication during the first year of the pandemic. Moreover, some interesting crisis communication stakeholders on Twitter in Germany emerged only after the study started. The separation between experts and authorities in this study should have been more specific or analyzed with more subgroups. In particular, differentiating authorities as science organizations vs

organizations with sovereign duties seems promising for future research.

It is important to note again that the comparison between the groups of experts and authorities is limited. The modes of crisis communication of these two groups are different. For example, authorities have many other communication channels (online and offline) that they can use for crisis communication, such as press conferences. Moreover, it can be questioned to what extent authorities use Twitter to inform the public in general or more specific target groups such as journalists or experts themselves. This study only analyzed tweets written in German. To communicate within the scientific community, experts especially use English; however, these tweets were not analyzed.

The study results further indicate that there might be other determinants for the success of specific stakeholders on Twitter, which cannot be observed by only using Twitter data, such as sympathy, reputation, publicity, reliability, and a general media presence during the study period. Overall, the tweets were downloaded on a specific date and as such represent a snapshot of events. The data, retrieved on January 15, 2021, cover a singular period amidst an ongoing crisis with an unforeseeable ending and are also designed to be analyzed retrospectively.

Conclusion

Twitter data represent a powerful information source and are suitable for crisis communication in Germany regarding COVID-19. Some important results can be highlighted. COVID-19 tweet activity mirrors the COVID-19 case numbers in Germany. Both authorities' and experts' COVID-19 tweets have higher spread when they are plain and for authorities when they address the public directly. Experts' success in crisis communication on Twitter outweighs the spread of authorities by far. Experts are more valued as an information source in the pandemic situation than authorities. For authorities, it appears difficult to win recognition during a crisis when their crisis communication is not only related to the specific crisis. Authorities should consider developing separate accounts on Twitter and using these accounts for more targeted communication.

Authors' Contributions

LD: study design, data adjustments, analysis, interpretation, and manuscript preparation; JR: study design, data retrieval, data analysis, and interpretation; KA: study design, literature review, and interpretation; KD: study design and interpretation; WS: study design and interpretation; AG: study design and interpretation.

Conflicts of Interest

The authors are researchers at a private research company and received funding from the German Federal Office for Radiation Protection.

Multimedia Appendix 1
List of stakeholders and number of followings and followers.
[DOCX File , 18 KB - publichealth_v7i12e31834_app1.docx]

Multimedia Appendix 2
Complete word lists.
[TXT File , 129 KB - publichealth_v7i12e31834_app2.txt]

Multimedia Appendix 3
Additional binomial regression results on likes count.
[DOCX File , 16 KB - publichealth_v7i12e31834_app3.docx]

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Abbreviations

API: application programming interface
IRR: incidence rate ratio
RKI: Robert Koch Institute

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Original Paper

Infoveillance of the Croatian Online Media During the COVID-19 Pandemic: One-Year Longitudinal Study Using Natural Language Processing

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Abstract

Background: Online media play an important role in public health emergencies and serve as essential communication platforms. Infoveillance of online media during the COVID-19 pandemic is an important step toward gaining a better understanding of crisis communication.

Objective: The goal of this study was to perform a longitudinal analysis of the COVID-19–related content on online media based on natural language processing.

Methods: We collected a data set of news articles published by Croatian online media during the first 13 months of the pandemic. First, we tested the correlations between the number of articles and the number of new daily COVID-19 cases. Second, we analyzed the content by extracting the most frequent terms and applied the Jaccard similarity coefficient. Third, we compared the occurrence of the pandemic-related terms during the two waves of the pandemic. Finally, we applied named entity recognition to extract the most frequent entities and tracked the dynamics of changes during the observation period.

Results: The results showed no significant correlation between the number of articles and the number of new daily COVID-19 cases. Furthermore, there were high overlaps in the terminology used in all articles published during the pandemic with a slight shift in the pandemic-related terms between the first and the second waves. Finally, the findings indicate that the most influential entities have lower overlaps for the identified people and higher overlaps for locations and institutions.

Conclusions: Our study shows that online media have a prompt response to the pandemic with a large number of COVID-19–related articles. There was a high overlap in the frequently used terms across the first 13 months, which may indicate the narrow focus of reporting in certain periods. However, the pandemic-related terminology is well-covered.

KEYWORDS

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Introduction

Background

Media coverage plays an important role in public health emergencies such as the COVID-19 pandemic and serves as a key communication platform during global health crises [1]. The media represent a bridge between science and society and have great power in forming collective opinions, attitudes, perspectives, and behaviors [2]. Recent studies proposed new disease-spreading models integrating media coverage as a strong factor that may influence human behavior in the context of disease transmission [3-5]. All of these studies confirm that the media may affect the spread and control of infectious diseases. Wang et al [4] explained that media coverage has an impact on the implementation of public intervention and control policies. They pointed out that one of the measures is to educate people and explain how to prevent the disease through all available sources of information.

On the other side, the media, especially internet-based information sources, may cause an infodemic, which is described as an overabundance of information, misinformation, and disinformation. Coping with these phenomena created the discipline of infodemiology [6,7]. Eysenbach [8] defined the four pillars of infodemic management, including information monitoring, or infoveillance, which enables gaining better insight into how the media respond to a crisis.

The infodemic is one of the severe consequences of the COVID-19 pandemic [9,10]. This raises many challenges for the task of infoveillance in terms of massive data sets, such as large communication volumes, new terminology related to COVID-19, various topics and domains present in the media (eg, health care, economy, politics, education), and the large number of users involved in communication in social media. Recently, natural language processing (NLP) technologies have enabled progress in dealing with the large amount of accumulating textual data [11] and thus are promising underlying methods as an integral part of infoveillance methodology.

Prior Work

The significance and impact of the media in the context of an epidemic has been extensively studied for several epidemics before COVID-19, such as H5N1 influenza [12], severe acute respiratory syndrome (SARS) [13], Middle Eastern Respiratory Syndrome (MERS) [14], H1N1 influenza [15], and Zika virus disease [16]. The outbreak of the COVID-19 pandemic resulted in numerous research publications focused on different aspects of public communication, including the linguistic perspective of the online news media [17], content analysis of global media framing of COVID-19 [18], politicization and polarization in COVID-19 news coverage [19], and amount of media coverage in the context of the pandemic [2]. The studies related to infoveillance have mostly focused on discovering topics [20,21], sentiment analysis [22,23], or fake news detection [24,25].

Most studies employed different NLP techniques for capturing specific aspects of the COVID-19 content published online. For discovering public perceptions, opinions, and attitudes toward specific COVID-19–related topics, researchers commonly combine topic modeling and sentiment analysis [21,26-28], which are also occasionally combined with named entity recognition (NER) [29].

Although COVID-19–related media coverage has been widely studied, there are still some aspects of the task of infoveillance that can be improved. For example, existing studies are largely focused solely on the content of the texts rather than on the volume of published texts. There are only a few exceptions in which the dynamics of publishing have been analyzed [2,20]. Moreover, the majority of analyzed data sets consist of texts published at the beginning of the pandemic, which only capture a short time span of 3 to 4 months. Given the lack of research applying longitudinal data monitoring over larger time spans (ie, the first year of the COVID-19 pandemic), our study might be worthy of attention.

In this study, we followed similar methodologies as described above. However, to more specifically address the mentioned gaps, we propose extensions of these methods contributing to the theoretical framework for the task of infoveillance. First, we combined statistical methods and NLP techniques to track the number of news articles and the content of news articles at the same time. Second, in the proposed approach, we applied the Jaccard similarity coefficient for measuring the similarity of the most frequent terms and entities in COVID-19–related online news articles.

Goal of This Study

In relation to prior work, we developed an approach for the task of infoveillance based on combining NLP and statistical methods, focused on the content from online news media.

By providing an analysis of the online media's response to the pandemic, we aimed to contribute to the discipline of information monitoring, particularly to gain a better understanding of: (1) the role that internet-based sources play in communication during the COVID-19 crisis and (2) the potential infodemic. Our goal was to achieve NLP-based longitudinal tracking of the dynamics of changes in the coverage of the Croatian online news space. Noting that the Croatian media are reported as being poorly trusted [30] further motivated us to explore how the media have treated one of the most challenging situations in the everyday life of the country's citizens.

This study addressed the following research questions related to the period of the first 13 months of the pandemic: (1) What is the number of COVID-19–related news articles and is this number correlated with the number of new COVID-19 cases? (2) What are the main key terms, the most frequent pandemic-related terms, and the most frequent entities in the focus of the online news media? (3) How has the COVID-19–related content (in terms of the most frequent words, most frequent pandemic-related terms, and main entities related to the pandemic) in the online news changed during the first 13 months of the pandemic?

To answer these questions, we performed the following analyses. First, we carried out an exploratory statistical analysis of online media to provide an overview of the trends of

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COVID-19–related articles published during the first year of the pandemic. Next, we developed a set of statistical and NLP-based methods for the task of infoveillance of the content published on online news media. More specifically, we applied NER for the automatic extraction of the entities that play a key role during the pandemic. Next, we constructed a simple visualization monitor enabling the longitudinal tracking of the change of the pandemic-related terms contrasted between the first and second waves of the pandemic. Finally, we quantified and visualized the changes of the most frequent terms and entities using the Jaccard similarity coefficient over the 13 months.

Methods

Data Collection

In this longitudinal study, the collected data covered a period of more than 1 year, specifically the period from January 1, 2020, to January 15, 2021, thereby covering the time period corresponding to the first two pandemic waves in the Republic of Croatia (see Table 1). We included January and part of February 2020 in the study period, although this represents the time before the first reported COVID-19 case in Croatia. With

the inclusion of this short period before the pandemic outbreak, the data set contains the emergence of seed pandemic-related terminology. Moreover, the captured antecedent period served as the control for the comparison with the official pandemic period. More details about the duration of the epidemic (pandemic) waves can be found in Section-A1 of Multimedia Appendix 1.

The data were selected among publications from eight mainstream online news media sources, distributed to cover the geographical and media space of the Republic of Croatia. The articles were collected on a daily basis, resulting in 270,359 articles in total, 121,095 of which were COVID-19–related news articles. Collected articles represent the full sample of all articles published in these eight portals in the defined period. We refer to the data set of the COVID-19–related articles as "Cro-CoV-texts2020" (see Multimedia Appendix 1 for a link to the publicly available lists of the word frequencies extracted from all news sources grouped by month). These eight portals included in the Cro-CoV-texts2020 data set do not cover the entire online news media space of Croatia. Nevertheless, they form a representative sample for our longitudinal study. The criteria for their selection are described in detail in Section-A0 of Multimedia Appendix 1.

Table 1. Duration of pandemic waves in Croatia.

Period	Start date	End date
First pandemic wave	January 1, 2020, February 25, 2020[a]	May 22, 2020
Pandemic subsides	May 23, 2020	June 14, 2020
Second pandemic wave	June 15, 2020	January 15, 2021

[a]Appearance of the first COVID-19 case in Croatia.

The filter used to determine the affiliation of an article to a COVID-19 class was the occurrence of keywords from the coronavirus thesaurus in the title, subtitle, or body of the text. The coronavirus thesaurus contains approximately 20 of the most important words describing the SARS-CoV-2 virus epidemic, as well as all inflectional variations (see Section-A2 of Multimedia Appendix 1). In addition to the general words (universal keywords related to the COVID-19 pandemic), the list was expanded with additional terms specific to Croatia, including the names of public administration authorities (eg, the Minister of Health, a leading state epidemiologist, the director of the National Civil Protection Headquarters).

The collected articles were preprocessed as follows: (1) only the textual part of the news was retained (related images and videos were discarded), and (2) titles, subtitles, and body of the texts were lemmatized to reduce the inflectional variations of the words as a standard NLP preprocessing procedure.

The epidemiological data related to COVID-19 (ie, the number of newly infected individuals) were obtained from the official government portal. The data are available in Section-A0 of Multimedia Appendix 1 for every day in the period from February 26, 2020 (when the first case of coronavirus infection was confirmed in Croatia), to January 15, 2021.

Statistical Analysis of Online Media Content Volume

After filtering the collected content according to the defined thesaurus of coronavirus terms, we first determined the ratio of the COVID-19–related and remaining publications. We then performed an exploratory statistical analysis of the COVID-19–related online publications.

Specifically, the time series of COVID-19 daily cases was compared with daily published COVID-19–related articles during the entire period from January 1, 2020, to January 15, 2021. Both time series have the same time resolution and the same length of 110 days in the first wave and 215 days in the second pandemic wave. For time-series data that did not follow a Gaussian distribution, nonparametric tests were used. The standard Spearman correlation coefficient (ρ) and Kendall coefficient (τ) were used to measure the strength and direction of the association between the two variables: the number of cases and the number of articles.

Additionally, the cross-correlation function (CCF) was applied to quantify a potential association, as well as the time lag between the two time series (see Equation 1 in Section-A3 of Multimedia Appendix 1). The interpretation of the CCF dictates that larger absolute values of cross-correlation at the time lag indicate a stronger association between the two time series. The correlation is considered to be significant when the absolute

value is greater than the threshold defined with Equation 3 in Section-A3 of Multimedia Appendix 1.

Another modality of the experiment aggregated the daily data into a 1-week window for both time series, resulting in the resolution of 15 weeks in the first wave and 32 weeks in the second pandemic wave (46 weeks in total), which is also suitable for calculating the CCF.

The autocorrelation function (ACF) was used to calculate the strength of the relationship between a time-series observation and observations at prior time steps, referred to as "lags." Because the correlation of the time-series observations is calculated with values of the same series at previous times, this is known as a serial correlation analysis. A plot of the autocorrelation of a time series by a lag is often called the ACF, correlogram, or an autocorrelation plot.

The graphs for the ACF of the autoregressive integrated moving-average residuals include lines that represent the significance limits, which are calculated by Equation 4 in Section-A3 of Multimedia Appendix 1. The values that extend beyond the significance limits are considered to be statistically significant at approximately $\alpha=.05$, providing evidence that the autocorrelation does not equal zero [31].

The mutual information (MI) between the new COVID-19 case counts and the number of published articles related to COVID-19 from February 26, 2020, to January 15, 2021, was quantified to further evaluate the mutual dependence of the two time series. The MI was calculated as the expected value of the pointwise MI of the two time series. The calculations of point-wise MI, MI, and normalized MI are defined by Equations 5, 6, and 7, respectively, in Section-A3 of Multimedia Appendix 1.

As suggested by Safarnejad et al [16], the CCF provides an overview of the association between real-world COVID-19 case counts and the published COVID-19–related articles over a certain time period. In our case (for 325 observations and 28 lags), a CCF above 0.116 would indicate a strong association between the two time series. However, the MI complements the CCF and was used to further quantify this association with an exact numerical value.

Identification of the Most Frequent Terms and Change Dynamics

In the next step, we analyzed the most frequent terms related to COVID-19 and how the vocabulary trends are changing over time. Specifically, we calculated the frequencies of all of the terms in the lemmatized data set. We performed the same analysis in two different time spans: on a monthly level (13 months in total) and for the two pandemic waves. In the analysis by months, the number of time units (days) depends on the total number of calendar days. In the second case, the duration of the pandemic waves was 281 days in total, with the first wave being shorter at 166 days and the second wave stretching over the

remaining 215 days. Roughly speaking, the first and second waves can be considered to have lasted for approximately 6 and 7 months, respectively.

Being aware of the fact that other countries might not relate to the recognition and differentiation of pandemic waves, chunking for Croatia is justified by the collected data. The monthly level analysis is certainly appropriate for further comparison with other countries. In the analysis of coronavirus-related concepts, we compared the trends of how the most frequently used terms were changing during the 13 months and across two different pandemic waves by quantifying the Jaccard similarity that indicates the overlap of the terms between two different periods. There are many approaches available for the extraction of key terms [32]; however, we decided to apply a simple approach based on the word frequencies.

NER Extraction

NER is an NLP task aimed at the extraction of named entities such as people, locations, organizations, and numeric expressions (ie, time, money, dates). NER extraction can be modeled as a text sequence annotation problem. In this case, the conditional random field (CRF) as a nondirected graphical model was trained to maximize the log likelihood, calculated from the conditional probabilities of the output labels' sequences over the features of the input sequences and CRF states. Performance of NER for Croatia has been reported previously [33] based on an experiment with three named entity classes (organization, person, location) and yielded an F1 score of 89.8%. In this work, we used the NER system trained for the related Slavic languages Slovenian, Croatian, and Serbian [33,34] to automatically extract entities from the large COVID-19–related data set. The implemented NER was a slight modification of the CRF-based reldi-tagger with Brown clusters information added, capable of the recognition of person, person derivatives (adjectives derived from a person's name), location, organization, and miscellaneous entities.

Results

Descriptive Analysis of the Online Newspaper Space

In our previous work, we analyzed isolated online and social media content published in the Croatian language in a shorter time period [35-38]. In this study, we focused on the eight major representatives of online news media by scrutinizing their publications over a significantly longer period (from January 1, 2020, to January 15, 2021). The percentage of COVID-19–related articles was quantified according to the coronavirus vocabulary.

The percentage of COVID-19–related articles did not fall below 44% for any of the eight observed online news media sources (Figure 1A). The average ratio across all online news media sources of COVID-19–related publications occupied more than half of the total media space (approximately 57%).

Figure 1. Percentage of COVID-19–related articles summarized for each of the eight online news media sources during the pandemic in Croatia (February 25, 2020, to January 15, 2021) (A), and the percentage of COVID-19–related articles relative to the total number of articles summarized across the eight online news media sources for different periods during the pandemic (B).
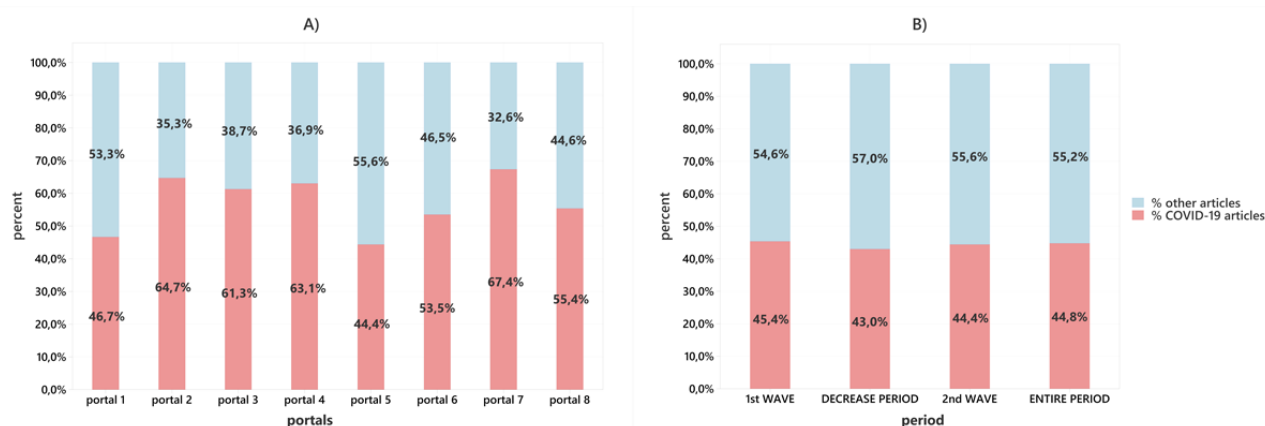

Figure 1B shows the percentage of COVID-19–related articles relative to the total number of published articles, summarized for all eight online news media sources for different time periods (ie, the two pandemic waves, the period in which the pandemic subsided marked as the decrease period, and for the entire period of 13 months). To gain a global picture for 2020, data from January 1 to February 25, 2020, were also analyzed despite the fact that there were no cases of COVID-19 in Croatia in that time. The percentage of COVID-19–related articles in the first wave would take on a much higher value if the analysis did not include days in which there were no cases of infection in Croatia (the period from the beginning of the year to February 26, 2020) and would rise to a value of 57%. Surprisingly, in the period between the two pandemic waves, when the number of cases of infection dropped to zero (the decrease period), the number of publications related to COVID-19 remained high at 43%, despite expectations that the media would write significantly less about COVID-19.

Association Between the COVID-19 Pandemic and Writing Dynamics in the News Media

Many factors may influence the increased interest in COVID-19–related issues in the media, including the number of patients on mechanical ventilation due to deterioration of their condition, the number of people in self-isolation, the daily or total number of deaths from COVID-19, and the number of companies and entrepreneurs who had to stop their regular business due to the pandemic. The testing of all of these claims was impeded by the unavailability of reliable data. Nevertheless, we examined an isolated variable with potential to influence COVID-19–related publications and from which we could obtain reliable data. Hence, we aimed to determine whether there is a correlation between the number of daily cases of newly infected people with SARS-CoV-2 and the number of published news articles related to the topic of COVID-19.

The time-series plot in Figure 2 shows the number of new COVID-19 cases per day (red line) and the number of published

COVID-19–related articles (blue line). The blue line has the same pattern of wavy repetition throughout the observation period, regardless of the epidemic wave, whereas the red line has an elongated left tail and then a high ridge in the second epidemic wave. In addition, slight repetitive wave-like oscillations can be seen along the time axis (days). Data distributions are shown with the histograms of the frequencies for both observed time series in Figure A4-1 of Section-A4 in Multimedia Appendix 1.

We next examined whether there is a linear relationship between the number of new cases of COVID-19 per day and the number of publications of COVID-19–related news articles per day using the Spearman rank correlation coefficient. The null hypothesis was that there is no correlation between the number of COVID-19 cases and the number of published articles related to COVID-19 (α=.05), which was rejected given a weak but statistically significant correlation (n=325; ρ=0.253, P<.001); this was additionally confirmed with Kendall τ=0.173 (P<.001). More detailed results, including the 95% CIs for the 2-tailed test, are reported in Section-A4 of Multimedia Appendix 1.

Although statistically significant, the correlation was extremely weak. To obtain a direct interpretation of results, we used the Kendall τ coefficient in terms of the probabilities for observing the agreeable (concordant) and nonagreeable (discordant) pairs. The ratio of the occurrence of concordant to discordant pairs was 1:1.4 (ie, $1+\tau/1-\tau$), which means that the probability of occurrence of concordant pairs is 1.4 times higher than the occurrence of discordant pairs.

Realistically, it is to be expected that the number of publications on the topic of COVID-19 will not increase on the same day as the number of COVID-19 cases increases (or decreases), but that the media will write about it subsequently (ie, the next day or a few days later). Therefore, we next examined whether the correlation can be stronger if we observe the publication of COVID-19–related articles with a time delay compared to the daily number of COVID-19 cases.

Figure 2. Time-series plot comparing the number of published COVID-19–related articles per day (blue) and the number of new COVID-19 cases (red) from February 25, 2020, to January 15, 2021.
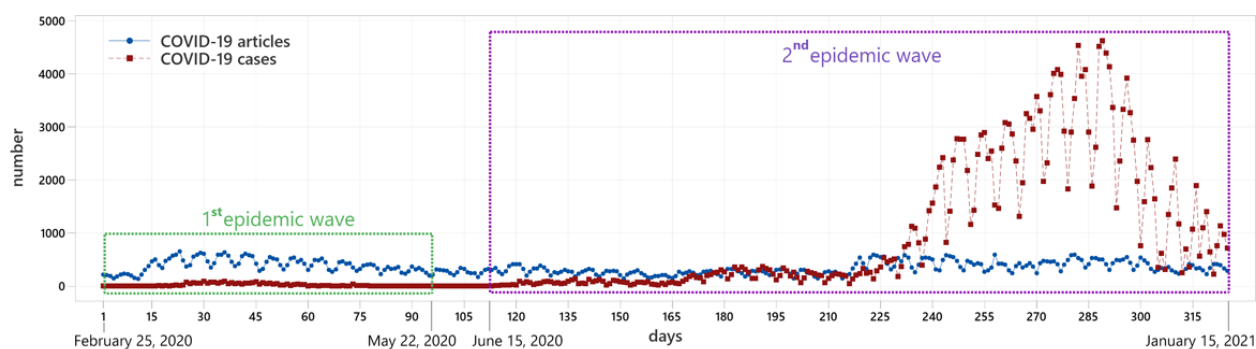
Given that cycles can be seen in the time-series data that repeat regularly over time in the form of a sine wave (see Figure 2), this could represent seasonal variations. However, a cycle structure in a time series may or may not be seasonal. Correlograms in Section-A4 in Multimedia Appendix 1 show plots of the ACF on time-series data of new COVID-19 cases (left plot) and published COVID-19–related articles by a lag (right plot). This autocorrelation measures the linear relationship between the lagged values of a time series. The ACF for both COVID-19–related articles and new COVID-19 cases showed several significant peaks after a lag of 7 days. This determines the cyclic behavior in the time-series data in which the cycles are repeated every 7 days. The reason for this is that on nonworking days (ie, Saturday and Sunday), less news is written and published and thus a minimum cycle value is achieved. By contrast, during working days (usually in the middle of the week), there is a larger number of published news articles (ie, the maximum cycle value is reached). It is important to emphasize that there is no complete regularity in the cycles (ie, there is no seasonality on a 7-day basis). The reason for this is that the maximum number of news articles does not always occur on the same day of the week. The peak can shift among Tuesdays, Wednesdays, or Thursdays. The same holds for the number of new confirmed cases of COVID-19. On weekends, a smaller number of people are tested (corresponding to the same days when less news is published), whereas more people are tested on work days, so that the number of confirmed infections is higher. The peak is reached again in the middle of the week, but not always on the same day, so the regularity in the form of seasonality cannot be credibly confirmed for the entire epidemic year. The results could suggest the presence of a weekly seasonal component for certain shorter periods of the year. Finally, for the entire year, we observed with certainty a cyclical behavior on a weekly or 7-day basis.

According to these insights, we aggregated the data on the time series by week (7 days), and observed them in the 1-week time window. The Kolmogorov-Smirnov normality test showed that the data do not follow the Gaussian distribution (test details are available in Section-A4 of Multimedia Appendix 1). Again, the null hypothesis was that the correlation does not exist (α=.05).

Spearman correlation of ranks indicated the existence of a slight positive correlation (n=47; ρ=0.277), which was slightly higher than that obtained in the previous case analyzed on a per-day basis, but was not statistically significant (*P*=.06). Additionally, this was confirmed with Kendall τ of 0.202 (*P*=.05); the 95% CIs are reported in Section-A4 of Multimedia Appendix 1.

Due to the vague picture of the existence or nonexistence of at least a weak positive correlation, we performed an additional cross-correlation test on the time-series data measured on a daily basis. A significant cross-correlation between the published COVID-19–related article counts and the number of confirmed COVID-19 cases per day was observed for the pandemic in Croatia (Figure 3). The CCF was substantially above the threshold of statistical significance, and the strongest positive correlation occurred at lag=2. This shows that the two variables are not contemporaneously correlated. However, the positive correlation at lag +2 suggests that higher numbers of COVID-19 cases lead to higher numbers of published articles related to COVID-19 themes 2 days later. Negative correlations were not detected in the observed lag range.

Cross-correlation tests indicated that publishing COVID-19–related news articles was not completely decoupled from the actual disease pandemic in the Republic of Croatia's online news space. This indicates the underlying effect of the COVID-19 pandemic on the writing about COVID-19. Finally, the strong dependence between the two time series was further quantified and confirmed by MI and the normalized MI measure (for details see Section-A4 of Multimedia Appendix 1).

Next, we asked whether there is a linear relation among the eight major online news media sources considering the number of COVID-19–related articles published per day. For all 28 possible cases, the correlations were statistically significant. In terms of the Spearman coefficient, all correlations were positive and a correlation was absent in only two cases. Furthermore, in 12 cases, the positive correlation was weak, in the next 12 cases, it was substantial, and in 2 more cases, it was strong. The correlations were confirmed with Kendall τ as a more conservative coefficient (see Section-A4 of Multimedia Appendix 1).

Figure 3. Cross-correlation function between the published COVID-19–related article counts per day and the number of confirmed COVID-19 cases per day.
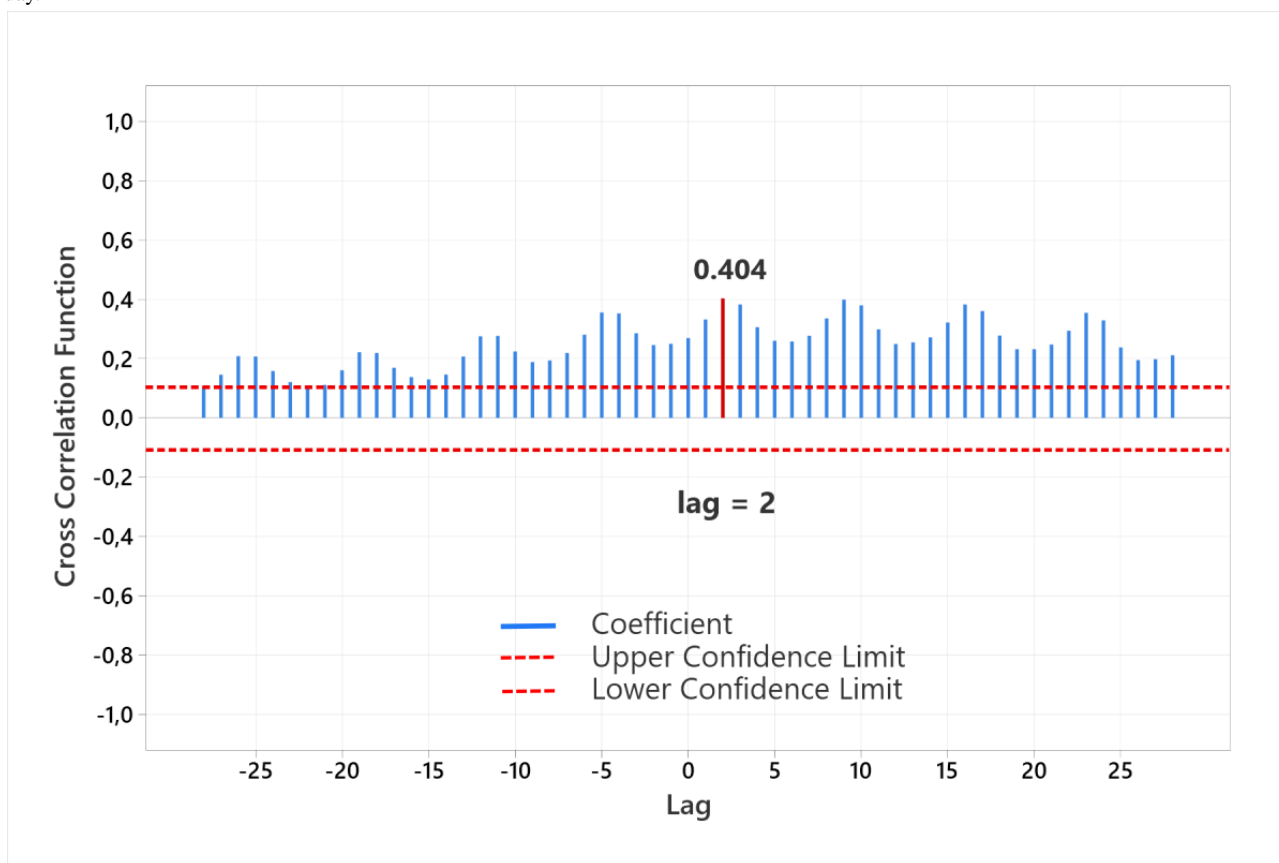
Pandemic-Related Terminology Analysis

The analysis of the most frequent terms was performed at the granularity of pandemic waves. The top eight highly frequent terms in the first and in the second epidemic waves were found to be identical, according to their frequency in COVID-19–related media releases. This is an indication that throughout the pandemic year, regardless of the epidemic wave, journalists most often mentioned the following terms: people, coronavirus, Croatia, year, measure, day, high/large, and new. This represents an extremely narrow vocabulary with a small set of three terms that consistently refer to the epidemic year in Croatia and five more terms that are used daily in the news describing the high daily number of newly infected people.

Expanding the monitored list to the top 250 most frequent terms during the first and second epidemic waves showed an average Jaccard similarity coefficient of 0.72 (see the curve oscillations in Figure 4, left). This is an indication of a significant overlap of the most frequent terminology between the pandemic waves, and hence the consistent content of pandemic-related writing in online media. Table A5-1 in Multimedia Appendix 1 lists the 50 most frequent terms used in news publications for the first and second epidemic waves, respectively.

Figure 4. Jaccard similarity coefficients of the most frequent words (terms) between the first and second waves (left) and among the 13 months of the COVID-19 pandemic in Croatia (right).

In the second step, the terminology analysis was performed at the month granularity. The Jaccard similarity coefficient was calculated for the 250 most frequent terms between every two months. The heat map in Figure 4 shows significant deviations in January and February (yellow squares), followed by some high overlaps in terms of the Jaccard similarity (red squares). The green triangle on the heat map indicates the period with the highest overlap (ie, the most used terminology in those months was the most similar). All angles of the green triangle have a value of 0.75 and thus delimit the months in which the epidemic subsided and people lived with less pressure from infection. During the "green triangle" months, the media virtually revolved around the same most frequent pandemic terms, and the reasons are related to two upcoming events: parliamentary elections and the tourist season. Moreover, the prime minister, who was running in the elections, announced that the income from tourism, which is always important for the Croatian gross domestic product, would be crucial during the pandemic.

The prevalence of pandemic terminology in the first and second epidemic waves was quantified and is visualized in Figure 5. The terms below the blue diagonal line are those that were more frequently identified in the media during the first wave and the terms above the line are those that were more frequent during the second wave.

Figure 5. Relationship of epidemiological vocabulary between the first (lower right) and second (upper left) pandemic waves.

According to the results, the symptoms that were more common in the first wave were cough, sore throat, and respiratory symptoms, whereas writing about symptoms during the second wave was more focused on the lungs and breathing, taste, smell, and dry cough. It is important to note that the differences in frequencies between all of these terms are small and that they were written about at almost equal rates in both waves. The symptoms of anosmia, ageusia, and parosmia appeared with the highest occurrence frequency.

The necessities for maintaining hygiene and preventing the spread of infection were predominantly mentioned in the first wave, including disinfectants, gloves, soap, visors, and even the pharmacies that trade in such supplies. The next important group of terms was related to drugs. Azithromycin (Sumamed), paracetamol, and hydroxychloroquine were mentioned more in the first wave. In the second wave, once we gained more knowledge about the disease, remdesivir was more frequently mentioned, accompanied by the rise of vaccination-related terminology (eg, CureVac, Pfizer, AstraZeneca, and Sputnik

V). In addition, the word "vitamins" was frequently identified, as well as "oxygen" due to intensification of the pandemic outbreak in the second wave.

Subjects from the political scene, such as the minister of the interior affairs (Božinović) or the minister of health (Beroš), the director-general of the Institute of Public Health (Capak), and the director of the largest Clinic for Infectious Diseases in Croatia (Markotić), were more frequently mentioned in the second wave. Scientists (eg, Lauc and Đikić) were more frequently mentioned in the second wave because they made more media appearances at that time. Nevertheless, politicians were mentioned more often than scientists.

During the first wave, more attention was paid to the ways of spreading the disease and infection prevention. Therefore, terms such as spread (infection or disease), isolation, quarantine, infection, and disinfection were mentioned more often in this wave. Interestingly, the terms "self-isolation," "newly infected," "infection," "transmission," "treatment," "sample," "positive test," "testing," "epidemiologist," "social distance," "to die," "patient," and "mechanical ventilation (respirator)" had a significantly higher incidence in the second wave. This might be a result of a significantly higher number of infections in the second epidemic wave, which was magnitudes higher than that in the first.

Among the terms that refer to diseases, "the plague" and "SARS" prevailed in the first wave, whereas "influenza," "SARS-CoV-2," and "COVID-19" dominated in the second wave.

General words used for describing COVID-19 infection and disease such as "virus," "coronavirus," "infection," "hospital and health care," "pandemic," "epidemic," "life," and "patient" are immediately close to the wave-dividing boundary. Due to their generality, their frequency was magnitudes higher than the frequency of terms that describe or name symptoms, medications, public figures, medical institutions, and similar.

We paid particular attention to drugs and vaccines that were most frequently mentioned at the time of the pandemic. The details of the observed word groups naming drugs and vaccines can be found in Table A5-2 in Multimedia Appendix 1. The

representation of the groups in the corpus is expressed as a percentage.

Results are reported separately for drug and vaccine terminology as normalized values for the first and second waves. The group of drug-related words occupied 0.38% of the corpus from the first wave and 0.61% of the second wave. The group of vaccine-related words occupied 0.24% and 4.63% of the corpus in the first and second wave, respectively. The occurrence of words from both groups increased in the second epidemic wave: 0.23% more terms referred to drugs in the second wave than in the first wave, and as many as 4.02% more terms referred to vaccines in the second wave. In the first wave, existing drugs that could help treat COVID-19 were reported, but with the emergence of some new drugs (eg, remdesivir), their mention in the second wave was relegated to the background. As the production of vaccines was announced mainly during the second wave, vaccine-related reporting became more exhaustive.

The Main Subjects in the Pandemic

Analysis of the ratio of unique entities and the total number of entities in the pandemic articles was obtained by NER. The results indicated that the proposed longitudinal tracking of focal entities can serve as one aspect of infoveillance, providing insights into the trends of public interest. Figure 6 reveals that the numbers of people and organizations were significantly higher than those of locations and general (miscellaneous) entities. Combined with the insights from Figure 6 (right), where the total number of detected entities in the categories people, organizations, and locations were fairly equal and the miscellaneous category was marginal, it is possible to enable the consistent tracking of the public interest during the pandemic. The left part of Figure 6 provides numerical insight into the representation of individual subjects in media coverage during the pandemic. In the first pandemic year, among the four studied groups of entities, people (the blue graph area) were the most frequent subjects in coronavirus-related news. In addition to personal names, nationalities also belonged to a group of entities collectively referred to as "person." The personal names mostly referred to leading figures of the political scene, the presidents of the state and government, the heads of the civil protection headquarters, ministers, scientists, hospital directors, and infectious diseases specialists.

Figure 6. Ratio of the representation of unique entities (left graph) and the total number of recognized entities (right graph) in COVID-19–related media releases in summary for all observed online news media. PER: person; ORG: organization; LOC: location; MISC: miscellaneous (general).
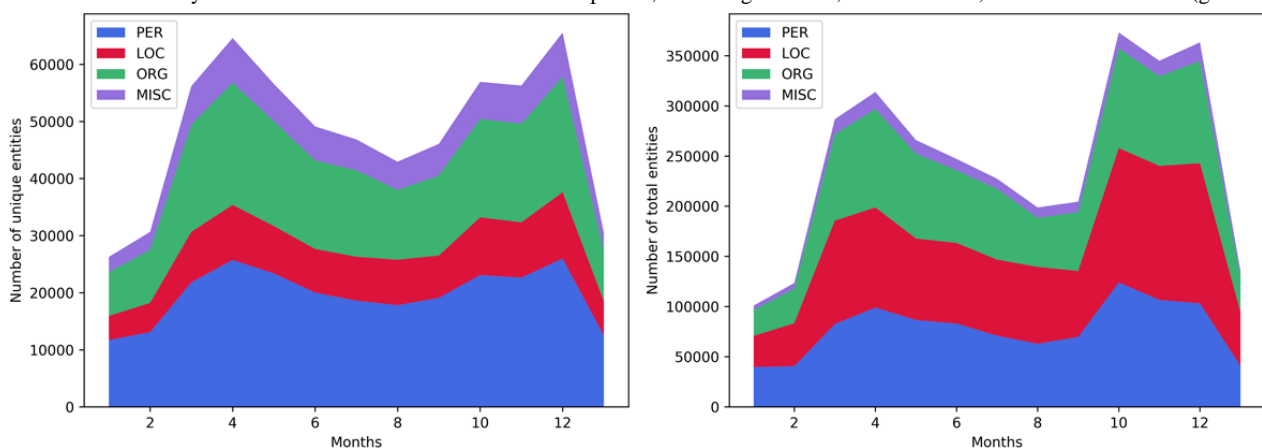
The second most frequent group was organizations (green). During the pandemic year, most journalists wrote about hospitals, public health schools, testing centers, civil protection headquarters, the World Health Organization (WHO), European Medicines Agency, vaccine companies, and, surprisingly, the most popular social networks such as Facebook and Twitter; occasionally, these sources referred to football or sports clubs organizations, whereas political organizations and parties were most frequently mentioned.

Locations was the third group of entities (red), including states, cities, and counties. The captured location entities involved the foci of the epidemic or areas where important pandemic-related events were happening, including where the first vaccines were available, antimasker protests, areas running out of oxygen for clinical treatment, infection entering nursing homes, state borders closing, borders opening for the tourist season, schools closing, presidential elections, and a massive earthquake that occurred twice in 2020 coinciding with the pandemic waves (during the first wave it occurred in Zagreb, the capital of Croatia, and during the second wave it occurred in the towns of Sisak and Petrinja in the vicinity of Zagreb). During the pandemic, the news articles mentioned only a limited and consistent set of locations since not much traveling and migration were allowed. Hence, the number of locations was constantly below the numbers of people and organizations.

The last rank was occupied by the group of general or miscellaneous entities (violet). This category includes the names of events, commercial products and brands, documents, TV channels, viruses, and diseases, among others. Their occurrence was highly dependent on the time of year or month in which an event, competition, concert, or promotion takes place.

Finally, both graphs in Figure 6 show that maximal values were reached during the peaks of the first and the second waves of the pandemic.

Quantifying the similarity of the top 100 entities by months during the observed pandemic period, the heat map in Figure 7 reveals higher similarity (Jaccard) values between sets of people and locations than between sets of organizations and miscellaneous entities. The bright red color indicates a stronger overlap, whereas the dark blue indicates disjunction (ie, no overlap) between the observed entities. The yellow color indicates only a mediocre overlap.

Figure 7. Jaccard similarity coefficients between the 13 months for the 100 most frequent entities per four traditional categories: person (A), location (B), organization (C), and other general entities (miscellaneous) (D).
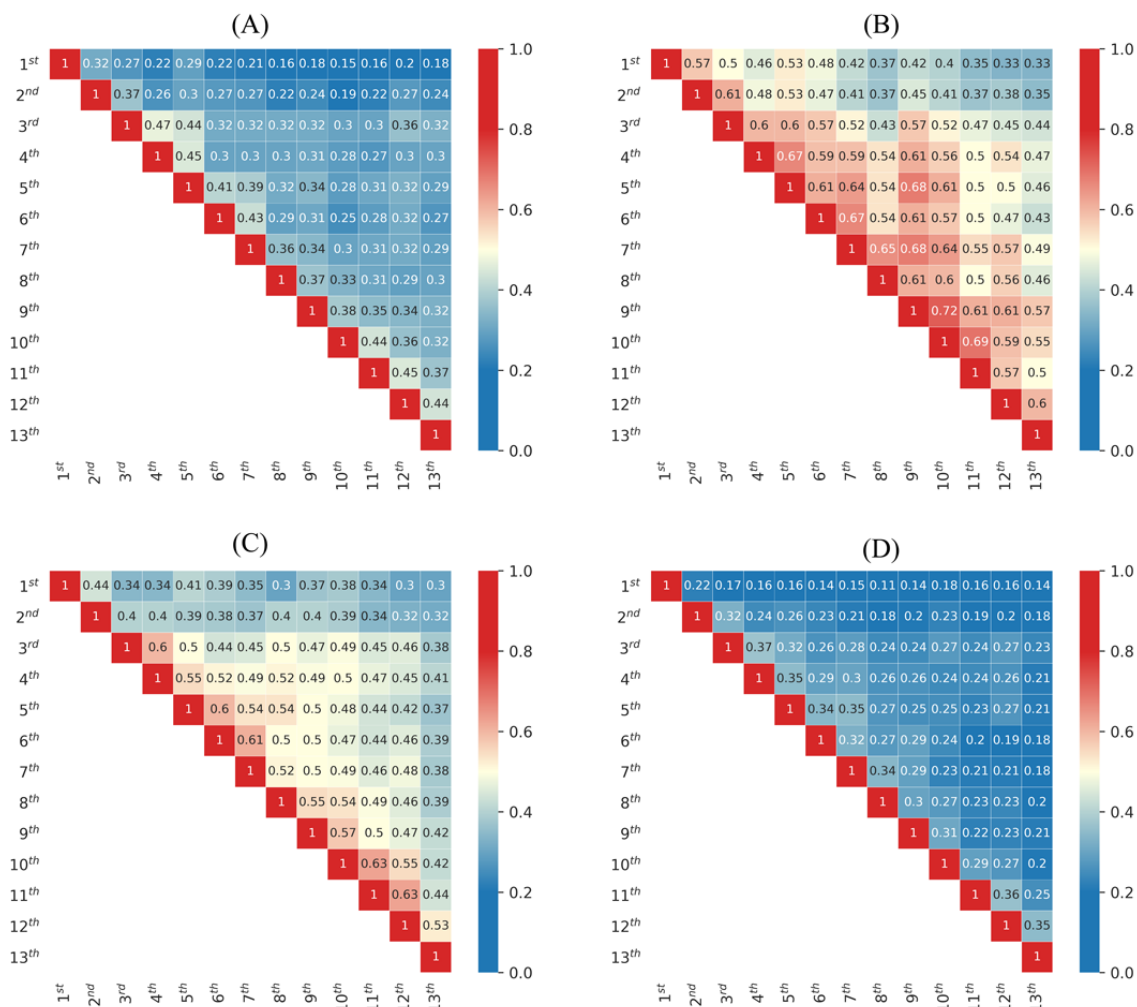
Locations showed the highest overlap, whereas person and miscellaneous entities showed the lowest overlap across the months. This indicates that news was dispersed across many people appearing in daily events. In contrast, locations were fairly constant during the pandemic due to the low number of total locations. These results indicate that the focus was on a narrow area restricted to Croatia, the neighboring countries, the European Union, and international locations such as Wuhan and Lombardy. This reflects the fact that countries closed their borders and the majority of events took place inside the country. That is why Croatian cities and regions were the predominant location entities throughout the study period. Similar observations were made for organizations as well. The principal organizations of focus were the WHO, local infectious disease clinics, and hospitals. Besides medical institutions, the focus was on government entities such as the national headquarters, ministries, the Croatian parliament, and political parties. In the second wave, the focused entities were related to vaccination. The names of the most popular social networks (ie, Facebook and Twitter) were also always present because news articles were reporting COVID-19–related discussions on Facebook and Twitter. A difference can be noticed (Figure 7) for January and February 2020 (when the epidemic had not yet been declared in Croatia). These fields are in shades of blue, which indicates that online news media wrote about different organizations until the epidemic broke out. After that (from March 2020 onward), the color changes to yellow and slightly red. The online news media then predominantly wrote about the same set of organizations for the entire duration of the pandemic, even in the month of June in which there was a break between the two epidemic waves.

Furthermore, we performed an entity analysis between the two pandemic waves. In this case, we focused on the 250 most frequent entities per entity type (person, location, organization, and miscellaneous) and observed their overlap between the two epidemic waves. The Jaccard similarity coefficients showed the largest overlaps for the location entity type (0.5337), which was slightly lower for organizations (0.4793) than for people (0.4045) and was the lowest for the miscellaneous (0.333) category. The interpretation of the results is identical to that described above for the analysis by months.

Discussion

Principal Results

In this work, we characterized the online media response to the COVID-19 pandemic in Croatia by examining the amount and the content of news articles related to COVID-19. Since most of the studies dealing with the media response to previous world epidemics were performed without using NLP for the task of infoveillance (eg, [12-16]), our study is not fully comparable with this previous work. In response to the other infoveillance studies related to COVID-19 media coverage [20-23,26,27,29], this study offers methodological extension. Specifically, we propose an integrative infoveillance approach based on NLP methods combined with the Jaccard similarity coefficient for longitudinal tracking of the dynamics of changes across the first 13 months of the pandemic.

Our results show that the number of COVID-19–related articles was relatively high, representing approximately 40% of total news articles, on average. This property remained the same during both waves of the pandemic. These results differ from those described by Pearman et al [2], who showed that COVID-19 media coverage decreased after the initial intense attention at the beginning of the crisis. It seems that the online news media in Croatia tended to highly focus on the pandemic during both waves, as well as during the period after the first wave (which, in the following 3 weeks, turned out to be a break before the second wave).

The high amount of pandemic-related articles is one of the three indicators of dramatized media coverage [15], which may indicate an infodemic. However, this alone is not a sufficient condition to confirm an infodemic. Clearly, during the first wave, it was necessary to inform the public about the COVID-19 pandemic. The online media play an important role in informing the public, and perhaps this is the main reason for the high number of COVID-19–related articles despite the relatively lower number of COVID-19 cases during the first wave. Consequently, our findings show that there is no strong correlation between the number of news articles related to COVID-19 and the number of new cases of COVID-19. This finding is in line with a previous study [26] showing that Zika-related tweeting dynamics were not significantly correlated with the underlying Zika epidemic. Additionally, we found that the number of articles and the number of new COVID-19 cases repeated in cycles within the time window of 1 week. There was a constant pattern: the number of articles was smaller during the weekends, and fewer new cases of COVID-19 were reported on Sundays and Mondays.

Capturing the dynamics of changes in the most frequent terms across the 13 months showed the highest similarities from May to September 2020. This was the period with a lower number of COVID-19 cases and it is probable that the news articles were less informative and featured similar topics. Additional examination of the similarities between pandemic-related terms indicated that all of the general terms (such as coronavirus, infection, pandemic, and hospital) were equally present in both waves. The pandemic-related terminology shifted from some possible remedies and medicines that could be used to prevent or cure COVID-19 (eg, disinfectant, paracetamol, Sumamed, azithromycin, hydroxychloroquine) in the first wave to the vaccination process (Pfizer, AstraZeneca, Sputnik V, vaccination) in the second wave. This can be interpreted as a sign of adequate online media coverage in the sense that the online media provided the available information.

The results of NER showed that the online news media concentrates mostly on the people from the state administration; even the scientists featured are often involved as members of the various state bodies. A similar pattern was reported by Hart et al [19], showing that politicians appear in media coverage more frequently than scientists. The online news media showed low dynamics of changes regarding the locations, whereas people, organizations, and other entities were frequently changing over the monitored months.

The inclusion of NER as a method for infoveillance enriches the longitudinal tracking of the dynamics of changes by introducing the insights of focal entities. However, this approach is not a replacement for the topic modeling that is also used as a part of infoveillance methodology [39,40]. In fact, owing to its certain advantages, NER can be a complementary approach to the characterization of the content of information sources. In contrast to topic modeling, which relies on the annotator's viewpoint and thus raises potential ambiguities in detecting and naming the topics along with challenges regarding interannotator agreement or consistency [32], NER enables unambiguous monitoring since there is no need for an additional interpretation of annotation, which clearly speaks in favor of NER as the complement method of topic modeling.

To the best of our knowledge, this longitudinal study is the first of its kind to use NLP techniques in combination with Jaccard similarity for tracking the changes in the most frequent subjects. In addition, since this study was oriented to the Croatian online news media response during the first year of the pandemic, it can provide useful data for further comparisons with data collected from other countries.

Limitations

This research has several limitations. First, we characterized media content related to the COVID-19 pandemic by considering only Croatian online news media. However, a large amount of information is present in social media, especially the social networks that were not included in this study. Additionally, individuals are also exposed to COVID-19–related information through traditional sources. Therefore, to obtain a more realistic picture of media content related to the pandemic, it would be advisable to extend the analysis to cover all sources. Hence, in future work, we plan to extend this study by integrating heterogeneous data sources such as online social networks and similar social media platforms, online forums, and all other sources of textual data in social media such as user comments on online news media. Second, this study focused only on the Croatian language; however, the same longitudinal approach can be applied to any other language and/or country, and the entire methodology is transferable and only dependent on the available data sources and the maturity of the NLP methods per selected language.

Furthermore, there are many possible extensions of the reported research. For example, in the inferential statistical analysis, we used only one variable (the number of new COVID-19 cases), but there are also some other variables (eg, number of deaths, number of hospitalizations, number of patients in the intensive care unit or on a respirator) that can be studied as potentially related to the number of published articles. Moreover, several NLP methods can be applied to infoveillance (eg, topic modeling combined with polarity of the sentiment or attitudes in comments). Another important direction of our future research is to develop a full stack of NLP-based methods focused on longitudinal monitoring of the infodemia, infoveillance, health-crisis communication, and infodemic management.

Conclusion

The presented approach enables the infoveillance of online media in response to the COVID-19 pandemic through quantification of the share of COVID-19–related articles. Specifically, in this study, we addressed three open research questions and our main findings are as follows.

The low correlation between the number of COVID-19–related articles and new cases indicates that the amount of media content is not driven solely by the number of new COVID-19 cases, but rather by external processes. In the first wave, the large amount of news articles was necessary to inform the public about the new disease and the pandemic outbreak. In the second wave, the large number of news articles was important to communicate findings such as vaccines and other epidemiological measures.

Deeper insights can be obtained by analyzing the media content. Quantification of the dynamics of the changes captured by the Jaccard similarity coefficients revealed that there are slow changes in key terminology, locations, and institutions. The similarity between the most frequent terms was higher than 50% across all of the observed months (except for January 2020) and was higher than 70% from May to September 2020. This may indicate the narrow focus of reporting by online media during certain periods. However, additional analysis of the frequencies of the pandemic-related terms between the two waves indicated that there was a shift from the initial medical terminology known in the first wave to the novel medicine approaches and vaccines in the second wave.

To conclude, the online media had a prompt response to the pandemic in the sense of quantity (the number of articles) in both waves that occurred during the first 13 months of the pandemic. Despite the high number of COVID-19–related articles, the key terms and entities encountered slow changes. However, the results based on tracking the dynamics of the changes of pandemic-related terminology suggest that the media covered the important changes during the pandemic (eg, the number of infected people, prevention measures, vaccine production).

Overall, the proposed infoveillance approach based on NLP for longitudinal tracking of the dynamics of changes enables gaining deeper insight into the online news media response to the pandemic. This study thus contributes a better understanding of the published content related to COVID-19 in the Croatian online news media and can be further exploited for improving crisis communication.

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Conflicts of Interest

None declared.

Multimedia Appendix 1

Additional information on data, list of COVID-19–related terms used for article filtering, epidemiological data and used data sets, mathematical formulas used in experiments, result details (additional tables and graphs) of inferential statistical analysis, and obtained table of coronavirus-related concepts.

[DOCX File , 721 KB - publichealth_v7i12e31540_app1.docx]

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Abbreviations

ACF: autocorrelation function
CCF: cross-correlation function
CRF: conditional random field
MERS: Middle East respiratory syndrome
MI: mutual information
NER: name entity recognition

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NLP: natural language processing
SARS: severe acute respiratory syndrome
WHO: World Health Organization

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Original Paper

Accuracy of Self-reported Human Papillomavirus Vaccination Status Among Gay and Bisexual Adolescent Males: Cross-sectional Study

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Abstract

Background: Men who have sex with men are a risk group for anal human papillomavirus (HPV) and anal cancer. Australia introduced a universal school-based HPV vaccination program in 2013. Self-reported HPV vaccination status has been widely used in clinical and research settings, but its accuracy is understudied.

Objective: We aimed to examine the accuracy of self-reported HPV vaccination status among gay and bisexual adolescent males.

Methods: We included 192 gay and bisexual males aged 16-20 years from the Human Papillomavirus in Young People Epidemiological Research 2 (HYPER2) study in Melbourne, Australia. All participants had been eligible for the universal school-based HPV vaccination program implemented in 2013 and were asked to self-report their HPV vaccination status. Written informed consent was obtained to verify their HPV vaccination status using records at the National HPV Vaccination Program Register and the Australian Immunisation Register. We calculated the sensitivity, specificity, positive predictive value, and negative predictive value of self-reported HPV vaccination status.

Results: The median age of the 192 males was 19 (IQR 18-20) years. There were 128 males (67%) who had HPV vaccination records documented on either registry. Self-reported HPV vaccination had a sensitivity of 47.7% (95% CI 38.8%-56.7%; 61/128), a specificity of 85.9% (95% CI 75.0%-93.4%; 55/64), a positive predictive value of 87.1% (95% CI 77.0%-93.9%; 61/70), and a negative predictive value of 45.1% (95% CI 36.1%-54.3%; 55/122).

Conclusions: Self-reported HPV vaccination status among Australian gay and bisexual adolescent males underestimates actual vaccination and may be inaccurate for clinical and research purposes.

KEYWORDS

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Introduction

Multiple countries have implemented national human papillomavirus (HPV) vaccination programs and demonstrated significant reductions in HPV infection, genital warts, and cervical cancer and its precursors [1-4]. Self-reported HPV vaccination status has been widely used in clinical and research settings to monitor the effectiveness of the HPV vaccination program.

Australia introduced a school-based HPV vaccination program for girls in 2007, with expansion to include 12- and 13-year-old boys in 2013. Additionally, Australia established robust population-based vaccination registries to document HPV vaccination coverage [5]. Several studies have examined the accuracy of self-reported HPV vaccination status among women and adolescent girls; however, the proportion who report their HPV vaccination status correctly varies across populations and settings, ranging from 54% to 92% [6-15]. Low sensitivity (54%) of self-reported HPV vaccination status against medical records is reported among adolescent girls aged 14-17 years in the United States [6]. The sensitivity seems to be improved among older populations. Another US study has shown that the sensitivity of self-reported HPV vaccination status against medical records is 91% among women aged 18-49 years [10]. A reasonable but lower sensitivity of self-reported HPV vaccination status is also reported when immunization registry data are used as the reference standard, with a sensitivity of 85% among women aged 20-22 years in Japan and 86% among women aged 22-30 years in Australia [7,12].

Most previous studies verified self-reported HPV vaccination status from parents or electronic medical records instead of vaccination registries. One study examined the accuracy of self-reported HPV vaccination status in men, but the authors did not separate the data of heterosexual men and gay/bisexual men [16]. Australia is one of very few countries that has implemented a school-based HPV vaccination program coupled with a national vaccination registry recording HPV vaccination. This study aimed to determine the accuracy of self-reported HPV vaccination status from the school-based program verified against the national vaccination registry among gay and bisexual adolescent males.

Methods

The Human Papillomavirus in Young People Epidemiological Research 2 (HYPER2) study was a cross-sectional study aimed at examining HPV prevalence among young gay and bisexual males after the implementation of the school-based gender-neutral HPV vaccination program in Australia, with the main findings published elsewhere [17]. A total of 200 same-sex attracted men aged 16-20 years who were residents in Australia in 2013 were recruited via the HYPER2 study to ensure they had been eligible for the gender-neutral HPV vaccination program at the time. All males were recruited at the Melbourne Sexual Health Centre (Victoria, Australia) between January 2017 and March 2019. All men were asked to complete a questionnaire that collected demographic characteristics, sexual practices, and self-reported HPV vaccination status. Men could

choose "unsure" for vaccination status and the number of doses. Written consent was obtained from all the men. Ethics approval was granted from the Alfred Hospital Ethics Committee, Melbourne, Australia (429/16).

The National HPV Vaccination Program Register (NHVPR) was established in 2008 to monitor HPV vaccination coverage in Australia. State Health Departments and local councils were mandated to report individuals who received the vaccine from the school-based program to the NHVPR [5]. The NHVPR also received vaccination records on a voluntary basis from general practices (who received notification payments for doing so in the initial 3 years when mass catch-up through general practice occurred) and other immunization providers across Australia. The NHVPR ceased at the end of 2018 and HPV vaccination records moved to the Australian Immunization Register (AIR); therefore, NHVPR and AIR were both used to verify HPV vaccination records [18]. A probabilistic matching based on identifying details (eg, first and last name, date of birth) was used to identify an individual's corresponding vaccination records in the registers.

Only men who received the vaccine via the school-based program were eligible for inclusion in this study. Self-reported HPV vaccination status was stratified into "vaccinated" and "not vaccinated or unsure" based on self-reported data on the survey. The sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio for self-reported HPV vaccination status were calculated using data from the registers as the reference standard. The positive likelihood ratio is the probability of individuals who self-reported being vaccinated in those who were vaccinated divided by the probability of individuals who self-reported being vaccinated in those who were not vaccinated (ie, dividing the sensitivity by 1 minus the specificity). The negative likelihood ratio is the probability of individuals who self-reported being not vaccinated in those who were vaccinated divided by the probability of individuals who self-reported being not vaccinated in those who were not vaccinated (ie, dividing 1 minus the sensitivity by the specificity). A positive likelihood ratio >10 is useful for ruling in being vaccinated, while a negative likelihood ratio <0.1 is useful for ruling out being vaccinated [19,20]. The κ statistics were also calculated to determine the agreement between self-reported vaccination status and registry records. The level of agreement was categorized based on the κ statistics as none (0-0.20), minimal (0.21-0.39), weak (0.40-0.59), moderate (0.60-0.79), strong (0.80-0.90), and almost perfect (>0.90) [21]. We also performed analyses by excluding individuals who were unsure about their vaccination status. All statistical analyses were performed in Stata (version 17; StataCorp LLC).

Results

Of the 200 men, 8 were excluded from the analysis because they were not vaccinated as part of the school-based vaccination program. Median age of the 192 men was 19 (IQR 18-20) years. Most men completed secondary school (n=138, 71.9%). The median number of lifetime male sex partners was 9 (IQR 5-25). There were 70 (36.5%) men who self-reported being vaccinated,

13 (6.8%) reported being unvaccinated, and 109 (56.8%) men were unsure about their vaccination status (Table 1).

Table 1. The 2×2 tables comparing self-reported vaccination status to the reference standard of national vaccine registry vaccination data among gay and bisexual adolescent males.

Self-reported vaccination status	Vaccination registries		Total
	Vaccinated	Not vaccinated	
All men (N=192)			
Self-reported vaccinated	61	9	70
Self-reported not vaccinated/unsure	67	55	122
Total	128	64	192
All men excluding those who were unsure about their vaccination (N=83)[a]			
Self-reported vaccinated	61	9	70
Self-reported not vaccinated	1	12	13
Total	62	21	83

[a]This value excludes the 109 men who were unsure about their vaccination status.

At least one dose of HPV vaccination was recorded in the HPV vaccine registry for 66.7% (128/192) of men, 63.0% (121/192) completed 3 doses of vaccination, 6 men received 2 doses, and 1 man received 1 dose. Only 61 of the 128 men correctly reported they were vaccinated (sensitivity=47.7%; Table 2). Of those 64 men who did not have any registry record, 55 men reported being unvaccinated or unsure of their vaccination status (specificity=85.9%). The positive predictive value was 87.1% (61/70) and the negative predictive value was 45.1% (55/122). The positive likelihood ratio was 3.4 and the negative likelihood ratio was 0.61.

Table 2. Accuracy of self-reported human papillomavirus vaccination status among gay and bisexual adolescent males using national vaccine registry data as the reference standard.

Diagnostic accuracy	All men (N=192), value (95% CI)	All men excluding those who were unsure about their vaccination (N=83)[a], value (95% CI)
Sensitivity, %	47.7 (38.8-56.7)	98.4 (91.3-100)
Specificity, %	85.9 (75.0-93.4)	57.1 (34.0-78.2)
Positive predictive value, %	87.1 (77.0-93.9)	87.1 (77-93.9)
Negative predictive value, %	45.1 (36.1-54.3)	92.3 (64.0-99.8)
Positive likelihood ratio	3.4 (1.8-6.4)	2.3 (1.4-3.8)
Negative likelihood ratio	0.61 (0.50-0.74)	0.03 (0-0.20)
κ value	0.274 (0.166-0.382)	0.635 (0.435-0.836)

[a]This value excludes the 109 men who were unsure about their vaccination status.

After excluding 109 men who were unsure about their vaccination status, there was an improvement in the sensitivity (61/62, 98.4%) and negative predictive value (12/13, 92.3%), but a decrease in the specificity (12/21, 57.1%). The positive likelihood ratio remained similar (2.3) but with a relatively low negative likelihood ratio (0.03).

The agreement between self-reported vaccination status and registry record was minimal (κ=0.274) when including men with unsure vaccination status in the unvaccinated group. However, the level of agreement between self-reported vaccination status and registry record improved to moderate (κ=0.635) when excluding men with unsure vaccination status.

Discussion

This study examines the accuracy of self-reported HPV vaccination status among gay and bisexual adolescent males using national vaccine registry data as the reference standard. Our study showed that, of those vaccinated with at least one dose, only 48% of men correctly recalled their vaccination status, with over half of men unsure. However, the sensitivity improved to 98% after excluding men who were unsure about their vaccination status.

The low sensitivity of self-reported vaccination status in our study is similar to a US study showing only 54% of 74 adolescent girls aged 14-17 years correctly reported their HPV vaccination status as verified via medical records [6]. To our best knowledge, there has been only one study examining the accuracy of self-reported HPV vaccination status among men. Consistent with our findings, a US study has also reported a minimal agreement (κ=0.35) between self-reported vaccination status and medical records among men aged 13-26 years [16]. The authors also reported a positive predictive value of 62% [16], which is lower than our estimate (87%); this is likely due

to the United States having lower vaccination coverage compared to Australia. However, the authors did not report the sensitivity and specificity for heterosexual men and gay/bisexual men separately. Past studies have reported that the sensitivity of self-reported HPV vaccination status is higher among young adults compared to adolescents [16], and this may be because adolescents may receive multiple vaccines at school around the same time and they may not remember which specific vaccine they received. Several countries have also implemented catch-up HPV vaccination programs for gay and bisexual men aged up to 45 years [22-24]. Further studies examining the accuracy of self-reported HPV vaccination status among gay and bisexual men in these populations would be beneficial.

We found that the positive likelihood ratios were relatively small regardless of whether the unsure vaccination group was included or not. Given the positive likelihood ratios are <10 [19], this suggests that self-reported vaccination status is not useful for ruling in being vaccinated. However, there was a significant change in the negative likelihood ratio from 0.61 when including men who were unsure about their vaccination status to 0.03 when excluding men who were unsure about their vaccination status. A negative likelihood ratio that is <0.1 would be useful for ruling out being vaccinated [20]. Given not all individuals would be aware of their vaccination status, the high negative likelihood ratio in our study suggests that self-reported vaccination status is not useful for ruling out being vaccinated.

There are several limitations to this study. First, this study was conducted among adolescent gay and bisexual men; therefore, our findings may not be generalizable to other populations such as heterosexual men and adults. Second, adolescents also receive the meningococcal ACWY and whooping cough booster vaccines at school around the age they receive the HPV vaccine [25], and it is likely many adolescents cannot distinguish between the vaccines. Third, the vaccines given in general practice may not have been recorded in the registers and therefore we may have underestimated the proportion of vaccinated individuals in this population.

In conclusion, the accuracy of self-reported HPV vaccination status among gay and bisexual adolescent males was low, and most men were unsure about their vaccination status. Underreporting HPV vaccination suggests that self-reported vaccination status may be inaccurate for clinical practice to guide vaccination and for research evaluating the effectiveness of vaccination programs. This highlights the benefit of using data on actual vaccination status from vaccination registries to verify vaccination status and dosage. The AIR is the national register that records vaccines that are given to individuals in Australia. Individuals can access their immunization history statement online. Additionally, general practitioners or other vaccination providers can also access the immunization history statement online.

Authors' Contributions

EPFC, MYC, CKF, SNT, AMC, and SMG were the study investigators for the HYPER2 study. EPFC and MYC conceived the study idea, designed this study, and oversaw the HYPER2 study. RW was involved in study recruitment and data collection and oversaw study recruitment for the HYPER2 study. EPFC conducted the statistical analyses and wrote the first draft of the manuscript. All authors provided data interpretation, revised the manuscript for intellectual content, and approved the final version of the manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Conflicts of Interest

EPFC and AMC have received educational grants from Seqirus Australia and bioCSL for educational, training, and academic purposes in the area of HPV outside the submitted work. EPFC has received an honorarium from Merck Sharp & Dohme outside the submitted work. CKF has received research funding from CSL Biotherapies and owns shares in CSL Biotherapies. SMG has received advisory board fees and lecture fees from Merck & Co for work in private time and through her institution (Royal Women's Hospital) funding for an Investigator-Initiated grant from Merck & Co for a young women's study on HPV; SMG is a member of the Merck Global Advisory Board for HPV vaccines. All other authors have no conflicts of interest to declare.

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Abbreviations

AIR: Australian Immunization Register
HPV: human papillomavirus
HYPER2: Human Papillomavirus in Young People Epidemiological Research 2
NHVPR: National HPV Vaccination Program Register

Original Paper

Comparing Social Media and In-Person Recruitment: Lessons Learned From Recruiting Substance-Using, Sexual and Gender Minority Adolescents and Young Adults for a Randomized Control Trial

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Abstract

Background: Recruiting large samples of diverse sexual and gender minority adolescent and young adults (AYAs) into HIV intervention research is critical to the development and later dissemination of interventions that address the risk factors for HIV transmission among substance-using, sexual and gender minority AYAs.

Objective: This paper aimed to describe the characteristics of the samples recruited via social media and in-person methods and makes recommendations for strategies to recruit substance-using, sexual and gender minority AYAs, a hardly reached population that is a priority for HIV prevention research.

Methods: Using data from a randomized control trial of an HIV and substance use intervention with sexual and gender minority AYAs, aged 15 to 29 years in southeastern Michigan (n=414), we examined demographic and behavioral characteristics associated with successful recruitment from a range of virtual and physical venues.

Results: We found that paid advertisements on Facebook, Instagram, and Grindr offered the largest quantity of eligible participants willing to enroll in the trial. Instagram offered the largest proportion of transgender masculine participants, and Grindr offered the largest proportion of Black/African American individuals. Although we attempted venue-based recruitment at clubs, bars, community centers, and AIDS service organizations, we found it to be unsuccessful for this specific hardly reached population. Social media and geobased dating applications offered the largest pool of eligible participants.

Conclusions: Understanding factors associated with successful recruitment has the potential to inform effective and efficient strategies for HIV prevention research with substance-using, sexual and gender AYAs.

Trial Registration: ClinicalTrials.gov NCT02945436; https://clinicaltrials.gov/ct2/show/NCT02945436

International Registered Report Identifier (IRRID):   RR2-10.2196/resprot.9414

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Introduction

Hardly reached populations refer to groups that are traditionally under-recruited into health research. Such populations were, until recently, referred to as hard-to-reach, but recent literature has redefined them as *hardly reached*, switching the emphasis to researchers' inability to recruit rather than the population's inability to be recruited [1]. Hardly reached populations often experience high levels of structural vulnerability (ie, homelessness or incarceration), creating significant barriers to their participation in research. These hardly reached groups may also experience high levels of stigma and discrimination associated with their identity (ie, transphobia or homophobia) or behaviors (ie, people who use substances) that act as a barrier to their research in participation [2,3]. An alternative term, *hidden population*, is often used to refer to those who may not wish to be found or contacted (eg, people who use substances or undocumented migrants) [4]. For example, people who use or misuse substances may be reluctant to disclose behaviors that would make them eligible for research participation due to fears of illegal behaviors being reported to authorities or the high level of stigma associated with this behavior [5-7].

