JMIR Public Health and Surveillance

Impact Factor (2023): 3.5
Volume 8 (2022), Issue 5 ISSN 2369-2960 Editor in Chief: Travis Sanchez, PhD, MPH

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Original Paper

Korea's Response to COVID-19 According to Set Time Frames, With a Focus on the Network Between the Government and Responding Agencies: Social Network Analysis

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Abstract

Background: In December 2019, COVID-19 was first confirmed in Wuhan, China, and as the respiratory disease spread around the globe, there was a spike in interest worldwide in combating such contagious diseases. When such disasters occur, the central government of South Korea and its affiliated local governments—together with nongovernmental organizations—play a crucial role in crisis management systems.

Objective: The purpose of this paper is to corroborate the characteristics government ministries and domestic and foreign institutions exhibit through their interconnection when the parties are undergoing a disease-related catastrophe such as the COVID-19 pandemic.

Methods: Using the social network analysis technique, the span of the COVID-19 pandemic was segmented into 3 time frames, and the relational characteristics of the COVID-19 contagious disease response department and related agencies at home and abroad were analyzed based on 3 centralities.

Results: Evidence from the second and third time frames indicates that the agents reacting to contagious diseases do not necessarily hold the central position in the network. From this, it can be inferred that it is not only the primary host that plays a pivotal role but the key to a successful response to various disasters also lies in cooperation with the relevant parties.

Conclusions: The incongruency between the findings of this paper and the existing disaster response system gives rise to the corollary that both the essential parties and the adjoining ones need to collaborate for a coordinated crisis response in disaster situations. Furthermore, much significance lies in the fact that this paper explores the various aspects that could surface among the host and relevant parties in a real-life pandemic.

(JMIR Public Health Surveill 2022;8(5):e35958) doi:10.2196/35958

KEYWORDS

COVID-19; government departments' networks; network structure; contagious disease response; social network analysis

Introduction

Background

In December 2019, COVID-19 (a respiratory disease informally known as coronavirus) originated in Wuhan, China [1-3]. Since then, interest in responding to contagious diseases has increased worldwide as it spread across China and around the globe [4].

With the first contraction of the disease on South Korean territory being reported on January, 20, 2020, an exponential growth of cases occurred, with the largest number of infections

traced back to Daegu; a local blockade was seriously considered [5]. In the event of such a disaster, the foremost mission of the standing government is to protect its citizens from harm, which is why the crisis management system operates for the safety of the people. Perry [6] stated that local, state, federal, and private organizations play a central role in a crisis management system. Putting this into the context of South Korea, this translates to the central government, local governments, private organizations, and nongovernmental organizations (NGOs), and in defense of the rapid transmission of COVID-19, the nation has ensured communication with the Infectious Disease Response Center and its affiliated departments for assured support and cooperation.

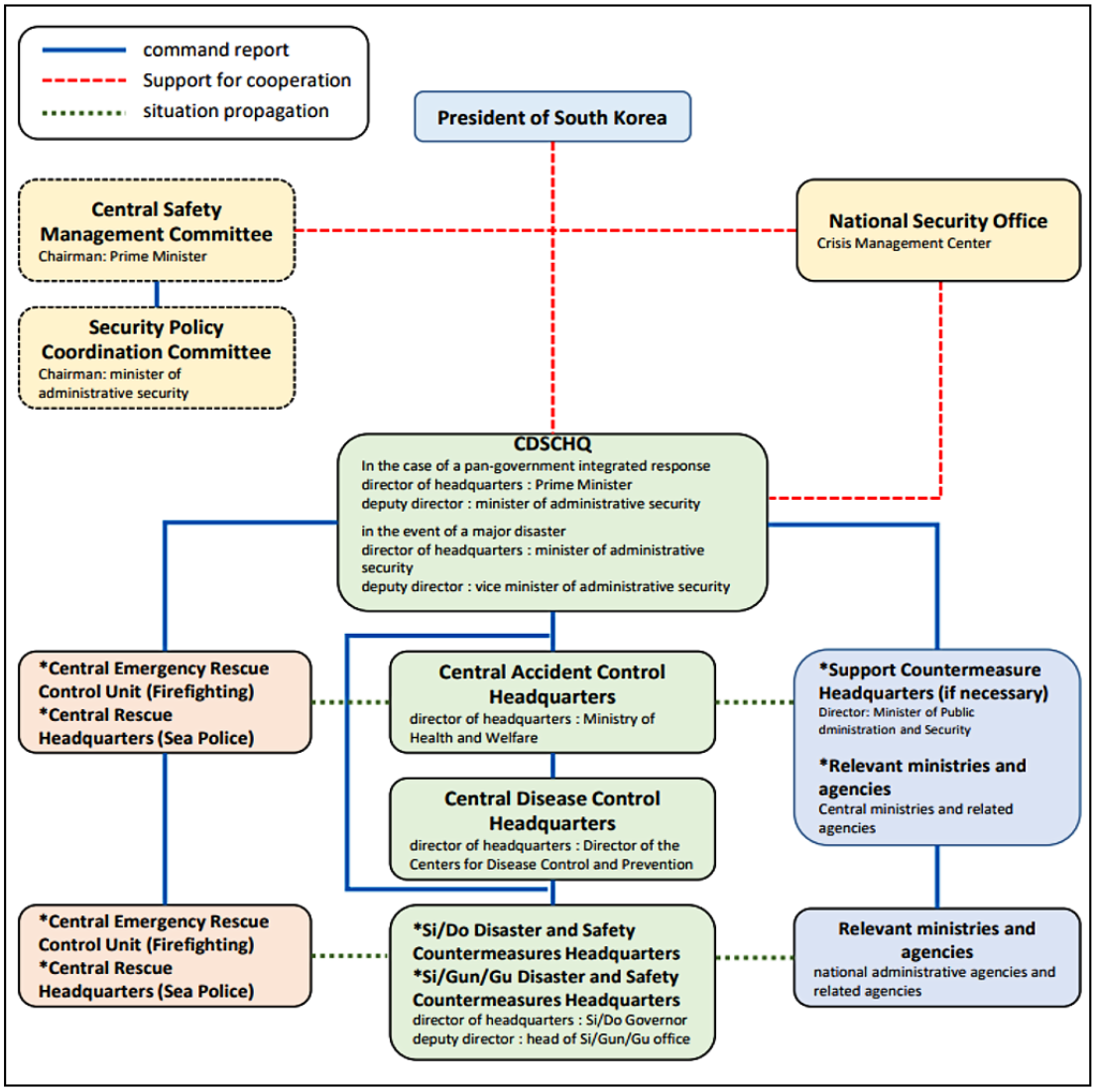
Social network analysis (SNA) has been applied to understand the network characteristics of contagious disease control and the relevant departments in Korea during emergency responses. Disaster-related studies, usually using SNA, have been conducted with social media to analyze the emotions about a particular event [7-9] or analyze certain sections of organizational networks on disaster frameworks [10-12]. The patterns of network formation among every organization related to contagious disease responses were able to be proven, and through this—by identifying the disaster response agencies that play a crucial role in the network structure of response agencies if a substantially sized disaster were to occur—pragmatic policies were provided.

Korea's Disaster Response System for Contagious Diseases

The constitution of South Korea states that the government consists of a president and its executive branches [13]. At the apex of the hierarchy stands the president, from which orders are given to the Prime Minister who supervises and directs the secretaries of the central administrative agencies. The executive branch consists of 18 departments, 5 offices, 4 offices in 2 houses, 7 committees, and the Deputy Prime Minister (who performs specially delegated affairs), which all fall under the Prime Minister. More often than not, the government—equipped with advice from experts in relevant fields—reaches out to disaster management agencies in the event of a large-scale disaster such as COVID-19. In simpler terms, the Central Disaster and Safety Countermeasures Headquarters (CDSCH) and Central Disaster Management Headquarters (CDMH) are operated by Korea's disaster response system on a level that is on par with the central government in the case of a national disaster. Figure 1 shows the contagious disease management and response system entailed in the disaster management standard manual. One should take note that the Ministry of Security and Public Administration directs the CDSCH and the CDMH, while the Ministry of Health and Welfare has a central disease management headquarters under its wing to respond to contagious diseases [5].

The Ministry of Health and Welfare, shown in Figure 1, plays a central role in the infectious disease management and response system. Naturally, the CDMH, which falls under the Ministry of Health and Welfare, was also a subject for this study. See Multimedia Appendix 1 for all the institutions and countries included in this study.

Figure 1. Contagious disease disaster management system. CDSCHQ: Central Disaster and Safety Countermeasures Headquarters; Si/Do: It is an administrative district of the Republic of Korea classified as a metropolitan local government and has a total of 17 'Si' & 'Do'; Si/Gun/Gu: The 'Si' has subordinate administrative districts called 'Gun' and 'Gu,' and the 'Do' has subordinate administrative districts called 'Si' and 'Gu.'.



Methods

Social Network Analysis for COVID-19

Concept of Social Network Theory

A social network consists of a web of interpersonal relationships that can be characterized by interactions and interconnections in social relationships [5,14,15]. The actors may be individuals, but the term also refers to entities such as groups, organizations, and companies [16]. The social network theory can be explained through the duality of structure, which is a concept proposed by the British social scientist, Giddens [17]. He defined structure as a medium of action and simultaneously as a product of reproducing an action—determined by the duality of the structure. In essence, in light of the social network theory, the structure of social networks is formed by the actors, and it affects their behavior.

Social Network Analysis

It can be said that SNA manages the following: deriving the characteristics of a structure or from the endpoint of a period, explaining a system's characteristics from a relationship point of view, and the behavior of the units that constitute a system [18]. The main focus of network analysis is identifying the patterns of interactions between the entities making up the network or from the results [19]. Nodes represent actors (eg, people, organizations, groups, events), while the links represent the relationships among the actors. A connection network composed of nodes and lines can be analyzed by grafting them onto social phenomena—hence, SNA [20].

The main approach in SNA is to establish the centrality of the actor where it can be expressed as a value between 0 and 1: 0 means that it is an isolated node without any connection, while 1 means that it is connected to every other node. In other words, the closer the value is to 1, there is greater involvement of a node within a network [21]. The concept of centrality is classified further into "degree of centrality," "closeness centrality," and "betweenness centrality." Degree of centrality simply represents how much one actor is connected to another, which is obtained by adding the total number of connected relationships [22]. Closeness centrality measures the distance between actors within a relationship to identify the network

with the most influence [19]. Finally, betweenness centrality measures the extent to which a network is on a path in breaking the flow of information: It sums up the rate of an actor between 2 other actors in the shortest path possible [23].

SNA comprises social units such as events and organizations, as well as information such as the relationships among people [24]. By paying attention to the structure and actions, it can investigate social facts in regards to which agencies have certain relationships and how they are organized.

Collaboration With Government Agencies in the Event of a Disaster

Not only do contagious diseases such as COVID-19 pose a threat, but various natural disasters—such as wind, floods, and wild fires—occur repeatedly every year, and the scale of damage continues to increase. It is during the times when a large-scale disaster causes calamitous damage that a government-orientated disaster response system is established, and in order for this to be true, a mutual, organic, cooperation system is essential [25]. Moreover, in order to effectively control a disaster response, a network of cooperation consisting of local governments, private organizations, and NGOs hinging on the central government is vital [26,27]. Many studies have been conducted on disaster response systems, and in particular, collaboration among organizations participating in disaster response has been confirmed in light of a network approach [27-29]. An example of this would be from Quarshie and Leuschner [28], where the New Jersey state government interacted with government and NGOs during Hurricane Sandy. As can be seen from the study, the government played a major role in organizing, facilitating, and supplying network members, and it served as the central hub among institutions. A study by Jovita et al [30] analyzed the causes for failing to respond adequately to typhoon Washi, which caused mass destruction to the Philippines in 2010. From the analysis, the networks of each institution participating in the disaster response in the region were very low, which equates to fragile cooperation among the institutions [30].

By analyzing the cooperative system among the government and other related organizations that are involved in a disaster response system, the aforementioned cases confirm the relationship-perspective characteristics and the effectiveness of disaster response systems among the relevant organizations. Thus, the purpose of this paper was to understand the relational characteristics of each institution in a disaster response system.

Research Design

In order to conduct a proper analysis of social networks, the ranking and roles of responding agencies to COVID-19 were examined to clarify the networks that had been formed to respond to the pandemic (Table 1). When conducting the case study of the organizations, the following criteria were used: First, the agencies included in the contagious disease management and response system suggested in the Korean Disaster Management Standard Manual were the primary focus. Second, agencies that were involved in responding to contagious disease outbreaks were mainly selected. Finally, COVID-19 response was conducted not only among domestic agencies but also with other countries, which amounts to a total of 63 agencies and countries.

This research sought to define relationship aspects among agencies in networks. Therefore, based on the official documents of activities uploaded on the website of the contagious disease disaster response department and the agencies pertinent to it, a node was defined as a contagious disease response organization only if it were noted that a “meeting” was held or “support” or “cooperation” occurred.

This study was conducted using the NetMiner software from CYRAM, a data science group, for efficient data analysis. NetMiner is a professional software that is appropriate for analyzing enormous data [31], and it is able to produce data by applying different methods such as SNA techniques, statistics, data mining, and machine learning.

Table 1. Concept of this study.

Designation	Significance
Node	This signifies the agency involved in responding to COVID-19.
Link	This signifies bidirectional communication as part of overall communication, such as via meetings, support, and cooperation among institutions.
Network	This signifies a set of links among agencies, such as meetings, response support, and collaboration for COVID-19 as well as COVID-19 response agencies (nodes).

Hypotheses

The study intended to determine the degree to which COVID-19 response agencies are centered, assuming that the contagious disease response center (in Korea, the Ministry of Public Administration and Security and the Ministry of Health and Welfare) is more central than the other agencies (Hypothesis 1 [H1]). It was also assumed that the contagious disease response center maintained a closer distance than other agencies and formed a network (Hypothesis 2 [H2]). Finally, the study intended to determine which agencies played a key role among COVID-19 response agencies through their betweenness centrality and also posited that collaboration or information transmission would occur through the contagious disease response center (Hypothesis 3 [H3]). Through this, this study proposes the following 3 hypotheses:

1. H1: The COVID-19 response center will have a high degree of centrality.
2. H2: The COVID-19 response center will have a high closeness centrality.
3. H3: The COVID-19 response center will have a high betweenness centrality.

Data Collection

The data used in this study were based on the official documents of activities uploaded on the website of the department in charge of responding to contagious diseases and the agencies related to it, which amounted to a total of 11,832 documents. Based on the official documents, it was assumed that a 2-way network was formed between the relevant ministries when preparing for and supporting COVID-19 response measures. The total number of connected networks in this study collected through this method came to 11,909.

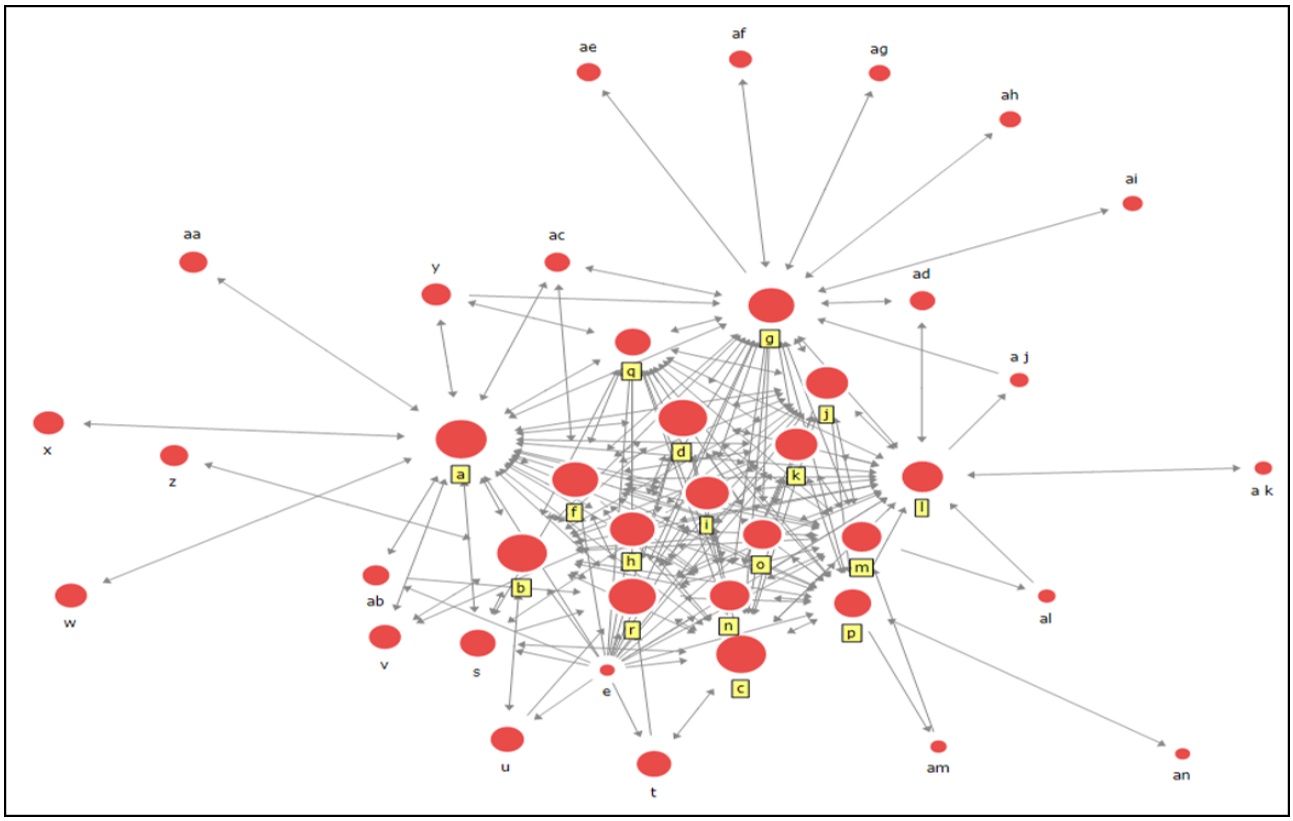
The course of the data collection ranges from the date of the first infection in Korea until the time when the number of infected people fell to double digits, which amounted to a total of 102 days, with the various activities confirmed by each ministry. The first period starts from the day of the first infection in Korea until when Korean citizens who were residing in Wuhan moved into temporary residential facilities—from January 20, 2020, until February 18, 2020. The second period is from February 19, 2020, to March 14, 2020. This is when the number of domestic cases surged due to the pseudoreligious group, Shincheonji (SCJ), in Daegu and Gyeongsangbuk province. The final period is when the figures began to fall to double digits—from March 15, 2020, to April 30, 2020. Simply put, the 102 days were categorized into 3 periods, with 2079, 5016, and 4814 links being verified, respectively, for each period in chronological order.

Results

Overview

Figure 2 is a diagram of the social networks of the COVID-19 response department of management and related agencies in the first period. Figure 2 presents the characteristics of social networks that can be identified simply by the node's name. As seen in the corresponding figures, certain institutions have very tight connections. In the diagram, the nodes located in the center and the nodes around it signify centrality, which means that it generally has a higher centrality than other agencies and shows that it plays a key role in the COVID-19 response. A note to take is that, in the first period, the Korea Disease Control and Prevention Agency (KDCA; formally known as Korea Centers for Disease Control and Prevention), which is the department managing the contagious disease response, has the largest node, meaning that it has the most connections with other institutions.

Figure 2. Corresponding management department and associated agencies in a social network with regards to COVID-19 in the first period (January 20, 2020, to February 18, 2020), in which the first case of COVID -19 in Korea was confirmed as well as the transfer of Korean residents from Wuhan to temporary living facilities. The 5 institutions with high centrality are the Korea Disease Control and Prevention Agency, Blue House & President, Prime Minister, Ministry of Economy and Finance, and the Ministry of Oceans and Fisheries.



Centrality During the First Period

The results for degree centrality in the first period are shown in Table 2. In addition to responding to contagious diseases, the Ministry of Strategy and Finance showed the next highest centrality. For that reason, it can be said the Ministry of Economy and Finance is related to agencies responsible for contagious disease responses. During that particular period, events, such as dispatching chartered planes to Wuhan, China, and isolating the infected patients in domestic temporary facilities, occurred. As a result, the Ministry appears to have

formed many networks with other agencies as additional revenue had been set aside.

The results for closeness centrality in the first period are shown in Table 3. In-closeness centrality means that the KDCA received the most requests for network formation, maintaining a close distance directly or indirectly to other agencies. Unlike the degree, the Ministry of Food and Drug Safety shows a high out-closeness centrality value. The reason why the Ministry of Food and Drug Safety shows a high out-closeness centrality value is the chaos associated with the regulation that masks be worn to prevent the dissemination of COVID-19. Therefore, in the first period, the KDCA—the management department responsible for responding to contagious diseases—supported H2, since it showed the highest closeness centrality value.

The results for betweenness centrality in the first period are shown in Table 4. The Ministry of Economy and Finance, having shown the highest value in the analysis of betweenness centrality, is the most essential intermediary among other agencies in responding to COVID-19. Following the KDCA, the Ministry of Oceans and Fisheries also showed a high level of betweenness centrality because of previous events such as naval quarantine and the suspension of 16 ports. Judging from these results, the Ministry of Economy and Finance and the related agencies, rather than the department in charge of responding to infectious diseases, showed the highest value in terms of mediated centrality in the first period. Therefore, H3 is not supported.

Figure 3 is a diagram of the social networks of the department handling COVID-19 responses and the related agencies in the second period, which is also when the largest number of institutions was involved in the COVID-19 response to form a network out of all 3 periods. The number of infected people increased exponentially due to the mass infection that originated from one of the pseudoreligions in Korea—SCJ. SCJ refers to the Korean leader as Jaerim Jesus, and missionary activities are carried out throughout Korea. As a result, confirmed patients at the SCJ Church in Daegu constantly travelled beyond North Gyeongsang Province in Korea to other regions such as Seoul, Gyeonggi Province, and Jeolla Province—dispersing the virus and further heightening the severity of the situation. With this background, the interpretation is that an active network with various institutions was formed to respond to the exponential increase in the number of infected people in the second period.

Table 2. Degree centrality of the top 5 agencies in the first period.

Top 5 agencies	Degree centrality	
	In-degree centrality	Out-degree centrality
Korea Disease Control and Prevention Agency (KDCA)	0.619048	0.595238
Ministry of Economy and Finance	0.595238	0.547619
Ministry of Health and Welfare	0.547619	0.52381
The Korean presidential residence (Cheongwadae, the Blue House)	0.52381	0.5
Ministry of Oceans and Fisheries	0.47619	0.452381

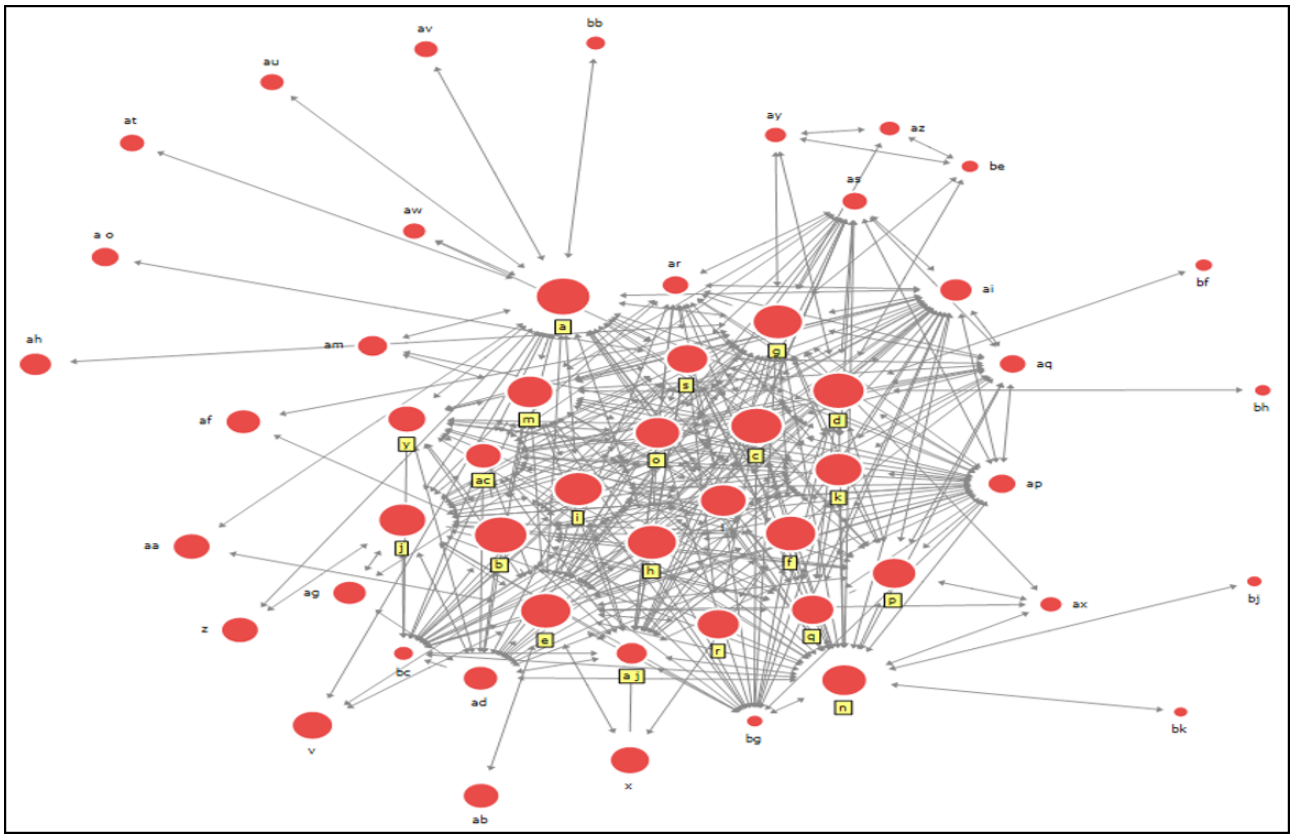
Table 3. Closeness centrality of the top 5 agencies in the first period.