While hardly reached populations often include groups with minority identities (ie, racial and ethnic minorities or sexual and gender minorities) [4,8,9], they may also include other populations that are under-recruited due to geographical location (ie, rural populations), lack of access to health services (for the recruitment of clinic-based populations), or access to technology (for recruitment of online samples) [1,3,4]. Difficulties experienced in engaging hardly reached populations in research studies may be particularly heightened when individuals live with the intersectionality of being a sexual or gender minority and engaging in a stigmatized behavior of substance use. The stigma associated with underage drinking or use of illegal drugs could significantly decrease the likelihood of participation in research [2]. In HIV research, the potential under-recruitment of substance-using young men who have sex with men (YMSM) is particularly problematic given data illustrating the growing incidence of HIV and striking associations between substance use and HIV risk [10]. Sexual and gender minority youth are increasingly important to recruit into prevention research to accurately develop prevention strategies that represent and are tailored toward diverse communities. Strategies are needed to recruit youth that represent local demographics and geography (ie, in states such as Michigan with large rural populations) and risk groups in localized epidemics [11].

Venue-based recruitment is a modified venue-time-spaced screening approach implemented by behavioral surveillance and involves listing physical venues where target populations can be found and using this list to identify times to recruit potential participants. Venue-based recruitment has served as a viable way to connect with substance-using, sexual and gender minority, adolescent and young adults (AYAs) and can occur through locations such as bars and clubs, AIDS service organizations, or street outreach by research study staff. Multiple studies have demonstrated that recruitment through venues such as bars or nightclubs can often yield high numbers of substance-using, sexual and gender minority AYAs [12-14].

However, the age restrictions of bars and clubs poses a barrier to the recruitment of YMSM under the age of 21 years. This age requirement could possibly result in fewer adolescents recruited or additional effort required from research staff, leaving online-based recruitment as a more effective way to recruiting sexual and gender minority AYAs into HIV research [15].

To counteract the challenges of venue-based sampling and community-based outreach, researchers are increasingly using internet-based recruitment to recruit populations who may be hardly reached through traditional sampling methods [16]. Using the internet for social media–targeted recruitment has been reported as a feasible strategy for recruiting large samples of men who have sex with men (MSM) [16-19] as well as AYAs who engage in substance use [20,21]. Compared with traditional recruitment strategies, social media is attractive for its wide geographic reach, cost effectiveness, usability, and capacity for engaging hardly reached, isolated, or minority populations [22-24]. Social media (eg, Facebook, Instagram, and other socially oriented platforms such as Grindr) has been shown to be a cost-effective recruitment strategy [25-27] to recruit AYAs who have demographic profiles reflective of the general AYA population. Additionally, social media and internet-based recruitment efforts can reach rural areas, where opportunities for venue-based recruitment can be limited [28]. Based on a sample of 8252 participants, Christensen et al [29] found that social media recruitment was more efficient (total number of participants enrolled); had an average lower cost per recruited participant, compared with in-person methods; and was found to be cost-effective and rapid, with researchers paying, on average, US $17 per completer (range US $1.36–$110). Thornton et al [30] reported that 86% of studies reported similar representativeness between online and offline samples, with no systematic gender or age differences. The use of social media platforms can allow for a broader range of hardly reached YMSM populations (ie, rural areas) [31]. Facebook [32-34] and the dating application Grindr [18,35,36] have yielded successful recruitment of YMSM, though Grindr at a higher cost [24]. However, recruitment via the internet has the potential to exclude YMSM without access to the internet, which often includes individuals who are ethnic minorities or socioeconomically disadvantaged.

Here, we describe a case study of recruiting substance-using, young, sexual and gender minority AYAs (aged 15-29 years) in southeastern Michigan for a randomized controlled trial of a substance use and HIV prevention counseling intervention. This paper describes and contrasts 2 recruitment methods (in-person, venue-based recruitment and recruitment via the internet using social media targeted advertising), describes the characteristics of the samples recruited via each method, and adds recommendations to the literature for programs aiming to recruit substance-using YMSM, a hardly reached population that it is urgent to include in HIV prevention research.

Methods

Study Design

Project Swerve is a randomized control trial testing the efficacy of a substance use brief intervention for creating gains in HIV and sexually transmitted infection (STI) testing among young, substance-using, sexual and gender minority communities, aged 15 to 29 years. Full details of the intervention and research protocol can be found in [32].

Eligibility

Eligibility criteria for the trial participants included self-reported (1) sex assigned male at birth and currently identifying as man/male, woman/female/trans feminine, and/or gender nonbinary or assigned female at birth and currently identifying as man/male/trans masculine; (2) age between 15 and 29 years at the time of screening; (3) negative or unknown HIV status at screening; (4) past 3-month drug use or binge drinking (eg, stimulants, hallucinogens, opioids, sedatives, amyl-nitrite, or club drugs with alcohol and/or cannabis); (5) condomless anal or oral sex with a self-identified man in the 6 months prior to enrollment; and (6) resident of southeastern Michigan at the time of screening.

Recruitment

Overview

Recruitment of participants took place from April 2017 to September 2019 and consisted of 2 modes of recruitment: (1) online recruitment through social media and dating applications and (2) in-person recruitment at local venues. Online recruitment consisted of paid advertisements on social media platforms, including those aimed at general audiences—Facebook, Instagram, Snapchat, Reddit, and Google Ads—as well as networking mobile apps targeted toward sexual and gender minorities—Grindr, Scruff, Jack'd, and Bareback Realtime. Web-based recruitment also included unpaid advertisements through a health research portal based at the university, Tumblr, and Twitter. We used Completely Automated Public Turing test to tell Computers and Humans Apart (CAPTCHA) during the screening process to verify for fraud. Additionally, email addresses could only register once and were sent verification links to complete registration.

Online Recruitment

Online advertisement photos were purchased from stock photo websites and included people from a range of gender identities, races, and ethnicities. Language used in online advertisements included "Get paid to participate in an HIV testing program" and "Participate in a paid university study about health and HIV testing." To supplement paid online static advertising, recruitment videos were also created through an online video creation platform that provides stock footage and images. These short, <15-second videos consisted of people holding hands and pride flags and used the same language as the static advertisements. These were posted as video advertisements on Facebook, Instagram, Reddit, Tumblr, and Twitter.

We ran 3 campaigns at a time on Facebook and Instagram: 2 for cisgender MSM and 1 for transgender individuals. Facebook and Instagram allow advertisers to target populations based on age, location, and interests, which allowed us to narrow our impressions to those between 15 and 29 years old, residing within southeastern Michigan, and within specific search interests (eg, gay pride, Gay Straight Alliance [GSA], gay, bisexual, transgender, gay bars). Facebook and Instagram offer an advertisement boost option, which costs US $20 and increases the advertisement's reach for a limited amount of time.

Snapchat advertisements cost US $50 a day and could be targeted by interests (eg, lifestyle, sports, technology), location (eg, cities within our participant range), and demographics (eg, age, gender, language). We began Snapchat advertisements at the end of June 2018, running them every weekend through the end of July 2018 to see if they would bring in any new participants. After we found Snapchat ads to bring in some new eligible participants, we increased the frequency of our advertisements to 7 days every other week during August 2018 and increased once more to month-long advertisements from September to mid-November 2018. Snapchat did not bring in enough new eligible participants for the project, and we decided to end advertisements in November 2018.

Reddit advertisements were developed in November 2018 and ran through December 2018. After consideration of our project and its inclusion of minors, Reddit chose not to allow us to advertise our project through their platform, where recruiting only people aged ≥18 years old is acceptable. Our advertisements were reported by users 5 times in 2 months, and organic posts were deleted from threads by owners.

Grindr, a geosocial networking application, offered 2 different advertisements: banner (at the top of the screen) and interstitial (a full-page advertisement). We created an advertisement for each: a banner "Interested in getting paid to test for HIV/STIs? Swerve is a testing program looking for young gay men and Trans folks. Click here!" and a full-page, interstitial advertisement "Get paid to test for HIV/STIs by joining Swerve - A testing program for young gay men and Trans folks." Grindr advertisements target MSM and can target specific cities, which helps to narrow down the impressions for people within the enrollment criteria. Grindr cannot target age. We ran 2 flat-rate advertisements: April to October 2017 and November 2017 to April 2018. In 2018, Grindr changed their advertisement approach to bids to be advertised on the platform. We ran this set of Grindr campaigns from August 2018 to August 2019, with a typical banner campaign running at US $1250 total, with a US $40 a day spending cap in place. A typical interstitial campaign with a capped budget cost US $1000 total, had a US $35 a day spending cap, and was auto-placed throughout the day.

Scruff, a networking application also targeting MSM, offered advertisements that cost a flat rate of a minimum US $500 for 2 weeks, with a cost per 1000 impressions option. At the time, Scruff's advertisements were full page with a call-to-action button, which linked the advertisement directly to the landing page. Scruff can target by location and, similarly to Grindr, cannot target by age. We ran a full-page advertisement, the same as on Grindr, for 1 month and targeted Detroit, Michigan with a 50-mile radius. Jack'd, another geosocial networking

application for the gay, bisexual, and transgender community, offered only banner ads for public health–based research projects when we were using their advertising platform from June 2018 to July 2018. The same banner advertisement used on Grindr was used on Jack'd and cost US $2000 for 1 month of advertisements.

We created a Twitter account in October 2017 and used it to boost our online presence. We had a pinned tweet with a link to the Swerve landing page and would tweet our recruitment materials (videos and photos), post when we were at a conference, and share articles related to sexual health. Our final post was in October 2019. Similarly, we created a Tumblr account to boost engagement and posted recruitment materials with tags (eg, pride, gay, Michigan, bisexual, transgender, mtf, ftm, HIV, HIVtesting, knowyourstatus, healthyliving, publichealth). We made a total of 10 posts to Tumblr between January 2018 and February 2019.

Bareback Realtime is a web service that MSM use to meet other men. They offer free Quick Connect Ads, which are typically used to meet other people. We made our advertisements last for 6 hours at a time and used language similar to that used with Grindr. Bareback Realtime was posted an average of once per week in varying cities in southeastern Michigan, and we ran the advertisements from May 2017 to September 2019. Bareback Realtime was not successful, and advertisements were placed sparingly throughout the recruitment period.

The university at which this trial is housed offers a health research portal for research staff to share their trials with the public. The name, description, study topic, participant involvement, compensation, location, inclusion and exclusion criteria, and additional screening questions were options for development of the research page. We used HIV, substance abuse, and sexual health as our study topics; explained what the project entailed; explained the breakdown of compensation per visit; listed Ypsilanti, Detroit, and Flint as study locations; listed age of 15-29 years old and "male identifying" as inclusion criteria; and did not include any additional screening questions. When people marked that they were interested in the study, we sent them a link to the landing page to participate in the eligibility screener.

Venue-Based Recruitment

Venue-based recruitment took place from October 2017 to September 2019. To reach our target population, potential participants were systematically sampled from a predeveloped list of public venues where sexual and gender minority AYAs were known to frequent, which included lesbian, gay, bisexual, transgender, queer, plus (LGBTQ+)–friendly bars, clubs, drag shows, restaurants, and cafés; events in Michigan (eg, Pride); health fairs and wellness centers (testing centers); campus-based events at high schools and colleges in southeastern Michigan; and social organizations (eg, local GSA chapters).

Staff went to at least 10 locations each week and always to 2 different locations on Friday and Saturday nights. Approximately 30 locations were potential venues for each month's selection, where some venues were attended more than once per week. Some venues were not chosen to attend due to

lack of permission from management, weather concerns for outdoor events, seasonal events, or lack of regular attendance by patrons. An average of 40 locations were attended each month.

All potential participants were approached within staffing and time limits. Staff were required to spend at least 2 hours recruiting during each scheduled shift, and if a venue had a low turnout, staff would move on to a second location to ensure at least 10 people were screened during each recruitment shift. Participants were offered to take the screener at the time of recruitment and if they refused, were handed a palm card (a small postcard-sized flyer with information regarding the trial). Palm cards and coasters were left at locations for people to pick up on days and at times when staff were not actively recruiting. We purchased or signed up for table space at local pride events, conferences, and health fairs at colleges and community centers. At these events, we passed out recruitment materials and approached potential participants to take the eligibility screener on tablets and left a sign-up sheet on the table for people to leave their name, phone number, email address, and age so we could contact them for screening if they decided not to take the eligibility screener on-site.

Staff were trained to approach potential participants by introducing themselves, the project, and their purpose of recruiting. T-shirts with the project logo were worn to show legitimacy of the project. Staff always recruited in groups of 2 or more after 6 pm to ensure safety, and groups of 4 or more would split up and attend events in different cities (ie, Detroit and Ann Arbor) to recruit more participants in each shift.

Measures

Sociodemographic Characteristics

In the eligibility screening survey, we asked demographic questions on sexual orientation, gender identity, sex assigned at birth, age, race, ethnicity, zip code, and school enrollment status. Participants were asked to identify their gender, using the check all that apply method, with options being female, male, trans woman, trans man, gender queer/nonconforming, and other. Participants indicated their sexual orientation as straight or heterosexual, gay or homosexual, bisexual, same gender loving, queer, or other. Participants were not eligible if they stated their gender was female and their sexual orientation was bisexual, same gender loving, or queer or if their gender was male and sexual orientation was heterosexual. Participants indicated their race as White/Caucasian, Black/African American, Asian/Pacific Islander, Middle Eastern, or other, and ethnicity was identified by Hispanic/Latino or not. Participants were asked to check all that apply, allowing us to identify racial and ethnic subgroups (eg, Black Latino, Asian Latino).

HIV Status and Sexual Experience

We asked participants to indicate if they had ever tested positive for HIV, and those with self-reported unknown or presumed negative HIV status were eligible. We asked participants to identify if they had condomless oral or anal sex with someone who identifies as a man in the past 6 months at the time of screening.

Substance Use

We asked participants to identify any substances used in the last 3 months using the check all that apply method. Substances included tobacco or nicotine products, more than 5 standard alcoholic drinks in each day or night, cannabis, cocaine or crack, heroin, hallucinogens, inhalants, prescription pain relievers, prescription tranquilizers, prescription stimulants, prescription sedatives, methamphetamine, or none of the above. Participants were eligible if they reported using substances other than tobacco or alcohol and/or if they reported alcohol use at a rate of 5 or more standard drinks per day.

Statistical Analysis

We conducted a descriptive analysis across all recruitment platforms to examine differences in demographic characteristics (ie, gender identity, race, age) and substance use. The second step of our analysis focused on eligibility and enrollment from each recruitment source, where total eligibility and enrollment rates were calculated for the study overall as well as each recruitment source. Models were run in Stata Statistical Software version 16 (StataCorp LLC, College Station, TX).

Results

Eligibility

We had a total of 17,328 visits to the eligibility screener on the landing page, with 6274 (36.2%) completing screeners. Of those who completed the screener, 623 (623/6274, 9.92%) consented and were eligible for the trial, and 580 (580/623, 93.10%) of those who were eligible responded with their source of recruitment in their eligibility screener (Table 1). This question was added to the eligibility screener after 43 participants had taken the screener.

Table 1. Participant eligibility and enrollment by recruitment source.

Recruitment source	Screened eligible (n=580), n (%)	Enrolled (n=217), n (%)	Enrollment rate (total=37.4%), %
BBRT	1 (0.2)	1 (0.5)	100
Facebook	244 (42.1)	85 (39.2)	34.8
Friend	31 (5.3)	12 (5.5)	38.7
Google Ad	2 (0.3)	1 (0.5)	50.0
Grindr	135 (23.2)	54 (24.9)	40.0
Instagram	63 (10.8)	24 (11.1)	38.1
Jack'd	3 (0.5)	1 (0.5)	33.3
Other	3 (0.5)	1 (0.5)	33.3
Reddit	4 (0.7)	3 (1.4)	75.0
Scruff	10 (1.7)	3 (1.4)	30.0
Snapchat	2 (0.3)	1 (0.5)	50.0
Tumblr	13 (2.2)	5 (2.3)	38.5
Twitter	2 (0.3)	1 (0.5)	50.0
University health research	42 (7.2)	20 (9.2)	47.6
Venue	23 (3.9)	6 (2.8)	26.1

Recruitment

Of the 580 participants who reported their source of recruitment, Facebook advertisements offered the largest quantity of eligible participants (244/580, 42.1%) followed by advertisements on Grindr (135/580, 23.2%) and Instagram (63/580, 10.8%; Table 2). Other paid advertisements on the dating application Jack'd (3/580, 0.5%) yielded a low number of eligible participants. The health research portal website, an unpaid university level study participant portal, enrolled 42 (42/580, 7.2%) of eligible participants. A small number of eligible participants indicated a friend (31/580, 5.3%) or other (3/580, 0.5%) referred the eligible participants to the study for enrollment.

Unpaid social media advertisements including Google Ads (2/580, 0.51%), Snapchat (2/580, 0.3%), Reddit (4/580, 0.7%), Tumblr (13/580, 2.2%), Twitter (2/580, 0.3%), and the dating applications Scruff (10/580, 1.7%) and BBRT (1/580, 0.2%) offered the smallest quantities of eligible participants.

Table 2. Demographics of the eligible participants by recruitment source.

Characteristic	Total eligible sample, n (%)	Recruitment source[a], n (%)														
		A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
Sample size	580	1	244	31	3	135	63	3	3	4	10	2	13	2	42	23
Gender identity																
Female	2 (0.3)	0 (0)	2 (0.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Male	475 (76.2)	1 (100)	185 (75.8)	27 (87.1)	4 (100)	121 (89.6)	51 (80.9)	2 (0.3)	2 (66.7)	0 (0)	10 (100)	2 (100)	9 (69.2)	2 (100)	40 (95.2)	19 (82.6)
Trans woman/female		0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		0 (0)	0 (0)
Trans man/male	66 (10.6)	0 (0)	35 (14.3)	4 (12.9)	0 (0)	5 (3.7)	12 (19.1)	0 (0)	0 (0)	3 (75.0)	0 (0)	0 (0)	2 (15.4)	0 (0)	2 (4.8)	3 (13.0)
Gender queer/non-conforming	16 (69.6)	0 (0)	6 (2.5)	0 (0)	0 (0)	6 (0.7)	0 (0)	1 (0.2)	1 (33.3)	1 (25.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4.3)
Other	1 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7.7)	0 (0)	0 (0)	0 (0)
Race and ethnicity																
White/Caucasian	352 (60.7)	1 (100)	155 (63.5)	18 (58.0)	2 (66.7)	69 (51.1)	38 (60.3)	0 (0)	1 (33.3)	4 (100)	7 (70.0)	1 (50.0)	6 (46.1)	1 (50.0)	29 (69.0)	19 (82.6)
Black/African American	90 (15.5)	0 (0)	38 (15.6)	4 (12.9)	0 (0)	28 (10.7)	7 (11.1)	3 (100)	1 (33.3)	0 (0)	0 (0)	1 (50.0)	4 (30.8)	0 (0)	4 (9.5)	0 (0)
Asian/Pacific Islander	20 (3.4)	0 (0)	7 (2.8)	0 (0)	0 (0)	5 (3.7)	6 (9.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4.8)	0 (0)
Middle Eastern	13 (2.2)	0 (0)	3 (1.2)	2 (6.4)	0 (0)	4 (2.9)	2 (3.2)	0 (0)	0 (0)	0 (0)	2 (20.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hispanic or Latinx	45 (7.8)	0 (0)	13 (5.3)	3 (9.7)	1 (33.)	17 (12.6)	7 (11.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7.7)	0 (0)	1 (2.4)	2 (8.7)
Native or American Indian	8 (1.4)	0 (0)	3 (1.2)	1 (3.2)	0 (0)	1 (0.7)	1 (1.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (15.4)	0 (0)	0 (0)
Biracial	49 (8.4)	0 (0)	24 (9.8)	2 (6.4)	0 (0)	11 (8.1)	2 (3.2)	0 (0)	1 (33.3)	0 (0)	1 (10.0)	0 (0)	0 (0)	0 (0)	6 (14.3)	2 (8.7)
Multiracial (≥3)	3 (0.5)	0 (0)	1 (0.4)	1 (3.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.0)	0 (0)	0 (0)
Age (years)																
15-19	120 (20.7)	0 (0)	43 (17.6)	6 (19.4)	1 (33.3)	29 (21.5)	23 (36.5)	2 (66.7)	0 (0)	3 (75.0)	0 (0)	1 (50.0)	3 (23.1)	0 (0)	4 (9.5)	7 (30.4)
20-24	284 (48.9)	0 (0)	117 (47.9)	18 (58.1)	2 (66.7)	68 (50.4)	28 (44.4)	1 (33.3)	2 (66.7)	1 (25.0)	3 (30.0)	1 (50.0)	6 (46.2)	1 (50.0)	20 (47.6)	15 (65.2)
25-29	176 (30.3)	1 (100)	84 (34.4)	7 (22.6)	0 (0)	38 (28.1)	12 (19.0)	0 (0)	1 (33.3)	0 (0)	7 (70.0)	0 (0)	4 (30.8)	1 (50.0)	18 (42.8)	1 (4.3)
Substance use																
Illicit substances with alcohol and/or marijuana (polysubstance use)	231 (39.8)	1 (100)	96 (39.3)	20 (32.3)	2 (66.7)	50 (37.0)	19 (30.1)	1 (33.3)	2 (66.7)	2 (50.0)	6 (60.0)	1 (50.0)	9 (69.2)	2 (100)	20 (47.6)	9 (39.1)

Characteristic	Total eligible sample, n (%)	Recruitment source[a], n (%)														
		A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
Sample size	580	1	244	31	3	135	63	3	3	4	10	2	13	2	42	23
Illicit substances only	15 (2.6)	0 (0)	9 (3.7)	0 (0)	0 (0)	2 (1.5)	4 (6.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Alcohol and marijuana only	166 (28.6)	0 (0)	77 (31.6)	13 (41.9)	1 (33.3)	31 (22.9)	19 (30.1)	0 (0)	1 (33.3)	0 (0)	2 (20.0)	0 (0)	3 (23.1)	0 (0)	11 (26.1)	8 (34.7)
Alcohol only	44 (7.6)	0 (0)	14 (5.7)	3 (9.7)	0 (0)	15 (11.1)	6 (9.5)	0 (0)	0 (0)	1 (25.0)	1 (10.0)	0 (0)	0 (0)	0 (0)	3 (7.1)	1 (4.3)
Marijuana only	124 (21.4)	0 (0)	48 (19.7)	5 (2.0)	0 (0)	37 (27.4)	15 (23.8)	2 (66.7)	0 (0)	1 (25.0)	1 (10.0)	1 (50.0)	1 (7.7)	0 (0)	0 (0)	5 (21.7)

[a]A: BBRT; B: Facebook; C: Friend; D: Google Ad; E: Grindr; F: Instagram; G: Jack'd; H: Other; I: Reddit; J: Scruff; K: Snapchat; L: Tumblr; M: Twitter; N: University; O: Venue.

The screened eligible participant sample (n=580) was composed mostly of those who self-identified as male (475/580, 81.9%), followed by transgender men (66/580, 11.4%), and transgender women (20/580, 3.4%). Most identified as White/Caucasian (382/580, 65.8%), followed by Black/African American (90/580, 15.5%) and biracial (49/580, 8.4%). The largest proportion of participants who screened eligible were in the age range of 20-24 years (314/580, 54.1%). Facebook offered the largest volume of transgender women (16/244, 6.6% of those eligible on Facebook), where Grindr (3/135, 2.2%) and Tumblr (1/13, 8%) were the only other sources to recruit transgender women. Again, Facebook recruited the highest volume of transgender men (35/244, 14.3%), but friend referral (4/31, 13%), Grindr (5/135, 3.7%), Instagram (12/63, 19%), Reddit (3/4, 75%), Tumblr (2/13, 15%), and the university research portal (2/42, 5%) also recruited transgender men.

Of those recruited on Facebook, 155 (155/244, 63.5%) were White, and 38 (38/244, 15.6%) were Black/African American, compared with Grindr, where 69 (69/135, 51.1%) were White and 28 (28/135, 20.7%) were Black/African American, and Instagram, where 38 (38/63, 60.3%) were White and 7 (7/63, 11%) were Black/African American. Reddit recruited 100% (4/4) White participants, and the university research portal primarily recruited White participants (29/42, 69%). Reddit and Jack'd recruited the highest percentage of those aged 15-19 years (3/4, 75%; 2/3, 67%, respectively), although the volume was very low.

Of the 580 eligible participants, polysubstance use (eg, stimulants, hallucinogens, opioids, sedatives, amyl-nitrite, or club drugs) with alcohol or cannabis was the most commonly self-reported substance use behavior (231/580, 39.8%), followed by alcohol and cannabis use only (166/580, 28.6%) and cannabis use only (124/580, 21.4%). This pattern was relatively consistent across participants from all recruitment sources. Facebook and Grindr offered the largest proportions of polysubstance and alcohol users. The highest percentages of those reporting alcohol use only were on Instagram (15/63, 10%), via friend referral (3/31, 10%), and on Reddit (1/4, 25%, although this was only 1 participant), showing most participants were using more than alcohol. The use of cannabis only was most reported by those recruited through Jack'd (2/3, 67%), Reddit (1/4, 25%), Grindr (37/135, 27.4%), and venue-based sampling (5/23, 22%), although this only represents 7.8% (45/580) of the recruited participants.

Recruiting this hardly reached population was costly for the study, as it cost US $281.14 per participant to enroll in the study, and over US $61,000 of our budget to recruit (Table 3). Snapchat, Jack'd, and venue-based recruitment were the most expensive per enrolled participant, costing 26.4% ($16,131/$61,006.94) of the total recruitment cost and only enrolled 8 participants.

Table 3. Cost of participant recruitment by recruitment source.

Recruitment source	Total cose (US $)	Eligible participants		Enrolled participants	
		Number of participants	Cost per participant (US $)	Number of participants	Cost per participant (US $)
BBRT	0	1	0	1	0
Facebook and Instagram	16,904.58	307	55.06	109	155.09
Friend	0	31	0	12	0
Google Ad	226.70	3	75.56	1	226.70
Grindr	27,085.55	135	200.63	54	501.58
Jack'd	2000.00	3	666.67	1	2000.00
Other	0	3	0	1	0
Reddit	159.11	4	39.77	3	53.04
Scruff	500.00	10	50.00	3	166.67
Snapchat	5330.00	2	2665.00	1	5330.00
Tumblr	0	13	0	5	0
Twitter	0	2	0	1	0
University health research	0	42	0	20	0
Venue	8801.00	23	382.66	6	1466.83
Total	61,006.94	580	105.18	217	281.14

Discussion

We learned several lessons from recruiting and enrolling young, substance-using, sexual and gender minority AYAs into a large, randomized control trial in southeastern Michigan. Online advertising across a variety of platforms led to more success in recruiting a large volume of diverse, young, substance-using, sexual and gender minority individuals than more traditional, in-person, venue-based recruitment. Previous research showed that venue-based recruitment can be successful [14,37,38], although many components factor into the success. Ott et al [39] explained that recruiting through local AIDS service organizations and testing centers may be a successful route for recruiting MSM engaging in risky sexual behaviors, although not all who are engaging in risky sexual behaviors will be engaged at AIDS service organizations. Although previous research has found engaging with AIDS service organizations to be a successful form of recruiting hardly reached populations, we found that engaging with local AIDS service organizations, community centers, shelters, youth groups, and churches did not offer any participants into our sample. Further research is warranted to explore the factors that lead to the very different levels of research engagement among young, substance-using, sexual and gender minority communities approached in virtual and physical spaces. It is possible that stigma and fear of being identified as substance-using may be a deterrent for in-person enrollment, especially if they are required to report their substance use or sexual behavior face to face to an in-person recruiter, compared with the anonymity that is offered online [6]. Additionally, individuals attending these venues, which included AIDS service organizations, shelters, youth groups, churches, bars, clubs, and community centers, could have had

other purposes for attending, where screening for research was not a priority.

Facebook, Grindr, and Instagram yielded the largest number of eligible participants for the study from paid advertisements, while unpaid social media and dating applications yielded smaller enrollment numbers. The health research recruitment website, financially supported by the university, had a high recruitment rate, perhaps as people who received notifications from the portal had already indicated an interest in research participation and felt the project to be more legitimate if coming from a university-based email. Venue-based recruitment, however, yielded low numbers of participants recruited into the study (23/580, 3.9%), despite significant personnel and financial resources attributed to in-person recruitment. The enrollment rates for venue-based recruitment were consistently lower compared with paid social media advertising. Similar racial distributions were identified among online recruitment methods, but most participants who were recruited from venue-based sampling were White men, demonstrating that social media was more successful in terms of participant volume and racial diversity.

It was challenging to rapidly build relationships with venues, and we were denied from recruiting in some locations. Hiring and retaining Community Outreach Specialists proved to be more difficult than expected, with scheduling and driving complications being the most common issues. The distance for some outreach events, bars, and clubs extended up to 60 miles one way, and shifts were often in the late evening or night hours when venues were busiest. Rental cars and reimbursement for travel were expensive and time-consuming, which posed difficulties for active venue-based recruitment and maintaining Community Outreach Specialists throughout the recruitment

time frame. We did not record data on recruiters' perceptions of the barriers to venue-based recruitment.

There are several limitations in this paper; first, this analysis may not be generalizable to all young, substance-using, sexual and gender minority communities, as this sample included those based in southeastern Michigan only, and the analysis should be considered as a case study of recruitment for a specific trial in a specific context. Second, these responses may be subject to recall error, as all answers to the pretest survey were self-reported, and participants in the pretest survey may have suffered from desirability bias. Third, the length of the eligibility screener (~10 minutes to complete) was a limitation of venue-based recruitment, as potentially eligible participants often did not want to spend time completing the survey. Fourth, when tailoring advertisements, we focused imagery and keywords for those identifying as a man or male, which may have missed a large group of transgender and gender-diverse individuals. In the future, programs should offer a shorter eligibility screener to be taken on-site or a way to sign up to be contacted to take an eligibility screener. Additionally, tailoring verbiage to be more inclusive of gender-diverse and transgender communities is warranted. This analysis offers future researchers' insight into recruiting into HIV- and STI-focused programs in southeastern Michigan.

Ultimately, web-based advertisements allow for potential participants to screen for eligibility at their convenience and are more convenient for programs looking to recruit young, substance-using, sexual and gender minority communities in southeastern Michigan. Generating a substantial sample of young, substance-using, sexual and gender minority communities in southeastern Michigan requires advertisements to be placed on multiple platforms, where resources are concentrated on web-based platforms such as Facebook, Instagram, and Grindr. Additionally, recruiting online offers a more cost-effective way to reach large numbers of people [22,23,29], including those who are hardly reached in southeastern Michigan. However, not everyone has access to a smartphone, computer, or internet, and future research efforts should consider this when designing recruitment efforts and screening surveys. Although online-based recruitment has shown to be cost-effective for some programs, we found it to be quite expensive. For example, recruiting from Snapchat cost over US $5000 per enrolled participant. Future programs aiming to recruit participants in southeastern Michigan should focus on paid, online advertisements, specifically Facebook, Instagram, and Grindr, rather than venue-based sampling to recruit hardly reached populations and young, substance-using sexual and gender minority communities.

Conflicts of Interest

None declared.

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Abbreviations

AYAs: adolescents and young adults
CAPTCHA: Completely Automated Public Turing test to tell Computers and Humans Apart
GSA: Gay Straight Alliance
LGBTQ+: lesbian, gay, bisexual, transgender, queer, plus
MSM: men who have sex with men
STI: sexually transmitted infection
YMSM: young men who have sex with men

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Original Paper

Acceptance, Use, and Barriers of Telemedicine in Transgender Health Care in Times of SARS-CoV-2: Nationwide Cross-sectional Survey

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Abstract

Background: The global incidence in the treatment of transgender people is increasing. During the COVID-19 pandemic, many consultations had to be cancelled, postponed, or converted to a virtual format. Telemedicine in the management of transgender health care could support physicians.

Objective: The aim of this study was to analyze the acceptance, use, and barriers of telemedicine in transgender health care in times of SARS-CoV-2 in Germany.

Methods: This prospective cross-sectional study was based on a survey of gynecological endocrinologists and transgender patients undergoing gender-affirming hormone treatment in Germany during the COVID-19 pandemic. Descriptive statistics were calculated, and regression analyses were performed to show correlations.

Results: We analyzed responses of 269 transgender patients and 202 gynecological endocrinologists treating transgender patients. Most believed that telemedicine was useful. Physicians and patients rated their knowledge of telemedicine as unsatisfactory. The majority of respondents said they did not currently use telemedicine, although they would like to do so. Patients and physicians reported that their attitudes toward telemedicine had changed positively and that their use of telemedicine had increased due to COVID-19. The majority in both groups agreed on the implementation of virtual visits in the context of stable disease conditions. In the treatment phases, 74.3% (150/202) of the physicians said they would use telemedicine during follow-ups. Half of the physicians said they would choose tele-counseling as a specific approach to improving care (128/202, 63.4%). Obstacles to the introduction of telemedicine among physicians included the purchase of technical equipment (132/202, 65.3%), administration (124/202, 61.4%), and poor reimbursement (106/202, 52.5%).

Conclusions: Telemedicine in transgender health care found limited use but high acceptance among doctors and patients alike. The absence of a structured framework is an obstacle for effective implementation. Training courses should be introduced to improve the limited knowledge of physicians in the use of telemedicine. More research in tele-endogynecology is needed. Future studies should include large-scale randomized controlled trials, economic analyses, and the exploration of user preferences.

KEYWORDS

telemedicine; health services research; COVID-19; transgender health care; acceptance; usage; barrier; telehealth; gender; identity; transgender; cross-sectional; survey; Germany; framework; implementation

Introduction

The global incidence in the treatment of transgender people is increasing. Approximately 15,000 to 25,000 persons in Germany are affected [1]. According to the World Health Organization, transgenderism refers to people whose perceived gender and the physical gender they were assigned at birth do not coincide [2]. As a socially and medically vulnerable group, transgender people face numerous inequalities in terms of health and mental health problems as compared to cisgender people [3]. The COVID-19 pandemic has exacerbated international health problems and is creating devastating mental health strains on a global scale for many populations. Transgender people today face problems related to social, physical, and mental well-being, as well as difficulties in accessing health care. Even before the COVID-19 pandemic, there were many barriers to accessing health care for transgender people, such as a shortage of skilled health professionals, resulting in very few transgender people receiving gender-specific surgery and hormone interventions, especially in low- and middle-income countries [4]. As a fringe group, inequalities faced by transgender people in politics and society, such as legislation based on binary gender norms, could increase the risk of disease and mortality during the COVID-19 pandemic [5]. To prevent overloading the health care system with COVID-19 cases, planned operations as well as examinations and therapies for non–life-threatening conditions have been postponed [5].

Due to pandemic containment measures, many patient appointments had to be cancelled or were switched to telephone or video counseling. However, the clinical care of patients had to continue. This made it even more difficult for transgender people to access hormone interventions and sex-affirming operations [6]. Because of the difficulties caused by COVID-19, it is likely that transgender people also face difficult situations in terms of their mental health. Recent studies found that difficulties in accessing hormones were associated with high levels of anxiety and depression, as the availability of future therapies was uncertain and transgender people still wanted treatment during the COVID-19 pandemic [7,8]. In particular, transgender patients are dependent on regular medical consultations. Follow-up checks are frequently carried out to monitor ongoing endocrine hormone therapy. Endocrine hormone therapy is essential for the physical transition; with its help, sufferers could have a normal life. New concepts and ideas have recently been introduced. The topic of digitalization was driven forward by the COVID-19 pandemic. The use of digital applications in everyday clinical practice is well established among cisgender people. While some medical disciplines have made more progress in the implementation and application of digital media, other disciplines remain largely untouched [9]. Digital media and applications can positively influence patient care and open up new treatment pathways. In general, many physicians believe that telemedicine has great potential for managing patient care. Digitalization affects 90% of the health care system and has already brought many changes for patients and doctors, which have decisively influenced the patient-doctor relationship [10]. Patients are willing to use mobile health technologies to improve their disease status and monitor symptoms and disease activity. The use of digital health applications has also increased in recent years [11]. Data from these applications have been obtained from patients and health care professionals. As with the general population, the internet and social media have been useful in reducing isolation during lockdowns and for this marginalized group (ie, transgender persons); they have also been important in helping this group maintain contact with health facilities through telemedicine services [12]. The perspective of transgender people and physicians is crucial for the successful development and implementation of telemedicine concepts for the management of transgender patient care [13]. The central question is whether and how adequate treatment can be delivered digitally in the future for this special group. This study explored the acceptance, use, and barriers of telemedicine in times of SARS-CoV-2 in transgender health care in Germany, as well as how the medical and mental health care of this special group of patients can be improved by the use of telemedicine applications. Changes in these aspects were observed, particularly during the COVID-19 pandemic.

Methods

Surveys were conducted among gynecological endocrinologists (specialists and trainees) who provide gender-specific hormone treatments to transgender patients. In addition, we evaluated the perspectives of transgender patients undergoing gender-affirming hormone therapy (GAHT) regarding the use of digital health applications in the form of telemedicine in the times of COVID-19 during their GAHT. The responsible ethics committee of the University of Jena was informed of the study and did not object to it (registration No. 2019-1456-Bef). Web-based surveys were conducted by members of the Youth Working Group Forum of the German Society for Gynecology and Obstetrics (DGGG). In order to investigate the identified areas of interest, a panel of experts administered the study questionnaire during two separate online meetings based on individual literature searches, similar to the standard operating procedures drafted by the EULAR (European League Against Rheumatism) recommendation working group [14]. Four areas were investigated: (1) epidemiological data of respondents, (2) basic use of digital health applications, (3) knowledge and use of telemedicine, and (4) barriers and benefits of tele-endogynecology. The web-based study questionnaires were designed according to published guidelines for questionnaire research [15-17]. The choice of questions for the questionnaires was based on both comparable work and on the quality criteria for online questionnaires [18]. The two web-based surveys were created in SurveyMonkey (Momentive). The surveys were administered from November 1, 2020, to March 30, 2021. The data were collected anonymously. The methodology and results

of the study were reported according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) [19]. Content of the questionnaires was developed based on the published research results on digitalization among patients, a 23-part, self-managed online questionnaire. Members of the Youth Working Group Forum of the DGGG were asked to provide feedback on the format, completeness, clarity, and procedure of the validation process [16]. Both surveys were pilot-tested. The survey for physicians was tested on 10 physicians, and the patient survey was tested on 10 transgender patients; this was done to gauge the need to refine the wording and format and to check whether predefined response options were exhaustive. Minor revisions were made; accordingly, the questionnaires were modified. The surveys consisted of binominal questions, questions in categorical Likert-scale formats (6 levels), and open questions; the surveys were entitled "Telemedicine in the era of COVID-19 in gynecological endocrinology for the treatment of transgender patients."

The main sections were as follows: (1) epidemiological data of respondents, (2) basic use of digital health applications, (3) knowledge and use of telemedicine, and (4) barriers and benefits of tele-endogynecology.

We aimed to shorten the interview duration using the surveys to a maximum of 15 minutes in order to keep the dropout rate as low as possible and to motivate the respondents, as much as possible, to answer all of the questions [20,21]. The physician questionnaire was distributed via email to the physicians. In an information letter, participants were informed that their data would be treated in a strictly confidential and anonymous manner and that they would be able to access the online questionnaire via a QR (Quick Response) code or survey link. All participants gave their consent digitally before the start of the study. To do this, they had to manually participate in the study by clicking the button "I agree to participate in the study." If participants refused to participate in the study, their participation was terminated and was not evaluated. The physician survey was sent digitally to 2287 gynecological endocrinologists (specialists and trainees) in Germany who provide GAHTs to transgender patients. The contact details of potential participants in Germany were provided by the Association of Statutory Health Insurance Physicians [22] and are available to the public. In 2020, a total of 2942 consultations were conducted during the special consultation hours at the University Women's Hospital Jena, and a total of 421 patients undergoing GAHT were treated by four gynecological endocrinologists. GAHTs were administered to female-to-male and male-to-female patients. All of these patients were contacted by postal letter. In an information letter, participants were informed that their data would be treated in a strictly confidential and anonymous manner, and that they would be able to access the online questionnaire via a QR code or survey link.

Exclusion criteria included the following: patients under 18 years of age, patients not currently undergoing GAHT, physicians without the medical designation of gynecological endocrinology, physicians not performing GAHT, and digital refusal to participate in the study.

The results were analyzed using SurveyMonkey and SPSS Statistics for Windows (version 27.0; IBM Corp). Descriptive statistics included quantities, percentages, median scores, and ranges for ordinal variables. The chi-square test was applied for the analyses of influencing parameters. P values of less than .05 were considered significant.

Results

Overview

From November 2020 to March 2021, a cross-sectional, self-administered, web-based survey regarding the acceptance, use, and barriers of telemedicine in times of SARS-CoV-2 in transgender health care in Germany was completed by gynecological endocrinologists and transgender patients in Germany. Of the 2287 physician questionnaires that were sent out, 286 (12.5%) were returned. Of the 286 responses, 84 (29.4%) were excluded from the analysis because fewer than half of the questions were answered. The final response rate for physicians was 8.8% (202/2287). In the period from November 2020 to March 2021, 333 out of 421 (79.1%) transgender patients participated in the study. Of the 333 responses, 64 (19.2%) were excluded from the analysis because fewer than half of the questions were answered. The final response rate for patients was 63.9% (269/421).

Epidemiological Data of Respondents

A total of 202 gynecological endocrinologists and 269 patients completed the surveys. Most patients (n=115, 42.8%) were between 21 and 30 years old. The majority (n=187, 69.5%) of the participating patients had been undergoing GAHT for more than 24 months. Most of the GAHTs among the study participants were being carried out in the context of the transformation from female to male (n=148, 55.0%).

Of the 202 physician respondents, almost one-third were between 41 and 50 years old (n=69, 34.2%) and most of them were specialists in the field of GAHT (n=175, 86.6%). One-quarter of them were still in training to become gynecological endocrinologists (n=51, 25.2%) and around two-fifths were between the ages of 21 and 30 years (n=32, 15.8%). The smallest proportion of these respondents were over 60 years of age (n=25, 12.4%). Almost all of the physicians were women (n=148, 73.3%). A total of 44.1% (n=89) of the physicians worked in a private practice, 32.2% (n=65) were clinicians in a university hospital, and about one-quarter worked in a nonuniversity hospital (n=48, 23.8%). Details of the participants are given in Multimedia Appendix 1.

Basic Use of Digital Health Applications

Out of 269 patients, 82.5% (n=222) reported using apps several times a day on a smartphone, 9.7% (n=26) used apps once daily, and 6.2% (n=17) used apps once weekly. Only 1.5% (n=4) of the patients stated that they never used apps. A total of 91.1% (n=245) of the patients were able to use digital health applications. In addition, 79.9% (n=215) said that the use of digital health applications can have a positive impact on their disease treatment, while 20.1% (n=54) disagreed. The higher the age of the patients, the lower their overall app usage ($P<.001$) and the lower their confidence in using apps ($P<.001$),

adjusted for gender and time of treatment. All physicians were able to use digital health applications. A total of 66.8% (n=135) of the gynecological endocrinologists described the use of digital health applications for managing a patient's disease as useful, while only 3.0% (n=6) disagreed. No significant difference in gender, age, degree of training, and workplace was noted. Due to the COVID-19 pandemic, the attitude toward digital health applications changed positively in 54.3% of patients (n=146) and 40.1% of physicians (n=81). A total of 88.8% of the patients (n=239) and 64.4% of the gynecological endocrinologists (n=130) reported using digital health applications more regularly (Multimedia Appendix 2).

At the time of the survey, patients were most likely to use video consultations (n=214, 79.6%), informative digital health applications (n=210, 78.1%), and symptom checkers (n=115, 42.8%). Therapy-based digital health applications and self-drawn blood samples with digital access to the results showed different levels of acceptance: 58.7% of patients (n=158) said they had no interest and 41.3% (n=111) could imagine a future application of these techniques, respectively. Physicians were most likely to use therapy-based digital health applications (n=160, 79.2%), digital diaries (n=134, 66.3%), and video consultations (n=132, 65.3%). Self-drawn blood samples with digital access to the results showed different levels of acceptance: 57.4% of physicians (n=116) said they had no interest and 42.6% (n=86) could imagine a future application of this technique. The majority of gynecological endocrinologists rejected the use of symptom checkers (n=61, 30.2%). Details of the participants are given in Figure 1. Patients were most likely to say that video consultations for aftercare (n=200, 74.3%) and emergency appointments (n=148, 55.0%) were possible. A total of 63.9% (n=172) of patients said that time-synchronous digital consultation could complement physical appointments. In addition, 75.5% (n=203) of patients and 64.4% (n=130) of gynecological endocrinologists indicated that they should cancel an appointment on-site if the patient's disease is stable and if he or she can indicate his or her well-being using a digital health application (Figure 2).

Figure 1. Details of the participants in the study. Numbers of respondents are reported on the plot bars.
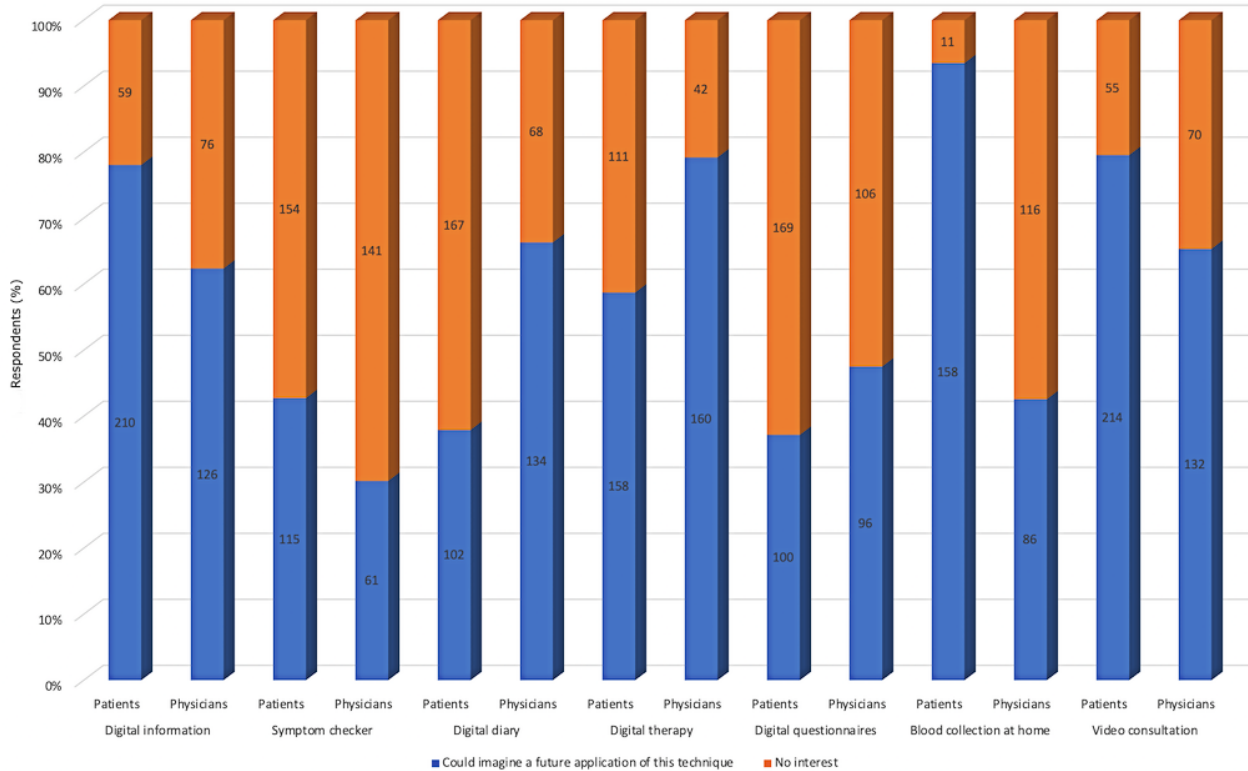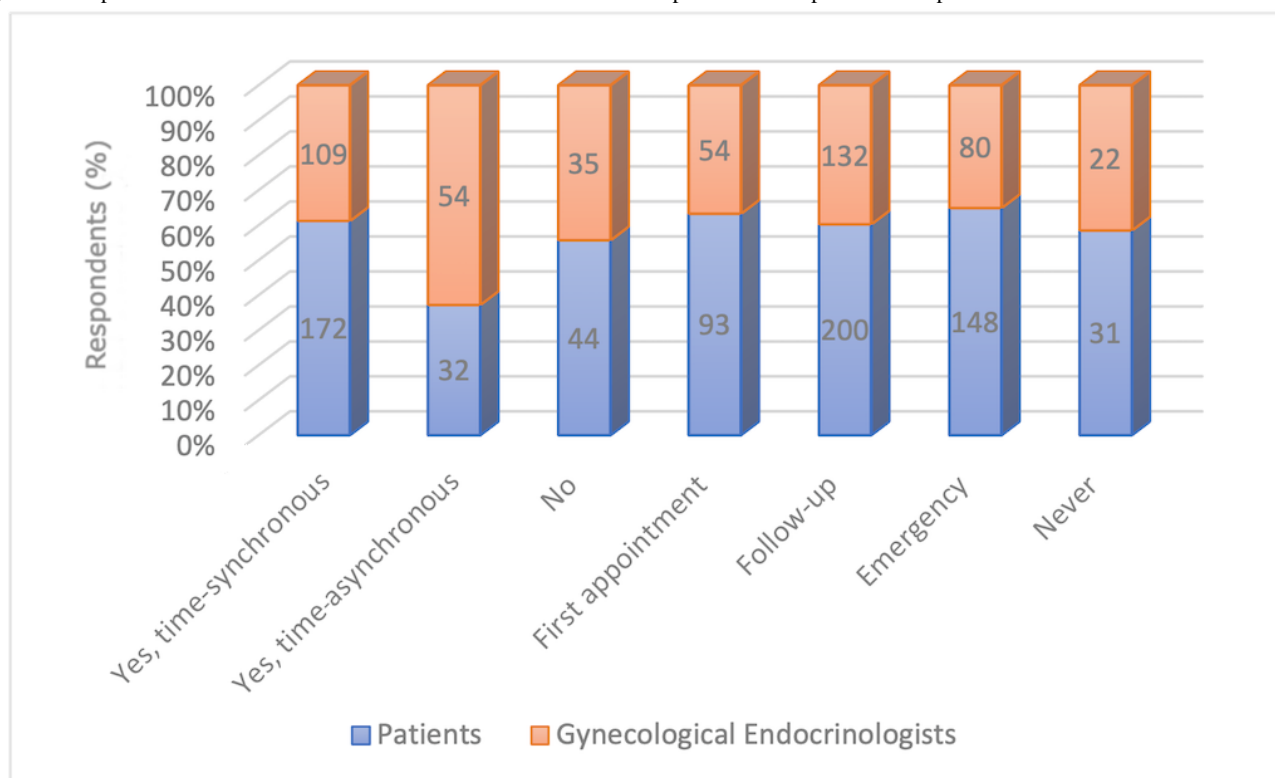
Figure 2. Respondents' attitudes to video consultation hours. Numbers of respondents are reported on the plot bars.

Telemedicine From a Medical Point of View: Knowledge and Use

A total of 71.3% (n=144) of the 202 physicians rated their knowledge of telemedicine as 4 (unsatisfactory), 5 (bad), or 6 (very poor). The minority (n=58, 28.7%) rated their knowledge of telemedicine as 1 (very good), 2 (good), or 3 (satisfactory). At the time of the survey, the majority (n=175, 86.6%) of the physicians did not use telemedicine, but 69.3% (n=140) said they would like to use it. A total of 89.1% (n=180) of the physicians pointed out that they do not use telemedicine due to barriers. According to the respondents, the main obstacles to the introduction of telemedicine were the purchase of technological equipment (n=132, 65.3%), administration (n=124, 61.4%), poor reimbursement (n=106, 52.5%), lack of data security (n=92, 45.5%), less participation by colleagues (n=67, 33.2%), technical comprehension of patients (n=55, 27.2%), and poor internet connection (n=52, 25.7%) (Multimedia Appendix 3).

Tele-endogynecology in Transgender Patient Care Management: Barriers and Benefits

Out of 202 physician respondents, 74.8% (n=151) considered telemedicine to be useful in gynecological endocrinology in transgender patient care management. When asked which interactions should occur within telemedicine, 82.2% (n=166) answered doctor-doctor interactions, 66.8% (n=135) answered doctor-patient interactions, and 35.6% (n=72) answered physician-assistant interactions (multiple answers were possible). The preferred therapeutic phases for the use of telemedicine in the treatment of transgender patients were the follow-up phase (n=150, 74.3%), first contact (n=68, 33.7%), and preventive examinations (n=39, 19.3%). Participants were

asked to provide specific digital tools that could support endocrinological care for transgender patients undergoing GAHT. The most frequently selected topics were teleconsulting (n=128, 63.4%), video consultations (n=90, 44.6%), and tele-diagnostics (n=75, 37.1%). This was followed by online appointments (n=64, 31.7%), e-learning (n=45, 22.3%), patient apps (n=37, 18.3%), digital screening (n=35, 17.3%), portable devices (n=22, 10.9%), and other instruments (n=9, 4.5%) (Multimedia Appendix 4).

Discussion

Principal Findings

This study was the largest nationwide survey on the use of telemedicine in the field of gynecological endocrinology for the promotion and implementation of tele-endogynecology for the treatment of transgender patients in Germany. For this purpose, transgender patients undergoing GAHT and gynecological endocrinologists performing GAHT were interviewed. The two surveys evaluated the perspectives of patients and gynecological endocrinologists on the acceptance of, attitudes toward, and possible barriers to the use of telemedicine applications during GAHT and the impact of the COVID-19 pandemic on their use. The survey contained the following main topics: (1) epidemiological data of respondents, (2) basic use of digital health applications, (3) knowledge and use of telemedicine, and (4) barriers and benefits of tele-endogynecology.

In line with previous surveys [23,24], the respondents reported that they regularly used mobile apps on their smartphones and believed that they would be able to follow digital health advice. Other general studies on the use of digital media showed that

with age, interest in digital health applications decreases among patients and physicians [25,26]. The patients in this study were very young compared to other studies. The age of the interviewed physicians compared to that of the patients was twice as high and ranged from 41 to 50 years. Comparing the user behavior of the young patient group with the group of physicians in this study, there was no significant difference in the basic attitude toward the acceptance and use of telemedicine applications. In this survey, transgender patients and gynecological endocrinologists reported a general positive attitude toward telemedicine and at least regular use of telemedicine applications. This may be the reason that transgender patients and gynecological endocrinologists reported a general positive attitude toward telemedicine. Both believed that the use of telemedicine in the form of digital health applications (eg, medical apps, video consultations, and online pharmacies) can improve disease management. This study's findings about the fundamental benefits of using telemedicine for treatment in disease management are in line with previous work. For example, Enam et al found that the use of telemedicine can be evidence based if appropriate media are used; the data from Enam et al are from the time before the COVID-19 pandemic [27].

Respondents to our study indicated that the COVID-19 pandemic had a positive impact on attitudes toward telemedicine applications in the form of digital health applications. Not only was attitude toward telemedicine applications influenced by the COVID-19 pandemic, but user behavior was as well. More than three-quarters of the respondents said that the COVID-19 pandemic had increased their personal use of digital health applications. Transgender patients reported a higher use of these applications than physicians. As with the general population, during the lockdown, the internet and social media were useful in reducing isolation among transgender people and were also relevant for keeping in touch with associations and health care facilities with the support of telemedicine services [28]. Physicians' use behavior had increased as a result of the COVID-19 pandemic; they were using digital health applications more often than before the pandemic. This seems to be a general development in the medical field, as shown by other studies [29]. The general increase in interest and acceptance of telemedicine among patients and physicians may provide the basis for longer-term use and increasing development of the use of telemedicine in the treatment of diseases, regardless of the disease or group of persons. This can be underlined by the findings of this study, which also showed that the patient population of this study is a special group of patients.

In their study, Winter et al [30] described the difficult access that transgender patients have to general health care facilities, the associated hurdles and barriers, and the mental health and social consequences they faced compared to the general population before the COVID-19 pandemic. The COVID-19 pandemic has particularly exacerbated the situation for this particular societal group. In Italy and a number of other countries, access to health care has been difficult or impossible for transgender people. This has obstructed the beginning or continuation of hormonal and psychic treatment among this group. In addition, planned gender-equalizing operations have

been postponed. These obstacles have led to several problems for transgender patients. There has been an additional mental strain, and the positive effects of medical and surgical treatments on their well-being has been absent. Stressors have increasingly been directly and indirectly triggered, such as discrimination at work, social inequalities, and a deterioration in health care for this particular patient group [31]. This was investigated in a study by van der Miesen et al, in which they concluded that transgender patients are disadvantaged and often indeterminate; they determined that some organizational aspects should also be considered, since inequalities and marginalization of transgender subjects potentially increase the risk of morbidity and mortality [7]. This is where telemedicine can be used to limit such consequences and problems.

A study by Gava et al investigated endocrinological care of transgender patients during the COVID-19 pandemic [31]. They investigated the use of telemedicine in transgender patients as part of hormone treatment. Between May and June 2020, they conducted an anonymous web-based survey of transgender people in Italy. Among the 108 respondents, who had a mean age of 34.3 (SD 11.7) years, 73.1% were transgender men and 26.9% were transgender women. A total of 88.9% of respondents were undergoing GAHT. A total of 1 in 4 patients experienced a moderate to severe impact from the pandemic event. The availability of tele-endocrinological visits was associated with improved mental health scores. The survey suggested that there was a positive effect from telemedicine, as the availability of tele-endocrinological consultations may have relieved the distress caused by the COVID-19 pandemic by offering the opportunity to avoid halting GAHT. The age of the transgender patients and the proportion of female-to-male transgender patients in that study were almost identical to our study. We also investigated the use of telemedicine in transgender patients receiving hormone therapy in times of COVID-19. In the study by Gava et al, only transgender patients were interviewed, while the statements and attitudes of medical staff were completely lacking. Other published studies on transgender health and telemedicine dealt exclusively with the attitudes of the affected people themselves [12].

There is a complete lack of knowledge about the attitudes toward, and opinions on, telemedicine by the medical staff who would administer the therapy and, thus, be responsible for its administration. It is precisely these attitudes toward acceptance and application and barriers to telemedicine in the treatment of transgender people that are important, as they can fuel the basis for enabling change and progress of telemedicine when the individual backgrounds are known by the doctors who perform the treatment. With our study, we were able to identify initial insights into the relevance, application, and potential barriers to the use of telemedicine by physicians treating transgender people and performing medical treatments in the form of hormone treatments. All the physicians in our studies reported being able to use telemedicine applications, regardless of age and gender, which is the first prerequisite for the implementation of these novel applications. The interviewed physicians in this study came from the field of endocrinological gynecology, and our survey reflected only their opinions. The survey was aimed at gynecological endocrinologists from all over Germany,

especially doctors from Thuringia and Bavaria, who participated in the recruitment strategy. A self-selection bias and a nonresponse bias in this study were possible because the survey was probably answered predominantly by doctors and patients interested in telemedicine. The survey was conducted in the time of COVID-19, and prepandemic data are pending in this area, so further research on the development of the acceptance of telemedicine applications in general and in relation to tele-endogynecology is urgently needed. An online survey was deliberately used to increase the response rate, since respondents could complete it quickly, regardless of place and time, and to achieve a reduced effort for data management. However, it is expected that this online survey will lead to a positive bias toward users of telemedicine. To answer the questionnaire, knowledge of the field of telemedicine was required (eg, preferences for specific tools were requested). Given the limited knowledge of doctors in the field of telemedicine, distortions were likely. In addition, we expect there to be rapid technological developments in the field of telemedicine, so the predefined response categories may not have been exhaustive enough.

Perspectives of Telemedicine in Transgender Health Care Management

COVID-19 has increased the importance of contactless approaches to medical care. Already in 2020, when we conducted the survey, transgender patients and gynecological endocrinologists were willing to use tele-endogynecology. It is assumed that as a result of the pandemic there has been an increase in the willingness to speed up the use of telemedicine as part of social action and new standards in health care [23]. However, the maximum potential of telemedicine has not been fully achieved. Further research on implementation is urgently needed. This includes large-scale randomized controlled studies on the effects and health effects, risks and incidents, and specific interventions. Since our results showed that there was no "one-size-fits-all" solution in the field of telemedicine, the perspectives and preferences of physicians, patients, and others telemedicine users in tele-endogynecology are indispensable. This can create the basis for individual patient- and physician-adapted telemedicine options and triage mechanisms to select patients for digital or analog consultation, as appropriate [32,33]. As doctors reported regarding the barriers to the use of telemedicine, it seems that the structural framework for the effective implementation of tele-endogynecology is not yet in place. The use of telemedicine by the doctors interviewed was hindered by considerable administrative burdens and inadequate reimbursement structures. The biggest obstacle, however, was the limited knowledge of physicians about the use of telemedicine, which is why it is necessary to provide early information on telemedicine in the introduction of low-threshold training courses.

Conclusions

Our study showed that gynecological endocrinologists and transgender patients support the implementation of tele-endogynecology, and two-thirds of those want telemedicine incorporated into their clinical routine. The medical professionals expressed an even greater willingness to use telemedicine. Respondents welcomed a variety of telemedicine approaches. However, at the time of the survey, only a minority of the interviewed physicians used telemedicine in their clinical routine. In addition, most physicians considered their knowledge of telemedicine to be rather poor. The provision of high-quality telemedical care requires additional research, a reduction in existing obstacles, and training for professionals and generalists. Transgender patients are very open to treatment with telemedicine applications. The foundations have been laid, and the concepts in this area have great potential for the future and should be developed.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Details of the participants.
[DOCX File , 14 KB - publichealth_v7i12e30278_app1.docx]

Multimedia Appendix 2
Usage of digital health applications before and after COVID-19 pandemic.
[DOCX File , 15 KB - publichealth_v7i12e30278_app2.docx]

Multimedia Appendix 3
Knowledge and use of telemedicine.
[DOCX File , 15 KB - publichealth_v7i12e30278_app3.docx]

Multimedia Appendix 4

Implementation of telemedicine in transgender health care management.
[DOCX File , 15 KB - publichealth_v7i12e30278_app4.docx]

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Abbreviations

CHERRIES: Checklist for Reporting Results of Internet E-Surveys
DGGG: Deutschen Gesellschaft für Gynäkologie und Geburtshilfe (German Society for Gynecology and Obstetrics)
EULAR: European League Against Rheumatism
GAHT: gender-affirming hormone therapy
QR: Quick Response

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Original Paper

Examining the Impact of Question Construction on Reporting of Sexual Identity: Survey Experiment Among Young Adults

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Abstract

Background: Compared with heterosexuals, sexual minorities in the United States experience a higher incidence of negative physical and mental health outcomes. However, a variety of measurement challenges limit researchers' ability to conduct meaningful survey research to understand these disparities. Despite the prevalence of additional identities, many national health surveys only offer respondents 3 substantive options for reporting their sexual identities (straight/heterosexual, gay or lesbian, and bisexual), which could lead to measurement error via misreporting and item nonresponse.

Objective: This study compared the traditional 3-option approach to measuring sexual identity with an expanded approach that offered respondents 5 additional options.

Methods: An online survey experiment conducted among New Jersey residents between March and June 2021 randomly assigned 1254 young adults (ages 18-21) to answer either the 3-response measure of sexual identity or the expanded item. Response distributions for each measure were compared as were the odds of item nonresponse.

Results: The expanded version of the question appeared to result in more accurate reporting among some subgroups and induced less item nonresponse; 12% (77/642) of respondents in the expanded version selected a response that was not available in the shorter version. Females answering the expanded item were less likely to identify as gay or lesbian (2.1% [10/467] vs 6.6% [30/457]). Females and Non-Hispanic Whites were slightly more likely to skip the shorter version than the longer version (1.1% [5/457 for females and 3/264 for Non-Hispanic Whites] vs 0% [0/467 for females and 0/277 for Non-Hispanic Whites]). About 5% (32/642) of respondents answering the longer item were unsure of their sexual identity (a similar option was not available in the shorter version). Compared with respondents answering the longer version of the question, those answering the shorter version had substantially greater odds of skipping the question altogether (odds ratio 9.57, 95% CI 1.21-75.74; *P*=.03).

Conclusions: Results favor the use of a longer, more detailed approach to measuring sexual identity in epidemiological research. Such a measure will likely allow researchers to produce more accurate estimates of health behaviors and outcomes among sexual minorities.

KEYWORDS

survey measurement; sexual identity; survey wording experiment

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Introduction

Compared with heterosexual individuals, those identifying as sexual minorities in the United States experience a higher incidence of negative physical and mental health outcomes [1-7]. They also report higher levels of risk behaviors including tobacco, alcohol, and drug use [1,2,8-13]. Given that sexual minorities bear a disproportionate burden of risk behaviors and poor health outcomes, research to understand and address these health inequities is essential [14]. However, survey measurement challenges limit the ability to conduct meaningful research inclusive of sexual minorities. Indeed, a variety of approaches to operationalizing sexual orientation exist across national surveys, complicating estimates of risk behaviors and health outcomes among this population [15,16]. In fact, the National Academies of Sciences, Engineering, and Medicine commissioned a panel to review current measures and methodological issues related to measuring sexual orientation, in addition to sex and gender identity [17].

In this short paper, we contribute to the literature on measuring sexual identity by presenting the results of a randomized experiment comparing 2 measurement approaches. It is well established in the literature on survey methods that question design can affect respondents' motivation to respond accurately, or even at all, to particular items [18]. If a question does not motivate respondents to answer accurately, or it encourages them to skip the item altogether (eg, item nonresponse), this can lead to measurement error [18]. One common approach to measure sexual identity asks participants to choose from 1 of 3 responses: heterosexual/straight, gay or lesbian, and bisexual. This 3-response approach, or a close variation of it, is the one taken by several national surveys, including the National Health Interview Survey [19], Behavioral Risk Factor Surveillance System [20], and the National Survey on Drug Use and Health [21]. Despite the popularity of this approach, these 3 responses do not constitute an exhaustive list of sexual identities that one may claim [22]. In failing to offer a broader range of options, surveys employing the 3-response approach are susceptible to measurement error, either because respondents report an inaccurate sexual identity or because they skip the item altogether if they believe it does not represent their actual identities.

Methods

To explore the impact of question construction on measurement of sexual identity, we randomly assigned a diverse group of 1254 young adults, aged 18-21 years, to answer either the traditional, 3-response version of the sexual identity item (n=612) or an expanded version offering more response options (n=642). Overall sample demographics and demographics by experimental condition are presented in Multimedia Appendix 1. The traditional, 3-category question read, "Do you consider yourself to be:" and offered 3 response options: "Heterosexual or straight," "Gay or lesbian," and "Bisexual." The longer version read, "Below is a list of terms that people often use to describe their sexuality or sexual orientation. Please select the term that best applies to you." It offered the responses, "Straight/Heterosexual," "Gay," "Lesbian," "Bisexual," "Queer," "Asexual," "Pansexual," "Questioning/Not sure," and "Another sexual orientation not listed above (please specify)." The experiment was embedded in the first wave survey of the Policy and Communication Evaluation: New Jersey (PACE NJ) study. The survey was fielded online between March 24 and June 21, 2021. In addition to the age requirement, participants in the PACE NJ study were required to report living in New Jersey for at least four months out of the year.

Results

The expanded version of the question offers a more complete picture of respondents' sexual identities (Tables 1 and 2). In fact, 12% (77/642) of respondents answering the longer question selected a response option that was not offered in the shorter, more commonly used version of the question. Cross-tabular results revealed that the proportion of females identifying as gay or lesbian was much lower in the expanded version compared with the shorter version (2.1% [10/467] vs. 6.6% [30/457]), as they presumably opted for terms such as queer (4.1% [19/467]) or pansexual (2.6% [12/467]). Females and Non-Hispanic Whites were slightly more likely to skip the shorter version than the longer version (1.1% [5/457 for females and 3/264 for non-Hispanic Whites] vs. 0% [0/467 for females and 0/277 for Non-Hispanic Whites]). Importantly, 6.6% (31/467) of females, 6.1% (22/359) of non-White respondents, and 5% (32/642) overall reported questioning or being unsure of their sexuality in the expanded version. It could be, then, that some individuals avoided answering the shorter item not only because they felt the choices did not represent their identities, but also because they were unsure of their identities in the first place.

Table 1. Response distributions by sex and race in experimental condition 1.[a]

Sexual identity	Overall (N=612)		Sex				Race			
			Male (n=155)		Female (n=457)		Non-White (n=339)		White, non-Hispanic (n=264)	
	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Condition 1: Do you consider yourself to be:										
Heterosexual or straight	426 (69.6)	66 to 73	125 (80.6)	74 to 87	301 (65.9)	62 to 70	254 (74.9)	70 to 80	165 (62.5)	57 to 68
Gay or lesbian	43 (7.0)	5 to 9	13 (8.4)	4 to 13	30 (6.6)	4 to 9	17 (5.0)	3 to 7	26 (9.8)	6 to 13
Bisexual	134 (21.9)	19 to 25	13 (8.4)	4 to 13	121 (26.5)	22 to 31	63 (18.6)	14 to 23	70 (26.5)	21 to 32
Queer	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Asexual	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Pansexual	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Questioning/not sure	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Other (specify)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Missing	9 (1.5)	0.5 to 2	4 (2.6)	0.1 to 5	5 (1.1)	0.1 to 2	5 (1.5)	0.2 to 3	3 (1.1)	0 to 2

[a]Percentages may not add to 100 due to rounding; race categories do not add to overall totals due to missing data.

[b]N/A: not applicable.

Table 2. Response distributions by sex and race in experimental condition 2.[a]

Sexual identity	Overall (N=642)		Sex				Race			
			Male (n=175)		Female (n=467)		Non-White (n=359)		White, non-Hispanic (n=277)	
	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Condition 2: Below is a list of terms that people often use to describe their sexuality or sexual orientation. Please select the term that best applies to you.										
Heterosexual or straight	423 (65.9)	62 to 70	133 (76.0)	70 to 82	290 (62.1)	58 to 67	250 (69.6)	65 to 74	170 (61.4)	56 to 67
Gay or lesbian	30 (4.7)	3 to 6	20 (11.4)	7 to 16	10 (2.1)	0.8 to 3	10 (2.8)	1 to 5	19 (6.9)	4 to 10
Bisexual	111 (17.3)	14 to 20	15 (8.6)	4 to 13	96 (20.6)	17 to 24	51 (14.2)	11 to 18	59 (21.3)	16 to 26
Queer	20 (3.1)	2 to 4	1 (0.6)	0 to 2	19 (4.1)	2 to 6	9 (2.5)	0.8 to 4	11 (4.0)	2 to 6
Asexual	5 (0.8)	0.1 to 2	1 (0.6)	0 to 2	4 (0.9)	0.04 to 2	3 (0.8)	0 to 2	2 (0.7)	0 to 2
Pansexual	15 (2.3)	1 to 3	3 (1.7)	0 to 4	12 (2.6)	1 to 4	10 (2.8)	1 to 5	5 (1.8)	0.2 to 3
Questioning/not sure	32 (5.0)	3 to 7	1 (0.6)	0 to 2	31 (6.6)	4 to 9	22 (6.1)	4 to 9	9 (3.2)	1 to 5
Other (specify)	5 (0.8)	0.1 to 2	0 (0)	0 to 0	5 (1.1)	0.2 to 2	3 (0.8)	0 to 2	2 (0.7)	0 to 2
Missing	1 (0.2)	0 to 0.5	1 (0.6)	0 to 2	0 (0)	0 to 0	1 (0.3)	0 to 0.9	0 (0)	0 to 0

[a]Percentages may not add to 100 due to rounding; race categories do not add to overall totals due to missing data.