Top 5 agencies	Closeness centrality	
	In-closeness centrality	Out-closeness centrality
Korea Disease Control and Prevention Agency (KDCA)	0.680233	0.680233
Ministry of Economy and Finance	0.667398	0.655039
Ministry of Health and Welfare	0.643129	0.643129
The Korean presidential residence (Cheongwadae, the Blue House)	0.631645	0.631645
Ministry of Food and Drug Safety	0.631127	0.631127

Table 4. Betweenness centrality of the top 5 agencies in the first period.

Top 5 agencies	Betweenness centrality
Ministry of Economy and Finance	0.229265
Korea Disease Control and Prevention Agency (KDCA)	0.190228
Ministry of Oceans and Fisheries	0.098866
Ministry of Health and Welfare	0.089269
The Korean presidential residence (Cheongwadae, the Blue House)	0.082255

Figure 3. Corresponding management department and associated agencies in a social network with regards to COVID-19 in the second period (February 19, 2020, to March 14, 2020), in which regional infections occurred as the number of confirmed cases surged due to the Shincheonji in Daegu, GyeongBuk Province. The 5 institutions with high centrality are the Korea Disease Control and Prevention Agency, Foreign Ministry, Prime Minister, Ministry of Health and Welfare, and Ministry of Economy and Finance.



Centrality During the Second Period

The results for degree centrality in the second period are as shown in Table 5. First, when looking at the centrality of internal connections, the 3 highest values came from the Ministry of Foreign Affairs (d), the Ministry of Economy and Finance (g), and Ministry of Health and Welfare (e), respectively.

The results for closeness centrality in the second period are shown in Table 6. The Ministry of Foreign Affairs had received the most requests for network formation, maintaining a close distance directly and indirectly from other agencies. The results indicate that, in the second period, the activities of the Ministry of Foreign Affairs (a related agency), surprisingly not the department of management in charge of responding to infectious diseases, did not support H2 because it showed the highest value in closeness centrality.

The results for betweenness centrality in the second period are shown in Table 7. The Ministry of Foreign Affairs showed the highest betweenness centrality, similar to the degree centrality and closeness centrality. Judging from these results, it can be concluded that the second period did not support H3 because the Ministry of Foreign Affairs showed the highest value in terms of betweenness centrality.

Figure 4 is a diagram of the COVID-19 response and management department and its relevant agencies in a social network within the third period. The agency in the center of the network is the Ministry of Foreign Affairs (d), indicated by the largest circle. It is during this period that more than 100 countries enforced restrictions on Koreans for entry, and in the second half of the period, the number of infected people decreased from 3 digits to 2 digits. A repercussion of this was that many overseas countries requested a more robust, international, cooperative system.

Table 5. Degree centrality of the top 5 agencies in the second period.

Top 5 agencies	Degree centrality	
	In-degree centrality	Out-degree centrality
Ministry of Foreign Affairs	0.617391	0.6
Ministry of Economy and Finance	0.504348	0.478261
Ministry of Health and Welfare	0.322740	0.313043
Ministry of Science and ICT	0.321739	0.330435
Korea Disease Control and Prevention Agency (KDCA)	0.313043	0.321739

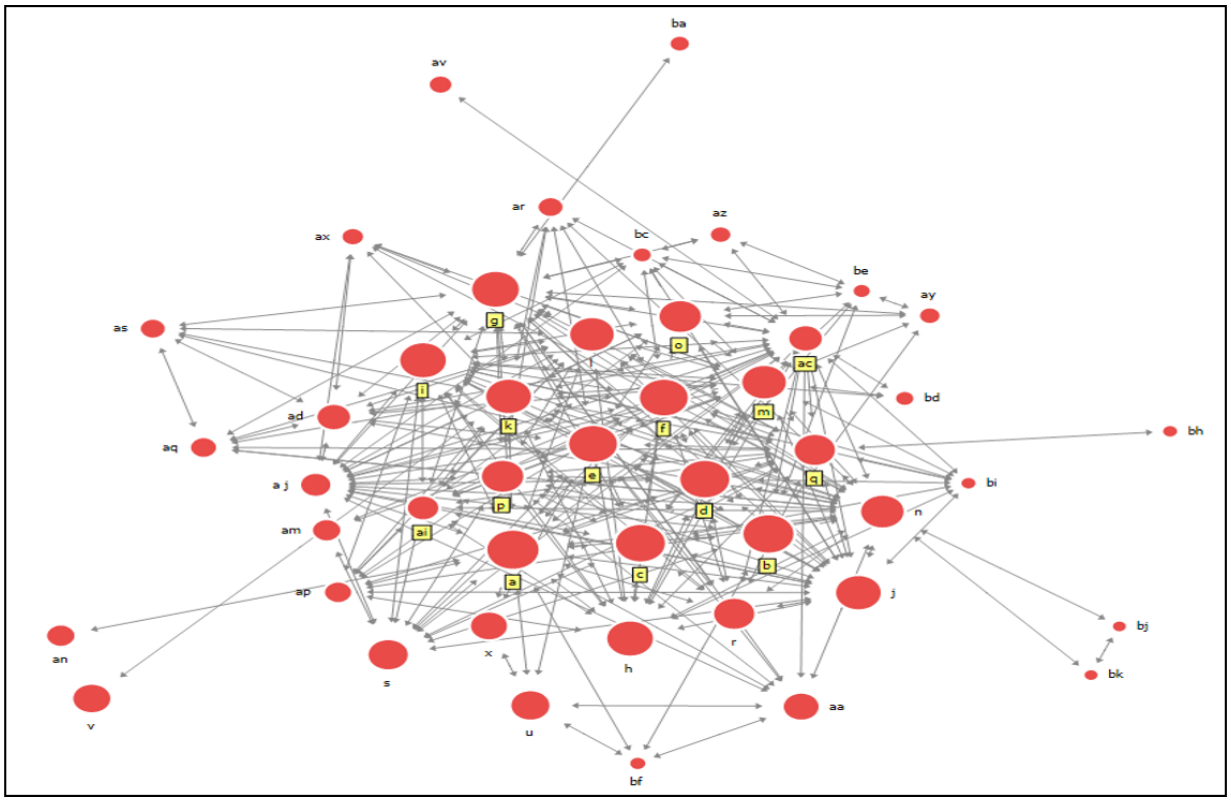
Table 6. Closeness centrality of the top 5 agencies in the second period.

Top 5 agencies	Closeness centrality	
	In-closeness centrality	Out-closeness centrality
Ministry of Foreign Affairs	0.656708	0.642809
Ministry of Economy and Finance	0.591037	0.574112
Ministry of Health and Welfare	0.50884	0.498071
Ministry of Science and ICT	0.502188	0.504756
The Korean presidential residence (Cheongwadae, the Blue House)	0.492531	0.485217

Table 7. Betweenness centrality of the top 5 agencies in the second period.

Top 5 agencies	Betweenness centrality
Ministry of Foreign Affairs	0.219257
Ministry of Economy and Finance	0.098854
Korea Disease Control and Prevention Agency (KDCA)	0.080244
Ministry of Health and Welfare	0.045238
Ministry of Trade, Industry and Energy	0.032122

Figure 4. Corresponding management department and associated agencies in a social network with regards to COVID-19 in the third period (March 15, 2020, to April 30, 2020), when the number of confirmed cases began to drop to double digits. The 5 institutions with high centrality are the Foreign Ministry, Ministry of Economy and Finance, Prime Minister, Korea Disease Control and Prevention Agency, and Cheong Wa Dae and President.



Centrality During the Third Period

The results for degree centrality in the third period are as shown in Table 8. From these results, it is not the department of management responding to contagious diseases, but rather the Ministry of Foreign Affairs (a related organization) that showed the highest value in degree centrality; thus, H1 was not supported.

The results for closeness centrality for this period are shown in Table 9. The Ministry of Foreign Affairs—a related institution—maintained the closest distance to other agencies, and instead of the contagious disease response management department, it showed the highest value in closed centrality, thereby dismissing H2.

The results for betweenness centrality in this period are shown in Table 10.

The Korean presidential residence was the most important intermediary among all other institutions, and this indicates that their activities do not support H3.

Table 8. Degree centrality of the top 5 agencies in the third period.

Top 5 agencies	Degree centrality	
	In-degree centrality	Out-degree centrality
Ministry of Foreign Affairs	0.44186	0.44186
The Korean presidential residence (Cheongwadae, the Blue House)	0.364341	0.364341
Ministry of Culture, Sports and Tourism	0.356589	0.356589
Ministry of Trade, Industry and Energy	0.325581	0.325581
Ministry of Health and Welfare	0.310078	0.310078

Table 9. Closeness centrality of the top 5 agencies in the third period.

Top 5 agencies	Closeness centrality	
	In-closeness centrality	Out-closeness centrality
Ministry of Foreign Affairs	0.531449	0.531449
The Korean presidential residence (Cheongwadae, the Blue House)	0.519017	0.519017
Ministry of Trade, Industry and Energy	0.513017	0.513017
Ministry of Health and Welfare	0.504272	0.504272
Ministry of Culture, Sports and Tourism	0.495821	0.495821

Table 10. Betweenness centrality of the top 5 agencies in the third period.

Top 5 agencies	Betweenness centrality
The Korean presidential residence (Cheongwadae, the Blue House)	0.124024
Ministry of Foreign Affairs	0.094018
Ministry of Trade, Industry and Energy	0.059094
Ministry of Health and Welfare	0.046297
Ministry of Science and ICT	0.044972

Comparison of Research Results by Period

Figure 5 shows the results from all 3 periods and the major institutions with a high centrality. The fact that more networks were formed in the second and third periods than in the first period since the COVID-19 outbreak stands out. The explanation for this is that the number of confirmed cases had increased exponentially since the first outbreak in the country, which contributed to the formation of an active network for each institution. In addition, under the Ministry of Health and Welfare, the KDCA had the highest centrality in the first and second periods. However, in the third period, the Ministry of Foreign Affairs—not the center responding to contagious diseases—was located at the center of the network; this can be attributed to 2 factors. First, the role of the Ministry of Foreign Affairs expanded as the number of countries imposing travel restrictions on Koreans rose due to mass infections in Korea at the time, and since then, the number of cases caused by a collective outbreak has decreased sharply. This resulted in the Ministry of Foreign Affairs forming many networks in response to carrying out requests in order to bolster the international cooperative system for the prevention of contagious diseases. In particular, the networks formed in the third period can be said that they show the roles of the host organization in charge of a disaster and that the related organizations are integral to responding to disaster situations.

From the perspective of degree centrality during the 3 periods, the first and second periods showed the highest centrality in the KDCA—a contagious disease agency (Table 11). However, in the third period, the Ministry of Foreign Affairs, an agency related to contagious diseases, showed the highest degree centrality. Degree centrality indicates the degree of information and resource exchange as a frequency linked to other agencies, meaning that the Ministry of Foreign Affairs has conducted many information and resource exchanges with other agencies during the COVID-19 response. Since the values for both in-degree centrality and out-degree centrality are high, this indicates that the desire for other institutions to establish a network with the Ministry of Foreign Affairs is also high, and vice versa.

Figure 5. Network diagram comparison of the 3 periods.

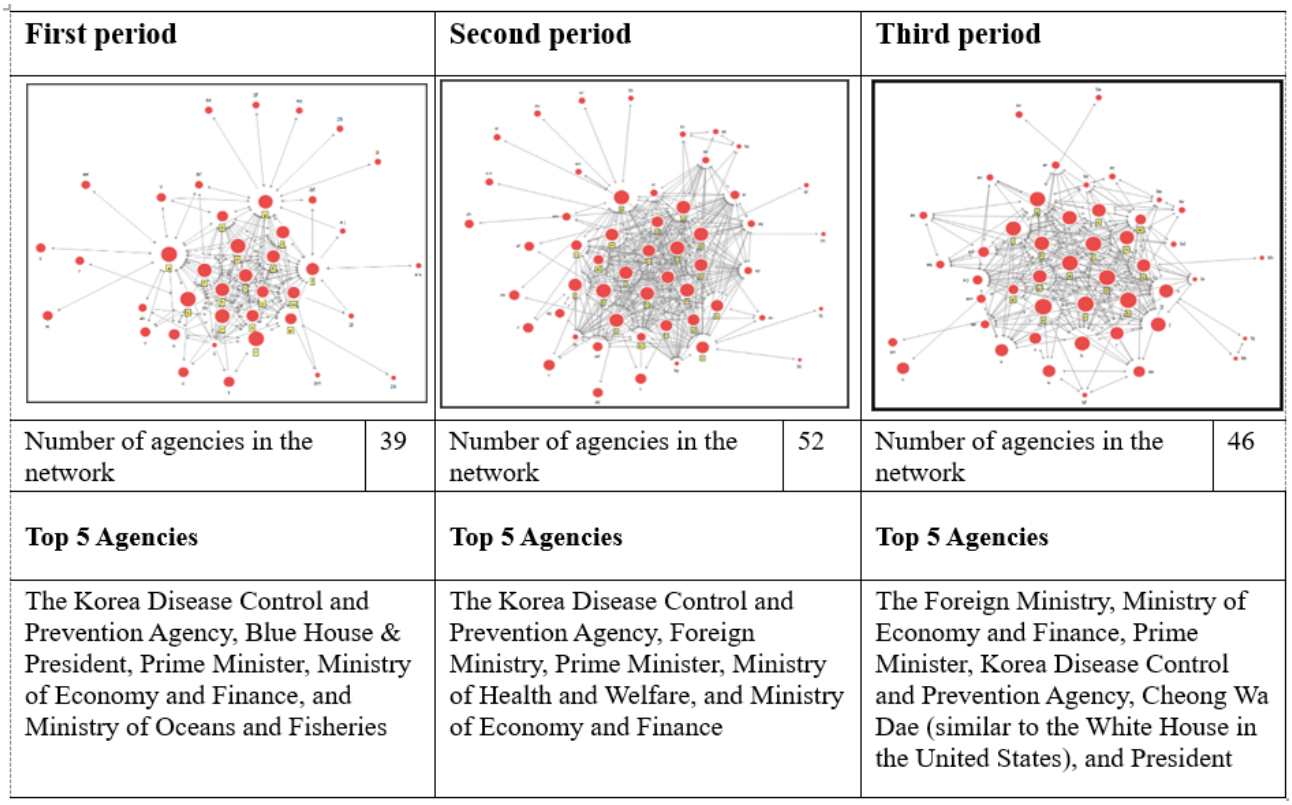


Table 11. Degree centrality of the top 5 agencies for all 3 periods.

Period and top 5 agencies	Degree centrality	
	In-degree centrality	Out-degree centrality
First		
Korea Disease Control and Prevention Agency (KDCA)	0.619048	0.595238
Ministry of Economy and Finance	0.595238	0.547619
Ministry of Health and Welfare	0.547619	0.52381
The Korean presidential residence (Cheongwadae, the Blue House)	0.52381	0.5
Ministry of Oceans and Fisheries	0.47619	0.452381
Second		
Ministry of Foreign Affairs	0.617391	0.6
Ministry of Economy and Finance	0.504348	0.478261
Ministry of Health and Welfare	0.322740	0.313043
Ministry of Science and ICT	0.321739	0.330435
Korea Disease Control and Prevention Agency (KDCA)	0.313043	0.321739
Third		
Ministry of Foreign Affairs	0.44186	0.44186
The Korean presidential residence (Cheongwadae, the Blue House)	0.364341	0.364341
Ministry of Culture, Sports and Tourism	0.356589	0.356589
Ministry of Trade, Industry and Energy	0.325581	0.325581
Ministry of Health and Welfare	0.310078	0.310078

From the perspective of closeness centrality during the 3 periods, it can be confirmed that the result is the same as the aforementioned degree centrality (Table 12). In the case of closeness centrality, the higher the value, the easier it is to reach other organizations in the network, so it usually plays the role of negotiation and coordination. This means that the Ministry

of Foreign Affairs oversaw the whole process with other agencies in response to COVID-19 in the second and third periods. In addition, this means that it was able to acquire information in responding to contagious diseases at a faster pace than other institutions.

From the perspective of betweenness centrality during the 3 periods, the Ministry of Economy and Finance had the highest betweenness centrality value in the first period and was the pinnacle agency of all the periods. The Ministry of Foreign Affairs had the highest betweenness centrality value in the second period, while the Blue House ranked first in the third period (Table 13). Organizations with high betweenness centrality have the potential to influence the distribution of information with regards to the control or regulation of information exchange within a network. This happens to be the case since they perform activities that have to do with mediating organizations that do not exchange information on their own. Therefore, the high betweenness centrality value of the related organizations translates to the manisfistation of cooperation among the agencies that support the ones dedicated to responding to contagious diseases. Therefore, those with a high betweenness centrality value (the Ministry of Economy and Finance, the Ministry of Foreign Affairs, and the Blue House) played a mediating role with other agencies because of their position at the core of the network of dedicated agencies.

Table 12. Closeness centrality of the top 5 agencies for all 3 periods.

Period and top 5 agencies	Closeness centrality	
	In-closeness centrality	Out-closeness centrality
First		
Korea Disease Control and Prevention Agency (KDCA)	0.680233	0.680233
Ministry of Economy and Finance	0.667398	0.655039
Ministry of Health and Welfare	0.643129	0.643129
The Korean presidential residence (Cheongwadae, the Blue House)	0.631645	0.631645
Ministry of Food and Drug Safety	0.631127	0.631127
Second		
Ministry of Foreign Affairs	0.656708	0.642809
Ministry of Economy and Finance	0.591037	0.574112
Ministry of Health and Welfare	0.50884	0.498071
Ministry of Science and ICT	0.502188	0.504756
The Korean presidential residence (Cheongwadae, the Blue House)	0.492531	0.485217
Third		
Ministry of Foreign Affairs	0.531449	0.531449
The Korean presidential residence (Cheongwadae, the Blue House)	0.519017	0.519017
Ministry of Trade, Industry and Energy	0.513017	0.513017
Ministry of Health and Welfare	0.504272	0.504272
Ministry of Culture, Sports and Tourism	0.495821	0.495821

Table 13. Betweenness centrality of the top 5 agencies for all 3 periods.

Period and top 5 agencies	Betweenness centrality
First	
Ministry of Economy and Finance	0.229265
Korea Disease Control and Prevention Agency (KDCA)	0.190228
Ministry of Oceans and Fisheries	0.098866
Ministry of Health and Welfare	0.089269
The Korean presidential residence (Cheongwadae, the Blue House)	0.082255
Second	
Ministry of Foreign Affairs	0.219257
Ministry of Economy and Finance	0.098854
Korea Disease Control and Prevention Agency (KDCA)	0.080244
Ministry of Health and Welfare	0.045238
Ministry of Trade, Industry and Energy	0.032122
Third	
The Korean presidential residence (Cheongwadae, the Blue House)	0.124024
Ministry of Foreign Affairs	0.094018
Ministry of Trade, Industry and Energy	0.059094
Ministry of Health and Welfare	0.046297
Ministry of Science and ICT	0.044972

Discussion

Principal Findings

In summary, for 102 days from January 20, 2020, the date of the first infection in Korea, to April 30, 2020, the development of the network of infectious disease response and those of related organizations were categorized into 3 periods, in which this study suggests a few notable findings: Frst, during the first and second periods, under the Ministry of Health and Welfare, the KDCA had the highest centrality, but in the third period, the Ministry of Foreign Affairs (not the center of the response to contagious diseases) was located at the center of the network. These results show that, in the event of a disaster, not only the leading agency in charge of responding to disasters but also the related agencies are of indusputable importance. Second, regarding closeness centrality, the relationship period, which is not the central agency for responding to contagious diseases, was found to have the highest values of the 2 periods, and looking at betweenness centrality, the related organizations had the highest values in all 3 periods. These results could be an indication of collaboration among related agencies to support dedicated response agencies for contagious diseases for their response. Third, as the hypothesis of this study, the agency dedicated to responding to contagious diseases was expected to have the highest values for all centralities. However, the analysis shows that there are numerous networks formed by related agencies other than the dedicated agencies.

Except in the first period, this study found that the contagious disease response agencies are not situated at the center of the network, which means that they are not in line with the disaster response system created in Korea. In particular, this study's results show that various institutions are vital for working together to respond to large-scale disasters. In other words, related organizations as well as the host organization should be able to collaborate during a response to a crisis. This means that it is imperative to expand and systemize manuals based on input from institutions that respond to contagious diseases and their related institutions. Therefore, institutional measures are needed to form networks among contagious disease response agencies, and modification of existing disaster response manuals is crucial.

Limitations

This study has limitations in that its research was contained to only a single type of disaster, COVID-19, and the pandemic has not ended as of the time of writing. In addition, when data were collected for the SNA, only 2-way networks were collected and analyzed, which resulted in the absence of analysis on the direction of each organization's network.

Conclusion

Based on the COVID-19 situation that led to the declaration of a pandemic, this study conducted an SNA to understand the characteristics of Korea's contagious disease control department and the related agencies from a network perspective. Therefore, to perform an exploratory analysis of the network formation of institutions that responded to COVID-19 in Korea, SNA studies were conducted on the management of contagious disease disaster response and the establishment of a system.

Except for the first period, the other 2 periods showed that contagious disease response agencies were not the center of the network. These findings reveal that not only the host

organization but also various organizations should cooperate to respond to disasters. These results are inconsistent with the existing disaster response system. Therefore, not only organizations that are in charge but also the related agencies should be aware of the cooperative function for crisis response in the event of a disaster. In addition, the study is meaningful in that it is an exploratory study on an actual network conducted between the organizer and related agencies in the outbreak of an actual contagious disease.

Acknowledgments

This paper was supported by Korea Institute for Advancement of Technology (KIAT) grant funded by the Korea Government (MOTIE; P0008703, The Competency Development Program for Industry Specialist).

Conflicts of Interest

None declared.

Multimedia Appendix 1
COVID-19 domestic and international response agencies and organizations.
[DOC File , 76 KB - publichealth_v8i5e35958_app1.doc]

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Abbreviations

CDMH: Central Disaster Management Headquarters
CDSCH: Central Disaster and Safety Countermeasures Headquarters
KDCA: Korea Disease Control and Prevention Agency
KIAT: Korea Institute for Advancement of Technology
NGO: nongovernmental organization
SCJ: Shincheonji
SNA: social network analysis

Edited by T Sanchez, A Mavragani; submitted 23.12.21; peer-reviewed by SY Paek, J Jung; comments to author 24.01.22; revised version received 08.02.22; accepted 26.04.22; published 23.05.22.

Please cite as:
Cho J, Kang W, Lee J
Korea's Response to COVID-19 According to Set Time Frames, With a Focus on the Network Between the Government and Responding Agencies: Social Network Analysis
JMIR Public Health Surveill 2022;8(5):e35958
URL: https://publichealth.jmir.org/2022/5/e35958
doi:10.2196/35958
PMID:35486100

Review

Evaluation of Digital Interventions for Physical Activity Promotion: Scoping Review

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Abstract

Background: Digital interventions are interventions supported by digital tools or technologies, such as mobile apps, wearables, or web-based software. Digital interventions in the context of public health are specifically designed to promote and improve health. Recent reviews have shown that many digital interventions target physical activity promotion; however, it is unclear how such digital interventions are evaluated.

Objective: We aimed to investigate evaluation strategies in the context of digital interventions for physical activity promotion using a scoping review of published reviews. We focused on the target (ie, user outcomes or tool performance), methods (ie, tool data or self-reported data), and theoretical frameworks of the evaluation strategies.

Methods: A protocol for this study was preregistered and published. From among 300 reviews published up to March 19, 2021 in Medline, PsycINFO, and CINAHL databases, 40 reviews (1 rapid, 9 scoping, and 30 systematic) were included in this scoping review. Two authors independently performed study selection and data coding. Consensus was reached by discussion. If applicable, data were coded quantitatively into predefined categories or qualitatively using definitions or author statements from the included reviews. Data were analyzed using either descriptive statistics, for quantitative data (relative frequencies out of all studies), or narrative synthesis focusing on common themes, for qualitative data.