An additional indicator of question performance is participants' willingness to respond to the question they received. As noted above, if some respondents felt that the shorter version of the question did not well represent their actual sexual identities, or if they were unsure of their identities, then we should expect to see a greater propensity toward item nonresponse than in the longer, more complete version of the question. To test this hypothesis, we estimated a logistic regression in which item nonresponse was regressed on a dummy treatment variable. Indeed, compared with respondents answering the longer version of the question, those answering the shorter version had substantially greater odds of skipping the question altogether (odds ratio 9.57, 95% CI 1.21-75.74; P=.03). Additionally, this has important implications for survey design: if survey questions are used as screeners and branch to additional items based on the sexual identity measure, then the magnitude of the impact of item nonresponse will increase.

Discussion

Considered together, the comparison of response distributions (Tables 1 and 2) and the analysis of respondents' willingness to answer the question they received cast doubt on the appropriateness of the shorter, 3-category approach to measuring sexual identity. The longer item presents a descriptively richer picture of respondents' identities and induced significantly lower odds of item nonresponse. Furthermore, if the limited, shorter survey question makes respondents feel excluded, it could result in further stigmatizing or marginalizing individuals with nonnormative sexual identities [23]. Given that sexual minorities are more likely to experience negative health outcomes and report higher levels of some risk behaviors, these findings warrant attention from those aiming to study such outcomes and accurately describe their prevalence among various groups in the United States [1]. This is especially so given that sexual minorities are not a homogenous group in terms of health outcomes [1].

This study has limitations. Given that respondents were randomized between question versions, the internal validity of the study is high. However, this sample consisted only of young adults between the ages of 18 and 21. Further research should explore whether the impact of receiving one question version over another varies by respondent age. Moreover, our experimental respondents all live at least four months of the year in New Jersey. If comfort levels with revealing information about one's sexual identity vary regionally, the sizes of the treatment effects presented here may also vary if this experiment were fielded in other parts of the country or nationally.

To conclude, the evidence presented here favors the use of a longer, more detailed approach to measuring sexual identity in epidemiological research. This measure will likely allow researchers to produce more accurate estimates of health behaviors and outcomes among sexual minorities, given that respondents are less likely to skip the question, compared with the shorter item. Furthermore, accounting for the fluidity of sexual identity in the survey question will help to improve inclusion and representation in survey research among sexual minorities [23].

Conflicts of Interest

None declared.

Multimedia Appendix 1
Sample Demographics.
[DOCX File , 32 KB - publichealth_v7i12e32294_app1.docx]

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Abbreviations

FDA: Food and Drug Administration
NCI: National Cancer Institute
PACE NJ: Policy and Communication Evaluation: New Jersey

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Original Paper

Patterns of SARS-CoV-2 Testing Preferences in a National Cohort in the United States: Latent Class Analysis of a Discrete Choice Experiment

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Abstract

Background: Inadequate screening and diagnostic testing in the United States throughout the first several months of the COVID-19 pandemic led to undetected cases transmitting disease in the community and an underestimation of cases. Though testing supply has increased, maintaining testing uptake remains a public health priority in the efforts to control community transmission considering the availability of vaccinations and threats from variants.

Objective: This study aimed to identify patterns of preferences for SARS-CoV-2 screening and diagnostic testing prior to widespread vaccine availability and uptake.

Methods: We conducted a discrete choice experiment (DCE) among participants in the national, prospective CHASING COVID (Communities, Households, and SARS-CoV-2 Epidemiology) Cohort Study from July 30 to September 8, 2020. The DCE elicited preferences for SARS-CoV-2 test type, specimen type, testing venue, and result turnaround time. We used latent class multinomial logit to identify distinct patterns of preferences related to testing as measured by attribute-level part-worth utilities and conducted a simulation based on the utility estimates to predict testing uptake if additional testing scenarios were offered.

Results: Of the 5098 invited cohort participants, 4793 (94.0%) completed the DCE. Five distinct patterns of SARS-CoV-2 testing emerged. Noninvasive home testers (n=920, 19.2% of participants) were most influenced by specimen type and favored less invasive specimen collection methods, with saliva being most preferred; this group was the least likely to opt out of testing. Fast-track testers (n=1235, 25.8%) were most influenced by result turnaround time and favored immediate and same-day turnaround time. Among dual testers (n=889, 18.5%), test type was the most important attribute, and preference was given to both antibody and viral tests. Noninvasive dual testers (n=1578, 32.9%) were most strongly influenced by specimen type and test type, preferring saliva and cheek swab specimens and both antibody and viral tests. Among hesitant home testers (n=171, 3.6%), the venue was the most important attribute; notably, this group was the most likely to opt out of testing. In addition to variability in preferences for testing features, heterogeneity was observed in the distribution of certain demographic characteristics (age, race/ethnicity, education, and employment), history of SARS-CoV-2 testing, COVID-19 diagnosis, and concern about the pandemic. Simulation

models predicted that testing uptake would increase from 81.6% (with a status quo scenario of polymerase chain reaction by nasal swab in a provider's office and a turnaround time of several days) to 98.1% by offering additional scenarios using less invasive specimens, both viral and antibody tests from a single specimen, faster turnaround time, and at-home testing.

Conclusions: We identified substantial differences in preferences for SARS-CoV-2 testing and found that offering additional testing options would likely increase testing uptake in line with public health goals. Additional studies may be warranted to understand if preferences for testing have changed since the availability and widespread uptake of vaccines.

Introduction

Screening and diagnostic testing for SARS-CoV-2 infection is a critical tool in the public health response to the COVID-19 pandemic, as early detection allows for the implementation of isolation and quarantine measures to reduce community transmission [1]. Negative tests are often required for work, school, and leisure activities. The importance of testing has been well demonstrated globally, such as in South Korea, where a "test, trace, isolate" strategy was largely credited for rapidly controlling transmission in spring 2020 [2]. Unfortunately, insufficient SARS-CoV-2 testing in the United States throughout the first several months of the pandemic led to both undetected cases transmitting disease in the community and an underestimation of the burden of COVID-19 [3]. Though the SARS-CoV-2 diagnostic testing supply has increased, maintaining testing uptake remains a major US public health priority in the efforts to control community transmission in the current pandemic phase of vaccinations and variants [4-6]. Currently, the US Centers for Disease Control and Prevention recommends diagnostic testing for individuals with symptoms of COVID-19 and unvaccinated individuals in close contact with a confirmed or suspected COVID-19 case; they also recommend screening tests for unvaccinated people, for example, for work, school, or travel [7-9]. Hereafter, we define SARS-CoV-2 testing as including both screening and diagnostic testing.

Individuals' preferences about testing, specifically about the test itself or the service model that delivers the test, are important to consider in determining strategies to increase and maintain the uptake of SARS-CoV-2 testing in the vaccine era. In other contexts, individual preferences about a health-related product or service have been shown to be predictive of adoption of health-related behaviors [10]. Discrete choice experiments (DCEs), which are surveys that elicit stated preferences to identify trade-offs that a person makes with a product or service, have emerged as a tool to understand patient preferences and barriers to health care engagement [11], and are increasingly being used to inform patient-centered health care [12,13]. We previously conducted a DCE to understand SARS-CoV-2 testing preferences and found strong preferences for both viral and antibody testing, less invasive specimen collection, and rapid result turnaround time [14]. However, as observed in DCEs on other topics, patient preferences are often heterogeneous, and

there may be distinct patterns of preferences within a population [15].

If indeed preferences are relevant to SARS-CoV-2 testing uptake and different patterns of preferences exist, these patterns may also be characterized by distinct demographic profiles. Previous work has documented demographic disparities in SARS-CoV-2 testing uptake [16-19]. For example, among individuals receiving care at US Department of Veterans Affairs sites, overall SARS-CoV-2 testing rates within the Veterans Affairs system were lowest among non-Hispanic White individuals, especially among those who were male and those who lived in rural settings; however, testing rates per positive case were lowest among non-Hispanic Black and Hispanic individuals [17]. Patterns of preferences may also differ based on experience with a product or service, as observed with the frequency of past testing in the preferences for HIV self-testing [20]. Concern or perceived risk is another component involved in making decisions about health, and since it is not uniformly distributed, it may also differ by patterns of preferences [21].

We hypothesized that discernable patterns of SARS-CoV-2 testing preferences would emerge and that individuals in these patterns would have distinct demographic profiles, SARS-CoV-2 testing history, and concern about infection. Identifying and characterizing heterogenous testing preferences could facilitate the design and implementation of an array of services and ultimately enhance testing uptake and engagement.

Methods

Recruitment and Study Ethics

The survey design of our DCE has been previously described [14], but here we provide a summary. Participants enrolled in the CHASING COVID (Communities, Households, and SARS-CoV-2 Epidemiology) Cohort Study [22] who completed a routine follow-up assessment from July 30 through September 8, 2020, were invited to complete the DCE via a unique survey link at the end of the follow-up assessment. A US $5 Amazon gift card incentive was offered to participants completing the DCE. All study procedures were approved by the City University of New York (CUNY) Graduate School of Public Health and Health Policy Institutional Review Board.

DCE Design

The DCE was designed and implemented using Lighthouse Studio 9.8.1 (Sawtooth Software). Prior to the main DCE tasks,

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participants who agreed to complete the DCE were presented with a sample task related to ice cream preferences to help demonstrate the method and orient them to the DCE format. Each participant was then presented with 5 choice tasks with illustrations where they were asked to indicate which of 2 different SARS-CoV-2 testing scenarios was preferable or if neither was acceptable, imagining that "...the number of people hospitalized or dying from the coronavirus in your community was increasing" (see Multimedia Appendix 1 for a sample choice task). Specific testing attributes and levels examined are described in Multimedia Appendix 2. These attributes and levels were based on the current options for SARS-CoV-2 testing in the United States at the time of study design, as well as aspirational features hypothesized by the study investigators to be relevant to individual preferences. The combination and order of attribute levels presented to each participant were randomized for a balanced and orthogonal design using Sawtooth's Balanced Overlap method [23,24]. However, we did constrain the combination of certain levels to reflect real-world possibilities. For example, we did not allow the nasopharyngeal (NP) swab specimen type level to be combined with either of the at-home specimen collection venue levels. The survey was tested internally by study team members prior to deployment.

Latent Class Analysis

For the unsegmented analysis reported previously [14], we estimated individual-level part-worth utilities for each attribute level and relative importance for each attribute using a hierarchical Bayesian multinomial logit (MNL) model, which iterates through the upper aggregate level of the hierarchy and the lower individual level of the hierarchy until convergence [25,26]. For this analysis, however, we used a latent class MNL model to identify different segments of respondents based on their response patterns. Latent class MNL estimation first selects random estimates of each segment's utility values, then uses those values to fit each participant's data and estimate the relative probability of each respondent belonging to each class [27]. Next, using probabilities as weights, logit weights are re-estimated for each pattern and log-likelihoods are accumulated across all classes. This process repeats until reaching the convergence limit. We estimated individual-level utilities as the weighted average of the group utilities weighted by each participant's likelihood of belonging to each group, and zero-centered the utilities using effects coding, so that the reference level is the negative sum of the preferences of the other levels within each attribute [28-31]. Compared to aggregate logit, the effect of the independence of irrelevant alternatives assumption is reduced in latent class MNL [28]. We calculated relative importance at the individual level as the range of utilities within an attribute over the sum of the ranges of utilities of all attributes, and then calculated the mean and 95% CI for each segment as the mean ± 1.96 × SE. We calculated the mean of the weighted utilities by segment, and 95% CIs in the same manner as previously described [29,32].

We ran the latent class analysis with 2 to 10 classes, 5 replications per class, and 100 iterations per replication to facilitate convergence. We used the Akaike information criterion, Bayesian information criterion, and log-likelihood to inform best model selection. In addition, we sought a segmentation model that balanced statistical fit with interpretability and reasonably sized groups. We ran the latent class analysis with multiple starting seeds to facilitate finding the globally best-fit solution.

Respondent Quality

To assess respondent quality, we computed DCE exercise completion time statistics and examined straightlining behavior (always picking the left-hand alternative or the right-hand alternative) [33]. We reran the latent class analysis excluding participants with a combination of straightlining behavior, or completion times in the 5th or 10th percentile of all participants, to determine whether these participants affected the final model. All latent class analyses were done using Lighthouse Studio 9.8.1.

Simulation

We then extrapolated the 2-alternative choice task to a multiscenario simulation to estimate preferences for 5 testing approaches, summarized in Table 1, using the individual-level part-worth utility estimates from the latent class MNL analysis and stratifying by the latent class segments. Our simulations included the following:

- Scenarios 1 and 2: "standard testing" scenarios were based on major health departments' testing programs in fall 2020—viral test (NP swab) and a result turnaround time of 48 hours. We included two unique scenarios to cover two variations in venue [34,35]—drive-through testing site and walk-in community testing site. Result turnaround time was based on reports from major health departments (eg, >85% of results within 2 days in California) [35].
- Scenario 3: "less invasive testing" was based on some jurisdictions offering less invasive specimen collection, such as saliva [34]—viral test, saliva specimen, walk-in community testing site, and a result turnaround time of 48 hours.
- Scenario 4: "dual testing" consisted of both viral and antibody testing and would necessitate a finger prick [36]—viral and antibody test, finger prick specimen, walk-in community testing site, and a result turnaround time of 48 hours.
- Scenario 5: "at-home testing" was based on a commercially available at-home testing kit [37]—viral test, shallow nasal swab, home collection, receiving and returning the kit in the mail, and a result turnaround time within 5 days, as additional time would be required for mailing the specimen.

We conducted two sets of simulations to predict testing uptake: (1) the 2 standard testing scenarios, with a "no test" option to capture the proportion of participants in each class who would opt out of testing altogether, given the choices, and (2) the 2 standard test scenarios as well as the less invasive, dual testing, and at-home testing scenarios, including a "no test" option. Predicted uptake for the 3 total options for the first simulation and 6 total options for the second simulation were generated using the Randomized First Choice (RFC) method with utilities from the latent class MNL as inputs [25,38,39]. The RFC approach assumes that participants would choose the testing scenario with the highest total utility summed across attributes

using each participant's own individual estimated utilities, with some perturbation around the utilities to account for test scenario similarities and reduce the independence of an irrelevant alternatives problem. The simulator performs thousands of simulated draws per participant, then computes the proportion of participants who would choose each testing scenario based on its total utility. The simulations were done using Lighthouse Studio 9.8.1.

Table 1. Testing approaches used in the simulations.

	Testing scenario	Test	Specimen type	Venue	Result turnaround time	Included in simulation 1	Included in simulation 2
1.	Standard testing, drive-through	PCR[a]	NP[b] swab	Drive-through community testing site	48 hours	✓[c]	✓
2.	Standard testing, walk-in	PCR	NP swab	Walk-in community testing site	48 hours	✓	✓
3.	Less invasive testing	PCR	Spit sample	Walk-in community testing site	48 hours		✓
4.	Dual testing	PCR and serology	Finger prick	Walk-in community testing site	48 hours		✓
5.	At-home testing	PCR	Shallow nasal swab	Home collection, receiving and returning the kit via mail	Within 5 days		✓
6.	None	N/A	N/A	N/A	N/A	✓	✓

[a]PCR: polymerase chain reaction.

[b]NP: nasopharyngeal.

[c]✓: Check marks indicate whether the testing scenario was included in each simulation.

Additional Measures

Other measures of interest were merged from participants' responses from the CHASING COVID Cohort Study [22] baseline interview (age, gender, race/ethnicity, education, region, urbanicity, comorbidities) and a combination of baseline, visit 1, and visit 2 follow-up interviews (employment, concern about infection, previous SARS-CoV-2 testing) [40] (see Multimedia Appendix 3 for details on how the variables were defined).

We computed descriptive statistics (frequencies and proportions) for these characteristics by class and compared the distributions of these variables using Pearson chi-square tests. An alpha level of .05 was the criterion for statistical significance. The descriptive statistics and bivariate analyses were done using SAS 9.4 (SAS Institute).

Results

Participant Demographic Characteristics

Of the 5098 invited cohort participants, 4793 participants completed the DCE (response rate 94.0%). The median age was 39 (IQR 30-53) years, 51.5% (n=2468) were female, 62.8% (n=3009) were non-Hispanic White, 16.4% (n=788) were Hispanic, 9.2% (n=442) were non-Hispanic Black, 7.4% (n=361) were Asian or Pacific Islander, and 3.9% (n=189) were another race.

Respondent Quality

We assessed respondent quality and reran the 5-group latent class analysis four times excluding participants who exhibited combinations of either straightlining behavior (n=392), completion times in the 5th (n=239) or 10th (n=473) percentile of all responders, or combinations of straightlining and speeding. Though there was some volatility in the part-worth utility estimates for the smallest class size in the models with exclusions, there were no qualitative differences to class sizes or relative attribute importance. Therefore, we used the model that retained all 4793 participants (see Multimedia Appendix 4 for additional details).

Patterns of Preferences: Relative Attribute Importance and Preferences for Levels of Attributes

Among the 4793 participants who completed the DCE, 5 distinct classes were identified balancing quantitative measures of model fit (Akaike information criterion, Bayesian information criterion, and log-likelihood) with class size and the ability to interpret the final solution. Multimedia Appendix 5 presents a summary of these criteria. Each class had a distinct profile or pattern of attribute relative importance (Figure 1) and preferences for specific levels of attributes (Table S1, Multimedia Appendix 6). We characterized the patterns based on the preferences within each class: noninvasive home testers (n=920, 19.2%), fast-track testers (n=1235, 25.8%), dual testers (n=889, 18.5%), noninvasive dual testers (n=1578, 32.9%), and hesitant home testers (n=171, 3.6%).

Figure 1. Mean relative attribute importance for SARS-CoV-2 testing by preference pattern.
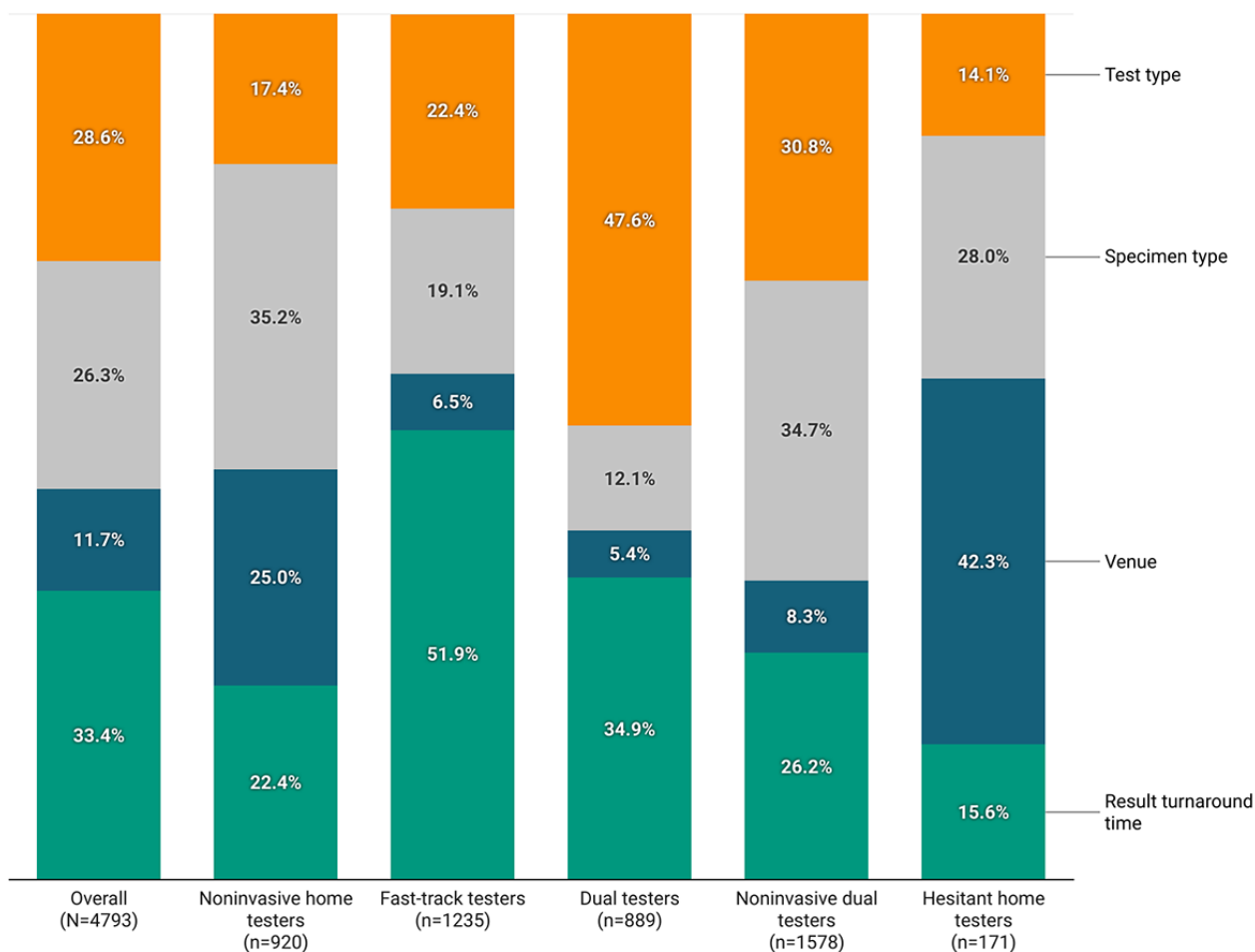
To elaborate, among noninvasive home testers, specimen type had the highest relative importance (35.2%, 95% CI 34.8%-35.5%), followed by venue (25.0%, 95% CI 24.4%-25.5%), result turnaround time (22.4%, 95% CI 22.0%-22.9%), and test type (17.4%, 95% CI 16.9%-17.9%). Participants in this pattern favored less invasive specimen types, with saliva being most preferred (utility 48.6) and NP swab and blood draw specimen types being least preferred (utilities –92.1 and –41.3, respectively). They preferred home sample collection, either returning the sample for testing by mail (utility 55.3) or to a collection site (utility 42.7), and least preferred testing at a doctor's office or urgent care clinic (utility –41.6) or walk-in community testing site (utility –44.5). Participants in this pattern most preferred a fast turnaround time for their results (immediate, utility 42.0; same day, utility 30.4) and antibody and viral tests together (utility 39.5). The none option had a large negative utility (–299.6).

The attribute with the highest relative importance for fast-track testers was result turnaround time (51.9%, 95% CI 51.6%-52.3%), followed by test type (22.4%, 95% CI 22.1%-22.8%) and specimen type (19.1%, 95% CI 18.8%-19.4%); venue was least important (6.5%, 95% CI 6.4%-6.6%). Participants in this pattern had the most extreme range of values for relative importance. They most preferred an immediate (utility 98.6) and same-day (utility 63.8) result turnaround time and both antibody and viral tests (utility 53.0).

They preferred less invasive specimen types, with a cheek swab being most preferred (utility 25.4) and NP swab and blood draw being least preferred (utilities –51.1 and –20.7, respectively). Although venue was the least important attribute for this group, among the specific options, testing at a community drive-through was most preferred (utility 10.8). Similar to noninvasive home testers, the fast-track testers had a large negative utility for the none option (–238.0).

Among dual testers, test type had the highest relative importance (47.6%, 95% CI 47.2%-47.9%), followed by result turnaround time (34.9%, 95% CI 34.7%-35.2%), with specimen type being less important (12.2%, 95% CI 11.8%-12.4%) and venue being least important (5.4%, 95% CI 5.3%-5.5%). Participants in this pattern most preferred both antibody and viral tests (utility 93.3) and fast turnaround times for results (immediate: utility 64.9; same day: utility 40.5). Less invasive specimen types were preferred, with saliva (utility 14.2) and cheek swab (utility 16.4) being most preferred, and NP swab being least preferred (utility –30.5). Regarding venue, testing at drive-through community sites was most preferred (utility 12.2). Dual testers had a large negative utility for the none opt-out choice (utility –217.4).

Among noninvasive dual testers, specimen type had the highest relative importance (34.7%, 95% CI 34.5%-34.8%), followed by test type (30.8%, 95% CI 30.7%-31.0%) and then result turnaround time (26.2%, 95% CI 26.0%-26.5%), with venue least important (8.3%, 95% CI 8.2%-8.4%). In this pattern, the

most preferred specimen types were saliva (utility 28.1) and cheek swab (utility 37.8), and the least preferred was NP swab (utility –100.9). Both antibody and viral tests were preferred (utility 73.3), as well as fast turnaround times for results (immediate: utility 54.7; same day: utility 25.1). Regarding venue, home collection with returning the sample to a collection site was most preferred (utility 16.8). Similar to the previous three patterns, noninvasive dual testers had a large negative utility for the none opt-out choice (–226.6).

Finally, among participants in the hesitant home testers pattern, venue had the highest relative importance (42.3%, 95% CI 41.4%-43.1%) followed by specimen type (28.0%, 95% CI 27.7%-28.2%); result turnaround time (15.6%, 95% CI 14.9%-16.4%) and test type (14.1%, 95% CI 13.8%-14.5%) were similarly less important. In contrast to the other 4 patterns, hesitant home testers had a positive utility (32.5) for the none option, hence the use of "hesitant" in this pattern's name. Participants in this pattern preferred less invasive specimens, including urine (utility 33.5), finger prick (utility 24.5), cheek swab and saliva (utilities 25.6 and 18.7, respectively), and least preferred NP swab (utility –77.7) and blood draw (utility –21.1). They most preferred home sample collection either returning the sample for testing by mail (utility 93.2) or to a collection site (utility 60.2), and least preferred testing at a walk-in community site (utility –75.9) or a doctor's office/urgent care clinic (utility –44.6). Although test type and turnaround time were the least important attributes for hesitant home testers, participants with this pattern preferred both antibody and viral tests (utility 36.1) and fast turnaround times for results (immediate: utility 32.5; same day: utility 21.2).

Simulated Preferences for Standard Testing, Less Invasive Testing, Dual Testing, and At-Home Testing

Predicted testing uptake for the 2 standard scenarios among all participants was 81.6%, ranging from 34.8% for hesitant home testers to 92.9% for dual testers (Figure 2). By including less invasive testing, dual testing, and at-home testing scenarios in our second simulation, predicted testing uptake among all participants increased by 16.4 percentage points to 98.0%. The addition of these 3 scenarios had the biggest impact on hesitant home testers, with an increase in uptake from 34.8% to 66.7% (31.9 percentage points), and noninvasive dual testers, with an increase in uptake from 75.4% to 99.4% (24.0 percentage points).

In our simulation of all 6 scenarios (Table S2, Multimedia Appendix 6), the standard testing scenarios generally had the lowest predicted uptake, though with higher uptake for the drive-through option (overall 6.6%) compared with the walk-in community site option (overall 0.9%). Of the 3 additional scenarios, the dual testing scenario combining polymerase chain reaction and serology had the highest predicted uptake overall (61.8%) and was highest for fast-track testers (60.8%), dual testers (65.0%), and noninvasive dual testers (80.9%). The at-home testing scenario had the highest predicted uptake for noninvasive home testers (37.9%) and hesitant home testers (38.2%); however, for noninvasive home testers, there was also similar uptake for the dual testing scenario (35.5%). For hesitant home testers, one-third (33.3%) were predicted to opt out of testing altogether.

Figure 2. Simulated uptake of SARS-CoV-2 testing for 2 standard testing scenarios versus the addition of less invasive dual testing and at-home scenarios, overall and by preference pattern.
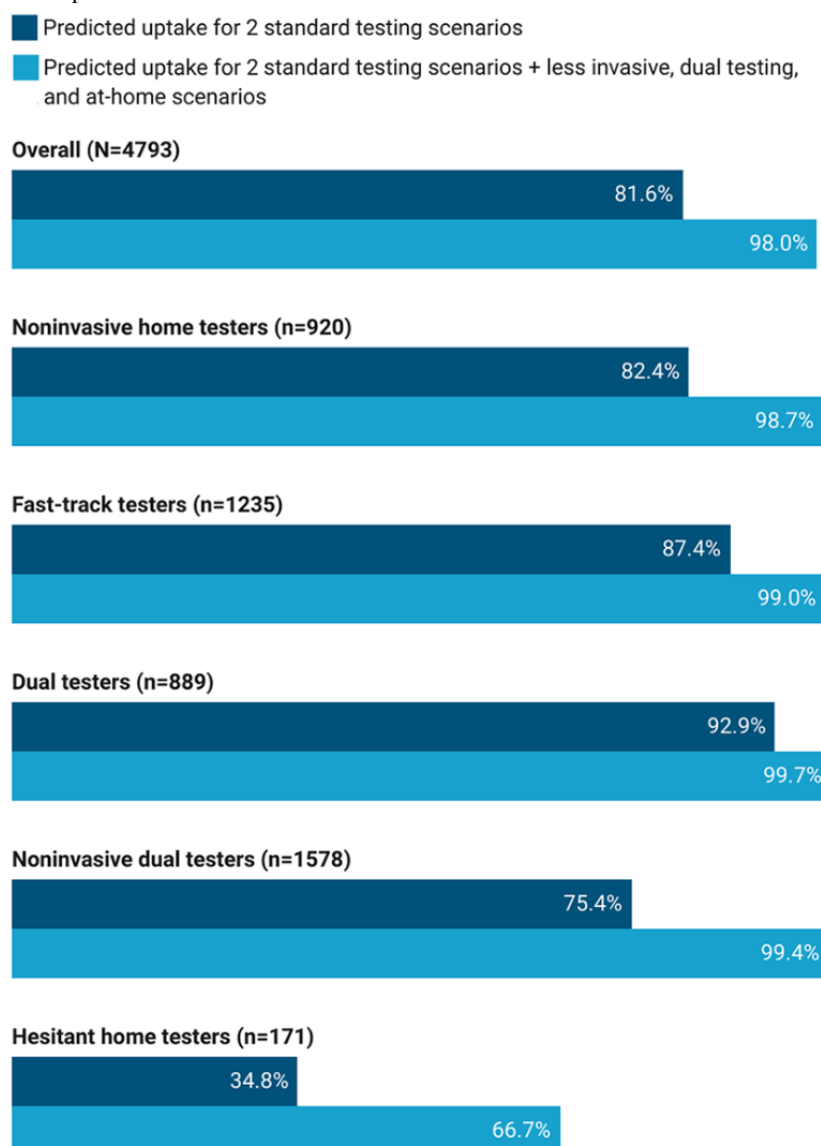
Demographic Characteristics of Participants by Preference Pattern

There were statistically significant differences by preference pattern in age group, gender, race/ethnicity, education, and employment, but not in geographic region, urbanicity, or presence of any comorbidity (Table S3, Multimedia Appendix 6). Hesitant home testers were older with less representation in the youngest age group of 18 to 39 years (69/171, 40.4%) compared with participants in other patterns (range 49.3%-56.1%). Fast-track testers were less often female (583/1235, 47.2%), especially when compared with hesitant home testers (100/171, 58.5%) and to a lesser extent when compared with participants in other patterns (range 50.5%-53.6%). Dual testers (625/889, 70.3%) and noninvasive dual testers (1059/1578, 67.1%) were more often non-Hispanic White, especially compared with hesitant home testers (85/171, 49.7%) and to a lesser extent with noninvasive home testers (516/920, 56.1%) and fast-track testers (725/1235, 58.6%). Dual testers tended to be college graduates (628/889, 70.6%), especially compared with noninvasive home testers (508/920,

55.2%) and to a lesser extent when compared with participants in other patterns (range 59.1%-64.3%). Regarding employment, hesitant home testers were more often out of work (37/171, 21.6%) compared with participants in other patterns (range 9.3%-13.8%).

Previous SARS-CoV-2 Testing, COVID-19 Diagnosis, and Infection Concern by Preference Pattern

There were statistically significant differences by preference pattern for previous SARS-CoV-2 testing, reported COVID-19 diagnosis, concern about getting infected, concern about loved ones getting infected, concern about hospitals being overwhelmed, personally knowing someone who had died from COVID-19, and submitting a dried blood spot (DBS) for testing as part of our cohort study (Table S3, Multimedia Appendix 6). Fast-track testers (424/1235, 34.3%) and dual testers (298/889, 33.5%) more often had previously tested for SARS-CoV-2 compared with participants in other patterns (range 23.4%-25.9%). Reporting a previous laboratory-confirmed diagnosis of COVID-19 was lowest among dual testers (35/889, 3.9%) and noninvasive dual testers (51/1578, 3.2%) compared

with participants in other patterns (range 5.3%-7.5%). Among those who did not report being previously diagnosed with COVID-19, dual testers were less often not at all worried or not too worried about getting infected with SARS-CoV-2 (179/889, 21.0%), especially when compared with hesitant home testers (52/171, 32.1%) and to a lesser extent participants in other patterns (range 23.9%-29.6%). A similar pattern was observed for concern about loved ones getting infected with SARS-CoV-2, where dual testers had the lowest proportion of people who reported being not at all worried or not too worried about loved ones getting infected (82/889, 9.2%) compared with hesitant home testers (38/171, 22.2%) and to a lesser extent compared with participants in other patterns (range 13.0%-17.5%). Likewise, dual testers had the lowest proportion of people who reported being not at all worried or not too worried about hospitals being overwhelmed by COVID-19 (112/889, 12.6%) compared to participants in other patterns (range 19.3%-32.2%).

Fast-track testers were more likely to personally know someone who had died from COVID-19 (320/1235, 25.9%) than hesitant home testers (34/171, 19.9%) and participants in other patterns (range 21.0%-22.5%). Noninvasive dual testers (1323/1578, 83.8%) and dual testers (741/889, 83.4%) were more likely to have submitted at least one DBS specimen for serology as part of our cohort study, compared with hesitant home testers (121/171, 70.8%), noninvasive home testers (671/920, 72.9%), and fast-track testers (915/1235, 74.1%).

Discussion

Principal Results

A one-size-fits-all approach to SARS-CoV-2 testing may alienate or exclude segments of the population with preferences for different testing modalities. If the goal is to increase and maintain testing uptake and engagement, then the identification of patterns of heterogeneous testing preferences could inform the design and implementation of complementary testing services that support greater coverage.

We identified substantial differences in preferences for aspects of SARS-CoV-2 testing, as shown by the differences in attribute relative importance and part-worth utilities. Overall, participants preferred getting both antibody and viral tests with less invasive specimens and fast turnaround time for results; however, the degree to which these features influenced participants' choices varied across patterns. Our 6-scenario simulation showed that offering additional venues and test type options would increase testing uptake at a time when case numbers were increasing in many parts of the United States, with dual viral and antibody testing expected to have the biggest uptake. Though identifying previous infections via antibody tests does not help control transmission, including antibody tests with diagnostic testing could incentivize some people to get tested. An at-home testing option would also be expected to increase uptake, especially for participants in the noninvasive home testers and hesitant home testers patterns, which comprised about one-fifth of the sample.

Since this study was undertaken, there have been developments in SARS-CoV-2 viral and serologic testing that could address many of the distinct preferences across patterns, including the expansion of at-home specimen collection, affordable fully at-home tests commercially available without a prescription, rapid point-of-care tests, and less invasive specimens [41-44]. Though not yet approved by the US Food and Drug Administration, a promising saliva-based antibody test is in development [45], which may, in the future, allow for a single saliva specimen to be used for both serology and molecular testing. In our study, noninvasive home testers and hesitant home testers, who placed most importance on specimen type and venue, respectively, were more often non-Hispanic Black and Hispanic. These testing developments may provide a pathway to increase lower testing rates among Black and Latino individuals, who have experienced a disproportionate burden of cases, hospitalization, and deaths due to COVID-19 [46].

We also observed differences in sample characteristics by preference pattern, including demographic characteristics, previous testing, and COVID-19 diagnosis, and concern about infection. These differences could be leveraged to promote testing through media tools and campaigns targeting specific populations, similar to "The Conversation: Between Us, About Us" [47], created by the Kaiser Family Foundation's Greater than COVID and the Black Coalition Against COVID and designed to address "some of the most common questions and concerns Black people have about COVID-19 vaccines," or targeting specific behaviors, such as New York City's Test and Trace Corps' "Do it for them. Get Tested for COVID-19" advertisements on Twitter, bus shelters, and pizza boxes [48-50] with pictures of families of different races and ethnicities, sometimes multigenerational.

Across most of the preference patterns, the large negative utilities that we observed for the no-test option indicated a willingness to test. The exception was the hesitant home testers pattern, which had a positive utility for the none option, suggesting that this group of participants would be more likely to opt out of testing altogether compared to participants in the other patterns. Though hesitant home testers were least prevalent in our study, qualitative work may be warranted to understand the factors that influence their willingness to test.

Limitations

Our results should be interpreted in the context of their limitations. An important limitation of our analysis is related to latent class analysis in general, as best practices for using it to study heterogeneity in preferences in health-related research are still evolving [15]. We selected 5 classes after comparing sample size, fit statistics, and overall interpretability of 2 to 10 classes. On the one hand, the hesitant home testers pattern was small relative to the other patterns, and one could argue that it could have been combined with a larger class in a solution with fewer groups. However, in every lower dimension solution, a similarly small-sized class was identified that was strongly influenced by venue and specimen type, and had a nonnegative utility for opting out of testing. On the other hand, it is possible that additional distinct patterns of preference remained undetected with only 5 classes.

Another potential limitation is that the stated preferences regarding SARS-CoV-2 testing in our DCE may not necessarily align with actual behavior (ie, revealed preferences); however, a systematic review and meta-analysis found that, in general, stated preferences in DCEs did align with revealed preferences [10]. To minimize cognitive burden, DCE design must balance the inclusion of relevant and actionable attributes and levels with the complexity of each choice task [51]. However, one reason for lack of concordance between stated and revealed preferences in general is the omission of attributes in DCEs that may influence real-life decisions [10,29]. Aspects of accessibility including cost, transportation time, availability of testing, and wait time could be explored in future studies, as well as how participants' prior knowledge of test options may have influenced their decisions, the effects of operator error, and test validity (ie, sensitivity and specificity). Nevertheless, the different patterns of preferences for features of the test and testing experience as ascertained in our study could be used to inform the development of strategies deployed by public health agencies, who can account for the operating characteristics of tests. In some instances, even a less accurate test implemented at scale could have a larger public health impact than a more accurate test with lower uptake [52].

Although our sample was large and geographically diverse, it was not a nationally representative sample, so it may be that there are additional patterns of preferences that exist beyond our study in other populations. Not all testing options are available in every jurisdiction, and different patterns of testing preferences may emerge in different settings. Furthermore, most participants (78.3%) in the DCE had already completed at-home self-collection of a DBS specimen as part of our larger cohort study, which may have influenced preferences regarding the venue of testing.

Lastly, participants' preferences about SARS-CoV-2 testing may change over time as the pandemic continues to evolve.

Research on other topics has demonstrated that choices stated in a DCE are generally consistent, with good test-retest reliability [53,54]; however, knowledge about SARS-CoV-2 and COVID-19 has rapidly evolved and is widely disseminated in mainstream media [55], which could plausibly impact preferences. The first report of reinfection and the potential waning of antibodies appeared in the United States in October 2020 [56], approximately 1 month after the completion of our DCE, and could influence current preferences about antibody testing. In addition, the availability of highly efficacious vaccines starting in December 2020 [57] could have an impact on testing service preferences more globally, potentially causing more people to opt out of testing when case numbers, hospitalizations, and deaths decrease. It will also be important to examine preferences since new testing modalities have become available, such as fully at-home molecular tests that provide rapid results [58-60], and as vaccine uptake increases.

Conclusions

Our study may inform ways to better design and deliver SARS-CoV-2 testing services in line with pandemic response goals. The heterogeneity in preferences observed across patterns highlights that having more options available (and educating the public about their availability) is one way to increase testing uptake in an emerging and ongoing pandemic. Importantly, our analysis highlights that preferences for SARS-CoV-2 testing differ by population characteristics, including demographics, which must also be considered in the context of existing health disparities in the United States. Even as increasing proportions of the population are vaccinated, we anticipate that testing will remain a critical tool in the pandemic response until vaccine coverage and herd immunity are sufficiently high to reduce transmission and control more pathogenic or virulent variants; offering a mix of testing options is an important aspect of increasing and maintaining testing uptake.

Authors' Contributions

RZ, SGK, AB, WY, CM, DAW, AMP, LW, MSR, SK, MMR, ARM, CG, and DN designed and conducted the cohort study and discrete choice experiment. MLR and RZ conducted the statistical analysis. RZ, MLR, and DN interpreted the results. RZ and MLR drafted the manuscript. All authors critically reviewed the manuscript and approved the final version.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Desktop example of SARS-CoV-2 testing preferences choice task.
[PDF File (Adobe PDF File), 369 KB - publichealth_v7i12e32846_app1.pdf]

Multimedia Appendix 2
SARS-CoV-2 testing discrete choice experiment attributes and levels.
[PDF File (Adobe PDF File), 151 KB - publichealth_v7i12e32846_app2.pdf]

Multimedia Appendix 3
Definition of variables from the CHASING COVID Cohort Study.
[PDF File (Adobe PDF File), 156 KB - publichealth_v7i12e32846_app3.pdf]

Multimedia Appendix 4
Respondent quality details.
[PDF File (Adobe PDF File), 100 KB - publichealth_v7i12e32846_app4.pdf]

Multimedia Appendix 5
Summary of best replications of latent class analysis multinomial logit.
[PDF File (Adobe PDF File), 139 KB - publichealth_v7i12e32846_app5.pdf]

Multimedia Appendix 6
Supplementary tables on zero-centered part-worth utilities for SARS-CoV-2 testing attribute levels by preference pattern (Table S1); simulated uptake of standard testing, less invasive testing, dual testing, and at-home testing scenarios by preference pattern (Table S2); and sample characteristics, previous testing, COVID-19 diagnosis, and concern about infection stratified by preference pattern for SARS-CoV-2 testing (Table S3).
[PDF File (Adobe PDF File), 210 KB - publichealth_v7i12e32846_app6.pdf]

Multimedia Appendix 7
CHERRIES (Checklist for Reporting Results of Internet E-Surveys) checklist.
[PDF File (Adobe PDF File), 171 KB - publichealth_v7i12e32846_app7.pdf]

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Abbreviations

CHASING COVID Cohort Study: Communities, Households, and SARS-CoV-2 Epidemiology Cohort Study
CUNY: City University of New York
DBS: dried blood spot
DCE: discrete choice experiment
MNL: multinomial logit
NIH: National Institutes of Health
NP: nasopharyngeal
RFC: Randomized First Choice

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Original Paper

Web-Based Discussion and Illicit Street Sales of Tapentadol and Oxycodone in Australia: Epidemiological Surveillance Study

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Abstract

Background: Opioid use disorder and its consequences are a persistent public health concern for Australians. Web activity has been used to understand the perception of drug safety and diversion of drugs in contexts outside of Australia. The anonymity of the internet offers several advantages for surveilling and inquiring about specific covert behaviors, such as diversion or discussion of sensitive subjects where traditional surveillance approaches might be limited.

Objective: This study aims to characterize the content of web posts and compare reports of illicit sales of tapentadol and oxycodone from sources originating in Australia. First, post content is evaluated to determine whether internet discussion encourages or discourages proper therapeutic use of the drugs. Second, we hypothesize that tapentadol would have lower street price and fewer illicit sales than oxycodone.

Methods: Web posts originating in Australia between 2017 and 2019 were collected using the Researched Abuse, Diversion, and Addiction-Related Surveillance System Web Monitoring Program. Using a manual coding process, unstructured post content from social media, blogs, and forums was categorized into topics of discussion related to the harms and behaviors that could lead to harm. Illicit sales data in a structured format were collected through a crowdsourcing website between 2016 and 2019 using the Researched Abuse, Diversion, and Addiction-Related Surveillance System StreetRx Program. In total, 2 multivariable regression models assessed the differences in illicit price and number of sales.

Results: A total of 4.7% (28/600) of tapentadol posts discussed an adverse event, whereas 10.27% (95% CI 9.32-11.21) of oxycodone posts discussed this topic. A total of 10% (60/600) of tapentadol posts discussed unsafe use or side effects, whereas 20.17% (95% CI 18.92-21.41) of oxycodone posts discussed unsafe use or side effects. There were 31 illicit sales reports for tapentadol (geometric mean price per milligram: Aus $0.12 [US $0.09]) and 756 illicit sales reports for oxycodone (Aus $1.28 [US $0.91]). Models detected no differences in the street price or number of sales between the drugs when covariates were included, although the potency of the pill significantly predicted the street price ($P<.001$) and availability predicted the number of sales ($P=.03$).

Conclusions: Australians searching the web for opinions could judge tapentadol as safer than oxycodone because of the web post content. The illicit sales market for tapentadol was smaller than that of oxycodone, and drug potency and licit availability are likely important factors influencing the illicit market.

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Introduction

Background

With a steady increase in opioid prescribing [1], opioid use disorder and its consequences are a persistent public health concern for Australians despite the lack of national research on the topic. The few papers presenting national data show that most people who inject drugs use opioids [2], and opioid deaths rose through 2012 [3]. Prescription opioids continue to be misused, and the prevalence of use differs for each drug [2]. The most recent reports show that ambulance attendances involving prescription opioids are rising in Victoria, Australia [4]. Diversion, which is the sale or acquisition of a controlled substance outside the regulatory system, contributes to serious medical consequences. In other parts of the world, there is evidence that at least one-fourth of opioid overdose deaths involve a diverted drug [5]. Without the direction of a health care provider to provide safe use information and guidance (such as using multiple drugs at once), individuals using diverted drugs could be at higher risk of adverse events, such as fatality. Understanding the availability of diverted drugs and desirability differences between these drugs will help guide effective policies to control drug harms and create postmarketing systems that monitor safety and efficacy across all populations of users. Given the relatively limited country-wide surveillance, evaluation of data from internet sources could provide an initial understanding of how Australians perceive the safety of drugs and how frequently a drug is sold outside of the licit drug distribution channels. Investigations of street sale volume and web-based discussion of drug misuse together provide complementary perspectives on the desirability of drugs in the Australian market.

The anonymity of the internet offers several advantages for surveilling and inquiring about specific covert behaviors, such as diversion or discussion of sensitive subjects, where traditional surveillance approaches might be limited. Crowdsourcing of street prices has been used to discern factors that influence differences in prices between oxycodone and oxymorphone [6], identify unmet needs for buprenorphine assisted opioid therapy [7], and demonstrate the rarity of tapentadol diversion relative to other controlled drugs [8]. The monitoring of blogs and forums and social media has shown divergent trends in the discussion of addiction and overdose between drugs [9], tracked the popularity of marijuana concentrates [10], and identified tampering methods for reformulated oxycodone [11].

Objectives

The aim of this study is to characterize safety-related web post content and compare reports of illicit sales of tapentadol and oxycodone products from sources originating in Australia. Tapentadol is a relatively new drug in Australia and was first approved in 2011. It is possible that the diversion and desirability of a new drug are different from those of drugs with a longer history and larger market availability, such as oxycodone. First, these 2 drugs were compared to describe the differences in web-based discussions of serious health consequences. The textual content of the posts was evaluated to determine whether internet discussion encouraged or discouraged the proper therapeutic use of the drugs. Second, 2 hypotheses were tested using street sales data. As patients exposed to tapentadol have lower odds of physician shopping [12], we hypothesized that tapentadol would have lower street prices and fewer illicit sales. Differences between drugs were modeled with covariates to account for other effects on sales.

Methods

Overview

The Researched Abuse, Diversion, and Addiction-Related Surveillance System is a compilation of individual data collection programs that monitor drug use–related outcomes and behaviors. In total, 2 systems, the Web Monitoring Program and the StreetRx Program, were used to characterize web posts and reports of street sales involving tapentadol or oxycodone in Australia. The Web Monitoring Program, established in 2014, focuses on the collection and organization of real-time web content about prescription drugs from >150 million websites on the internet, including social media, blogs, and forums. The StreetRx Program collects crowdsourced information related to illicit street sales of drugs. StreetRx users select drugs purchased or sold from a drop-down menu of substances and formulations (pill or tablet, syrup or liquid, film, patch, etc). All statistical analyses were conducted using SAS (version 9.4; The SAS Institute).

Data Collection and Analysis of Internet Posts

Methods of data collection, cleaning, and estimation procedures for the Web Monitoring Program have been described elsewhere [9]. Briefly, all data were collected using a web-crawling platform (Salesforce.com Inc) that scrapes data from public websites that permit content viewing by a third party. Examples of sites that permit this type of crawling include Twitter, Reddit, public blogs and forums, and comment sections on many news sites. Private sites, such as personal Facebook pages, Bluelight, and other password-protected sites do not permit this type of crawling. For this study, posts mentioning either tapentadol or oxycodone were collected from websites that permit public scraping of data, and the weekly number of posts was calculated. Posts mentioning tapentadol or oxycodone were identified based on specified search-string criteria (such as drug name, associated misspellings, product names, and unique slang terms). The keywords for each drug substance and product were generated using a phonetic algorithm and then validated using the number of hits when entered into a common search engine. Other keywords were identified during the manual coding process. The search strings used are listed in Multimedia Appendix 1. Posts between 2017 and 2019 were collected, and only posts that originated in Australia as determined by the IP address of the post were included in this study. Nonsubstantive posts, such as nonsensical posts or posts from web-based pharmacies, were removed. The remaining posts had substantive content about a person's experience, opinion, or understanding of the drugs. The content of the posts was manually categorized into topics by a team of trained coders, who pass at least a 90% biannual interrater reliability test [9], into a series of safety-related topics based on the definitions listed in Textbox 1. Grounding theory was previously used to develop topics and definitions [11]. In

brief, topics were identified by trained researchers reviewing samples of the posts for emergent topics. These data-driven topics were identified in a 2-round process, and a standard definition was created for coding purposes. The percentages of posts discussing each topic and 95% CIs were calculated. All scraped posts mentioning tapentadol were coded. Therefore, the statistics presented here are exact and represent the total volume of tapentadol posts from Australia during the period.

Owing to the volume of scraped posts mentioning oxycodone, a sample of posts was coded. A stratified, random sample without replacement and with proportional allocation was obtained from the population of identified posts. Strata included both time (by week) and origin (social media or blogs and forums) of the web posts. Therefore, statistics for oxycodone are estimates presented with a 95% CI.

Textbox 1. Coding definitions for web posts.

Coding definitions

- Abuse

    - A mention that indicates the use of a drug to gain a high, euphoric effect or some other psychotropic effect

- Addiction—a mention that indicates one or more of the following:

    - Psychological or physical dependence on a drug

    - Tolerance to the psychotropic effects of a drug

    - Withdrawal effects when discontinuing use of a drug

- Adverse event

    - Any untoward medical occurrence in a patient or clinical investigation participant (individual) administered a medicinal product and which does not necessarily require to have a causal relationship with this treatment. An adverse event can therefore be any unfavorable and unintended sign (eg, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether considered related to this medicinal product or not.

    - Adverse events include misuse, abuse, overdose, death, drug dependency, side effect, exposure during pregnancy, exposure during breastfeeding, medication error, lack of effect, off-label use, suspected transmission of infectious agents, quality defect or falsified medicine (counterfeit product), and occupational exposure.

- Concomitant use

    - The concurrent administration of 2 or more substances of interest such that the effects of the substances overlap

- Death

    - A mention that indicates that death has occurred because of a drug of interest

- Injection or intranasal administration

    - A mention that discusses the route of administration for a drug, defined as the path by which a drug is taken into the body

- Overdose

    - A mention that indicates the accidental or intentional overdose of a drug using a dangerous amount of a drug (ie, a quantity greater than that recommended or generally prescribed) or use which may result in a medical intervention

- Post

    - A single point of communication entered by 1 individual at 1 specific time point

- Tampering with product

    - A mention of a drug that discusses manipulating a product formulation to change its drug delivery in a way not specified by the manufacturer

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All posts were categorized as conveying negative, positive, or neutral sentiment. Sentiment was defined as the dominant view or opinion of a drug within the post. Positive sentiments promoted the therapeutic benefits or safe use of a drug. Negative sentiments encouraged unsafe or inappropriate use of a drug or reported ineffectiveness or side effects. Positive and negative sentiments were further broken down into mutually exclusive sentiment categories. Positive sentiment must have (1) promoted

therapeutic benefit, (2) discouraged abuse, or (3) referred to a product in another positive way. Negative sentiment must have (1) discouraged therapeutic benefit, (2) promoted abuse, or (3) referred to a product in another negative way (eg, side effects). Posts categorized as having neutral sentiment were those in which no predominant opinion existed, or the sentiment could not be determined. Posts were categorized as part of ongoing data collection using the Researched Abuse, Diversion, and

Addiction-Related Surveillance System; therefore, coders were blind to the study purpose. The content of the posts was redacted to preserve the anonymity of the authors. The content of each post was changed so that the post could not be found using web-based search engines, but it did not alter the message or context of the post. Changes included the correction of grammar and spelling, replacement of words with synonyms, and reordering of sentence structure.

Street Sales Data Collection and Analysis

Methods of data collection for the StreetRx Program have been described elsewhere [13]. In brief, a website with an Australian domain name collected product identity, geographic location, and sale price in Australian dollars, as entered by the website user. Reports of illicit street sales were entered by website users who had either participated in the transaction or heard about the prices. Website users were prompted to select the drug name from a list of licit and illicit drugs sold in Australia and were required to enter the Australian state or territory where the sale occurred. The website also requires the user to enter the price paid per unit, dose, and date of the transaction. The price per milligram is calculated from the price paid per unit and the dose. Website users are not compensated for entering information; however, they are shown a list of other sales for the same drug that occurred in the same area before entering the data. Sales data for tapentadol and oxycodone were collected from 2016 to 2019. For summarizing in this report, prices were converted to US dollars at a conversion of Aus $1 to US $0.71, which was the conversion on December 1, 2021.

The number of reports, geometric mean of the sale price per milligram, and percentages of release type and reason for sale were calculated. The geometric mean was used as the distribution of prices reported was not symmetrical, and it better represented the central tendency than the arithmetic mean [6].

Regression models were run to test 2 separate hypotheses. First, we hypothesized that there was a difference in price between oxycodone and tapentadol. Differences in price were tested using a linear multivariable model while controlling for the year the sale occurred. The potency of the drug in morphine milligram equivalents (MME) was added separately to the simplified model to test if differences in price were predicted by potency. The outcome for the first hypothesis was a log-transformed price. Conversion factors for MME from the United States Centers for Disease Control and Prevention were used [14]. Influential points were defined as a Cook distance

>0.01. Second, we hypothesize that there is a difference in the number of sales between oxycodone and tapentadol. The difference in the likelihood of reporting a sale was tested using a Poisson multivariable model while controlling for general site use. Standard units sold (ie, licit availability) were added separately to test if differences in the number of illicit sales were predicted by licit availability. The outcome in the second model was the number of quarterly reports. Standard units sold are estimates of the number of drug units sold from manufacturers to dispensing outlets (eg, pharmacies and supermarkets); data were obtained from IQVIA. Estimates of standard units sold were used to control for the amount of drug available for diversion. Drug availability data were only obtained from 2016 to 2018; therefore, the models for the second hypothesis did not include reports from 2019.

Results

Characteristics of Web-Based Discussion

The weekly number of posts for tapentadol and oxycodone were steady across the study period, with a potential increase in posts in early 2019 (Figure 1). A total of 17,634 oxycodone posts were collected for sampling and 695 tapentadol posts were collected for coding. After coding to remove nonsubstantive posts, there were 600 substantive tapentadol posts originating in Australia. After sampling and coding, an estimated 8598 (95% CI 8456-8739) substantive oxycodone posts were identified. The percentages of posts on discussion topics are listed in Table 1. Most of the posts shared an experience or opinion regarding the drug. An adverse event was discussed in 4.7% (28/600) of tapentadol posts and 10.27% (95% CI 9.32-11.21) of oxycodone posts. A total of 2.7% (16/600) of tapentadol posts and 5.42% (95% CI 4.72-6.12) of oxycodone posts discussed addiction. Discussion of concomitant use was higher among tapentadol posts than among oxycodone posts. The use of another drug was discussed in 14.7% (88/600) of tapentadol posts compared with 6.05% (95% CI 5.31-6.79) of oxycodone posts. When tapentadol was concomitantly used, paracetamol, oxycodone, and pregabalin were the 3 most frequently used second drug. When oxycodone was concomitantly used, paracetamol, morphine, and tramadol were the 3 most frequently used second drug. For either drug, <1% of posts discussed abuse, overdose, death, product tampering, injection of the product, or intranasal administration of the product.

Figure 1. Weekly number of web posts from Australian sources: total number of posts per week that mention tapentadol and oxycodone.
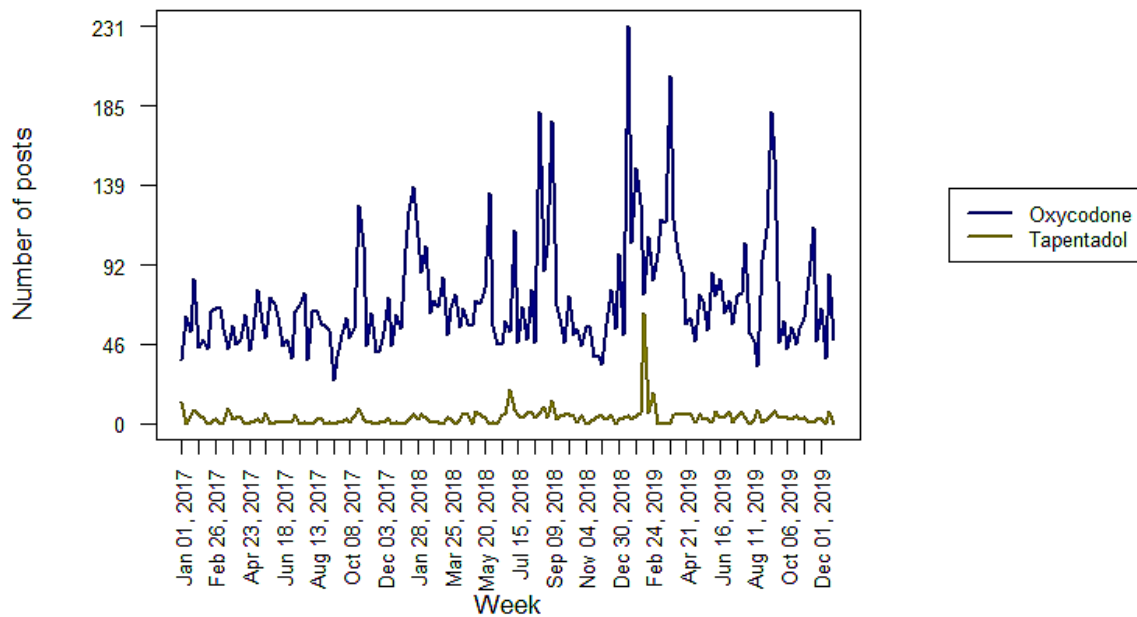
Table 1. Web-based discussion topics (2017-2019).

Characteristics	Tapentadol[a]	Oxycodone
Number of substantive posts, n (95% CI)	600	8598 (8456-8739)
Discussion topic, % (95% CI)		
Sharing experience or opinion	98.33	99.79 (99.64-99.94)
Seeking information	3.33	1.16 (0.83-1.50)
Abuse	0.17	0.79 (0.52-1.07)
Overdose	0.17	0.38 (0.19-0.57)
Addiction	2.67	5.42 (4.72-6.12)
Death	0.00	0.79 (0.51-1.07)
Adverse events	4.67	10.27 (9.32-11.21)
Concomitant use with another product	14.70	6.05 (5.31-6.79)
Tampering with product	0.00	0.05 (0.00-0.13)
Injection of product	0.17	0.06 (0.00-0.14)
Intranasal administration of product	0.00	0.19 (0.05-0.33)
Overall sentiment, % (95% CI)		
Positive	16.83	9.87 (8.94-10.80)
Negative	10.00	20.17 (18.92-21.41)
Neutral	73.17	69.96 (68.54-71.39)
Positive sentiment,[b] % (95% CI)		
Promoting therapeutic use	50.50	27.70 (23.25-32.15)
Discouraging abuse	0.00	0.96 (0.02-1.89)
Others	50.50	71.81 (67.34-76.28)
Negative sentiment,[b] % (95% CI)		
Discouraging therapeutic use	0.00	0.00 (0.00)
Promoting abuse	6.67	20.91 (18.10-23.72)
Others	95.00	82.12 (79.48-84.77)

[a]All tapentadol posts were coded, and therefore, values are exact; CIs are not applicable.

[b]Posts could be identified with more than one discussion topic or sentiment; therefore, percentages would not sum to 100% within each category.

The overall sentiment of tapentadol posts was more positive and less negative than that of oxycodone posts (Table 1). Among positive sentiment posts, a higher percentage of posts encouraged the therapeutic benefit of tapentadol than that of oxycodone. A total of 50.5% (51/101) of positive tapentadol posts encouraged therapeutic benefit compared with 27.7% (95% CI 23.25-32.15) of positive oxycodone posts. Among negative posts, a lower percentage of posts promoted abuse of tapentadol compared with that of oxycodone. A total of 7% (4/60) of negative tapentadol posts encouraged abuse compared with 20.91% (95% CI 18.10-23.72) for negative oxycodone posts. Side effects were more prevalent among negative tapentadol posts. A total of 40% (24/60) of negative tapentadol posts and 24.21% (95% CI 21.23-27.18) of negative oxycodone posts discussed side effects.

Representative redacted posts demonstrate coding practices for topics and sentiments (Table 2). Both simple and challenging posts are shown here. Nearly all posts involved the author of

the post sharing an experience or opinion of the drugs. Some posts were clear in how the author of the post intended to use the drug. Posts 1, 2, and 3 show how the coding of topics was conducted. Post 1 demonstrates a post coded for sharing an experience but not coded for abuse. In post 1, the intention was clearly suicidal and not to gain a high, euphoric effect or some other psychotropic effect. In post 2, a clear description of drug-related death of a person was provided. In post 3, the author of the post indicates the intention to use in the future to "not feel." Given that the activity is in the future, it was challenging to assign intention to the post. Ultimately, this post was not assigned to abuse, given the ambiguity. Posts 4, 5, and 6 show differences in how sentiment was assigned; challenging posts are shown here to demonstrate how sentiment might be assigned and to demonstrate the pitfalls in the manual coding of drug-related sentiment. In post 4, the author of the post discussed the use of a tapentadol product without concomitant use, switched to another opioid product, and encouraged others to use tapentadol. This post was coded as promoting the safe use

of the drug (ie, positive sentiment). In post 5, the author of the post discussed sickness from combining drugs. This post was coded as describing a negative effect from use (ie, negative sentiment). In post 6, the author of the post took an excessive amount of the drug, thinking it was a different drug, and the author of the post indicated that the experience was *pretty interesting*. This post was coded as promoting unsafe use of the drug (ie, negative sentiment).

Table 2. Redacted, representative posts from web-based discussion.

Redacted post	Coded topics	Coded sentiment
Oxycodone		
Post 1: "I'm 30 now, and when I was 28 I tried my hardest to end my life. I took a pack of oxycontin on a ten story balcony. The next day, I woke up covered in vomit under a piano. I didn't tell a soul because it seemed dumb."	Sharing experience	Negative
Post 2: "I've just heard that the husband of my cousin, who is only in his 30s, had pneumonia and died in his sleep. A doctor gave him oxycodone for muscle pain in his chest. The oxycodone suppressed his breathing and he just stopped breathing in his sleep."	Sharing experience and death	Negative
Post 3: "I am emotional, plus my dog just puked on the rug. I'm going to drink wine and take oxycodone until I can't feel."	Sharing experience	Negative
Tapentadol		
Post 4: "I've been off tapentadol for four months now and the withdrawal was terrible, but I put up with the pain and went down to Tramadol SR. The pain relief is sometimes not worth the mental price. I hope tapentadol works out for you."	Sharing experience and addiction	Positive
Post 5: "Throughout the day I had a few glasses of white wine which caused me to be sick at night. I've realized that Alcohol with Clonazepam or Tapentadol does not mix well together. Clonazepam is only potent at a low dose and about 0.5 mg of it equals about 10 mg of Diazepam."	Sharing experience and concomitant use (alcohol and clonazepam)	Negative
Post 6: "Today has been pretty interesting! Here's a suggestion: store medicines that look similar in different locations not near each other. I took tapentadol thinking it was nizatidine. I had 500 mg of tapentadol in my body, all at the same time, and that is a lot!"	Sharing experience	Negative

Characteristics of Street Sales

Most number of street sales was reported in New South Wales, Australia, and 6 states or territories had at least one sale reported (Figure 2). Nationally, there were 31 reports of tapentadol sales and 756 reports of oxycodone sales (Table 3), and reports were concentrated in states with larger cities. The geometric mean sale price per milligram for oxycodone (Aus $1.28 [US $0.91]/mg) was higher than that of tapentadol (Aus $0.12 [US $0.09]/mg). When stratified by release type, there was little difference in geometric mean price per milligram between extended-release and immediate-release tapentadol. The geometric mean price per milligram of immediate-release oxycodone was more than twice that of extended-release oxycodone. A total of 57.8% (436/756) of oxycodone sales were for immediate-release products; 16% (5/31) of tapentadol sales were for immediate-release products. The reasons for sale were generally similar between products. Notably, a higher proportion of sales of tapentadol was for self-treatment of pain or other medical conditions than for oxycodone. No report of a tapentadol sale included getting high as the reason for the sale; a total of 45 reports indicated this reason for oxycodone. However, a substantial portion of reports did not list a reason for the sale as the website users might have been more reluctant to enter sensitive or illegal use (such as to resell).

Figure 2. Geographic distribution of illicit sales in StreetRx. More illicit sales were reported for oxycodone than tapentadol, and reports were concentrated in states with larger city populations.
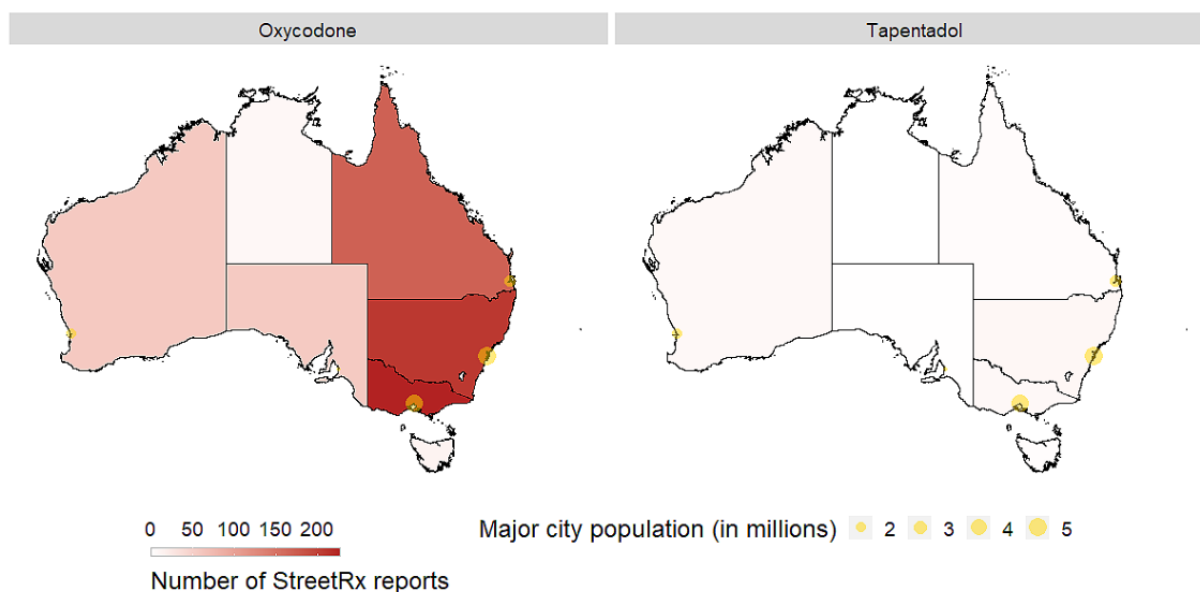

Table 3. Characteristics of street sales entered in the StreetRx website.

Variables	Tapentadol	Oxycodone
Number of reports, n (%)		
All reports	31 (100)	756 (100)
Extended-release	11 (35.48)	218 (28.84)
Immediate-release	5 (16.13)	437 (57.8)
Unknown	15 (48.39)	101 (13.36)
Geometric mean price per milligram, Aus $ (US$)		
All reports	0.12 (0.09)	1.28 (0.91)
Extended-release	0.09 (0.06)	0.69 (0.49)
Immediate-release	0.10 (0.07)	1.84 (1.31)
Unknown	0.16 (0.11)	1.08 (0.77)
Reason for purchase, n (%)		
To prevent or treat withdrawal	0 (0)	10 (1.32)
For enjoyment or to get high	0 (0)	45 (5.95)
To resell	1 (3.23)	8 (1.06)
To self-treat pain or another medical condition	14 (45.16)	219 (28.97)
To come down	0 (0)	3 (0.4)
Missing or did not report[a]	16 (51.61)	471 (62.3)

[a]Website users might skip this question, indicate they do not wish to answer, do not know the answer, or the question was not asked; the question was added in September 2016.

Regression models were used to test whether there were differences in street prices or the number of sales between tapentadol and oxycodone (Table 4). The first set of models were linear models that tested the differences in street prices. In a simplified model that used only the year of sale as a covariate, the effect between drugs was not significant ($P=.67$). However, in the simplified model, there were 9 influential points in the regression. Of these 9 points, 8 (89%) were from tapentadol, and many were at relatively high prices. These points strongly influence the estimate of the difference in price toward the null hypothesis (ie, no difference between drugs). Given the small number of observed points, removing these points would substantially hamper the power of the model. When adjustments for potency of the drug were added, the effect of the drug was

still not significant (P=.34). Only the MME of drug sales significantly predicted the price. For a 10-MME increase in the strength of the drug, the illicit price increased by 7.8% (P<.001) after adjusting for the year and drug. The second set of models were Poisson models that tested the differences in the number of sales. The simplified model used only total website activity as a covariate, and the effect of the drug was significant (P<.001). However, when adjustments for licit availability were added, the effect of the drug was no longer significant (P=.98). The effect of standard units sold was significant (P=.03), but

the effect on the number of illicit sale reports was relatively small. A 100,000 unit increase in standard units sold increased the likelihood of an illicit report by only 0.1%. Over the 3-year period, there were relatively few reports of sales, particularly for tapentadol. Notably, the second model to estimate the number of reports had only 10 tapentadol reports from 2016 to 2018. It is likely that both models are underpowered to detect meaningful differences between drugs in models with more covariates.

Table 4. Modeling differences in street price and number of sales.

Parameters	Model estimate	P value	Exponentiated parameter (95% CI)
Differences in street price[a]			
Simplified linear model			
Intercept	2.36	<.001	10.6 (6.93-16.3)
Drug (reference: tapentadol)	0.089	.67	1.09 (0.729-1.64)
Year	−0.032	.35	0.968 (0.904-1.04)
Linear model with potency added			
Intercept	2.10	<.001	8.19 (5.36-12.5)
Drug (reference: tapentadol)	0.191	.34	1.21 (0.816-1.79)
Year	−0.0326	.33	0.968 (0.906-1.03)
10-MME[b] increase	0.0754	<.001	1.08 (1.05-1.10)
Quarterly number of sales			
Simplified Poisson model			
Intercept	−1.23	.004	0.294 (0.127-0.677)
Drug (reference: tapentadol)	3.99	<.001	54.2 (27.0-109)
Total website reports	0.00465	<.001	1.005 (1.003-1.007)
Poisson model with availability added			
Intercept	−2.03	<.001	0.131 (0.0457-0.378)
Drug (reference: tapentadol)	0.0482	.98	1.05 (0.0289-38.1)
Total website reports	0.00557	<.001	1.006 (1.003-1.008)
100,000-unit increase in standard units sold	0.00882	.03	1.01 (1.00-1.02)

[a]Street price, the dependent variable, was log-transformed for modeling.

[b]MME: morphine milligram equivalents.

Discussion

Principal Findings and Policy Implications

The results presented here indicate that Australians using the web perceive tapentadol as safer and less desirable for illicit activities than oxycodone. The overall sentiment of tapentadol posts tended toward promoting therapeutic use, implying that the population using the web uses tapentadol as intended more so than oxycodone. If reflective of the larger national population, the web-based content presented here could indicate that major consequences of addiction, overdose, death, and other adverse events are less common for those who use tapentadol than for those who use oxycodone. The conclusions were strengthened as multiple types of posts were analyzed. Collecting data from both forum-type sources and social media sources allows for

more diverse discussion topics to be analyzed [9]. Both the low percentage of posts promoting abuse and the lack of reports of tapentadol street sales suggest there is little desire for tapentadol as a drug of abuse. As tapentadol is a drug with a mixed mechanism of action [15], there are pharmacological reasons that account for its lower desirability. We originally hypothesized that because tapentadol had a lower μ-opioid receptor affinity [16], there would be lower street prices once potency was accounted for. Neither the simplified model nor one with potency added detected significant differences between the drugs. Although no evidence was detected for the original hypothesis, once potency was added to the model, higher potency drug sales led to significantly higher prices. If higher prices indicate higher desirability, this suggests that a drug control policy that gives more attention to high potency doses

could be effective in curbing market desirability. However, given the relatively recent approval of tapentadol, more familiarity among individuals who use drugs might increase the desirability (and therefore, the street price) independent of potency.

Control of prescription drug supply can improve health outcomes. In the United States, declining prescriptions for opioids has contributed to declining adverse health outcomes from prescription painkillers [17]. As diverted drugs are frequently found in overdose deaths [5], prevention of diverted supply could mitigate overdose mortality and other adverse outcomes. The difference in illicit market activity between the drugs suggests that differences in diversion control policies should be considered. Both substances are Schedule 8 drugs, but more nuanced policies with stricter controls on more desirable drugs could be more appropriate.

Public Health Surveillance Implications

Ongoing pharmacoepidemiological surveillance of prescription opioid use and harms in Australia is scarce. A review found 15 reports from 2000 to 2018 [18]. The National Drug and Alcohol Research Centre produces annual reports on illicit drug harms [2], but information on prescription drugs is limited. Not all drugs have the same desirability, effect on the body, or potential for harm. Our study has reinforced the differences between the 2 opioids in illicit availability and web-based perceptions of safety, 2 factors that could influence eventual harm. Differences among other prescription drugs are likely to exist. Elucidating these differences on a broader scale than in this work would help identify the drugs best suited to have the highest benefit to those needing opioid pain relief and lowest risk to the Australian public. Given the scarcity of surveillance data, descriptive results derived from internet sources can be used as a primer for more complex approaches, such as system models quantifying trafficking or risky behaviors (eg, injection or concomitant use).

The approach to analyzing web content presented here used a systematic manual coding method combined with random sampling of the entire population of scraped posts, which presented several advantages. This avoided limitations that might arise when using natural language processing and machine learning to train on rare outcomes (such as drug tampering). Although internet posts can be ambiguous and lack context [19], manual coding is advantageous in identifying novel or rare content. Manual coding allowed for a large list of safety-related drug use topics, and this study is the first to characterize

sentiment in terms of safe drug use, rather than as a form of approval [20]. Furthermore, the entire population of scraped posts was available for sampling, which eliminated several (but not all) sources of selection bias that might arise from smaller scale studies. Web posts were collected from all publicly scrapable Australian websites (including social media, blogs, and forums). Other approaches to internet surveillance tend to focus on social media, which could exclude certain types of content [9]. Sampling leverages frequentist methods for CIs, permitting valid inferences within the context of the sampling frame, even for rare outcomes. Finally, the overall approach presented here derived results from (1) unstructured web content and (2) structured, crowdsourced data entry. This combined study design allowed complementary interpretation of drug desirability using different methodological approaches.

Limitations

The primary limitation of this study is that the sampling frames limit generalizability. The sampling frame of web posts does not include private websites (eg, private Reddit forums and Bluelight.org), which likely contain pertinent information. Australians also have access to forums outside the country, which could influence their opinions. If the keyword list was incomplete, then some posts would not be scraped, resulting in a selection bias. Illicit sales data are collected through crowdsourcing from the StreetRx website [21], and bias could exist between illicit sales reported to the website and the universe of all illicit sales. This would primarily cause the number of illicit sales to be underestimated because not all illicit sales would be entered into the website. Self-report data could also be subject to recall bias. Unless there is a differential bias in the underestimation between tapentadol and oxycodone, there would be a small impact on the comparative conclusions from this study. No information on the activities before the sale is available via the StreetRx website. Information describing causal elements that lead to diversion would be beneficial in crafting policies targeted toward drugs at the highest diversion risk. Finally, as an observational study, the number of reported street sales could not be controlled, leading to lower power to detect differences between drugs.

Conclusions

Australians searching the web for opinions about drug use will generally view discussion of tapentadol as safer than oxycodone. Although strength and licit availability are significant factors in the illicit market, the illicit sales market for tapentadol was smaller than that of oxycodone.

Authors' Contributions

JB contributed to the design and drafting of the work; ZRM and GB contributed to the design, analysis, and drafting; and JLI and RCD contributed to the design and critical intellectual content of the work. All authors have approved this work.

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Conflicts of Interest

Multimedia Appendix 1
Keywords for web content search.
[DOCX File , 16 KB - publichealth_v7i12e29187_app1.docx]

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Abbreviations

MME: morphine milligram equivalents

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<u>Original Paper</u>

Utility of Facebook's Social Connectedness Index in Modeling COVID-19 Spread: Exponential Random Graph Modeling Study

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Abstract

Background: The COVID-19 (the disease caused by the SARS-CoV-2 virus) pandemic has underscored the need for additional data, tools, and methods that can be used to combat emerging and existing public health concerns. Since March 2020, there has been substantial interest in using social media data to both understand and intervene in the pandemic. Researchers from many disciplines have recently found a relationship between COVID-19 and a new data set from Facebook called the Social Connectedness Index (SCI).

Objective: Building off this work, we seek to use the SCI to examine how social similarity of Missouri counties could explain similarities of COVID-19 cases over time. Additionally, we aim to add to the body of literature on the utility of the SCI by using a novel modeling technique.

Methods: In September 2020, we conducted this cross-sectional study using publicly available data to test the association between the SCI and COVID-19 spread in Missouri using exponential random graph models, which model relational data, and the outcome variable must be binary, representing the presence or absence of a relationship. In our model, this was the presence or absence of a highly correlated COVID-19 case count trajectory between two given counties in Missouri. Covariates included each county's total population, percent rurality, and distance between each county pair.

Results: We found that all covariates were significantly associated with two counties having highly correlated COVID-19 case count trajectories. As the log of a county's total population increased, the odds of two counties having highly correlated COVID-19 case count trajectories increased by 66% (odds ratio [OR] 1.66, 95% CI 1.43-1.92). As the percent of a county classified as rural increased, the odds of two counties having highly correlated COVID-19 case count trajectories increased by 1% (OR 1.01, 95% CI 1.00-1.01). As the distance (in miles) between two counties increased, the odds of two counties having highly correlated COVID-19 case count trajectories decreased by 43% (OR 0.57, 95% CI 0.43-0.77). Lastly, as the log of the SCI between two Missouri counties increased, the odds of those two counties having highly correlated COVID-19 case count trajectories significantly increased by 17% (OR 1.17, 95% CI 1.09-1.26).

Conclusions: These results could suggest that two counties with a greater likelihood of sharing Facebook friendships means residents of those counties have a higher likelihood of sharing similar belief systems, in particular as they relate to COVID-19 and public health practices. Another possibility is that the SCI is picking up travel or movement data among county residents. This suggests the SCI is capturing a unique phenomenon relevant to COVID-19 and that it may be worth adding to other COVID-19 models. Additional research is needed to better understand what the SCI is capturing practically and what it means for public health policies and prevention practices.

Introduction

The COVID-19 (the disease caused by the virus SARS-CoV-2) pandemic has underscored the need for additional data, tools, and methods that can be used to combat emerging and existing public health concerns. Since March 2020, there has been substantial interest among researchers, public health professionals, infectious disease experts, and social media companies themselves in using social media data to both understand and intervene in the pandemic [1-7]. This is understandable given that nearly half of the world's population (49% or 3.8 billion people) are social media users, with as many as 7 in 10 Americans reporting using at least one social media site.

One early example of using social media for novel purposes related to the pandemic was done by economists with expertise in modeling geographic and social data, who used a relatively new data set from Facebook called the Social Connectedness Index (SCI) to understand the spread of COVID-19 in the emerging hot spots of Italy and Westchester, New York [8]. The SCI is a measure of the strength of connectedness between two geographic areas as measured by Facebook friendships [9,10]. The researchers found that the SCI was associated with confirmed COVID-19 cases after controlling for geographic distance to the two early hot spots as well as income and population density [8].

Other researchers with backgrounds in economics, engineering, and management have also explored the utility of this data set as it relates to COVID-19. One group of researchers found that households in counties with relatively stronger social connections to early hot spots in China and Italy (as measured by the SCI) were more likely to comply with stay-at-home orders [11]. Others found that public health prevention practices that people in a given region adopt are significantly influenced by the policies and behaviors of people in other regions with whom there is a relatively strong SCI [12]. In other words, even between distant regions, the SCI was associated with people in those two regions having similar COVID-19–related behaviors, suggesting people are influenced by their social connections.

Building off this work, we sought to use the SCI to examine how social similarity of Missouri counties could explain similarities of COVID-19 cases over time. Additionally, we aimed to add to the body of literature on the utility of the SCI by using a novel modeling technique that allows for the modeling of relational data [13]. To our knowledge, this technique has not been used with the SCI, which is a relational data set, thus making it a highly relevant and appropriate method.

Methods

Study Design

In this cross-sectional study, we analyzed publicly available data to test the association between the SCI and COVID-19 spread in Missouri using exponential random graph models (ERGMs). This study was reviewed by the institutional review board and deemed nonhuman participant research.

Data Sources

Social Connectedness Index

The SCI was obtained through the Facebook Data for Good program. The Facebook Data for Good program creates and makes available a variety of tools and data sets that are built from privacy-protected data from the Facebook platform and other publicly available data sources such as satellite imagery. Data sets in the program include the SCI, electrical distribution grid maps, the Inclusive Internet Index (a measure of internet accessibility), the Climate Change Survey, and more.

The SCI measures the relative probability of a Facebook friendship link between a given Facebook user in location A and a user in location B. It is calculated by dividing the number of Facebook friends between two locations divided by the number of Facebook users in location A multiplied by the number of users in location B. The SCI data set includes values for locations from the zip code level up to the country level and is an anonymized snapshot from a single point in time. The locations of Facebook users are assigned based on their information and activity on Facebook, including their public profile information as well as device and connection information.

The SCI is a single data set calculated based on Facebook friendships in March 2020; therefore, additional time points of the SCI could not be included in the model or in sensitivity analyses.

COVID-19 Data

To determine which Missouri counties had similar COVID-19 spread, we used data obtained from the Johns Hopkins University's Coronavirus Resource Center. The data on United States COVID-19 cases and deaths made available through the Center are compiled by the Johns Hopkins Center for Systems Science and Engineering, which is updated daily. They retrieve all state data from their respective state departments of health or other local government reporting agency, and for Missouri, those sources are the Missouri Department of Health, St. Louis City Department of Health, St. Louis County Department of Health, and Nodaway County Health Center. We obtained daily new case counts for every county in Missouri starting on March 8, 2020 (the day the first case of COVID-19 was recorded in

the state), through September 30, 2020, which was the time we conducted the analyses.

Population, Rurality, and Distance Data

Data on each county's population and its rurality were obtained from the United States Census Bureau from the 2010 Census database [14]. Distance between each county pair was obtained from the 2020 TIGER/Line shapefiles, also available from the US Census Bureau [15].

Analysis

All analyses were conducted using R version 4.0.3 (R Foundation for Statistical Computing) with the packages statnet and ergm. Alpha levels were set at .05.

Data Management

Every county pair has an SCI value, so this variable did not need to be computed, though this variable was log transformed.

To create a measure of two counties' similarity in COVID-19 case counts, we used the daily new case counts as each county's "trajectory" of COVID-19 and conducted a Pearson correlation test between each county's trajectory. We then used a 0.60 correlation coefficient cutoff to classify each county pair as either having highly correlated COVID-19 case count trajectories or not. The 0.60 cutoff was chosen based on established recommendations [16]. This binary variable was our primary outcome.

The total county population was log transformed, and the distance between every county pair was calculated using the distance between the centroids of each county in the shapefiles. The percent of the county that was classified as rural was not computed or transformed before being entered into the analytical model.

We originally intended to include demographic characteristics of residents at the county level, but given the lack of diversity on characteristics such as age, race, and ethnicity across Missouri, including these data in the model caused it to not converge. Therefore, we were unfortunately unable to include them.

Modeling

Our basic modeling approach was to examine the relationship between the social media connections (as measured by the SCI) and COVID-19 case counts across Missouri counties. To do this, we used exponential random graph modeling.

ERGMs model relational data, and the outcome variable must be relational and binary, representing the presence or absence of a relationship. In our model, this was the presence or absence of a highly correlated COVID-19 case count trajectory between two given counties in Missouri. The model was built sequentially, starting with a null model. Next, all covariates except the SCI were entered into the model. Distance between every county pair was entered into the model as a relational term, meaning it represented a relationship between every county pair. Total county population and the percent of the county classified as rural were both entered into the model as object-level terms, meaning instead of the data representing a relationship between every county pair, these data were singular attributes of each county. After running this model, the SCI was entered into the last model and the Akaike information criterion (AIC) was used to compare overall model fit. Odds ratios (ORs) and 95% CIs are also reported.

Results

COVID-19 Case Count Trajectories

Missouri reported its first COVID-19 case on March 8, 2020, and at the time of analysis (September 30, 2020) the state had reported 129,733 cumulative cases with a 7-day average of 1127. Each county's average daily new case count data are available in Multimedia Appendix 1.

Of the 6555 different county pairs ([115 counties * 114] / 2 = 6555), the range of correlations was –0.09 to 0.90 with an average correlation of 0.36. Of those, 1114 county pairs had COVID-19 case count trajectories correlated at 0.60 or greater. These 1114 county pairs then represented the relationship we predicted in the model.

Exponential Random Graph Model

The results of the sequential model building process are presented in Table 1. In the final model, we assessed the likelihood that two counties in Missouri had highly correlated COVID-19 case count trajectories based on their level of social connectedness, controlling for the total population size of the counties, the percent of the counties that were rural, and the distance between the two counties. The model fit improved sequentially as evident by the decreasing AIC value as more covariates were entered into the model.

Table 1. Sequential building of an exponential random graph model of the relationship between the Social Connectedness Index (SCI) and Missouri counties' similar COVID-19 case counts from March to September 2020.

	Null model[a]		Model 1[b]		Model 2[c,d]		
	b (SE)	P value	b (SE)	P value	b (SE)	OR[e] (95% CI)	P value
Intercept	–2.40 (0.04)	<.001	–14.63 (0.12)	<.001	–14.85 (0.94)	0.00 (0.00-0.00)	<.001
Total county population (logged)	N/A[f]	N/A	0.44 (0.04)	<.001	0.51 (0.07)	1.66 (1.43-1.92)	<.001
Percent of county that is rural	N/A	N/A	0.01 (0.00)	.001	0.01 (0.00)	1.01 (1.00-1.01)	<.001
Distance in miles between county pairs	N/A	N/A	–0.62 (0.16)	<.001	–0.55 (0.15)	0.57 (0.43-0.77)	<.001
SCI[g] (logged)	N/A	N/A	N/A	N/A	0.16 (0.04)	1.17 (1.09-1.26)	<.001
Model fit							
Akaike information criterion	3251	N/A	2707	N/A	2691	N/A	N/A
Bayesian information criterion	3773	N/A	2741	N/A	2731	N/A	N/A
Log likelihood (*df*)	–1882.008 (1)	N/A	–1485.785 (4)	N/A	–1477.192 (5)	N/A	N/A

[a]Null model with no covariates.

[b]Model 1 included all covariates, except the SCI.

[c]Model 2 included all covariates, including the SCI.

[d]The geometrically weighted edgewise shared partner term *gwesp* was included in models 1 and 2.

[e]OR: odds ratio.

[f]N/A: not applicable.

[g]SCI: Social Connectedness Index.

All covariates were significantly associated with two counties having highly correlated COVID-19 case count trajectories. As the log of a county's total population increased, the odds of two counties having highly correlated COVID-19 case count trajectories increased by 66% (OR 1.66, 95% CI 1.43-1.92). (Log scales are commonly used when examining population growth; it also is helpful here for comparing changes in ratios or proportions.) As the percent of a county classified as rural increased, the odds of two counties having highly correlated COVID-19 case count trajectories increased by 1% (OR 1.01, 95% CI 1.00-1.01). As the distance (in miles) between two counties increased, the odds of two counties having highly correlated COVID-19 case count trajectories decreased by 43% (OR 0.57, 95% CI 0.43-0.77). For our main outcome, we found that as the log of the SCI increased between two counties, the odds of those two counties having highly correlated COVID-19 case count trajectories increases by 17% (OR 1.17, 95% CI 1.09-1.26), controlling for the counties' population size, rurality, and the distance between the two counties.

Discussion

Principal Findings

We found that as the likelihood of Facebook friendships between two counties increases, as measured with the SCI, the odds of those two counties having strong, positive correlations of their COVID-19 daily new case count trajectories also significantly increased. This relationship remained significant when controlling for the distance between the two counties, their rurality, and their total population sizes.

These results build upon and align with prior, preliminary research using the SCI to understand COVID-19 spread. [8,11,12] These results also confirm the "signal" in the SCI "noise," meaning there is something uniquely captured in the SCI and Facebook friendships that cannot be explained by geography, distance, or population size.

The primary reasons for conducting this study were to assess if the relationship between the likelihood of Facebook friendships and COVID-19 spread could be explained by other factors. For example, it makes intuitive sense that two urban counties are more likely to have similar COVID-19 case count trajectories because, in general, urban areas had more cases earlier in the pandemic than rural areas [17]. It also makes sense that two urban counties would be more likely to share Facebook friendships than an urban and a rural county [18]. Likewise, it is reasonable to expect that two counties next to each other would be more likely to share Facebook friendships than two counties hundreds of miles apart [9]. Could the SCI signal as it relates to COVID-19 spread be explained by these other factors? Our results suggest there is something above and beyond these other factors that the SCI represents; however, it is not clear what exactly that is.

One possibility is that people tend to form friendships and social connections to those who share similar belief systems [12,19]. This could suggest that two counties with a greater likelihood

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of sharing Facebook friendships means residents of those counties have a higher likelihood of sharing similar belief systems, in particular as they relate to COVID-19 and public health practices. For example, perhaps residents of two counties with a relatively high SCI value are equally likely to wear masks or not, restrict travel or not, etc. Residents sharing similar public health practices could explain why counties with relatively high SCI values are also more likely to have similar COVID-19 case count trajectories. Similar results have been found in earlier studies using the SCI [12].

Another possibility is that the SCI is picking up travel or movement data among county residents. People are more likely to form Facebook friendships with people they have offline connections with, and these offline connections may stem from a physical location such as a school, place of worship, or place of employment [20,21]. Therefore, a resident of one county may have a lot of Facebook friends in a neighboring county because that resident works at a large business in that neighboring county and travels there multiple days a week. That resident may also frequent restaurants and other businesses near their place of employment, increasing the opportunities to form friendships in this neighboring county. In rural areas, residents often travel long distances [22,23], so the SCI may indeed be capturing, in part, a person's likelihood of traveling to another county. This has relevance, of course, to COVID-19 spread.

In particular, the results of this study could be relevant for state and county public health departments in Missouri that are trying to implement COVID-19 prevention practices, such as setting event/business capacity limits or enacting mask requirements. Knowing that social connectedness, as measured through Facebook friendships, is associated with COVID-19 spread even after controlling for the distance between two counties might suggest that mitigation practices should extend beyond a regional approach and be implemented statewide.

Additional investigation is needed to more fully understand the SCI. Our study and others' prior work have demonstrated a signal, but now more research is needed to fully decipher that signal. We also encourage Facebook to continue to update and refine the SCI, so that researchers can understand more of what in the signal it is capturing and how it relates to COVID-19. However, while that work is underway, there may be utility in using the SCI in models of COVID-19 spread even without knowing what it is capturing. In the case of a global pandemic, the need for timely data and models to inform mitigation efforts is critical. If including the SCI in these models can improve model fit and serve as a control for more fully understood variables, then it is worth including in the model.

Limitations

There are key caveats that must be acknowledged. First, more granular data are not included in the SCI, which would add greater clarity to the results. For example, we would have liked to have known the demographics of Facebook users in a given county and if the SCI was different for certain demographic subgroups in each county (eg, are older Facebook users in county 1 more likely to form friendships with older users in county 2). Second, the SCI was a cross-sectional data set created in March 2020, while our COVID-19 data were longitudinal from March to September 2020. It is unknown if, and by how much, the SCI changes over time and if this would impact our modeling. Third, we are network analysis and modeling experts; we are not epidemiologists or infectious disease experts. Therefore, we approached this study from a methodological perspective, not a public health perspective, and we acknowledge there are additional factors that should be studied before any policies or prevention practices are enacted based on these results.

Conclusions

This study further validated the signal raised by the SCI as it relates to COVID-19 spread. It is also the first study to use ERGM to model Facebook friendships as they relate to COVID-19 spread. We found that as the social connectedness increases between two counties, the odds of those two counties having highly correlated COVID-19 case count trajectories increases by 18%, controlling for the counties' population size, rurality, and the distance between the two counties. This suggests that the SCI is capturing a unique social connection phenomenon that is important in understanding disease transmission and is specifically relevant to COVID-19. Additional research is needed to better understand what the SCI is capturing practically and what it means for public health policies and prevention practices, but in the short term, researchers may consider adding it to other COVID-19 models to improve model fit.

Authors' Contributions

BP was responsible for the study design. BP, KP, JML, and DAL were responsible for the data analysis. BP was responsible for drafting the manuscript, with KP, JML, and DAL revising.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Missouri Counties' COVID-19 Daily Case Counts.
[DOCX File , 22 KB - publichealth_v7i12e33617_app1.docx]

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Abbreviations

AIC: Akaike information criterion

ERGM: exponential random graph model
OR: odds ratio
SCI: Social Connectedness Index

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Original Paper

Understanding Health Communication Through Google Trends and News Coverage for COVID-19: Multinational Study in Eight Countries

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Abstract

Background: Due to the COVID-19 pandemic, health information related to COVID-19 has spread across news media worldwide. Google is among the most used internet search engines, and the Google Trends tool can reflect how the public seeks COVID-19–related health information during the pandemic.

Objective: The aim of this study was to understand health communication through Google Trends and news coverage and to explore their relationship with prevention and control of COVID-19 at the early epidemic stage.

Methods: To achieve the study objectives, we analyzed the public's information-seeking behaviors on Google and news media coverage on COVID-19. We collected data on COVID-19 news coverage and Google search queries from eight countries (ie, the United States, the United Kingdom, Canada, Singapore, Ireland, Australia, South Africa, and New Zealand) between January 1 and April 29, 2020. We depicted the characteristics of the COVID-19 news coverage trends over time, as well as the search query trends for the topics of COVID-19–related "diseases," "treatments and medical resources," "symptoms and signs," and "public measures." The search query trends provided the relative search volume (RSV) as an indicator to represent the popularity of a specific search term in a specific geographic area over time. Also, time-lag correlation analysis was used to further explore

the relationship between search terms trends and the number of new daily cases, as well as the relationship between search terms trends and news coverage.

Results: Across all search trends in eight countries, almost all search peaks appeared between March and April 2020, and declined in April 2020. Regarding COVID-19–related "diseases," in most countries, the RSV of the term "coronavirus" increased earlier than that of "covid-19"; however, around April 2020, the search volume of the term "covid-19" surpassed that of "coronavirus." Regarding the topic "treatments and medical resources," the most and least searched terms were "mask" and "ventilator," respectively. Regarding the topic "symptoms and signs," "fever" and "cough" were the most searched terms. The RSV for the term "lockdown" was significantly higher than that for "social distancing" under the topic "public health measures." In addition, when combining search trends with news coverage, there were three main patterns: (1) the pattern for Singapore, (2) the pattern for the United States, and (3) the pattern for the other countries. In the time-lag correlation analysis between the RSV for the topic "treatments and medical resources" and the number of new daily cases, the RSV for all countries except Singapore was positively correlated with new daily cases, with a maximum correlation of 0.8 for the United States. In addition, in the time-lag correlation analysis between the overall RSV for the topic "diseases" and the number of daily news items, the overall RSV was positively correlated with the number of daily news items, the maximum correlation coefficient was more than 0.8, and the search behavior occurred 0 to 17 days earlier than the news coverage.

Conclusions: Our findings revealed public interest in masks, disease control, and public measures, and revealed the potential value of Google Trends in the face of the emergence of new infectious diseases. Also, Google Trends combined with news media can achieve more efficient health communication. Therefore, both news media and Google Trends can contribute to the early prevention and control of epidemics.

Introduction

In late December 2019, a cluster of patients with pneumonia of unknown etiology was reported in Wuhan, China [1]. Soon after, a new type of coronavirus was identified as the pathogen causing this pneumonia [2], which was named COVID-19 by the World Health Organization (WHO) [3,4]. As the number of COVID-19 infections continued to increase, the WHO declared COVID-19 a pandemic on March 11, 2020 [5]. Globally, as of July 2020, there have been more than 10.3 million confirmed cases and more than half a million deaths in over 200 countries [6], which caused global supply chain disruptions during the COVID-19 pandemic [7]. Therefore, the prevention and control of the epidemic require a great deal of urgency.

Surveillance is an essential component of infectious disease control [8,9]. Nevertheless, traditional public health surveillance of epidemic diseases is based on government-implemented data gathering, resulting in data that can take years to become available [10]. Traditional laboratory monitoring is still used in most countries, but in recent years, some countries have tried to use internet search query data to assist traditional public health surveillance, such as Google Flu Trends (GFT) and Google Dengue Trends [11-14]. In the future, various types of internet data, such as search data, will offer more possibilities for better disease prevention and control [11,12]. Google Trends is one of the most popular open online tools for assessing data from public internet searches and has multiple advantages [11]. Specifically, it collects real-time data automatically, and provides quantitative and qualitative data applied to the informatics research of various communicable and noncommunicable diseases [13,15]. For example, Ginsberg et al [16] employed Google to track influenza-like illness in a

population. Ocampo et al [17] were the first to use Google search queries in malaria surveillance. Glynn et al [18] assessed the relationship between breast cancer awareness campaigns and internet search activity from 2004 to 2009 using Google Trends. All of the above research drew similar conclusions: Google Trends can supplement traditional public health surveillance and help us to better understand public response and sentiment to the pandemic. Moreover, Google Trends can help reveal the need for health-related information [11,19].

In addition, news coverage of COVID-19 by mass media played an important role during the outbreak [20]. As a source of information, news coverage can provide important information to the public and, in turn, guide people to form positive, healthy behaviors or prevent the development of unhealthy behaviors. News coverage influences the behaviors of the public by both direct and indirect routes: news content can directly influence the behavior of the recipients or indirectly influence interpersonal discussion and transmission of coverage content [21,22]. For instance, the public's online search behaviors for information about diseases increase during disease awareness months [18,23]. Moreover, some researchers have noted that internet search behaviors and news coverage were relevant to traditional data monitoring, and the latter appeared to promote internet searches for health topics [24,25]. In the area of public health [26], when there is an emerging pandemic, news media as a tool can inform the public about prevention and control strategies. On the other hand, news media can also have a negative side. For example, news coverage might not be based on expert assessments and may hold relatively independent views. Also, news coverage might cause public panic. Although newsworthiness is complex, analyzing internet data can help improve the effectiveness of public communication [19]. In other words, news coverage plays an important role in health

communication. Hence, acquiring available online data, including internet search query data and social media information, can provide novel insights for the prevention and control of COVID-19 [27].

To date, only a few studies have focused on internet search data combined with news coverage data. This study, therefore, used Google query data, news coverage data, and new COVID-19 case data to understand health communication during the early stage of this epidemic.

Methods

Overview

In this study, we collected data from Google Trends, news coverage, and new COVID-19–related daily cases from January 1 to April 29, 2020 (120 days), which is considered the early period of the epidemic in eight countries: the United States, the United Kingdom, Canada, Singapore, Ireland, Australia, South Africa, and New Zealand. We then described different Google Trends search queries and news coverage trends in different countries to understand the situation of health communication, and we explored the connection between the above and the prevention and control of COVID-19 at the early epidemic stage.

Data Collection

Google Query Data

Google Trends is one of the most popular online tools used to track internet hit search volumes. Users of Google Trends [28] can obtain the search trend data of terms [8]. Google Trends provides a relative search volume (RSV) to depict the popularity of a specific search term in a specific geographic area over a period of time. The value of RSV ranges from 0 to 100. A value of 0 means there was not enough data for this term, and a value of 100 represents the peak popularity for the term [10,29].

Based on a previous study [20], symptoms, treatments and medical resources, measures, and the virus itself were the major topics covered by online media during the early period of the COVID-19 pandemic. Therefore, we selected "diseases," "treatments and medical resources," "symptoms and signs," and "public measures" as search topics, and we used their terms as search terms. Also, due to the limited language of Google Trends, only English-speaking countries were included in this study [30]. According to population size, we selected eight English-speaking countries for the study: the United States, the United Kingdom, Canada, Singapore, Ireland, Australia, South Africa, and New Zealand. RSV data for the above topics in these eight countries, between January 1 and April 29, 2020, were collected and then exported into CSV files. The topics and their query terms are shown in Table 1.

Table 1. Query topics and search terms related to COVID-19.

Query topic	Search terms
Diseases	"coronavirus," "covid-19," and "pneumonia"
Treatments and medical resources	"ventilator," "vaccine," and "mask"
Symptoms and signs	"fever," "cough," "shortness of breath," and "tiredness"
Public measures	"quarantine," "lockdown," and "social distancing"

News Coverage Data

Meltwater is a platform that provides real-time monitoring of domestic and overseas news, and covers more than 300,000 online websites, news clients, and other news media [31]. With wide geographical coverage, Meltwater provides rich news data from different countries. To compare and analyze the news media coverage on COVID-19, we selected news media from eight countries (ie, the United States, the United Kingdom, Canada, Singapore, Ireland, Australia, South Africa, and New Zealand) and searched the news coverage from January 1 to April 29, 2020, with "covid-19" or "coronavirus" as the keywords.

New Case Data

The number of new daily cases of COVID-19 was obtained from the WHO with surveillance data [32].

Analytical Framework

First, we used line graphs to show search trends for different topics in eight countries and attached the epidemic curves of new COVID-19 cases. We then assessed the most popular terms at the country level by comparing their search peaks to determine the characteristics of various terms in different

countries. We then explored the reason for trend fluctuation of search query terms and the fluctuation impact on the prevention and control of COVID-19. Additionally, in Google Trends, the plus sign (+) has the function of "OR" and can be used to connect multiple terms to form an overall term [33]. Thus, we used "+" to integrate multiple terms in different topics into the overall term of the topic, and its RSV represents the overall RSV of the topic. For example, we used the RSV of "coronavirus + covid-19 + pneumonia" to represent the overall RSV of "diseases."

Second, we used the neighborhood average method to smooth the news coverage data [34,35]. Then we used line charts to show news coverage longitudinal trends and identified the similarities and differences of news coverage between eight countries. Furthermore, to further discuss the relationship between news coverage and internet search queries, as well as the relationship between search queries and daily news, we summed the overall RSVs of the four topics to obtain the total RSV and attached it to the line chart along with the epidemic curve of new daily cases to more intuitively observe the changes of the three in the different countries. Moreover, we conducted time-lag correlation analysis between the overall RSVs of search queries for different topics and the number of new COVID-19

cases each day, as well as between the overall RSVs of search queries for different topics and the number of daily news items. The cross-correlation function of the "tseries" package from R software (version 4.0.5; The R Foundation) was used to compute time-lag correlations. In the analysis, a time lag between –17 and +17 days was used, and the Pearson correlation coefficient was used as the correlation measure.

Finally, the interrupted time series analysis was used to evaluate the impact of the appearance of the first COVID-19 case on the four search terms of the topic "symptoms and signs." Taking the date of the first COVID-19 case as the change point, we used the generalized least squares estimator to fit the segmented linear regression model to evaluate the change in the level and slope of the RSV after the first case was discovered. Also, the residual autocorrelation was tested using the Durbin-Watson test. All hypothesis tests used a significance level (α) of .05.

Results

Figures 1 to 4 depict the trends of a specific query topic by its associated query terms, accompanied by new daily cases in the eight countries studied.

For the topic "diseases," we used the search terms "coronavirus," "covid-19," and "pneumonia" (Figure 1). Regarding the term "coronavirus," its RSV increased around January 20, 2020, with a small peak at the end of January 2020. Except for Singapore, the RSV of "coronavirus" in other countries all formed an obvious peak in mid to late March 2020. Regarding the term "covid-19," its RSV began to increase on February 11, 2020, and generated the top search peak from late March to early April 2020; around April 2020, the RSV value of this term surpassed that of "coronavirus." Compared to these two terms, the trend for "pneumonia" fluctuated very little between January and April 2020.

Figure 2 shows the trends of the topic "treatments and medical resources," including the query terms "ventilator," "vaccine," and "mask." The term "mask" was the most searched term, followed by "vaccine" and "ventilator." Regarding the term "mask," there was one main search peak that occurred in April 2020 for all eight countries despite multiple spikes found in specific countries (ie, Singapore, Ireland, Australia, and New Zealand). Regarding the term "vaccine," its RSV for most countries rose starting in March and generated several small spikes near mid-March 2020.

Figure 1. Search query trend of the "diseases" topic and the trend of new daily COVID-19 cases for eight countries from January 1 to April 29, 2020. WHO: World Health Organization.
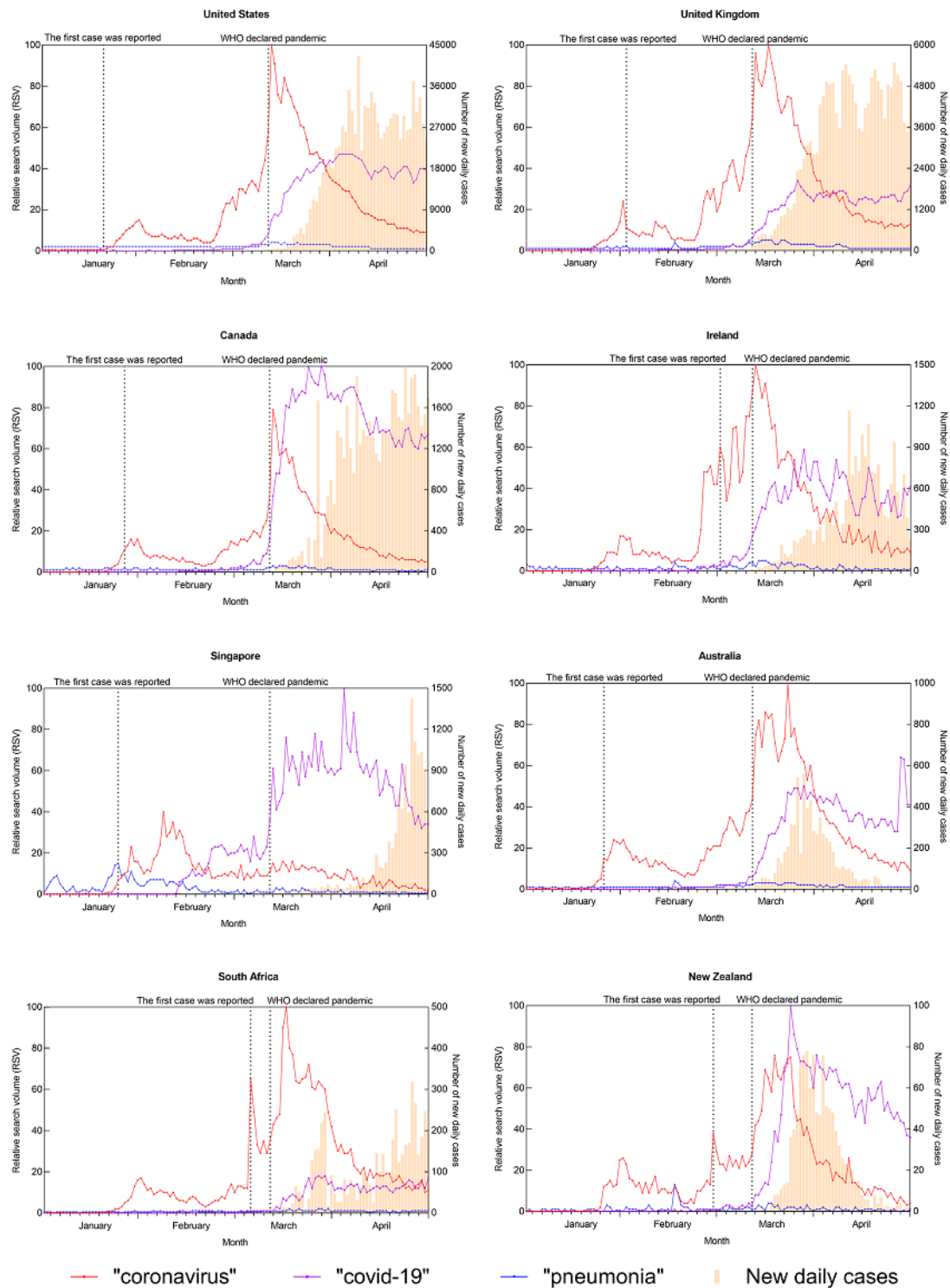
Figure 2. Search query trend of the "treatments and medical resources" topic and the trend of new daily COVID-19 cases for eight countries from January 1 to April 29, 2020. WHO: World Health Organization.
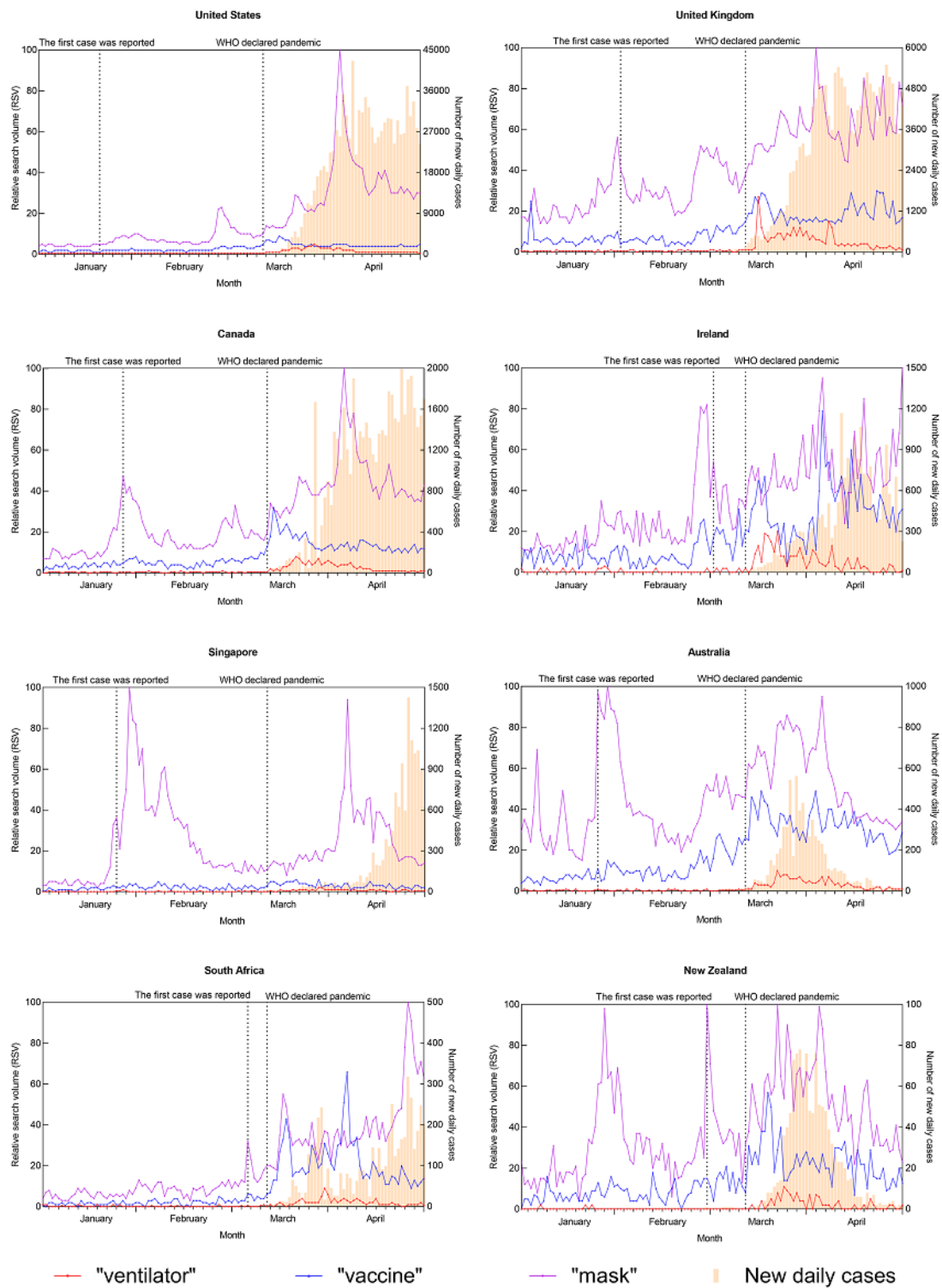

Figure 3 shows the trends for the topic "symptoms and signs" related to COVID-19. Among its query terms, "fever" was the most searched term, followed by "cough," "shortness of breath," and "tiredness." Regarding the terms "fever" and "cough," their top search peaks were formed around mid-March 2020 for all countries except Singapore, slightly earlier than the peak of new daily cases. In Singapore, the search peaks of "fever" and "cough" appeared between late January and mid-February 2020.

Figure 3. Search query trend of the "symptoms and signs" topic and the trend of new daily COVID-19 cases for eight countries from January 1 to April 29, 2020. WHO: World Health Organization.
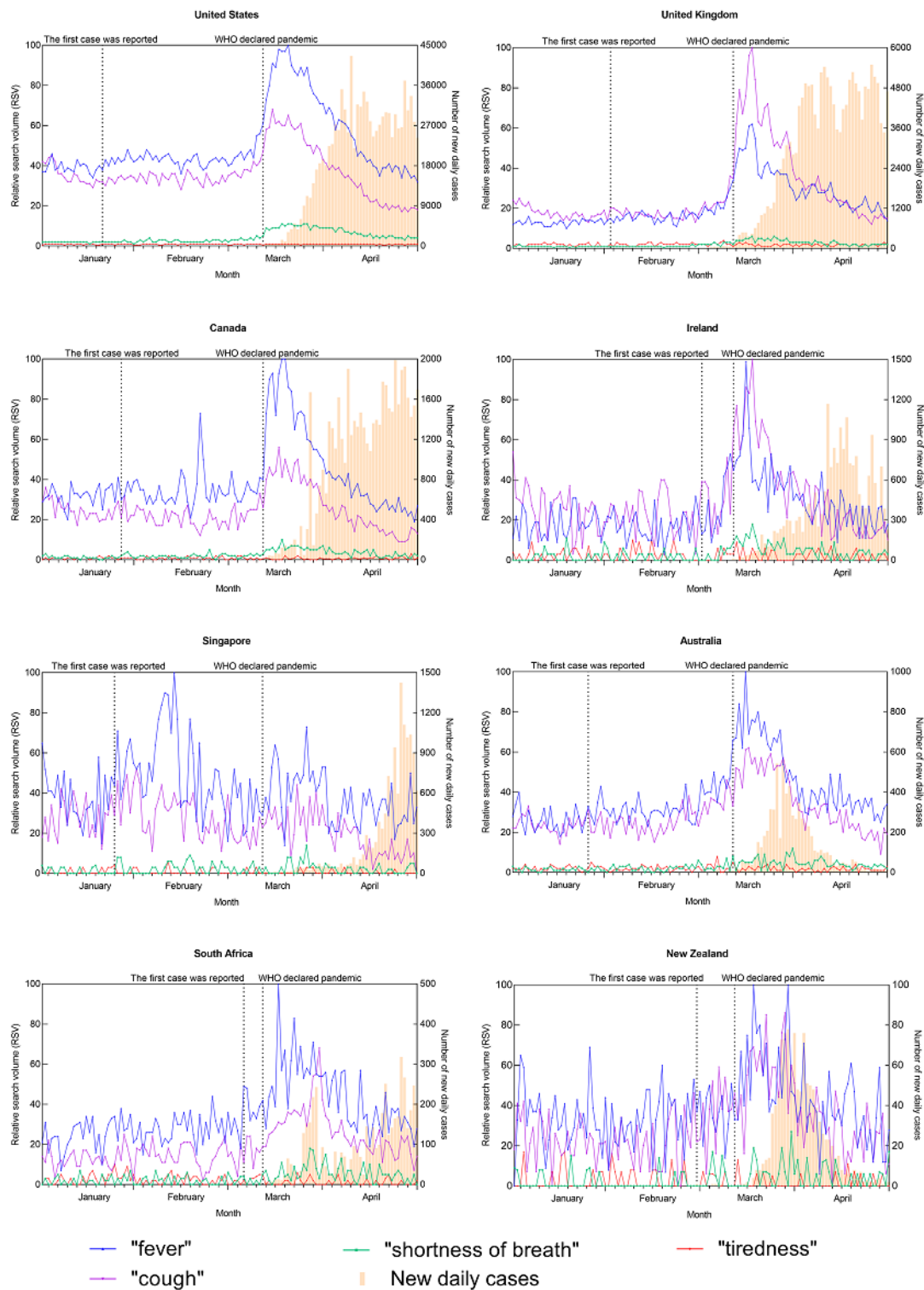

Figure 4 shows the trend for the topic "public measures," using the query terms "quarantine," "social distancing," and "lockdown" during this study period. The RSV of "lockdown" was the highest, followed by "quarantine" and "social distancing." For all these terms, their RSVs were very low before March 2020, and the RSVs of "quarantine" and "lockdown" increased and formed search peaks after mid-March 2020.

Figure 4. Search query trend of the "public measures" topic and the trend of new daily COVID-19 cases for eight countries from January 1 to April 29, 2020. WHO: World Health Organization.
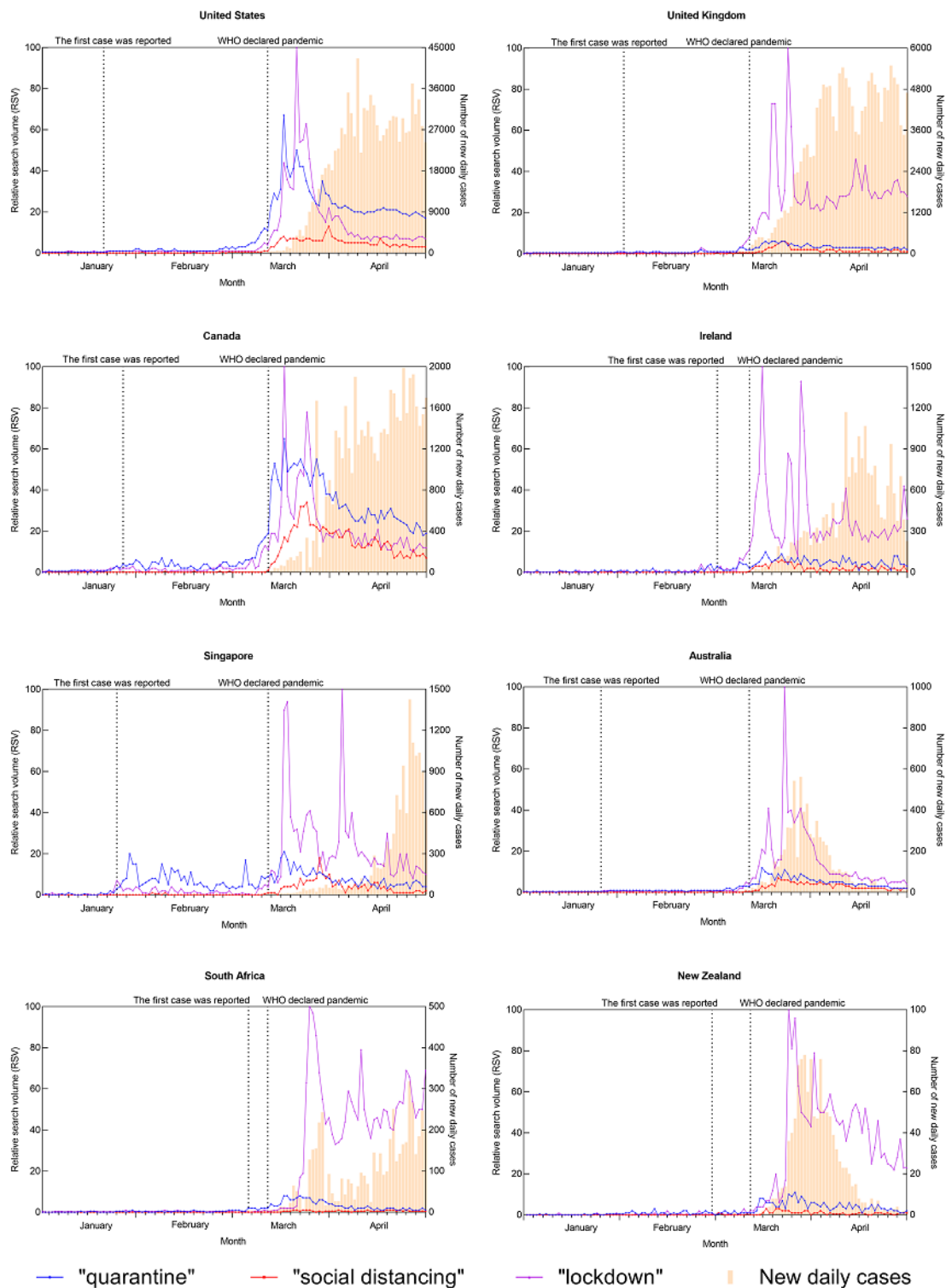
News coverage trends related to COVID-19 are shown in Figure 5. According to the neighborhood average method, we set 7 days as a base period to smooth the number of news coverage items. With the United States as an example, $y_1, y_2,..., y_n$ were the true number of news coverage items from January 1 to April 29, 2020, where n=120. Therefore, the fitted value of news reports S_t could be obtained by $S_t = (y_{t-3} + y_{t-2} + y_{t-1} + y_t + y_{t+1} + y_{t+2} + y_{t+3}) / 7$, where $y_{t-3}, y_{t-2}, y_{t-1}$ represents the true number of news coverage items about 3 days, 2 days, and 1 day before

day t, and $y_{t+3}, y_{t+2}, y_{t+1}$ represents the true number of news coverage items about 3 days, 2 days, and 1 day after day t, where $t=4,..., 117$. Across eight countries, the number of news reports remained low before February 2020. From the end of January, the news report number gradually increased until the end of March 2020 and remained stable afterward. This trend was consistently observed in all countries, except the United States. In contrast, the coverage in the United States soared from around March 29, 2020, far outpacing that in any other country by

nearly 300 times. Also, when comparing the trends of the total RSVs and news coverage, we identified three main patterns across the eight countries, which we have termed Singapore, the United States, and other country patterns. In Singapore, the trends of total RSVs formed two major peaks between late January and mid-February and between mid-March and early April, respectively, and the number of news reports increased gradually to a relatively high level starting from the end of January 2020. In the United States, as the total RSVs reached

a peak around mid to late March 2020, the total RSVs began to decline, while the amount of low-level news coverage suddenly increased to a relatively high level at the end of March 2020. In other countries, the total RSVs and the number of news coverage items spiked in mid-March, but the growth of total RSVs occurred slightly earlier than that of news coverage items. Across all patterns, the total RSVs gradually dropped to the baseline level after the peaks from mid-March to early April, while the news coverage items remained at a higher level.

Figure 5. News coverage trends, new daily cases, and total relative search volumes (RSVs) of four topics for eight countries from January 1 to April 29, 2020. WHO: World Health Organization.
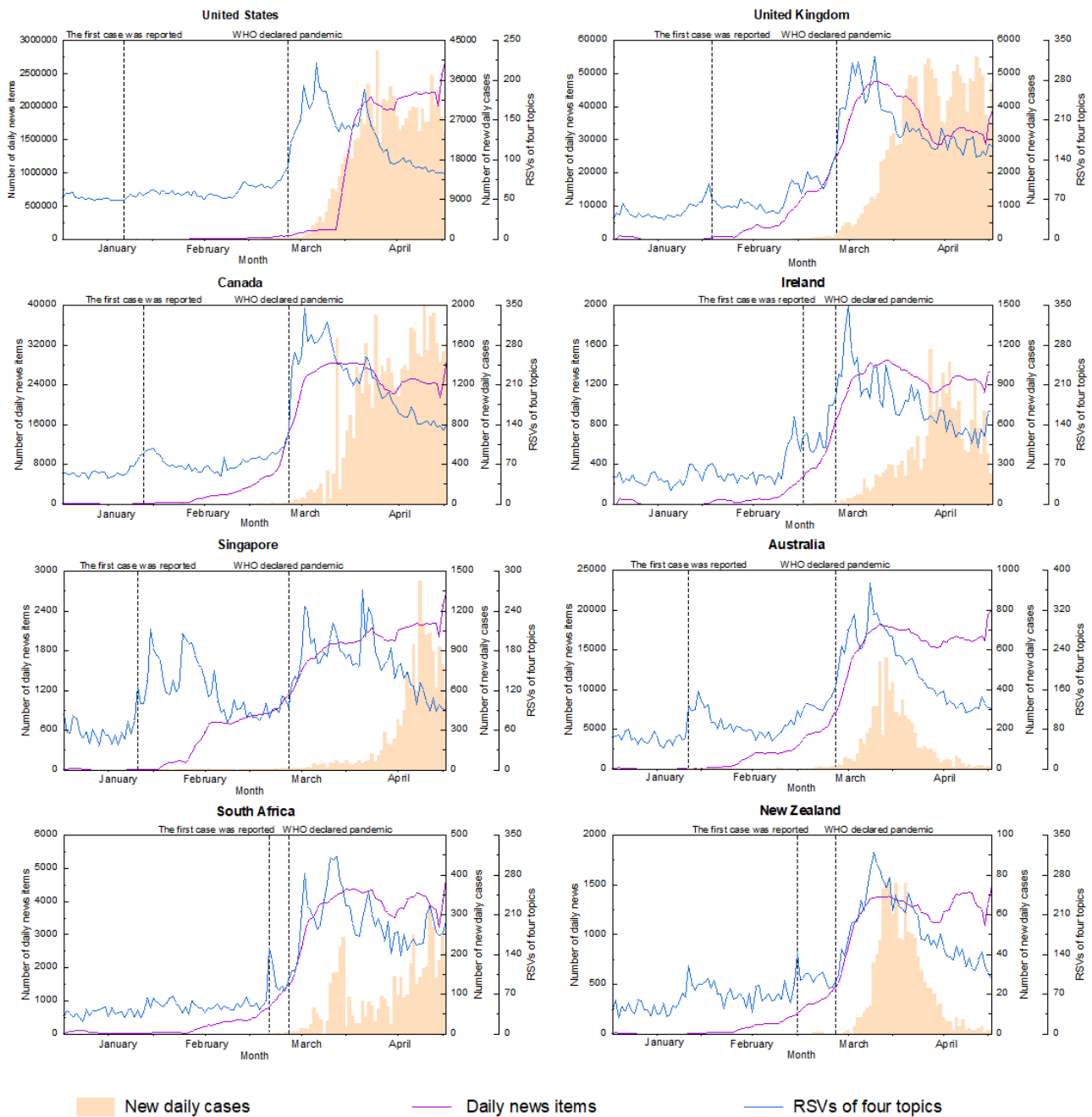

Figure 6 shows the time-lag correlation between the overall RSV for the topic "treatments and medical resources" and the new daily cases. With the exception of Singapore, there was a positive correlation between the overall RSV for the "treatments and medical resources" topic and the new daily cases in all

countries, with the highest correlation being 0.8 for the United States. Also, we divided the eight countries into three categories: (1) Singapore; (2) the United States, the United Kingdom, Canada, South Africa, and Ireland; and (3) Australia and New Zealand. In Singapore, the overall RSV for the "treatments and

medical resources" topic gradually decreased within 17 days before the peak of new daily cases of COVID-19; after forming the peak of new cases, there was a clear negative correlation. In the second category of countries (ie, the United States, the United Kingdom, Canada, South Africa, and Ireland), the overall RSV for the "treatments and medical resources" topic was maintained at a high level for about 17 days before the peak of new daily cases was formed, and then decreased gradually; the correlation remained above 0.2. In other words, the correlation between the overall RSVs of these countries and the new daily cases was maintained at a medium to high level during the time lag of –17 to 17 days. In the third category of countries (ie, Australia and New Zealand), about 1 day and 6 days before forming the peak of new daily infections, the overall RSV for the "treatments and medical resources" topic reached the highest levels, with the maximum correlations being close to 0.8 and 0.7. The time-lag correlation between –17 and 17 days showed a high curve trend in the middle and was low on both sides.

Figure 7 shows that there was a positive correlation between the overall RSV for the topic "diseases" and the number of daily news items in eight countries, with the highest correlation coefficient exceeding 0.8; this indicated that as the number of search queries on the topic of "diseases" increased, the number of daily news items related to COVID-19 also showed an increasing trend. We divided the eight countries into two categories. The first category included only the United States; its maximum correlation appeared in the 17 days before the largest number of daily news reports, and then the correlation gradually decreased within the time lag from –17 to 17 days and showed an obvious negative linear trend. That is, the public's interest in the topic of "diseases" reached its peak 17 days before the peak of news coverage and then gradually decreased over time. The second category included the United Kingdom, Canada, Ireland, Singapore, Australia, South Africa, and New Zealand. During the 17 days before the largest amount of daily news, public interest in the topic of "diseases" remained high. Most of these countries reached the highest level of public interest in "diseases" in about 1 day before the largest amount of daily news; the maximum correlation was close to 0.8. However, within 17 days after the largest amount of daily news, the public gradually lost interest, but most of the correlations remained above 0.2; that is, the correlations maintained a moderate level.

Figure 6. Time-lag correlations of the overall relative search volume (RSV) for the "treatments and medical resources" topic and new daily cases for eight countries from January 1 to April 29, 2020. The area between the two dotted blue lines is the 95% CI of the white noise. If the correlation coefficient of the time lag z days falls between the two blue dotted lines, we could believe that the new daily cases are not related to the overall RSV of "treatments and medical resources" within the lag (pre) z days when the maximum number of new daily cases was reported, with 95% confidence level.
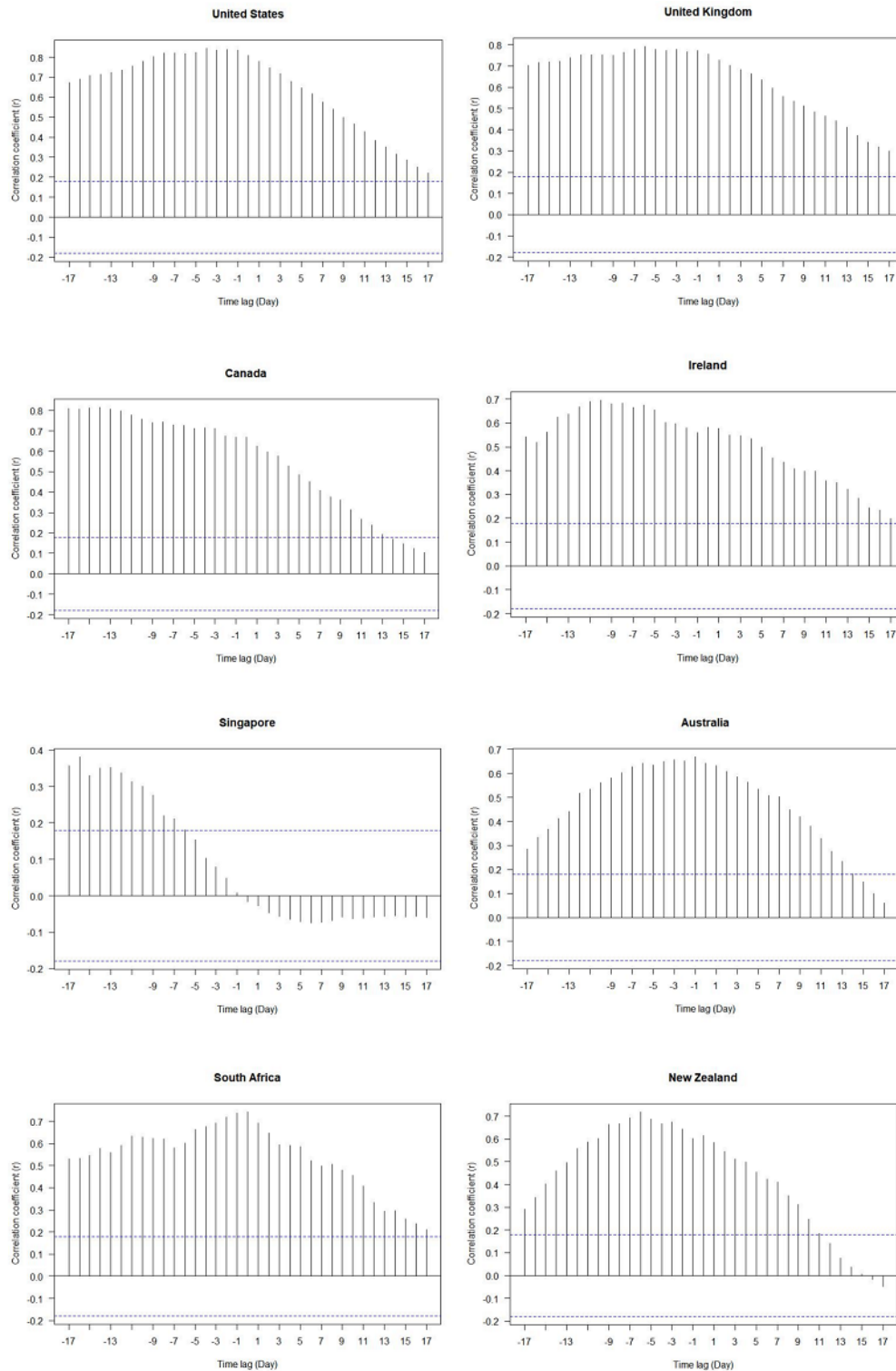
Figure 7. Time-lag correlations of the overall relative search volume (RSV) for the "diseases" topic and daily news items for eight countries from January 1 to April 29, 2020. The area between the two dotted blue lines is the 95% CI of the white noise. If the correlation coefficient of the time lag z days falls between the two blue dotted lines, we could believe that the daily news items are not related to the overall RSV of "diseases" within the lag (pre) z days when the amount of daily news coverage reached the maximum, with 95% confidence level.
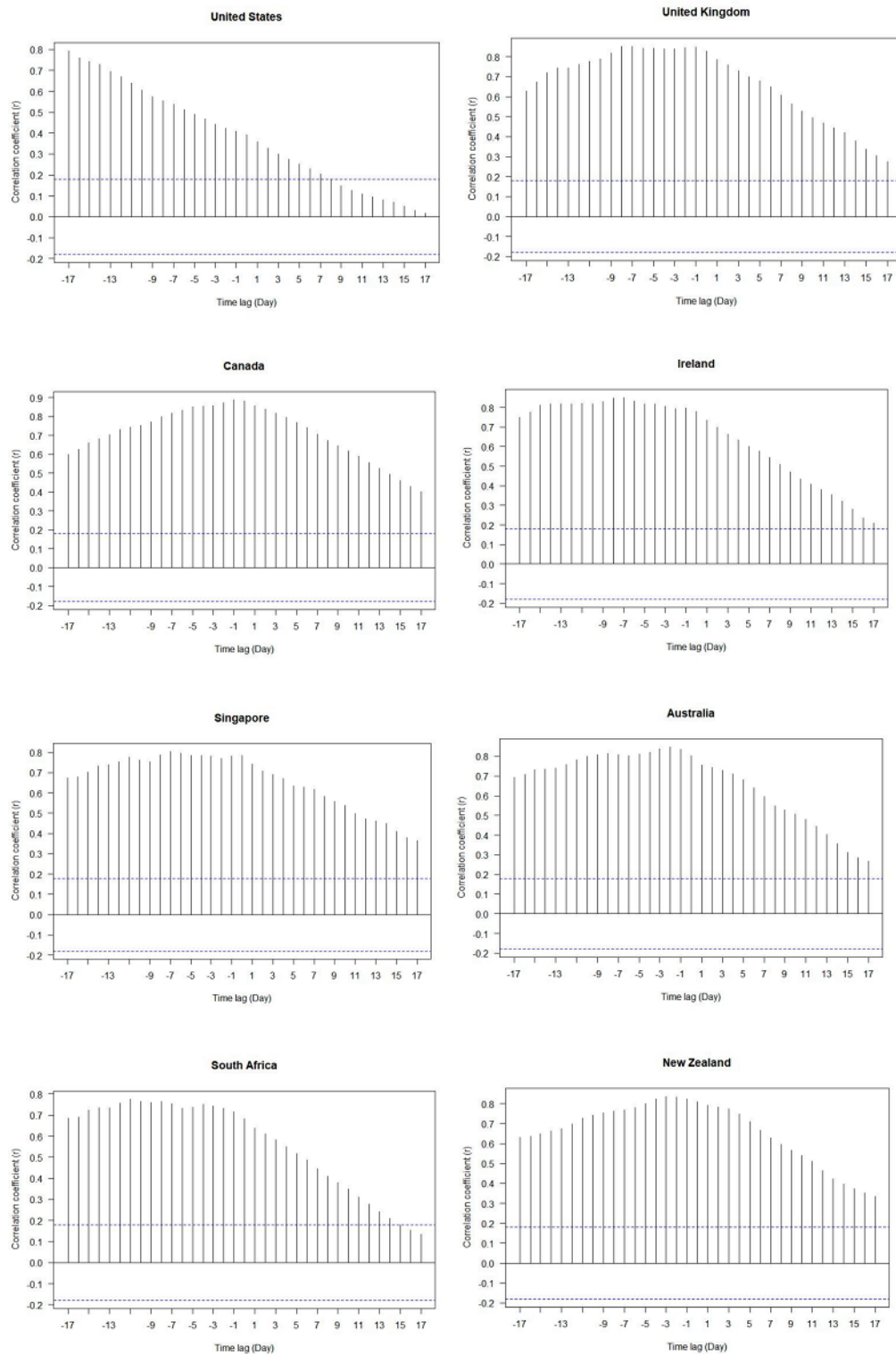
Figures S1 to S3 in Multimedia Appendix 1 show the results of the time-lag analysis between the overall RSVs for the topics "diseases," "symptoms and signs," and "public measures" and the number of new daily cases. Figures S4 to S6 in Multimedia Appendix 1 show the results of the time-lag analysis between the overall RSVs of the topics "treatments and medical resources," "symptoms and signs," and "public measures" and the number of daily news items. Table S1 in Multimedia Appendix 1 reports the effect of the first COVID-19 case on the RSVs of the search terms for the topic "symptoms and signs."

Discussion

Principal Findings

Regarding the search trends of the topic "diseases," all of the search peaks were earlier than new cases of COVID-19; this was similar to other studies [25,36,37]. When "coronavirus" was used as a search term, this term caused a spike of interest in all countries around January 20, 2020. On that day, the Chinese authorities announced that the virus was contagious, and the first case was found in the United States, which may have prompted the public to quickly recognize the threat and raised public interest. The term "covid-19" was first published by the WHO on February 11, 2020. Since then, its search volume has gradually increased and surpassed the terms "coronavirus" and "pneumonia" to become the main search term for this pandemic. The above findings showed that there were changes in public interest in external events related to the COVID-19 outbreak, indicating that Google Trends had the potential to be used as a tool to monitor public reaction and emotion regarding threatening events [38].

Regarding the search trends of the topic "treatments and medical resources," the public was the least interested in the term "ventilator," despite this being an important piece of medical equipment for the treatment of COVID-19 patients, and there was a shortage of ventilators in some countries or regions during the epidemic, such as New York City [39]. However, the majority of healthy persons were more concerned with masks than ventilators. Furthermore, wearing masks is an important means of preventing infection and plays a crucial role in curbing the COVID-19 epidemic [40]. In the situation of mask shortages [41], the public's interest in the term "mask" showed great fluctuation; although the reasons for the change in search behaviors were complex, it largely reflected public concern about the shortage of masks to some extent. In addition to masks, vaccination is an important way to end the COVID-19 pandemic [4]; as such, rising public concern reflected by the term "vaccine" was observed in our study, which was consistent with the findings in a previous study by Paguio et al [38]. In the face of the rapid spread of COVID-19 and the lack of effective vaccines, the public has paid much attention to vaccine research, in part reflected by the panic related to the urgent public need for COVID-19 vaccines, which might also indicate hope in ending the current pandemic [38].

Furthermore, in the time-lag correlation analysis, there was a positive correlation between the overall RSV for the topic "treatments and medical resources" and new daily cases for all countries except Singapore, where the maximum correlation coefficient exceeded 0.8 for the United States. In addition, the overall RSV peak for the topic "treatments and medical resources" occurred 0 to 17 days earlier than the peak for new daily cases. The positive correlation coefficient showed that as the search volume increased in this study, the number of new daily cases also showed increasing trends. These results were similar to those from other studies [25,42,43]; therefore, Google Trends has the potential to become a useful tool for disease prevention and control. Moreover, Ali et al [44] found that by observing Google Trends, the public's interest in telemedicine

continued to increase. However, in most countries and regions, the health care system's digital equipment was unable to meet growing public demand, which reminded relevant stakeholders to incorporate telemedicine into the health care system to combat pandemics. In a study by Nikolopoulos et al [7], the researchers also used Google Trends data and simulated government policies to model and successfully predict the excessive demand for products and services during the pandemic. The results showed that Google Trends data could identify the dynamic process of prediction and supply chain management directions in order to assist decision makers in making many key decisions on supply chain and disease prevention strategies. Therefore, Google Trends could be used to capture the public's early concerns or needs in order to identify fluctuations in public demands [7]. During a public health crisis, the RSV increase for specific topics or terms could be regarded as public demands or needs; we could translate these public demands into practice to formulate reasonable countermeasures to respond quickly [45]. For example, Google Trends could provide an opportunity to formulate production plans to avoid supply chain disruptions and ensure reasonable allocation of resources. Specifically, the government could arrange special fiscal budgets in advance to cover expenses related to public health emergencies and their associated impacts, such as subsidies for companies that produce masks and ventilators [45]. However, we still need more research to provide much more evidence about the predictive value in supporting decision-making policies.