Results: Most reviews that were included in our scoping review were published in the period from 2019 to 2021 and originated from Europe or Australia. Most primary studies cited in the reviews included adult populations in clinical or nonclinical settings, and focused on mobile apps or wearables for physical activity promotion. The evaluation target was a user outcome (efficacy, acceptability, usability, feasibility, or engagement) in 38 of the 40 reviews or tool performance in 24 of the 40 reviews. Evaluation methods relied upon objective tool data (in 35/40 reviews) or other data from self-reports or assessments (in 28/40 reviews). Evaluation frameworks based on behavior change theory, including goal setting, self-monitoring, feedback on behavior, and educational or motivational content, were mentioned in 22 out of 40 reviews. Behavior change theory was included in the development phases of digital interventions according to the findings of 20 out of 22 reviews.

Conclusions: The evaluation of digital interventions is a high priority according to the reviews included in this scoping review. Evaluations of digital interventions, including mobile apps or wearables for physical activity promotion, typically target user outcomes and rely upon objective tool data. Behavior change theory may provide useful guidance not only for development of digital interventions but also for the evaluation of user outcomes in the context of physical activity promotion. Future research

should investigate factors that could improve the efficacy of digital interventions and the standardization of terminology and reporting in this field.

International Registered Report Identifier (IRRID): RR2-10.2196/35332

(JMIR Public Health Surveill 2022;8(5):e37820) doi:10.2196/37820

KEYWORDS

evaluation; digital interventions; physical activity; scoping review; review; health promotion; behavior change theory; digital health; public health; digital technology

Introduction

The field of digital public health aims to promote and improve the health of people and communities through the application of digital technologies [1,2]. Digital technologies specifically designed to promote and improve health have emerged on a large scale and already permeate seemingly all aspects of daily life. For example, interventions supported by digital technologies (ie, digital interventions) are becoming increasingly popular in the context of healthy lifestyles and behavior change, including physical activity promotion [3]. Given the rapid growth in the number and sophistication of digital technologies, the use of mobile wearable devices or smartphone apps has been found to be a scalable and cost-effective way of promoting physical activity–related behavior change [4].

Digital technologies have tremendous potential to be incorporated into health interventions that are grounded in behavioral theory. Such digital interventions can include a variety of potentially useful behavior change techniques and can be tailored to meet the needs of individuals or populations [5]. Behavior change theory refers to the active ingredients of any given intervention that aim to evoke a change in behavior (eg, increase physical activity), which have been classified according to their nature [6,7]. Various components of behavior change theory have been used in digital interventions for physical activity promotion, including goal setting, activity monitoring with feedback, and shaping knowledge [8,9]. In particular, the use of goal setting, social incentives, and graded tasks may improve the physical activity outcomes of digital interventions [10].

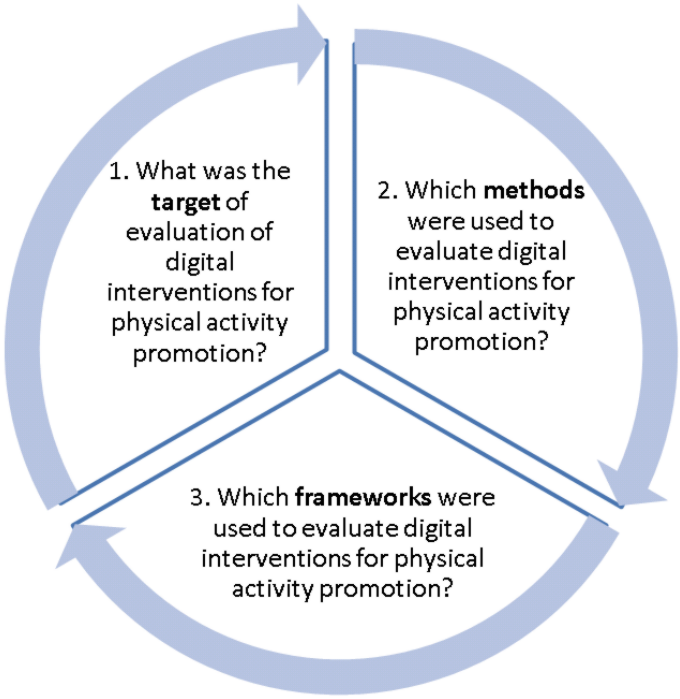
Little is known about how digital interventions help shape behavior in real-world settings. This suggests there is a need to evaluate and understand factors related to intervention success or failure [11,12]. Success or failure depends on the context of use, including structural issues in the environment in which an intervention is used, available infrastructure, the health needs that are being addressed, and the ease of use of the technology [3,13]. Thus, an evaluation of novel digital interventions is important, not only in terms of efficacy but also, to justify and inform policy, program, and funding decisions. In Germany, digital health apps that are used as medical devices must undergo an evaluation process similar to that undergone by other medical procedures, while other digital interventions with a primary focus on prevention, such as digital interventions for physical activity promotion, are not required to undergo such an evaluation process [14]. More importantly, when evaluations are omitted, it becomes the user's responsibility to identify which digital interventions may be effective and useful, and consequently, users bear the risk of using ineffective, or even potentially harmful, solutions.

One key issue in this area of research is the lack of frameworks or guidelines specifically addressing the evaluation of digital interventions. Although assessment criteria for health-related technologies in general have been developed previously, their focus is generally neither on digital technologies [15] nor on a public health context [16]. Health technology assessment, for example, is a methodology for the systematic and transparent evaluation of medical procedures and technologies under medical, economic, social, ethical, and economic aspects with the aim of supporting associated decision-making processes [17]. While health technology assessment is not specifically designed for digital interventions, various organizations that are engaged in health technology assessment were involved in creating or guiding the development of standards for the evidence required for digital interventions. For example, the National Institute for Health and Care Excellence recently developed an Evidence Standards Framework for Digital Health Technologies for assessing the effectiveness and cost-effectiveness of digital interventions within the UK health care system [18]. Currently, however, health technology assessment frameworks such as this [18] mainly focus on evaluating the clinical rather than the public health outcomes of novel digital interventions.

We initially planned to conduct a scoping review in two phases: (1) scoping review of existing reviews (ie, review of reviews) and (2) scoping review of primary studies [19]. As explained in a subsequent study protocol [20], this scoping review addresses phase 1 of the study. Phase 2 will depend on the outcomes of phase 1 of the study; specifically, phase 1 of the study will provide evidence to support a decision for or against conducting a new scoping review of primary literature. Such a decision needs to be evidence-based to prevent any research waste that occurs when new reviews are conducted despite the existence of other reviews that address the same aims.

The aim of this scoping review was to investigate the evaluation strategies in the context of digital interventions for physical activity promotion that were addressed in other published reviews. The 3 main objectives of this scoping review address the target (ie, user outcomes or tool performance), methods (ie, tool data or self-reported data), and theoretical frameworks of such evaluations (Figure 1). In addition, we also aim to summarize the evidence gaps identified in other published reviews.

Figure 1. Objectives of this scoping review.



Methods

Study Design

This study was a scoping review and adheres to PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension for Scoping Reviews) guidelines [21]. The PRISMA-ScR checklist is reported in Table S1 in Multimedia Appendix 1.

Protocol and Registration

The protocol for this scoping review was prospectively registered [19] and published [20]. We chose a scoping review methodology because our objectives focus broadly on the strategies required to evaluate digital interventions rather than the efficacy of digital interventions (which is typically the case in overviews). We apply 2 aspects taken from the overview methodology: (1) we assessed the overlap among primary studies cited in the included reviews to investigate the uniqueness of existing evidence, and (2) we appraised the included systematic reviews to investigate the sources of weaknesses in existing evidence. Since the methods applied in this scoping review were already reported in detail in our published protocol [20], only a short summary is provided here. There were no changes between the published protocol [20] and the objectives, methods, and results reported in this scoping review.

Eligibility Criteria

The eligibility criteria ([20], Textbox 1) for this scoping review were derived from the Population, Intervention, Comparison, Outcome, and Study type (PICOS) criteria.

Textbox 1. Inclusion criteria for this scoping review.

Population

- Any health status (healthy or clinical human samples)
- Any age (children or adults)

Intervention

- Digital interventions for physical activity promotion

Comparison

- Any other intervention or no intervention

Outcome

- Evaluation of any outcome in the context of physical activity promotion

Study type

- Any review (systematic, scoping, rapid, narrative, overview)
- Papers published in peer-reviewed journals, in English or German, available in full-text

Information Sources

We used (1) international databases (MEDLINE, PsycINFO, and CINAHL) and (2) the reference sections of studies (reviews) included in our scoping review.

Search

The electronic search strategy (Multimedia Appendix 2) was developed and performed under the supervision of an experienced librarian. The electronic search was performed from database inception to March 19, 2021, without any limits, in 3 international databases.

Selection of Sources of Evidence

The electronic search returned 8272 records that were stored and processed in EndNote X9 (Clarivate); after duplicates were removed, 4912 records remained. Reviews of any type were identified using smart group settings in EndNote and assessed for eligibility by any 2 authors independently. Based on title and abstract screening, reviews that met the inclusion criteria were selected for full-text screening. The reference sections of eligible full-text reviews were also manually screened to identify additional relevant reviews. Final eligibility was decided by consensus. Final list of included and excluded studies is shown in Table S2 in Multimedia Appendix 1).

Data Charting

Data were coded into a self-developed spreadsheet (Excel, version 10; Microsoft Inc). The spreadsheet was pilot-tested and calibrated within the team. Data coding was performed independently by 2 authors, and consensus was reached by discussion.

Data Items

Data items (Textbox 2) were coded either quantitatively into predefined categories or qualitatively using definitions or author statements from the included reviews.

The operational definitions of the 2 key concepts (digital interventions and physical activity promotion) are summarized in Textbox 3.

Textbox 2. Data items in this scoping review.

1. Bibliographic information (publication year, author region, conflict of interest)
2. Population details (health status and age)
3. Digital intervention details
4. Comparison condition
5. Outcome in the context of physical activity promotion
6. Study details
   - Review type
   - Primary studies in review (number, designs, overlap among primary studies cited in reviews)
7. Evaluation strategy details (target, methods, theoretical frameworks)
8. Evidence gaps (requirements for efficacy and ideas for future research)

Textbox 3. Operational definitions applied in this scoping review.

Digital intervention

- Digital intervention was defined as any intervention delivered or supported by digital tools or digitally supported technologies for automated and continuous self-monitoring and feedback. This includes mobile apps, wearable activity trackers and web-based software but excludes pedometers and accelerometers that do not offer feedback throughout time [22]. Reviews were included if only a minority of their primary studies incorporated pedometers or accelerometers.

Physical activity promotion

- Physical activity promotion was defined as any primary outcome targeting general fitness or mobility. Reviews were excluded if physical activity promotion was assessed as part of healthy lifestyle, as a secondary outcome to management of weight or blood sugar, or as part of rehabilitation after sport injuries, surgeries, or in neurological disorders.

Critical Appraisal of Individual Sources of Evidence

We performed critical appraisals using AMSTAR2 (A Measurement Tool to Assess Systematic Reviews, version 2) [23]) of all systematic reviews to identify weaknesses in existing evidence. The appraisal procedure was explained in detail in the published protocol [20]. Two authors appraised all systematic reviews independently and reached consensus by discussion. The overall confidence ratings in the results of each systematic review (high, moderate, low, or critically low) were established based on the type and the number of weaknesses in each review [23] (Multimedia Appendix 3).

Synthesis of Results

Coded data were synthesized using either descriptive statistics of quantitative data (relative frequencies out of all studies) or narrative descriptions of qualitative data (by identifying common themes). The AMSTAR2 appraisal outcomes (overall confidence

ratings) were synthesized for all systematic reviews using a bar graph. Evidence maps were used to visualize the results based on the objectives of this scoping review (Figure 1).

Results

Included Studies

Study Selection

Of 4912 records identified in our electronic search, 300 were designated as reviews of any type based on the titles or abstracts (Table S2 in Multimedia Appendix 1), and 40 reviews were found to meet eligibility criteria: 36/40 reviews from the electronic search and 4/40 reviews from the manual search of reference sections of these 36 reviews. The majority of the 40 included studies were systematic reviews, followed by scoping reviews; there was 1 rapid review (Table 1). All 40 reviews addressed the evaluation strategies for any outcome in the context of digital interventions for physical activity promotion in healthy or clinical samples. The digital interventions in all reviews were supported by digital tools, such as mobile phones, smartphone apps, wearable activity trackers, or the internet (ie, websites). The physical activity promotion outcomes in all reviews were general fitness or mobility measures (ie, steps per day, frequency of physical exercise at various intensities, meeting physical activity guidelines; Multimedia Appendix 4).

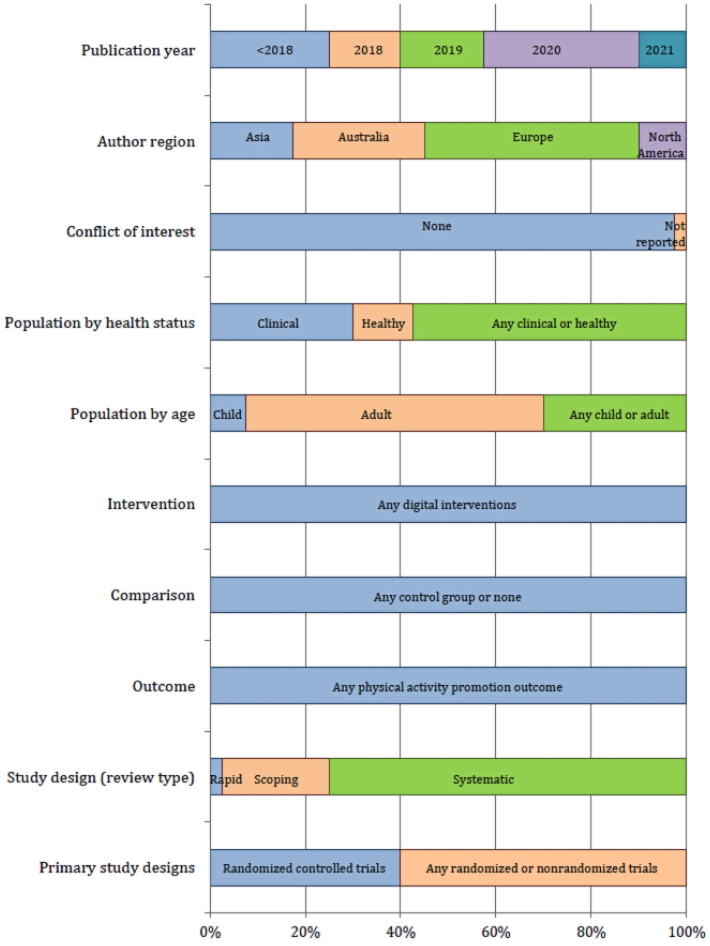
Table 1. A list of studies (40 reviews) included in this scoping review.

Study type	Studies (n=40)	Citation
Rapid review	1	[24]
Scoping review	9	[8,9,25-31]
Systematic review	30	[11,22,32-59]

Study Characteristics

Study characteristics of the individual reviews are shown in Figures S1 and S2 in Multimedia Appendix 1. Synthesis of study characteristics of all 40 reviews is shown in Figure 2. All 40 reviews were published in the period from 2007 to 2021. The majority were systematic reviews (30/40), published from 2019 to 2021 (24/40), originated from Europe (18/40) or Australia (11/40), and reported no conflicts of interest (39/40). All 40 reviews addressed any digital interventions for any physical activity promotion outcome relative to any control condition (other interventions or baseline physical activity). Most reviews included primary studies with any design (randomized controlled trials or non–randomized controlled trials: 24/40 reviews) adult populations (25/40 reviews), and any health setting (clinical or nonclinical: 23/40 reviews).

Figure 2. Study characteristics of 40 reviews.



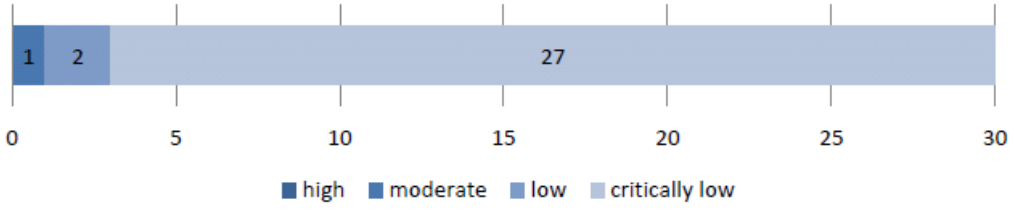
Overlap Among Primary Studies Cited in Reviews

The assessment of the overlap among primary studies showed that most primary studies were cited only once in any review (Textbox S1 in Multimedia Appendix 1). The 10 rapid or scoping reviews cited 278 unique published primary studies. Most of these studies (244/278, 87.8%) were cited only once in any review while the rest (34/278, 12.2%) were cited twice. The 30 systematic reviews cited 320 unique published primary studies. Most of these studies (249/320, 77.8%) were cited only once, others (67/320, 20.9%) were cited 2 to 4 times, and the minority (4/320, 1.2%) were cited either 5 times [60,61] or 6 times [62,63].

Quality Appraisal in Systematic Reviews

The majority of systematic reviews (27/30, 90%) received critically low confidence ratings, and the remaining systematic reviews received either low (2/30, 6.7% [38,41]) or moderate (1/30, 3.3% [22]) confidence ratings (Figure 3). None of the systematic reviews received high confidence ratings. The 3 most common weaknesses among the 30 systematic reviews were that a list of excluded studies was not reported, a review protocol was not mentioned, and the sources of funding for the primary studies included in review were not reported.

Figure 3. Overall confidence in the results of 30 systematic reviews.

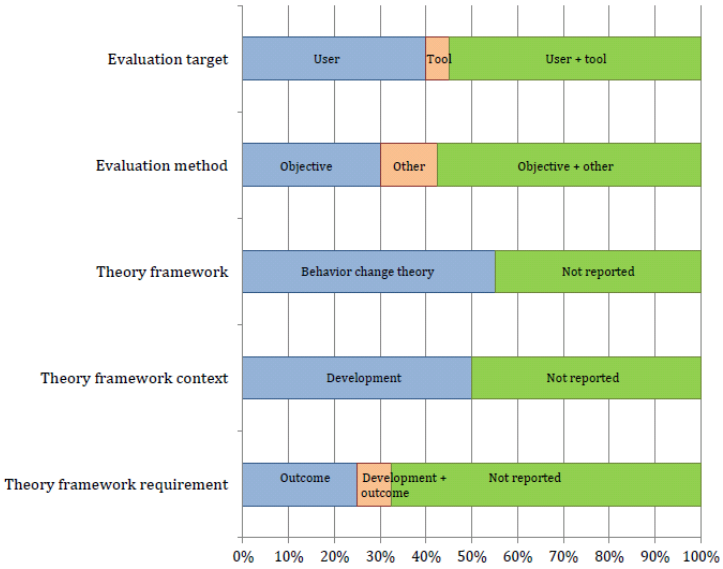


Evaluation of Digital Interventions for Physical Activity Promotion

Overall

Evaluation strategies of digital interventions for physical activity promotion addressed in the individual reviews are shown in Figure S3 in Multimedia Appendix 1. The synthesis of evaluation strategies in all reviews (Figure 4) showed that, while all 40 reviews addressed evaluation targets and evaluation methods used to assess digital interventions for physical activity promotion, only just over half of reviews mentioned the evaluation frameworks.

Figure 4. Evaluation strategies addressed in 40 reviews.



Evaluation Targets

Evaluation target was either any user outcome (in 38/40 reviews) or tool performance (in 24/40 reviews). Both evaluation targets (user outcomes and tool performance) were mentioned in 22/40 reviews. User outcomes were described as efficacy, acceptability, usability, feasibility, or engagement with digital interventions for promoting physical activity while tool performance was typically mentioned in the context of tool validation (Multimedia Appendix 4).

Evaluation Methods

Evaluation methods relied upon either objective data (in 35/40 reviews) or other data (in 28/40 reviews). Both types of data (objective and other) were mentioned in 23/40 reviews. Objective data were automatic, tool-generated data, such as continuous recording of physical activity with wearable activity trackers or smartphone apps. Other data included self-reported data from questionnaires or rating scales (used to assess tool performance), tests, or assessments of user outcomes as well as various measures of engagement or coaching (Multimedia Appendix 4).

Evaluation Frameworks

Only just over half of all reviews (22/40) mentioned evaluation frameworks. All 22 reviews focused on various aspects of behavior change theory, such as goal setting, self-monitoring, feedback on behavior, and educational or motivational content. Among the 22 reviews, 20 discussed the context of evaluation frameworks and concluded that aspects of behavior change theory were predominantly used to develop digital interventions for physical activity promotion. Among all 40 reviews, 13 mentioned a need to incorporate evaluation frameworks to assess user outcomes of digital interventions in the context of physical activity promotion (Multimedia Appendix 4).

Evidence Gaps

Overall

There were several evidence gaps identified in the 40 reviews (Table 2). The evidence gaps mentioned by the authors of the 40 reviews were synthesized with respect to two main themes: (1) requirements for efficacy and (2) ideas for future research.

Table 2. Evidence gaps in 40 reviews.

Review type, theme, and category	Studies, n
Rapid and scoping reviews	10
Requirements for efficacy	
Identify factors that could improve the effectiveness of digital interventions by increasing compliance and adherence to digital interventions (personalization, feedback, engagement with the tool, human support, and digital literacy)	7
Need for guidelines for evaluation and reporting / better reporting of digital interventions	3
Need for objective and homogeneous outcome measures required to evaluate digital interventions	3
Ideas for future research	
Use and grounding of behavioral theory or include theoretical framework for digital interventions	3
Perform long-term studies / use longer follow-up for digital interventions	1
Systematic reviews	30
Requirements for efficacy	
Identify factors that could improve the effectiveness of digital interventions by increasing compliance and adherence to digital interventions (personalization, feedback, engagement with the tool, human support, and digital literacy)	18
Need for objective and homogeneous outcome measures required to evaluate digital interventions	11
Need for guidelines for evaluation and reporting and better reporting of digital interventions	2
Ideas for future research	
Perform long-term studies and use longer follow-up for digital interventions	13
Evaluation or better understanding of (clinical) effectiveness of digital interventions	9
Need for an appropriate study design in future studies (eg, high quality trials, rigorous study designs)	8
Use and grounding of behavioral theory or include theoretical framework for digital interventions	5
Investigation of cost-effectiveness of digital interventions	5
Inclusion of more diverse samples in the studies (eg, low-income countries, age groups)	3

Requirements for Efficacy

Three main themes emerged in the context of assessing the efficacy of digital interventions for physical activity promotion. Most reviews mentioned the need to identify factors that could improve the effectiveness of digital interventions. The other themes were the need to objectively and homogeneously define the outcomes of digital interventions and the need for evaluation guidelines and better standardized reporting of digital interventions components and outcomes.

Ideas for Future Research

There were several ideas for future research. Two common themes among the reviews were a need for theoretical frameworks to evaluate digital interventions and a need for evaluation of digital interventions using studies with long-term follow-up. In addition, systematic reviews mentioned a need to understand the clinical effectiveness of digital interventions that should be studied using rigorous and high-quality study designs. Some systematic reviews also suggested investigating the cost-effectiveness of digital interventions and evaluating digital interventions in more diverse settings and samples, such as in samples with different sociodemographic characteristics.

Discussion

Principal Results

This scoping review shows that 40 reviews (rapid, scoping, or systematic) that had been published within the last 15 years mentioned the issue of evaluation of digital interventions for physical activity promotion. All reviews addressed different evaluation targets, which included user outcomes or tool performance in the context of physical activity promotion. The reviews mentioned that evaluation methods relied predominantly upon objective tool data, although data from self-reports or assessments were also used. Only approximately half of all reviews mentioned evaluation frameworks and concluded that various aspects of behavior change theory were applied to develop digital interventions but not to evaluate the user outcomes of such digital interventions.