For risk surveillance of emerging infectious diseases, syndromic surveillance might detect health threats faster than traditional surveillance systems, thus making timely public health action more likely [46]. Recently, Google Trends data have been applied to syndromic surveillance: this is based on the principle that when patients have a certain symptom, they are likely to search for the description of this symptom on Google. When the RSV of one particular symptom is increasing, the syndromic monitors can be alerted after a series of extensive analyses [11]. In this study of "symptoms and signs" search trends, fever and cough were symptoms that the public was most concerned about in most countries, which have been reported as the most common symptoms of COVID-19 [47]. Meanwhile, the results of the time-lag correlation analysis showed that the search peaks for the "fever" and "cough" terms were 1 to 17 days earlier than the peak of new cases in each country, with the maximum correlation coefficient being close to 0.9 for Australia; this supports Google Trends data indicating that the above symptoms seemed to act as a warning function during the early epidemic period. Also, many researchers had used specific search data to accurately estimate the level of weekly influenza activity [16,48]. In other words, there might be a certain relationship between search query data and the number of new cases, which is likely to be useful for surveillance, prevention, and control of COVID-19. However, there has been debate about the usefulness of Google search query data for predicting pandemics; the cancellation of GFT suggests that the predictions by this tool might not be sufficiently accurate [49]. Generally, syndromic surveillance often cannot fully reflect the epidemic status of the disease and will be affected by other factors, such as news coverage and important events [36,50]. In other studies, media reports have been proven to be an important factor

affecting search query interest [51]. In this study, the peak RSV was earlier than the peak number of news reports, and the trend of RSV was still positively correlated with the number of news reports (Figure S5 in Multimedia Appendix 1). Therefore, although the predictive value of Google Trends is questionable, future research studies might need to eliminate the influence of factors such as media reports.

For the prevention and control of infectious diseases, quarantine, social distancing, and lockdown are all public measures that are used to control the source of infection and block the route of transmission, which are extremely important for the prevention and control of COVID-19 [52]. Regarding the "public measures" topic, the search trend peak was formed in mid to late March, and the corresponding important event was that the lockdown policies of most countries were also released and implemented in mid to late March [51]. Similarly, from the results of the time-lag correlation analysis, the peak public interest in all countries except the United States was close to the peak number of news reports, but the peak of reporting on COVID-19–related news was slightly later than the peak of the public's interest (Figure S6 in Multimedia Appendix 1). Moreover, the RSV of the term "lockdown" was significantly higher than that of the term "social distancing." In addition to indicating that citizens in most countries were more interested in the term "lockdown," it might be that the public was not clear about the meaning of the public measure of "lockdown." The effectiveness of public measure interventions depends not only on strong policies but also on the correct cognition and compliance of the public measures. Thus, if the public lacked interest or understanding in public measures, this could jeopardize COVID-19 prevention and control [47,52,53]. Also, news media is an important tool for achieving good risk communication at the early stage of an infectious disease epidemic and for improving the control effect of policies or measures [26]. Therefore, before or at the initial stage of implementing new policies or measures, the government can use the news media to propagate policies and develop a good risk communication strategy to obtain high-quality health communication effects to better control the spread of COVID-19 [54].

When comparing search query trends with news coverage, the search query trends showed public interest, and the news reflected mass health communication. Also, the number of new cases was one indicator reflecting the severity of the epidemic and the level of prevention and control. Under the eight countries' different cultural, political, and epidemic situations, there were three health communication patterns: (1) the pattern for Singapore, (2) the pattern for the United States, and (2) the pattern for the other countries. Regarding the pattern for Singapore, it was quite different from that of the other countries. The biggest difference was that the search query peaks appeared earlier than those of the other countries, indicating that Singaporeans were more concerned in the early period of the epidemic. Moreover, in Singapore, the results of the time-lag analysis between the "treatments and medical resources" topic, the "symptoms and signs" topic, the number of daily news items, and the number of new daily cases were also different from those of the other countries. The correlation was negative and low. Among them, the correlation between the Singaporean

public's search interest in "treatments and medical resources" and the number of daily news items was low (Figure S4 in Multimedia Appendix 1), indicating that at the early stage of the COVID-19 epidemic, the Singapore public's early attention toward "treatments and medical resources" was less likely to be affected by the number of news reports, but was likely to be affected by other factors. Two main reasons could be used to explain the Singapore public's interest. One was that Singapore, as a tourism hub, has frequent tourism-business exchanges with neighboring China. The other was that Singapore had learned hard lessons from SARS in 2003 [55], so it had taken various measures to control the spread of the virus early in the epidemic, such as temperature checks and health screening, public education, and quarantine. These measures potentially made the public aware of a new threat and relevant health information as soon as possible and, thus, improved the public's sensitivity and vigilance to COVID-19 via health communications [56,57]. In other words, Singapore had done a good job of containment and prevention at the early stage. Similarly, the Singaporean public's early interest in symptoms was likely affected by other factors or events, such as the first COVID-19 case (Table S1 in Multimedia Appendix 1), though the determination of the cause of RSV changes needs further analysis.

Regarding the patterns of the United States and other countries, the amount of news coverage in the United States was much higher than in other countries. The number of new cases was also far higher than in other countries. Therefore, to some extent, their level of news coverage related to COVID-19 was justifiable, but that might also be an illusion caused by the irregularity of the data collection methods. In general, news coverage in most countries was highly responsive to the COVID-19 epidemic in late March. In addition, the results of the time-lag correlation analysis between the number of daily news items and the overall RSV for the topic "diseases" also reflected the fact that news reports appeared later than search queries, with lag times ranging from 0 to 17 days. Moreover, the correlation between the two was relatively high and gradually decreased over time, indicating that in this study, the public's interest in the COVID-19 outbreak occurred earlier than the appearance of news media reports. Based on Dutta-Bergman's channel complementarity theory, Zillmann and Bryant's selective exposure theory, and Rubin's use and satisfaction theory, which assume that active audiences use different media channels to meet their needs [58], we may use these to explain the relationship between news coverage and search query trends. To be specific, in the uncertainty of this COVID-19 epidemic, there was initially little news coverage, indicating that the public was probably not sufficiently informed, so the public's search volume was higher. As the news coverage increased, more information was available, and uncertainty decreased, as did the online search behavior of the public. However, the number of overall RSVs in the same period began to decline, which might be a kind of public desensitization for COVID-19, likely caused by continuous extensive news coverage [59-61]. That is, at the early stage of the COVID-19 epidemic, there was an increase in health information–seeking behaviors because the public lacked relevant information [42]. Therefore, in this case, Google Trends could reflect information needs and potentially provide appropriate window periods and

locations for risk communication and health communication [42,62].

In the face of emerging infectious diseases, the public lacks relevant information, and timely and effective risk communication is necessary. News media is a key resource in shaping public awareness of risks and communicating relevant health information; it has great potential to become an effective partner in health communication, which could promote risk communication and the implementation of disease prevention and control strategies [26]. In this research, the public's interest in different topics had different characteristics, and their interest was related to factors such as the development of the epidemic and media reports. This also reminded countries or public health departments that when communicating with the public, they should unite with the news media as soon as possible, pay close attention to changes in public interests by monitoring Google Trends search data and media reports, plan the nature and content of news items, and provide the information needed by the public in a more reasonable manner, in order to better prevent and control epidemics at their early stages, such as the COVID-19 epidemic [26,43,54]. However, the RSVs of the search terms from Google Trends are relative values and do not provide the exact values of the actual search volumes. As some search terms with higher search volumes appear, the change in trend of search terms may be underestimated [63]. As a result, it somewhat reduces the usability of Google Trends, though the linear trend of individual search terms does not change. However, in some studies, by collecting more data to analyze seasonal differences and long-term trends, we can further analyze whether there are changes in search terms and explore the meaning and reasons of these changes [17,38]. In addition, Google Trends has the characteristic of being available in real time, which can not only be used to monitor public emotions, reactions, and needs in real time, but can also be used to evaluate the effects of risk communication and public health interventions and the impact of major events or policies, among other factors. For example, interrupted time series analysis was used to assess the impact of celebrity suicides on search volumes, as well as the impact of tobacco control policies on search rates for smoking cessation information, in order to evaluate the effectiveness of the policy implementation [64,65]. In the internet era, with the popularity of mobile terminals, online searching is a two-way communication process, including sending search requests and receiving search results. Sending a search request reflects the public's response to the severity and urgency of the risk and actual needs, and receiving search results provides feedback in response to the public's views on their ability and effectiveness to manage or respond to risks [66]. Therefore, timely responses and exploration of data are very important, and Google Trends has the characteristic of real-time availability. In addition, Google Trends can also integrate more data sources, such as Twitter and Facebook, among others, so Google Trends data are still valuable [39,67-69].

Limitations

Google Trends has its own limitations. For example, it is more applicable to study high-prevalence diseases in countries where the internet is popular [8] and when providing a relative versus exact value for search volume. Due to Google's existing language limitations [23], we only studied the major English-speaking countries. Also, Google search data and news data might not be comprehensive enough and might not have included all of the search terms or topics related to COVID-19. For example, we did not include some important symptoms (eg, "loss of taste or smell"), and we omitted some similar terms such as "Wuhan virus." In addition, "pneumonia" was not related only to COVID-19, but could also be related to influenza. Also, there was no one-to-one correspondence between news coverage data and search terms and topics. Therefore, further studies should apply detailed search terms and extract more news data to explore additional values.

Conclusions

Through Google Trends, we identified the level of public interest for various aspects at the early stages of the COVID-19 epidemic, learned about public concern and neglect, and revealed the potential value of Google Trends in monitoring public response and demand, prediction, and other aspects in the face of the occurrence of emerging infectious diseases. In addition, news media as an essential source of information, combined with Google Trends, could achieve more effective health communication. Therefore, both news coverage and Google search trends could potentially contribute to the prevention and control of epidemics at the early epidemic stage.

Authors' Contributions

QL and W-KM conceived the original idea and designed the entire research process. QL, W-KM, FH, and QC collected and cleaned the data. W-KM, FH, QC, and BL performed the data analysis and data interpretation. W-KM, QL, FH, QC, and TL wrote the first version of the manuscript. FH, HW, QC, and BL constructed the figures. JH, CJPZ, and BA contributed to the administration of the project, data analysis, and data interpretation. W-KM, QL, QC, FH, AJ, and TL contributed to the final version of the manuscript. QL, JH, CJPZ, and BA reviewed the manuscript. All authors contributed to the interpretation of the results and the final manuscript. All authors discussed and agreed on the implications of the study findings and approved the final version to be published.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Supplementary materials.
[DOCX File , 511 KB - publichealth_v7i12e26644_app1.docx]

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Abbreviations

GFT: Google Flu Trends
RSV: Relative Search Volume
WHO: World Health Organization

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The Standardization of Hospital-Acquired Infection Rates Using Prediction Models in Iran: Observational Study of National Nosocomial Infection Registry Data

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Abstract

Background: Many factors contribute to the spreading of hospital-acquired infections (HAIs).

Objective: This study aimed to standardize the HAI rate using prediction models in Iran based on the National Healthcare Safety Network (NHSN) method.

Methods: In this study, the Iranian nosocomial infections surveillance system (INIS) was used to gather data on patients with HAIs (126,314 infections). In addition, the hospital statistics and information system (AVAB) was used to collect data on hospital characteristics. First, well-performing hospitals, including 357 hospitals from all over the country, were selected. Data were randomly split into training (70%) and testing (30%) sets. Finally, the standardized infection ratio (SIR) and the corrected SIR were calculated for the HAIs.

Results: The mean age of the 100,110 patients with an HAI was 40.02 (SD 23.56) years. The corrected SIRs based on the observed and predicted infections for respiratory tract infections (RTIs), urinary tract infections (UTIs), surgical site infections (SSIs), and bloodstream infections (BSIs) were 0.03 (95% CI 0-0.09), 1.02 (95% CI 0.95-1.09), 0.93 (95% CI 0.85-1.007), and 0.91 (95% CI 0.54-1.28), respectively. Moreover, the corrected SIRs for RTIs in the infectious disease, burn, obstetrics and gynecology, and internal medicine wards; UTIs in the burn, infectious disease, internal medicine, and intensive care unit wards; SSIs in the burn and infectious disease wards; and BSIs in most wards were >1, indicating that more HAIs were observed than expected.

Conclusions: The results of this study can help to promote preventive measures based on scientific evidence. They can also lead to the continuous improvement of the monitoring system by collecting and systematically analyzing data on HAIs and encourage the hospitals to better control their infection rates by establishing a benchmarking system.

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Introduction

Many factors contribute to the spreading of hospital-acquired infections (HAIs), and controlling nosocomial infections is now a global priority. Because accurate measurements are needed to improve any situation, infection control measures must first include accurate determination of the infection incidence at the hospital level [1]. On the other hand, statistics in low- and middle-income countries show that the exact rate of HAIs in such countries depends on 2 groups of factors: (1) factors related to the hospital, such as the hospital bed size (number of beds), the grade of the referral hospital, whether the hospital is teaching or nonteaching, the presence or absence of monitoring programs, the ward types, the facilities, and the adequacy of financial resources for such care programs, and (2) factors beyond the hospital's control, such as the age and gender of patients [2-4]. Therefore, it is necessary to determine the rate of HAIs by adjusting and considering these variables and to obtain a suitable statistical model to calculate these rates.

On the other hand, environmental and sociocultural factors also contribute to rate of HAIs. In addition, the relation between HAI rates and the socioeconomic level showed that a lower country socioeconomic level was correlated with a higher infection risk [5,6]. The environmental factors include contaminated air-conditioning systems and the physical layout of the facility, and factors related to cultural issues include lack of or poor hand hygiene practice and awareness by health care workers and lack of use of sterile methods [6,7].

In the United States, the Centers for Disease Control and Prevention (CDC) uses the National Nosocomial Infections Surveillance (NNIS) risk index to determine the incidence of infections, especially for surgical site infections (SSIs) [8]. Despite the use of this risk index in many countries, the NNIS risk index has several drawbacks, including the following: using only 4 factors (including the American Society of Anesthesiologists score, wound class, procedure duration, and endoscope use) to calculate the risk index and its inadequacy, considering all variables as binary variables and not quantitative variables, and considering the same weights for different procedures and their inaccuracy (different weights are needed). For this reason, in 2009, the United States National Healthcare Safety Network (NHSN) introduced a new statistical model to replace the NNIS risk index to estimate the expected infection incidence for all infections, which was then used as a denominator in the new measurement: the standardized infection ratio (SIR) based on a statistical model [9,10]. The use of a statistical model–based SIR solved the problems of utilizing an SIR based on the conventional risk index in the United States and significantly improved international comparisons in this field [11]. The SIR is a summary measure used to track HAIs at a national, state, or local level over time. This measure compares the actual number of reported HAIs with the number that would be predicted, adjusting for the factors that are associated with differences in the infection incidence. By calculating the SIR, the relevant and significant variables for each hospital are adjusted.

In Iran, the Center for Disease Control and Prevention of the Ministry of Health and Medical Education is responsible for establishing a hospital infection surveillance system for regular and continuous data collection related to nosocomial infections, analysis, publication of periodic reports, and providing feedback. However, calculating only a crude rate without adjusting for the variables that affect HAIs and using this rate for planning and policy in this field may not be very efficient. Therefore, this study aimed to standardize the HAI rate using prediction models in Iran based on the NHSN method.

Methods

Surveillance System

In 2010, a surveillance system for infectious diseases was created in Iran, and all hospitals were requested to record information about HAIs in the hospital. The Iranian Nosocomial Infections Surveillance System (INIS) was revised in 2017. In 2018, it collected data from 863 hospitals in all the provinces of Iran and recorded different types of information. INIS uses the CDC/NHSN definitions to report all infections. In this study, INIS (126,314 patients with HAIs in 2018) and the hospital statistics and information system (AVAB), a web-based system for monitoring and evaluation of different hospitals (ie, data on 942 hospitals in Iran in 2018), were used to standardize the HAI rate. With the help of these systems and their linkage, we have access to data on the observed number of HAIs in different hospitals during the year of the study. More details about the data source, linkage of the data source, and national standard for hospital performance indicators (ie, average length of stay [LOS], bed occupancy rate [BOR], bed turnover [BTO] rate, death-to-bedridden ratio, and Pabon Lasso model) are available elsewhere [12,13].

Ethics Approval and Consent to Participate

All procedures performed in this study were approved by the ethical committee of the National Institute for Medical Research Development (IR.NIMAD.REC.1399.074). All methods were carried out in accordance with relevant guidelines and regulations.

Variable Selection

In this study, there were about 40 variables for the prediction model. Using univariable regression analysis ($P<.20$) and expert opinions, the important variables (24 variables) for the prediction model were selected: type of ward, hospital affiliation, type of hospital, hospital expertise, accreditation, number of active beds, average LOS, BTO rate, nurse-to-hospital bed ratio, number of devices used daily in each ward (device-day), number of catheters used daily in each ward (catheter-day), number of ventilators used daily in each ward (ventilator-day), mean age, length of hospitalization until infection, duration of hospitalization, male-to-female patient ratio, number of deaths in each ward, number of device-related infections, number of ventilator-related infections, number of catheter-related infections, BOR, surgery-to-surgery bed ratio, death-to-bedridden ratio, ventilator-day to catheter-day ratio.

Well-Performing Hospitals in Terms of the Accreditation Degree and Reporting of HAIs for Modeling and Obtaining Coefficients for SIR Calculation

To develop a model that identifies the infection predictors in a normal hospital, first, well-performing hospitals were defined as follows: (1) hospitals with excellent and first grade "accreditation" and (2) hospitals with an HAI rate of 4%-15%.

Considering all the aforementioned criteria, the number of records decreased to 687. Missing items were also removed for the variable "surgery-to-surgery bed ratio" (23 records).

For the number of expected (predicted) infections (denominator of the SIR indicator), first, well-performing hospitals (with similar distribution of hospital expertise, type of ward, type of hospital, and affiliation compared with the total data) were selected, including 357 hospitals from 31 provinces and 54 universities in the country (664 records). Poisson regression analysis was performed on the data, and over/underdispersion was examined in the model. Then, due to overdispersion ($\mu < \sigma^2$) and because there was an excess of zero counts, generalized negative binomial and hurdle negative binomial regression analyses were performed on the data. Also, the "number of hospitalizations" logarithm was considered as an offset for the model. The previously mentioned predictors were entered into the model. Then, using the Akaike information criterion and both directions of the stepwise method (forward/backward), the candidate variables for the final models were determined.

Model Validation

In this study, the data were randomly split into training (70%) and testing (30%) data sets. The final model for each type of HAI was developed on the training data, and then, the validity of the models was measured on the testing data using "pseudo R^2" metrics including:

In addition, the model results from the training, test, and total data sets were compared based on the prediction error, which is the mean square error (MSE):

where O is observed and P is predicted.

Finally, the root mean square error (RMSE) was obtained by taking the root of the model prediction error value, and the final models were extracted to calculate the SIR using the lowest value of RMSE.

SIR

This ratio is a summary measure that compares the observed number of HAIs and the number that would be predicted, adjusting for several risk factors that are associated with differences in the infection incidence. In other words, an SIR greater than 1.0 means that the observed number of HAIs is more than predicted; conversely, an SIR less than 1.0 indicates that fewer HAIs were observed than predicted.

For each type of infection, the regression model on the total data (3449 records) was updated using regression coefficients of the model based on the data from well-performing hospitals (664 records), and the number of infections was predicted. Then, the SIR was calculated for the HAIs with different variables in Iran using the INIS data as the observed number of HAIs.

Corrected SIR

To calculate the correction factor (CF), linear regression analysis was used (no constant). The number of observed as the outcome variable (y) and the number of predicted (expected) obtained from the regression model for each infection from the data of well-performing hospitals (664 records) were defined as independent variables (x), and the coefficient obtained in the linear regression analysis was considered the CF. In the next step, the CF was multiplied by the number of expected (predicted) infections for the total data (3449 records). Finally, the corrected SIR was calculated (Figure 1).

The corrected SIR was calculated as follows: CF × number of expected (predicted) infections for the total data (3449 records).

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Figure 1. Data preparation steps and calculation of standardized infection ratio (SIR). AVAB: hospital statistics and information system; HAI: hospital-acquired infection; INIS: Iranian Nosocomial Infections Surveillance System; RMSE: root mean square error.
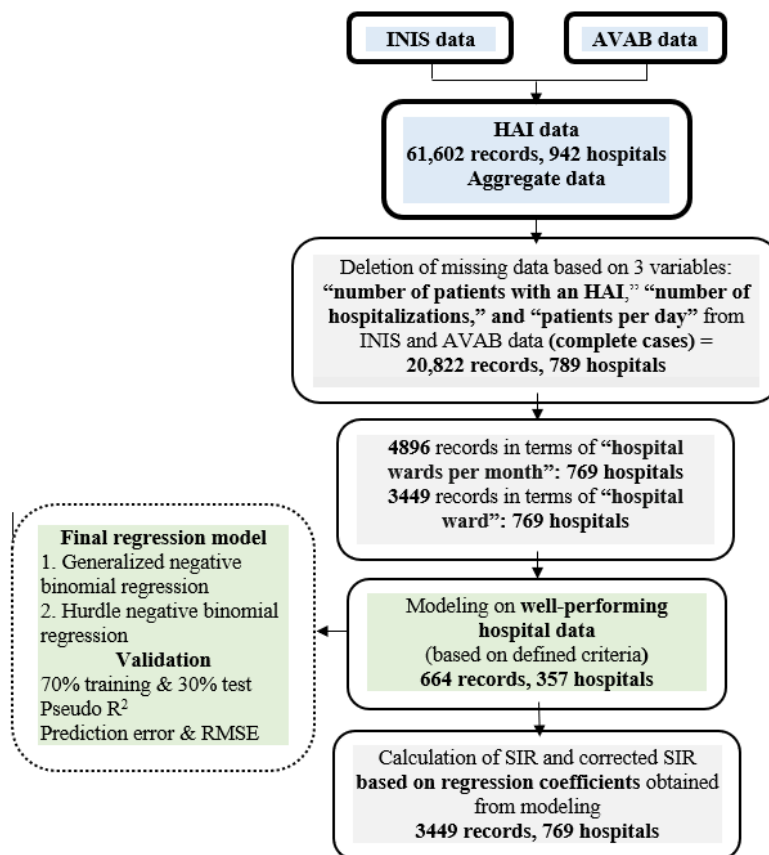
Results

The mean age of the 100,110 patients with an HAI was 40.02 (SD 23.56) years. The median hospitalization length until infection and hospital LOS were 6.97 (Q1-Q3 2.67-12.6) days and 15.2 (Q1-Q3 7.75-24.9) days, respectively.

Model Development and Performance Measurement

The most important predictor variables in the training and test data and on well-performing hospital data were the type of ward,

hospital affiliation, mean age of patients, male-to-female patient ratio, number of device-related infections, number of catheter-related infections, surgery-to-surgery bed ratio, death-to-bedridden ratio, and ventilator-day to catheter-day ratio. Table 1 shows the Cox and Snell R^2, Nagelkerke R^2, and RMSE values in the training, test, and total data sets for each type of infection.

Table 1. Performance measures for the hospital-acquired infection prediction model on the training, test, and total data sets from well-performing hospitals.

Performance measures	Training data (n=466)	Test data (n=198)	Total data (n=664)
RTI[a]			
Pseudo R^2: McFadden	0.19	0.22	_[b]
Pseudo R^2: Cox and Snell (maximum likelihood)	0.74	0.79	-
Pseudo R^2: Nagelkerke (Cragg and Uhler)	0.74	0.79	-
Prediction error (MSE[c])	344.47	466.99	354.57
RMSE[d]	18.56	21.61	18.83
UTI[e]			
Pseudo R^2: McFadden	0.20	0.19	-
Pseudo R^2: Cox and Snell (maximum likelihood)	0.73	0.72	-
Pseudo R^2: Nagelkerke (Cragg and Uhler)	0.73	0.72	-
Prediction error (MSE)	213.45	306.95	248.37
RMSE	14.61	17.52	15.76
SSI[f]			
Pseudo R^2: McFadden	0.17	0.20	-
Pseudo R^2: Cox and Snell (maximum likelihood)	0.54	0.62	-
Pseudo R^2: Nagelkerke (Cragg and Uhler)	0.54	0.62	-
Prediction error (MSE)	367.87	632.01	334.15
RMSE	19.18	25.14	18.28
BSI[g]			
Pseudo R^2: McFadden	0.17	0.14	-
Pseudo R^2: Cox and Snell (maximum likelihood)	0.58	0.55	-
Pseudo R^2: Nagelkerke (Cragg and Uhler)	0.59	0.56	-
Prediction error (MSE)	1078.46	102.01	673.4
RMSE	32.84	10.1	25.95

[a]RTI: respiratory tract infection.

[b]Not calculated for the total data set.

[c]MSE: mean square error.

[d]RMSE: root mean square error.

[e]UTI: urinary tract infection.

[f]SSI: surgical site infection.

[g]BSI: bloodstream infection.

SIR and Corrected SIR by Type of Ward

The SIR for respiratory tract infections (RTIs; ie, ventilator-associated events, pneumonia events and lower respiratory tract infections, urinary tract infections [UTIs], surgical site infections [SSIs], and bloodstream infections [BSIs]) were 0.024 (95% CI 0-0.071), 0.93 (95% CI 0.86-0.99), 0.86 (95% CI 0.79-0.93), and 0.4 (95% CI 0.23-0.56), respectively. In addition, the corrected SIRs for RTI, UTI, SSI, and BSI were 0.03 (95% CI 0-0.09), 1.02 (95% CI 0.95-1.09), 0.93 (95% CI 0.85-1.007), and 0.91 (95% CI 0.54-1.28), respectively. Also, the corrected SIRs for RTI in the infectious disease, burn, obstetrics and gynecology, and internal medicine wards; for UTI in the burn, infectious disease, internal medicine, and intensive care unit wards; for SSI in the burn and infectious disease wards; and for BSI in most wards were >1. These findings showed that the number of observed HAIs was more than expected (Figure 2).

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Figure 2. The standardized infection ratio (SIR) and corrected SIR by ward type in Iran, 2018. BSI: bloodstream infection; CCU: cardiac care unit; ICU: intensive care unit; P,NICU: pediatric or neonatal intensive care unit; RTI: respiratory tract infection; SSI: surgical site infection; UTI: urinary tract infection.
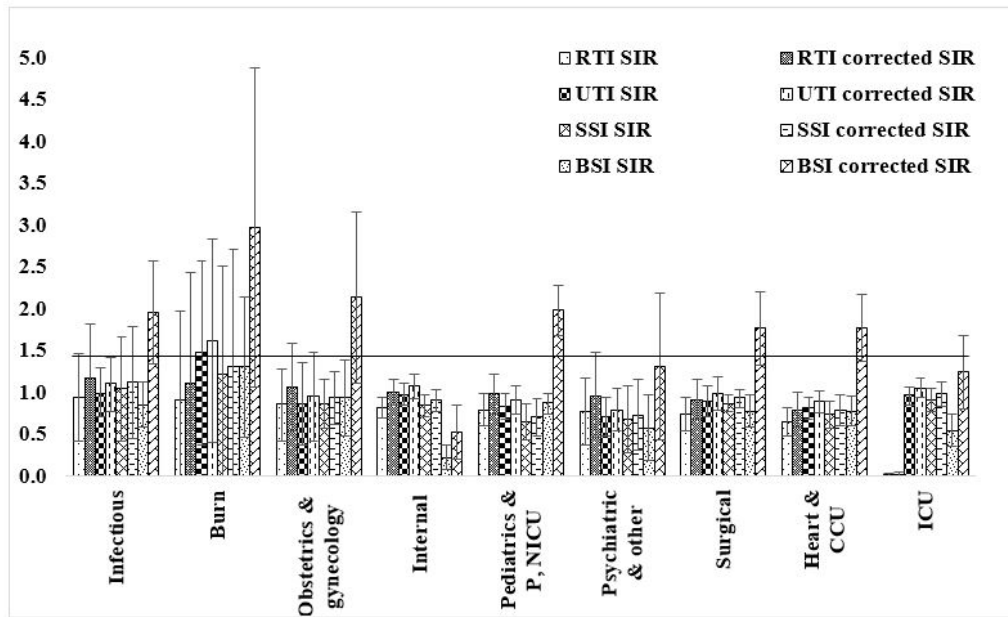
SIR and Corrected SIR by Other Variables

The corrected SIR was >1 for accident and burn hospitals, general hospitals, and for-profit hospitals, as well as hospitals with excellent or grade 2/3 accreditations. Considering hospital expertise, the highest SIR and highest corrected SIR were observed in accident and burn hospitals for RTI, UTI, and BSI and in pediatric hospitals for SSI. Also, the highest SIR and highest corrected SIR by hospital affiliation were observed in for-profit hospitals for RTI, government hospitals for UTI, and semigovernment hospitals for BSI. In terms of the type of hospital, the highest SIR and highest corrected SIR were related to nonteaching hospitals for RTI, SSI, and BSI and teaching hospitals for UTI (Table 2).

Table 2. Standardized infection ratio (SIR) and corrected SIR by different variables in Iranian hospitals in 2018.

Variables	Hospital number	RTI[a]		UTI[b]		SSI[c]		BSI[d]	
		SIR (95% CI)	Corrected SIR (95% CI)	SIR (95% CI)	Corrected SIR (95% CI)	SIR (95% CI)	Corrected SIR (95% CI)	SIR (95% CI)	Corrected SIR (95% CI)
National	769	0.31	0.4	0.93	0.99	0.86	0.99	0.4	1.14
Hospital expertise									
Accident & burn	6	1.05 (0.68-1.41)	1.3 (0.85-1.74)	2.41 (1.52-3.3)	2.65 (1.67-3.62)	1.14 (0-2.49)	1.23 (0-2.67)	1.58 (0.96-2.19)	3.59 (2.18-4.99)
General	578	0.94 (0.87-1)	1.16 (1.08-1.24)	0.98 (0.91-1.05)	1.07 (0.99-1.15)	0.88 (0.81-0.96)	0.95 (0.87-1.03)	0.34 (0.19-0.48)	0.77 (0.43-1.11)
Heart	11	0.71 (0.37-1.04)	0.87 (0.45-1.29)	0.57 (0.37-0.78)	0.63 (0.41-0.98)	1.06 (0.51-1.6)	1.13 (0.54-1.72)	0.7 (0.48-0.92)	1.6 (1.11-2.09)
Pediatrics	11	0.61 (0.42-0.8)	0.76 (0.71-1.72)	0.58 (0.38-0.77)	0.63 (0.42-0.84)	1.19 (0.62-1.76)	1.28 (0.66-1.89)	1.23 (0.91-1.55)	2.79 (20.6-3.52)
Obstetrics & gynecology	21	0.44 (0-0.89)	0.55 (0-1.09)	0.6 (0.3-0.89)	0.66 (0.33-0.98)	0.67 (0.31-1.03)	0.72 (0.33-1.11)	0.86 (0.57-1.14)	1.95 (1.31-2.6)
Other[e]	34	0.0003 (0-0.0009)	0.0004 (0-0.001))	0.63 (0.37-0.89)	0.69 (0.41-0.98)	0.39 (0.13-0.65)	0.42 (0.14-0.7)	1.49 (0.79-2.18)	3.39 (1.81-4.97)
Hospital affiliation									
Government	556	0.02 (0-0.06)	0.025 (0-0.07)	0.98 (0.9-1.05)	1.07 (0.99-1.15)	0.89 (0.81-0.97)	0.96 (0.87-1.05)	0.38 (0.22-0.53)	0.85 (0.49-1.21)
Semigovernment/other	78	0.79 (0.62-0.96)	0.98 (0.77-1.19)	0.8 (0.64-0.96)	0.88 (0.7-1.05)	0.76 (0.6-0.93)	0.82 (0.64-1.004)	1.05 (0.8-1.31)	2.39 (1.81-2.98)
For-profit	135	0.88 (0.69-1.07)	1.09 (0.86-1.33)	0.67 (0.57-0.77)	0.73 (0.62-0.84)	0.73 (0.56-0.89)	0.78 (0.6-0.95)	0.89 (0.71-1.07)	2.03 (1.61-2.45)
Accreditation									
Excellent	20	0.72 (0.46-0.98)	0.89 (0.56-1.22)	1.07 (0.84-1.3)	1.17 (0.92-1.43)	0.65 (0.49-0.81)	0.7 (0.52-0.87)	1.14 (0.75-1.52)	2.59 (1.71-3.47)
Grade 1	541	0.021 (0-0.062)	0.026 (0-0.077)	0.96 (0.89-1.03)	1.06 (0.98-1.13)	0.87 (0.79-0.96)	0.94 (0.85-1.02)	0.36 (0.21-0.52)	0.83 (0.47-1.18)
Grade 2/3	99	0.79 (0.62-0.98)	0.98 (0.77-1.19)	0.58 (0.43-0.73)	0.64 (0.47-1.43)	0.99 (0.8-1.18)	1.06 (0.85-1.27)	0.57 (0.39-0.74)	1.29 (0.89-1.69)
Hospital type									
Nonteaching	197	0.89 (0.81-0.97)	1.1 (1.004-1.2)	0.74 (0.66-0.82)	0.81 (0.73-0.9)	0.93 (0.81-1.06)	1.002 (0.87-1.13)	0.69 (0.6-0.78)	1.56 (1.36-1.76)
Teaching	465	0.014 (0-0.043)	0.02 (0-0.053)	1.13 (1.03-1.23)	1.24 (1.13-1.35)	0.8 (0.72-0.89)	0.86 (0.78-0.95)	0.36 (0.19-0.53)	0.82 (0.45-1.2)

[a]RTI: respiratory tract infection.

[b]UTI: urinary tract infection.

[c]SSI: surgical site infection.

[d]BSI: bloodstream infection.

[e]Orthopedic, surgery, cancer, psychiatric.

Discussion

Principal Findings

HAIs lead to longer hospital LOS and increased costs for patients and the health care system. Knowing the reasons for, type of, and rate of HAIs can be very helpful for optimal management and improving service quality. Therefore, the establishment of a nosocomial infection control committee, implementation of educational programs, attention to the physical structure of hospital wards, and providing motivational and attitudinal mechanisms in infection control are important factors that can reduce HAIs [14]. Based on the results, the type of ward, hospital affiliation, the mean age of patients, male-to-female patient ratio, number of device-related infections, number of catheter-related infections, surgery-to-surgery bed ratio, death-to-bedridden ratio, and

ventilator-day to catheter-day ratio were the predictor variables for HAIs.

In a study in Liguria, age >54 years, LOS, surgery, exposure to more devices, and exposure to vascular catheters were confirmed as factors associated with HAIs in a multivariable analysis. However, the type of ward and the size of the hospital (number of beds) had no relationship with the occurrence of HAIs [15].

Implementing infection prevention and control activities is critical for reducing the burden of HAIs and should be tailored to local needs. These standards are far from the goals of the infection prevention guidelines in the hospitals included in this study, which recommend that there should be one full-time infection control nurse for every 100 beds in acute care hospitals and every 150 beds in long-term acute care hospitals or every 250 beds, as defined by the WHO guidelines [16,17]. It is also important to note that staffing has been identified as a human resource for infection prevention [18].

In this study, the corrected SIR based on observed and predicted infections for RTI, UTI, SSI, and BSI were 0.03, 1.02, 0.93, and 0.91, respectively. Also, the corrected SIR for RTI in the infectious disease, burn, obstetrics and gynecology, and internal medicine wards; for UTI in the burn, infectious disease, internal medicine, and intensive care unit wards; for SSI in the burn and infectious disease wards; and for BSI in most wards were >1, indicating that the observed number of HAIs was more than expected. This index was >1 for accident and burn hospitals, general hospitals, and for-profit hospitals, as well as for hospitals with excellent or grade 2/3 accreditations.

Since the highest SIR was related to UTI, prevention strategies for reducing the risk of these infections, such as educating health care personnel regarding the indications for catheter use, proper procedures for the insertion and maintenance of catheters, appropriate infection control measures to prevent catheter-related infections, hand hygiene, and aseptic procedures, should be considered [19,20].

Improving hand hygiene, reducing and avoiding unnecessary urinary catheters, placing urinary catheters using an aseptic method and keeping them according to the instructions, determining the need for a urinary catheter on a daily basis and removing it as soon as possible, and managing an incontinence catheter should be considered to reduce these infections if possible.

In a study by Martillo et al [21], there were 102 central line–associated BIs (CLABSIs) and 58,321 line-days in 2017. The CLABSI rate was 1.75 infections per 1000 days, and the SIR was 1.25. Also, in 2018, the number of CLABSIs decreased by 58% (59 infections and 56,893 line-days). The CLABSI rate was 1.03 infections per 1000 days, and the SIR was 0.91. In 2017, 58,621 central line-days were utilized across the hospital with a standardized utilization ratio of 0.73, while in 2018, there were 56,893 central line-days with a standardized utilization ratio of 0.81 [21]. Therefore, based on the results, the use of a specialized team such as the comprehensive vascular access service (VAS) team ensures adherence to the best practices during catheter insertion and enhances nurse training for device maintenance, especially in patients who are at risk for

complications. Reports have shown that using dedicated VAS teams seems to be a good and cost-effective strategy, as these teams are associated with greater success for first-time insertion and thus improve efficiency and safety and reduce side effects [21,22]. Another report by Brunelle [23] showed that a team dedicated to the maintenance of central venous catheters reduces BSI from 45 to 19 infections per year. On the other hand, a Cochrane systematic review that attempted to assess the role of specialized teams in device insertion failed to find clinical trials that supported the role of these teams compared with general practitioners [24].

In the study by Słowik et al [25], the SIR did not exceed 1, and the incidence of SSI after hip arthroplasties was at a level comparable to that of European countries (0.7 for patients without a risk factor, 0.8 for patients with 1 risk factor, and 0.3 for patients with 2 or 3 risk factors). The SIR for SSIs in knee arthroplasties exceeded 1 at all 3 levels and was obtained as follows: 7 for patients without risk factors, 2 for patients with 1 risk factor, and 2 for patients with 2 or 3 risk factors [25].

In a study in Italy, the prevalence of observed infections in 13 of 18 hospitals was lower than expected, while in 4 hospitals, the SIR was >1. One hospital had reached 4.9, which means a 390% increase in the observed infections compared with the expected number [15]. Boev et al [26], in an investigation using the results of various studies, reported the SIRs for CLABSI, catheter-associated UTI, and SSI (colon surgery only) to be 5, 1, and 0.98, respectively.

Strengths and Limitations

Conventional epidemiological indicators do not have the necessary efficiency to prioritize programs. Thus, new indicators were introduced, including the SIR, which corrects the prediction of the expected nosocomial infections by considering the variables affecting this rate. It can be said that one of the strengths of this study is to address this index and calculate it. Another strength of the study is the use of more than one source, namely INIS and AVAB; the use of registered data for a multicenter, comprehensive, and national-level study to more accurately estimate the HAIs in Iran; and the use of the NHSN method, which is considered less frequently by researchers. One other advantage of the study is the calculation of the corrected SIR.

On the other hand, the following factors can be considered as the study limitations: lack of a complete and comprehensive data source for HAIs and hospital-related variables; problems related to the data including underreporting, registration of false negatives, missing data, problems related to the definition of infections, and insufficient quality control of data, among others; failure to collect data from all hospitals in Iran; lack of new and similar studies in Iran that can be compared with the current study (the results were compared with those of only a few studies, which were not performed with the same method as this study); failure to calculate the SIR for SSIs according to the type of procedure; and the possibility of some biases due to the retrospective study. However, as mentioned earlier, in this study, to overcome the limitations of data sources and data problems, several sources as well as the NHSN codes were used to estimate HAIs more accurately and completely. Also,

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regarding the limitation of not collecting data from all hospitals in Iran, it can be said that this study was performed using recorded data with a coverage of about 75%, which were randomly collected from all the provinces in the country; therefore, it can be claimed that the results are reliable.

Conclusions

The results of this study can help to promote preventive measures based on scientific evidence. They can also lead to the continuous improvement of the monitoring system by collecting and systematically analyzing data on HAIs. Addressing HAIs in low-resource countries may require significant investment and commitment to an infection prevention and control program, which includes training and deployment of infection control care professionals, as an additional strategy to help implement the guidelines. As a result, although significant progress has been made in recent years in implementing prevention strategies in Iranian hospitals, HAI remains a public health concern. The higher observed number of HAIs than expected, especially for UTI, indicates the need for a nosocomial infection care system and effective policies for identifying the types of HAIs and the related factors and encourages the hospitals to better control their infection rates by establishing a benchmarking system.

Authors' Contributions

NI, KE, BE, SS, and HN contributed to conceiving the study. NI, BE, SS, and HN designed the study and acquired the data. NI, YM, SS, and HN analyzed the data, and NI, YM, BE, SS, and HN interpreted the findings. NI, KE, SS, and HN drafted the manuscript, and all authors read and approved the manuscript.

Conflicts of Interest

None declared.

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Abbreviations

AVAB: hospital statistics and information system
BOR: bed occupancy rate
BSI: bloodstream infection
BTO: bed turnover
CDC: Centers for Disease Control and Prevention
CF: correction factor
CLABSI: catheter line–associated bloodstream infection
HAI: hospital-acquired infection
INIS: Iranian Nosocomial Infections Surveillance System
LOS: length of stay
MSE: mean square error
NHSN: National Healthcare Safety Network
NNIS: National Nosocomial Infections Surveillance

RMSE: root mean square error
RTI: respiratory tract infection
SIR: standardized infection ratio
SSI: surgical site infection
UTI: urinary tract infection
VAS: vascular access service

Original Paper

Predicting COVID-19 Transmission to Inform the Management of Mass Events: Model-Based Approach

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Abstract

Background: Modelling COVID-19 transmission at live events and public gatherings is essential to controlling the probability of subsequent outbreaks and communicating to participants their personalized risk. Yet, despite the fast-growing body of literature on COVID-19 transmission dynamics, current risk models either neglect contextual information including vaccination rates or disease prevalence or do not attempt to quantitatively model transmission.

Objective: This paper attempted to bridge this gap by providing informative risk metrics for live public events, along with a measure of their uncertainty.

Methods: Building upon existing models, our approach ties together 3 main components: (1) reliable modelling of the number of infectious cases at the time of the event, (2) evaluation of the efficiency of pre-event screening, and (3) modelling of the event's transmission dynamics and their uncertainty using Monte Carlo simulations.

Results: We illustrated the application of our pipeline for a concert at the Royal Albert Hall and highlighted the risk's dependency on factors such as prevalence, mask wearing, and event duration. We demonstrate how this event held on 3 different dates (August 20, 2020; January 20, 2021; and March 20, 2021) would likely lead to transmission events that are similar to community transmission rates (0.06 vs 0.07, 2.38 vs 2.39, and 0.67 vs 0.60, respectively). However, differences between event and background transmissions substantially widened in the upper tails of the distribution of the number of infections (as denoted by their respective 99th quantiles: 1 vs 1, 19 vs 8, and 6 vs 3, respectively, for our 3 dates), further demonstrating that sole reliance on vaccination and antigen testing to gain entry would likely significantly underestimate the tail risk of the event.

Conclusions: Despite the unknowns surrounding COVID-19 transmission, our estimation pipeline opens the discussion on contextualized risk assessment by combining the best tools at hand to assess the order of magnitude of the risk. Our model can be applied to any future event and is presented in a user-friendly RShiny interface. Finally, we discussed our model's limitations as well as avenues for model evaluation and improvement.

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Introduction

Background

Evaluating the Safety of Live Events

More than a year after a global and unprecedented cancellation of live events in March 2020, the future of live events and the entertainment industry remains uncertain despite increasing vaccination rates and low community prevalence levels (at the time of writing). The main concern raised by these gatherings lies in their susceptibility to "super-spreading"—a scenario whereby a few contagious participants inadvertently infect a disproportionately large number of others [1-6] and that has been highlighted as a significant driver of the pandemic [7-10]. Despite the re-opening of live events in the United Kingdom on July 19, 2021, the threat of existing and emergent COVID-19 variants coupled with dwindling immunity from vaccination over time suggests that policy makers and event organizers will likely continue to struggle with the following 2 questions: (1) Is the COVID-19 transmission risk posed by these events tolerable? and (2) What additional safety measures can be feasibly deployed to reduce this risk?

The answer to these questions is inherently tied to the estimation of 2 quantities: the number of infections occurring at the event and the postevent secondary attack rate, or number of subsequent infections in the participants' social circles. Evaluating the safety (or lack thereof) of large public gatherings can then be reframed as quantifying the significance and magnitude of their effect on the distribution of the number of primary and secondary COVID-19 cases. Yet, despite the growing body of literature on COVID-19 risk evaluation and recent efforts to evaluate the safety of live events, this effect remains ill-characterized. Nevertheless, over the past several months, several calculators were developed to estimate this risk [11-14]. These methods can typically be placed in 1 of 3 categories: ranking heuristics, context-based heuristics, and transmission risk calculators.

Ranking Heuristics

These estimators typically rank events on a scale ranging from "low" risk to "high" risk based on the feedback of medical experts [13,15-17]. However, these heuristics do not take into account contextual information, including the prevalence. For example, the risk associated with an event would be classified as high regardless of whether it was held in August 2020 (background prevalence of 1 in 3000 individuals in the United Kingdom) or January 2021 (prevalence of 1 in 60 individuals [18]).

Context-Based Heuristics

These calculators estimate the probability of encountering 1 COVID-19 case based on the number of people attending an event [11,12]. While more context-aware than risk assessment charts, such estimators do not attempt to model transmission dynamics—which is undeniably one of the main unknowns in the spread of viral epidemics—and consequently rarely stratify risk by type of activity. To exemplify, a classical music recital of 1.5 hours for the BBC Proms would potentially be considered equally risky to a 3-hour concert in which participants could be expected to sing along.

Transmission Risk Calculators

Stemming from physics or fluid dynamics, these calculators focus on modelling the aerosolization and spread of microdroplets—typically in a closed or indoor environment [19-22]. These fine-grained models thus must be combined with extensive and often prohibitive simulations of crowd movements in order to model transmission dynamics during any given event.

Limitations of Existing Estimators

Regardless of their category, most of these models rely on a large number of input parameters, including (but not restricted to) the prevalence of the disease. While certain calculators attempt to bridge the gap between expert heuristics and physical models [11,23], they are not capable of predicting the risk of a future event. Moreover, all of these estimators provide point estimates—in other words, their output is a single number to quantify the risk. Given the uncertainty associated with all the inputs and the parametrization of the problem as well as the high stochasticity of viral transmission, the provision of a single consolidated outcome or number can potentially be misleading. This is because a singular focus on the expected outcome precludes consideration of the distribution of all possible outcomes, including worst-case scenarios. In the context of COVID-19, where the majority of new cases has been shown to be caused by a minority of index cases [24-26], the modelling of tail events and potential super-spreader phenomena takes on significant importance for risk assessment [26,27].

Mitigating Transmission Risk

Meanwhile, with the increasing vaccination rates in several countries around the world, a few initiatives have begun to evaluate the outbreak risk associated with live events empirically [28-31]. This is because vaccinated individuals may still be infected with SARS-CoV-2 [32,33], and even antigen-test based screening of ticket holders offers no guarantee due to false negatives [34,35]. The estimation of what constitutes an admissible level of risk thus poses a difficult conundrum to the live event industry. To begin answering these questions, the CAPACITY study [36]—a partnership between Certific (a private, remote testing, health status, and identify certification service) and Imperial College London—aims to predict and measure the outcomes of full capacity live events while ensuring rigorous implementation and alignment to current public health and recommended safety measures. Central to this study is the provision of a streamlined and efficient pre-event screening protocol of all ticket holders using professionally witnessed rapid at-home antigen tests followed by postevent monitoring based on antigen tests, surveys, and safety recommendations (see Multimedia Appendix 1). In this setting, providing risk estimates not only becomes essential in communicating to the ticket holders their own level of risk so that they may make an informed decision of whether to attend the event but also necessary to inform event managers and policy makers on the likelihood of an outbreak task that serves here as the motivating application behind this paper.

A Working Example: Concert at the Royal Albert Hall

In order to understand and illustrate the potential challenges that arise in the risk estimation for the CAPACITY study, we

considered as an example a concert at the Royal Albert Hall (RAH) and demonstrate how to estimate the associated risk assuming a near capacity attendance of 5000 in the main concert hall, which has a volume of 86,650 m^3 [37], with a dwell time of 3 hours. Attendees will be assumed to be a cross-section representative of the general British public and will be required to have a negative COVID-19 antigen test result within 2 days prior to the event, as well as satisfying other self-declared symptoms and exposure-risk questions. Vaccination status would be requested, but not required, for attendance, and full compliance with mask wearing was assumed in our default example.

Goals and Contributions

The objectives of our modelling approach were threefold: (1) enable the quantitative comparison of different activities and event characteristics, (2) estimate the efficacy of various safety protocols, and (3) provide a predictive risk assessment (ie, the risk associated with a scheduled future event). To this end, we delineated our approach into 3 sequential steps (see Figure 1): (1) estimating the number of contagious participants, (2) evaluating the transmission dynamics, and (3) comparing the risk of holding the event with the null model (ie, if the event had not taken place). We illustrated the application of our risk modelling pipeline in the RAH example to highlight the risk's dependency on factors such as prevalence, mask wearing, number of attendees, and event duration. In particular, we demonstrated how this particular event held on 3 different dates corresponding to 3 distinct COVID-19 prevalence regimes in

the United Kingdom (stable low prevalence: August 20, 2020; high prevalence peak: January 20, 2021; medium declining prevalence: March 20, 2021) would likely lead to transmission events that were on par with community transmission rates (0.06 vs 0.07, 2.38 vs 2.39, and 0.67 vs 0.60, respectively; see Table 1). However, the 99th percentile of the prediction interval for the infections at the event would likely be substantially higher than the background rate (1 vs 1, 19 vs 8, and 6 vs 3, respectively), further demonstrating that sole reliance on vaccination and antigen testing to gain entry would significantly underestimate the tail risk of the event. However, we emphasize that the goal of this paper is not to present a novel "state-of-the-art" risk estimation procedure. This is because COVID-19 transmission mechanisms remain poorly characterized, and we acknowledge that our approach requires certain simplifications and assumptions that we discuss at length in the last section of this paper. Rather, faced with the need to provide a risk evaluation tool despite many unknowns, our estimation pipeline combined the best tools at hand to assess the order of magnitude of the risk—thereby opening the avenue for further work on contextualized COVID-19 risk assessment. Consequently, in providing a pipeline for risk estimation, our objective was twofold: (1) developing a publicly available platform to increase risk awareness and promote informed consent for event organizers and participants, while simultaneously (2) encouraging the data collection that is currently so desperately needed for risk assessment. Our model can be applied to any event occurring in the near future and is presented in a user-friendly RShiny interface [38].

Figure 1. Summary of our modelling pipeline.
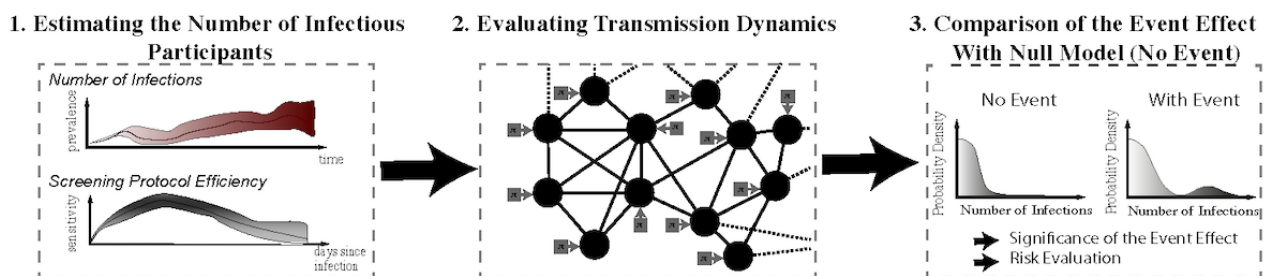
Table 1. Quantiles of the number of transmission events for the Royal Albert Hall concert, by event date, assuming that all participants were wearing masks, so that the exhalation of particles is reduced by 70% and inhalation by 50%.

Statistics	August 20, 2020		January 20, 2021		March 20, 2021	
	Event	Null	Event	Null	Event	Null
Median	0	0	1	2	0	0
Mean	0.06	0.07	2.38	2.49	0.67	0.63
1st percentile	0	0	0	0	0	0
2.5th percentile	0	0	0	0	0	0
97.5th percentile	1	1	10	7	3	3
99th percentile	1	1	19	8	6	3

Methods

Modelling the Risk of a Large Public Event

Step 1: Estimating the Number of Infectious Participants

Step 1a in our risk modelling procedure was determining the projected incidence, by predicting the number of infectious cases attending a given future event. COVID-19 forecasting is undeniably an involved task, as reflected by its impressive corresponding body of literature (eg, agent-based models or susceptible-exposed-infectious-removed models [39-49]). Predicting the number of new cases per day typically depends on the choice of a specific parameterization (eg, an exponential growth for computing the reproductive number R [50,51]), whose validity is severely hindered by continuous updates to public policies. To alleviate these concerns, we used a nonparametric k-nearest neighbor (kNN) approach. Using all trajectories of the disease incidence across countries and time since the beginning of the pandemic, we computed the k=100 closest trajectories (in terms of the l_2 loss) on time windows of 2 weeks. The historical trajectories of these kNNs were then used as a "dictionary of observed behaviors" to predict the daily incidence rate in the days leading to the event. We defer to Multimedia Appendix 2 for a more in-depth discussion of this estimation procedure, a description of the parameter selection process, and an evaluation of its performance compared with standard epidemic prediction methods. To briefly summarize, our kNN approach provides a nonparametric, model-agnostic approach to epidemic prediction that is more robust for nonstationarity in public policies than model-based approaches. We show in Multimedia Appendix 2 that these parameters (k=100 neighbors, fitted on trajectories of 14 days) are optimal in allowing an accurate estimation of the trajectory while providing adequate coverage and uncertainty quantification. In fact, we show that, while standard methods fail to provide reliable uncertainty estimates, our kNN methods provide a coverage greater than 95%. Despite coming at the price of wider prediction intervals, our pipeline privileges methods that allow us to correctly estimate the uncertainty in its outputs—thereby more accurately reflecting the state of our knowledge (or lack thereof). Figure 2 presents a comparison of the projected incidences for our 3 dates of interest (August 20, 2020; January 20, 2021; March 20, 2021) for the RAH concert using 2 weeks of fitting and predicting 4 weeks in advance. Note the good coverage provided by our method (the convex hull of the 95% prediction intervals for the projected incidences contains the actual observations). These plots also highlight the importance and variability of the incidence, which varied by orders of magnitude between August 2020 and January 2021.

Figure 2. Projected incidence (average and 95% prediction interval) using a 100-nearest neighbor approach, which provides good coverage (observed trajectory lies within the 95% prediction interval). The black line denotes observed incidence rates, while the red denotes the predicted rates, based on an initial period of observation of 14 days; the prediction interval for the predicted incidence over the next 4 weeks is highlighted in dark grey.
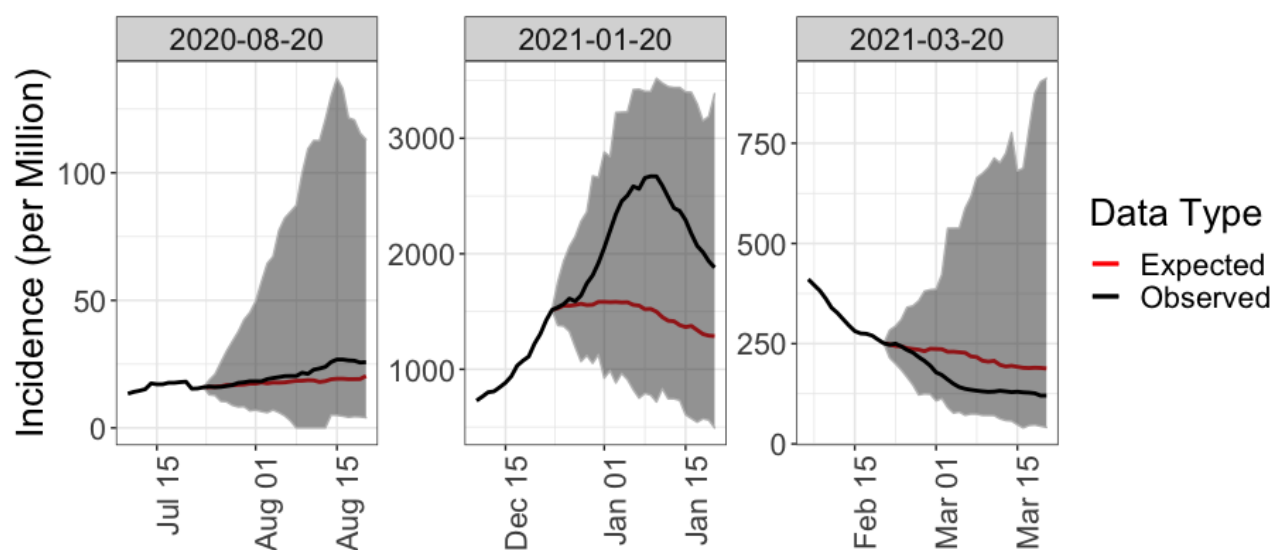
Step 1b was determining the under-ascertainment bias. The estimated number of new cases based on official incidence data will then need to be corrected for under-ascertainment. The latter refers to the downward bias of the reported prevalence in the population, due for instance, to limited testing capacity, low test sensitivity, or people being unwilling or unable to take a test. To this end, we compared the ratio of the number of deaths over reported cases (translated by 3 weeks) to an expected, age-stratified infection-fatality ratio [52] (see Multimedia Appendix 2 for more details). To highlight the potential importance of this correction step, the ascertainment rate for the United Kingdom was evaluated as over 90% for August 2020 but below 40% for December 2020.

Step 1c was determining the number of infectious participants at the event. Having predicted the background daily incidence rate, we turned to the estimation of the number of infectious participants who will attend the event despite the screening protocols. For an infectious individual to attend the event in spite of the CAPACITY study's screening protocol, they must (1) have no COVID-19–like symptoms or fail to report them on the morning of the event, (2) receive a (false) negative result during antigen testing D at 2 days prior to the event, and (3) be

contagious (rather than simply infected) at the time of the event. We evaluate the joint probability of these events as follows and, for the sake of clarity, refer the reader to Multimedia Appendix 2 for an in-depth explanation of our estimation procedure.

Regarding symptom-check failure, one of the main challenges associated with the COVID-19 crisis is the number of asymptomatic cases—that is, infected individuals who do not express symptoms and are thus unaware of their potential infectiousness. This group includes individuals that are either presymptomatic or completely asymptomatic during the course of their illness—the latter are estimated to represent roughly 25% of all cases [53]. For symptomatic patients, the probability of having symptoms on the day of the event is also a function of time since infection. To account for this temporal dependency, we used estimates of the incubation period (defined as the number of days between infection and symptom onset) from McAloon et al [54] and data on symptom duration from van Kampen et al [55] to estimate the probability for a ticket holder infected k days before the event to exhibit symptoms on the day of the event. A density plot of this probability is displayed in red in Figure 3A.

Figure 3. (A) Density of the COVID-19 incubation time and percentage culture positive and (B) probability that an individual is infectious (light grey), that the screening protocol will miss them (black), and that they will be missed and so attend the event (red) as a function of days since infection. The shaded regions denote the uncertainty of this estimate due to the uncertainty on the sensitivity of the test.
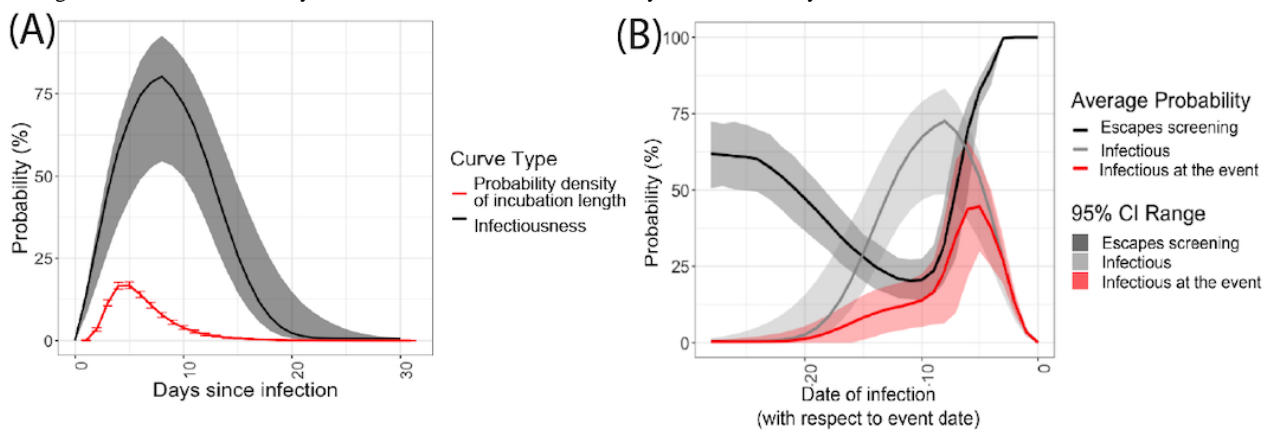
Regarding antigen test failure, the sensitivity of COVID-19 tests depends heavily on the time since infection—whether these are the gold-standard polymerase chain reaction (PCR) or lateral flow antigen assays [56]. Moreover, studies have shown that lateral flow antigen tests have much lower sensitivity on asymptomatic individuals than symptomatic: In particular, according to a recent Centers for Disease Control and Prevention report [57], rapid antigen testing has 80% sensitivity on symptomatic individuals, but only 40% sensitivity on asymptomatic individuals. Coupling the sensitivity estimates [56,57] with the distribution of the incubation period and estimated percentage of asymptomatic cases [53,54], for each individual infected at day k taking an antigen test D days before the event, the probability of getting through the filtering protocol is thus given by the formula:

$$\boxed{\times}$$

where $s^{(symptomatic)}_{t-k-D}$ and $s^{(symptomatic)}$ are the sensitivities of the test taken D days before the event for a symptomatic participant infected $t-k$ days before the event and an asymptomatic individual, respectively. The parameter $p^{(symptom)}_{t-k}$ denotes the probability for a symptomatic individual to exhibit symptoms $t-k$ days after infection, whereas $p^{(symptom)}$ is the probability of being asymptomatic. Finally, the variable p_{sc} denotes the probability of the symptom check failing—namely, that the participant does not want to report their symptoms (see Multimedia Appendix 2 for more details). The curve in black on Figure 3B shows the probability of the failure of the screening protocol as a function of days after infection. The shaded areas denote the uncertainty around this estimate due to the variability of the incubation time.

The infectiousness of the participants—that is, the propensity of an infected ticket holder to contaminate others—is a function of time since infection. In order to estimate this relationship, we build upon the existing literature studying the link between reverse-transcription PCR thresholds and cultivable virus [58,59]. The percentage of culturable viral material in the sample can indeed be used as a proxy for infectiousness. Using the estimated percentages of viable samples [58,59] as a function of time since symptom onset, compounded with distribution of the incubation period duration [54], we computed an estimate of the infectiousness as a function of time since infection (black curve in Figure 3A). A more complete description of this estimation procedure is presented in Multimedia Appendix 2. The results are presented in Figure 3B. The red line in Figure 3B shows the resulting probability for an infectious ticket holder to pass through the screening protocol and be allowed into the event. Note that ticket holders that have been infected 5 days before the event are the most likely to be infectious and let in the venue on the day of the event.

Step 1d was determining the number of participants at risk. Finally, the last quantity that we needed to infer before getting into the specifics of the transmission mechanisms was the number of participants at risk of being infected who present at the event. This requires a knowledge of the participants' COVID-19 susceptibility status (ie, has the participant already had COVID-19 in the previous year, or has the participant been vaccinated?) While previous history could be imputed through additional questions (eg, previous positive test for COVID-19

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and symptoms combined in a model such as in [60]), for the sake of simplicity, we only considered the vaccination status of the participants—thus leaving out the proportion of the population that had COVID-19 but was not yet vaccinated. This induces a risk estimate that is biased upward and is thus more conservative. We imputed missing data (cases where the participants have not filled in their vaccination status) using linear regression, expressing vaccination rate as a function of time. This assumes that vaccinations are operating at capacity (see Multimedia Appendix 2 for a longer discussion on the reasons for this approximation and further ways of improving this model). Having imputed the rate of new vaccinations $\pi_s, s=1\ldots t$ days leading to the event, we turned to the estimation of the number of individuals that are likely to be susceptible. Recent reports indicate that vaccine-acquired immunity is a function of both time since vaccination and number of doses [61]. To compute the effective number of participants at risk in the event, we used a compound Poisson distribution: On each day s in the weeks leading to the event, the number X of new participants vaccinated (having either their first or second dose) is expressed as a Poisson($\pi^{(dose\ j)}$), where $j \in \{1,2\}$. Each of these newly vaccinated individuals then has a probability $\rho^{(dose\ j)}$ of being immune, depending on the date and dose j that they

have received. The resulting number of immune people Z attending the event can thus be modelled as:

We discuss in Multimedia Appendix 2 how this estimation can easily be modified as the vaccination rates increase and the Poisson approximation becomes no longer valid.

Royal Albert Hall Example

For the RAH example, we present a comparison of each quantity for 3 different dates (see Table 2). Of note is that the screening safety protocol is effective in more than 60% of cases, that when combined with the expected infectiousness of participants and self-reporting of COVID-19–like symptoms, implies that 95% of infected cases are removed. We also note that prevalence is very important in determining the number of infectious cases at the event—thereby highlighting the importance of a context-aware risk calculator. The combined effect of the screening protocol and the natural time-dependent infectiousness of infected ticket holders means that the number of infectious participants at the event is likely to be very low (~ of the order of tens in times of extremely high prevalence).

Table 2. Comparison of the efficiency of the screening protocol and the number of infectious participants at the event by date.

Measurement	August 20, 2020	January 20, 2021	March 20, 2021[a]
Projected incidence (in 1,000,000)	20	1286	188
Number of infected participants	3.6	299.3	50.2
Number of infectious participants at the event	0.22	7.96	2.00
Percentage of caught cases, %	94	97	96
Number of susceptible participants	4996.4	4700.7	3860.4

[a]Vaccination rates started to account for a substantial proportion of the British public, so that the sum of the number of susceptible participants and the number of infected participants does not equate 5000.

Step 2: Modelling Transmission Dynamics

Having estimated the number of infectious participants at the event, the second major component of our model consists of estimating the number of transmission events during the event itself.

Identification of Transmission Mechanisms

More than a year after the start of the epidemic, the precise mechanisms by which COVID-19 is transmitted are still unclear. Aside from direct physical contact, experts continue to debate the significance of the following 2 main routes of infection: droplet transmission and airborne transmission.

In the scenario of droplet transmission, transmission happens through the inhalation of droplets (particles of 5-10 μm in diameter [62]) and typically occurs when a person is in close proximity (within 1 meter) of someone who has respiratory symptoms (eg, coughing or sneezing).

Increasing concerns around airborne transmission have been raised by a number of experts over the past few months [63,64]. Airborne transmission refers to the presence of the virus within droplet nuclei remaining in the air for long periods of time and

with the potential to travel long distances [63] and penetrate more deeply in respiratory tracts. Airborne transmission has been estimated to be nearly 19 times more likely indoors than outdoors [65]. In the context of large public events, this transmission route thus has more diffusive power and hence could explain several super-spreader events (SSEs) [6], making it a major cause for concern [2,63,66-72].

While droplet emission is undeniably a source of concern and a major source of transmission, simple safety precautions such as mask wearing have been shown to efficiently control this transmission source [73,74]: It is estimated that face masks can block 80% of exhaled droplets and reduce inhaled droplets by up to 50% and so, on average, reduce the transmission probability by 70% [73]. Conversely, the evidence concerning the efficiency of standard protective equipment in filtering aerosol droplets varies widely across studies probably due to "variation in experimental design and particle sizes analyzed" [73]. Airborne transmission in indoor settings can thus represent one of the main risk factors in live events, which we focus on modelling using the aerosol model proposed by Jimenez and collaborators [21,69,75]. This aerosol transmission model is currently one of the only COVID-19 transmission models that

provide enough granularity to quantify the risk associated with an event. This recognized model has been used several times in the literature over the course of the pandemic [76], including to allow in-class teaching at the University of Illinois at Chicago [70]. Based on the Wells-Riley model [77-79], this estimator calibrates the quanta to known transmission events and considers important factors to compute a risk estimate, including event-specific (eg, number of people, local prevalence) and venue-specific (ventilation rate, size of the venue, UV exposure) variables. This Wells-Riley–based model relies on the evaluation of 3 quantities: (1) the quanta exhalation rate, which is contingent on the activity performed and the number of infectious participants; (2) quanta concentration, which is a function of the volume of the space, the room ventilation rate, and the quanta exhalation rate; and (3) quanta inhalation rate, which is a function of the quanta concentration and breathing rate associated with the activity performed. The probability for each susceptible individual to be infected can then be written as $p_{infection} = 1 - e^{-qinhalation}$. See Multimedia Appendix 3 for more details.

Modelling the Uncertainty of the Model

To estimate the uncertainty associated with this model, we used Monte-Carlo simulations. We simulated random input parameters (number of infectious and susceptible individuals) using the distributions and uncertainty estimates discussed in the previous section. In order to model the uncertainty associated with the aerosol transmission model, we added a sampling step at the end of the Jimenez and Peng pipeline. This allowed us to account for individual variations in infectious participants' ability to spread the disease and to remain consistent with the extensive literature on the heavy-tailed Pareto nature of COVID-19 transmission and superspreading [24-27]. For each infected participant, we sampled the number of quanta that they exhale using a Pareto distribution with shape $\theta = 1.16$ and rate $\eta = \theta/(\theta - 1)q^{exhalation}$. This produces a distribution centered around $q^{exhalation}$ but skewed to the right and heavy-tailed—thereby modelling the heterogeneity in infected participants' ability to spread. This choice of parameters allowed us to abide by the Pareto principle, according to which 80% of transmissions are due to 20% of those infected. In accordance with the uniform mixing assumption of the aerosol transmission models, susceptible participants then all inhale a quanta concentration that is a function of the sum of the exhaled quanta: All have an identical probability of becoming infected. In mathematical terms, infections are thus simulated using a binomial distribution such that $n_{infected} \sim \text{Binomial}(n_{susceptible}, 1 - e^{-qinhaled})$. We discuss the limitations of this approach and its assumptions in the discussion section of this paper.

The code for the model can be found online on the authors' Github [80].

Results

Step 3: Comparison With the Null Model

To quantify the effect of the event, it is necessary to put it in context of the background rate of infections: Even if the participants had not been to the event, they could have been infected elsewhere. In this null model, the number of infections is binomially distributed, such that the number infections Y is $Y \sim \text{Binom}(n_{susceptible}, \pi)$.

We present the results for the RAH example in Table 2. This table shows in grey the values of the different quantiles of this distribution. We note the skewed distribution that we obtain is expected given the modelling of the uncertainty around inhalation rate. If the event did not occur, then on each respective date, there would be an expected community transmission of 0.07 (95% prediction interval: 0-1), 2.5 (95% prediction interval: 0-7), and 0.63 (95% prediction interval: 0-3) events on August 20, 2020, January 20, 2021, and March 20, 2021, respectively. However, with the event taking place on these dates and calculating the expected number of infectious individuals, susceptible individuals, and transmission dynamics within the venue, the distribution of the number of transmission events would in general widen to 0.06 (0-1), 2.38 (0-19), and 0.67 (0-6) in that same order. In this case, it is important to note the similarity in mean transmission between the "event" and "no event" scenarios and their substantial deviation in the tails. This highlights the importance of modelling the distribution of the risk and highlighting its substantial heavy tails, rather than providing point estimates.

It is likely, although not inevitable, that the event will have an impact on the transmission and increase it irrespective of the level of the prevalence. However, for low levels of prevalence and higher vaccination rates, this substantially decreases. Having computed the number of expected transmission events, we can then compute several complementary metrics of interest including, for example, the secondary attack rate (SAR)—that is, the number of COVID-19 cases in the participants' community in both the null and event models. SAR can be calculated from the predicted reproductive rate (R) in the regions where the ticket holders dwell. In the United Kingdom, R rates are updated on a weekly basis at regional levels (eg, East Midlands, London) and available from the Office for National Statistics or can be derived from the kNN modelling previously described. An opportunity for further research would be to estimate SAR within households by gathering contextual data from ticket holders. Equally, estimates of hospitalizations and deaths might be possible based on individual characteristics and comorbidities; however, this is beyond the scope of the current article.

Evaluating the Effectiveness of the Screening Protocol

This risk modelling pipeline also allows comparison of different protocols and situations. For example, this pipeline highlights (1) the importance of event duration (the longer the dwell time at the event, the more at risk the participants) and (2) the importance of wearing masks. Table 3 quantifies the outcomes of holding the event on our 3 dates, assuming that either 0%, 50%, or 100% of participants are wearing masks or varying parameters such as the density or length of the concert. Figure 4 completes that analysis by providing a visual representation of the effect of these parameters on the distribution of the number of infections. The distributional nature of these results is essential in highlighting nuances between scenarios: While

holding an event at half capacity or for half the duration produces average transmission risks that are roughly similar, holding the event at half capacity seems to more substantially reduce the effect of the event in the tails of the distribution.

Table 3. Effect of different input parameters on the quantiles of the number of infections for an event at the Royal Albert Hall across all 3 dates.

Event	August 20, 2020, median, mean (99% CI)	January 20, 2021, median, mean (99% CI)	March 20, 2021, median, mean (99% CI)
No mask wearing, 3 hours, n=5000	0, 0.3 (0-4)	5, 9.9 (0-76)	1, 2.4 (0-21)
50% mask wearing, 3 hours, n=5000	0, 0.2 (0-3)	3, 5.5 (0-40)	1, 1.3 (0-13)
100% mask wearing, 3 hours, n=5000	0, 0.1 (0-1)	1, 2.4 (0-19)	0, 0.7 (0-6)
100% mask wearing, 1.5 hours, n=5000	0, 0.04 (0-1)	0, 1.4 (0-10)	0, 0.4 (0-3)
100% mask wearing, 3 hours, n=2500	0, 0.2 (0-1)	0, 0.9 (0-8)	0, 0.2 (0-3)

Figure 4. Boxplots showing the distribution of the number of infections across different scenarios, for our Royal Albert Hall event held on March 20, 2021: Where variables are not mentioned, the number of attendees is 5000, the duration is 3 hours, and the proportion of attendees wearing masks is 100%.
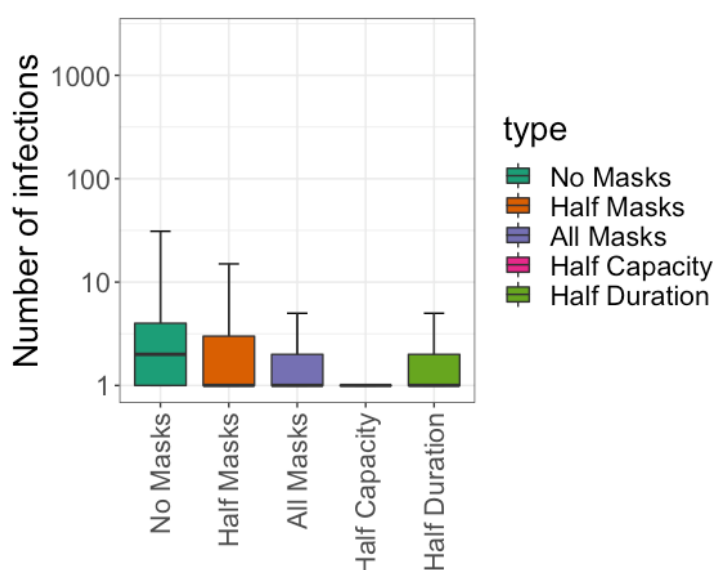
In addition to the aggregated risk that a live event presents, individual risk of transmission can be estimated and can be communicated to ticket holders so that they can gauge whether the risk of attending the event outweighs their desire to attend. For the first person to purchase a ticket, risk of transmission will be calculated based on their own immunity status (eg, vaccination, regional prevalence) and a synthetic population based on national prevalence at that time. As more bookings are assigned to ticket holders, the reliance on the synthetic population decreases as understanding of the number of susceptible and potentially infectious individuals attending the event increases. Therefore, the confidence in the risk score increases as the event draws closer and as the proportion of tickets sold increases. This can be reflected in the updated risk scores provided to ticket holders as the event approaches. The individual risk scores can be modified based on alternative scenarios imputed into the risk algorithm. For example, for an individual not yet vaccinated, their risk could be also presented as if they had been vaccinated, offering an opportunity for the individual to appreciate how vaccination could have modified their risk. Such an approach could form the basis for behavior change interventional studies for promoting health literacy and tackling vaccine hesitancy (see Multimedia Appendix 1). By working in partnership with the live events organizer, individuals that chose to opt out can be reimbursed without delay and the ticket re-sold.

Discussion

The modelling we propose is based on prevalence estimates and screening protocols to calculate the number of infectious and susceptible individuals attending the event as well as transmission dynamics at the venue to predict the number of new infections. Our paper demonstrates the value of estimating attack rates from live events so that they can be appropriately managed. We also demonstrate how individual ticket holders can receive personalized risk scores for contracting COVID-19 at the event, which would, for the first time, enable genuine informed consent to be obtained. Although this methodology provides clear benefit to event organizers, local public health authorities, and individual ticket holders, our approach is based on several assumptions that group in 2 categories: modelling assumptions and parameter sensitivity.

Modelling Assumptions

As they combine data and tools from different sources, the computations in our pipeline rely on assumptions at 3 main levels: predicting COVID-19 prevalence, assessing the

efficiency of the screening protocol, and transmission at the event.

Predicting COVID-19 Prevalence

To predict future COVID-19 incidence, we chose a kNN approach as it yields a more robust prediction and better uncertainty quantification than most existing parametric methods. One of the downsides of this approach is that it might not generalize very well to entirely novel behaviors or viral variants—in which case well-parameterized methods may outperform our approach as knowledge of transmission, vaccination, and other relevant model parameters continues to improve. While prevalence predictions are important for event planners and attendees alike, on the day of the event, the more important metric is whether official case rates reflect actual cases (ie, the ascertainment rate). Historically, this rate has been low due to limited testing facilities, and our method to determine ascertainment using cases, deaths, and infection-fatality rates reflects this, but also indicates that ascertainment may exceed 100% in times of widespread testing and low prevalence. It was beyond the scope of this paper to further investigate ascertainment, but we expect that future research will clarify the impact of different test types, their false negative and positive rates, and their frequency of use in determining the ascertainment rate.

Assessing the Efficiency of the Screening Protocol

Our modelling framework assumes that events will screen participants with COVID-19 tests, such as virtually witnessed lateral flow antigen tests. Assessing the efficiency of this screening step requires the estimation of (1) the sensitivity of the test, (2) the probability of having symptoms, and (3) the probability of being infectious—all of these quantities being a function of days since infection. Our estimation of each of these quantities is based on published data—with the exception of the probability of symptom check failure (ie, the probability that a participant lies about their symptoms to get in). By default, we select this probability to be 50%, a choice that will be improved upon as the CAPACITY and other similar studies gather behavioral data. However, as shown in Multimedia Appendix 4, this factor has a relatively minor impact on the outcome of the model compared with the uncertainty of the other inputs. Of potentially greater concern is our assumption that the probability of testing negative 2 days before the event is independent (conditionally on time since infection) of a participant's infectiousness during the event. A potential avenue for improvement could consist of determining both test sensitivity and infectiousness as a function of viral load and estimating the joint probability of the viral load 2 days apart. However, the data required for this approach are—to the best of our knowledge—still lacking and given the variability of the viral load or PCR cycle threshold behavior, this conditional independence assumption seemed a reasonable first-order approximation.

Transmission at the Event

The airborne transmission model that we use relies on a homogeneous (well-mixed) air hypothesis for an indoor environment. While several other models have been proposed (either breaking the room into compartments or using a distance index) to counter this hypothesis, we highlight (following the discussion by Jimenez and Peng [75]) that this is a first-order approximation: Some participants will have more risk and others less, so that at low quanta concentration, this effect will be averaged out. At very high concentration, the model will likely underestimate the number of infections, but given the efficiency of the screening protocol and density limitations, we do not expect this scenario to be common. Moreover, while this model was originally developed for indoor transmission, its application to an outdoor setting—where the ventilation rate can be considered infinite and transmission is more likely to occur through droplets rather than aerosolized particles—can nonetheless provide a conservative estimate of the risk. We are however currently working on developing a better model for outdoor transmission, relying on a modelling of droplet transmission in crowd bottlenecks. We leave the detail of this separate transmission model to future work. Finally, we note that our model is not tied to any specific transmission mechanism, and as our knowledge of COVID-19 transmission improves, we can refine and supplant the transmission dynamics with a superior alternative or another model that is deemed more suitable.

Parameter Sensitivity

While we try to limit the number of input parameters in our pipeline, the sensitivity of the estimates to these inputs (namely, the mask efficiency and population of interest) has to be studied. We refer the reader to Multimedia Appendix 4 for a quantitative sensitivity analysis and highlight our conclusions here. In terms of the model parameters, the greatest unknown consists in determining the efficiency of masks and protective equipment—the latter having been shown to vary depending on the mask type and activity. However, we hope to make use of the growing body of literature on the topic to update and refine this important factor. Second, our prediction framework assumes that participants at the event have the same probability of infection and vaccination as their regional average. However, this might not be the case as participation in the event may be an incentive to get vaccinated or conversely might select for less cautious subpopulations. The importance of this sampling frame assumption nonetheless decreases as participants' vaccination status and behavioral data from the CAPACITY study will result in more precise estimates.

Model Validation

Finally, one of the main current hurdles for developing risk estimators lies in the absence of quality data to validate and benchmark different transmission models—thereby making the task of validating our transmission pipeline a rather daunting task. Indeed, while we can (and have, see Multimedia Appendix 2) check the accuracy of the vaccination and prevalence estimation step, the validation of the transmission model itself is inherently difficult: There are no, or very few, available datasets on COVID-19 spread following live events or rigorous accounts of SSEs, nor are there any statistics on how likely SSEs are. As such, the majority of SSEs that are documented currently (1) are generally not detailed enough to untangle the huge variability in context (eg, outdoors vs indoors, activity

performed, background prevalence) and (2) suffer from selection bias—and might not be reflective of the general distribution of live events. To make up for the current lack of testing data, we resort here to the following 3 strategies: model checking, model validation on (scarce) existing data, and prospective data gathering.

For model checking, we begin by validating the behavior of our model estimates on documented SSEs [81]—that is, we confirm that the model outputs (1) present similar tail behavior as these documented SSEs and (2) are predicted as outlier SSE events by our model.

For model validation on (scarce) existing data, we also consider 2 documented live indoor concert events [82,83] and use the event parameters as well as the documented transmission statistics to verify that these numbers fall within the realm of feasible outcomes.

For prospective data gathering, finally, to overcome the lack of available data, we propose using the RShiny app [38] as a data collection platform and encourage users (event organizers and participants alike) who use the app to record their event in our dataset by filling in a survey [84]. This paves the way for a larger-scale and more detailed record of transmission events at large gatherings, as well as a more precise modelling of transmission dynamics.

This validation and model assessment step is further described in Multimedia Appendix 5.

Conclusion

A nuanced, data-driven system is required to assess risk at each event informed by the characteristics of all ticket holders and the background risk of transmission concurrent to the event, so that proportionate and specific action can be taken by event organizers and public health authorities. We have detailed our attempt to create such a system and have outlined its predictions and limitations. Our end-to-end risk model is provided in the form of an RShiny interface. At times of high prevalence, this type of system will ensure events likely to increase transmission can be halted. At times of low prevalence, this will ensure events can potentially continue to operate. Learning to live with SARS-CoV-2 will be about implementing systems that support hyperlocal, data-driven decisions so that far-reaching and highly damaging sector-specific lockdowns can be avoided as much as possible.

Conflicts of Interest

JK is the medical director and co-founder of Certific. None of the remaining authors have any competing interests.

Multimedia Appendix 1
Prediction.
[DOCX File , 537 KB - publichealth_v7i12e30648_app1.docx]

Multimedia Appendix 2
Model and assumptions of the Jimenez aerosol transmission model.
[DOCX File , 146 KB - publichealth_v7i12e30648_app2.docx]

Multimedia Appendix 3
Sensitivity analysis.
[DOCX File , 178 KB - publichealth_v7i12e30648_app3.docx]

Multimedia Appendix 4
Risk communication.
[DOCX File , 236 KB - publichealth_v7i12e30648_app4.docx]

Multimedia Appendix 5
Model validation.
[DOCX File , 350 KB - publichealth_v7i12e30648_app5.docx]

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Abbreviations

ARC: Applied Research Collaboration
kNN: k-nearest neighbor
NIHR: National Institute for Health Research
PCR: polymerase chain reaction
RAH: Royal Albert Hall
SAR: secondary attack rate
SSE: super-spreader event

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Original Paper

Risk Factors Associated with a Dengue Fever Outbreak in Islamabad, Pakistan: Case-Control Study

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Abstract

Background: On October 23, 2016, 79 dengue fever cases were reported from the Union Council Tarlai to Federal Disease Surveillance and Response Unit Islamabad. A team was established to investigate the suspected dengue outbreak.

Objective: The aim of this study was to determine the extent of the outbreak and identify the possible risk factors.

Methods: Active case finding was performed through a house-to-house survey. A case was defined as an acute onset of fever $\geq 38°C$ in a resident of Tarlai from October 2 to November 11, 2016, with a positive dengue virus (nonstructural protein, NS-1) test and any of the two of following signs and symptoms: retroorbital/ocular pain, headache, rash, myalgia, arthralgia, and hemorrhagic manifestations. A structured questionnaire was used to collect data. Age- and sex-matched controls (1:1) were identified from residents in the same area as cases. Blood samples were taken and sent to the National Institute of Health for genotype identification.

Results: During the active case search, 145 cases of dengue fever were identified by surveying 928 houses from October 23 to November 11, 2016. The attack rate (AR) was 17.0/10,000. The mean age was 34.4 (SD 14.4) years. More than half of the cases were male (80/145, 55.2%). Among all cases, 29% belonged to the 25-34 years age group and the highest AR was found in the 35-44 years age group (35.6/10,000), followed by the 55-64 years age group (35.5/10,000). All five blood samples tested positive for NS-1 (genotype DENV-2). The most frequent presenting signs/symptoms were fever and headache (both 100%). Stagnant water around houses (odds ratio [OR] 4.86, 95% CI 2.94-8.01; *P*<.001), presence of flower pots in the home (OR 2.73, 95% CI 1.67-4.45; *P*<.001), and open water containers (OR 2.24, 95% CI 1.36-3.60; *P*<.001) showed higher odds among cases. Conversely, use of bed nets (OR 0.44, 95% CI 0.25-0.77; *P*=.003), insecticidal spray (OR 0.33, 95% CI 0.22-0.55; *P*<.001), door screens (OR 0.27, 95% CI 0.15-0.46; *P*<.001), mosquito coil/mat (OR 0.26, 95% CI 0.16-0.44; *P*<.001), and cleanliness of the house (OR 0.12, 95% CI 0.05-0.26; *P*<.001) showed significant protective effects.

Conclusions: Stagnant water acting as breeding grounds for vectors was identified as the probable cause of spread of the dengue outbreak. Establishment of surveillance and an early reporting system along with use of protective measures against the vector are strongly recommended.

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Introduction

Dengue fever is a vector-borne viral disease transmitted by *Aedes aegypti* and *Aedes albopictus* [1] carrying dengue virus, which is a single-stranded RNA virus from the *Flaviviridae* family [2]. There are four distinct serotypes of dengue virus: DEN-1, DEN-2, DEN-3, and DEN-4 [3]. Recovery from infection by dengue virus provides lifelong immunity against that particular virus serotype. However, this immunity confers only partial and transient protection against subsequent infections by the other three serotypes of the virus. If the same individual is infected with another serotype, they can become seriously ill and develop complications of dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) [4]. Clinical features include flu-like symptoms with high-grade fever, headaches, nausea, vomiting, body aches, retroorbital pain, swollen glands/joints, bone or muscle pain, and rash [5].

Since 1970, the upsurge in all dengue virus serotypes has increased the danger of severe disease pertaining to secondary infections, resulting in steady growth in the frequency of epidemics [6]. During the last two decades of the 19th century and in the first two decades of the 20th century, dengue became sporadic in tropical and subtropical countries of the world [7]. Worldwide, the incidence is 50-100 million dengue cases and 250,000-500,000 cases of DHF per year. DHF/DSS is associated with a mortality rate up to 5%-10%. Dengue fever affects both genders; however, males are predominantly more affected [8,9].

In Pakistan, the first outbreak of dengue fever was reported from Karachi in 1994. Subsequently, huge outbreaks were reported from Karachi in 2005, Lahore in 2011, and Swat in 2013 with 6376 cases and 23 deaths. DEN-2 and DEN-3 were identified as the most prevalent serotypes in Pakistan [9]. Research has shown that a humid/warm environment favors the breeding of the mosquito vectors [10]. Various studies have also reported certain risk factors for dengue fever. Small puddles of stagnant water in plants, tires, and ditches have been identified as the preferred breeding sites of vectors. Clothing with long sleeves and legs, use of mosquito repellent, and vector control (insecticide residual spray and thermal fogging) have been determined to be the most effective preventive measures against dengue fever.

On October 23, 2016, the medical officer of a first-level health care facility (Basic Health Unit) in Union Council (UC) Tarlai telephonically communicated with the Federal Disease Surveillance and Response Unit at the National Institute of Health, Islamabad, that he had witnessed 79 dengue cases in only 3 days. On the same day, a team comprising members of the Field Epidemiology and Laboratory Training Program along with the local medical officer was deployed to investigate the dengue outbreak. The aim of this study was to determine the extent of the outbreak and identify the possible risk factors responsible for spread of the disease.

Methods

The investigation team performed a descriptive study and identified all cases that presented with fever. A case-control study was then performed from October 23 to November 11, 2016. Active cases, along with the cases reported earlier, were enrolled through a house-to-house case search. Diagnostic criteria set by the district government were used to enroll the cases in which a dengue virus antigen detection test targeting nonstructural protein-1 (NS-1) was used as a confirmatory test.

A case was defined as acute onset of fever ≥38℃ in a resident of Tarlai from October 2, 2016, to November 11, 2016, with a positive NS-1 test and any two of the following signs and symptoms: retroorbital pain, headache, rash, myalgia, arthralgia, and hemorrhagic manifestations (petechial spots, purpura, bleeding from the gums or nose).

Age- and sex-matched controls were selected from the neighborhood of the cases. Controls were residents who did not have fever and associated signs and symptoms, and had not tested positive for NS-1 during this time period. Information from inhabitants of the area, fitting the case definition, was collected using a structured questionnaire. Information was collected on demographics; dates of onset of illness, sign/symptoms, and laboratory confirmation; along with other relevant possible risk factors. A line list was prepared and a total of five blood samples were taken from the patients of UC Tarlai for laboratory confirmation.

Data were analyzed using Epi-info version 7. The mean age was calculated. Age groups were created to compute age group–specific attack rates (ARs). Frequencies of each variable were calculated. Multivariate analysis was performed to determine the risk factors. A *P* value <.05 was considered statistically significant.

Results

Patient Characteristics

During the active case search, 145 cases of dengue fever were identified by surveying 928 houses from October 23 to November 11, 2016. The overall AR was 17.0/10,000 (the total population of UC Tarlai was 84,810 during the study period). The mean age of the cases was 34.4 (SD 14.4) years (range 6-80 years). More than half of the cases (80/145, 55.2%) were men. Approximately 30% of the cases belonged to the age group 25-34 years, followed by 35-44 years, and 15-24 years. The age-specific AR per 10,000 individuals in the population showed the highest incidence among the 35-44 years age group, followed by the 55-64 years age group (Table 1).

Table 1. Age distribution of dengue fever cases among residents of Union Council Tarlai, Islamabad, from October 23 to November 11, 2016 (N=145).

Age group (years)	Cases, n (%)	Population, n	Attack rate (per 10,000)
<5	0 (0)	11,024	0.00
5-14	10 (6.9)	22,975	4.3
15-24	26 (17.9)	17,836	14.5
25-34	42 (29.0)	12,602	33.3
35-44	31 (21.4)	8700	35.6
45-54	20 (13.8)	5808	34.4
55-64	12 (8.3)	3374	35.5
65-74	2 (1.4)	1703	17.7
≥75	2 (1.4)	788	25.3

Signs and Symptoms

As shown in Table 2, the most frequent signs/symptoms were fever and headache, followed by myalgia and joint/bone pain, whereas only few patients presented with mucosal bleeding. Five blood samples were taken from the patients; all were positive for dengue fever (NS-1 antigen) and one was identified as genotype DEN-2.

Table 2. Clinical presentation of dengue fever cases in Union Council Tarlai, Islamabad, from October 23 to November 11, 2016 (N=145).

Signs and symptoms	Cases, n (%)
Fever	145 (100.0)
Headache	145 (100.0)
Myalgia	122 (84.1)
Joint/bone pain	121 (83.4)
Retroorbital pian	113 (77.9)
Nausea/vomiting	113 (77.9)
Abdominal pain	90 (62.1)
Petechia	64 (44.1)
Impaired consciousness	32 (22.1)
Rash	24 (16.6)
Mucosal bleeding	8 (5.5)

Preventive Measures and Distribution of Risk Factors

The use of different preventive measures was determined from the surveys with the 145 dengue fever cases. The majority of patients wore full cloth for protection against mosquito bites, approximately half used insecticide spray or a mosquito coil/mat stand, a third used repellent lotion, and bed net use was the least frequent preventive measure adopted. The possible risk factors were stagnant water around the house, presence of flower pots in the house, and open containers of water in the house (Table 3).

Table 3. Distribution of preventive measures adopted and possible risk factors among 145 dengue fever cases in Union Council Tarlai, Islamabad, from October 23 to November 11, 2016.

Variables	Cases, n (%)
Preventive measures	
Use of full clothing	129 (89.9)
Presence of door screening	82 (56.6)
Use of insecticide spray	80 (55.2)
Use of mosquito coil/mat	72 (49.7)
Use of repellent lotion	48 (33.1)
Use of bed net	24 (16.6)
Possible risk factors	
Stagnant water around house	106 (73.1)
Presence of flower pots in house	74 (51.0)
Open container of water in house	63 (43.4)
Uncleaned house	47 (32.4)
Water pools	22 (15.2)
Old tires in or around house	14 (11.2)
Travel history	16 (11.3)
History of blood donation	0 (0)

Epidemiologic Curve

The epidemiologic curve showed that the first case had a date of onset of illness of October 2, 2016, and most of the cases developed signs/symptoms on October 6 (n=22), followed by October 5 and October 7 (Figure 1).

Approximately 99 mm of rain fell on September 1, with two additional rain showers occurring in the middle of September.

Figure 1. Epidemic curve. Number of cases by the date of onset of illness (month/year) during the dengue fever outbreak in Union Council Tarlai, Islamabad (October 23 to November 11, 2016).
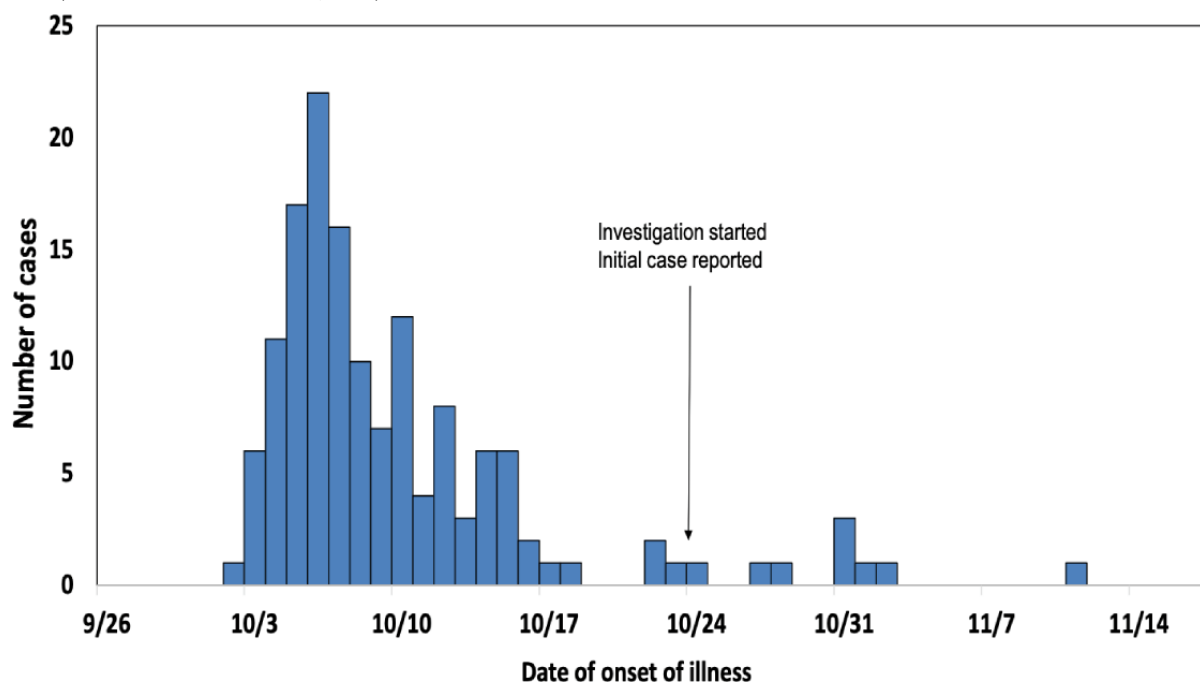
Factors Associated With Dengue Fever

In the bivariate analysis, stagnant water around houses, use of flower pots, and open water containers were significantly associated with increased odds of dengue fever among cases. Use of bed nets, insecticidal spray, a door screen, and a mosquito coil/mat, along with cleanliness in the house showed significant protective effects (Table 4).

On multivariate logistic regression, stagnant water (adjusted odds ratio 4.25, 95% CI 2.42-7.46, *P*<.001) and open containers in the house (adjusted odds ratio 1.94, CI 1.09-3.42, *P*=.02) showed significant associations with dengue fever incidence.

Table 4. Bivariate analysis of factors associated with dengue fever in Tarlai, Islamabad (October 23 to November 11, 2016).

Factor	Cases, n	Controls, n	OR[a]	95% CI	*P* value
Stagnant water	106	52	4.86	2.94-8.01	<.001
Flower pots	74	40	2.73	1.67-4.45	<.001
Open water container	63	37	2.24	1.36-3.60	<.001
Use of bed nets	24	45	0.44	0.25-0.77	.003
Insecticide spray	80	114	0.33	0.20-0.55	<.001
Door screen	82	120	0.27	0.15-0.46	<.001
Use of mosquito coil/mat	72	114	0.26	0.16-0.44	<.001
Cleanliness	98	137	0.12	0.05-0.26	<.001
Water pool	22	11	2.17	1.01-4.67	.04
Use of full clothing	129	139	0.34	0.13-0.91	.03

[a]OR: odds ratio.

Discussion

Principal Findings

Dengue fever is one of the most rapidly spreading diseases in the world, with a 30-fold increase in incidence in the last 50 years [11]. In this study, a dengue fever outbreak was investigated in a rural area of Islamabad capital territory. This study showed that the number of males with dengue fever exceeded the number of females affected by dengue fever. This finding is consistent with findings of another study [12] and might be explained by the fact that males are more involved in outdoor activities in Pakistani culture and hence are more prone to infection. Moreover, the extreme age groups (under 14 and above 65 years) were less commonly affected as compared to the working age groups, which is attributed to the fact that the former age groups tend to stay at home most of the time. This finding supports the conclusions of a similar study performed in Swat [9].

Meteorological data showed that the local clustering of cases is likely due to the accumulation of stagnant water that facilitates the endemic vector species *Aedes aegypti* to breed. Strong associations of dengue fever with the presence of stagnant water around houses and flower pots in houses were determined. Stagnant water was previously identified as a risk factor in another outbreak in Lahore, Pakistan [13]. However, this study in Lahore in 2012 showed that dengue fever was associated with the piped water supply, which is in contrast to our findings.

Open fields and empty plots are the main sites for accumulation of stagnant water that become breeding sites for mosquitoes. Similarly, accumulated rainwater around houses and uncovered receptacles serve as important breeding grounds for these vectors.

A detailed environmental survey is called upon to understand the mechanism of hatching of larvae after the first rain, in which mosquitos reach the adult stage and are therefore capable of disease transmission. Our findings showed that cases clusters in the village (Figure 2), suggesting a link with previous rainfall at the start of September and October. Therefore, routine entomological surveillance for dengue virus is of great importance to enable early detection of spatial and temporal links of the outbreaks.

The NS-1 test is widely used for diagnostic purposes [14]. A positive NS-1 test has equal sensitivity as real-time polymerase chain reaction in the early phase of disease; however, the NS-1 test is a cheaper and more readily available tool for the early diagnosis of dengue [13]. Previously reported outbreaks showed the presence of the DEN-2 and DEN-3 genotypes, which is consistent with our finding that DEN-2 was the only serotype identified in the Tarlai outbreak [15]. Only one sample was sent to the public health laboratory for genotyping due to lack of resources, which confirmed the DEN-2 genotype.

The main limitations of this study are the lack of environmental analysis related to vector prevalence and the possibility of recall bias, especially in the control group.

Figure 2. Spot map of Union Council Tarlai, Islamabad, during the dengue fever outbreak from October 23 to November 11, 2016.
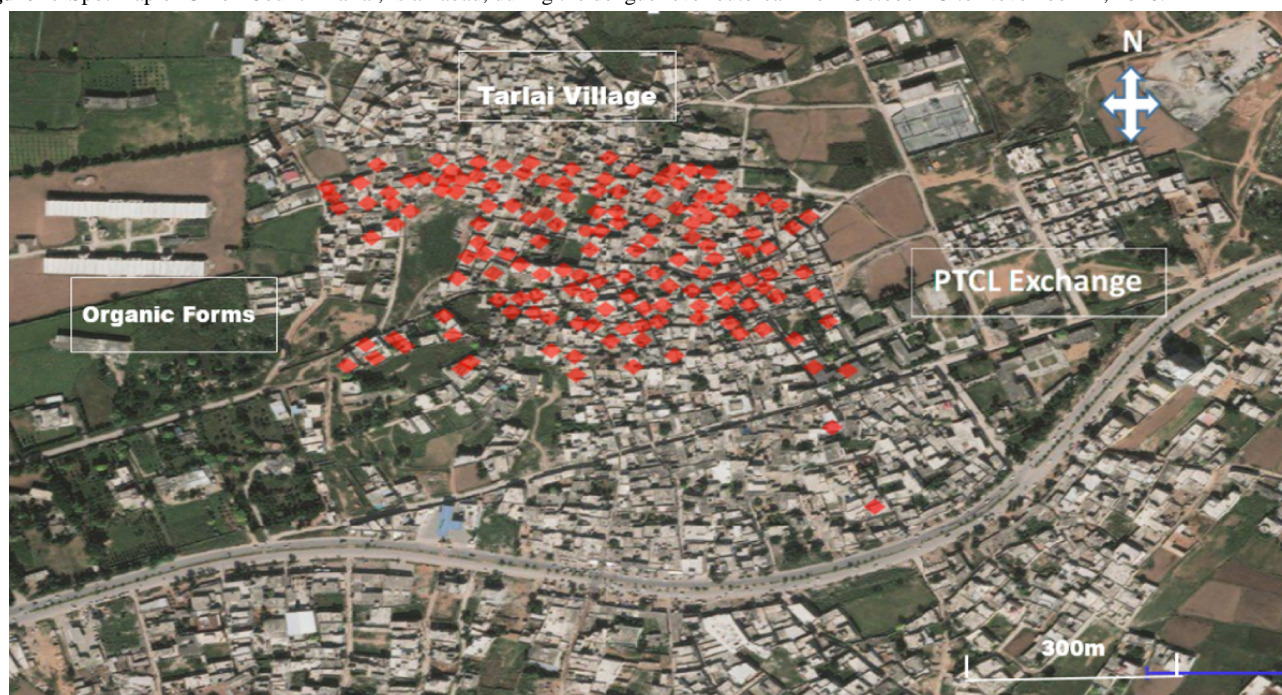
Conclusion

Stagnant water was significantly associated with a dengue fever outbreak in UC Tarlai, Islamabad, which is the most probable cause for spread of the disease. Therefore, the community should have been educated about the normal habitat of the dengue virus vector. Use of protective measures against the vector is strongly recommended. Different control measures should be implemented, including a media campaign for awareness and health education of vector control (mosquito), capacity building of health staff for timely disease detection and control, proper disposal of solid waste, indoor residual spray/fumigation for larval control, and a flower pot dryness campaign to reduce the indoor breeding sites of mosquitoes. Moreover, awareness campaigns for the use of repellents and protective measures, and establishment of a surveillance system (sanitization of health staff for reporting) for detection of dengue fever are strongly recommended.

Conflicts of Interest

None declared.

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Abbreviations

AR: attack rate
DHF: dengue hemorrhagic fever
DSS: dengue shock syndrome
NS-1: nonstructural protein-1
UC: Union Council

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Using Venn Diagrams to Evaluate Digital Contact Tracing: Panel Survey Analysis

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Abstract

Background: Mitigation of the spread of infection relies on targeted approaches aimed at preventing nonhousehold interactions. Contact tracing in the form of digital proximity tracing apps has been widely adopted in multiple countries due to its perceived added benefits of tracing speed and breadth in comparison to traditional manual contact tracing. Assessments of user responses to exposure notifications through a guided approach can provide insights into the effect of digital proximity tracing app use on managing the spread of SARS-CoV-2.

Objective: The aim of this study was to demonstrate the use of Venn diagrams to investigate the contributions of digital proximity tracing app exposure notifications and subsequent mitigative actions in curbing the spread of SARS-CoV-2 in Switzerland.

Methods: We assessed data from 4 survey waves (December 2020 to March 2021) from a nationwide panel study (COVID-19 Social Monitor) of Swiss residents who were (1) nonusers of the SwissCovid app, (2) users of the SwissCovid app, or (3) users of the SwissCovid app who received exposure notifications. A Venn diagram approach was applied to describe the overlap or nonoverlap of these subpopulations and to assess digital proximity tracing app use and its associated key performance indicators, including actions taken to prevent SARS-CoV-2 transmission.

Results: We included 12,525 assessments from 2403 participants, of whom 50.9% (1222/2403) reported not using the SwissCovid digital proximity tracing app, 49.1% (1181/2403) reported using the SwissCovid digital proximity tracing app and 2.5% (29/1181) of the digital proximity tracing app users reported having received an exposure notification. Most digital proximity tracing app users (75.9%, 22/29) revealed taking at least one recommended action after receiving an exposure notification, such as seeking SARS-CoV-2 testing (17/29, 58.6%) or calling a federal information hotline (7/29, 24.1%). An assessment of key indicators of mitigative actions through a Venn diagram approach reveals that 30% of digital proximity tracing app users (95% CI 11.9%-54.3%) also tested positive for SARS-CoV-2 after having received exposure notifications, which is more than 3 times that of digital proximity tracing app users who did not receive exposure notifications (8%, 95% CI 5%-11.9%).

Conclusions: Responses in the form of mitigative actions taken by 3 out of 4 individuals who received exposure notifications reveal a possible contribution of digital proximity tracing apps in mitigating the spread of SARS-CoV-2. The application of a Venn diagram approach demonstrates its value as a foundation for researchers and health authorities to assess population-level digital proximity tracing app effectiveness by providing an intuitive approach for calculating key performance indicators.

Introduction

In recent efforts to limit the number of COVID-19 infections, a respiratory disease caused by SARS-CoV-2, digital proximity tracing apps have been deployed in multiple countries [1,2]. In Switzerland, the SwissCovid digital proximity tracing app complements conventional manual contact tracing procedures that are carried out by cantonal authorities to track the spread of SARS-CoV-2, regardless of whether an individual has the voluntary digital proximity tracing app installed or not [3]. Manual contact tracing, in the form of interviews of identified cases, is labor-intensive and prone to errors due to its reliance on individuals' abilities to recall close-range proximity contacts [4]. Digital proximity tracing apps aim to overcome the limitations of manual contact tracing [5,6]. Most digital proximity tracing apps use Bluetooth low-energy beacons to track proximity contacts within a radius of 2 meters and notify individuals of a recent exposure to a SARS-CoV-2 clinically confirmed digital proximity tracing app user [7]. Digital proximity tracing apps promise to deliver notifications at a faster rate, with broader reach, and with greater scalability than manual contact tracing [5,8]. Their increased implementation in countries is widely associated with improved contact tracing and transmission mitigation in modeling studies [5,9,10].

There has been a surge of interest in evaluating the effectiveness of digital proximity tracing apps in mitigating the spread of SARS-CoV-2. Particular interest is placed on the added benefit of exposure notifications from digital proximity tracing apps relative to manual contact tracing in containing nonhousehold spread [11,12]. For example, recent studies in England [13] and Switzerland [14] revealed an average of 4 exposure notifications per index case were triggered by infected app users, which highlights the considerable breadth of digital proximity tracing apps over traditional manual contact tracing. However, attributing the contribution of digital proximity tracing apps on the mitigative actions taken by exposure notification recipients is a challenge due to inconsistent data availability [15]. This proves to be particularly challenging in countries such as Switzerland, where notified users of the digital proximity tracing app are not legally mandated to take action as a result of the exposure notification [16]. Furthermore, there is no unified methodology to evaluate the effectiveness of digital proximity tracing apps in mitigating the spread of infection. The lack of harmonization of terminology, indicator definitions, and monitoring goals has emerged in recent months as one of the key challenges in informing health policy about digital proximity tracing app effectiveness [8].

An approach based on Venn diagrams can be used to assess the effectiveness of digital proximity tracing apps in mitigating the spread of the SARS-CoV-2 infection. The use of Venn diagrams enables a structured approach to count outcomes across several subpopulations and for each period cross-sectionally. Very importantly, a Venn diagram approach also provides an intuitive framework for assessing generalizability and missing population segments of study data. Hence, when applied to population-level data, the approach enables the identification and construction of appropriate indicators in a reproducible manner, given the available data, to evaluate the impact of digital proximity tracing apps on users taking mitigative actions. The aim of this study was to demonstrate the use of Venn diagrams in assessing key indicators for exposure notification performance and effectiveness in mitigating the spread of SARS-CoV-2. We hope to guide health researchers and authorities in collecting relevant population-level data.

Methods

Overview

We applied a Venn diagram approach on data from COVID-19 Social Monitor, a nationwide panel study [17,18] of Swiss residents that allowed for the classification of (1) nonusers of the SwissCovid app, (2) users of the SwissCovid app and (3) users of the SwissCovid app who received exposure notifications, to provide a first description of the possible influence of exposure notifications on individuals taking mitigative actions against SARS-CoV-2 spread.

SwissCovid Digital Proximity Tracing App

The Swiss digital proximity tracing app (SwissCovid app) was launched on June 25, 2020. The adoption of the app in the Swiss health care system and pandemic mitigation response has been described extensively in previous studies [14,19]. The SwissCovid app employs a decentralized privacy-preserving proximity tracing protocol [2], has been downloaded almost 3 million times [20] for a population of 8.4 million in Switzerland, and has an estimated 1.7 million active users. App users who receive exposure notifications are eligible for a free SARS-CoV-2 test and are instructed to call a federal information hotline. The hotline elicits further information about the possible risk exposure and determines if entering into quarantining is necessary, which happens in approximately 20% of cases [14]. The hotline can only recommend quarantine, which makes entering into quarantine voluntary, and individuals who choose to quarantine do not receive salary compensation. By contrast, mandatory quarantine can be ordered by cantonal health authorities or a physician through manual contact tracing, and individuals who are quarantined are entitled to salary compensation. As of March 2021, 60,000 app users who have tested positive have triggered exposure notifications, and 70,000 telephone calls to the information hotline have been logged [20].

Venn Diagram Approach

This approach makes use of Venn diagrams to visualize the co-occurrence of SARS-CoV-2 outcomes of interest based on digital proximity tracing app use [21]. To construct the Venn diagrams, as recently formalized [21], requirements are established to define the appropriate data sets and time points, as well as identify subpopulations, to calculate digital proximity tracing app effectiveness. Based on our experience and extensive reporting of key indicators to mitigate the spread of SARS-CoV-2 [2,19,20], we proposed 4 attributes for Venn diagram development to facilitate the identification of subpopulations of interest: (1) having been tested for SARS-CoV-2, (2) having a positive SARS-CoV-2 test result, (3) having received an exposure notification, and (4) having entered into quarantine (Table 1).

Table 1. Descriptive attributes of Venn diagram subpopulations.

Group	Tested for SARS-CoV-2	Positive test for SARS-CoV-2	Exposure notification (exposure notification)	Quarantine	Remarks
A	True	True	False	False	N/A[a]
B	True	True	True	False	N/A
C	True	True	True	True	Tested positive; received exposure notification; quarantined
D	True	True	False	True	Tested positive; did not receive exposure notification; quarantined
E1	True	False	True	False	Tested negative; received exposure notification; not quarantined
E2	False	False	True	False	Not tested; received exposure notification; not quarantined
F1	True	False	True	True	Tested negative; received exposure notification; quarantined
F2	False	False	True	True	Not tested; received exposure notification; quarantined
G1	True	False	False	True	Tested negative; did not receive exposure notification; quarantined
G2	False	False	False	True	Not tested; did not receive exposure notification; quarantined
T	True	False	False	False	Tested negative; did not receive exposure notification; not quarantined
N	False	False	False	False	Not tested; did not receive exposure notification, not quarantined

[a]N/A: not applicable to the applied scope; all individuals who tested positive were immediately placed in isolation.

The allocation of individuals to each subsection, and their resulting overlap, enabled a more thorough definition of subpopulations. Once the subpopulations were identified, they were labeled according to the Venn diagram allocation. These labels facilitated the calculation of key digital proximity tracing effectiveness indicators by identifying relevant numerators and denominators (eg, the number of app users who received exposure notifications and entered into quarantine versus the number of app users who received exposure notifications but did not enter into quarantine). Furthermore, the data visualizations through Venn diagrams enabled an overview of available data, time horizons, as well as missing and available populations for analyses. A Venn diagram approach thereby provides a general methodology to facilitate the formulation of research hypotheses, aid the selection of suitable databases, and help to define key performance indicators by referencing to specific, labeled diagram segments. For our study, we defined a priori guiding criteria and definitions (Multimedia Appendix 1) to interpret Venn diagrams in the context of the SARS-CoV-2 pandemic in Switzerland. We also applied targeted questions (Multimedia Appendix 1) on digital proximity tracing app use in Switzerland from our panel survey to the Venn diagram population set.

Data Collection

Data from COVID-19 Social Monitor [17,18] comprise a representative stratified random survey panel of 3381 participants from Switzerland. Participants were randomly sampled from an existing web-based market research panel from a Swiss survey company. The study was launched in March

2020, with 14 survey waves (as of March 2021) which have been offered every 4 to 6 weeks. The sample was replenished in December 2020 by recruiting new participants from the same market research panel to counteract panel attrition.

Our study used data from 4 survey waves: December 14 to December 23, 2020 (December survey); January 25 to February 4, 2021 (January survey); February 22 to March 3, 2021 (February survey); and March 29 to 08 April 8, 2021 (March survey). The December survey was used as the baseline for this study due to high SARS-CoV-2 incidence in Switzerland at that time, which averaged approximately 4000 newly detected COVID-19 cases daily and a test positivity rate of 16% [22]. This period encompasses the peak of the second COVID-19 wave in December 2020 and the subsequent decline of infections in the following months. The January, February, and March follow-up surveys were used to record information on new outcomes of interest. Only participants with at least one follow-up survey were included in our analyses. The first instance of an event of interest (eg, testing positive for SARS-CoV-2) was included in our analyses; after the event of interest, the participant was excluded from further analyses. Participants with a self-reported positive SARS-CoV-2 test prior to or at baseline were excluded in order to include only new infection cases in the assessment period. We also expected that individuals were likely to react differently to a first receipt of an exposure notification in comparison to future exposure notification receipts. Therefore, we also excluded participants who received exposure notifications prior to or at baseline. National SARS-CoV-2 incidence and test positivity were also

extracted to provide context on the state of the pandemic at the time the surveys were conducted [22,23].

Statistical Analysis

Descriptive statistics were calculated for survey respondent demographics and to assess mitigative actions taken by the participants within the study period. Analyses were performed on the full study sample, as well as across the 3 subgroups of digital proximity tracing app nonusers and digital proximity tracing app users who did or did not receive an exposure notification.

Performance measures were constructed on the basis of labeled Venn segments representing subpopulations with the attributes shown in Table 1. We assessed the proportion of individuals who received SARS-CoV-2 testing, tested positive for SARS-CoV-2 (including the percentage of individuals who tested positive for SARS-CoV-2 among those who were tested), or entered into quarantine at the request of health care professionals or health authorities. The assessment of these indicators was stratified according to the 3 subgroups defined by digital proximity tracing app use or nonuse and exposure notification receipt.

We assessed the mitigative actions taken by individuals who received an exposure notification. These actions included (1) calling an information hotline to obtain advice on appropriate actions, (2) getting tested after receiving an exposure notification, and (3) entering into quarantine, including entering into quarantine as recommended by health care professionals or ordered by health authorities. The assessed key indicators are derived from the subpopulations observed in the Venn diagram based on digital proximity tracing app use.

We report 95% confidence intervals based on an exact binomial test for proportions for the estimation of subpopulation sizes and key indicators. Analyses were performed in Stata (version 16.1; StataCorp LLC). Continuous variables were represented as median (interquartile range), and categorical variables were represented as count (percentage) with corresponding 95% confidence intervals.

Ethics

For the COVID-19 Social Monitor project, the Ethics Committee of the Canton of Zurich confirmed that it does not fall under the Swiss Human Research Law (BASEC-Nr Req-2020-00323). This exemption was granted due to the fact that data were collected and treated anonymously throughout the project.

As per the decision of the Cantonal Ethics Commission of Zurich, explicit informed consent was not needed from participants for this particular study. However, participants gave their general permission to be part of research studies when accepting the invitation to the panel from which we sampled our respondents. Participation in the study was voluntary, and participants could withdraw from the study at any time.

Results

Study Population

We included 12,525 assessments from 2403 participants in the final study cohort (Figure 1). The median respondent age was 49 years (IQR 35-59) and most (2305/2403, 95.9%) respondents were Swiss nationals (Table 2).

From the study cohort, 319 (319/2403, 13.3%) respondents reported having at least one of the following chronic illnesses: asthma, chronic obstructive pulmonary disease, diabetes, hypertension, cardiovascular disease, stroke, and cancer.

At the baseline survey (December 2020), 19.3% (236/1222) of app nonusers, 28.2% (325/1152) of app users who did not receive an exposure notification, and 34.5% (10/29) of app users who received an exposure notification reported an average monthly household income greater than 10,000 CHF (approximately US $10,886.43).

Figure 1. Flowchart of assessed panel survey data and associated SARS-CoV-2 incidence values. For the national daily case numbers, the values represent the daily average of SARS-CoV-2 cases in each month, with the values in parentheses representing their respective standard deviations. EN: exposure notification.
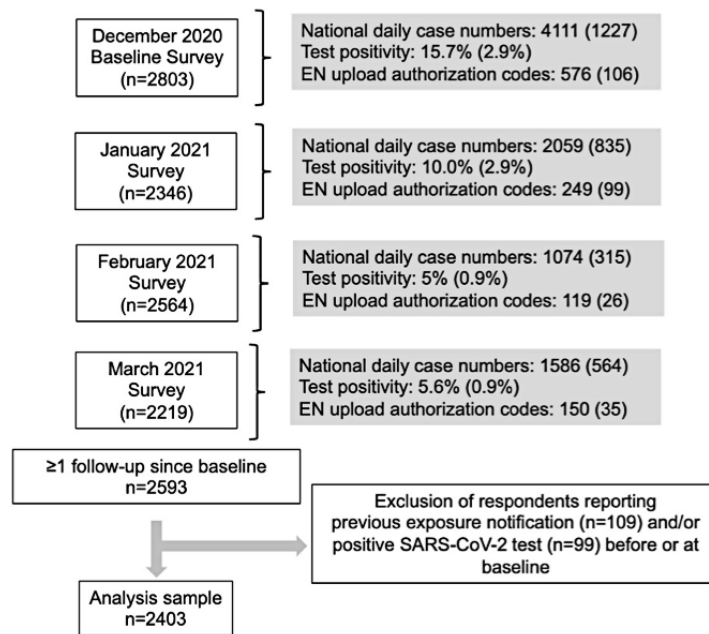
Table 2. Respondent demographics, self-reported health risks, and mitigative actions.

Characteristic	Full sample (n=2403)	Nonusers (n=1222)	App users (n=1152)	App users and received exposure notifications (n=29)
Age (in years), median (IQR)	49 (35-59)	49 (35-58)	49 (36-59)	40 (29-52)
Gender, n (%)				
Female	1171 (48.7)	593 (48.5)	566 (49.1)	12 (41.4)
Male	1232 (51.3)	629 (51.5)	586 (50.9)	17 (58.6)
Personal status, n (%)				
No partner	668 (27.8)	353 (28.9)	310 (26.9)	5 (17.2)
Living with partner	1518 (63.2)	755 (61.8)	739 (64.1)	24 (82.8)
Not living with partner	217 (9.0)	114 (9.3)	103 (8.9)	0 (0.0)
Family status, n (%)				
Has children	245 (10.2)	123 (10.1)	116 (10.1)	6 (20.7)
Does not have children	2158 (89.8)	1099 (89.9)	1036 (89.9)	23 (79.3)
Citizenship, n (%)				
Swiss	2173 (90.4)	1095 (89.6)	1051 (91.2)	27 (93.1)
Swiss and other	132 (5.5)	72 (5.9)	59 (5.1)	1 (3.4)
Non-Swiss	98 (4.1)	55 (4.5)	42 (3.6)	1 (3.4)
Language region, n (%)				
German	1964 (81.7)	973 (79.6)	965 (83.8)	26 (89.7)
French	274 (11.4)	160 (13.1)	113 (9.8)	1 (3.4)
Ticino	165 (6.9)	89 (7.3)	74 (6.4)	2 (6.9)
Education, n (%)				
Only mandatory schooling	64 (2.7)	42 (3.4)	22 (1.9)	0 (0.0)
Completed professional education	1737 (72.3)	901 (73.7)	811 (70.4)	25 (86.2)
University or university of applied sciences	602 (25.1)	279 (22.8)	319 (27.7)	4 (13.8)
Employment status, n (%)				
Not working	721 (30.0)	370 (30.3)	344 (29.9)	7 (24.1)
Currently working	1682 (70.0)	852 (69.7)	808 (70.1)	22 (75.9)
Monthly household income (CHF[a]), n (%)				
≤6000	657 (27.3)	392 (32.1)	260 (22.6)	5 (17.2)
6000-10,000	783 (32.6)	391 (32.0)	381 (33.1)	11 (37.9)
>10,000	571 (23.8)	236 (19.3)	325 (28.2)	10 (34.5)
No answer	392 (16.3)	203 (16.6)	186 (16.1)	3 (10.3)
Health risks, n (%)[b]				
Smoker	507 (21.1)	287 (23.5)	211 (18.3)	9 (31.0)
Self-reported chronic illness[c]	319 (13.3)	169 (13.8)	149 (12.9)	1 (3.4)
Mitigative actions, n (%)[b]				
Always used protective masks when recommended	2335 (97.2)	1167 (95.5)	1140 (99.0)	28 (96.6)
Always stayed at home except for essential tasks	1561 (65.0)	738 (60.4)	804 (69.8)	19 (65.5)
Always kept recommended distance	2225 (92.6)	1103 (90.3)	1097 (95.2)	25 (86.2)
Always refrained from visits	1583 (65.9)	743 (60.8)	824 (71.5)	16 (55.2)
Number of physical contacts, median (IQR)	3 (1-5)	3 (2-5)	3 (1-5)	3 (2-4)

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[a]CHF: Swiss franc; At the time of publication, the exchange rate was approximately US $1=0.92 CHF.

[b]More than one or no answer is possible; therefore, percentages in this category do not add to 100%.

[c]At least one of the following chronic illnesses: asthma, chronic obstructive pulmonary disease, diabetes, hypertension, cardiovascular disease, stroke, or cancer.

Baseline Adherence to Mitigation Strategies

During the high-incidence period in December 2020 (ie, baseline), most participants reported consistent adherence, as opposed to occasional or no adherence, to wearing protective masks (2335/2403, 97.2%) and maintaining appropriate distance (2225/2403, 92.6%) (Table 2). Despite the strongly recommended restrictions on mobility imposed in winter 2020 throughout Switzerland, 1561 (1561/2403, 65%) respondents reported leaving their households for nonessential tasks.

On average, 76.8% (938/1222) of app nonusers, 83.9% (966/1152) of app users who did not receive an exposure notification, and 75.9% (22/29) of app users who received an exposure notification reported adherence to at least one of the 4 mitigative measures (Figure 2).

Figure 2. Baseline respondent mitigative actions based on reported SwissCovid app use with 95% confidence intervals. DPT: digital proximity tracing; EN: exposure notifications.
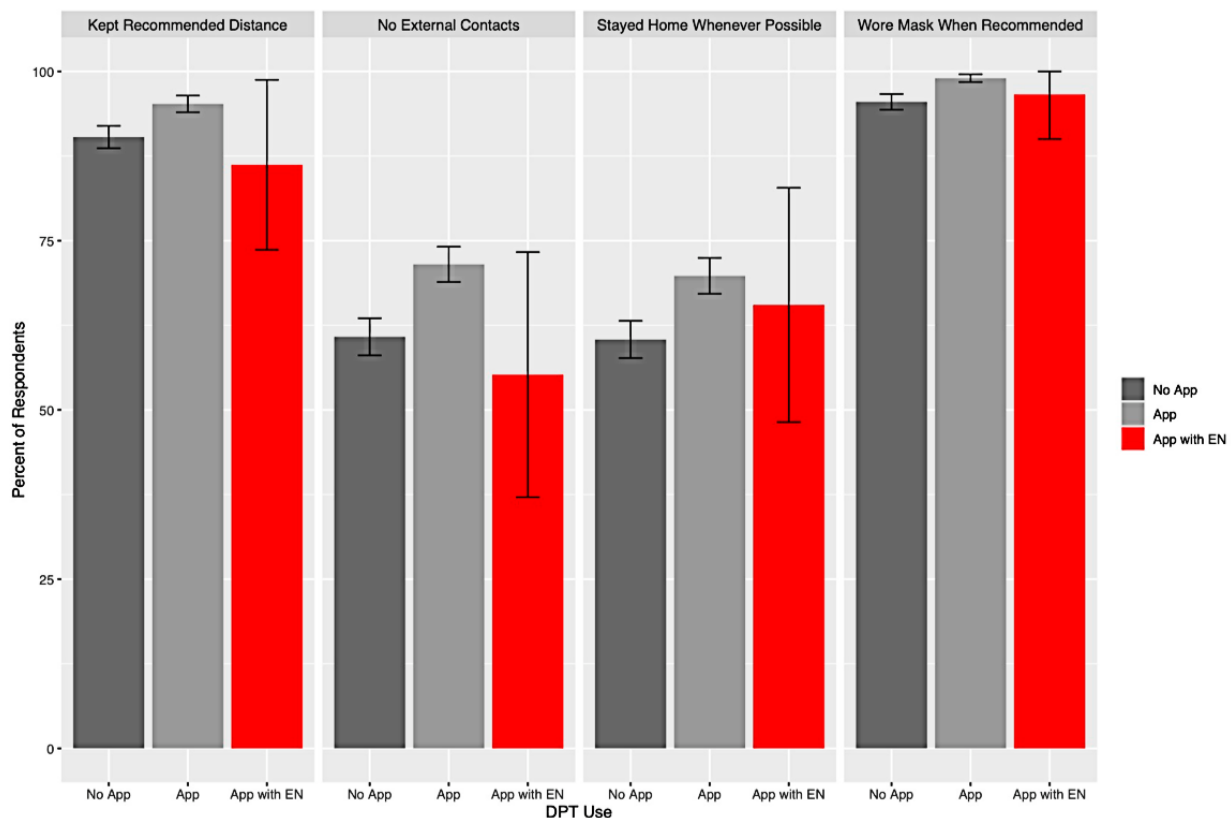
Population Sizes of Different Venn Diagram Segments

Based on outcomes reported across the 4 survey waves from December 2020 to March 2021, the respondent sample is visualized in a Venn diagram according to 4 categories (Figure 3). The corresponding subpopulation sizes for each Venn diagram segment are shown in Table 3. The sample is further divided into the 3 respondent subgroups based on digital proximity tracing app use and receipt of exposure notifications in order to calculate subgroup-specific indicators. Of note, segments A and B are empty by design, as all positive tested individuals are reported immediately to health authorities who, in turn placed these individuals in isolation (Table 3).

Overall (of the 2403 respondents), 46 (1.9%) respondents tested positive for SARS-CoV-2 in the follow-up period, 29 (1.2%) received exposure notifications, and 130 (5.4%) were placed into quarantine. In segment C, 6 (6/46, 13%) respondents who tested positive for SARS-CoV-2 reported having received an exposure notification. In segments E1 and F1 (14/29, 48.3%) were respondents who received exposure notifications and who tested negative for SARS-CoV-2, of whom 7 (7/29, 24.1%) respondents in segment F1 were placed into quarantine after having received exposure notifications. By contrast, in segments E2 and F2, 9 (9/29, 31%) respondents who received exposure notifications were not tested for SARS-CoV-2; the respondent in F2 was still placed into quarantine (Figure 3).

Figure 3. Venn diagram representation of mitigative actions taken by 4 survey subpopulations (in bold) after follow-up: (1) respondents who were tested for SARS-CoV-2 in the past 4 weeks (white circle), (2) respondents who tested positive for SARS-CoV-2 (yellow circle), (3) respondents who received exposure notifications (red circle), and (4) respondents who were placed in quarantine by Swiss cantonal health services or by a physician (blue circle). Sample sizes of specific segments are indicated in the diagram, with the values in [square brackets] reflecting the number of DPT app users in a given segment. Each (non)overlap represents a subpopulation of the survey respondents.
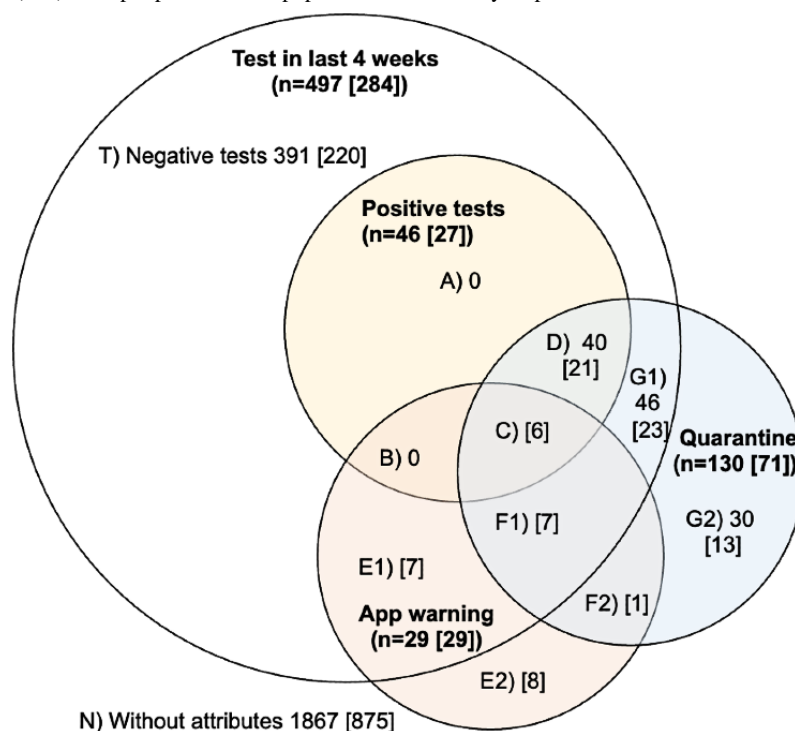
Table 3. Subpopulation cumulative mitigative actions and outcomes from the Venn diagram based on SwissCovid app use after respondent follow-up.

Group[a]	Nonusers, n	App users, n		All (n=2403), n	Percentage of entire sample (95% CI)
		No notifications	Received exposure notification		
C	0	0	6	6	0.2 (0.1-0.5)
D	19	21	0	40	1.7 (1.2-2.3)
E1	0	0	7	7	0.3 (0.1-0.6)
E2	0	0	8	8	0.3 (0.1-0.7)
F1	0	0	7	7	0.3 (0.1-0.6)
F2	0	0	1	1	0.04 (0.001-0.02)
G1	23	23	0	46	1.9 (1.4-2.5)
G2	17	13	0	30	1.2 (0.8-1.8)
N	992	875	0	1867	77.7 (76.0-79.3)
T	171	220	0	391	16.3 (14.8-17.8)

[a]The letters correspond to the subpopulations in the Venn diagram in Figure 3.

Indicators Derived From Venn Diagrams

Denominators of subpopulations were selected to assess key indicators of SwissCovid app performance in reducing the spread of SARS-CoV-2 based on the mitigative actions taken and outcomes of interest by respondent groups (Table 4).

Overall, 49.2% (95% CI 47.1%-51.2%) of all participants reported using the SwissCovid app in at least one follow-up survey. App users contributed to 57.1% (95% CI 52.7%-61.5%) of SARS-CoV-2 tests taken, 58.7% (95% CI 43.2%-73%) of positive SARS-CoV-2 tests and 54.6% (95% CI 45.7%-63.4%) of respondents who entered into quarantine in our sample.

Test positivity among those who sought SARS-CoV-2 testing was 8.9% (95% CI 5.5%-13.6%) among app nonusers, 8% (95% CI 5%-11.9%) among app users who did not receive exposure notifications, and 30% (95% CI 11.9%-54.3%) among app users who received exposure notifications.

Entering into quarantine was reported by 4.8% (95% CI 3.7%-6.2%) of the app nonusers, 5% (95% CI 3.8%-6.4%) of the app users who did not receive exposure notifications, and

48.3% (95% CI 29.5-67.5%) of the app users who received exposure notifications. Similarly, entering into quarantine following testing for SARS-CoV-2 was reported by 19.7% (95% CI 14.6%-25.7%) of the app nonusers, by 16.7% (95% CI 12.4%-21.7%) of the app users who did not receive exposure notifications, and by 65% (95% CI 40.8%-84.6%) of the app users who received exposure notifications.

The percentage of respondents who received exposure notifications among those who tested positive (22.2%, 95% CI 8.6%-42.3%) for SARS-CoV-2 at a later point in time was higher than app users who tested negative (5.5%, 95% CI 3%-9%).

Table 4. Selection of appropriate numerators and denominators from a Venn diagram based on SwissCovid digital proximity tracing app use after respondent follow-up. Letters in square brackets—[]—reflect subpopulations (Venn segments) of app users and those in curly brackets—{}— reflect the subset of individuals who did not use the app.

Indicator	Numerator	Denominator	% (95% CI)
Coverage of app users			
All	[C,D,E1,E2,F1,F2,G1,G2,N,T]	C,D,E1,E2,F1,F2,G1,G2,N,T	49.15 (47.13-51.17)
Tested	[C,D,E1,F1,G1,T]	C,D,E1,F1,G1,T	57.14 (52.66-61.54)
Tested positive	[C,D]	C,D	58.70 (43.23-73.00)
Quarantined	[C,D,F1,F2,G1,G2]	C,D,F1,F2,G1,G2	54.62 (45.65-63.36)
Individuals tested			
Nonuser	{D,G1,T}	{D,G1,G2,N,T}	17.43 (15.34-19.68)
App user	[D,G1,T]	[D,G1,G2,N,T]	22.92 (20.52-25.45)
App user and received exposure notifications	[C,E1,F1]	[C,E1,E2,F1,F2]	68.97 (49.17-84.72)
Test positivity			
Nonuser	{D}	{D,G1,T}	8.92 (5.46-13.58)
App user	[D]	[D,G1,T]	7.95 (4.99-11.90)
App user and received exposure notifications	[C]	[C,E1,F1]	30.00 (11.89-54.28)
Quarantined			
Nonuser	{D,G1,G2}	{D,G1,G2,N,T}	4.83 (3.70-6.18)
App user	[D,G1,G2]	[D,G1,G2,N,T]	4.95 (3.77-6.36)
App user and received exposure notifications	[C,F1,F2]	[C,E1,E2,F1,F2]	48.28 (29.45-67.47)
Quarantine (among those tested)			
Nonuser	{D,G1}	{D,G1,T}	19.72 (14.60-25.70)
App user	[D,G1]	[D,G1,T]	16.67 (12.38-21.72)
App user and received exposure notifications	[C,F1]	[C,E1,F1]	65.00 (40.78-84.61)
App users who received an exposure notification who later tested positive	[C]	[C,D]	22.22 (8.62-42.26)
App users who received an exposure notification who later tested negative	[E1,F1]	[E1,F1, G1,T]	5.45 (3.01-8.97)

Recommended Actions Taken Upon Receipt of Exposure Notifications

Recommended mitigative actions taken among respondents who received an exposure notification (segments C, E1, E2, F1, F2, n=29) are reported in Multimedia Appendix 1.

Most respondents (17/29, 58.6%) who received exposure notifications sought SARS-CoV-2 testing and 7 (7/29, 24.1%) respondents called the federal information hotline. From these respondents, 22 (22/29, 75.9%) who received an exposure notification undertook at least one recommended mitigative action, while 5 (5/29, 17.2%) respondents explicitly stated to have ignored the exposure notification (Figure 4).

In group C, all 6 individuals reported to have sought testing after receiving an exposure notification: 4 (4/6, 66.7%) respondents reported having symptoms, and 2 (2/6, 33.3%) respondents reported entering into quarantine in response to the exposure notifications, even though one of these respondents reported not having symptoms.

Having contact with positive tested individuals or household members was almost always cited as a quarantine reason in groups C, F1, and F2 (with 1 exception). However, 5 (71.4%) out of 7 individuals in group E1 did not report possible contacts to positive tested individuals as a quarantine reason and yet still sought testing for SARS-CoV-2.

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Figure 4. Tree diagram of subpopulation mitigative actions after follow-up in response to exposure notifications from the SwissCovid app. MCT: manual contact tracing.
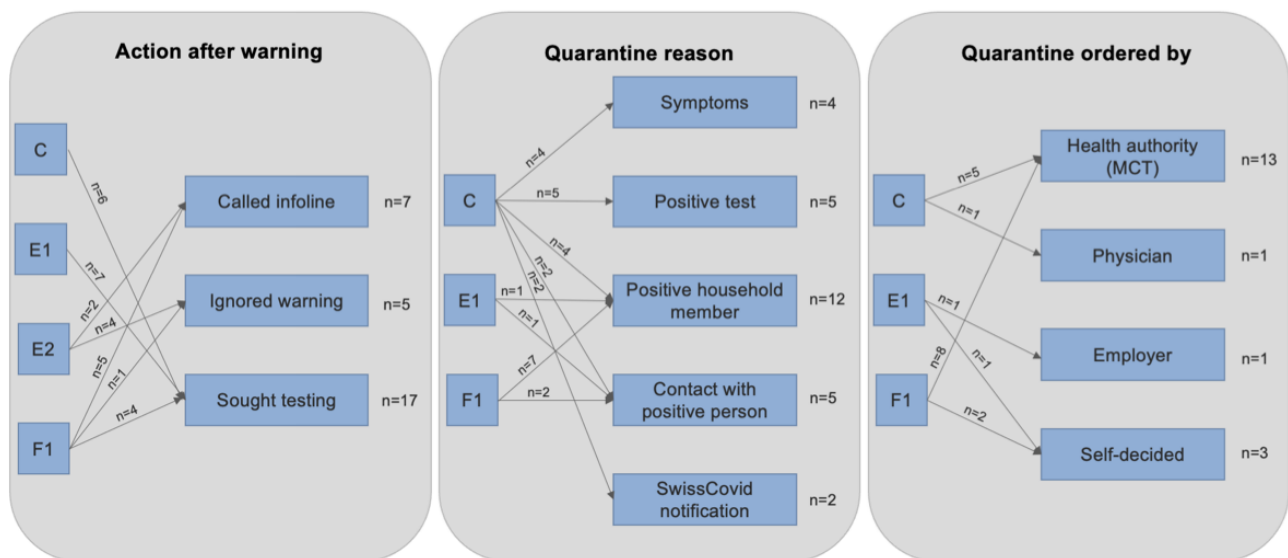
Discussion

We were able to isolate subpopulations of interest and define performance indicators for digital proximity tracing app effectiveness. From our assessment, we found that a greater proportion of digital proximity tracing app users who received an exposure notification tested positive, in comparison to digital proximity tracing app users who did not receive an exposure notification and digital proximity tracing app nonusers. Our findings also suggest that the receipt of exposure notifications may contribute to SARS-CoV-2 transmission mitigation, as observed with most users from our cohort who voluntarily sought testing or called the federal information hotline, while half of these users received recommendations to self-isolate or quarantine as a result of manual contact tracing. Possible transmission mitigation was also observed in respondents who sought testing and who tested positive after receiving exposure notifications.

A previous cross-sectional analysis [17] of the same database revealed similar differences between app users and those who do not use digital proximity tracing apps to those in our study, namely with respect to citizenship status, household income, and adherence to mask-wearing. Furthermore, findings on user response to exposure notifications from our study complement those from an experimental study [24] in Spain that simulated exposure notification cascades. The findings of the study [24] suggested that 10% of individuals who received exposure notifications called the federal hotline. In our study, follow-up was sought by 24.1% (7/29) of digital proximity tracing app users who called the federal hotline after receiving exposure notifications..

Subpopulations visible in segments E1 (ie, individuals who tested negative, did not enter into quarantine and received an exposure notification) and E2 (ie, individuals who did not get tested, did not enter into quarantine and received an exposure notification) are currently not captured by any official statistics in Switzerland. Tracking responses to exposure notifications is

challenging in Switzerland, since no data are systematically collected on individuals seeking testing after they have received exposure notifications, such as recording the reason for testing [25]. Responses to exposure notifications are also voluntary in Switzerland, making outgoing exposure notification data from the SwissCovid app inconclusive regarding the actual resulting mitigative measures taken by the users. In our study, our results suggest that approximately 1 in 2 individuals who receive exposure notifications may remain undetected and approximately 1 in 4 individuals do not respond to exposure notifications.