Interest in the Evaluation of Digital Interventions for Physical Activity Promotion in Past Reviews

We found that many reviews that have been published to date mentioned the issue of evaluation of digital interventions for physical activity promotion. While evaluation targets and methods were mentioned in all reviews, only some reviews addressed evaluation frameworks. Among these reviews, most suggest that evaluation frameworks seem to be considered in development of digital interventions; however, it is unclear if

evaluation frameworks are used to evaluate the outcomes of digital interventions. There are several possible explanations for these findings First, most reviews aimed to synthesize the literature on the effects of digital interventions on various user outcomes, and information on evaluation frameworks may not have been coded from the primary studies by review authors. This seems unlikely because evaluation was often discussed in reviews meaning that details on evaluation frameworks were probably not reported in primary studies. Indeed, the description of the respective theoretical background of digital interventions may not be sufficiently reported in primary studies for it to be coded by reviewers [51]. Second, a focus on theoretical frameworks for development but not for the evaluation of user outcomes suggests that some digital interventions may be developed for profit, while benefits to users remain secondary or unclear. Theoretical frameworks appear to inform mechanisms of action (how digital interventions work) but are also required to define how digital interventions affect user outcomes and contribute to behavior change [25]. Third, the highly heterogeneous terminology used in the field of digital interventions means that the terms *evaluation* or *evaluation frameworks* may not have been explicitly mentioned in primary studies or reviews. Since the term *evaluation* was included in our search syntax, we only identified reviews that specifically referred to evaluation in titles, abstracts, or key words. Thus, more literature on theoretical frameworks in the context of digital interventions likely exists but was not located using our strategy. Indeed, the reviews included in this scoping review cited different primary studies meaning that the overlap in the primary literature among the reviews was very low despite the common topic (digital interventions for physical activity promotion). There were only 4 primary studies [60-63] that were cited in 5 to 6 systematic reviews. Interestingly, all 4 studies are reasonably old (published 2014-2017), given the rapid technological advancement and interest in digital tools to support physical activity. In general, all 4 studies [60-63] compared the physical activity outcomes of digital interventions supported by different digital tools with or without other engagement methods, such as human coaching, reminders, or feedback. The results and implications of these 4 studies can be summarized as follows: (1) physical activity outcomes were evaluated using objective tool data, (2) similar physical activity benefits were evident when using modern digital tools with feedback, such as smartphone apps or activity trackers, to those evident when using traditional tools, such as pedometers, (3) physical activity benefits were higher when digital interventions were combined with human support or feedback, and (4) preference for and acceptance of modern digital tools was high based on feedback from participants and use patterns recorded by the tools. Future research is required to determine the benefits of digital interventions relative to baseline physical activity and to evaluate the effectiveness of complex interventions incorporating digital tools and human coaching for physical activity promotion.

Evidence Gaps and Ideas for Future Research

Our results suggest that the production of yet another scoping review of primary literature on the topic of evaluation of digital interventions for physical activity promotion (planned as part 2 of this review) may not be necessary and could contribute to research waste. Instead, based on our results of part 1 of our study (this scoping review of reviews) we propose the following topics for future research.

First, more work is needed to identify factors that could improve the effectiveness of digital interventions for physical activity promotion. According to the majority of the included reviews, the identification of such factors could help to increase adherence to digital interventions and contribute to evaluation of efficacy of digital interventions. Digital interventions are typically complex interventions that require several elements for their effectiveness, such as personalization, feedback, engagement with the tool, or human support [64]. The contribution of these elements to the success or failure of digital interventions for physical activity promotion is unclear, primarily because this information was either not coded in reviews or not reported in the primary studies. Furthermore, sociodemographic factors, including age, gender, education, income, and digital health literacy, affect the use of and interest in digital health technologies [1] and could also facilitate or hinder the efficacy of digital interventions. Further research is needed to identify health needs or barriers associated with digital health technology use in low socioeconomic settings [65] to improve the efficacy of digital interventions for physical activity promotion in such populations [66].

Second, evaluation guidelines are required for digital interventions because complex interventions, such as digital interventions, are often insufficiently reported [67]. Until these guidelines are in place, for the description of digital interventions, authors could use already established reporting guidelines, such as the TIDieR Checklist [68], which includes a description of the rationale, theory, or goal of the elements essential to the intervention in item 2. Therefore, adherence to this reporting guideline could improve the inclusion of theoretical frameworks for digital interventions in future studies.

Third, standardized reporting of digital intervention components and outcomes is needed. The key difficulty is that a standardized and universally accepted definition of digital interventions does not exist yet. Generic terms, such as eHealth, mobile health (mHealth), or telehealth typically refer to very different digital health approaches. A recent guideline from the World Health Organization [69] refers to digital interventions as digitally supported interventions delivered via the internet or digital tools with mobile apps. This definition includes the elements of eHealth and mHealth and encompasses the modern digital tools, such as smartphone apps, but also established technologies, such as the internet in general (websites and email), mobile phones able to deliver SMS reminders or wearable sensors able to quantify physical activity. There are two main differences among any of these digital interventions: (1) the level of digital health literacy required to operate or interact with the digital technologies included in the digital intervention, which can be low for noninteractive wearable sensors to high when operating a smartphone app, and (2) the level of engagement and feedback, which can range from a passive use of a website, obtaining reminders via email or SMS to continuous tracing and feedback from smartphone apps or activity trackers. Furthermore, similar to that of nondigital interventions, the development of core

physical activity outcome sets is necessary to evaluate digital interventions in different populations [70,71].

Fourth, objective and homogeneous outcome measures should be evaluated for digital interventions using appropriate study designs with long-term follow-up. The potential for digital interventions to improve health has been scarcely realized, partly due to an insufficient knowledge base of guiding principles in the development and evaluation of such interventions [72]. While the gold standard for evaluating a health intervention is conducting a randomized controlled trial, these can take a long time and typically require many participants and extensive financial resources. Long delays to evaluate novel digital interventions in the rapidly evolving field might result in the digital interventions becoming obsolete or nonfunctional by the time the trial is completed [73]. Thus, the evaluation of digital interventions potentially requires new study designs and methods that take the iterative and rapidly evolving nature of such interventions and continuous data collection into account. Furthermore, digital interventions are at the intersection of various fields, such as behavioral, biomedical, and computing sciences. Thus, methods taken from multiple disciplines are required for development and outcome evaluation of digital interventions [74].

Fifth, the reviews included in this scoping review predominantly focused on mixed healthy or clinical samples and predominantly adult populations. Since digital interventions can support health promotion and disease prevention [1], future research should focus on the evaluation of digital interventions or digital tools in healthy populations to promote healthy lifestyle, including physical activity. Furthermore, children and adolescents are important target populations for digital interventions that focus on physical activity promotion because the use of digital technologies contributes to sedentary behavior, especially in early childhood [75]. Therefore, future research should consider potential benefits but also harms of digital technologies and thus, evaluate if digital interventions promote or hinder physical activity in children and adolescents [76].

Evidence Appraisal

Although this scoping review focused on evaluation strategies rather than outcomes of such evaluations, we performed an appraisal of the 30 systematic reviews included in our study with the AMSTAR2 tool. We found that the overall methodological quality of systematic reviews of digital interventions for physical activity promotion needs improvement, which has already been suggested in the context of other health interventions [77-79]. The overall confidence in the results of systematic reviews of digital interventions for physical activity promotion could be improved by better adherence to established reporting guidelines for systematic reviews and the prospective registration of review protocols. Due to potential financial interests in the field of digital interventions, the sources of funding for primary studies should be documented in systematic reviews. Our results are in line with those of other studies [80-82] that assessed the methodological quality of systematic reviews in telemedicine [80]; digital methods for maximizing participant engagement, participation, and retention in cohort studies [81]; or digital interventions for reducing behavioral risks of cardiovascular disease [82]. These studies [80-82] demonstrated that the majority or all of the included systematic reviews regarding digital interventions had low methodological quality, and thus, the overall confidence in the results of these systematic reviews was considered to be critically low.

Limitations

There were several limitations in this scoping review. First, the search strategy for literature was conservative due to the inclusion of the term *evaluation* in the syntax. Thus, we did not find reviews of digital interventions for physical activity promotion that omitted the term *evaluation* from their titles, abstracts, or keywords. A manual search for such reviews was beyond the scope of this review. Second, study selection and data coding were difficult due to highly heterogeneous terminology for digital interventions, physical activity outcomes and evaluation. These difficulties contributed to partially superficial coding of data with little detail on specific aspects of evaluation. We also struggled to code the data item *evaluation target* into user outcomes or tool performance. While the evaluation of well-defined user outcomes (ie, promotion of a specific physical activity outcome) was a focus of most reviews, the focus on tool performance was less clear and sometimes included as part of user outcomes (eg, acceptance of the tool). Although any 2 authors coded the data and reached consensus by discussion, a coding manual with more detail could have improved the quality of coding.

Conclusions

The evaluation of digital interventions is a high priority based on the 40 reviews included in this scoping review. Evaluations of digital interventions, including mobile apps or wearables for physical activity promotion, typically target any user outcomes and rely on objective tool data. While the development of digital interventions appears to be guided by various aspects of behavior change theory, evaluation frameworks are also required to evaluate user outcomes. Behavior change theory may provide useful guidance not only for the development of digital interventions but also for the evaluation of user outcomes in the context of physical activity promotion. Evidence gaps mentioned in most reviews included a need to (1) identify factors that could improve the effectiveness of digital interventions for physical activity promotion, such as personalization, feedback, engagement with the tool, human support, and digital literacy; (2) develop evaluation guidelines; and (3) standardize the reporting of digital intervention components and outcomes. The implementation of evaluation frameworks at the development stage and to assess user outcomes is required to ensure that digital interventions are effective for physical activity promotion.

Acknowledgments

We thank the librarian, Lara Christianson, MLS, and the team assistant, Lisa Kühne, MSc, for their assistance in designing the search strategy and performing the electronic search, respectively. We gratefully acknowledge the support of the Leibniz-Science Campus Bremen Digital Public Health (lsc-diph.de), which is jointly funded by the Leibniz Association (W4/2018), the Federal State of Bremen and the Leibniz Institute for Prevention Research and Epidemiology – BIPS.

Authors' Contributions

KKDS conceptualized the study, developed the methodology, selected the studies, coded the data, processed and analyzed the data, visualized the results, wrote the first draft of the manuscript, and reviewed and edited the manuscript. TJ conceptualized the study, coded the data, wrote the first draft of the manuscript, and reviewed and edited the manuscript. KM conceptualized the study, developed the methodology, selected the studies, performed the critical appraisals, processed and analyzed the data, visualized the results, wrote the first draft of the manuscript, and reviewed and edited the manuscript. LM selected the studies, coded the data, performed the critical appraisals, processed and analyzed the data, and reviewed and edited the manuscript. HAK selected the studies, coded the data, and reviewed and edited the manuscript. HZ conceptualized the study, developed the methodology, and reviewed and edited the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Additional material.
[PDF File (Adobe PDF File), 866 KB - publichealth_v8i5e37820_app1.pdf]

Multimedia Appendix 2
Search strategy and results.
[XLSX File (Microsoft Excel File), 19 KB - publichealth_v8i5e37820_app2.xlsx]

Multimedia Appendix 3
Overall confidence ratings (using AMSTAR2).
[XLSX File (Microsoft Excel File), 12 KB - publichealth_v8i5e37820_app3.xlsx]

Multimedia Appendix 4
Coded data.
[XLSX File (Microsoft Excel File), 43 KB - publichealth_v8i5e37820_app4.xlsx]

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Abbreviations

AMSTAR2: A Measurement Tool to Assess Systematic Reviews, version 2
mHealth: mobile health
PICOS: Population, Intervention, Comparison, Outcome, Study
PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension for Scoping Reviews

Edited by Y Khader; submitted 08.03.22; peer-reviewed by AS Aslam, S Bhattacharjee; comments to author 26.03.22; revised version received 06.04.22; accepted 09.04.22; published 23.05.22.

Please cite as:
De Santis KK, Jahnel T, Matthias K, Mergenthal L, Al Khayyal H, Zeeb H
Evaluation of Digital Interventions for Physical Activity Promotion: Scoping Review
JMIR Public Health Surveill 2022;8(5):e37820
URL: https://publichealth.jmir.org/2022/5/e37820
doi:10.2196/37820
PMID:35604757

Original Paper

Exploring the Risk of Suicide in Real Time on Spanish Twitter: Observational Study

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Abstract

Background: Social media is now a common context wherein people express their feelings in real time. These platforms are increasingly showing their potential to detect the mental health status of the population. Suicide prevention is a global health priority and efforts toward early detection are starting to develop, although there is a need for more robust research.

Objective: We aimed to explore the emotional content of Twitter posts in Spanish and their relationships with severity of the risk of suicide at the time of writing the tweet.

Methods: Tweets containing a specific lexicon relating to suicide were filtered through Twitter's public application programming interface. Expert psychologists were trained to independently evaluate these tweets. Each tweet was evaluated by 3 experts. Tweets were filtered by experts according to their relevance to the risk of suicide. In the tweets, the experts evaluated: (1) the severity of the general risk of suicide and the risk of suicide at the time of writing the tweet (2) the emotional valence and intensity of 5 basic emotions; (3) relevant personality traits; and (4) other relevant risk variables such as helplessness, desire to escape, perceived social support, and intensity of suicidal ideation. Correlation and multivariate analyses were performed.

Results: Of 2509 tweets, 8.61% (n=216) were considered to indicate suicidality by most experts. Severity of the risk of suicide at the time was correlated with sadness (ρ=0.266; *P*<.001), joy (ρ=–0.234; *P*=.001), general risk (ρ=0.908; *P*<.001), and intensity of suicidal ideation (ρ=0.766; *P*<.001). The severity of risk at the time of the tweet was significantly higher in people who expressed feelings of defeat and rejection (*P*=.003), a desire to escape (*P*<.001), a lack of social support (*P*=.03), helplessness (*P*=.001), and daily recurrent thoughts (*P*=.007). In the multivariate analysis, the intensity of suicide ideation was a predictor for the severity of suicidal risk at the time (β=0.311; *P*=.001), as well as being a predictor for fear (β=–0.009; *P*=.01) and emotional valence (β=0.007; *P*=.009). The model explained 75% of the variance.

Conclusions: These findings suggest that it is possible to identify emotional content and other risk factors in suicidal tweets with a Spanish sample. Emotional analysis and, in particular, the detection of emotional variations may be key for real-time suicide prevention through social media.

(JMIR Public Health Surveill 2022;8(5):e31800) doi:10.2196/31800

KEYWORDS

suicide; prevention; social media; Twitter; emotional analysis; eHealth; big data; content analysis; emotional content; risk factors; mental health; public health; suicide prevention

Introduction

As the cause of more than 800,000 deaths every year, suicide has become a global public health priority. It is the second leading cause of death in young people aged 15 to 29 years, and for every death, it is estimated that there are 20 other suicide attempts [1]. In Spain, suicide has been the main cause of unnatural death since 2012 [2].

According to the World Health Organization [3], suicidal behavior refers to a range of behaviors that includes thinking about suicide (or ideation), planning to commit suicide, attempting suicide, and suicide itself.

Until a few decades ago, research efforts have been focused on curbing suicide deaths by trying to predict their occurrence. This predictive approach consisted of semistructured risk assessment using lists of risk factors and sometimes included suicide risk questionnaires or scales to express risk as low, moderate, or high [4,5]. Because suicide deaths are statistically a rare event, it has been difficult to develop sensitive tools with sufficient predictive value [6]. Recent reviews [5,7-10] of these models advocate a shift from models based on suicide prediction to those that emphasize assessment and management of the risk of suicide by identifying variables related to suicide behavior and stratifying risk in terms of severity and temporality.

Suicidal behavior has been consistently found to be associated with emotional states such as depression and hopelessness [11,12]. Bryan and Rudd [9] collected different variables that have been empirically demonstrated to be essential for risk assessment: predisposition to suicidal behavior (ie, psychiatric diagnoses, previous suicidal behavior), identifiable precipitants or stressors (ie, significant loss, relationship instability), a patient's symptomatic presentation (eg, anhedonia, low self-esteem, sadness, dyssomnia, fatigue), presence of hopelessness, nature of suicidal thinking (eg, ideation, suicidal plan, lethality of means, explicit suicidal intent), impulsivity and self-control, and protective factors (eg, social support, life satisfaction). Emotional dysregulation seems to be also an important predictor of suicidal outcomes [13,14].

To improve accuracy in risk evaluations, ecological momentary assessment has been used to study suicidal behavior [15], which involves repeated sampling of people's behavior in real time in their natural environments, now typically collected via smartphones. This approach attempts to minimize recall bias and maximize ecological validity. Recent research using mobile phone–based momentary ecological assessments showed that suicidal ideation varied over short periods of time [16], indicating that real-time assessments and ecological validity could be a crucial approach for suicide prevention.

With more than 3.8 billion users around the globe [17], social media has transformed the world. People express their thoughts and emotions through social media [18]. These new forms of social interaction have been linked to suicidal behavior, nevertheless, recent studies [19] have highlighted the potential for social media to offer assistance in suicide prevention.

Twitter currently has 340 million users [20] who, in microblogging format, communicate what they are thinking or doing at a particular moment publicly with a limited number of characters. People express suicidal tendencies on Twitter [21], and although there is a support mechanism among users, this system is not automatic or in real time.

According to Christensen [22], web-based interventions for suicide prevention have focused mainly on three directions: (1) web-based screening for suicidality, (2) web-based therapeutic interventions for suicide prevention, and (3) real-time identification of individuals at risk, either by people or by computer language processing systems.

The use of social media in the real-time detection of mental health has already been proven. Specifically, Twitter has been proven useful in predicting depression [23-25], postpartum depression [24], and even posttraumatic stress disorder [26,27]. Machine learning algorithms have been used to assess the risk of suicide and identify suicidal individuals. Automatic machine learning classification systems that are able to effectively differentiate people who are at risk of suicide from those who are not [28-30] and identify temporal patterns in posts before suicide [31] have been developed. Reviews on the subject [22,32] yield similar results: social media is an empirically tested tool for suicide detection, but further validation is needed.

Recent studies have incorporated human coders in order to create language classification systems or validate machine learning results from natural language processing systems [33]. Nevertheless, the need to incorporate mental health experts in suicide assessments for the improvement of accuracy has been noted [34]. Furthermore, the detection of the risk of suicide for social media users located in Spain has yet to be explored.

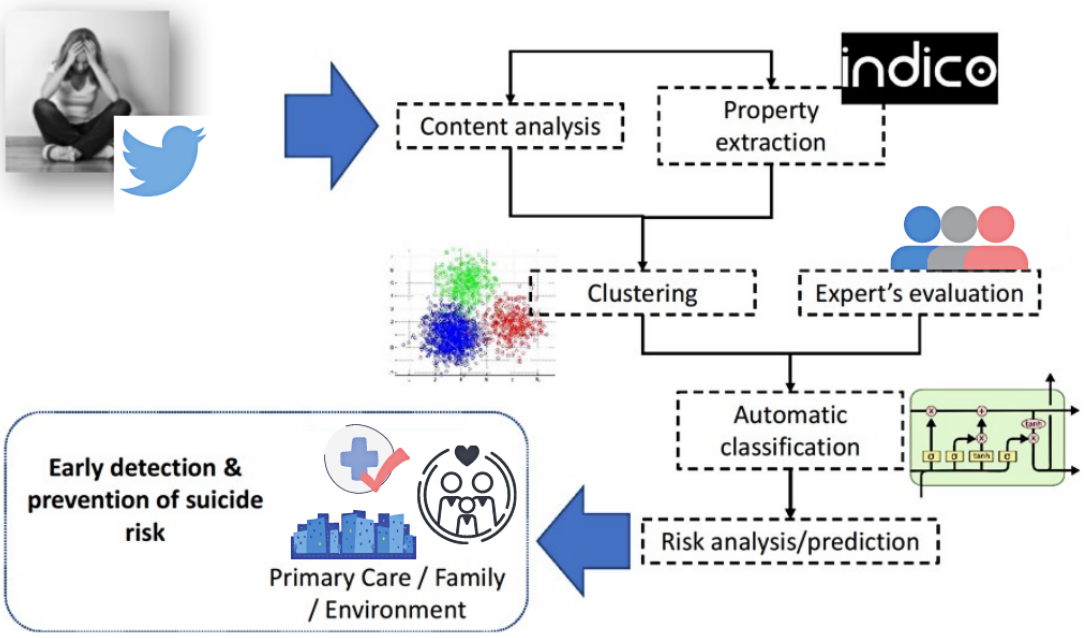
Our objective was to analyze the risk of suicide among Twitter users who post in Spanish, by assessing the emotional content of their posts and other variables that have been identified as being related to suicidal behavior, such as perception of defeat, helplessness, and social support.

Methods

Design

We conducted a cross-sectional exploratory study. To collect and analyze tweets, we used a framework based on computer technologies that we had developed previously [35]. This is a full framework (Figure 1) that has been engineered and implemented using various technologies and has been structured around a multidisciplinary team of professionals from health sciences and professionals with specialization in information technology. We focused on the Expert's evaluation stage. The first step was to obtain the Twitter entries from keywords related to suicide. To identify potentially emotional tweets, a large vocabulary of emotional terms was compiled from different sources, including the Spanish adaptation of Affective Norms for English Words [36], which provides a set of emotional normative scales for a set of words, and the Spanish dictionary of the Linguistic Inquiry and Word Count [37], which is an analysis software that calculates the degree to which people use different categories of words across a wide spectrum of texts. The use of Linguistic Inquiry and Word Count software to assess positive and negative emotions has been validated [38,39].

Figure 1. Methodology for the early detection and prevention of the risk of suicide on Twitter.



Adding properties to the text contained in the tweet facilitates and improves the identification and classification of groups at risk of suicide. Therefore, a series of properties associated with the text were obtained and added. The properties were based both on external natural language processing systems and platforms, and on internal algorithms that obtained the information through a text evaluation platform, which is completed by selected reviewers. The emotional vocabulary was organized by combining the hierarchy of emotions [40] and the tree of emotions [41]. Each emotional word was classified into 6 categories of primary emotions (love, joy, surprise, anger, sadness, and fear) and 25 subgroups of secondary emotions using affective and emotional text processing software (Indico, version 2020) that provides a toolkit of application programming interfaces (APIs). We used the following APIs for text-based analysis: Sentiment Analysis, Text Tags, Language Detection, Emotions, Personality and Personas. These APIs do not support the use of emoticons, and they ignore the appearance of these elements during text processing. A low or moderate use of emojis was observed in the content captured from Twitter that were relevant to the study. However, given that the use of emojis is ubiquitous, this fact must be taken into account when extending this work. The study of the criteria for matching between emojis and suicide or suicidal tendency is an aspect that we propose in future work in the short term.

To cluster data groups with similar characteristics—in our case, we wanted to identify groups at risk of suicide—we selected *k*-means clustering [42]. This method is based on partitioning data into *k* well-defined groups. To select the *k* value, a cross-validation method was used [43].

The clusters were analyzed in order to understand the characteristics of each one. This step needed to be carried out by a group of reviewers who were experts in the subject in order to understand the quality of the groups. The objective of this analysis was to validate that the clusters corresponded to groups at risk of suicide. At this stage, human coding was used to determine the degree of relationships of the classified tweets, based on the judgment of researchers from the fields of mental health and medicine who specialized in suicide prevention and had training in detecting the risk of suicide.

An automatic classifier with clusters and tweets as input was created. This classifier was capable of receiving new tweets and classifying them into one of the groups in order to determine whether there was a risk of suicide or not. We used a long short-term memory neural network.

Tweets were selected using Twitter's API. Because most Twitter accounts were not geolocated, we selected posts written in Spanish. We checked this using both the Twitter information obtained through the API and by using a Language Detection API (Indico). We excluded posts in Latin-Spanish language because the cultural context of the tweet could be unknown. These tweets were collected between November 2019 and February 2020. The study included 25 psychologist evaluators with clinical or research experience who were trained to assess the tweets for the variables of the study. Each tweet was randomly assigned to 3 different evaluators. Each expert evaluated a tweet independently, without knowing to which other evaluators the tweet had been assigned. Assessments were carried out using a smartphone-based software. The tweets were evaluated between the months of March and April 2020.

Study Variables

Primary

Only posts from the data set that were considered to be relevant by most experts were subsequently analyzed. Tweets were considered relevant if the content of the text was related to a potential risk of suicide of the author of the tweet. Tweets in which—(1) the text did not correspond to content related to a possible risk of suicide or associated emotional states; (2) the text was written in a language other than Spanish or the text was written in Latin Spanish; (3) the text of the tweet was

ambiguous (ie, the context was unknown); or (4) the text of the tweet was not suicide-relevant for any other reason were and discarded.

Secondary

Outcome Variable

The outcome variable was the severity of the risk of suicide at the moment of writing the tweet. We used a scale based on a suicide risk continuum with 5 levels [9]: (0) nonexistent risk, (1) mildly suicidal, (2) moderately frequent, (3) severely frequent, and (4) extremely frequent with intense and enduring suicidal ideation, specific plans, clear subjective and objective intent, impaired self-control, severe dysphoria, many risk factors, and no protective factors (ie, extreme risk).

Valence

Valence represented if the emotional valence of the tweet was positive or negative. If the value was greater than 50, it was considered that the text expressed a positive or pleasant feeling. If it was less than 50, it was considered to have a negative valence, that is, it expressed a negative, aversive, or unpleasant feeling. This was assessed on a scale from 0 and 100, using 2 decimal places.

Emotional Content

The level of anger, joy, fear, sadness, and surprise expressed in each tweet was evaluated on a scale from 0 and 100 (with 2 decimal places), with values closest to 100 being the highest level of the emotion.