Positive test results for SARS-CoV-2 among app users who did not receive exposure notifications (8%, 95% CI 5%-11.9%) nonusers were similar (8.9%, 95% CI 5.5-13.6%) and of comparable magnitude to the officially reported test positivity values in Switzerland [22]. Notably, test positivity among app users who received exposure notifications was more than 3 times higher (30%, 95% CI 11.9%-54.3%). A recent report [26] also revealed similar findings of test positivity among app users in the Netherlands, which were recently found to be higher for users who received exposure notifications in comparison to those who did not. This raises the question of whether exposure notifications are reflective of an increased exposure risk [27]. Addressing this question is particularly relevant due to concerns that Bluetooth technology may not be able to capture exposure risks accurately [28,29]. By using data on digital proximity tracing app use with Venn diagrams, we presented a novel approach that evaluates the effect of exposure notifications on users' mitigative actions as well as the risk of SARS-CoV-2 transmission through test positivity. However, such interpretations must account for national risk scoring schemes to allow for the identification of relevant exposure notifications. Switzerland, as an example, operates on conservative Bluetooth attenuation signal thresholds [3], whereas the United Kingdom has recently adopted lower thresholds in order to capture more exposures [30].

Our study also illustrates the usability and value of a Venn diagram approach to contextualize population- or survey-based

evaluations of exposure notifications. We find that this method, and the extensive database used in this approach, provide a visual and analytical basis for assessing digital proximity tracing app effectiveness. Despite being based on over 12,500 follow-up surveys, our outcomes of interest such as SARS-CoV-2 infections (46/2403, 1.9%) and exposure notifications (29/2403,1.2%) were relatively rare. Nevertheless, the sample is likely well reflective of the population of app users as the sociodemographic characteristics associated with a higher propensity for electronic survey participation and SwissCovid app use likely overlap [17]. In contrary to the findings of another study [31], however, our database managed to cover all relevant segments of the Venn diagram, including groups of exposed contacts who received exposure notifications but did not respond to the warning. With even larger sample sizes, researchers can fulfill large enough subpopulation sizes to generate possible direct inference on digital proximity tracing effectiveness from the associated denominators. A current approach to evaluate the role of digital proximity tracing in the SARS-CoV-2 pandemic was presented in a recent study on factors associated with app use in Switzerland [17] and their associated effectiveness on the app notification cascade [14,19]. Another recent study [13] conducted in the United Kingdom also traced exposure notifications to a substantial number of individuals with nonhousehold risk exposures. By providing subpopulation-level granularity, a Venn diagram approach complements current evaluations of the role of digital proximity tracings in curbing SARS-CoV-2 transmission. This is particularly relevant in countries similar to Switzerland, where exposure notifications do not mandate mitigative actions from users [16].

Limitations

Our study has some limitations. Due to the scarcity of relevant digital proximity tracing–related exposure notification outcomes, our study had limited statistical power. Owing to the mode of data collection (web-based panel surveys), the respondents in our sample may reflect subpopulations with above-average literacy and, possibly, higher adherence to recommended preventive actions against the SARS-CoV-2 infection. Therefore, our results might not be generalizable to the broader Swiss population. Also, while survey respondents are provided full anonymity, partial non- or overreporting of having received exposure notifications, of SARS-CoV-2 testing and positivity, as well as of nonadherence to measures, might have occurred. Furthermore, considering the small sample size of participants

who received an exposure notification, findings of possible associated mitigative responses should be viewed as preliminary. Nevertheless, given the privacy-preserving nature of digital proximity tracing app design, survey-based exposure notification studies are among the few sources of data available to make assessments on their effectiveness in mitigating the spread of infection. As such, despite the limitations presented by surveys in including participants who received exposure notifications, our results are some of the first available to provide quantitative insights on the contribution of exposure notifications in digital proximity tracing app users taking mitigative actions. Lastly, the panel data did not provide enough granularity to recreate the full cascade sequence of risk exposure. Rather, the panel survey focused on gathering information on digital proximity tracing usage and associated mitigative actions yet not information on the premise surrounding any possible exposure notifications. Therefore, our data cannot univocally demonstrate causality of exposure notifications and SARS-CoV-2 transmission prevention.

Conclusion

In our paper, we presented the Venn diagram as a tool to facilitate and streamline the evaluation of the role of digital proximity tracing apps in curbing the spread of the SARS-CoV-2 virus. By isolating subpopulations through a Venn diagram approach, a higher proportion of digital proximity tracing app users who tested positive after receiving an exposure notification was observed in comparison to digital proximity tracing app users who did not receive an exposure notification or digital proximity tracing app nonusers. Our findings also revealed that more than 3 out of 4 digital proximity tracing app users who received exposure notifications performed at least one recommended mitigative action, such as seeking SARS-CoV-2 testing or calling a federal information hotline, while half of these users received a recommendation to self-isolate or quarantine. An assessment, using a Venn diagram approach, of a larger population than the one presented in our study would allow the opportunity to assess the effectiveness of digital proximity tracing apps on users taking mitigative actions and their associated exposure risk with greater statistical power. This could, in turn, assist health authorities and researchers in identifying possible areas of improvement for digital proximity tracing apps alone, or in combination with manual contact tracing, by assessing effectiveness in curbing the spread of infection in a reproducible manner.

Authors' Contributions

PD wrote the first draft of the manuscript, analyzed data, and approved the final manuscript. VN analyzed data and revised and approved the final manuscript. AM and MH collected and analyzed data and revised and approved the final manuscript. VvW designed the study, interpreted data, wrote the first draft, and approved the final manuscript.

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Conflicts of Interest

VvW had a mandate by the Swiss Federal Office of Public Health to evaluate the SwissCovid App; however, this study was planned and executed independently, without any involvement of the Swiss Federal Office of Public Health.

Multimedia Appendix 1
Subpopulation mitigative actions, Venn diagram analysis, and standardized questions on SwissCovid app use.
[PDF File (Adobe PDF File), 124 KB - publichealth_v7i12e30004_app1.pdf]

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Abbreviations

CHF: Swiss franc

Original Paper

Learning From a Massive Open Online COVID-19 Vaccination Training Experience: Survey Study

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Abstract

Background: To prepare key stakeholders for the global COVID-19 vaccination rollout, the World Health Organization and partners developed online vaccination training packages. The online course was launched in December 2020 on the OpenWHO learning platform. This paper presents the findings of an evaluation of this course.

Objective: The aim of this evaluation was to provide insights into user experiences and challenges, measure the impact of the course in terms of knowledge gained, and anticipate potential interest in future online vaccination courses.

Methods: The primary source of data was the anonymized information on course participants, enrollment, completion, and scores from the OpenWHO platform's statistical data and metric reporting system. Data from the OpenWHO platform were analyzed from the opening of the courses in mid-December 2020 to mid-April 2021. In addition, a learner feedback survey was sent by email to all course participants to complete within a 3-week period (March 19 to April 9, 2021). The survey was designed to determine the perceived strengths and weaknesses of the training packages and to understand barriers to access.

Results: During the study period, 53,593 learners enrolled in the course. Of them, 30,034 (56.0%) completed the course, which is substantially higher than the industry benchmark of 5%-10% for a massive open online course (MOOC). Overall, learners averaged 76.5% on the prequiz compared to 85% on the postquiz, resulting in an increase in average score of 9%. A total of 2019 learners from the course participated in the survey. Nearly 98% (n=1647 fully agree, n=308 somewhat agree; N=1986 survey respondents excluding missing values) of respondents fully or somewhat agreed that they had more confidence in their ability to support COVID-19 vaccination following completion of this course.

Conclusions: The online vaccine training was well received by the target audience, with a measurable impact on knowledge gained. The key benefits of online training were the convenience, self-paced nature, access to downloadable material, and ability to replay material, as well as an increased ability to concentrate. Online training was identified as a timely, cost-effective way of delivering essential training to a large number of people to prepare for the COVID-19 vaccination rollout.

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Introduction

To address the need for timely training on COVID-19 vaccination, the Access to COVID-19 Tools Accelerator's Country Readiness and Delivery (CRD) workstream rapidly produced the *COVID-19 vaccination training for health workers* course. The course was launched on the OpenWHO platform in mid-December 2020. The objective was to ensure that health workers responsible for COVID-19 vaccination deployment had timely access to World Health Organization (WHO) recommendations and information that could help them prepare for a safe and efficient vaccine rollout. Although the course was targeted to health workers, it was open to all and was accessed by others, such as policy makers, community leaders, and students.

As the COVID-19 pandemic limited travel and the ability to gather learners together in a typical classroom environment, the health workers course was developed as an online learning curriculum. The health workers course includes a series of video lectures presented by technical experts, with accompanying multiple-choice questions delivered before and after the lectures. The transcripts and videos are downloadable. The health workers course contains 6 modules and provides information on organizing the vaccination session, including infection prevention and control measures; COVID-19 vaccine storage, handling, administration, and safe disposal; recording and monitoring, including adverse events following immunization (AEFI); and communication with the community.

OpenWHO is one of the WHO's online learning platforms, offering free online courses with the aim to improve responses to health emergencies [1]. The platform hosts over 100 courses on COVID-19 and other health topics, has over 5 million enrollments, and offers courses in 55 languages. Within the OpenWHO platform, registration includes an option to self-declare the registrant's occupation. The occupation selection is not validated and may be subjective, depending on the registrant's consideration of their role in the workforce.

Given that online learning to prepare for vaccine introduction is a relatively new approach for many countries, this course was evaluated to understand participants' online learning experience. The aim of this analysis is to increase the effectiveness of OpenWHO training packages and to plan for future online immunization learning.

The COVID-19 pandemic emphasized the need for trusted, accurate information to help health workers and the public respond to the outbreak. Online learning to prepare for vaccine introduction is a relatively new approach [2]. This paper provides an overview of the OpenWHO COVID-19 vaccine introduction training for health workers, shares insights on participants' online learning experiences, and provides key findings that can be used to improve future real-time online training.

The title of the course (*COVID-19 vaccination training for health workers*) uses the WHO definition of health workers as all people engaged in actions whose primary intent is to enhance health.

Methods

The analysis is based on quantitative data collected from the OpenWHO integrated statistical data and analytics reporting system. Anonymized course reports data sets were extracted from the OpenWHO reporting tool, providing raw data including basic demographics on OpenWHO users (eg, self-declared age, gender, professional affiliation, and nationality information), which were entered at the time of registration to the platform. OpenWHO course reports also include course-specific learners' performance and course activity indicators (such as module completion), including videos, self-assessments, download activity status, quiz performance, and obtention of the certificate, as well as tracked average session duration and time-stamped activity usage patterns.

Course registration and completion data captured by the OpenWHO analytics systems were analyzed to understand user demographics, certifications, and dropout rates. Completion of the course was defined as watching all videos and completing the postquiz with a score of at least 80%. Questions were scored as correct or incorrect—no partial credit was granted. Demographic information, including age, gender, and professional affiliation were not mandatory; therefore, analyses on these variables were based on the learners who provided information voluntarily. The course activity data of individual learners—including modules visited, videos watched, and resources downloaded—were collected and analyzed to understand the usability of the training course. Data on the scores of individual learners for pre- and postquizzes were collected and used in the analysis to measure knowledge gained. Learner's knowledge gain was assessed by comparing average postquiz scores to prequiz scores (where data were available). Both pre- and postquizzes had the same questions. Pre- and postquizzes were included before and after each module, respectively. The number of questions was limited (2-4 questions per module) to avoid overburdening the learners. Learners had a single attempt for prequizzes, but multiple attempts were allowed for postquizzes. For each learner's postquiz scores, the scores from the first postquiz attempts were used. Due to the limited number of questions per module, statistical significance by module could not be analyzed. Analysis of the course data was based on the total number of enrolled learners from the course opening date (December 18, 2020) until the date when the course analyses for this paper began (April 18, 2021).

In addition, an exit survey was added at the end of the course to collect participant feedback on course content to better understand the usability and virtual learning experiences of the learners, as well as strengths, weaknesses, and barriers of the training package. The learner feedback survey was composed of 21 questions (Multimedia Appendix 1). The survey was implemented on the OpenWHO platform and opened for a period of 3 weeks (March 19-April 9, 2021). For those learners who enrolled and completed the health workers course prior to March 19, 2021, survey invitation emails were sent. The survey was voluntary and indicated that it was conducted to collect feedback and that results may be used for research purposes.

The two sets of anonymized statistical data from the course report and survey data were overlaid by using a unique pseudo-ID for each OpenWHO learner, thus allowing the two data sets to be merged for analysis.

All analyses were conducted using Python (version 3.8.3; Python Software Foundation). OpenWHO data and the survey data were collected in line with the OpenWHO Terms of Use, which every enrolled user accepts. All OpenWHO users agree to the following statement, which was provided by the Office of the Legal Counsel of the WHO: "Records of your participation in OpenWHO courses may be used for education research. In the interest of this research, you may be exposed to variations in the course content. Research findings will typically be reported at the aggregate level. Your personal identity will not be publicly disclosed in any research findings without your express consent." As the survey was conducted to provide feedback on the course, ethical clearance was not required.

Results

Summary Statistics

During the study period, the total number of enrolled learners was 53,595. Of all enrolled learners in the health workers course, 30,034 (56.0%) completed the course. Out of 2019 survey participants, 1857 (92.0%) completed the course and 432 (8.0%) did not. All survey responses were included in the survey analysis, as this paper considers the knowledge gained and experiences of participants who did and did not complete the course.

Demographic characteristics of the enrolled learners for the course are described in Table 1. Of the enrolled learners, 34,746 (64.8%) provided their gender, 33,557 (62.6%) provided their age, and 46,909 (87.5%) provided their professional affiliation. There were more female learners (n=18,388, 52.9%) than male learners (n=16,311, 47.0%) and the age group of 20-29 years was most dominant in the course (n=11,444, 34.1%). The top 3 professional affiliations of learners were the following: health care professionals (n=21,487, 45.8%), students (n=6874, 14.7%), and ministry of health officials (n=4666, 9.9%).

The course was also translated into 11 additional languages: Arabic, Chinese, Dutch, French, Indonesian, Kazak, Macedonian, Spanish, Russian, Portuguese, and Vietnamese. This analysis considers the English version, as it was the original course launched and it has the largest enrollment of the language versions. Learners from 191 countries participated in the English version of the course. The four countries with the highest number of participants in the English course were India (n=3998, 11.8%), Philippines (n=2700, 7.9%), Nigeria (n=2297, 6.8%), and Rwanda (n=2163, 6.4%).

When asked about their motivation to enroll in the health workers course, 58.5% (n=1177) of survey respondents replied that they participated in the course to prepare themselves for specific professional responsibilities, 12.6% (n=255) out of private interest, 10.9% (n=220) because it was mandatory, 8.0% (n=161) to strengthen their resume, 7.0% (n=142) to be able to teach others, and 3.0% (n=64) for other and unknown reasons. However, there were substantial differences in motivation between countries, professional affiliations, and years of experience (Figure 1 and Table S1 in Multimedia Appendix 2 for numerical values). For example, most learners from the United States were students and took the course because it was required. In comparison, a large proportion of the learners from Ministries of Health took the course to be able to teach others.

Table 1. Demographic characteristics of the total enrolled learners in the English version of the *COVID-19 vaccination training for health workers* course on OpenWHO from December 18, 2020, to April 18, 2021.

Characteristics	Values, n (%)
Total enrollments	53,595 (100)
Number of learners that completed the course	30,034 (56)
Gender[a]	
Female	18,388 (52.9)
Male	16,311 (47)
Other	47 (0.1)
Age group (years)[a]	
<20	1279 (3.8)
20-29	11,444 (34.1)
30-39	10,756 (32)
40-49	5711 (17)
50-59	3146 (9.4)
60-69	1094 (3.3)
>70	127 (0.4)
Professional affiliation (top 3)[a]	
Health care professionals	21,487 (45.8)
Students	6874 (14.7)
Health ministry	4666 (9.9)
Country of residence (top 4)[a]	
India	3998 (11.8)
Philippines	2700 (7.9)
Nigeria	2297 (6.8)
Rwanda	2163 (6.4)

[a]Among those who provided information.

Figure 1. Survey participants' motivation for taking the health workers course by selected country, professional affiliation, and years of experience (total survey participants=2019; survey period from March 19 to April 9, 2021). MoH: Ministry of Health; USA: United States of America.
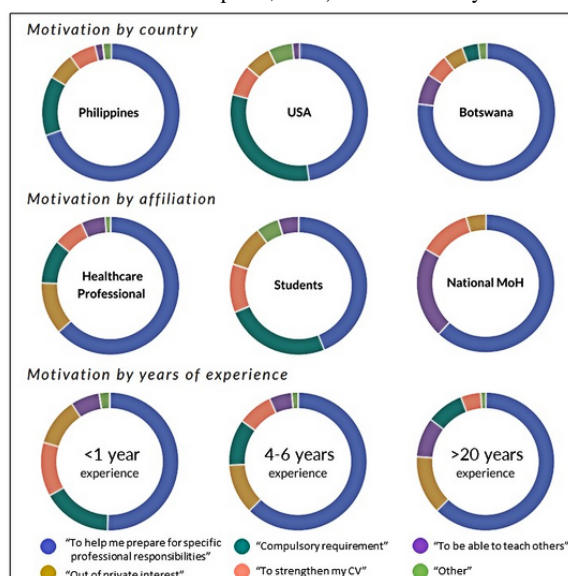
Usability of Course

Survey respondents indicated that they primarily watched the videos as the main resource for the training, which corresponds to the intended training method. Based on the total enrollment course data, on average, Module 2, which focused on supply chains and logistics, was the most watched video of the course, while Module 5, which focused on reporting and monitoring COVID-19 vaccination, was the least watched video among all enrolled learners (Figure 2). More than half of the survey respondents also read the transcripts (n=1070, 53.0%) and downloaded the presentations (n=1083, 53.6%).

For all modules, the postquiz was the course component deemed most useful by the enrolled learners. Although the quizzes were not mandatory, the postquizzes were highly used.

Males aged 40-49 years and females aged 50-59 years were most likely to complete the course. The demographics of learners least likely to complete the course were females under the age of 20 years and learners from a health expert group or other ministry.

For this course, learners spent a median of 25.7 minutes per session and typically completed the course in three sessions (total duration of 72.1 minutes). As the run time for all videos in this course is approximately 1.5 hours, learners may have played videos at a faster speed (OpenWHO allows for participants to speed up the videos by up to 2 times the speed of the original recording) or skipped some parts of the videos.

Figure 2. Usability (by average percent completion) of modules by total enrolled learners (n=53,595) in the COVID-19 vaccination training for health workers course on OpenWHO from December 18, 2020, to April 18, 2021. AEFI: adverse events following immunization.
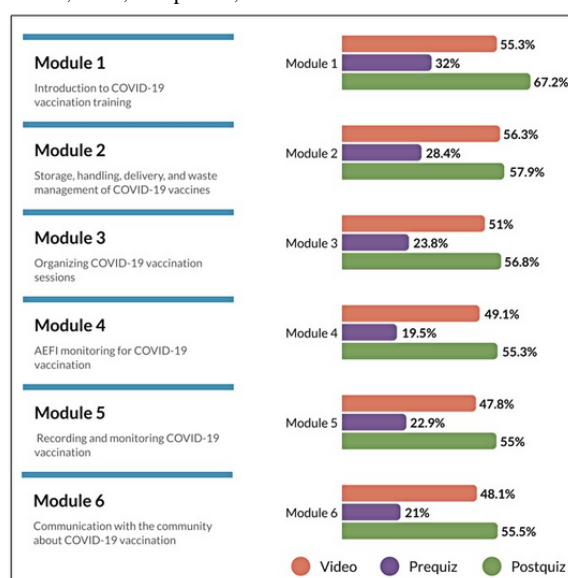
Knowledge and Confidence Gained

As the increase in scores varied by module, the breakdown by module is included below, along with the average change in score from pre- to postquiz. Notably, the module with the highest increase in score was Module 4, which focuses on AEFI monitoring. In Module 4, learners averaged 62% on the prequiz and 78% on the postquiz, for an overall increase of 16%. Overall, learners averaged 76% on the prequiz compared to 85% on the postquiz, resulting in an increase in average score of 9% (Table 2).

Survey respondents were asked whether they had more confidence in their ability to perform their professional role related to COVID-19 vaccination after this training. Overall, nearly 83% (n=1647) of respondents fully agreed with this statement and an additional 15.5% (n=308) somewhat agreed with this statement. Among the top 3 professional affiliation groups, health care professionals were most likely to fully agree with this statement (n=1136, 85.4%) compared to students (n=171, 77.7%) and those working in the public health sector (n=66, 71.0%). Individuals with 4-6 years of experience in their field had the highest "fully agree" rate (n=240, 86.1%), while those with <1 year of experience had the lowest "fully agree" rate (n=196, 78.7%).

Table 2. Pre- and postquiz scores of 53,595 enrolled learners for the *COVID-19 vaccination training for health workers* course on OpenWHO from December 18, 2020, to April 18, 2021.

Modules	Prequiz score[a], %	Postquiz score[a], %	Improvement, %	Number of questions
Module 1: Introduction to COVID-19 vaccination training	88	93	5	2
Module 2: Storage, handling, delivery, and waste management of COVID-19 vaccines	81	88	7	2
Module 3: Organizing COVID-19 vaccination sessions	72	85	13	4
Module 4: AEFI[b] monitoring for COVID-19 vaccination	62	78	16	3
Module 5: Recording and monitoring COVID-19 vaccination	75	84	9	2
Module 6: Communication with the community about COVID-19 vaccination	81	81	0	2
Total	76	85	9	15

[a]Among those who participated in the quiz.

[b]AEFI: adverse events following immunization.

Considerations for Future Virtual Trainings

The health workers course was particularly well received by health care professionals. About 99% (n=1966) of survey respondents indicated that they would recommend this course to others, with 91.3% (n=1832) fully agreeing and 7.6% (n=134) somewhat agreeing. Among the top 3 professional affiliation groups, health care professionals had the highest fully agree rate (n=1244, 93.7%), while students had the lowest (n=188, 86.2%).

When asked their preferred training methods, 65.6% (n=1293) of the survey respondents preferred online training, 29.3% (n=579) preferred blended (combination of online and in-person training), 3.7% (n=73) preferred in-person training, and 1.4% (n=27) were unsure. The reasons respondents preferred online training (multiple responses were possible) included the convenience of the timing (n=1204, 59.6%), the self-paced nature (n=1039, 51.5%), the ability to download the materials (n=907, 44.9%), the ability to replay sections (n=890, 44.1%),

and the increased ability to concentrate (n=520, 25.8%). As these responses were from learners who participated in the online training and completed the online survey, it is important to note that this may reflect an overestimate of overall willingness to participate in online learning among the general population.

When asked about areas for future improvement, 32.9% (n=604) of survey respondents requested that OpenWHO offer more COVID-19 vaccination courses (particularly vaccine-specific resources).

In addition, 17.9% (n=362) of survey respondents requested the course be available in their national language and 4% (n=81) asked for more interaction with technical experts.

At the time of the submission of this article (July 2021), the health workers course has been provided in 12 languages and has had more than 110,000 enrollments (Table 3). The average completion rate is 65% and the highest is 89%, for the Spanish-language course.

Table 3. Total number of enrollments and completion certificates awarded by language version for the *COVID-19 vaccination training for health workers* course on OpenWHO from December 18, 2020, to April 18, 2021.

Course number in order of launch date	Language	Number of enrollments N=110,836	Number of certificates (completion rate) N=71,770
1	English	68,267	37,284 (55)
2	Bahasa	4660	2786 (60)
3	Russian	350	159 (45)
4	Macedonian	84	39 (46)
5	Chinese	424	240 (57)
6	Arabic	1324	665 (50)
7	Spanish	32,672	29,178 (89)
8	French	1959	970 (50)
9	Portuguese	501	209 (42)
10	Vietnamese	394	195 (49)
11	Dutch	182	44 (24)
12	Kazakh	19	1 (5)

Discussion

Principal Findings

Although the completion rate for this course was substantially higher than the industry benchmark of 5%-10% for a massive open online course (MOOC), the findings from this OpenWHO course correspond to other online training experiences for OpenWHO and other virtual training platforms [3-9].

Health care professionals are OpenWHO's largest user group, accounting for nearly one-third of users [10]. In the context of COVID-19 vaccination, primary health workers may serve as "knowledge ambassadors" [11] or "knowledge brokers" [12] and, as such, may have the greatest chance to increase confidence about the vaccine among their patients. For example, it was demonstrated that the acceptability of the COVID-19 vaccine was greater among individuals who thought their health care provider would recommend it [13].

Online and blended learning can provide substantial cost savings by reducing the need for travel, per diems, and other related expenses, as well as rapidly increasing the potential number of people that can be trained [14,15]. As online learning is still relatively new for the training of health workers, the modality has received mixed reviews. Several systematic reviews report that online learning approaches may be at least as effective as traditional learning approaches [11-14], while others show that online learning may make little or no difference in patient outcomes or health professionals' behaviors, skills, or knowledge [16]. However, included studies have used different study designs to measure the effectiveness of online learning, from cross-sectional approaches with pre- and post-test assessments (ie, testing before and after the learning activity) [17] to longitudinal research, where knowledge retention was assessed up to 6 months or a 1-year follow up was carried out [18], which makes comparing these studies difficult.

Although the health workers course was well received, feedback did include the need for additional vaccine-specific training content, more translated versions of the course, opportunities to ask questions to technical experts, and the ability to participate in peer-to-peer learning. Following the request for more vaccine-specific content, CRD launched the vaccine-specific resources course in all United Nations languages (Arabic, Chinese, English, French, Russian, and Spanish) as well as Portuguese [19]. This course provides short instructional videos for COVID-19 vaccines that received Emergency Use Listing, such as Pfizer-BioNTech, Moderna, AstraZeneca, and Janssen. In addition, this new course provides job aides (ie, resources providing vaccine-specific information) to support stakeholders involved in COVID-19 vaccine deployment. To support the development of additional language versions, CRD worked with WHO Country Offices to provide translated versions of both this OpenWHO course for health workers and the Orientation to National Deployment and Vaccination Planning for COVID-19 vaccines course [20]. In response to participants' requests for more interaction and peer learning, CRD developed and implemented the COVID-19 Vaccination: Building Global Capacity webinar series, which brought together technical experts and learners for 15 live sessions dedicated to different aspects of COVID-19 vaccination. This webinar series ultimately reached more than 13,000 learners in 181 countries.

Ideally, virtual training could include recorded and live components, allowing for a combination of the flexibility offered by virtual self-paced learning with the opportunity to interact during the live sessions [21-25]. Considering the speed with which learners completed this course, it may be beneficial to provide shorter versions of the content.

In addition, when considering virtual courses, internet connectivity and the potential for system- or IT-related issues are important to consider, in particular at the subnational level in low-resource settings. In our analysis, nearly one-third of survey respondents noted that they had at least some internet

connection issues during their learning. Similarly, recent research demonstrated that accessibility of online learning activities may be hampered by the required baseline level of digital literacy, equipment, and internet connection, which might be of particular importance for certain populations, including refugees or people with vision problems and those living in low-resource settings [26-29]. If the WHO, governments, and partners plan to increase the use of online learning, it is critical to also consider the infrastructure necessary to ensure learners can fully participate.

Limitations of this research include that we focused this analysis on the English-speaking course. Additional analyses could be conducted on the other language versions of the course. This research also reflects a snapshot in time, as the survey was conducted in March and April 2021. Follow-up surveys could be conducted a year or two after the launch of the course to understand the evolution of the course experience and to understand how participants used the information they received from the course in their professional and personal lives. An additional limitation of these findings is the potential bias of people more comfortable with online learning having taken the course and completed the survey. Finally, this analysis may include potential self-reporting bias among survey respondents, while the limited number of questions in the pre- and postquizzes precludes robust statistical analysis of the impact of each module. It would be beneficial for future analyses to consider differences in the characteristics and perspectives of participants who complete virtual courses compared with participants who do not complete virtual courses.

Overall, this analysis highlights a strong interest in online learning among participating health professionals. This willingness to participate in virtual training is important for the WHO and partners to consider when developing educational materials for other vaccine introductions. Online learning may serve as a viable alternative to face-to-face training, particularly in an emergency context when physical distancing is recommended. It would be beneficial for future studies to look at how health workers applied the knowledge gained from this training and to consider the cost-effectiveness and/or cost-benefit of online learning for vaccine introduction, particularly during health emergencies.

Conclusion

The COVID-19 vaccination trainings were developed for OpenWHO due to the global need for rapidly available training, the need for rapid dissemination to a large number of learners, and the travel and operational limitations posed by the pandemic. This article provides an overview of the usability and utility of this global virtual training, as well as insights from the experience.

In summary, this analysis indicates that this course served its intended purpose of supporting participating health workers in preparing for COVID-19 vaccination deployment. Considering this analysis and the increasing desire of learners to have training materials and performance scores rapidly accessible, Ministries of Health and health facilities should consider the potential of training their health professionals using virtual or blended approaches to increase rapid accessibility and exchange of information [23,25].

Conflicts of Interest

All authors were surveyed for potential conflicts of interest using the WHO Declaration of Interest form. No conflicts of interest were identified. Laerdal Medical (SYJK) was contracted by the WHO to conduct this analysis.

Multimedia Appendix 1
Survey questions.
[PDF File (Adobe PDF File), 213 KB - publichealth_v7i12e33455_app1.pdf]

Multimedia Appendix 2
Supplementary table.
[PDF File (Adobe PDF File), 136 KB - publichealth_v7i12e33455_app2.pdf]

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Abbreviations

AEFI: adverse events following immunization
CRD: Country Readiness and Delivery
MOOC: massive open online course
WHO: World Health Organization

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Original Paper

COVID-19 Vaccine Perceptions, Intentions, and Uptake Among Young Adults in the United States: Prospective College-Based Cohort Study

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Abstract

Background: Uptake of the COVID-19 vaccine among US young adults, particularly those that belong to racial and ethnic minorities, remains low compared to their older peers. Understanding vaccine perceptions and their influence on vaccination uptake among this population remains crucial to achieving population herd immunity.

Objective: We sought to study perceptions of COVID-19 vaccines as well as intended and actual vaccine uptake among one population of college students, faculty, and staff.

Methods: As part of a larger study aimed at investigating the dynamics of COVID-19 transmission, serology, and perception on a college campus, participants were asked about their views on the COVID-19 vaccine in February 2021. Vaccination status was assessed by self-report in April 2021. Logistic regression was used to calculate prevalence ratios with marginal standardization.

Results: We found that non-White participants were 25% less likely to report COVID-19 vaccination compared to White participants. Among those who were unvaccinated, Black and other non-White participants were significantly more likely to indicate they were unwilling to receive a COVID-19 vaccine compared to White participants. The most common reason for unwillingness to receive the vaccine was belief that the vaccine approval process was rushed.

Conclusions: There are racial differences in perceptions of the COVID-19 vaccine among young adults, and these differences might differentially impact vaccine uptake among young racial and ethnic minorities. Efforts to increase vaccine uptake among college populations might require campaigns specifically tailored to these minority groups.

Introduction

Since its first reported case in the United States in January 2020, the ongoing COVID-19 pandemic has caused over 4 million deaths globally, and has severely disrupted global economies, educational and workplace practices, social gatherings, and daily behaviors [1]. To combat the spread of SARS-CoV-2, the virus that causes COVID-19, numerous vaccines targeting components of the virus have been rapidly developed. Since February 2021, three vaccines against SARS-CoV-2 have been granted Emergency Use Authorization (EUA) by the US Food and Drug Administration: BNT162b2 (Pfizer-BioNTech),

mRNA-1273 (Moderna), and Ad26.COV2.S (Janssen/Johnson & Johnson) [2]. Although there is wide variability in vaccination rates among and within states, over 330 million total doses have been administered nationwide as of July 7, 2021, with 55.1% of adults having received one or more doses [3].

To support programs to increase vaccination, greater attention is now being paid to community perceptions of these vaccines and how they relate to vaccine uptake and hesitancy, particularly among racial and ethnic minorities [4]. Several studies have found sociodemographic differences in vaccine hesitancy across the population, with significantly higher rates of vaccine hesitancy among those who are non-White compared to Whites and those without a 4-year advanced degree compared to those with a 4-year advanced degree [5]. Many attribute this concentration of hesitancy among non-White groups, particularly among Black Americans, to centuries of structural and medical racism that have resulted in unequal treatment of minority populations in the American health care system [6]. Understanding the unequal distribution of COVID-19 vaccine uptake and hesitancy is important as vaccination campaigns across the United States aim to reach sufficient community coverage to surpass the herd immunity threshold, estimated to be between 80%-90% for COVID-19 [7].

Young adults, including college or university students, are more likely to be asymptomatic or paucisymptomatic carriers of SARS-CoV-2 compared to their older counterparts [8]. American college students also frequently live together with other students in congregate dormitory settings or off-campus housing, which has led to numerous outbreaks of COVID-19 among young adults on college campuses [9-11]. These outbreaks have had spillover effects into neighboring communities and act as super-spreader–like events [12]. Despite this increased potential for viral spread, young adults are among the least likely age group to receive vaccines against other respiratory pathogens, such as for seasonal influenza strains [13]. Seasonal influenza vaccination uptake, which has been suggested as a possible predictor of COVID-19 vaccination uptake [14], has historically been low on college campuses, estimated to be between 8%-39% based on a survey of college students [15] conducted at a time when many schools did not require seasonal influenza vaccination. Current national data reveal that 18- to 29-year-olds are the least likely age group to be vaccinated for COVID-19 [3]. Because of this, it is vital to understand perceptions of the COVID-19 vaccines and predictors of vaccine uptake and willingness among college student communities, overall and stratified by racial and ethnic minority groups. Understanding these patterns of uptake and willingness among college students will help public health officials and student health programs to better promote vaccination opportunities to increase the uptake of vaccines for young adults and college-aged persons.

In this study, we describe results of behavioral and perception surveys administered as part of a longitudinal cohort study of students, faculty, and staff at a small liberal arts college located in Milton, Massachusetts, a suburb of Boston. This college has approximately 2000 undergraduate students, about 1000 of which live on campus in congregate dormitory settings, as well as 300 faculty and 400 staff members. Data were collected at two time points during the Spring 2021 semester: in the first week students returned to campus in early February, and immediately prior to final exams in late April 2021. We report the perceptions and intentions of this population regarding the COVID-19 vaccine as well as vaccine uptake.

Methods

All students, faculty, and staff members of Curry College electronically received an invitation to learn more about the study and enroll via a HIPAA-compliant, online survey-hosting platform. Interested individuals completed the informed consent process online in either text or video format; we have previously demonstrated that video consent is associated with higher comprehension of consent elements [16]. Consent to participate was documented online. Eligibility criteria were as follows: aged ≥18 years, ability to read and understand English without assistance, being a member of the Curry College residential community during the Spring 2021 semester (February-May 2021); completing at least part of their instruction or job in-person on the Curry College campus in Milton, Massachusetts; intention to remain in the vicinity of Curry College for the entire study period, willingness to comply with Curry College COVID-19 weekly screening requirements, willingness to answer biweekly study surveys electronically sent via email, willingness to participant in venipuncture for blood sample collection, and having no bleeding disorder preventing the use of venipuncture. Eligible participants who did not complete consent before returning to campus were offered enrollment on-site during their first week of classes.

Enrolled participants completed an online baseline survey. The survey collected demographic and socioeconomic information, as well as perceptions regarding COVID-19 risk and the COVID-19 vaccines, vaccine hesitancy, and self-reported vaccine uptake, with individual questions adapted from a validated, national probability-sampled survey used in a larger study of SARS-CoV-2 seroprevalence [17]. Vaccine hesitancy and concerns about the vaccine were assessed with a single item asking about willingness to receive the vaccine when eligible. At the time of the baseline survey in February 2021, most states were only offering the vaccine to those aged >65 years, health care workers, and essential workers. By the time of the final survey in late April 2021, all US adults were eligible for the COVID-19 vaccine. Participants were also asked about their perception of the safety and efficacy of the vaccines and perceptions about the timing of the EUA approval for the vaccines. At the end of the Spring 2021 semester in late April, participants completed a final survey including the same questions about perceptions about COVID-19 vaccines and receipt of vaccination.

Participant status as a health care worker or student (HCW) was established after identifying the primary major or department with which the student, faculty, or staff member was primarily affiliated via school records. Students were categorized as HCWs if their major course of study was either nursing or exploratory health professions. Faculty and staff were categorized as HCWs if their primary department was either the Department of Nursing or the Student Health Center.

Selection fractions and ratios will be calculated for students as a whole as well as for on-campus residential and off-campus commuter students and to assess for possible selection bias among these student subpopulations.

All statistical analyses were conducted with SAS (version 9.4; SAS Institute). Descriptive statistics and frequencies among the study sample results were obtained for all categorical demographic, exposure, and outcome variables in the survey. Fisher exact test was used to determine if there were statistical differences in attitudes toward and willingness to receive the COVID-19 vaccine between several sociodemographic groups, including racial and ethnic groups. To determine whether there were statistical differences in sociodemographic variables and perception of/intention to receive vaccine between those who were vaccinated and unvaccinated in April, predicted prevalence ratios with marginal standardization and confidence intervals were calculated using logistic regression [18]. We also used Fisher exact test to determine if there were statistically significant differences in self-reported vaccine uptake at the final time point between those who reported at baseline that they were unwilling to receive the COVID-19 vaccine and those who reported they were willing.

This longitudinal cohort study was conducted with the approval of the Emory University (STUDY00002096) and Curry College Institutional Review Boards in accordance with all applicable regulations.

Results

Between February 14-19, 2021, a total of 454 participants enrolled in the study and completed the baseline survey and venipuncture. Of these, 328 (72.8%) completed the second venipuncture and final survey in late April 2021. Most participants were female (333/454, 70.9%), White (366/433, 71.3%), non-Hispanic/Latinx (402/453, 69.2%), and students (308/450, 60.4%; Table 1). The median age of participants was 21 years. Most participants were not HCWs (313/454, 68.9%), as classified by department affiliation and student major (Table 1). In total, about 14% (308/2200) of the total student body participated in the study ulti(Table S1 in Multimedia Appendix 1).

Table 1. Demographic characteristics and self-reported COVID-19 vaccination status among students, faculty, and staff at Curry College, Milton, Massachusetts, February 2021.

Demographics	All participants (N=454), n	Characteristic by self-reported vaccination status		
		Unvaccinated (N=149), n (%)[a]	Vaccinated (N=305), n (%)[a]	Prevalence ratio (95% CI)[b]
Natal sex				
Male	121	52 (43)	69 (57)	Reference
Female	333	90 (27)	243 (73)	1.11 (0.94-1.30)
Race				
White	366	105 (29)	261 (71)	Reference
Black	33	19 (58)	14 (42)	0.79 (0.63-0.98)[c]
Other	34	17 (50)	17 (50)	0.79 (0.63-0.98)
Ethnicity				
Non-Hispanic/Latinx	402	124 (31)	278 (69)	Reference
Hispanic/Latinx	51	25 (49)	26 (51)	0.94 (0.75-1.19)
Affiliation				
Student	308	122 (40)	186 (60)	Reference
Staff	86	17 (20)	69 (80)	1.45 (1.28-1.64)[c]
Faculty	56	8 (14)	48 (86)	1.45 (1.28-1.64)
Work or study in health care setting				
Non–health care workers	313	119 (38)	194 (62)	Reference
Health care workers	141	30 (21)	111 (79)	1.35 (1.18-1.54)[c]

[a]Unless otherwise stated, percentages shown are row percentages.

[b]Prevalence ratios with marginal standardization with 95% CI are from multivariate modified logistic regression models testing associations between predictors and vaccination status.

[c]$P<.05$.

Participants were asked about their willingness to receive a COVID-19 vaccine and their attitudes regarding COVID-19 vaccines at the baseline time point in February and at the final

study survey in April 2021. At baseline, over two-thirds of those who reported they were unvaccinated indicated that they were willing or very willing to receive the COVID-19 vaccine once

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they became eligible (Figure 1, Table S2 in Multimedia Appendix 1). In comparison, in the final survey, among the 105 participants who reported not having received a dose of a COVID-19 vaccine, nearly 65% reported that they were willing or very willing to get vaccinated once they were able (Figure 1, Table S3 in Multimedia Appendix 1). All Massachusetts residents ≥16 years old have been eligible to receive the COVID-19 vaccine since April 19, 2021. However, in many areas, demand for vaccines exceeded supply, leading to delays in obtaining appointments [19]. Attitudes regarding the COVID-19 vaccine differed by race and ethnicity (Figure 1). In the baseline survey, 28% (8/28) of Black and 21% (6/29) of other non-White respondents reported they were unwilling or very unwilling to receive the COVID-19 vaccine, compared to only 13% (34/268) of White respondents. Among Hispanic/Latinx individuals, 40% (12/40) reported they were unwilling or very unwilling to receive the COVID-19 vaccine compared to 11% (39/300) of non-Hispanic/Latinx respondents.

Figure 1. Percentage of participants who self-reported they are unlikely to receive a COVID-19 vaccine. Only those who were unvaccinated at each time point were asked this question (N=341 for time point 1 and N=105 for time point 2). HCW: health care worker.
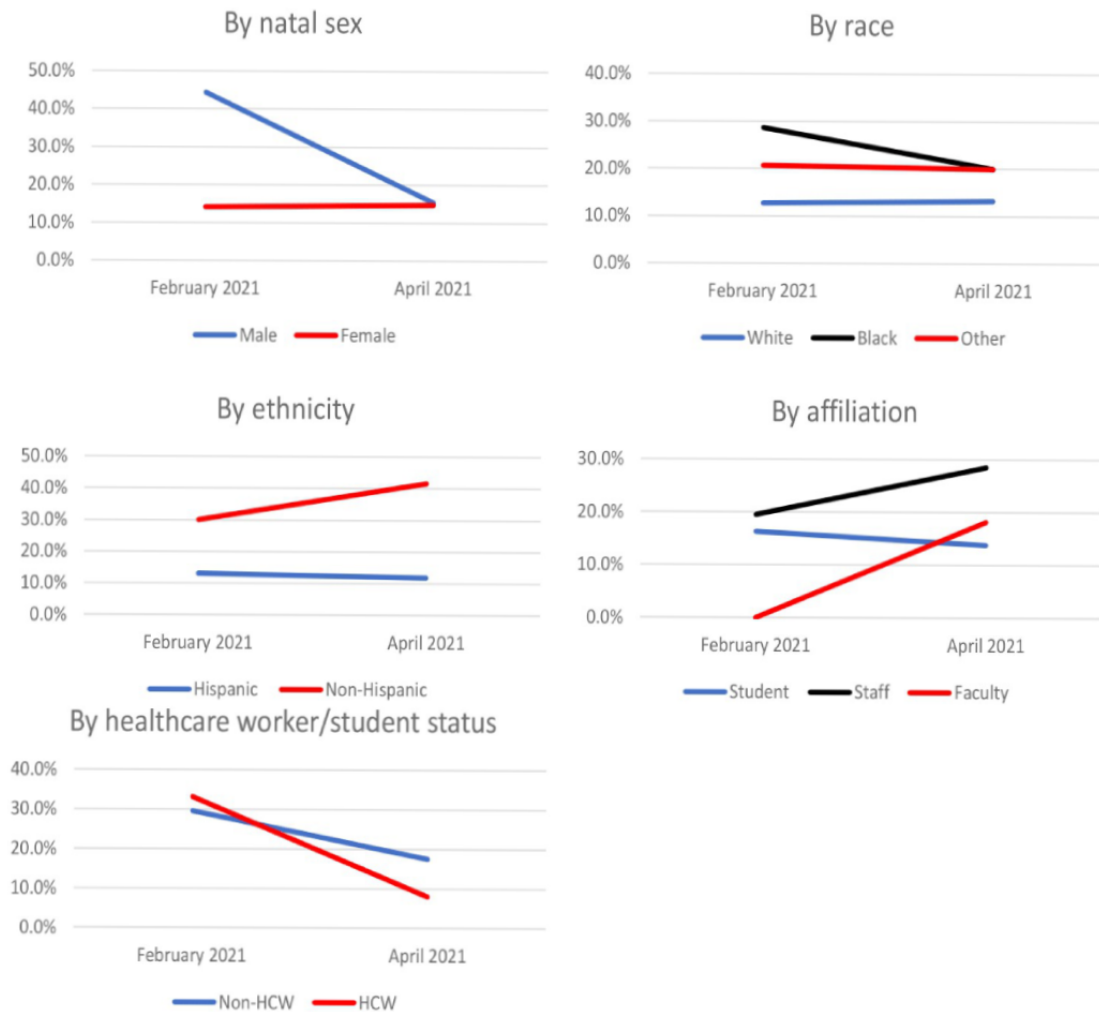
Participants were also asked about their perceptions of the speed with which the COVID-19 vaccines were granted Emergency Use Authorization by the US Food and Drug Administration. In the baseline survey, 30.4% (137/451) of participants believed the COVID-19 vaccine was approved too quickly (Figure 2, Table S2 in Multimedia Appendix 1). These perceptions differed across racial and ethnic groups: 29% (104/363) of White, 50.0% (15/30) of Black, 37.8% (14/37) of other non-White respondents, and 53.8% (29/52) of Hispanic/Latinx participants believed the COVID-19 vaccine was approved too quickly. In the April survey, 25.1% (95/365) of respondents believed the COVID-19 vaccines were approved too quickly. By race and ethnicity, about 23.3% (74/318) of White, 43% (9/21) of Black, 34.6% (9/26) of other non-White, and 37.8% (14/37) of non-Hispanic/Latinx participants believed the COVID-19 vaccine was approved too quickly in the April survey.

Figure 2. Percentage of participants who believed the COVID-19 vaccine was approved too quickly. This question was directed to the entire cohort (N=451 for time point 1 and N=365 for time point 2). HCW: health care worker.

At the final study assessment during late April 2021, about two-thirds (305/454) of all participants reported having received the COVID-19 vaccine (Table 1); this was similar to the Massachusetts statewide vaccination rate at the time [20]. However, in this study, 60.3% (186/308) of student participants reported having received the COVID-19 vaccine; this was much higher than the Massachusetts age-specific vaccination rate among 20- to 29-year-olds at that time, which was approximately 46% [20]. Participants who were natal sex women were about 10% more likely to self-report having received the COVID-19 vaccine compared to natal sex men (Table 1). Black and other non-White participants were 25% less likely to report vaccination compared to White participants. Overall Massachusetts data from the same point in time revealed a similar but weaker relationship between race and vaccination status [20]. However, there was not significant evidence of a relationship between self-reported vaccination uptake among Hispanic/Latinx participants when compared to non-Hispanic/Latinx participants. Taken together, these data indicate disparities in vaccine uptake among Black participants.

Other demographic variables were also found to be significantly associated with self-reported vaccination rate. Staff and faculty were nearly 50% more likely to report vaccination compared to students (Table 1). Of note, the average age among students was 21.5 years, while the average ages among faculty and staff were 50.7 years and 48.2 years, respectively; as such, faculty and staff had a longer window of time during which they could have received the COVID-19 vaccine by the time the survey was conducted due to the age-bracketed rollout in Massachusetts.

Further, we analyzed the relationship between work and/or study in health care settings and self-reported vaccination. Participants who identified as students or workers in health care settings were nearly 30% more likely to report COVID-19 vaccination compared to those who do not work or study in these settings (Table 1). Those who worked/studied in health care settings

were given earlier eligibility to receive the COVID-19 vaccine; however, all residents of Massachusetts had been eligible to receive the vaccine since April 19, 2021, and the time of final survey collection was in late April. At the time, there were no workplace requirements for vaccination in the state of Massachusetts.

We examined the relationship between vaccine intention measured at baseline and vaccine uptake in the final survey. Those who responded at baseline that they were likely or very likely to receive the COVID-19 vaccine were significantly more likely to have received the vaccine by the final time point compared to those who said they were unlikely or very unlikely to receive the COVID-19 vaccine, which may indicate that

vaccine perception and intentions were formed early in the vaccine rollout process (Figure 3).

Respondents who reported being unwilling to receive the COVID-19 vaccine at the final time point were asked to indicate possible reasons for being hesitant (Table 2). Although the plurality of respondents indicated "None of the above," the most commonly selected prespecified reason was that the vaccine approval process was rushed. These results were consistent with results regarding questions about whether the vaccine approval timeline was rushed, suggesting that participants' skepticism of the speed with which the COVID-19 vaccines were approved might have influenced their hesitancy in uptake of the vaccine.

Figure 3. COVID-19 vaccine willingness in February 2021, and follow-up vaccine uptake in April 2021. Participants' self-reported willingness to receive the COVID-19 vaccine in February 2021 and self-reported vaccine status as of late April 2021. Fisher exact t test revealed a significant ($P<.001$) difference in the distribution of baseline vaccine willingness among those unvaccinated versus vaccinated in April 2021.
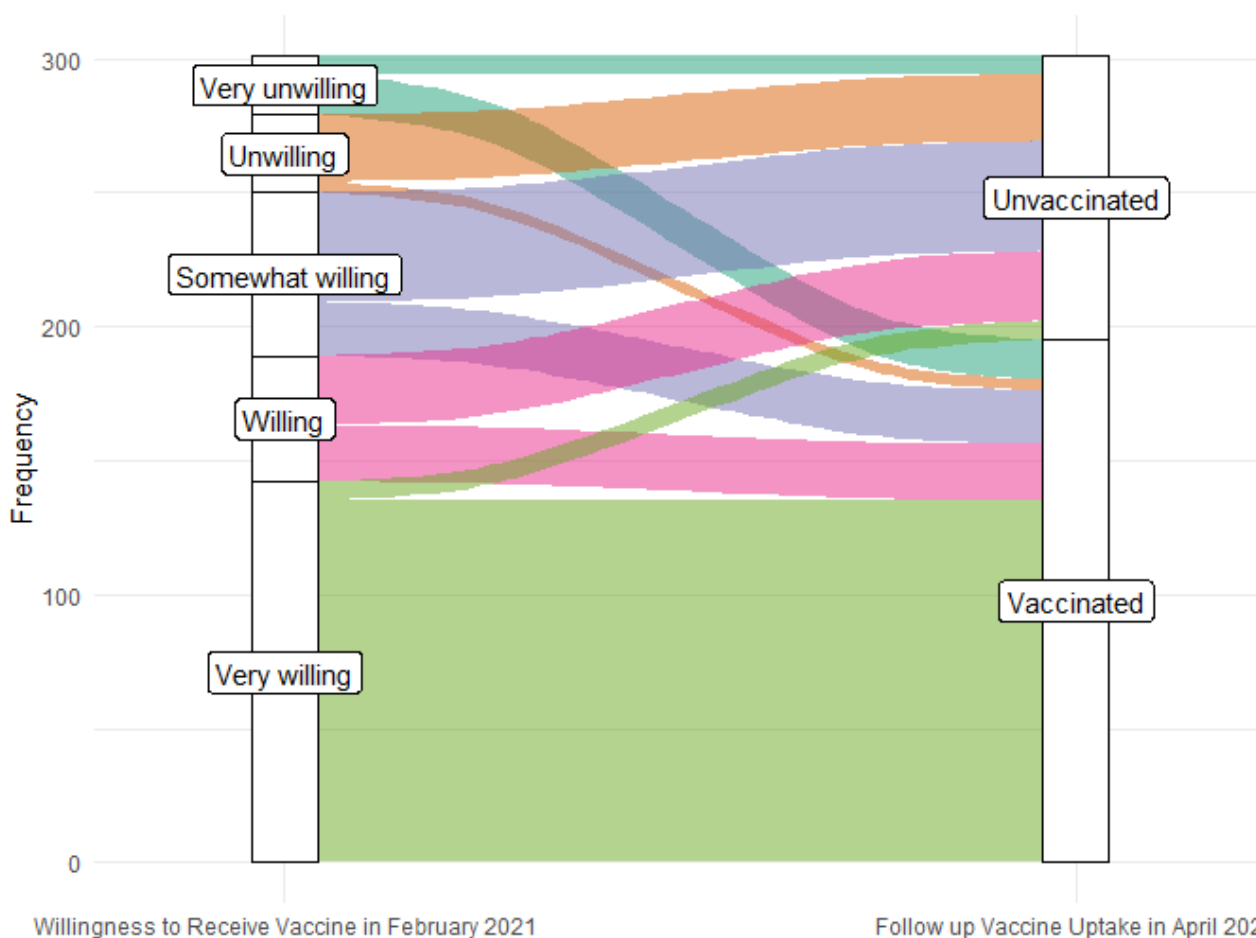
Table 2. Self-reported reasons for hesitancy regarding the COVID-19 vaccine among those in the Curry College Community who were unvaccinated as of April 2021 (N=145; respondents could indicate more than one response)[a].

Reason(s) for hesitancy	The vaccine will give me COVID-19, n (%)	The vaccine affects fertility, n (%)	Natural infection will protect me, n (%)	The approval process was rushed, n (%)	The vaccine is new technology, n (%)	Don't perceive risk for COVID-19, n (%)	None of the above, n (%)
Responses to this question (N=145)	4 (2.8)	22 (15.2)	5 (11.1)	34 (23.4)	18 (12.4)	9 (6.2)	53 (36.6)

[a]This question was directed at those who reported they were unvaccinated as well as those who said they were unlikely or very unlikely to receive the COVID-19 vaccine.

Discussion

Principal Findings

In a cohort of university students, faculty, and staff at a small liberal arts college near Boston, Massachusetts, over two-thirds of participants reported receiving the COVID-19 vaccine by late April 2021. At this time, the COVID-19 vaccine was approved for Massachusetts adults, and the Commonwealth had entered Phase IV of reopening, with some limited indoor gathering and dining [21]. In the previous 2 weeks, there were 53 new cases in Milton, Massachusetts, and 9740 across the state of Massachusetts, down from a high of 72,000 statewide cases in January [20]. About two-thirds of those who were unvaccinated at the completion of the study reported that they would be willing to receive the COVID-19 vaccine once it was available. These findings are reassuring as they indicate the potential to reach a high population vaccination rate that may surpass the community herd immunity threshold [22]. Moreover, these findings indicate that young adult and college student populations may be more amenable to receiving the COVID-19 vaccine than vaccines for other respiratory pathogens, such as the annual influenza vaccine, when compared to previous reports [15]. This could be due for several reasons, including the relative attention placed on the ongoing COVID-19 pandemic compared to other respiratory pathogen epidemics and the extent to which the COVID-19 pandemic has disrupted daily life.

We found significant differences in self-reported vaccination rates by race. The rates of self-reported vaccination among those who were White were significantly higher than the rates among those who were non-White. These results are consistent with statewide data from the Massachusetts Department of Public Health regarding disparities across racial and minority groups, indicating that racial and ethnic minorities, even among college student populations, are comparatively hesitant to receive the COVID-19 vaccine [20]. Thus, although this college population as a whole may achieve population herd immunity, there may be minority subpopulations still at risk for viral spread. This is particularly concerning, as numerous studies have noted racial disparities in clinical outcomes among those infected with COVID-19: not only are these individuals more at risk of becoming infected with COVID-19, but they are also more likely to have adverse outcomes compared to White individuals [23].

Furthermore, among those who were unvaccinated, we found significant differences in perceptions surrounding the willingness to receive the COVID-19 vaccine and perceptions of the vaccine across natal sex and race strata. We observed that Black and other non-White individuals were significantly more likely to say they were unwilling to receive the COVID-19 vaccine when available compared to their White counterparts. We found that Black and other non-White participants were significantly more likely to say that the COVID-19 vaccine was approved too quickly, and many cited this as being a reason they were hesitant to receive the COVID-19 vaccine. These disparities persisted in our cohort from the baseline survey to the final survey, despite increasing national attention focusing on disparities in vaccine uptake.

Lastly, we examined the relationship between intention to be vaccinated and self-reported receipt of vaccine. We found an association between baseline vaccine intention (ie, intent to receive the vaccine or lack thereof) and self-reported vaccination, which may indicate that perceptions and personal intent surrounding the vaccine formed early on in the vaccine rollout process influenced the decision to be vaccinated. This result may inform future public health messaging campaigns aimed at minority community outreach.

The disparities in vaccine uptake and vaccine hesitancy reported in many settings in the United States [24-26] were also observed among these college students, staff, and faculty. This highlights the need for targeted approaches and interventions among racial and ethnic minorities to increase vaccine uptake on college campuses. Particularly with the prevalent Delta variant's increased transmissibility, college administrators and public health officials must understand racial differences in vaccine perceptions to help prevent the spread of COVID-19 in their communities.

Limitations

Our data have important limitations. First, the data were collected using a convenience sample of Curry College community members and are therefore subject to selection bias. Recruitment was completed by mass email to all students, faculty, and staff that would be on campus at Curry College at least part-time in the Spring 2021 semester, as well as in-person at the Student Health SARS-CoV-2 polymerase chain reaction testing site. In total, about 14% of the total student population participated. Of student participants, nearly three-quarters reported living on campus compared to about 40% of the overall student population. It is possible that those who chose to complete some in-person instruction/work were less risk-averse and/or were self-assessed to be at less risk of severe COVID-19 compared to those who chose entirely virtual instruction/work. This difference in risk aversion may or may not correlate with other beliefs surrounding COVID-19, including perceptions and behaviors regarding the vaccine. However, due to the nature of this study and the necessity of on-campus presence to collect venipuncture samples, inclusion of fully remote students and workers was not possible. Moreover, the sampled population of students was more likely to be White and non-Hispanic compared to the overall Curry College student population. There are many possible reasons for fewer non-White students electing to participate. This may indicate that non-White students opted to pursue virtual instruction at a different rate than White students. Non-White students may also have been less likely to self-enroll in a health-related study due to distrust of the medical/public health system due to historic mistreatment and institutionalized racism [27,28].

Additionally, the Curry College campus population from which the cohort of participants was drawn is itself largely non-Hispanic White. Furthermore, Curry College is a private liberal arts school located in Milton, Massachusetts, a suburb of Boston, with a median income of $133,718 [29]. As such, this community has a higher education level and higher income compared to the state as a whole, which may limit the transferability of these data. Indeed, at the time of the conclusion

of the study, Milton had a higher local vaccination rate (57%) compared to the overall Massachusetts average (52.3%) [15], which may indicate that this community's perceptions surrounding COVID-19 vaccine uptake differ from elsewhere in the state. In addition, our sample also had a substantial proportion of health care workers, even among students, many of whom were vaccinated once vaccines were made available. Therefore, our cohort may not be representative of all university students nationwide or Massachusetts as a whole.

Conclusion

In a population of students, faculty, and staff at a New England residential college, a large majority were either vaccinated or willing to be vaccinated against COVID-19 by late April 2021. However, Black and other non-White racial groups were significantly less likely to be vaccinated or willing to be vaccinated. Perceptions of the COVID-19 vaccine in February 2021 predicted vaccination uptake by April, suggesting that views of the vaccine formed soon after it was approved shaped vaccine adoption behaviors. In this unique cohort, we observed lower vaccination willingness and uptake among racial/ethnic minority populations, similar to studies of other US populations. Additional research and programmatic activities are needed to understand reasons for vaccine hesitancy and to overcome hesitancy to work toward equitable vaccine coverage.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Supplemental Tables: Sampling Fractions and Survey Responses of Curry College community members, Milton, Massachusetts, in February and April 2021.
[DOCX File , 39 KB - publichealth_v7i12e33739_app1.docx]

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Abbreviations

EUA: Emergency Use Authorization
HCW: health care worker/student

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Original Paper

COVID-19 Vaccine–Related Attitudes and Beliefs in Canada: National Cross-sectional Survey and Cluster Analysis

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Abstract

Background: There are concerns that vaccine hesitancy may impede COVID-19 vaccine rollout and prevent the achievement of herd immunity. Vaccine hesitancy is a delay in acceptance or refusal of vaccines despite their availability.

Objective: We aimed to identify which people are more and less likely to take a COVID-19 vaccine and factors associated with vaccine hesitancy to inform public health messaging.

Methods: A Canadian cross-sectional survey was conducted in Canada in October and November 2020, prior to the regulatory approval of the COVID-19 vaccines. Vaccine hesitancy was measured by respondents answering the question "what would you do if a COVID-19 vaccine were available to you?" Negative binomial regression was used to identify the factors associated with vaccine hesitancy. Cluster analysis was performed to identify distinct clusters based on intention to take a COVID-19 vaccine, beliefs about COVID-19 and COVID-19 vaccines, and adherence to nonpharmaceutical interventions.

Results: Of 4498 participants, 2876 (63.9%) reported COVID-19 vaccine hesitancy. Vaccine hesitancy was significantly associated with (1) younger age (18-39 years), (2) lower education, and (3) non-Liberal political leaning. Participants that reported vaccine hesitancy were less likely to believe that a COVID-19 vaccine would end the pandemic or that the benefits of a COVID-19 vaccine outweighed the risks. Individuals with vaccine hesitancy had higher prevalence of being concerned about vaccine side effects, lower prevalence of being influenced by peers or health care professionals, and lower prevalence of trust in government institutions.

Conclusions: These findings can be used to inform targeted public health messaging to combat vaccine hesitancy as COVID-19 vaccine administration continues. Messaging related to preventing COVID among friends and family, highlighting the benefits, emphasizing safety and efficacy of COVID-19 vaccination, and ensuring that health care workers are knowledgeable and supported in their vaccination counselling may be effective for vaccine-hesitant populations.

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Introduction

In the fall of 2020, regions of Canada were experiencing a second wave of COVID-19 with rising case counts, hospitalizations, and deaths [1]. Although several vaccines against SARS-CoV-2 were in development [2], they were not yet available as public health tools to mitigate the spread of COVID-19, as the first COVID-19 vaccine was not authorized by Health Canada until December 9, 2020 [2]. This meant that in the fall of 2020, nonpharmacologic interventions (NPIs), including practicing physical distancing, wearing a face mask if physical distancing is not possible, staying home when sick, and limiting large gatherings were the only means to reduce the transmission of COVID-19 [3].

Although there was great optimism about the potential emergence of safe and effective vaccines against SARS-CoV-2, COVID-19 vaccine hesitancy was becoming evident in the summer and fall of 2020 [4-7]. Vaccine hesitancy is defined by the Strategic Advisory Group of Experts (SAGE) Working Group as a "delay in acceptance or refusal of vaccination despite availability of vaccination services" [8]. The reasons for vaccine hesitancy are heterogeneous and complex [9]. The SAGE Working Group created a framework of vaccine hesitancy determinants, which consists of 3 domains: (1) contextual influences (eg, socioeconomic group, political climate), (2) individual and social group influences (eg, social norm, personal experience), and (3) vaccine characteristics (eg, perceived risks and benefits, health care provider attitudes) [8]. This framework can be used to determine the potential factors contributing to vaccine hesitancy with respect to a COVID-19 vaccine within the unique context of the COVID-19 pandemic.

Several studies have looked at the risk factors for vaccine hesitancy in populations around the world and have found that many different factors, including sociodemographic variables and concerns about efficacy and safety of COVID-19 vaccines, may contribute to COVID-19 vaccine hesitancy [10]. It has been noted, however, that factors associated with vaccine hesitancy identified in the general population may not be consistent with factors associated with vaccine hesitancy in specific subpopulations [11]. Therefore, to improve overall vaccine uptake, it is important to examine the risk factors for vaccine hesitancy in the specific population segments who report increased vaccine hesitancy.

In the summer of 2020, we designed a mixed methods study to examine COVID-19 attitudes, beliefs, and behaviors among Canadians with an overreaching goal of informing targeted public health messaging to improve adherence to NPIs and vaccine uptake. We have previously published the initial phases of this mixed methods study including a pilot survey [5] and a qualitative study [4]. This preliminary work found that there were mixed views regarding willingness to take a COVID-19 vaccine and identified a number of risk factors with respect to COVID-19 vaccine hesitancy, including low perceived risk of COVID-19 infection, vaccine-specific concerns, low adherence to NPIs, and sources of COVID-19 information [4,5].

Based on the findings from the initial work in our mixed methods study [4,5], we designed a national survey to further explore the risk factors for vaccine hesitancy to identify segmented populations of individuals with vaccine hesitancy to inform targeted public health messaging campaigns. The objectives of this study were to (1) identify which groups of people are more or less likely to take a COVID-19 vaccine among Canadian adults, (2) determine which attitudes toward COVID-19 are associated with vaccine hesitancy, (3) determine if vaccine hesitancy is associated with adherence to NPIs for COVID-19, and (4) evaluate the relationship between persons' vaccine attitudes and their sources of COVID-19 information.

Methods

Study Design, Participants, and Setting

We used a cross-sectional survey to assess the attitudes and beliefs about vaccines and vaccine hesitancy among adults aged 18 years or older living in Canada. The survey was administered online by the Angus Reid Institute [12], a national, not-for-profit, research foundation, from October 27 to November 2, 2020, as the preliminary data on vaccine efficacy and safety of the COVID-19 vaccine, Pfizer-BioNTech, was being submitted to Health Canada for review but before it was approved for use in Canada on December 9, 2020. Survey participants were drawn randomly from the Angus Reid Forum and contacted electronically. The Angus Reid Forum is comprised of 70,000 individuals from across Canada designed to be representative of the Canadian population with sociodemographic characteristics verified to match electoral and census data in each sampling region [12]. To obtain a sample size of 4500, the survey was distributed to 14,887 potential participants. Sampling was stratified for equal representation of Alberta residents and residents of the other Canadian provinces combined. This sampling strategy was used to allow for comparison of 2 Canadian applications used to facilitate contact tracing, that is, ABTraceTogether (a contact tracing application, which is only available in Alberta) and COVID Alert (an exposure notification application available in 8 provinces and the Northwest territories). A copy of the survey questions that were administered can be found in Multimedia Appendix 1.

This study was approved by the Conjoint Health Research Ethics Board at the University of Calgary (REB20-1228). Informed consent was obtained from each participant prior to commencing the survey, and participation was voluntary. Responses were deidentified at the time of collection to ensure participant anonymity and privacy. If participants started the survey but

did not complete it, it was assumed that consent was withdrawn and their survey responses were not saved. Consistent with Angus Reid Forum policy [12], members of the Angus Reid Forum who completed the survey received a small monetary incentive. The Strengthening Reporting of Observational Studies in Epidemiology (STROBE) checklist was used to report our findings [13].

Outcome Measure

The main outcome measure was vaccine hesitancy. Survey participants were asked what they would do if a COVID-19 vaccine were available to them and given the following 4 options: (1) get a vaccine as soon as possible, (2) eventually get a vaccine, but wait a while first, (3) not get a vaccine, or (4) not sure. Vaccine hesitancy was defined as any of the latter 3 responses consistent with the SAGE Working Group definition of vaccine hesitancy [8].

Risk Factors for Vaccine Hesitancy

We considered factors that could be associated with vaccine hesitancy in each of the domains of the SAGE framework (contextual influences, individual and group influences, and vaccine-specific factors) [8] based on a review of the literature, focus groups [4], and a pilot survey [5] that we completed in Alberta, Canada in the summer of 2020. For contextual influences, we determined demographic factors, including sex, age, geographical region, household income, highest level of education, ethnicity, and political leaning. In terms of individual and group influences, we determined participants' attitudes toward COVID-19 and the COVID-19 vaccine, adherence to NPIs (ie, physical distancing, masking, reducing interactions with others, staying home when sick), trusted sources of COVID-19 information, and trusted institutions. For vaccine characteristics, participants were asked about the perceived risks and benefits of COVID-19 vaccines.

Statistical Analysis

Descriptive statistics (percentage frequencies) were calculated for all participant characteristics, adherence to NPIs, attitudes toward COVID-19 and COVID-19 vaccines, and trusted sources of COVID-19 information. Respondents were excluded if they did not answer all survey questions, and therefore, there were no missing data. Negative binomial regression models were used to estimate crude prevalence ratios (PRs) for factors associated with being vaccine hesitant compared to not being vaccine hesitant. Each PR was reported with the associated 95%

CI. We used multiple models to examine the association between vaccine hesitancy and each of the following: (1) sociodemographic characteristics, (2) attitudes toward COVID-19 vaccine, (3) adherence toward NPIs, (4) attitudes toward COVID-19, and (5) trusted sources of COVID-19 information. We also calculated adjusted prevalence ratios (aPRs) by using sociodemographic characteristics identified through a literature search [10,14-16] as being associated with vaccine hesitancy, including sex at birth, age, ethnicity, province of residence, education, household income, and political leaning.

To identify data-driven patterns in survey responses with respect to vaccine hesitancy, we used cluster analysis. The cluster analysis was based on intention to take a COVID-19 vaccine, beliefs about COVID-19 and COVID-19 vaccine, and adherence to NPIs. The K-means algorithm was used to partition the data set into distinct clusters. This iterative algorithm assigns observations to a cluster such that within each cluster, the sum of the squared distance between observations and the arithmetic mean of all observations is minimized. Cluster analysis was used to integrate COVID-19 vaccine intention, COVID-19 beliefs, and adherence to NPIs into similar like-minded groupings to identify insights that can be utilized for targeted messaging and interventions. By using several exposures to establish these clusters, we aimed to create clusters with greater similarity in motivations and attitudes for vaccine intention and gain a deeper understanding of vaccine hesitancy. Negative binomial regression was used to estimate crude PRs and 95% CI comparing sociodemographic characteristics between each of the clusters with cluster 2 as the reference. Analyses were conducted using STATA Version 15.1 (Stata Corp). A P value of <.05 was set as significant.

Results

Survey Participation

Of the 14,887 survey invitations distributed, 5893 (39.6%) invitations were accepted in the 7 days the survey was available. Of those, 4498 (76.3%) participants completed the survey and were included in the analysis (Table 1), while 1395 (23.7%) participants were excluded owing to one or more incomplete responses. Participants who completed the survey were similar to those who started but did not complete the survey in terms of sex, age, province of residence, highest level of education, and ethnicity.

Table 1. Participant characteristics and association with COVID-19 vaccine hesitancy in October to November 2020 (N=4498).