Relevant Personality Traits

Traits—extroversion, if the author of the text showed extroversion(ie, is a person who is focused and interested in the outside world); sensory, if the author has a sensory tendency when processing information (ie, is a person who pays attention to details and prefers to work with concrete facts than with speculation or possibilities); rational, if the person has a tendency to make decisions based on logic, using an analytical and objective approach(ie, is a person who supports their decisions with impersonal analysis rather than with personal values); and judgment, if the author of the post has a preference for a planned (stable and organized, rather than spontaneous and flexible) life—were evaluated on a scale between 0 and 100 (with 2 decimal places), with values closest to 100 being the closest to that trait. These personality traits were collected from Myers-Briggs Type Indicators [44].

Other Variables

Other relevant variables on suicide risk assessments were also collected in the event that the information available was sufficient to assess them (or left blank if the parameter was not identifiable in the content of the tweet): (1) feelings of defeat, rejection, or both, if it was possible to identify a stressful event that generated feelings of defeat, rejection, or both feelings in the text of the author; (2) desire to escape from the situation, or if desire or will to run from a situation can be identified, evaluated using a dichotomous scale (yes or no); (3) social support or possibility of perceived help was evaluated dichotomously (yes or no); (4) feelings of helplessness or lack of coping resources were evaluated dichotomously (yes or no); (5) the general risk of suicide for the author of the tweet was evaluated on a scale between 0 and 4, with 0 being no risk and 4 being an extreme risk; (6) daily recurring thoughts of suicide was evaluated dichotomously (yes or no), and the intensity of autolytic thoughts was assessed on a scale from 0 to 10, with 0 being not intense and 10 being very intense; (7) content related to the tweet author's sleep, insomnia, or hypersomnia was evaluated dichotomously (yes or no).

Statistical Analysis

Statistical analyses were conducted using SPSS software (version 22; IBM Corp). First, the sample distribution was analyzed. Kolmogorov-Smirnov values <0.05 were obtained for all variables; thus, nonparametric statistics were used. For quantitative variables, median and interquartile range were calculated, and for qualitative variables, frequency and percentages were calculated. The dependent variable (the severity of the risk of suicide at the present time) was analyzed as a continuous scale with a minimum of 0 and a maximum of 4. Spearman correlations between the severity of the risk of suicide at the time and the variables were calculated. Severity of the risk of suicide at the time was compared between qualitative variables using the Mann-Whitney *U* test (when there were 2 different groups) or the Kruskal-Wallis test (when there were more than 2 groups). A multivariate model was developed for severity of the suicidal risk at the time of tweeting. The independent variable was added into the regression model [45], and a final model was obtained. Linear regression was used since the residuals of the model had a finite mean, constant variance, and normal distribution (above all, because the sample size was very high; with the central limit theorem, any distribution with constant mean and variance, if it has a large enough sample size, has a normally distributed mean). However, bootstrapping analysis with 2000 samples was also conducted. The mean value of the 2 or 3 evaluators was used for continuous and qualitative variables, and the coinciding value between 3 evaluators, or 2 of 3 evaluators, was used. The interrater reliability was calculated using Fleiss κ. *P* values <.05 were considered to be significant.

Ethical Issues

All procedures contributing to this work complied with the ethical standards of the Clinical Research Ethics Committee of Aragón (Department of Health, Government of Aragón, Spain) and with the Helsinki Declaration of 1975, as revised in 2013 [46]. The study protocol was approved by the Clinical Research Ethics Committee of Aragón, Spain (17/0127, with the number PI21/164).

Results

A total of 2509 tweets were obtained, of which 2018 were deemed not relevant by 3 evaluators, and 275 were deemed not relevant by 2 of 3 evaluators. There were 216 tweets that were found to be relevant by most evaluators, with 68 tweets considered to be relevant by all evaluators, exhibiting moderate reliability (Fleiss κ=0.41).

Tweets mainly conveyed sadness and defeat, with there being no desire to escape, no support, and no feelings of helplessness

(Table 1). The median overall risk of suicide was 1.50 (IQR 1.00) on a scale from 0 to 4. The median severity of risk was 1.00 (IQR 1.16); 96.9% (186/192) of tweets did not indicate the presence of daily recurring thoughts of suicide, and the median intensity of suicidal thoughts was 4.50 (IQR 3.00) on a scale from 0 to 10.

Table 1. Description of the tweets deemed relevant.

Variables	Value
Valence[a], median (IQR)	21.58 (24.25)
Emotional content[a] (n=216), median (IQR)	
Anger	24.00 (34.00)
Joy	0.00 (1.50)
Fear	17.25 (32.37)
Sadness	51.41 (39.12)
Surprise	0.50 (5.50)
Relevant personality traits[a] (n=216), median (IQR)	
Extroversion	28.00 (34.29)
Sensory	25.16 (29.25)
Rational	19.50 (27.37)
Judgement	19.00 (32.00)
Feelings of defeat or rejection (n=98), n (%)	
Defeat	61 (62.2)
Rejection	16 (16.3)
Both	21 (21.4)
Desire to escape (n=161), n (%)	
Yes	25 (15.5)
No	136 (84.5)
Social support or possibility of perceived help (n=196), n (%)	
Yes	4 (2.0)
No	192 (98.0)
Feelings of helplessness (n=152), n (%)	
Yes	57 (37.5)
No	95 (62.5)
Suicide risk variables[b] (n=216), median (IQR)	
General risk	1.50 (1.00)
Severity suicidal risk at present moment (real-time risk)	1.00 (1.16)
Daily recurrent thoughts of suicide (n=192), n (%)	
Yes	6 (3.1)
No	186 (96.9)
Intensity of autolytic thoughts[c], median (IQR)	4.50 (3.00)
Content related to insomnia or hypersomnia (n=210), n (%)	
Yes	4 (1.9)
No	206 (98.1)

[a]These variables were evaluated on a scale from 0 to 100.

[b]These variables were evaluated on a scale from 0 to 4.

[c]This variable was evaluated on a scale from 0 to 10.

There were direct correlations between severity of the risk of suicide at the time of generating the tweet and sadness, general risk, and intensity of suicide thoughts, as well as inverse correlations with extroversion, rational trait, and joy (Table 2).

The severity of risk of suicide at the time of generating the tweet was higher in people who expressed feelings of defeat, rejection, desire to escape, feelings of helplessness, lack of social support, and daily recurrent thoughts (Table 3).

The linear regression model (R^2=0.750; adjusted R^2=0.710) showed that the intensity of autolytic thoughts, fear, and valence were predictors of the severity of the risk of suicide at the time (Table 4). Both the intensity of autolytic thoughts and valence had positive coefficients, and fear had a negative coefficient. This indicated that when intensity was higher, valence was more positive, and when fear was lower, the severity of suicidal risk was higher. The model explained 75% of the variance.

Table 2. Spearman correlations between variables and severity of the risk of suicide at the time of writing the tweet.

Variables	ρ	*P* value
Valence	–0.069	.31
Emotional content		
Anger	–0.013	.85
Joy	–0.234	.001
Fear	–0.097	.16
Sadness	0.266	<.001
Surprise	–0.075	.27
Relevant personality traits		
Extroversion	–0.22	.001
Sensory	–0.115	.09
Rational	–0.244	<.001
Judgement	–0.128	.06
Suicide risk variables		
General risk	0.908	<.001
Intensity of autolytic thoughts	0.766	<.001

Table 3. Comparison of severity of the risk of suicide at the time of writing the tweet between qualitative variables.

Variables	Severity of the risk of suicide at the moment (real-time risk), median (IQR)	*P* value
Feelings of defeat or rejection		
Defeat	1.33 (1.42)	.003
Rejection	0.33 (1.25)	
Both	1.66 (1)	
Desire to escape		
Yes	1 (0)	<.001
No	1 (1.17)	
Social support or possibility of perceived help		
Yes	0.33 (0.66)	.03
No	1 (1.16)	
Feelings of helplessness		
Yes	1.5 (1)	.001
No	1 (1.17)	
Daily recurrent thoughts of suicide		
Yes	2.16 (1.30)	.007
No	1 (1)	
Content related to insomnia or hypersomnia		
Yes	0.75 (0.63)	.22
No	1 (1.16)	

Table 4. Linear regression model coefficients indicating the relationship to severity of the risk of suicide at the time of writing the tweet.

Variables	Coefficient (95% CI)	*P* value
Constant	0.110 (–0.169, 0.412)	.45
Intensity of autolytic thoughts	0.311 (0.250, 0.370)	.001
Fear	–0.009 (–0.015, –0.005)	.01
Valence	0.007 (0.002, 0.013)	.009

Discussion

Suicide prevention is a crucial field that needs to be developed to stop preventable deaths worldwide. The findings of our study reveal that social media can be used to help to identify individuals at risk. These findings suggest that it is possible to identify suicidal behavior through Spanish tweets, and it is possible to identify these posts, not only by using a suicide-related lexicon but also, by filtering tweets based on their emotional content. Tweets that show sadness, defeat, and perceived lack of social support suggest that there is a risk of suicide. These variables have been commonly associated with symptoms of depression and hopelessness [12,47].

One of the main challenges in suicide prevention is identifying not only the people at risk of experiencing suicidal behavior at some point in their lives but those who are at risk at a particular moment, in our case, while they are writing the tweet.

Suicidal ideation and its risk factors can fluctuate over short periods of time [16], which demonstrates the importance of differentiating general suicide risk (or suicide status, such as in individuals with long-term risk factors) from real-time suicide risk. In this exploratory study, we emphasized assessment of suicide risk at the moment of writing the post. Our results provide some clues about the phenomenon of suicidal behavior.

In our study, although the *variable desire to escape from the situation* was not identifiable in most posts showing potential risk, it was related to an increase in the severity of the risk at the time of writing the tweet in posts that expressed a desire to escape.This outcome could suggest that the variable of the desire to run from a suffering situation may be only relevant in situations with an increased risk of suicide at that time. We found the same pattern for feelings of helplessness at the time, which was only identifiable in high-risk tweets. These results are consistent with recent conceptualizations of acute suicidal behavior that suggest that this feeling of entrapment—"in which the escape from an unbearable life situation is perceived as both urgent and impossible" [48]—is linked with imminent suicidal behavior. Nevertheless, further research is needed.

Individuals exhibiting high levels of negative urgency and emotion reactivity might be more likely to develop suicidal ideation and resort to self-harm while experiencing negative affective states [14,49]. In our sample, tweets with higher risk (at the time of writing the tweets) were identified by higher sadness, higher general risk, and higher intensity of suicidal thoughts on a daily basis. In addition, they similarly showed feelings of defeat and rejection, as well as the perception of a lack of social support. These results are consistent with those in literature, with lack of social support or isolation being an especially well-established risk factor [3].

Although the role of impulsivity in suicidal behavior has not been clearly defined yet [50,51], it appears that a considerable proportion of suicide attempts are related to impulsive behavior [52,53]. In our study, we also included personality trait variables. Our results suggest that people at risk at the time of writing their tweet might show less extroversion and less rational personality traits in their posts, which could be associated with greater impulsiveness. Further research would shed more light on this subject.

Although insomnia or sleep problems variables have been identified as risk factors in suicide assessments, our findings suggest that this variable is not identifiable or relevant to social media posts. One study [54] notes that only nightmares are associated with suicidality.

We obtained preliminary data that might help us to predict increased real-time suicide risk. The interpersonal theory of suicide [55] posits that the simultaneous occurrence of 2 psychological states, a perceived burden to others, and a frustrated belonging or social isolation, as well as hopelessness regarding the potential of these states to change, results in the desire for suicide. Our findings are consistent with this theory, showing that sadness, feeling of defeat, or perceived lack of support are related to high-risk tweets. However, according to this theory, the simultaneous presence of suicidal desire and a high tolerance for pain and fear of death would be necessary to produce lethal or near-lethal behavior. The interpersonal theory of suicide also posits that high risk occurs when tolerance for pain and fear increases [49,56]. Our results seem to also suggest that real risk appears when ideation intensity increases and the fear of suicide decreases, making the resulting emotional valence less unpleasant. In other words, the detection of a decrease in fear and, therefore, a less aversive emotional state could predict an increased risk of suicidal behavior at the time on social media. If these variables effectively and consistently prove their ability to predict an increase in risk at the time, we could generate real-time machine learning systems that would detect predictor emotional states, such as the decrease in fear, to prevent potential deaths.

Our study has strengths but also limitations. The cross-sectional design of this study provided limited data about suicidal phenomenon on social networks. In the future, it would be interesting to be able to design a study that screens variation in emotional states and suicide risk over time as this may provide more relevant information on how the risk of suicide varies.

Twitter is considered to be one of the most popular social media platforms, with the greatest immediacy in posting, but because there is a character limit, some variables are barely detectable or measurable. More complex feelings or constructs are difficult to evaluate. Future research could include the evaluation of conversation threads or tweets in their context (for example, by taking into account tweets within the previous 24 hours), which would allow more accurate evaluations of relevant variables in suicide risk assessments.

The interrater reliability was moderate, differences between research and the clinical professional profile of the experts might have had an impact on reliability. In future investigations, reliability will be assessed based on expert profiles, and intensive specific training will be conducted.

One of the strengths of our study is that it incorporates experts in suicide risk assessment. In future research, it would be interesting to introduce validated scales to measure suicidality so that expert risk detection could be effectively validated. Moreover, it would be interesting for future research to use social media users with past suicide attempts to screen and validate our findings.

Our findings—identifying emotional content that might be relevant for real-time suicide prevention—can contribute to the development of new technology-based screening systems; however, more robust research is needed to establish whether social media screening can effectively reduce suicide outcomes and whether there is a way to ethically reach those individuals at risk.

Acknowledgments

We would like to thank Afda Aragón, the B21_20R, B03_20R and DisCo-T21-20R Research Groups of the Department of Research, Innovation and Universities of the Aragon Regional Authority (Spain); and the European Regional Development Fund *Otra forma de hacer Europa*.

Conflicts of Interest

None declared.

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Abbreviations

API: application programming interface

Edited by H Bradley; submitted 06.07.21; peer-reviewed by X Li, K Reuter; comments to author 08.11.21; revised version received 22.12.21; accepted 24.02.22; published 17.05.22.

Please cite as:
García-Martínez C, Oliván-Blázquez B, Fabra J, Martínez-Martínez AB, Pérez-Yus MC, López-Del-Hoyo Y
Exploring the Risk of Suicide in Real Time on Spanish Twitter: Observational Study
JMIR Public Health Surveill 2022;8(5):e31800
URL: https://publichealth.jmir.org/2022/5/e31800
doi:10.2196/31800
PMID:35579921

Original Paper

Cross-Verification of COVID-19 Information Obtained From Unofficial Social Media Accounts and Associated Changes in Health Behaviors: Web-Based Questionnaire Study Among Chinese Netizens

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Abstract

Background: As social media platforms have become significant sources of information during the pandemic, a significant volume of both factual and inaccurate information related to the prevention of COVID-19 has been disseminated through social media. Thus, disparities in COVID-19 information verification across populations have the potential to promote the dissemination of misinformation among clustered groups of people with similar characteristics.

Objective: This study aimed to identify the characteristics of social media users who obtained COVID-19 information through unofficial social media accounts and were (1) most likely to change their health behaviors according to web-based information and (2) least likely to actively verify the accuracy of COVID-19 information, as these individuals may be susceptible to inaccurate prevention measures and may exacerbate transmission.

Methods: An online questionnaire consisting of 17 questions was disseminated by West China Hospital via its official online platforms, between May 18, 2020, and May 31, 2020. The questionnaire collected the sociodemographic information of 14,509 adults, and included questions surveying Chinese netizens' knowledge about COVID-19, personal social media use, health behavioral change tendencies, and cross-verification behaviors for web-based information during the pandemic. Multiple stepwise regression models were used to examine the relationships between social media use, behavior changes, and information cross-verification.

Results: Respondents who were most likely to change their health behaviors after obtaining web-based COVID-19 information from celebrity sources had the following characteristics: female sex (P=.004), age ≥50 years (P=.009), higher COVID-19 knowledge and health literacy (P=.045 and P=.03, respectively), non–health care professional (P=.02), higher frequency of searching on social media (P<.001), better health conditions (P<.001), and a trust rating score of more than 3 for information released by celebrities on social media (P=.005). Furthermore, among participants who were most likely to change their health behaviors according to social media information released by celebrities, female sex (P<.001), living in a rural residence rather than first-tier city (P<.001), self-reported medium health status and lower health care literacy (P=.007 and P<.001, respectively), less frequent search for COVID-19 information on social media (P<.001), and greater level of trust toward celebrities' social media accounts with a trust rating score greater than 1 (P≤.04) were associated with a lack of cross-verification of information.

Conclusions: The findings suggest that governments, health care agencies, celebrities, and technicians should combine their efforts to decrease the risk in vulnerable groups that are inclined to change health behaviors according to web-based information but do not perform any fact-check verification of the accuracy of the unofficial information. Specifically, it is necessary to correct the false information related to COVID-19 on social media, appropriately apply celebrities' star power, and increase Chinese netizens' awareness of information cross-verification and eHealth literacy for evaluating the veracity of web-based information.

(JMIR Public Health Surveill 2022;8(5):e33577) doi:10.2196/33577

KEYWORDS

COVID-19; pandemic; social media; behavior change; information cross-verification; eHealth literacy

Introduction

Background

Because of the unprecedented magnitude of the COVID-19 pandemic and initial uncertainty about the virus, strategies, such as maintaining social distance and frequent hand washing, were deemed to be the most effective and feasible countermeasures [1]. In such public health crises, the general public always plays a crucial role in mitigating the spread of the disease by actively engaging in effective preventive health behaviors [2]. Thus, efficient and effective anti–COVID-19 information management in combination with public adherence to preventive health behaviors is essential for slowing the spread of the virus [3]. Social media use has increased tremendously over the last few decades because of the speed of communication, large volume of users, accessibility, and transparency [4]. Several social media platforms are available worldwide, including Facebook, Twitter, and YouTube [5], along with Chinese equivalents, such as WeChat [6], Sina Weibo [7], and TikTok [8], which offer timely updates, vivid descriptions with animated pictures, and short videos [9], and have emerged as the most preferred and actively used social media platforms among Chinese netizens [10]. Chinese netizens are defined by the China Internet Network Information Center (CNNIC) as Chinese citizens who use the internet for at least 1 hour per week, and the number has reached 1.032 billion as of December 2021 [11].

Because the pandemic put individuals at high risk of infection and created a situation of great uncertainty, individuals experienced high levels of concern and anxiety. Thus, they began to seek help through the most accessible avenues available to them, namely, social media [12], in the hope that these platforms would help them make sound decisions about their health and safety [13]. High use volume and nonphysical contact have made social media a powerful tool for facilitating the dissemination of information pertaining to COVID-19 prevention protocols and safety guidelines [14]. At the onset of the outbreak in China on January 23, 2020, there was an 87% increase in social media use [15]. These platforms also offer Chinese netizens an open and free space to make comments; interact with others; and produce, obtain, disseminate, and retransmit information about COVID-19 without extensive restrictions or censorship [16].

Prior Work

Previous studies have found that social media can be used to disseminate health improvement measures [17], promote individual adoption of healthier behavioral patterns [18], and prevent negative health behaviors [19]. However, individuals can also be influenced to make harmful or counterproductive behavioral changes by misinformation disseminated through social media [20]. Misinformation refers to false or inaccurate information that is spread intentionally or unintentionally [21], and can be easily disseminated to large audiences on social media platforms at a very low cost [22]. The extensive COVID-19 information disseminated on social media has been extremely multifarious, with various unofficial entities engaging in producing and spreading information or misinformation ranging from hard facts to unfounded conspiracy theories [23]. In China, nearly 87% of netizens said they had encountered misinformation during the pandemic [24]. Notably, this misinformation not only causes the spread of unnecessary fears and conspiracies, but also distorts individuals' behavioral responses to the disease [25].

Individuals with access to various sources of COVID-19 information are more likely to be knowledgeable about the correct preventive measures, which facilitates appropriate health behavioral changes [26]. Fact checking web-based information, especially that released by unofficial accounts, by finding a consensus with other official social media sources or by directly consulting physicians or specialists is a feasible approach [27]. Such cross-validation efforts help netizens perceive health issues accurately when both accurate information and misinformation coexist on social media [28]. In addition, past research has shown that people's trust in social media accounts affects their tendency to follow preventive health information posted by that account and their decision to validate that information [29]. Therefore, it is crucial to identify vulnerable netizens who are

likely to change their health behaviors based on information from unofficial social media accounts, but are also unlikely to verify that information.

The Goals of This Study

The original contribution of this study is related to its aim to increase knowledge of the behaviors of Chinese netizens during the pandemic by addressing some gaps in the literature. In particular, this study identified the characteristics of Chinese netizens who primarily obtain COVID-19 information from unofficial social media and who are (1) more likely to change their health behaviors based on information from unofficial social media and (2) inclined to directly change their health behaviors without cross-referencing the veracity of web-based information released by unofficial sources.

Methods

Setting

West China Hospital (WCH), Sichuan University, is one of the largest single-site hospitals in the world, ranking second among general hospitals in China [30]. WCH has official social media accounts on WeChat, Weibo, and TikTok that are operated by its publicity department. As of May 2020, the numbers of active followers of WCH's social media accounts were 1,500,000 (WeChat), 495,000 (Weibo), and 421,000 (TikTok). Taking advantage of WCH's large number of Chinese netizens based on its official social media accounts, this study distributed a web-based cross-sectional survey using convenience sampling through WCH's official social media accounts. Data were collected through an anonymous online questionnaire from May 18 to May 31, 2020.

Ethical Considerations

The study was approved by the Research Ethics Committee of WCH. The manuscript adhered to the reporting standards outlined by the Checklist for Reporting the Results of Internet E-Surveys (CHERRIES) and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [31,32].

Study Design and Recruitment

The questionnaire was created on the online survey platform *Wen Juan Xing* (similar to Qualtrics) and generated with a URL link for dissemination. Thereafter, the URL link to access the questionnaire was posted on the social media accounts of WCH. Specifically, the followers of WCH's social media accounts who met the inclusion criteria were invited to visit the URL link and answer the questionnaire, and were encouraged to share the link with others. Because of the nature of the questionnaire, the inclusion criteria were individuals who (1) were at least 18 years old; (2) were able to read and complete the online questionnaire independently; and (3) voluntarily agreed to participate in the survey after being provided with information about the objectives and scope of the study, as well as privacy measures and instructions for completing the survey. The privacy of each participant was protected because the questionnaire did not collect individually identifiable information. Participants were free to exit from the questionnaire at any point. All participants were only allowed to submit 1 survey response, which was verified through *Wen Juan Xing* by automatically verifying that each participant's IP address only submitted 1 response.

Instruments and Measures

Instruments

The authors initially developed a questionnaire that contained 21 questions based on a literature review of relevant studies, as well as World Health Organization materials on COVID-19 [33,34] and the COVID-19 Protection Manual [35], and it was presented in Mandarin Chinese. To ensure its readability, first, the researchers stopped pedestrians at a central intersection and asked if they would be willing to answer the survey. Then, the questionnaire was modified according to the respondents' feedback regarding any ambiguities or areas of confusion.

To ensure the validity of the questionnaire, 20 experts from different fields were selected from the Sichuan Provincial health service system, including respiratory physicians, epidemiologists, medical informaticists, and health care policy-makers. The questionnaire was evaluated by the panel of experts to validate its content with intended constructs and theories. The content validity of the questionnaire was assessed by the item-level content validity index (CVI), which was measured on a 4-point Likert scale, including different parameters such as relevance, clarity, simplicity, and ambiguity [36]. Items with a CVI >0.8 were retained, and context-specific adjustments were made according to the feedback provided by the experts. As a result, the final questionnaire consisted of 17 questions, and of these, 10 were single choice, 2 were multiple choice, and 5 were ranking questions (Multimedia Appendix 1). After the questionnaire was revised according to the experts, 30 Chinese netizens were randomly selected to read the survey. All feedback was used to adjust the survey, including rectification and clarification of words or phrases. Finally, it included 4 subsets of questions described in the following sections.

Sociodemographic Information

A set of sociodemographic variables was collected in the first section of the questionnaire, including gender, age (referenced from the categorization by the National Bureau of Statistics of China), educational status, occupation (referenced from the standard occupational classification in China [37]), living area (classified by the National Statistics Bureau), perceived health status, and self-assessed health literacy.

Social Media Use and Trust Rating

Social media use was measured by the amount of time (in hours) spent on social media per day and the frequency of searching for information related to COVID-19. A multiple-choice question was asked about which of the 5 types of accounts were preferred when searching for information about COVID-19 on social media. To measure the trustworthiness of a specific source of web-based information on social media, the participants were asked to rate the perceived trustworthiness of each type of information source using a 5-point Likert scale from 1 (least trustworthy) to 5 (most trustworthy).

Basic Knowledge of COVID-19

Participants' basic knowledge of COVID-19 was evaluated using 4 questions developed based on the COVID-19 Protection Manual (China Mainland Version, January 2020), including 1 multiple-choice question related to COVID-19 transmission and 3 single-choice questions centered around the proper use of masks. Each correct answer was assigned 1 point, and incorrect answers were assigned 0 points for a maximum of 6 points.

Behavioral Changes and Cross-Verification of Information

To measure whether the individuals would change their health behaviors, participants were asked, "Did you change health behaviors based on the COVID-19 information on social media?" with answer options "Yes" and "No." Subsequently, a question ("Did you cross-verify the authenticity of COVID-19 information on social media?") was asked to identify the participants' cross-verification behavior, with answer options "Yes" and "No." Although the Likert approach is more accurate in capturing the variation and degree of behavioral change and cross-validation, the criterion here was the presence or absence of respondents' actual action; thus, binary measurement was used for analysis.

Statistical Analysis

Descriptive statistics were used to assess all sociodemographic characteristics of the participants. Frequency and case-weighted percentages were calculated to describe sociodemographic parameters and level distributions among participants. Differences in characteristics between groups were investigated with descriptive analyses performed according to the characteristics of the data, including the chi-square test and Kruskal-Wallis test.

Multiple stepwise regression was used to examine the association between the independent and dependent variables [38]. Specifically, the authors first included sociodemographic information, social media use, sources of information on social media, and the trust rating as control variables for Model 1, with the dependent variable "COVID-19 knowledge score." Then, participants who obtained web-based information from less reliable sources, namely, celebrity social media accounts, were further evaluated in Models 2 and 3. In Model 2, the COVID-19 knowledge score was introduced with the dependent variable "behavior change." Finally, those participants who changed or did not change their behaviors were introduced as a control variable in Model 3, with the dependent variable "information cross-verification." Key outcomes were presented according to standardized regression coefficients, adjusted odds ratios (aORs), and 95% CIs, and were analyzed using SPSS version 23 (IBM Corp). A P value <.05 was considered to be statistically significant.

Results

Sample Characteristics

A total of 15,055 Chinese netizens completed the survey, and 14,509 responses were included in the study after incomplete survey responses were excluded (14,509/15,055, 96.4%). The descriptive analysis shown in Table 1 indicates that socioeconomic attributes varied by age group. Among the respondents, 20.7% (3008/14,509) were male and 42.4% (6151/14,509) were between 30 and 39 years old. Furthermore, more than half (9792/14,509, 67.5%) of the participants had a bachelor's degree or higher, while 5.9% (849/14,509) reported that they lived in rural areas. Moreover, older participants were more likely to report a poor health status and low health care literacy. Furthermore, younger participants were generally more active in web-based activities (P<.001). In contrast, older respondents (≥40 years) used social media more often to seek COVID-19 information than other age groups (P<.001).

Table 1. Demographic characteristics of the participants.

Characteristic	Total (N=14,509), n (%)	Age groups (years)				*P* value
		18-29 (N=5723), n (%)	30-39 (N=6151), n (%)	40-49 (N=1714), n (%)	≥50 (N=921), n (%)	
Gender						<.001[a]
Male	3008 (20.7)	1297 (22.7)	1139 (18.5)	349 (20.4)	223 (24.2)	
Female	11,501 (79.3)	4426 (77.3)	5012 (81.5)	1365 (79.6)	698 (75.8)	
Educational status						<.001[b]
Junior high school or below	407 (2.8)	100 (1.7)	89 (1.4)	118 (6.9)	100 (10.9)	
High school	1242 (8.6)	368 (6.4)	420 (6.8)	240 (14.0)	214 (23.2)	
Junior college	3068 (21.1)	1218 (21.3)	1115 (18.1)	439 (25.6)	296 (32.1)	
Undergraduate degree	7685 (53.0)	3182 (55.6)	3480 (56.6)	742 (43.3)	281 (30.5)	
Master's degree or above	2107 (14.5)	855 (14.9)	1047 (17.0)	175 (10.2)	30 (3.3)	
Occupation						<.001[a]
Student	1661 (11.4)	1637 (28.6)	22 (0.4)	1 (0.1)	1 (0.1)	
Staff member in the government	2436 (16.8)	656 (11.5)	1282 (20.8)	367 (21.4)	131 (14.2)	
Health care provider	2192 (15.1)	1075 (18.8)	879 (14.3)	183 (10.7)	55 (6.0)	
Staff member in a company	3258 (22.5)	978 (17.1)	1737 (28.2)	463 (27.0)	80 (8.7)	
Self-employed entrepreneur	965 (6.7)	270 (4.7)	518 (8.4)	142 (8.3)	35 (3.8)	
Other	3997 (27.5)	1107 (19.3)	1713 (27.8)	558 (32.6)	619 (67.2)	
Current residence						<.001[a]
First-tier city	549 (3.8)	280 (4.9)	202 (3.3)	47 (2.7)	20 (2.2)	
Second-tier city	9133 (62.9)	3562 (62.2)	4078 (66.3)	980 (57.2)	513 (55.7)	
Other city	3978 (27.4)	1444 (25.2)	1646 (26.8)	564 (32.9)	324 (35.2)	
Rural area	849 (5.9)	437 (7.6)	225 (3.7)	123 (7.2)	64 (6.9)	
Perceived health status						<.001[b]
Good	9251 (63.8)	4106 (71.7)	3679 (59.8)	962 (56.1)	504 (54.7)	
Medium	4515 (31.1)	1393 (24.3)	2153 (35.0)	643 (37.5)	326 (35.4)	
Poor	743 (5.1)	224 (3.9)	319 (5.2)	109 (6.4)	91 (9.9)	
Health care literacy						<.001[b]
High	5978 (41.2)	2589 (45.2)	2373 (38.6)	666 (38.9)	350 (38.0)	
Medium	7090 (48.9)	2598 (45.4)	3155 (51.3)	871 (50.8)	466 (50.6)	
Low	1441 (9.9)	536 (9.4)	623 (10.1)	177 (10.3)	105 (11.4)	
Time spent on social media per day (hours)						<.001[b]
≤1	797 (5.5)	266 (4.6)	327 (5.3)	119 (6.9)	85 (9.2)	
>1 to ≤3	7108 (49.0)	2435 (42.5)	3233 (52.6)	925 (54.0)	515 (55.9)	
>3 to ≤5	4376 (30.2)	1916 (33.5)	1737 (28.2)	485 (28.3)	238 (25.8)	
>5 to ≤7	1418 (9.8)	670 (11.7)	565 (9.2)	122 (7.1)	61 (6.6)	
>7	810 (5.6)	436 (7.6)	289 (4.7)	63 (3.7)	22 (2.4)	
Frequency of browsing information related to COVID-19						<.001[b]
Rarely	573 (3.9)	267 (4.7)	230 (3.7)	47 (2.7)	29 (3.1)	
Sometimes	2107 (14.5)	922 (16.1)	912 (14.8)	177 (10.3)	96 (10.4)	

Characteristic	Total (N=14,509), n (%)	Age groups (years)				*P* value
		18-29 (N=5723), n (%)	30-39 (N=6151), n (%)	40-49 (N=1714), n (%)	≥50 (N=921), n (%)	
Often	11,829 (81.5)	4534 (79.2)	5009 (81.4)	1490 (86.9)	796 (86.4)	

[a]Chi-square test.

[b]Kruskal-Wallis test.

Use of and Trust in Various Social Media Sources and COVID-19 Knowledge

Table 2 presents Chinese netizens' use of and trust in different sources of web-based information on social media. The participants sought COVID-19 information through a variety of social media channels, favoring professional news media (12,706/14,509, 87.6%), government agencies (12,255/14,509, 84.5%), and health care media (8124/14,509, 56.0%), followed by hospital institutions (7107/14,509, 49.0%) and celebrities (4017/14,509, 27.7%). The trust scores for different sources were averaged to generate an overall score, which indicated that the most trusted source of COVID-19 information was hospital institutions (mean 4.52, SD 0.69), followed by government agencies (mean 4.46, SD 0.76), professional news media (mean 4.18, SD 0.79), health care media (mean 3.86, SD 0.87), and celebrities (mean 3.21, SD 1.07).

Table 3 shows that the sample of Chinese netizens had a high level of knowledge of preventive measures against COVID-19, but few participants lacked awareness of COVID-19 "airborne" transmission (correct option: 8990/14,509, 62.0%). In addition, 5.0% (723/14,509) chose the incorrect types of masks for preventing COVID-19 and 7.2% (1052/14,509) selected incorrect options for mask use methods. In total, 3.1% (448/14,509) of the respondents perceived "drinking alcohol," "sauna or steaming," and "rinsing with light saltwater'' as feasible COVID-19 countermeasures.

Table 2. Sources of COVID-19 information on social media and source trust scores.

Variable	Total (N=14,509)	Age groups (years)				*P* value
		18-29 (N=5723)	30-39 (N=6151)	40-49 (N=1714)	≥50 (N=921)	
Social media outlets used to search for COVID-19 information, n (%)						
Government agencies						.04[a]
Yes	12,255 (84.5)	4773 (83.4)	5241 (85.2)	1460 (85.2)	781 (84.8)	
No	2254 (15.5)	950 (16.6)	910 (14.8)	254 (14.8)	140 (15.2)	
Professional news media						<.001[a]
Yes	12,706 (87.6)	5024 (87.8)	5432 (88.3)	1483 (86.5)	767 (83.3)	
No	1803 (12.4)	699 (12.2)	719 (11.7)	231 (13.5)	154 (16.7)	
Health care media						<.001[a]
Yes	8124 (56.0)	3570 (62.4)	3357 (54.6)	812 (47.4)	385 (41.8)	
No	6385 (44.0)	2153 (37.6)	2794 (45.4)	902 (52.6)	536 (58.2)	
Hospital institutions						<.001[a]
Yes	7107 (49.0)	2743 (47.9)	2964 (48.2)	911 (53.2)	489 (53.1)	
No	7402 (51.0)	2980 (52.1)	3187 (51.8)	803 (46.8)	432 (46.9)	
Celebrities						<.001[a]
Yes	4017 (27.7)	1671 (29.2)	1595 (25.9)	447 (26.1)	304 (33.0)	
No	10,492 (72.3)	4052 (70.8)	4556 (74.1)	1267 (73.9)	617 (67.0)	
Trust score for different sources of information, mean (SD)						
Government agencies[b]	4.46 (0.76)	4.49 (0.75)	4.46 (0.76)	4.39 (0.77)	4.40 (0.82)	<.001[c]
Professional news media[d]	4.18 (0.79)	4.18 (0.80)	4.21 (0.77)	4.15 (0.79)	4.11 (0.87)	.002[c]
Health care media[e]	3.86 (0.87)	3.87 (0.88)	3.89 (0.85)	3.80 (0.86)	3.78 (0.89)	<.001[c]
Hospital institutions[f]	4.52 (0.69)	4.53 (0.67)	4.53 (0.68)	4.50 (0.71)	4.51 (0.74)	.76[c]
Celebrities[g]	3.21 (1.07)	3.27 (1.07)	3.18 (1.04)	3.15 (1.10)	3.14 (1.13)	<.001[c]

[a]Chi-square test.

[b]Government agencies, such as the Chinese State Council, which often serve as the voice of official or administrative institutions.

[c]Kruskal-Wallis test.

[d]Professional news media outlets, such as Sina Release, which focus on instant news reporting in the professional domain.

[e]Health care institutions, such as the US Centers for Disease Control and Prevention, which often cover trends in the medical field and issue public health advisories.

[f]Hospital institutions, such as West China Hospital accounts, which disseminate prevention and treatment information.

[g]Celebrities who have a large number of social media followers and overall social and consumer influence [39].

Table 3. Participants' knowledge about COVID-19.

Questions and responses	Value (N=14,509), n (%)
Modes of transmission[a]	
Droplet (correct option)	14,214 (98.0)
Airborne (correct option)	8990 (62.0)
Close contact (correct option)	12,353 (85.1)
Which of the following is not suitable for preventing COVID-19 in the choice of masks?	
Cloth mask (correct option)	13,786 (95.0)
Disposable medical mask	254 (1.8)
Medical-surgical mask	292 (2.0)
N95 protective mask	177 (1.2)
Which of the following statements is incorrect about the use of masks?	
If conditions permit, populations in dense areas should change their disposable masks around 4 hours	522 (3.6)
Once contaminated, it should be replaced as soon as possible	291 (2.0)
Avoid touching the inner face of the mask with your hands	239 (1.6)
Cotton masks resist the coronavirus better than medical masks (correct option)	13,457 (92.8)
Which of the following measures is recommended by the Chinese Centers for Disease Control to protect against COVID-19 transmission?	
Rinsing with light saltwater	148 (1.0)
Sauna or steaming	102 (0.7)
Drinking alcohol	198 (1.4)
Wearing masks (correct option)	14,061 (96.9)

[a]There were multiple correct options.

Multivariable Analyses of the COVID-19 Knowledge Score, Behavioral Change, and Cross-Verification

We identified the following groups as having a higher likelihood of obtaining accurate COVID-19 preventive information: female participants (P<.001), those aged 30-39 or 40-49 years (both P<.001), health care workers (P=.01), those living in cities (P<.001), those having a poor health status (P<.001), those having an online time of 1-5 hours (P=.005) or more than 7 hours per day (P=.02), and those having a high frequency of searching for COVID-19 information on social media (P=.001) (Table 4). In addition, those with high trust in web-based information from professional media and hospital institutions with a trust rating score more than 3 had a higher level of COVID-19 prevention knowledge (P<.05). On the other hand, those with trust rating scores of 5 for online information released from celebrities' social media accounts were more likely to have insufficient COVID-19 preventive knowledge (P<.001).

Among 4017 participants who searched for COVID-19 information on celebrities' social media accounts, those who were female, were aged ≥50 years, were non–health care workers, had a higher perceived health condition and health literacy, and had a higher frequency of searching had greater odds of behavioral changes based on COVID-19 web-based information (Table 5). Additionally, having high COVID-19 knowledge was associated with significantly higher odds of behavioral changes (aOR 1.085, 95% CI 1.036-1.191; P=.045). Those with high trust rating scores of more than 3 for social media information from celebrities were more likely to change their behaviors according to online information (P<.001).

In terms of subgroups who searched for COVID-19 web-based information released by celebrities and who were more likely to change their health behaviors, we found that being female (aOR 0.767, 95% CI 0.544-0.928; P<.001), having a self-reported medium health condition (aOR 0.789, 95% CI 0.664-0.939; P=.007), having a self-reported medium and low health literacy (aOR 0.596, 95% CI 0.505-0.703; P<.001 and aOR 0.441, 95% CI 0.323-0.600; P<.001, respectively), and having a high trust score of more than 1 for online information released by celebrities (P<.05) were associated with lower odds of information cross-validation (Table 5). Nevertheless, participants who resided in first-tier cities (aOR 1.455, 95% CI 1.260-2.144; P<.001) and those who often browsed internet information related to COVID-19 (aOR 3.239, 95% CI 1.632-6.788; P<.001) had greater odds of performing COVID-19 information cross-validation.

Table 4. Multiple linear regression results of the association of COVID-19 knowledge with demographic characteristics and social media use.

Variable	COVID-19 knowledge score		
	Coefficient	Standard error	*P* value
Gender (female vs male)	0.172	0.018	<.001
Age (years, vs 18-29 years)			
30-39	0.075	0.017	<.001
40-49	0.108	0.025	<.001
≥50	−0.138	0.032	<.001
Educational status (vs junior high school or below)			
High school	0.050	0.049	.30
Junior college	0.052	0.046	.26
Undergraduate degree	0048	0.046	.30
Master's degree or above	−0.016	0.049	.75
Occupation (vs student)			
Staff member in the government	−0.003	0.030	.91
Health care provider	0.073	0.029	.01
Staff member in a company	0.006	0.029	.84
Self-employed entrepreneur	0.002	0.037	.95
Other	0.053	0.028	.06
Current residence (vs rural area)			
First-tier city	0.158	0.037	<.001
Second-tier city	0.160	0.039	<.001
Other city	0.168	0.047	<.001
Perceived health status (vs good)			
Medium	0.001	0.016	.96
Poor	0.131	0.033	<.001
Medical information literacy (vs high)			
Medium	0.019	0.016	.22
Low	−0.026	0.027	.33
Time spent on social media (hours, vs ≤1 hour)			
>1 to ≤3	0.111	0.032	.001
>3 to ≤5	0.093	0.033	.005
>5 to ≤7	0.060	0.038	.11
>7	0.101	0.043	.02
Frequency of browsing information related to COVID-19 (vs rarely)			
Sometimes	0.305	0.040	<.001
Often	0.379	0.037	<.001
Sources of information about COVID-19 on social media			
Government agencies (no vs yes)	0.188	0.020	<.001
Professional news media (no vs yes)	0.245	0.022	<.001
Health care media (no vs yes)	0.063	0.015	<.001
Hospital institutions (no vs yes)	0.094	0.015	<.001
Celebrities (no vs yes)	0.087	0.017	<.001
Trust rating score for different sources of information			

Variable	COVID-19 knowledge score		
	Coefficient	Standard error	*P* value
Government agencies (vs 1)			
2	—[a]	—	N/A[b]
3	—	—	N/A
4	—	—	N/A
5	—	—	N/A
Professional news media (vs 1)			
2	0.064	0.123	.60
3	0.384	0.116	.001
4	0.364	0.115	.002
5	0.421	0.116	<.001
Health care media (vs 1)			
2	−0.037	0.085	.67
3	−0.127	0.080	.11
4	−0.135	0.080	.09
5	−0.183	0.081	.06
Hospital institutions (vs 1)			
2	−0.163	0.143	.25
3	0.256	0.122	.04
4	0.376	0.119	.002
5	0.444	0.119	<.001
Celebrities (vs 1)			
2	0.000	0.032	.99
3	0.025	0.029	.39
4	−0.045	0.030	.14
5	−0.120	0.035	.001

[a]The corresponding variable has not been included in the final multiple regression model.

[b]N/A: not applicable.

As shown in Table 5, among those who were less likely to change their behaviors according to web-based information released by celebrities, those who were female (aOR 1.419, 95% CI 1.050-1.921; *P*=.02) and who more frequently browsed internet information related to COVID-19 (aOR 4.077, 95% CI 1.906-9.742; *P*<.001) had higher odds of cross-validating COVID-19 information. However, participants who self-reported medium and low health literacy (aOR 0.614, 95% CI 0.476-0.791; *P*<.001 and aOR 0.529, 95% CI 0.338-0.822; *P*=.005, respectively) were less likely to check the veracity of COVID-19 information when determining their personal behaviors.

Table 5. Multiple logistic regression results of the association between behavior change and verification.

Variable	Behavior change		Information verification (among netizens searching web-based COVID-19 information released by celebrities)			
	Change vs no change		Behavior change group		No behavior change group	
	aOR[a] (95% CI)	*P* value	Verify vs not verify, aOR (95% CI)	*P* value	Verify vs not verify, aOR (95% CI)	*P* value
COVID-19 knowledge score	1.085 (1.036-1.191)	.045	—[b]	N/A[c]	—	N/A
Gender (female vs male)	1.301 (1.085-1.556)	.004	0.767 (0.544-0.928)	<.001	1.419 (1.050-1.921)	.02
Age (years, vs 18-29 years)						
30-39	1.161 (0.981-1.374)	.08	—	N/A	—	N/A
40-49	1.284 (0.998-1.660)	.054	—	N/A	—	N/A
≥50	1.519 (1.116-2.089)	.009	—	N/A	—	N/A
Educational status (vs junior high school or below)						
High school	—	N/A	0.695 (0.386-1.233)	.22	—	N/A
Junior college	—	N/A	0.786 (0.452-1.345)	.39	—	N/A
Undergraduate degree	—	N/A	0.613 (0.357-1.034)	.07	—	N/A
Master's degree or above	—	N/A	0.725 (0.409-1.268)	.27	—	N/A
Occupation (vs student)						
Staff member in the government	1.053 (0.779-1.425)	.74	—	N/A	—	N/A
Health care provider	0.721 (0.550-0.943)	.02	—	N/A	—	N/A
Staff member in a company	1.130 (0.850-1.499)	.40	—	N/A	—	N/A
Self-employed entrepreneur	1.140 (0.797-1.639)	.48	—	N/A	—	N/A
Other	1.045 (0.792-1.378)	.75	—	N/A	—	N/A
Current residence (vs rural area)						
First-tier city	—	N/A	1.455 (1.260-2.144)	<.001	—	N/A
Second-tier city	—	N/A	1.281 (0.899-1.419)	.06	—	N/A
Other city	—	N/A	0.799 (0.526-1.200)	.28	—	N/A
Perceived health status (vs good)						
Medium	1.046 (0.893-1.226)	.58	0.789 (0.664-0.939)	.007	—	N/A
Poor	0.578 (0.419-0.801)	<.001	0.770 (0.509-1.167)	.22	—	N/A
Medical information literacy (vs high)						
Medium	0.718 (0.454-0.956)	<.001	0.596 (0.505-0.703)	<.001	0.614 (0.476-0.791)	<.001
Low	0.845 (0.570-0.989)	.03	0.441 (0.323-0.600)	<.001	0.529 (0.338-0.822)	.005
Time spent on social media (hours, vs ≤1 hour)						
>1 to ≤3	—	N/A	1.156 (0.741-1.790)	.52	—	N/A
>3 to ≤5	—	N/A	0.809 (0.514-1.262)	.35	—	N/A
>5 to ≤7	—	N/A	1.258 (0.770-2.044)	.36	—	N/A
>7	—	N/A	1.009 (0.602-1.683)	.97	—	N/A
Frequency of browsing information related to COVID-19 (vs rarely)						
Sometimes	1.379 (0.827-2.295)	<.001	1.077 (0.458-1.786)	.92	1.545 (0.675-3.885)	.33
Often	2.477 (1.541-3.974)	<.001	3.239 (1.632-6.788)	<.001	4.077 (1.906-9.742)	.001
Trust rating score for different sources of information (celebrities, vs 1)						
2	1.043 (0.668-1.617)	.85	0.803 (0.681-0.939)	.04	—	N/A
3	1.330 (0.889-1.972)	.16	0.518 (0.374-0.777)	<.001	—	N/A

Variable	Behavior change		Information verification (among netizens searching web-based COVID-19 information released by celebrities)			
	Change vs no change		Behavior change group		No behavior change group	
	aOR[a] (95% CI)	*P* value	Verify vs not verify, aOR (95% CI)	*P* value	Verify vs not verify, aOR (95% CI)	*P* value
4	1.771 (1.182-2.629)	.005	0.625 (0.322-0.909)	<.001	—	N/A
5	2.497 (1.630-3.794)	<.001	0.386 (0.107-0.519)	<.001	—	N/A

[a]aOR: adjusted odds ratio.

[b]The corresponding variable has not been included in the final multiple regression model.

[c]N/A: not applicable.

Discussion

Principal Findings

Social Media Use and COVID-19 Knowledge

Overall, with the advancement of smart device technology, the use of the internet has penetrated various age groups. More than 90% of those investigated reported surfing social media for more than 1 hour per day, including middle-aged and older participants. The findings also showed that social media use and the credibility of web-based information among different age groups varied. The age gap should be considered as much as possible in broadening the diffusion of preventive measures for COVID-19 via social media platforms. The results also indicated that "frequency" had a more significant impact on COVID-19 literacy than the length of time spent using social media. In other words, "how often" individuals consulted social media directly, rather than "how long," had a strong relationship with preventive behaviors [12]. Since frequency may be a direct indicator of motivation for various types of social media use, such as self-expression, social learning, social comparison, and filtering [40], this study cautiously suggests that the frequency of social media use may be a more essential predictor of social media effects than time spent using social media [41].

Similar to a prior study that found that women had higher COVID-19 literacy [12], this survey detected that female netizens self-reported engaging in more correct preventive behaviors than male netizens. This finding may be explained by women usually having higher levels of disease knowledge and health care literacy than men [42]. A previous study also suggested that women were more sensitive to and interested in health information on social media [43], which may be another reason for their higher COVID-19 literacy, since females seem to search the internet more frequently for COVID-19 information [44]. Alternatively, the gender difference may be partly attributed to the self-reported health literacy bias in this study and previous studies. An objective measurement tool for health literacy, rather than self-ratings, is warranted to examine the gender disparity in future research. However, in our study, current residence was a direct indicator of higher COVID-19 literacy, whereas education level was nonsignificant. This inconsistency could be explained by the fact that those in rural areas usually have lower education levels [45]. These results highlight the need to pay attention to populations in remote regions in order to prevent the deterioration of their health outcomes from causing the education level to fall behind again, thus resulting in a vicious cycle [46,47].

Differing levels of trust in 5 web-based information sources on social media were found to be another significant predictor of preventive behaviors. For web-based information released by professional media and hospital institutions, higher trust was associated with a positive relationship with COVID-19 literacy. However, Chinese netizens with high trust in web-based information released by celebrities seemed to have less COVID-19 knowledge. The results indicate that the accuracy of COVID-19 information from individual and unofficial social media accounts, including those of movie stars and singers, deserves more attention than official social media accounts in terms of the effect on preventive measures, particularly for Chinese netizens. Celebrities were more influential in disseminating the related information via social media platforms, especially among young Chinese netizens [48]. The higher incidence of insufficient COVID-19 knowledge among followers of celebrities reflects the need to cross-reference web-based information released by unofficial sources with information from official sources.