Characteristic	Total, n (%)	Vaccine hesitancy, n (%) No	Yes	Prevalence ratio[a] (95% CI)	Adjusted prevalence ratio[b] (95% CI)
Participants	4498 (100)	1622 (36.1)	2876 (63.9)	N/A[c]	N/A
Sex at birth					
Female	2294 (51)	815 (35.5)	1479 (64.5)	Ref[d]	Ref
Male	2204 (49)	807 (36.6)	1397 (63.4)	0.98 (0.91-1.06)	0.93 (0.86-1.01)
Age (years)					
18-34	1341 (29.8)	505 (37.7)	836 (62.3)	Ref	Ref
35-54	1585 (35.2)	504 (31.8)	1081 (68.2)	1.09 (1.00-1.20)	1.04 (0.95-1.14)
55+	1572 (35)	613 (39)	959 (61)	0.98 (0.89-1.07)	0.90 (0.82-0.99)
Province of residence					
Alberta	1998 (44.4)	672 (33.6)	1326 (65.4)	Ref	Ref
British Columbia	502 (11.2)	176 (35.1)	326 (64.9)	0.98 (0.87-1.10)	1.04 (0.92-1.17)
Prairie provinces[e]	445 (9.9)	156 (35.1)	259 (58.2)	0.98 (0.76-1.11)	0.95 (0.84-1.08)
Ontario	800 (17.8)	311 (38.9)	489 (61.1)	0.92 (0.83-1.02)	0.96 (0.87-1.07)
Quebec	502 (11.2)	203 (40.4)	299 (59.6)	0.90 (0.79-1.02)	0.97 (0.85-1.10)
Atlantic provinces[e]	251 (5.6)	104 (41.4)	147 (58.6)	0.88 (0.74-1.05)	0.95 (0.80-1.13)
Household income[f] (CAD)					
<$50,000	1030 (22.9)	342 (33.2)	688 (66.8)	Ref	Ref
$50,000-$99,999	1353 (30.1)	486 (35.9)	867 (64.1)	0.96 (0.87-1.06)	0.97 (0.88-1.08)
$100,000-$199,999	1300 (28.9)	511 (39.3)	789 (60.7)	0.91 (0.82-1.01)	0.93 (0.84-1.04)
≥$200,000	229 (5.1)	102 (44.5)	127 (55.5)	0.83 (0.69-1.00)	0.85 (0.70-1.03)
Rather not say	586 (13)	181 (30.9)	405 (69.1)	1.03 (0.92-1.17)	1.02 (0.90-1.15)
Highest level of education					
High school graduate or less	897 (19.9)	256 (28.5)	641 (71.5)	Ref	Ref
Some college or trade school	840 (18.7)	240 (28.6)	600 (71.4)	1.00 (0.89-1.12)	1.01 (0.90-1.13)
College or trade school	996 (22.1)	301 (30.2)	695 (69.8)	0.98 (0.88-1.09)	0.98 (0.88-1.10)
Some university	454 (10.1)	185 (40.7)	269 (59.3)	0.83 (0.72-0.96)	0.85 (0.73-0.97)
University degree	1311 (29.1)	640 (48.8)	671 (51.2)	0.72 (0.64-0.80)	0.73 (0.65-0.81)
Ethnicity					
Caucasian	3862 (85.9)	1430 (37)	2432 (63)	Ref	Ref
Indigenous/First Nations/Metis/Inuit	228 (5)	68 (29.8)	160 (70.2)	1.11 (0.95-1.31)	1.09 (0.93-1.27)
Asian	193 (4.3)	65 (33.7)	128 (66.3)	1.05 (0.88-1.26)	1.15 (0.96-1.37)
Caribbean/African/South American	70 (1.6)	19 (27.1)	51 (72.9)	1.16 (0.88-1.53)	1.16 (0.88-1.54)
Other	145 (3.2)	40 (27.6)	105 (72.4)	1.15 (0.95-1.40)	1.10 (0.91-1.34)
Political leaning					
Liberal	1841 (40.9)	936 (50.8)	905 (49.2)	0.73 (0.66-0.80)	0.74 (0.67-0.82)
Moderate/middle of the road	1029 (22.9)	334 (32.5)	695 (67.5)	Ref	Ref
Conservative	1628 (36.2)	352 (21.6)	1276 (78.4)	1.16 (1.06-1.27)	1.18 (1.07-1.29)

[a]Prevalence ratio is the prevalence of vaccine hesitancy compared with the prevalence of planning to take a COVID-19 vaccine.

[b]Adjusted for sex, age, province of residence, household income, education level, ethnicity, and political leaning.

[c]N/A: not applicable.

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[d]Ref: reference value.

[e]Prairie provinces include Saskatchewan and Manitoba; Atlantic provinces include Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador.

[f]CAD $1=US $0.75.

Participant Characteristics

Participant demographic and socioeconomic characteristics are presented in Table 1. The majority of the participants were females (2294/4498, 51%) and Caucasian (3862/4498, 85.9%). The mean participant age was 47 (SD 16) years with participant ages ranging from 18 to 94 years. The majority of the participants indicated that they were vaccine hesitant and reported they would delay taking a COVID-19 vaccine when offered one (1817/4498, 40.4%), not take a COVID-19 vaccine (708/4498, 15.7%), or were not sure about taking a COVID-19 vaccine (351/4498, 7.8%). The remaining one-third (1622/4498, 36.1%) of the participants reported that they would take a COVID-19 vaccine as soon as possible. Participants aged 55 years or older had lower prevalence of vaccine hesitancy compared with those aged 18-34 years (aPR 0.90, 95% CI 0.82-0.99). University education was also associated with lower prevalence of vaccine hesitancy. Compared with participants who reported their highest level of education as high school graduate or less, the adjusted prevalence was 0.85 (95% CI 0.73-0.97) for some university education and 0.73 (95% CI 0.65-0.81) for participants who had completed a university degree. Liberal political leaning was associated with lower prevalence of vaccine hesitancy compared with participants who reported moderate or middle of the road political leaning (aPR 0.74, 95% CI 0.67-0.82), while conservative political leaning was associated with higher prevalence of vaccine hesitancy (aPR 1.18, 95% CI 1.07-1.29). Biological sex, household income, ethnicity, and province of residence were not associated with vaccine hesitancy.

Attitudes Toward COVID-19 Vaccine

More than half of the participants (2501/4498, 55.6%) felt that the benefits of taking a vaccine outweigh its risks, while 969 (22%) were unsure and 1028 (22%) disagreed (Table 2).

Table 2. Associations between COVID-19 vaccine hesitancy and attitudes toward COVID-19 vaccines in October to November 2020 (N=4498).

	Total, n (%)	Vaccine hesitancy, n (%)		Prevalence ratio[a] (95% CI)	Adjusted prevalence ratio[b] (95% CI)
		No	Yes		
Participants	4498 (100)	1622 (36.1)	2876 (63.9)	N/A[c]	N/A
Attitudes toward COVID-19 vaccines					
Would take a vaccine to protect family					
Agree	3293 (73.2)	1603 (48.7)	1690 (51.3)	Ref[d]	Ref
Disagree	810 (18)	17 (2.1)	793 (97.9)	1.91 (1.75-2.08)	1.77 (1.62-1.94)
Not sure	395 (8.8)	2 (0.5)	393 (99.5)	1.94 (1.74-2.16)	1.85 (1.66-2.07)
A vaccine will end the pandemic					
Agree	1265 (28.1)	691 (54.6)	574 (45.4)	Ref	Ref
Disagree	2214 (49.2)	587 (26.5)	1627 (73.5)	1.62 (1.47-1.78)	1.54 (1.40-1.70)
Not sure	1019 (22.7)	344 (33.8)	675 (66.2)	1.46 (1.31-1.63)	1.43 (1.28-1.61)
Usually get the flu vaccine					
Agree	2523 (56.1)	1301 (51.6)	1222 (48.4)	Ref	Ref
Disagree	1901 (42.3)	301 (15.8)	1600 (84.2)	1.74 (1.61-1.87)	1.67 (1.55-1.80)
Not Sure	74 (1.6)	20 (27)	54 (73)	1.51 (1.15-1.98)	1.50 (1.14-1.97)
Concern about short-term side effects					
Agree	2583 (57.4)	533 (20.6)	2050 (79.4)	Ref	Ref
Disagree	1443 (32.1)	922 (63.9)	521 (36.1)	0.45 (0.41-0.50)	0.47 (0.43-0.52)
Not Sure	472 (10.5)	167 (35.4)	305 (64.6)	0.81 (0.72-0.92)	0.83 (0.73-0.93)
Concern about long-term side effects					
Agree	2703 (60.1)	542 (20.1)	2161 (79.9)	Ref	Ref
Disagree	1294 (28.8)	881 (68.1)	413 (31.9)	0.40 (0.36-0.44)	0.42 (0.38-0.46)
Not sure	501 (11.1)	199 (39.7)	302 (60.3)	0.75 (0.67-0.85)	0.78 (0.69-0.88)
Vaccine developed too fast					
Agree	1985 (44.1)	162 (8.2)	1823 (91.8)	Ref	Ref
Disagree	1874 (41.7)	1248 (66.6)	626 (33.4)	0.36 (0.33-0.40)	0.38 (0.35-0.42)
Not sure	639 (14.2)	212 (33.2)	427 (66.8)	0.73 (0.65-0.81)	0.75 (0.67-0.83)
Vaccine benefits outweigh the risks					
Agree	2501 (55.6)	1457 (58.3)	1044 (41.7)	Ref	Ref
Disagree	1028 (22.9)	40 (3.9)	988 (96.1)	2.30 (2.11-2.51)	2.17 (1.98-2.38)
Not sure	969 (21.5)	125 (12.9)	844 (87.1)	2.09 (1.91-2.28)	2.02 (1.85-2.22)
Would take vaccine if family/friends do					
Agree	1681 (37.4)	745 (44.3)	936 (55.7)	Ref	Ref
Disagree	2296 (51)	717 (31.2)	1579 (68.8)	1.24 (1.14-1.34)	1.17 (1.08-1.27)
Not sure	521 (11.6)	160 (30.7)	361 (69.3)	1.24 (1.10-1.41)	1.21 (1.07-1.37)
Would take vaccine if advised by family doctor/pharmacist/public health official					
Agree	2775 (61.7)	1422 (51.2)	1353 (48.8)	Ref	Ref
Disagree	1319 (29.3)	131 (10)	1188 (90.1)	1.85 (1.71-2.00)	1.73 (1.59-1.87)
Not sure	404 (9)	69 (17.1)	335 (82.9)	1.70 (1.51-1.92)	1.65 (1.46-1.86)

[a]Prevalence ratio is the prevalence of vaccine hesitancy compared with the prevalence of planning to take a COVID-19 vaccine.

[b]Adjusted for sex, age, province of residence, household income, education level, ethnicity, and political leaning.

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Those who disagreed had higher prevalence of vaccine hesitancy compared with those who agreed (aPR 2.17, 95% CI 1.98-2.38; Table 2). Opinions were mixed on whether a COVID-19 vaccine would end the pandemic with 1265 (28.1%) in agreement, 2214 (49.2%) in disagreement, and 1019 (22.7%) being undecided. Participants who disagreed that the vaccine would end the pandemic had a higher prevalence of vaccine hesitancy than those who agreed (aPR 1.54, 95% CI 1.40-1.70).

Participants reported that they would be more likely to take a COVID-19 vaccine if it was recommended by a family doctor, pharmacist, or public health nurse (2775/4498, 61.7%) or if their friends or family took a vaccine (1681/4498, 37.4%). However, the prevalence of vaccine hesitancy was higher in participants who disagreed that they would take a vaccine if their friends/family do (aPR 1.17, 95% CI 1.08-1.27) or if it was recommended by a family doctor, pharmacist, or public health nurse (aPR 1.73, 95% CI 1.59-1.87). Numerous participants (3293/4498, 73.2%) said they would take a COVID-19 vaccine to protect their family; participants who disagreed with this statement had a higher prevalence of vaccine hesitancy compared with those who agreed (aPR 1.77, 95% CI 1.62-1.94). Many participants were concerned about the short-term side effects (2583/4498, 57.4%) and long-term side effects (2703/4498, 60.1%). Participants (1874/4498, 41.7%) who disagreed with the statement that vaccines were developed too fast had a lower prevalence of vaccine hesitancy compared with those who agreed (aPR 0.38, 95% CI 0.35-0.42).

NPIs

The majority of the participants reported physical distancing (3782/4498, 84.1%), wearing face masks (3873/4498, 86.1%), avoiding crowded spaces (3517/4498, 78.2%), and staying home when sick (3857/4498, 85.7%) all or most of the time (Table 3). Participants who reported only adhering to any of these NPIs sometimes, rarely, or never had higher odds of vaccine hesitancy. Participants who reported rarely or never wearing a face mask had an adjusted prevalence of vaccine hesitancy of 1.38 (95% CI 1.22-1.56) compared with those who reported wearing a face mask all the time or most of the time. For physical distancing, those who reported adhering to this NPI sometimes had higher prevalence of vaccine hesitancy than those who practiced physical distancing all the time or most of the time (aPR 1.32, 95% CI 1.18-1.48). Compared with those who reported avoiding crowded spaces all the time or most of the time, participants who reported rarely or never avoiding public spaces had higher prevalence of vaccine hesitancy (aPR 1.35, 95% CI 1.21-1.50).

Table 3. Associations between COVID-19 vaccine hesitancy, adherence to public health measures, and attitudes toward COVID-19 in October to November 2020 (N=4498).

Characteristic	Total, n (%)	Vaccine hesitancy, n (%)		Prevalence ratio[a] (95% CI)	Adjusted prevalence ratio[b] (95% CI)
		No	Yes		
Participants	4498 (100)	1622 (36.1)	2876 (63.9)	N/A[c]	N/A
Adherence to nonpharmaceutical interventions					
Physical distancing					
All the time/most of the time	3777 (84)	1523 (40.3)	2254 (69.7)	Ref[d]	Ref
Sometimes	457 (10.2)	68 (14.9)	389 (85.1)	1.43 (1.28-1.59)	1.32 (1.18-1.48)
Rarely/never	264 (5.8)	31 (11.7)	233 (88.3)	1.48 (1.29-1.69)	1.31 (1.13-1.50)
Wearing face masks					
All the time/most of the time	3868 (86)	1566 (40.5)	2302 (69.5)	Ref	Ref
Sometimes	274 (6.1)	36 (13.1)	238 (86.9)	1.46 (1.28-1.67)	1.34 (1.16-1.54)
Rarely/never	356 (7.9)	20 (5.6)	336 (94.4)	1.59 (1.41-1.78)	1.38 (1.22-1.56)
Avoiding crowded places					
All the time/most of the time	3513 (78.1)	1434 (40.8)	2079 (59.2)	Ref	Ref
Sometimes	457 (10.2)	129 (28.2)	328 (71.8)	1.21 (1.08-1.36)	1.16 (1.03-1.31)
Rarely/never	528 (11.7)	59 (11.2)	469 (88.8)	1.50 (1.36-1.66)	1.35 (1.21-1.50)
Staying home when sick					
All the time/most of the time	3852 (85.6)	1505 (39.1)	2347 (60.9)	Ref	Ref
Sometimes	232 (5.2)	47 (20.3)	185 (79.7)	1.31 (1.13-1.52)	1.22 (1.05-1.42)
Rarely/Never	414 (9.2)	70 (16.9)	344 (83.1)	1.36 (1.22-1.53)	1.27 (1.13-1.42)
Attitudes toward COVID-19					
Ever tested positive for COVID-19					
No	4385 (97.5)	1583 (36.1)	2802 (63.9)	Ref	Ref
Yes	113 (2.5)	39 (34.5)	74 (65.5)	1.02 (0.81-1.29)	1.05 (0.83-1.32)
Know someone who had COVID-19					
No	3162 (70.3)	1101 (34.8)	2061 (65.2)	Ref	Ref
Yes	1336 (29.7)	521 (39)	815 (61)	0.94 (0.86-1.01)	0.98 (0.90-1.06)
Anticipated effect of COVID-19 on own health					
Mild or no symptoms	1085 (24.1)	201 (18.5)	884 (81.5)	Ref	Ref
Manageable symptoms	1940 (43.1)	747 (38.5)	1193 (61.5)	0.75 (0.69-0.82)	0.80 (0.73-0.86)
Severe symptoms	1026 (22.8)	452 (44.1)	574 (55.9)	0.69 (0.62-0.76)	0.73 (0.66-0.82)
Possible death	447 (9.9)	222 (49.7)	225 (50.3)	0.62 (0.53-0.72)	0.65 (0.56-0.76)
Concern for friends/family getting sick					
Not concerned	1204 (26.8)	165 (13.7)	1039 (86.3)	Ref	Ref
Concerned	3294 (73.2)	1457 (44.2)	1837 (55.8)	0.65 (0.60-0.70)	0.70 (0.64-0.76)
Live with someone who is high risk for COVID-19					
No	2649 (58.9)	874 (33)	1775 (67)	Ref	Ref
Yes	1849 (41.1)	748 (40.5)	1101 (59.5)	0.89 (0.82-0.96)	0.89 (0.83-0.97)

[a]Prevalence ratio is the prevalence of vaccine hesitancy compared with the prevalence of planning to take a COVID-19 vaccine.

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[b]Adjusted for sex, age, province of residence, household income, education level, ethnicity, and political leaning.

[c]N/A: not applicable.

[d]Ref: reference value.

Attitudes Toward COVID-19

A small proportion of participants had tested positive for COVID-19 (113/4498, 3%) and almost one-third (1336/4498, 29.7%) knew someone who had tested positive for COVID-19 (Table 3). Participants who were concerned about their friends or family getting sick from COVID-19 had lower prevalence of vaccine hesitancy compared with those who were not concerned (aPR 0.70, 95% CI 0.64-0.76). Participants who reported living with an individual at high risk had lower prevalence (aPR 0.89, 95% CI 0.83-0.97) of vaccine hesitancy. Compared with participants who anticipated experiencing mild or no symptoms in the event of contracting COVID-19, participants had lower prevalence of vaccine hesitancy if they reported they anticipated experiencing manageable symptoms (aPR 0.80, 95% CI 0.73-0.86), severe symptoms (aPR 0.73, 95% CI 0.66-0.82), or possible death (aPR 0.65, 95% CI 0.56-0.76).

Trusted Sources of COVID-19 Information and Institutions

Participants who trusted chief medical officers of health (aPR 0.54, 95% CI 0.47-0.61) and public health websites (aPR 0.68, 95% CI 0.59-0.77) had lower prevalence of vaccine hesitancy compared with participants who did not (Table 4). Those who reported trusting internet searches for COVID-19 information had a higher prevalence of vaccine hesitancy compared to those who did not (aPR 1.34, 95% CI 1.21-1.49). Participants who reported that their most trusted social media platform was Reddit (aPR 0.64, 95% CI 0.51-0.80) had lower vaccine hesitancy than those who did not trust this source. We found that distrust in health care institutions, government, technology companies, finance industries, and professional services was associated with vaccine hesitancy (Table 4). Participants who reported that they did not trust government institutions had higher prevalence of vaccine hesitancy (aPR 1.61, 95% CI 1.46-1.78) compared with those who reported trust in government institutions. The prevalence of hesitancy was also higher in those who did not trust health care (aPR 1.43, 95% CI 1.25-1.62), technology (aPR 1.22, 95% CI 1.08-1.38), and finance (aPR 1.14, 95% CI 1.03-1.25) compared with those who reported trust in these institutions.

Table 4. Associations between COVID-19 vaccine hesitancy, trusted sources of COVID-19 information, and trust in institutions in October to November 2020 (N=4498)[a].

Sources	Total (N)	Vaccine hesitancy, n (%)		Prevalence ratio[b] (95% CI)	Adjusted prevalence ratio[c] (95% CI)
		No	Yes		
Most trusted sources for COVID-19 information					
Chief Medical Officer of Health	1933	904 (46.8)	1029 (53.2)	0.76 (0.70-0.82)	0.80 (0.73-0.86)
Public health websites	1754	778 (44.4)	976 (55.6)	0.83 (0.77-0.90)	0.86 (0.80-0.94)
Health care provider	1239	514 (41.5)	725 (58.5)	0.91 (0.84-1.00)	0.93 (0.85-1.01)
Television/radio news	607	233 (38.4)	374 (61.6)	0.98 (0.88-1.10)	0.96 (0.86-1.07)
Internet searches (eg, Google)	529	81 (15.3)	448 (84.7)	1.43 (1.29-1.58)	1.34 (1.21-1.49)
Friends and family	159	33 (20.8)	126 (79.2)	1.28 (1.07-1.53)	1.16 (0.97-1.39)
Print newspaper	134	55 (41)	79 (59)	0.94 (0.75-1.18)	0.96 (0.77-1.21)
Most trusted social media platforms for COVID-19 information					
Facebook	2167	778 (35.9)	1389 (64.1)	1.00 (0.93-1.08)	0.98 (0.91-1.06)
YouTube	976	297 (30.4)	679 (69.6)	1.12 (1.02-1.22)	1.08 (0.99-1.17)
Twitter	797	342 (42.9)	455 (57.1)	0.87 (0.79-0.96)	0.91 (0.82-1.00)
Instagram	450	144 (32)	396 (88)	1.07 (0.95-1.21)	1.09 (0.96-1.22)
Reddit	407	196 (48.2)	211 (51.8)	0.79 (0.69-0.91)	0.84 (0.72-0.97)
Trust in institutions					
Health care					
Trust	3370	1440 (42.7)	1930 (57.3)	Ref[d]	Ref
Neutral	828	154 (18.6)	674 (81.4)	1.42 (1.30-1.55)	1.33 (1.22-1.45)
Do not trust	300	28 (9.3)	272 (90.7)	1.58 (1.39-1.80)	1.43 (1.25-1.62)
Government					
Trust	1401	744 (53.1)	657 (46.9)	Ref	Ref
Neutral	1414	569 (40.2)	845 (59.8)	1.27 (1.15-1.41)	1.24 (1.12-1.38)
Do not trust	1683	309 (18.4)	1374 (81.6)	1.74 (1.59-1.91)	1.61 (1.46-1.78)
Technology					
Trust	579	261 (45.1)	318 (54.9)	Ref	Ref
Neutral	1707	648 (38)	1059 (62)	1.13 (1.00-1.28)	1.15 (1.01-1.30)
Do not trust	2212	713 (32.2)	1499 (67.8)	1.23 (1.09-1.39)	1.22 (1.08-1.38)
Finance					
Trust	1325	537 (40.5)	788 (59.5)	Ref	Ref
Neutral	1824	641 (35.1)	1183 (64.9)	1.09 (1.00-1.19)	1.09 (0.99-1.19)
Do not trust	1349	444 (32.9)	905 (67.1)	1.12 (1.03-1.24)	1.14 (1.03-1.25)

[a]Participants could pick more than one most trusted source from each list.

[b]Prevalence ratio is the prevalence of vaccine hesitancy compared with the prevalence of planning to take a COVID-19 vaccine.

[c]Adjusted for sex, age, province of residence, household income, education level, ethnicity, and political leaning.

[d]Ref: reference value.

Cluster Analysis

Three distinct nonoverlapping clusters were identified through cluster analysis (Multimedia Appendix 2). Cluster 1 (the vaccine and NPI-accepting cluster) consisted of 1652 (36.7%) participants who reported willingness to take a COVID-19 vaccine and adherence to NPIs, including physical distancing, wearing a face mask in public spaces, staying home when sick, and avoiding public spaces. The 2099 (46.7%) participants in Cluster 2 (the vaccine waiting and NPI accepting cluster) also reported adherence to NPIs but were vaccine hesitant, with 1652 (78.7%) reporting that they would eventually get a vaccine;

however, they planned to wait a while (Figure 1). Cluster 3 (the vaccine and NPI nonaccepting cluster) consisted of 747 (16.6%) participants who reported less adherence to NPIs and were vaccine hesitant, with 557 (74.6%) reporting that they would not take a COVID-19 vaccine when offered (Table 5).

Figure 1. Willingness of the survey participants, by cluster, to take the COVID-19 vaccine when available.
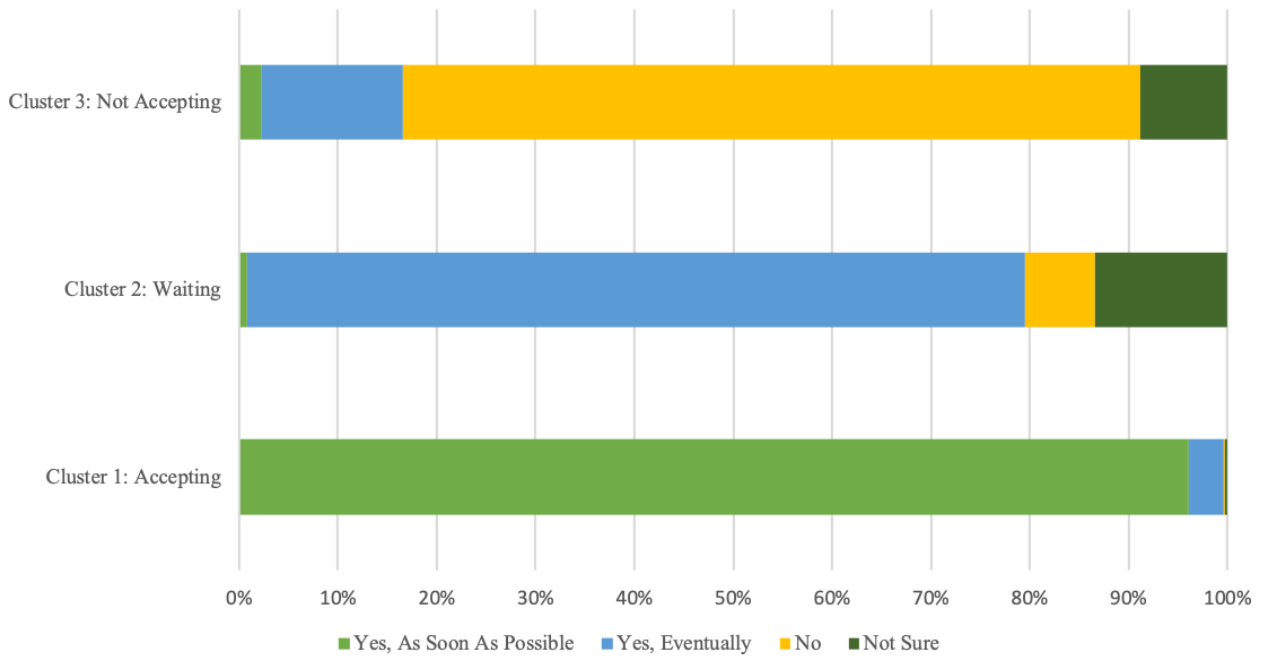
Table 5. Participant characteristics by cluster (N=4498) in October to November 2020.

Characteristic	Total, n (%)	Cluster, n (%)			Prevalence ratio[a] (95% CI)	
		Cluster 1: Accepting	Cluster 2: Waiting	Cluster 3: Not accepting	Cluster 1 versus Cluster 2	Cluster 3 versus Cluster 2
Participants	4498 (100)	1652 (36.7)	2099 (46.7)	747 (16.6)	N/A[b]	N/A
Sex at birth						
Female	2294 (51)	837 (36.5)	1171 (51)	286 (12.5)	Ref[c]	Ref
Male	2204 (49)	815 (37)	928 (42.1)	461 (20.9)	1.12 (1.02-1.24)	1.69 (1.46-1.96)
Age (years)						
18-34	1341 (29.8)	511 (38.1)	621 (46.3)	209 (15.6)	Ref	Ref
35-54	1585 (35.2)	516 (32.5)	741 (46.8)	328 (20.7)	0.91 (0.80-1.03)	1.22 (1.02-1.45)
55+	1572 (34.9)	625 (39.8)	737 (46.9)	210 (13.3)	1.02 (0.890-1.14)	0.88 (0.73-1.06)
Province of residence						
Alberta	1998 (44.4)	684 (34.2)	836 (41.8)	478 (23.9)	Ref	Ref
British Columbia	502 (11.2)	185 (36.9)	273 (54.4)	44 (8.8)	0.90 (0.76-1.06)	0.38 (0.28-0.52)
Prairie provinces[d]	445 (9.9)	158 (35.5)	215 (48.3)	72 (16.2)	0.94 (0.79-1.12)	0.69 (0.54-0.88)
Ontario	800 (17.8)	318 (39.7)	404 (50.5)	78 (9.8)	0.98 (0.86-1.12)	0.44 (0.35-0.57)
Quebec	502 (11.2)	202 (40.2)	250 (49.8)	50 (10)	0.99 (0.85-1.16)	0.46 (0.34-0.61)
Atlantic provinces[d]	251 (5.6)	105 (41.8)	121 (48.2)	25 (10)	1.03 (0.84-1.27)	0.47 (0.31-0.70)
Household income[e] (CAD)						
<$50,000	1030 (22.9)	341 (33.1)	532 (51.7)	157 (15.2)	Ref	Ref
$50,000-$99,999	1353 (30.1)	489 (36.1)	644 (47.6)	220 (16.3)	1.10 (0.96-1.27)	1.12 (0.91-1.37)
$100,000-$199,999	1300 (28.9)	532 (40.9)	559 (43)	209 (16.1)	1.25 (1.09-1.43)	1.19 (0.97-1.47)
≥$200,000	229 (5.1)	100 (43.7)	87 (38)	42 (18.3)	1.37 (1.10-1.71)	1.43 (1.02-2.01)
Rather not say	586 (13)	190 (32.4)	277 (47.3)	119 (20.3)	1.04 (0.87-1.24)	1.32 (1.04-1.67)
Highest level of education						
High school graduate or less	897 (19.9)	262 (29.2)	433 (48.3)	202 (22.5)	Ref	Ref
Some college or trade school	840 (18.7)	240 (28.6)	421 (50.1)	179 (21.3)	0.96 (0.81-1.15)	0.94 (0.77-1.15)
College or trade school	996 (22.1)	304 (30.5)	491 (49.3)	201 (20.2)	1.01 (0.86-1.20)	0.91 (0.75-1.11)
Some university	454 (10.1)	190 (41.8)	197 (43.4)	67 (14.8)	1.30 (1.08-1.57)	0.80 (0.61-1.05)
University degree	1311 (29.2)	656 (50)	557 (42.5)	98 (7.5)	1.43 (1.24-1.66)	0.47 (0.37-0.60)
Ethnicity						
Caucasian	3862 (85.9)	1455 (37.7)	1765 (45.7)	642 (16.6)	Ref	Ref
Indigenous/First Nations/Metis/Inuit	228 (5.1)	71 (31.1)	107 (46.9)	50 (21.9)	0.88 (0.70-1.12)	1.19 (0.90-1.59)
Asian	193 (4.3)	67 (34.7)	115 (59.6)	11 (5.7)	0.81 (0.64-1.04)	0.33 (0.18-0.59)
Caribbean/African/South American	70 (1.5)	16 (22.9)	43 (61.4)	11 (15.7)	0.60 (0.37-0.98)	0.76 (0.42-1.39)
Other	145 (3.2)	43 (29.6)	69 (47.6)	33 (22.8)	0.85 (0.63-1.15)	1.21 (0.85-1.72)
Political leaning						
Liberal	1841 (40.9)	971 (52.7)	821 (44.6)	49 (2.7)	1.48 (1.30-1.68)	0.29 (0.21-0.40)
Moderate/middle of the road	1029 (22.9)	327 (31.8)	565 (54.9)	137 (13.3)	Ref	Ref
Conservative	1628 (36.2)	354 (21.7)	713 (43.8)	561 (34.5)	0.91 (0.78-1.05)	2.26 (1.87-2.72)

[a]Determined using negative binomial regression.

[b]N/A: not applicable.

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[c]Ref: reference value.

[d]Prairie provinces include Saskatchewan and Manitoba; Atlantic provinces include Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador.

[e]CAD $1=US $0.75.

Compared with participants in Cluster 2 (the vaccine waiting and NPI-accepting cluster), participants in Cluster 3 (the vaccine and NPI nonaccepting cluster) were more likely to be male (PR 1.69, 95% CI 1.46-1.96), 35-54 years of age (PR 1.22, 95% CI 1.02-1.45), have a household income of CAD $200,000 (USD $150,200; CAD $1=US $0.75) or more (PR 1.32, 95% CI 1.04-1.67), and report a conservative political leaning (PR 2.26, 95% CI 1.87-2.72). Participants in Cluster 1 (the vaccine and NPI-accepting cluster) were more likely to be Liberal leaning (PR 1.48, 95% CI 1.30-1.68), have some university education (PR 1.30, 95% CI 1.08-1.57), or a university degree (PR 1.43, 95% CI 1.24-1.66), have an annual household income of CAD $100,000-$199,999 (PR 1.25, 95% CI 1.09-1.43) or CAD $200,000 or more (PR 1.37, 95% CI 1.10-1.71), and male (PR 1.12, 95% CI 1.02-1.24) compared with participants in Cluster 2 (the vaccine-waiting and NPI-accepting cluster).

Discussion

Principal Findings

In this national cross-sectional survey completed in the fall of 2020 prior to the approval of COVID-19 vaccines in Canada, we found that 63.9% (2876/4498) of the participants reported COVID-19 vaccine hesitancy, ranging from delaying vaccine administration when offered to not planning to take a vaccine. Vaccine hesitancy was associated with several sociodemographic factors including (1) younger age (18-39 years), (2) lower education, and (3) non-Liberal political leaning. Participants who reported vaccine hesitancy had higher prevalence of reporting being concerned about vaccine side effects, did not believe that a COVID-19 vaccine would end the pandemic or that the benefits of a COVID-19 vaccine outweighed the risks, and had lower prevalence of reporting being influenced by peers or health care professionals. We identified 3 distinct participant clusters: (1) participants who reported adherence to NPIs and did not have vaccine hesitancy, (2) individuals who reported adherence to NPIs but did have vaccine hesitancy, and (3) individuals who reported less adherence to NPIs and vaccine hesitancy.

The 3 distinct clusters of vaccine acceptance can inform targeted vaccination campaign messaging in a novel way by directing messages to address cluster-specific concerns with respect to vaccine hesitancy. The majority of the participants in Cluster 2 (the vaccine waiting and NPI-accepting cluster) planned to delay taking a vaccine when offered, while the majority in Cluster 3 (the vaccine and NPI nonaccepting cluster) did not intend to take a vaccine at all. Messaging related to preventing COVID among friends and family, highlighting the benefits, and ensuring health care workers are knowledgeable and supported in their vaccine counselling may be more helpful for those in Cluster 2 relative to those in Cluster 3. Participants in Cluster 3 were more likely to be male, 35-54 years of age, have an annual household income of CAD $200,000 or more, report Conservative political leaning, and live in Alberta compared

with participants in Cluster 2. The characteristics of Cluster 3 are consistent with current trends in vaccine uptake in that less uptake has been seen among Albertans, males, and individuals aged 18 to 59 years as of October 23, 2021 [17]. Based on our findings, Cluster 3 appears quite challenging to target messaging toward and further qualitative research is needed to determine how best to target this subgroup of vaccine-hesitant individuals to increase vaccine uptake.

As of October 27, 2021, more than 1,700,000 Canadians have been infected with COVID-19 and more than 28,000 Canadians have died [1]. Reported intention to get vaccinated has been variable [18-23], and as supply of vaccine outweighs demand among eligible individuals within Canada [24], there are growing concerns about vaccine hesitancy with respect to COVID-19 vaccines. The Government of Canada reports that as of October 23, 2021, 29,613,930 (77%) individuals 12 years of age or older had received 1 dose of COVID-19 vaccine and 28,086,337 (73%) were fully vaccinated [17]. Vaccine hesitancy among Canadians has decreased since the time our survey was administered, which is likely multifactorial. A recent qualitative study in the United States found that vaccine uptake among individuals who were initially vaccine hesitant is related to 3 factors: (1) intrinsic factors (eg, protecting oneself from COVID-19), (2) extrinsic factors (eg, protecting family or friends), and (3) structural factors (eg, vaccine mandates) [25].

While there has been a decrease in vaccine hesitancy over time, many of the underlying predictors of hesitancy have remained stable over time [5,7,10,26-29]. Many studies [10,19-21,30,31] have reported that female sex at birth was associated with COVID-19 vaccine hesitancy [18]. We found that lower education level was associated with COVID-19 vaccine hesitancy. Both low [10,19,20,30] and high [32] education level have been associated with COVID-19 vaccine hesitancy, while lower household income has more consistently been associated with vaccine hesitancy [10,18,30]. The conflicting associations between these sociodemographic factors and vaccine hesitancy suggest that these associations may be region-specific on a global scale as was identified by Lazarus et al [32] or may be time-dependent, as these cross-sectional surveys were completed at different points of time in the COVID-19 pandemic.

We did not find an association between ethnicity and COVID-19 vaccine hesitancy, although an association has been reported in several other studies [19,29,30,33]. In a qualitative study, Momplaisir et al [33] found several themes that contributed to vaccine hesitancy among individuals who identified as Black, including mistrust in the medical community, racial injustice, and COVID-19–specific concerns, including the speed of development and concerns about potential side effects. This highlights that COVID-19 vaccine hesitancy is complex with many contributing factors, all of which need to be addressed to effectively combat vaccine hesitancy and encourage individuals to take a COVID-19 vaccine when offered. Although population segments that are more likely to be vaccine hesitant can be

identified and messages can be tailored to those population segments, the content and delivery of the messaging needs to consider the complex interaction of all the domains of the SAGE working group vaccine hesitancy determinant framework (ie, contextual influences, vaccine characteristics, and individual/social group influences) [8]. Messaging needs to be designed in collaboration with these population segments through partnership-based community-embedded work to address the complex and unique circumstances contributing to vaccine hesitancy.

The influences of COVID-19 vaccine characteristics and administration of COVID-19 vaccines on vaccine hesitancy are unique compared to annual influenza campaigns or childhood immunization schedules. In response to the COVID-19 pandemic, the scientific community has come together to develop safe and effective vaccines [2]. At the time of survey administration, prior to the regulatory approval of COVID-19 vaccines in Canada, we found that almost half of the respondents were concerned that these vaccines had been developed too quickly and the majority were concerned about the short- and long-term vaccine side effects. These concerns about COVID-19 vaccines have been reported in other studies [19,31,33], and we found that they were associated with vaccine hesitancy. We also found that COVID-19 vaccine hesitancy was associated with lower concern about the consequences of becoming infected with COVID-19 or concern about family or friends becoming infected. Vaccination campaigns need to address these COVID-19–specific factors in their messaging.

Trust in government has been identified as a factor associated with acceptance of a COVID-19 vaccine [18]. Consistent with this, we found that vaccine hesitancy was associated with a lack of trust in government and health care institutions. When developing messaging to combat COVID-19 vaccine hesitancy, it is important to consider the importance of trust, which has been highlighted in previous pandemics, including the H1N1 pandemic [34]. To improve trust and consistency of messaging,

supportive programs need to be available for health care workers to build knowledge and confidence in their messaging. The trusted sources of COVID-19 information should also be considered when designing targeted vaccination campaigns.

Limitations

The major limitation of this cross-sectional study was that it represents one snapshot in time in the fall of 2020 prior to the approval of COVID-19 vaccines in Canada and as the country was entering the second wave of the pandemic; therefore, the responses provided by participants at that time have evolved. The survey recruited participants from an existing voluntary nationwide panel designed to be representative of the Canadian population; however, by using a panel, there will be a component of selection bias as participants have volunteered to partake in research surveys through an electronic platform, which may lead to increased selection of individuals with higher socioeconomic status or education level leading to an underestimation of vaccine hesitancy. We included all provinces and territories in our sampling strata; however, we did oversample Alberta, which could lead to bias in the results and make these findings less generalizable to the Canadian population. To minimize this bias, province of residence was included in all adjusted analyses. Response bias should also be considered as individuals who chose to respond to the web-based survey may differ systematically from those who chose not to respond.

Conclusion

COVID-19 vaccines are an important tool in the fight against the COVID-19 pandemic; yet, vaccine hesitancy is a concern. We have identified population segments that are associated with vaccine hesitancy (eg, younger age, lower education level) that can be targeted with public health messaging as well as attitudes toward COVID-19, COVID-19 vaccines, and NPIs that can inform messaging content. Effectively addressing vaccine hesitancy is important to increase vaccine uptake.

Authors' Contributions

JLB, RL, OA, BS, HS, MM, MMF, TT, BJM, DAM, JH, and RJO were all involved in study design. RL, JLB, BS, HS, MM, MMF, TT, BJM, DAM, JH, and RJO developed the survey. JLB, OA, BS, and RJO performed the analysis. JLB, OA, and RL wrote the initial draft of the paper. All authors reviewed the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Survey questions.
[DOCX File , 987 KB - publichealth_v7i12e30424_app1.docx]

Multimedia Appendix 2
Cluster analysis.
[DOCX File , 24 KB - publichealth_v7i12e30424_app2.docx]

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Abbreviations

aPR: adjusted prevalence ratio
NPI: nonpharmacologic intervention
PR: prevalence ratio
SAGE: Strategic Advisory Group of Experts
STROBE: Strengthening Reporting of Observational Studies in Epidemiology

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Original Paper

Presenting Characteristics, Comorbidities, and Outcomes Among Patients With COVID-19 Hospitalized in Pakistan: Retrospective Observational Study

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Abstract

Background: COVID-19 became a pandemic rapidly after its emergence in December 2019. It belongs to the coronavirus family of viruses, which have struck a few times before in history. Data based on previous research regarding etiology and epidemiology of other viruses from this family helped played a vital role in formulating prevention and precaution strategies during the initial stages of this pandemic. Data related to COVID-19 in Pakistan were not initially documented on a large scale. In addition, due to a weak health care system and low economic conditions, Pakistan's population, in general, already suffers from many comorbidities, which can severely affect the outcome of patients infected with COVID-19.

Objective: COVID-19 infections are coupled with a manifestation of various notable outcomes that can be documented and characterized clinically. The aim of this study was to examine these clinical manifestations, which can serve as indicators for early detection as well as severity prognosis for COVID-19 infections, especially in high-risk groups.

Methods: A retrospective observational study involving abstraction of demographic features, presenting symptoms, and adverse clinical outcomes for 1812 patients with COVID-19 was conducted. Patients were admitted to the four major hospitals in the Rawalpindi-Islamabad region of Pakistan, and the study was conducted from February to August 2020. Multivariate regression analysis was carried out to identify significant indicators of COVID-19 severity, intensive care unit (ICU) admission, ventilator aid, and mortality. The study not only relates COVID-19 infection with comorbidities, but also examines other related factors, such as age and gender.

Results: This study identified fever (1592/1812, 87.9%), cough (1433/1812, 79.1%), and shortness of breath (998/1812, 55.1%) at the time of hospital admission as the most prevalent symptoms for patients with COVID-19. These symptoms were common

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but not conclusive of the outcome of infection. Out of 1812 patients, 24.4% (n=443) required ICU admission and 21.5% (n=390) required ventilator aid at some point of disease progression during their stay at the hospital; 25.9% (n=469) of the patients died. Further analysis revealed the relationship of the presented symptoms and comorbidities with the progression of disease severity in these patients. Older adult patients with comorbidities, such as hypertension, diabetes, chronic kidney disease, and asthma, were significantly affected in higher proportions, resulting in requirement of ICU admission and ventilator aid in some cases and, in many cases, even mortality.

Conclusions: Older adult patients with comorbidities, such as hypertension, diabetes, asthma, chronic obstructive pulmonary disorder, and chronic kidney disease, are at increased risk of developing severe COVID-19 infections, with an increased likelihood of adverse clinical outcomes.

Introduction

COVID-19 is a worldwide pandemic that has proliferated across the globe since its spread from Wuhan, China, in December 2019 [1-3]. Since then, full clinical presentations of this viral infection are still not fully understood, as being an RNA virus with many variants, its clinical manifestations are always different [4]. Nevertheless, cough, fever, dyspnea, body ache, fatigue, and pneumonia are some of the most presented symptoms; however, due to its contagious nature and a wide array of asymptomatic, mild to severe, and, in some cases, life-threatening clinical manifestations [5], as well as a dearth of a standardized effective treatment strategies [6], the COVID-19 case count is escalating with time. According to the World Health Organization (WHO), Pakistan hastily entered the race of having the maximum COVID-19 cases per day and could be classified as having Level 4 COVID-19 transmission, where community transmission of the virus is the main reason for increasing COVID-19 cases [7]. Despite its proximity with China, India, and Iran, the total number of confirmed cases in Pakistan has never risen above 7000 per day, and the death toll per day has also been under control [8].

As of December 11, 2020, the total number of COVID-19 cases worldwide was 71,070,927, with 49,384,495 recoveries; 1,594,772 deaths; and 20,091,660 active cases awaiting outcomes [9]. In Pakistan as of December 11, 2020, the total number of COVID-19 cases was 432,327,149, with 379,092 recoveries; 8653 deaths; and 44,582 active cases awaiting outcomes [8]. The twin cities Rawalpindi and Islamabad in Pakistan have a combined population of around 3 million people and were a hot spot during various waves of COVID-19 [8]. A few small-scale studies have been reported from Pakistan, but there is a dire need to regularly gather, document, and analyze epidemiological data from patients with COVID-19 in Pakistan in a systematic way; this is needed in order to identify high-risk groups and determine risk factors associated with poor disease prognoses, in relation with resultant morbidity or mortality [10-14].

There is a lack of standardized treatment regimens because of varying symptoms associated with COVID-19 infections. The treatment so far has been symptomatic or supportive therapy instead of fixed regimens. A retrospective cohort study on hospitalized patients in China revealed that more men (median age 56 years) than women required intensive care unit (ICU) facilities and had a 28% mortality rate [15]. Nevertheless, health care conditions, prevalence of comorbidities, and lifestyle in Pakistan are quite different than in other countries, in general. We hereby performed a retrospective analysis study aimed at describing the demographic and clinical characteristics and subsequent clinical outcomes that are associated with COVID-19 infections; our cohort included 1812 cases confirmed by real-time reverse transcription–polymerase chain reaction (rRT-PCR) and that were admitted to the four major hospitals in the Rawalpindi-Islamabad region of Pakistan from February to August 2020. The objective was to identify the clinical outcomes and determine the impact of various factors, such as age, gender, and number and types of underlying comorbidities in patients with COVID-19, that can resultantly contribute to adverse clinical outcomes, including COVID-19 severity, requirement of ICU admission, ventilator aid, and mortality.

We analyzed the characteristics and outcomes of patients; these were correlated with the number and types of comorbidities as indicators of COVID-19 severity and prognostic values in pandemic viral infectious diseases, such as COVID-19. More studies are required to assess the clinical manifestations associated with COVID-19 infections, as well as the time and duration of each symptom after viral invasion, in order to provide concrete data about the course of action needed to counter or avoid symptoms by taking necessary prophylactic steps, especially among high-risk patients.

Methods

This retrospective study was conducted using clinical data acquired from 1812 patients with confirmed COVID-19 who were admitted to four major tertiary care hospitals in Islamabad-Rawalpindi from February to August 2020. The Islamabad-based hospitals were Pakistan Air Force Hospital and Pakistan Institute of Medical Sciences Hospital; the Rawalpindi-based hospitals were Holy Family Hospital and Benazir Bhutto Shaheed Hospital. The study was approved by the ethics review board of Rawalpindi Medical University before data collection, and the data were collected with approval from the National Institute of Health, Pakistan, by HA and SA. In addition to this, the data were systematically organized and recorded using a standardized data collection form specifically designed for the study.

Diagnosis of COVID-19 was confirmed using a polymerase chain reaction (PCR) test on nasal and oropharyngeal swab samples taken at the time of admission to the hospital. A detailed medical history was collected for each patient, including age, gender, exposure history, and clinical manifestations of COVID-19, including fever, cough, and respiratory symptoms. A total of 12 comorbidities were each marked as absent or present and these were categorized into four groups: (1) absence of comorbidities, (2) presence of one comorbidity, (3) presence of two comorbidities, and (4) presence of more than two comorbidities. Communicable comorbidities included hepatitis C (Hep C) and tuberculosis (TB). Noncommunicable disease comorbidities included hypertension (HT), diabetes mellitus (DM), cardiovascular diseases (CVDs), asthma, chronic kidney disease (CKD), nervous system disorders (NSDs), chronic obstructive pulmonary disorder (COPD), cancer, allergies, and anemia. A number of other chronic and acute conditions, such as rheumatoid arthritis, typhoid, stomach ulcers, hypothyroidism, and musculoskeletal injuries, were also reported and were grouped together as a 13th category termed "others."

The study was performed in line with the Declaration of Helsinki. Patients with COVID-19 who had immunological diseases or missing data were excluded from the analysis to avoid any confounding factors affecting the inflammatory markers assessed in this study.

COVID-19 severity was classified into two groups based on symptoms of patients within the first week of COVID-19 infection: (1) mild to moderate, including patients with fever, cough, and oxygen saturation of 90% or greater on room air along with other symptoms consistent with COVID-19, and (2) severe to critical, including patients with dyspnea (ie, oxygen saturation of less than 90% on room air), pneumonia, and varying degrees of respiratory distress (ie, respiratory rate >30 breaths/min), along with other symptoms. Clinical outcomes studied were COVID-19 severity, requirement of ICU admission, requirement of ventilator, and mortality. This classification was based on WHO guidelines regarding the clinical management of patients with COVID-19 [5].

Chest radiographs and computed tomography scans, including presence or absence of ground-glass or crazy-paving appearance, were noted. Moreover, hematological and biochemical parameters, including blood complete picture, serum ferritin, liver function test, creatinine, and a few others, were also recorded to assist in categorizing the patients. PCR test results of the patients and clinical outcomes, such as admission to ICU, requirement for noninvasive or invasive ventilation provided at the hospital at some stage of disease progression, and mortality, were also recorded.

Statistical analysis was conducted using SPSS Statistics for Windows (version 24; IBM Corp). Categorical variables were described using frequencies and percentages. We used t tests to compare two sets of quantitative data. Chi-square tests and Fisher exact tests were used to compare percentages of qualitative variables, where appropriate. Multivariate logistic regression analyses were carried out to determine the indicators of COVID-19 severity and mortality. P values of <.05 were considered statistically significant.

Results

This retrospective study included a total of 1812 patients; 69.2% (n=1253) of the patients were male. Patients included in the study ranged in age from 1 to 79 years, with a mean age of 47.32 years. The percentage of patients in the severe to critical group increased with age: 9.8% (31/315) were less than 30 years of age, 59.8% (177/296) were 60 to 69 years of age, and 74.5% (155/208) were 70 years of age or older. Nevertheless, of the 1812 patients with COVID-19 who were admitted to the one of the four hospitals, upon admission, 1153 (63.6%) fell into the category of mild to moderate COVID-19 infection, whereas 659 (36.4%) patients fell into the severe to critical category. Of these 659 patients, some went on to require admission to ICU (n=443) or ventilator support (n=390) during their stay at the hospital, some recovered and were discharged, and some passed away (n=469). Interestingly, we observed equivalent prevalence of male and female patients in the mild to moderate and the severe to critical categories of patients with COVID-19.

In addition to this, regarding the frequency of comorbidities among 1812 patients, 884 patients (48.8%) had none, 364 patients (20.1%) had one, 335 patients (18.5%) had two, and 229 patients (12.6%) had more than two. The most prevalent comorbidity was HT (n=625, 34.5%), followed by DM (n=532, 29.4%), CVDs (n=243, 13.4%), asthma (n=93, 5.1%), CKD (n=93, 5.1%), Hep C (n=84, 4.6%), TB (n=35, 1.9%), NSDs (n=30, 1.7%), COPD (n=18, 1.0%), cancer (n=13, 0.7%), allergies (n=13, 0.7%), and anemia (n=12, 0.7%) (Table 1).

Moreover, the prevalence of comorbidity stayed higher than 60% for all types in the severe to critical COVID-19 infection category. The prevalence was significant for all types of comorbidities included in this study, except for allergies. Surprisingly, only 111 patients out of 884 (12.6%) with no comorbidities were admitted to hospital or moved into the severe to critical category; this increased to 48.4% (176/364) for patients with a single comorbidity, 60.9% (204/335) for patients with two comorbidities, and 72.5% (166/229) for patients with more than two comorbidities; these results were significant. Table 1 presents the complete picture of COVID-19 severity in patients with respect to age, gender, and the number and types of comorbidities.

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Table 1. Basic demographic characteristics and COVID-19 severity in hospitalized patients.

Variables	Total cases (N=1812), n (%)[a]	COVID-19 severity, n (%)[b]		P value
		Mild to moderate	Severe to critical	
Cases (N=1812)	1812 (100)	1153 (63.6)	659 (36.4)	N/A[c]
Age (years)				
<30	315 (17.4)	284 (30.2)	31 (9.8)	<.001[d]
30-49	653 (36.0)	510 (78.1)	143 (21.9)	
50-59	340 (18.8)	187 (55.0)	153 (45.0)	
60-69	296 (16.3)	119 (40.2)	177 (59.8)	
≥70	208 (11.5)	53 (25.5)	155 (74.5)	
Gender				
Male	1253 (69.2)	801 (63.9)	452 (36.0)	.70
Female	559 (30.8)	352 (63.0)	207 (37.0)	
Number of comorbidities				
None	884 (48.8)	773 (87.4)	111 (12.6)	<.001
1	364 (20.1)	186 (51.1)	176 (48.4)	
2	335 (18.5)	131 (39.1)	204 (60.9)	
>2	229 (12.6)	63 (27.5)	166 (72.5)	
Type of comorbidity				
Hypertension	625 (34.5)	248 (39.7)	377 (60.3)	<.001
Diabetes mellitus	532 (29.4)	201 (37.8)	331 (62.2)	<.001
Cardiovascular diseases	243 (13.4)	80 (32.9)	163 (67.1)	<.001
Asthma	93 (5.1)	29 (31.2)	64 (68.8)	<.001
Chronic kidney disease	93 (5.1)	32 (34.4)	61 (65.6)	<.001
Hepatitis C	84 (4.6)	33 (39.3)	51 (60.7)	<.001
Tuberculosis	35 (1.9)	11 (31.4)	24 (68.6)	<.001
Nervous system disorders	30 (1.7)	7 (23.3)	23 (76.7)	<.001
Chronic obstructive pulmonary disorder	18 (1.0)	2 (11.1)	16 (88.9)	<.001
Cancer	13 (0.7)	4 (30.8)	9 (69.2)	.01
Allergies	13 (0.7)	5 (38.5)	8 (61.5)	.06
Anemia	12 (0.7)	2 (16.7)	10 (83.3)	.001
Others	84 (4.6)	22 (26.2)	62 (73.8)	<.001

[a]Percentages in this column are based on the total number of patients (N=1812).

[b]Percentages in these columns are based on the number of patients reported in the respective rows in the "Total cases" column.

[c]N/A: not applicable; a P value was not calculated for this item.

[d]The P value for a group of variables is reported in the top row of that group.

The frequency of clinical manifestations in the form of fever, cough, dyspnea, anosmia, ageusia, sore throat, and others are shown in Table 2; fever was the most common symptom among 1812 patients (n=1592, 87.9%), followed by cough (n=1433, 79.1%) and dyspnea (n=998, 55.1%). Loss of taste and smell (n=809, 44.6%), sore throat (n=499, 27.5%), and body aches (n=490, 27.0%) were comparatively less prevalent symptoms.

Indicators of severity varied among 1812 patients included in this study. A total of 443 (24.4%) patients required ICU admission, and 390 (21.5%) required ventilator aid at some point of disease progression during their stay at the hospital. Nevertheless, 469 (25.9%) patients died with or without ICU admission or ventilator aid.

A significant increase in ICU admissions, ventilator aid events, and mortality was observed with an increase in age and number of comorbidities. No significant differences in ICU admission, ventilator aid events, and mortality were observed between males and females. A significant increase in ICU admissions, ventilator aid events, and mortality was observed with the presence of any type of studied comorbidity, except for allergies.

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Patients with no known comorbidities had minimal requirements for ICU admission (47/884, 5.3%), ventilator aid events (34/884, 3.8%), and mortality (50/884, 5.7%); these proportions were approximately 10 times higher with patients who had two or more comorbidities. Delving into each type of comorbidity revealed that approximately half of the patients with any type of comorbidity required ICU admission with or without ventilator aid, and a significant number of them expired.

Table 2. Prevalence of reported signs and symptoms in patients with COVID-19 at the time of hospital admission.

Signs and symptoms	Patients experiencing these signs and symptoms (N=1812), n (%)
Chest pain	45 (2.5)
Headache	81 (4.5)
Nausea or vomiting	115 (6.3)
Diarrhea	130 (7.2)
Flu	150 (8.3)
Body aches, fatigue, or malaise	490 (27.0)
Sore throat	499 (27.5)
Anosmia or ageusia	809 (44.6)
Dyspnea	998 (55.1)
Cough	1433 (79.1)
Fever	1592 (87.9)

Table 3 shows the clinical outcomes of the hospitalized patients with COVID-19 with respect to age, gender, and number and types of comorbidities.

Multivariate regression analysis was carried out to identify significant indicators of COVID-19 severity, ICU admission, ventilator aid, and mortality. Factors such as age, gender, and number and types of comorbidities were included, except for anemia, which was excluded due to small sample size.

Our results indicate that old age was a significant indicator of COVID-19 severity, ICU admission, ventilator aid, and mortality. Although our data reported a greater number of male patients, male gender had no significant relationship with COVID-19 severity, ICU admission, ventilator aid, and mortality.

In addition, the results of this study revealed that an increase in the number of comorbidities was a significant predictor of COVID-19 severity, ICU admission, ventilator aid, and mortality. HT, DM, COPD, CKD, and asthma were significant predictors COVID-19 severity, ICU admission, ventilator aid, and mortality. NSDs, on the other hand, were a significant predictor of COVID-19 severity, ICU admission, and mortality, but not ventilator aid. TB was a significant predictor of COVID-19 severity and ICU admission, but not ventilator aid and mortality. In addition, Hep C and cancer were both significant predictors of ventilator aid and mortality, whereas CVDs were only a significant predictor of mortality. Presence of allergies was not a significant predictor of any of the study outcomes.

Table 4 shows the multivariate analysis of factors associated with COVID-19 severity, ICU admission, ventilator aid, and mortality.

Table 3. Clinical outcomes of patients with COVID-19.

Variables	Total cases (N=1812), n (%)[a]	ICU[b] admission, n (%)[c]	P value	Ventilator aid, n (%)[c]	P value	Mortality, n (%)[c]	P value
Cases (N=1812)	1812 (100)	443 (24.4)	N/A[d]	390 (21.5)	N/A	469 (25.9)	N/A
Age (years)							
<30	315 (17.4)	22 (7.0)	<.001	17 (5.4)	<.001	19 (6.0)	<.001
30-49	653 (36.0)	84 (12.9)	<.001	75 (11.5)	<.001	88 (13.5)	<.001
50-59	340 (18.8)	101 (29.7)	<.001	90 (26.5)	<.001	100 (29.4)	<.001
60-69	296 (16.3)	126 (42.6)	<.001	109 (36.8)	<.001	135 (45.6)	<.001
≥70	208 (11.5)	110 (52.9)	<.001	99 (47.6)	<.001	127 (61.1)	<.001
Gender							
Male	1253 (69.2)	297 (23.7)	.27[e]	263 (21.0)	.41	313 (25.0)	.19
Female	559 (30.8)	146 (26.1)		127 (22.7)		156 (27.9)	
Number of comorbidities							
None	884 (48.8)	47 (5.3)	<.001	34 (3.8)	<.001	50 (5.7)	<.001
1	364 (20.1)	124 (34.4)	<.001	110 (30.2)	<.001	126 (34.6)	<.001
2	335 (18.5)	141 (42.1)	<.001	128 (38.2)	<.001	147 (43.9)	<.001
>2	229 (12.6)	131 (57.2)	<.001	118 (51.5)	<.001	146 (63.8)	<.001
Type of comorbidity							
Hypertension	625 (34.5)	274 (43.8)	<.001	245 (39.2)	<.001	294 (47.0)	<.001
Diabetes mellitus	532 (29.4)	235 (44.2)	<.001	207 (38.9)	<.001	245 (46.1)	<.001
Cardiovascular diseases	243 (13.4)	123 (50.6)	<.001	112 (46.1)	<.001	135 (55.6)	<.001
Asthma	93 (5.1)	51 (54.4)	<.001	45 (48.4)	<.001	53 (57.0)	<.001
Chronic kidney disease	93 (5.1)	50 (53.8)	<.001	47 (50.5)	<.001	56 (60.2)	<.001
Hepatitis C	84 (4.6)	37 (44.0)	<.001	32 (38.1)	<.001	44 (52.4)	<.001
Tuberculosis	35 (1.9)	21 (60.0)	<.001	17 (48.6)	<.001	18 (51.4)	<.001
Nervous system disorders	30 (1.7)	19 (63.3)	<.001	16 (53.3)	<.001	21 (70.0)	<.001
Chronic obstructive pulmonary disorder	18 (1.0)	15 (83.3)	<.001	16 (88.9)	<.001	16 (88.9)	<.001
Cancer	13 (0.7)	7 (53.8)	.01	7 (53.8)	.004	9 (69.2)	<.001
Allergies	13 (0.7)	6 (46.2)	.07	6 (46.2)	.03	6 (46.2)	.09
Anemia	12 (0.7)	10 (83.3)	<.001	10 (83.3)	<.001	10 (83.3)	<.001
Others	84 (4.6)	51 (60.7)	<.001	48 (67.1)	<.001	54 (64.3)	<.001

[a]Percentages in this column are based on the total number of patients (N=1812).

[b]ICU: intensive care unit.

[c]Percentages in this column are based on the number of patients reported in the respective rows in the "Total cases" column.

[d]N/A: not applicable; a P value was not calculated for this item.

[e]The P value for a group of variables is reported in the top row of that group.

Table 4. Multivariate analysis of factors associated with COVID-19 severity and clinical outcomes of patients with COVID-19.

Covariates	COVID-19 severity		ICU[a] admission		Ventilator aid		COVID-19 mortality	
	OR[b] (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age (years) (vs <30 years)								
30-49	1.9 (1.2-2.9)	.004	1.4 (0.8-2.4)	.19	1.6 (0.9-2.9)	.09	1.8 (1.0-3.1)	.04
50-59	3.5 (2.2-5.6)	<.001	2.6 (1.5-4.5)	<.001	2.9 (1.7-5.3)	<.001	3.1 (1.8-5.6)	<.001
60-69	5.1 (3.2-8.3)	<.001	3.8 (2.2-6.6)	<.001	3.9 (2.1-7.0)	<.001	5.4 (3.0-9.7)	<.001
≥70	11.0 (6.4-18.7)	<.001	5.9 (3.3-10.4)	<.001	6.3 (3.4-11.6)	<.001	10.7 (5.9-19.5)	<.001
Gender (male vs female)	0.9 (0.7-1.2)	.68	1.1 (0.8-1.4)	.55	1.1 (0.8-1.4)	.71	1.2 (0.9-1.5)	.30
Number of comorbidities (vs no comorbidities)								
1	4.6 (3.4-6.2)	<.001	6.9 (4.7-10.1)	<.001	8.2 (5.3-12.6)	<.001	6.2 (4.3-9.0)	<.001
2	6.8 (4.9-9.5)	<.001	8.8 (5.9-13.1)	<.001	10.8 (7.0-16.7)	<.001	8.2 (5.6-12.0)	<.001
>2	10.8 (7.2-16.0)	<.001	14.9 (9.7-23.0)	<.001	17.4 (10.8-27.8)	<.001	16.9 (11.0-26.1)	<.001
Type of comorbidities (yes vs no)								
Diabetes mellitus	2.3 (1.7-3.0)	<.001	1.8 (1.4-2.4)	<.001	1.7 (1.3-2.2)	<.001	1.6 (1.2-2.2)	<.001
Hypertension	1.9 (1.5-2.5)	<.001	2.0 (1.5-2.7)	<.001	2.0 (1.5-2.7)	<.001	2.0 (1.5-2.7)	<.001
Cardiovascular diseases	1.4 (1.0-2.0)	.08	1.4 (1.0-1.9)	.08	1.4 (1.0-2.0)	.054	1.5 (1.1-2.2)	.02
Chronic kidney disease	2.1 (1.3-3.5)	.005	2.5 (1.5-4.1)	<.001	2.7 (1.6-4.4)	<.001	3.3 (2.0-5.4)	<.001
Asthma	2.4 (1.4-4.0)	.001	2.4 (1.5-4.0)	<.001	2.1 (1.3-3.5)	.003	2.4 (1.5-4.0)	<.001
Tuberculosis	2.6 (1.1-6.2)	.03	3.3 (1.4-7.5)	.005	2.1 (0.9-4.6)	.08	1.6 (0.7-3.8)	.27
Cancer	3.0 (0.7-12.8)	.13	2.7 (0.7-10.1)	.15	3.3 (0.9-12.4)	<.001	6.3 (1.5-26.2)	.01
Nervous system disorders	6.7 (2.6-17.6)	<.001	6.2 (2.7-14.7)	<.001	4.5 (2.0-10.4)	.82	8.5 (3.4-21.1)	<.001
Allergies	1.0 (0.2-4.3)	.96	0.9 (0.2-3.4)	.84	1.2 (0.3-4.5)	.54	0.7 (0.2-2.7)	.58
Hepatitis C	1.4 (0.8-2.4)	.18	1.3 (0.8-2.1)	.39	1.2 (0.7-2.0)	<.001	1.8 (1.1-3.0)	.03
Chronic kidney disease	8.2 (1.7-40.3)	.01	10.2 (2.6-40.3)	.001	21.7 (4.5-104.8)	<.001	17.5 (3.6-86.2)	<.001
Others	2.8 (1.6-5.1)	<.001	2.9 (1.7-4.9)	<.001	3.0 (1.8-5.1)	<.001	3.2 (1.9-5.5)	<.001

[a]ICU: intensive care unit.

[b]OR: odds ratio.

Discussion

Principal Findings

COVID-19 was declared a pandemic at the start of 2020 after emerging in December 2019 in Wuhan, China [3]. All the information related to COVID-19, including its risk factors, severity, mortality, clinical manifestations, and other complications, was not very clear, especially in Pakistan. We aimed to highlight and discuss some dependent and independent factors related to COVID-19 in this study.

In our study, the most prevalent presenting symptoms at the time of hospital admission were fever, cough, and shortness of breath. Anosmia, ageusia, sore throat, body aches, fatigue, and malaise were relatively less common presenting symptoms, whereas diarrhea, nausea, and vomiting were the least prevalent presenting symptoms reported by patients at the time of admission. One or more comorbidities, especially HT and DM, were more prevalent among older adults according to our results. Mild to moderate COVID-19 symptoms were highly prevalent

in younger groups. These findings were in accordance with those of other studies around the world [15-18]. The most prevalent comorbidities were HT, DM, and CVDs, followed by asthma, CKD, Hep C, TB, NSDs, COPD, cancer, allergies, and anemia, among others.

Two of the most significant findings of this study were related to the age and comorbidity of the patients, which can be explained as age-dependent weakened functionality of cell-mediated immunity with a decline in humoral immune support [15]. On the other hand, SARS-CoV-2 enters the host cell via attachment of its structural spike protein to the membrane-bound angiotensin-converting enzyme 2 (ACE-2) receptor of the host [19]. This attachment results in ACE-2 degradation and affects its role in the renin-angiotensin-aldosterone system (RAAS), resulting in abnormalities in maintaining blood pressure and homeostasis of electrolytes in the human body [20]. ACE-2 also catalyzes the conversion of angiotensin II into angiotensin (1-7), which regulates RAAS in the vasoconstriction of blood vessels, increase of sodium reabsorption in kidneys, and stimulation of

the hypothalamus, adrenal cortex, and sympathetic nervous system, to activate thirst centers in the brain and increase secretion of antidiuretic hormone, renin, and aldosterone, respectively [21,22]. Pathophysiological changes in RAAS due to distressed ACE-2 levels in patients with comorbid COVID-19 tend to show undesired outcomes, such as high levels of angiotensin II, which leads to angiogenesis, vascular aging, atherosclerosis, inflammation, and fibrosis, leading to diseases like hypertension, renal failure, and cardiac fibrosis [20]. In addition, angiotensin II also interferes with the anti-inflammatory action of insulin, which highlights its deleterious effect in patients with diabetes [23].

Moreover, following cell entry of SARS-CoV-2, a cascade of events leading to replication of viral nucleic acid and release of mature virus particles from the cell ensues, resulting in stimulation of the host's humoral and cellular immunity. Uncontrolled, systemic release of proinflammatory cytokines and chemokines as a part of the host immune response to SARS-CoV-2 infection results in a highly toxic "cytokine storm," or cytokine release syndrome, which is another hallmark of COVID-19 [19]. As a result, severe forms of COVID-19 can be described by three main phases: early infection, involvement of lungs, and systemic inflammation [24]. It can be concluded that factors that contribute to downregulation of ACE-2, dysregulation of RAAS, impairment of B- and T-cell immunity, and development of cytokine release syndrome also contribute to COVID-19 severity, ICU admission, ventilator aid, and mortality [22,24-27].

Similarly, several other meta-analyses reported that HT, DM, CVDs, and CKD were independent risk factors in patients with COVID-19 and indicators of poor prognosis [4,17,28,29]. A few small-scale studies from Pakistan investigating COVID-19 severity and mortality also reported similar trends [10-14]. Moreover, our findings are also in line with a few initial epidemiological reports from Wuhan, China, as well as more recent studies investigating the impact of comorbidities on patients with COVID-19 from China, the United States, the United Kingdom, Egypt, Spain, and Italy [17,18,30-36].

Multivariate analysis of results revealed that increased age of patients and the number of comorbidities were significantly associated with increased odds of COVID-19 severity, ICU admission, ventilator aid, and mortality. This establishes the fact that older patients with underlying conditions are not only at a higher risk of developing infection, but may also be at risk of severe progression that requires ventilator aid, which may result in death. No significant differences were found between males and females with respect to the odds of COVID-19 severity, ICU admission, ventilator aid, and mortality. Although HT and DM were the most prevalent among all comorbidities studied, with proportions of 34.5% and 29.4%, respectively, the mortality rates for all comorbidities were significantly higher, and were higher still among patients with two or more comorbidities, with an odds ratio (OR) of 16.9. Nevertheless, all comorbidities examined in this study had relatively higher ORs with respect to ICU admission, ventilator aid, and mortality, emphasizing the importance of considering these factors during COVID-19 treatment protocols.

In short, the COVID-19–associated downregulation of ACE-2, leading to an imbalance of RAAS, combined with an age-dependent impaired immune response and chronic inflammation in older patients, may lead to adverse clinical outcomes. Moreover, the likelihood of the presence of one or multiple chronic underlying comorbidities also increases with age, which may further contribute to a poor prognosis for older patients with COVID-19. Our findings are in line with several studies that have established old age to be a significant predictor of COVID-19 severity, ICU admission, ventilator aid, and mortality [15,37].

Conclusions

The ever-evolving nature of viruses makes them a difficult target for drug design and targeted therapies. In such confusing times, large studies monitoring several factors that might be associated in disease progression and severity are important for clarifying the picture and helping in the development of effective and targeted drugs and vaccines. Moreover, such studies help in the identification of high-risk groups that might have a more severe disease progression and may need a different treatment regime than others. In the current situation, most of the major government directives and guidelines are designed to help curtail the number of COVID-19 cases. These measures are focused on the following: (1) preventive strategies to control the rate of infection, where people are encouraged to take suitable preventative measures, such as improvement of hand hygiene, use of facial masks, and social distancing, and (2) management strategies, where patients who test positive with COVID-19 and report mild to moderate symptoms are directed to follow isolation protocols at home, are directed to monitor their progress by themselves while staying in contact with health care workers remotely via telephone, and are encouraged to report to hospitals only if severe symptoms manifest [38,39]. Studies that help in the identification of indicators for COVID-19 severity and mortality, specific to the Pakistani population, can help in the development of more refined public awareness programs and preventive strategies to encourage people who belong to high-risk groups to take more stringent preventive measures. Moreover, more sophisticated management strategies can be developed to evaluate risk assessment and ensure that high-risk groups can be identified in time and receive appropriate medical care when required, thereby helping to reduce the overall burden of disease on our already-weak health care infrastructure [40].

Conflicts of Interest

None declared.

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Abbreviations

ACE-2: angiotensin-converting enzyme 2
CKD: chronic kidney disease
COPD: chronic obstructive pulmonary disorder
CVD: cardiovascular disease
DM: diabetes mellitus
Hep C: hepatitis C
HT: hypertension

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ICU: intensive care unit
NSD: nervous system disorder
OR: odds ratio
PCR: polymerase chain reaction
RAAS: renin-angiotensin-aldosterone system
rRT-PCR: real-time reverse transcription–polymerase chain reaction
TB: tuberculosis
WHO: World Health Organization

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