Behavioral Changes and Social Media Use

The results showed that women were more likely than men to change their health care behaviors according to web-based information released by unofficial accounts. Women may be more sentimental and sensitive, may experience more severe stress and anxiety during the pandemic [49], and may use the internet and social media more frequently to search for related information [50]. Therefore, the authors cautiously conclude that concerns regarding this pandemic may accelerate women's health-related behavioral changes [51]. Additionally, non–health care workers were more inclined to change their behaviors after obtaining web-based COVID-19 information. Health care workers may choose to consult academic articles before making decisions about health care behaviors. Moreover, the higher possibility of behavioral changes based on social media information among those older than 50 years may be due to the presence of more health concerns and stronger emphasis on health among these age groups [52].

Additionally, social media use frequency had a significant relationship with Chinese netizens' adoption of web-based health care advice and changes to their preventive behaviors. Thus, "frequency" may be a more significant predictor of social media effects. Social media use frequency should therefore be

an effective strategy for public health promotion, especially when countries are confronted with COVID-19 vaccination hesitancy [53]. Furthermore, the authors also detected that the possibility of behavioral change was higher if netizens had higher trust in information from celebrities' social media outlets. Celebrities and public figures have long been shown to be important influencers of human behavior due to various proposed psychological, social, and biological mechanisms [54].

The relationship between health literacy and health behaviors has been widely recognized [55,56]. Consistent with a previous study, in this survey, the self-reported higher health literacy group seemed to change their behaviors, while less health literacy netizens were less likely to change their preventive behaviors based on information from social media as a result of a deficiency in basic medical knowledge associated with their education level. Similarly, the odds of behavioral change increased as individuals' COVID-19 knowledge increased, which may underscore that populations that have poor preventive knowledge are more likely to be stubborn and insist on their own perceptions of effective approaches to combat COVID-19. Thus, the knowledge gap should be considered to the greatest extent possible when using social media to publicize pandemic countermeasures [57]. Of note, the aforementioned disparities in behavioral change should be carefully considered since those netizens took web-based information from celebrities as an effective avenue for the dissemination of information during the pandemic.

Cross-Verification of Social Media Information

Although social media–based information may help specific groups improve their ability to deal with the pandemic, individuals may also take risks in their use of web-based resources, because web-based information released by individual accounts is not always accurate [58,59]. The survey findings can help identify vulnerable netizens who are likely to change their health behaviors according to less accurate web-based information without cross-verifying its accuracy and can provide insightful implications to promote better use of social media in the fight against COVID-19 [60].

As previous research has illustrated, health literacy has been underestimated, and more emphasis should be placed on it during the pandemic [61,62]. The positive effect of health literacy on the cross-verification of web-based information suggests that health literacy plays a fundamental role during the pandemic. Remarkably, the results also revealed that among the behavioral change groups, women were less likely than men to verify the veracity of web-based information. This finding is notable since the survey also found that female netizens had higher COVID-19 preventive knowledge and engaged in more preventive behaviors than men. Thus, the authors argue that compared with health literacy, eHealth literacy or digital literacy, which is defined as "the capacity for individuals to seek, find, understand, and appraise health information from electronic sources," might have a greater effect on the awareness of web-based information verification [63,64]. Even netizens who have high health literacy and COVID-19 knowledge may lack the eHealth literacy to be aware of, verify, and evaluate the veracity of COVID-19 web-based information posted by celebrities. Men have been reported to have higher digital literacy than women in relation to internet-based information [64]. Similarly, the low cross-verification among netizens living in rural areas extends the previous statement that there are distinct socioeconomic disparities in eHealth literacy [65]. Solving issues around limited digital health literacy, however, would benefit gender and residence disparities across cross-verification preferences in efforts to contain COVID-19 [66].

Furthermore, the high-frequency use of social media and search for information, rather than the time spent on social media, fostered the ability of groups to cross-verify information. This phenomenon was more commonly associated with the current practices of social media companies using algorithms that repeatedly drive similar content to users based on what they have recently browsed [67]. These algorithms reinforce COVID-19 misinformation for netizens who are incessantly immersed in social media and isolate them from reports on legitimate scientific evidence. Specifically, Chinese netizens who engage less frequently with social media should be encouraged to verify COVID-19 information through multiple searches for official internet sources.

The importance of cross-referencing was heavily based upon the likely veracity of the information obtained. In this context, web-based information released from official social media accounts, such as the government, the Centers for Disease Control and Prevention (CDC), and hospital institutions, is likely highly accurate, while that from individual social media accounts may be inaccurate and thus even more in need of cross-verification with official sources. Notably, in our research, Chinese netizens who trusted web-based COVID-19 information released by celebrities usually conducted little cross-verification of web-based information before changing their behaviors. Even worse, this survey found that netizens who highly trusted web-based information posted by celebrities were less knowledgeable of COVID-19 preventive measures and more likely to change their health care behaviors based on that online information. According to a Twitter survey, during the pandemic, the tweets of celebrities and politicians related to COVID-19 outperformed those of health and scientific institutions [68]. Many of the followers of celebrities, movie stars, and singers, also called blind adherents, trust everything said by their "idols." Celebrities should be aware of their social impact and foster positive values, including delivering more credible news and dispelling rumors, which may be helpful in controlling the pandemic [69,70]. Additionally, the government should act to raise fans' awareness of misinformation on social media and increase their eHealth literacy to improve their ability to verify web-based information related to COVID-19.

Policy Implications

The pandemic is accompanied by an infodemic that involves the abundant and uncontrolled spread of potentially harmful misinformation, mainly produced by unofficial social media accounts [71]. As cross-referencing of internet information via different released channels is perceived to be effective for identifying accurate information, netizens who lack awareness of such information verification are a vulnerable population

among those worst affected by the COVID-19 infodemic [72]. This study identified the characteristics of that vulnerable population and proposes the following measures to target them. Digital health or eHealth literacy can improve netizens' capacity to search, compare, and take the best advantage of web-based information [73]. The government should establish programs to improve netizens' eHealth literacy and strengthen their capacities to obtain, read, understand, and assess health care information so that they can use web-based COVID-19 information appropriately [74]. Moreover, natural language processing models and artificial intelligence (AI)-based approaches, including AI-augmented lifelong learning and AI-assisted translation, simplification, summarization, and filtering, may have the general advantages of building and enhancing netizens' levels of digital or eHealth literacy [75,76]. Referencing Eysenbach's fourth pillar of infodemic management, this study also suggests that data and information flow patterns on social media should be continuously monitored and analyzed [77]. Outbreaks of misinformation, rumors, and falsehoods can thus be detected immediately and countered with facts or other interventions, such as flagging or removing the content from social media platforms and decreasing the dissemination of negative information and panic among Chinese netizens [20,72]. Finally, the private accounts of celebrities should receive more relative attention since they have powerful appeal among netizens. Celebrities could help by providing valuable health information and convincing their fans to follow appropriate preventive COVID-19 measures and be vaccinated.

Strengths, Limitations, and Future Research

This study has several strengths. First, the sample was relatively large and widely representative, which provided the opportunity for accurate examination of potential variations. Moreover, this study extends the current literature on the characteristics of Chinese netizens who are likely to change their health behaviors according to unofficial web-based information, but seldom conduct cross-verification. As countries across the world continue to battle the pandemic and confront increased use of social media for health information dissemination, similar research in the infodemic management field is expected.

Despite its strengths, several limitations of our study should be acknowledged. First, it included only 3 WCH social media platforms and people who had access to the internet and electronic devices, thereby excluding people who did not. Additionally, since this was a cross-sectional study conducted between May 18 and May 31, 2020, the results may not be generalizable and thus may fail to capture changes over time due to rapid social development. The online survey had very low response rates among older people. Considering the low use of the internet among older groups, further studies should focus on the use of traditional media for older people during the pandemic. Moreover, the self-designed questionnaire failed to evaluate the actual age, obtain a more detailed educational degree, and use a 1-5 scale of medical knowledge, which would have allowed for the collection of more specific information from the respondents. In addition, the internal validity may be an issue because WCH social media followers were encouraged to distribute the questionnaire to their relatives and friends who met the inclusion criteria. However, considering that the questionnaire items did not involve any individual interests and emphasized voluntary and uncompelled survey participation, unintentional bias associated with participant relationships was a remote possibility. Moreover, the study was completely voluntary, so the characteristics of individuals who would actively choose to participate should be considered since self-reported health status and literacy levels are highly subjective. Similarly, the study could not accurately predict netizens' health behaviors based on self-reported behavioral change and cross-verification. However, it provides a preliminary analysis and clarifies associations between various characteristics.

Additionally, the behavioral change tendencies included in this study are not necessarily positive or negative because the survey could not discern what information a change was in response to and whether it was an effective change. Moreover, information verification is difficult to measure and is detrimental only when the information is inaccurate. Therefore, further studies regarding verification strategies are necessary. Furthermore, the sample included many more individuals with high education levels and netizens from urban areas. Future studies should include netizens with less education and those who live in rural areas to facilitate the generalizability of the findings. Moreover, this cross-sectional study focused mainly on investigating phenomena, and the barriers, facilitators, and causal loops for behavioral change and cross-verification were not included. Further research is necessary to explore what motivates individuals' social media use, as well as barriers to and facilitators of the validation of web-based information. Finally, with the increasing popularity of social media, people's health literacy and eHealth literacy have been continuously improving over the last few years, and future research with a wider time span could be conducted to investigate changes in cross-verification behaviors.

Conclusions

In general, this study made the first attempt to examine whether cross-verification was implemented before Chinese netizens engaged in changes related to health behavior–based information on unofficial social media. The study found that Chinese netizens who were female, lived in rural areas, had less health literacy, searched less frequently for online information, and had high trust in web-based information released by celebrities were more likely to be misled by misinformation on social media, since they were more likely to easily change their health behaviors without fact-checking and cross-verifying web-based information. These findings have practical implications for the government, health organizations, and health practitioners in designing and implementing health promotions and interventions in similar pandemics. Netizens with the aforementioned characteristics should be informed about the risk of misinformation and the strategies for verifying the accuracy of web-based COVID-19 information to protect them from using counterfeit, inappropriate, or unsafe preventive measures. More technical and policy efforts are needed to further address the dissemination of misinformation on social media.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (grant number 71874115) and the special funds for COVID-19 Prevention and Control of West China Hospital of Sichuan University (HX-2019-nCoV-023). The funder had no role in the design of the study; the collection, analysis, and interpretation of the data; or the writing of the manuscript. We sincerely thank Prof Jalali for insightful guidance and valuable discussion. The first author would like to express her gratitude to Mr Guanhua Qing for his continuous support and encouragement during this research.

Authors' Contributions

PL conducted the survey and statistical analysis, and drafted the manuscript. BC designed the study and questionnaire. GD consulted on the analysis and interpretation of the results, contributed to further development of the analysis and content, and revised the manuscript for important intellectual content. YL and WT helped to perform the statistical analysis and interpret the data. WL contributed to the manuscript revision. JW and YZ were the principal designers of the study and were responsible for all the results of the study, as well as the review and approval of the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Survey questionnaire.
[DOCX File , 27 KB - publichealth_v8i5e33577_app1.docx]

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Abbreviations

AI: artificial intelligence
aOR: adjusted odds ratio
CVI: content validity index
WCH: West China Hospital

Edited by A Mavragani, T Sanchez; submitted 14.09.21; peer-reviewed by C Mather, C Thornson; comments to author 17.01.22; revised version received 14.03.22; accepted 27.04.22; published 31.05.22.

Please cite as:
Li P, Chen B, Deveaux G, Luo Y, Tao W, Li W, Wen J, Zheng Y
Cross-Verification of COVID-19 Information Obtained From Unofficial Social Media Accounts and Associated Changes in Health Behaviors: Web-Based Questionnaire Study Among Chinese Netizens
JMIR Public Health Surveill 2022;8(5):e33577
URL: https://publichealth.jmir.org/2022/5/e33577
doi:10.2196/33577
PMID:35486529

Original Paper

A Novel Tool for Real-time Estimation of Epidemiological Parameters of Communicable Diseases Using Contact-Tracing Data: Development and Deployment

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Abstract

Background: The Surveillance Outbreak Response Management and Analysis System (SORMAS) contains a management module to support countries in their epidemic response. It consists of the documentation, linkage, and follow-up of cases, contacts, and events. To allow SORMAS users to visualize data, compute essential surveillance indicators, and estimate epidemiological parameters from such network data in real-time, we developed the SORMAS Statistics (SORMAS-Stats) application.

Objective: This study aims to describe the essential visualizations, surveillance indicators, and epidemiological parameters implemented in the SORMAS-Stats application and illustrate the application of SORMAS-Stats in response to the COVID-19 outbreak.

Methods: Based on findings from a rapid review and SORMAS user requests, we included the following visualization and estimation of parameters in SORMAS-Stats: transmission network diagram, serial interval (SI), time-varying reproduction number R(t), dispersion parameter k, and additional surveillance indicators presented in graphs and tables. We estimated SI by fitting lognormal, gamma, and Weibull distributions to the observed distribution of the number of days between symptom onset dates of infector-infectee pairs. We estimated k by fitting a negative binomial distribution to the observed number of infectees per infector. Furthermore, we applied the Markov Chain Monte Carlo approach and estimated R(t) using the incidence data and the observed SI computed from the transmission network data.

Results: Using COVID-19 contact-tracing data of confirmed cases reported between July 31 and October 29, 2021, in the Bourgogne-Franche-Comté region of France, we constructed a network diagram containing 63,570 nodes. The network comprises 1.75% (1115/63,570) events, 19.59% (12,452/63,570) case persons, and 78.66% (50,003/63,570) exposed persons, including 1238 infector-infectee pairs and 3860 transmission chains with 24.69% (953/3860) having events as the index infector. The distribution with the best fit to the observed SI data was a lognormal distribution with a mean of 4.30 (95% CI 4.09-4.51) days. We estimated a dispersion parameter k of 21.11 (95% CI 7.57-34.66) and an effective reproduction number R of 0.9 (95% CI 0.58-0.60). The weekly estimated R(t) values ranged from 0.80 to 1.61.

Conclusions: We provide an application for real-time estimation of epidemiological parameters, which is essential for informing outbreak response strategies. The estimates are commensurate with findings from previous studies. The SORMAS-Stats application could greatly assist public health authorities in the regions using SORMAS or similar tools by providing extensive visualizations and computation of surveillance indicators.

(JMIR Public Health Surveill 2022;8(5):e34438) doi:10.2196/34438

KEYWORDS

COVID-19; disease outbreak; contact tracing; serial interval; basic reproduction number; infectious disease incubation period; superspreading events; telemedicine; public health; epidemiology; surveillance tool; outbreak response; pandemic; digital health application; response strategy

Introduction

Background

During the course of 2020, there was a substantial increase in the number and use of eHealth applications, mainly in response to the COVID-19 outbreak [1-3]. These applications are being used in different areas of digital health intervention, such as disease surveillance, vaccine delivery, hospital management, laboratory management, symptom journals, and education [4].

The Surveillance Outbreak Response Management and Analysis System (SORMAS) is an open-source digital tool that supports disease control and outbreak management procedures [5-8]. The objective of SORMAS is to ensure the availability of real-time surveillance data for priority diseases at all administrative levels. SORMAS supports task management, complies with data protection and data security standards, and enhances interoperability with other applications.

Essential epidemiological parameters governing COVID-19 transmissions such as serial interval (SI), instantaneous reproduction number R(t), effective reproduction number R, and individual-level variation in transmission are context-specific, and thus often difficult to estimate precisely with publicly available data. Studies have been conducted to estimate these epidemiological parameters during the early phase of the outbreak, but most focused on coarse, aggregated, and publicly reported data sources that likely mask local specificities or are biased toward more severe cases [9-11]. The lack of easy access to outbreak data containing more epidemiological and clinical information has been reported as a limiting factor in improving the performance of epidemiological models [12]. Since then, most public health stakeholders used eHealth applications to document rich and large contact-tracing data in response to the COVID-19 outbreak. Nonetheless, such informative surveillance data are often not hosted on a centralized hub but scattered on different databases in the corresponding countries. In addition, the estimation of epidemiological parameters is frequently not done in real time and does not account for spatial and temporal variation, and thus, fails to provide comprehensive and timely information on outbreak evolution to best inform decision-making [13]. Further, public health stakeholders faced challenges in generating reproducible analyses for their routine situation reports because data are often manually exported from eHealth applications and analyzed with stand-alone statistical applications such as R, SAS, SPSS or STATA.

To address these challenges, we envisaged an approach whereby standardized statistical analysis methods are brought to where the rich and detailed surveillance data are hosted. To assist stakeholders (SORMAS users) with a reactive analytic platform that leverages the rich and detailed data documented in SORMAS, we developed the SORMAS Statistics (SORMAS-Stats) application. SORMAS-Stats is a user-friendly R Shiny web application to estimate epidemiological parameters, compute country or region-specific indicators, and provide visualizations in real time.

Objective

This study aims to describe the essential visualizations, epidemiological parameters, and surveillance indicators implemented in the SORMAS-Stats application. We illustrated its application in response to the COVID-19 outbreak using surveillance data captured with SORMAS in the Bourgogne-Franche-Comté region of France.

Methods

Design Process of SORMAS-Stats

We gathered the requirements essential to supporting outbreak response through SORMAS user requests (from Nigeria, Ghana, France, and Germany), which thus guided the design of SORMAS-Stats. SORMAS users are public health personnel of a country, such as field investigators and epidemiologists. We identified user requests through GitHub issues created by SORMAS users, the SORMAS user support platform, and the minutes of sprint planning meetings. The sprint planning meetings took place every 3 weeks, matching the software release cycle of SORMAS. In parallel, we conducted a rapid review of epidemiological publications and situation reports. Subsequently, we combined the essential requirements obtained from the review and the users' requests, implemented them, and released a beta version of the SORMAS-Stats application. Further, we conducted a field test of the beta version, got users' feedback, implemented them, and deployed a stable version. The time from requirement gathering to deployment was 12 months (July 2020 to June 2021).

Overview of SORMAS-Stats

SORMAS-Stats is a web application that can be installed locally and uses advanced visualization and statistical analysis methods to analyze surveillance data in real time. SORMAS-Stats assists public health officials in managing outbreaks and permits the execution of reproducible routine epidemiological analysis. The workflow of SORMAS-Stats consists of the preprocessing phase and the analytics phase.

In the preprocessing phase, SORMAS-Stats imports pseudonymized data from an external database. The default integration of SORMAS-Stats is with the SORMAS PostgreSQL database. Only the records and associated attributes reported within the time interval specified in the SORMAS-Stats configuration file are extracted from the external database. Further data processing steps are the deletion of error records, deduplication, categorization, and the computation of derived variables. In the analytics phase, SORMAS-Stats analyzes the preprocessed data. We classified the analytics phase into two types: (1) data visualization and the computation of summary

statistics and (2) the estimation of essential disease-specific epidemiological parameters through statistical modeling.

Epidemiological Data

The SORMAS-Stats application analyzes the entity-based surveillance data routinely collected by public health workers. Generally, surveillance data include the following entities: case person (a person infected with a disease), contact person (a noninfected person exposed to a case person), and event (any exposure or gathering that poses a threat to human health or may lead to the spread of diseases). The collection of all probable transmission chains (pairs of entities: case person–contact person or event–persons exposed to an event [event participants], that can result in disease transmission) forms the network data of the disease. During contact follow-up, a contact person or event participant may become symptomatic and meet the case definition of the disease in question, thus being converted or reclassified as a case. In such instances, 2 types of infector (ie, index case) and infectee (ie, secondary case) pairs are formed (infector-infectee pairs): first, between the case person and contact person, and second, between the event and the event participant.

The data used to illustrate the application of SORMAS-Stats consisted of confirmed cases of COVID-19 and their contacts documented using SORMAS between July 31 and October 29, 2021, in the Bourgogne-Franche-Comté region of France.

Estimation of Epidemiological Parameters and Surveillance Indicators

Serial Interval

We computed the observed SI as the difference in the number of days between symptom onsets of infector-infectee pairs. We excluded infector-infectee pairs for which the infector was an event or if one of a pair had missing data for symptom onset date. However, we only included symptomatic transmissions with available data for the date of symptom onset for both infector and infectee in a pair, as transmission data are often generated during contact-tracing under symptomatic settings [14]. We estimated the SI distribution by fitting lognormal, gamma, Weibull, and normal distributions to the observed SI data. The choice of these distributions was based on previous studies [15,16]. For all 4 types of distributions, we excluded observed SI greater than 30 days. For lognormal, gamma, and Weibull distributions, which do not take negative values, we dropped negative values before fitting the distributions. For each fitted distribution, we computed the goodness-of-fit criteria (Akaike information criterion and Bayesian information criterion) and goodness-of-fit statistics (Kolmogorov-Smirnov, Cramer-von Mises, and Anderson-Darling) [17]. We chose the distribution with the best fit by several approaches: the smallest Akaike information criterion, a plot of the density function of the fitted distribution with the histogram of observed data, and a plot of the empirical and theoretical cumulative distribution functions of each fitted model. We calculated the 95% CI of the mean SI using the formula $\mu \pm 1.96 \times (\sigma / \sqrt{n})$, where μ is the estimated sample mean, σ the estimated sample SD, and n the sample size. The analysis was performed using the R statistical software (R Foundation for Statistical Computing) package fitdistrplus [17].

Instantaneous Reproduction Number

We estimated R(t)—on a weekly basis—using the approach proposed by Cori et al [18,19]. This method mainly requires the incidence and contact-tracing data, which are the types of data captured by SORMAS. We implemented 2 approaches to specify the SI distribution used to estimate R(t). First, a parametric distribution for SI with values for the mean and SD, and second, a parametric distribution for SI and the observed data of infector-infectee pairs. For the second approach, we estimated the SI distribution by applying the Markov Chain Monte Carlo method. The possible choices of the parametric distribution for SI were gamma, Weibull, and lognormal. We computed the summary statistics of the posterior mean and plotted the posterior mean and 95% credible interval for R(t). The analysis was performed using the R statistical software package EpiEstim [19].

Variation in Transmission Heterogeneity and Effective Reproduction Number

Using the data for infector-infectee pairs of cases, we computed the observed offspring distribution as the number of infectees per infector. We applied the approach described by Lloyd-Smith et al [20] and fitted a negative binomial distribution to the observed offspring distribution. We estimated the effective reproduction number R and the variation in transmission heterogeneity as the mean and dispersion parameter k of the negative binomial distribution, respectively [20]. In addition, we computed the median and 95% percentile CI of both parameters using bootstrap. We performed the analysis using the R statistical software package fitdistrplus [17].

Visualizations and Surveillance Indicators

We computed 6 surveillance indicators that may be informative in managing disease outbreaks using transmission network data. Table 1 presents the definition of visualizations and surveillance indicators implemented in the SORMAS-Stats application.

Table 1. Description and application of epidemiological parameters, surveillance indicators, and visualizations in SORMAS-Stats application.

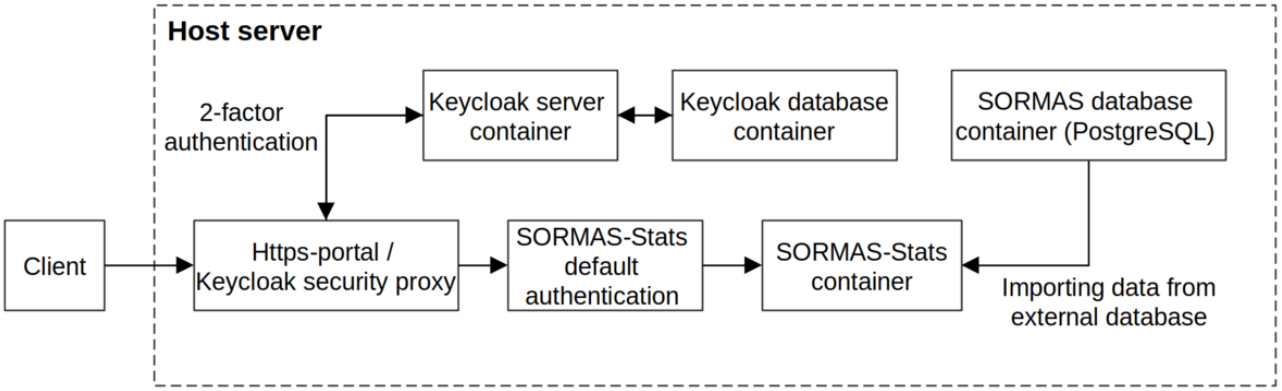
Name of output or indicator	Description	Applications in disease surveillance
Epidemiological parameters		
Serial interval (SI)	The difference in the number of days between symptom onsets of infector-infectee pairs (see Methods).	To distinguish disease variants, design follow-up and quarantine duration, and determine time window for effective intervention strategies.
Instantaneous reproduction number R(t)	The average number of infectees per infector at a particular time t (see Methods).	To assess the impact of intervention measures. R(t)>1 signify an increase in infectiousness at time t, R(t)<1 signify a decrease in infectiousness [18].
Effective reproduction number (R)	The average number of infectees per infector (see Methods).	Similar to R(t).
Dispersion parameter (k)	A measure of how the number of infectees per infector (offspring distribution) is distributed around the mean value (see Methods).	To assess the evidence of superspreading events or formation of clusters. This can help to devise relevant control measures. Smaller values of k indicate higher levels of dispersion, thus suggesting evidence of superspreading.
Surveillance indicators		
Proportion of exposed persons who became cases	The proportion of exposed persons—among all exposed persons—that converted to cases by exposure types.	To devise relevant control measures similar to the dispersion parameter k. To assess the quality of contact tracing and better allocate resources.
Proportion of index infectors	The proportion of index infectors among all infector nodes (infector person, infectee person, or event).	To determine the quality of contact-tracing. A smaller proportion indicates a greater coverage of identified linkages between infectors and infectees.
Variance-to-mean ratio (VMR)	The variance divided by the mean of the observed offspring distribution [21].	Similar to k. VMR>1 indicates higher levels of dispersion and thus signaling evidence of superspreading.
Edge density	The ratio of the number of edges (links between 2 nodes) and the maximum number of possible edges [22]. It represents how connected the nodes of the network diagram are to each other.	To assess the impact of control measures on overall societal behavior. Higher values may signify higher social interactions.
Number of individual transmission chains	The total number of transmission chains or index infector nodes in the network diagram.	Similar to proportion of index infectors.
Visualizations		
Network diagram	A directed graph of all disease transmission chains consisting of the following types of nodes: case persons, contact persons, events, and event participants.	To prioritize investigation and follow-up of events with known confirmed cases.
Time series plots	A bar graph or line plot of entity counts over time (day, week, or month).	To gauge the efficacy of control measures in place and the need to implement new ones.
Tables	Tables of entity count, proportions, or incidence proportions by administrative area (regions, districts, community).	To target intervention measures to specific areas of the country such as hotspots.
Charts	Pie charts and bar graphs of entity counts or proportions by entity attributes (eg, age and sex).	To protect vulnerable groups.
Maps	Spatial-temporal display of entity counts, proportion, and incidence proportion on a map by administrative area (regions, districts, community).	Similar to tables.

Architecture of SORMAS and SORMAS-Stats

The SORMAS application was developed on the VAADIN framework, JAVA EE, Payara server, and PostgreSQL database. SORMAS consists of 2 components: the mobile app and the web application. The mobile app communicates with the server via a REST-API and the VAADIN web client application. The SORMAS-Stats application analyzes the surveillance data documented in the PostgreSQL database of SORMAS. We developed SORMAS-Stats based on the R Shiny framework [23]. To secure the server hosting the application, we used an architecture with the following configuration: https-portal or secure proxy, 2-factor authentication with Keycloak, and the default authentication of SORMAS-Stats (Figure 1). The default authentication of SORMAS-Stats used the shinyauthr R package authentication module to hash the user password [24,25]. SORMAS-Stats can be executed as a default R Shiny application or a Docker application. We deployed SORMAS, SORMAS PostgreSQL, and SORMAS-Stats applications as separate Docker containers and managed them with one Docker-compose file. The test version of SORMAS-Stats based on demonstration

data is available online [26]. The code and description of deployment are hosted on GitHub [27].

Figure 1. Server setup for the SORMAS-Stats application. SORMAS: Surveillance Outbreak Response Management and Analysis System.



Ethical Considerations

The Agence Régionale de Santé de Bourgogne Franche-Comté, France, as an administrative public health institution, granted permission for using the anonymized COVID-19 outbreak data in this study, under article 11 of Law No. 2020-546 of May 11, 2020. Under this law, the secondary data used in this study did not require individual informed consent.

Results

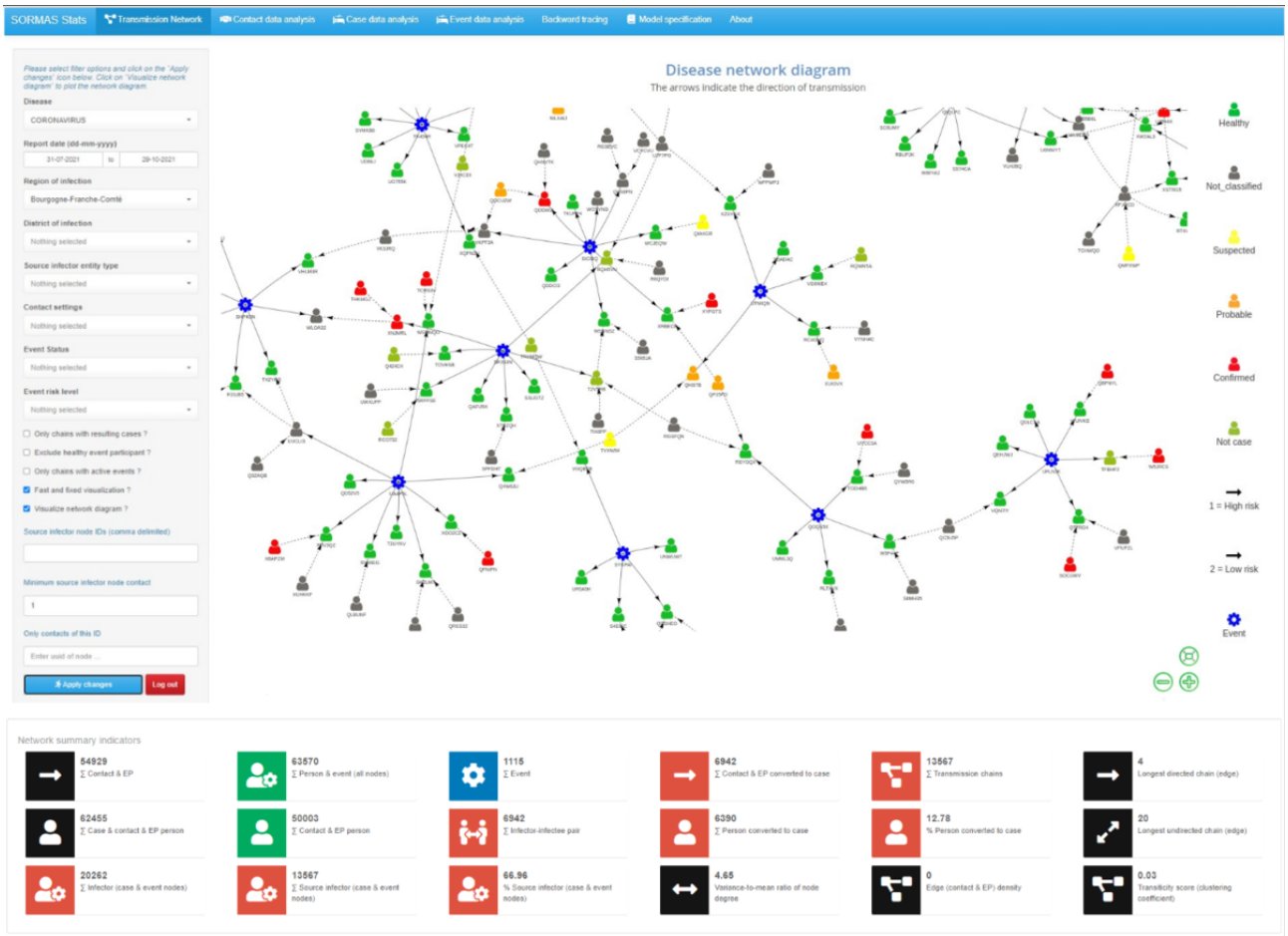
Contents of the SORMAS-Stats User Interface

The SORMAS-Stats application has multiple dashboards with filters, permitting users to execute analysis and download the output. Table 1 depicts the contents of the SORMAS-Stats user interface and their applications in disease surveillance or outbreak management. The contents of the interface are visualizations, epidemiological parameters, and surveillance indicators.

Description of the Epidemiological Data Used to Illustrate SORMAS-Stats

We used SORMAS-Stats to estimate epidemiological parameters and surveillance indicators by analyzing the contact-tracing data documented in SORMAS between July 31 and October 29, 2021, in the Bourgogne-Franche-Comté region of France. Figure 2 presents a network diagram constructed from the contact-tracing data consisting of 63,570 unique nodes, comprising 1.75% (n=1115) events, 19.59% (n=12,452) case persons, and 78.66% (n=50,003) exposed persons. Of the 50,003 exposed persons, 6390 (12.78%) subsequently converted to cases. The network diagram consisted of 3860 transmission chains, with each chain comprising a minimum of 1 exposed person and a source infector node (case person or event). The length of the longest directed chain was 4 generations of infection. The average number of exposed persons per node (node degree) was 1.73 (IQR 1-228), whereas the variance-to-mean ratio was 4.65.

Figure 2. Screenshot of SORMAS-Stats showing the COVID-19 transmission network diagram and surveillance indicators for 63,570 entities reported between July 31 and October 29, 2021, in the Bourgogne-Franche-Comté region of France. The diagram comprises 1115 events (blue gear node), 12,452 case persons (nongreen person node), 50,003 exposed persons (green person node), and 54,929 exposures (directed arrow from infector node). SORMAS-Stats: Surveillance Outbreak Response Management and Analysis System Statistical application.



Epidemiological Parameters and Surveillance Indicators

After subsetting the network diagram by considering chains with resulting cases only, 10,250 unique nodes remained, comprising 9.30% (n=953) events and 90.70% (n=9297) case persons. Of the 9297 case persons, 68.73% (n=6390) were infectees. There were 3860 transmission chains, with 24.69% (n=953) having an event as the index infector. The average node degree was 1.36 (IQR 1-36), whereas the variance-to-mean ratio was 1.05. The edge density of the complete or reduced network diagram considering chains with only resulting cases was <0.01.

Considering infector-infectee pairs consisting of person entities only (event nodes excluded) resulted in 1238 infector-infectee pairs, of which 31.26% (n=387) had available data for symptom onset date. Of the 387 pairs with available data for symptom onset date, 20.41% (n=79) were pairs of asymptomatic transmission for which the onset date of the infectee preceded or was on the same date as that of the infector. After excluding negative SIs, the mean of the observed SI was 3.96 (IQR 0-27**)** days. The distribution with the best fit to the observed SI data was the lognormal distribution with a mean of 4.30 (95% CI 4.09-4.51) days (Figure 3). The mean of the observed offspring distribution was 1.36 (IQR 1-36). By fitting a negative binomial distribution to the observed offspring distribution, we estimated a dispersion parameter k of 21.11 (95% CI 7.57-34.66) and a reproduction number R of 0.9 (95% CI 0.58-0.60). Using the observed transmission data with a lognormal distribution for SI, the estimate of the average weekly posterior mean for R(t) was 0.98 (IQR 0.80-1.61) (Figure 4). The estimated range of R(t) was congruent with the values obtained when plugging in values for SI mean and SD obtained from the literature (5.19 and 4.23 days, respectively) [9].

Figure 3. Screenshot of SORMAS-Stats showing the COVID-19 serial interval distribution for 1238 infector-infectee pairs reported between July 31 and October 29, 2021, in the Bourgogne-Franche-Comté region of France. AIC: Akaike information criterion; BIC: Bayesian information criterion; SORMAS-Stats: Surveillance Outbreak Response Management and Analysis System Statistical application.

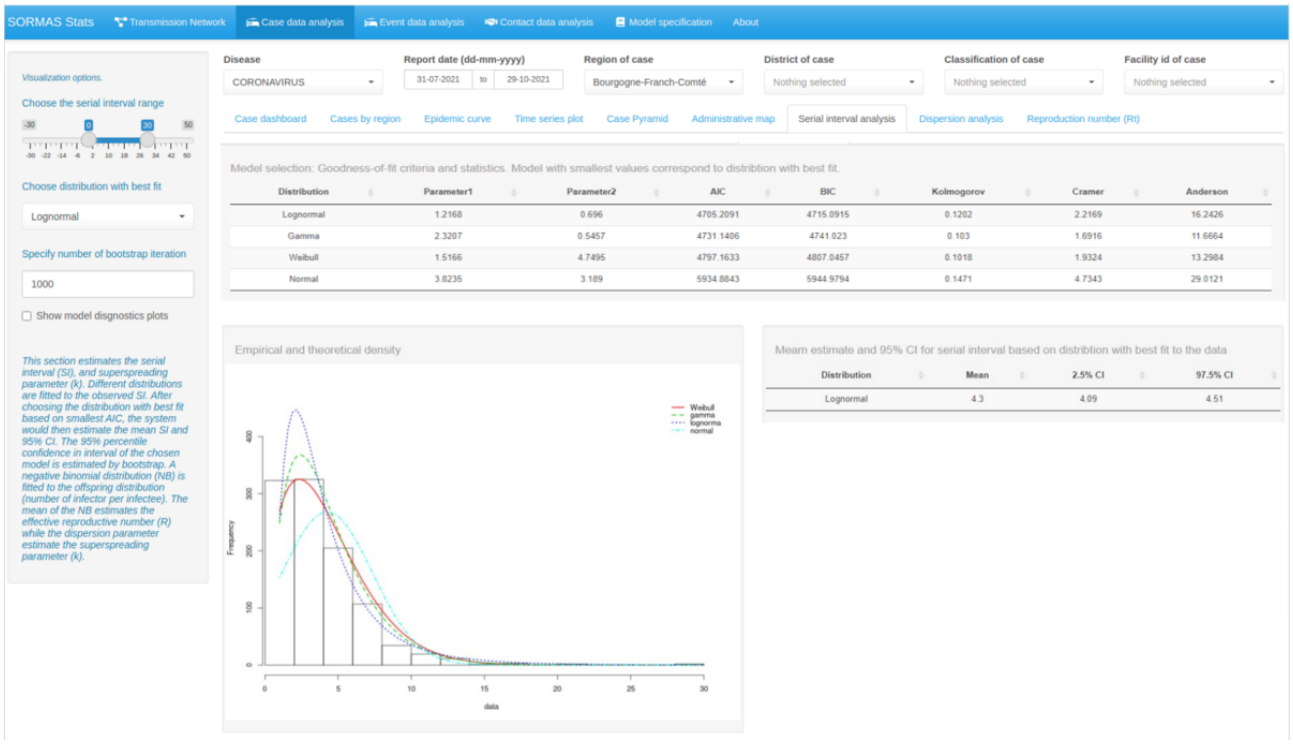


Figure 4. Screenshot of SORMAS-Stats showing an estimate of COVID-19 time-dependent reproduction number (line) with 95% credible interval (grey band) for 12,452 case persons reported between July 31 and October 29, 2021, in the Bourgogne-Franche-Comté region of France. SORMAS-Stats: Surveillance Outbreak Response Management and Analysis System Statistical application.

Discussion

Principal Findings

We developed and deployed SORMAS-Stats, an open-source web application for real-time visualization and the estimation of epidemiological parameters using contact-tracing data captured with the SORMAS eHealth application. SORMAS-Stats is easy to deploy and requires no programming skills to perform analyses. Some epidemiological parameters included in SORMAS-Stats are SI, time-varying reproduction number R(t), effective reproduction number R, and dispersion parameter k. We illustrated the use of SORMAS-Stats by

analyzing the contact-tracing data for COVID-19 captured between July 31 and October 29, 2021, in the Bourgogne-Franche-Comté region of France. The estimated mean SI was 4.30 days; this was commensurate with findings from previous studies [9,11]. The estimate for k was 21.11, whereas the variance-to-mean ratio of the offspring distribution was >1 (1.05), signifying a probable clustering of infections compatible with the observation of superspreading events. However, the estimate was not of the same magnitude as findings from 2 previous studies that used contact-tracing data from other countries at the early phase of the pandemic and reported k of 0.58 and 0.43 [28,29]. This difference in estimates could be related to various factors that may have prevented superspreading events, such as (1) intervention measures (such as the closure of bars, schools, and gatherings) that stakeholders may have enforced during the study period or (2) differences in the geographical area. The possibility of estimating k in real time may assist stakeholders in understanding the current local infection dynamics and thus inform which, if any, control measure would be most appropriate. The weekly estimated R(t) values ranged from 0.80 to 1.61. The maximum value of 1.61 was at the start of the study period; this value was not well estimated since there were no data for the preceding weeks. However, the subsequent values were well estimated and predominantly fluctuated slightly below and above 1, signifying that the infection dynamics were stable within the study period. The computed density of the transmission network diagram was small (<0.01), suggesting low social interactions among the persons in the population, thus resulting in a low transmission rate.

The visualizations included in SORMAS-Stats are maps, charts, tables, time series plots, and network diagrams. Further, SORMAS-Stats contains several filters to explore the network diagram by clusters, transmission chains, and superspreading events. The possibility to filter the network diagram was helpful to stakeholders, not only to assist the exploration of transmission chains but to also detect and correct errors created during the data collection phase. SORMAS-Stats is a stand-alone application, easily deployable owing to Docker technology and does not depend on the principal application or method used for data collection. Thus, users with programming skills in R statistical software only can easily configure and extend SORMAS-Stats to cover other types of statistical analyses.

SORMAS-Stats has a public GitHub repository that permits stakeholders from interested countries to make additional requests and contributions. In this way, it stays an application developed by and for public health workers.

Limitations

The current integration of SORMAS-Stats is with the SORMAS PostgreSQL database. However, with minor adjustment, SORMAS-Stats can be integrated with other databases or files that can be read by R statistical software as long as the relationship between the entities (such as case person, contact person, event, and event participant) are referenced across the tables in the database [30]. The range of the length of the directed transmission chain was 1 to 4; the majority of the chains had 2 or fewer generations of infection. This might be due to the short study period since the data for analysis were available for only 3 months. In France, data older than 3 months are deleted from the SORMAS database as demanded by the law. Some transmission chains may have continued to spread after the study period.

Recommendations for Future Research

Further development of the SORMAS-Stats application can focus on the following features: (1) implement more epidemiological indicators that can inform the management of outbreaks such as statistics on hospitalization, immunization, or symptoms; (2) integrate data from other eHealth applications other than SORMAS; and (3) include outbreak detection, change point detection, or prediction models (eg, compartment models). In addition, as more public health workers use SORMAS-Stats, further research can investigate users' experience, such as desirability, usefulness, and performance, through incorporating the concepts of human-computer interaction [31].

Conclusions

We have provided an application for the real-time estimation of communicable disease parameters, which are essential for outbreak response. The use of the application requires only basic statistical analysis skills. SORMAS-Stats may greatly assist public health authorities in countries using SORMAS or similar tools by providing extensive visualizations, the computation of surveillance indicators, the estimation of epidemiological parameters, and the facilitation of the generation of routine epidemiological reports. This study also showcases how epidemiologists with skills in R statistical software programming only can build a web application, integrate it with a database of another application, and deploy it in the field for outbreak response.

Acknowledgments

This research was supported by the Helmholtz Association of German Research Centres (grant number SO-094).

Authors' Contributions

GK conceived and designed the study. BCS was responsible for feature specification, implementation, and writing the original draft. SG contributed to supervision, code review, and testing. BBK, CV, OL, and CD contributed to feature specification and testing. All authors contributed to the writing of the final version of the manuscript.

Conflicts of Interest

None declared.

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Abbreviations

k: dispersion parameter
SI: serial interval
SORMAS: Surveillance Outbreak Response Management and Analysis System
SORMAS-Stats: Surveillance Outbreak Response Management and Analysis System Statistical application

Edited by T Sanchez, A Mavragani; submitted 27.12.21; peer-reviewed by O Ngwenyama, G Yuan; comments to author 25.01.22; revised version received 06.03.22; accepted 26.04.22; published 31.05.22.

Please cite as:
Silenou BC, Verset C, Kaburi BB, Leuci O, Ghozzi S, Duboudin C, Krause G
A Novel Tool for Real-time Estimation of Epidemiological Parameters of Communicable Diseases Using Contact-Tracing Data: Development and Deployment
JMIR Public Health Surveill 2022;8(5):e34438
URL: https://publichealth.jmir.org/2022/5/e34438
doi:10.2196/34438
PMID:35486812

Original Paper

The Impacts of the COVID-19 Pandemic on HIV Testing Utilization Among Men Who Have Sex With Men in China: Cross-sectional Online Survey

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Abstract

Background: The COVID-19 pandemic has created disruptions in HIV prevention and sexual health services for men who have sex with men (MSM).

Objective: This study compared HIV testing utilization in 3 different reference periods (period 1: before the COVID-19 outbreak, November 2019-January 2020; period 2: after the outbreak, February-April 2020; and period 3: after the pandemic was under initial control, May-July 2020). Factors associated with HIV testing utilization after the COVID-19 outbreak (combined periods 2 and 3) were also investigated.

Methods: Participants were MSM aged ≥18 years living in Shenzhen, China. Those self-reporting as HIV positive were excluded. A total of 595 participants recruited through multiple sources completed a self-administered online survey during August-September 2020. HIV testing utilization after the COVID-19 outbreak was the dependent variable, and multivariate logistic regression models were fitted.

Results: HIV testing utilization was significantly lower in period 2 than in period 1 (n=262 vs 363, 44.0% vs 61.0%, P<.001). However, HIV testing utilization was not significantly higher in period 3 than in period 2 (n=277 vs 262, 46.6% vs 44.0%, P=.21). The prevalence of HIV testing utilization after the COVID-19 outbreak was seen in 331 (55.6%) participants. After adjusting for significant background characteristics, condomless anal intercourse (CAI) with regular male sex partners (RPs; adjusted odds ratio [AOR] 2.15, 95% CI 1.29-3.57) and sexualized drug use (SDU; AOR 2.94, 95% CI 1.41-6.06) both before and after the COVID-19 outbreak, CAI with RPs (AOR 2.07, 95% CI 1.06-4.07) and nonregular male sex partners (NRPs; AOR 3.57, 95%CI: 1.43-8.89) only after the COVID-19 outbreak was positively associated with the dependent variable. Regarding HIV prevention service utilization, HIV testing utilization before the COVID-19 outbreak (AOR 10.75, 95% CI 7.22-16.02) and the use of sexually transmitted infection (STI) testing (AOR 7.02, 95% CI 4.10-12.02), other HIV/STI prevention (AOR 3.15, 95% CI 2.16-4.60), and preexposure prophylaxis (PrEP; AOR 3.58, 95% CI 1.54-8.34) after the COVID-19 outbreak were associated with higher HIV testing utilization. The current perceived risk of HIV infection was higher than that before the COVID-19 outbreak (AOR 1.15, 95% CI 1.01-1.30), and perceived COVID-19 preventive measures taken by HIV testing service providers to be effective (AOR 1.52, 95% CI 1.29-1.78) and perceived higher behavioral control to undergo HIV testing (AOR 1.18, 95% CI 1.00-1.40) were positively associated with HIV testing utilization. Concerns about COVID-19 infection during HIV testing (AOR 0.78, 95%

CI 0.68-0.89), avoiding crowded places (AOR 0.68, 95% CI 0.48-0.98), and HIV testing service providers reducing their working hours (AOR 0.59, 95% CI 0.48-0.98) were negatively associated with the dependent variable.

Conclusions: HIV testing utilization among Chinese MSM declined after the COVID-19 outbreak and did not increase after the pandemic was under initial control. Removing structural barriers to accessing HIV testing caused by COVID-19, modifying perceptions related to HIV testing, and making use of HIV self-testing (HIVST) might be useful strategies to improve HIV testing among MSM during the pandemic.

(JMIR Public Health Surveill 2022;8(5):e30070) doi:10.2196/30070

KEYWORDS

COVID-19; HIV testing; sexual risk behaviors; structural barriers; perception; men who have sex with men; China; MSM; HIV; testing; impact; utilization; cross-sectional; online survey; barrier; access

Introduction

High coverage of HIV testing (ie, >90%) among at-risk populations is the first and a crucial step to achieve the 90-90-90 targets established by the Joint United Nations Programme on HIV/AIDS (UNAIDS), which provides a hope of ending the global HIV epidemic by 2030 [1]. International health authorities recommend men who have sex with men (MSM) to undergo HIV testing every 6 months [2,3]. In China, the HIV epidemic among MSM has been worsening over time [4]. A recent systematic review showed an overall HIV prevalence of 5.7% among MSM in China [4], whereas the HIV incidence in this group was as high as 5.6 per 100 person-years [5]. However, HIV testing coverage remained low among MSM in China (about 60% in the past year) [6].

The COVID-19 pandemic is a serious health threat worldwide, with over 147 million confirmed cases and over 3 million deaths as of April 27, 2021 [7]. The COVID-19 pandemic and its control measures (eg, lockdown, physical distancing, and closure of business) had a direct impact on HIV prevention and sexual health services for MSM. In Japan, the number of HIV tests performed by public health centers significantly declined in the second quarter of 2020 (9584 vs 35,908 in the year-before period) [8]. A similar situation was observed in Melbourne, Australia, where the number of HIV tests decreased from 16,367 in 2019 to 11,270 in 2020, a 31% reduction [9]. An online survey of a global sample of MSM showed that only 30% and 19% of participants had similar levels of access to on-site HIV testing and HIV self-testing (HIVST) during the pandemic comparing to their situation in 2019 [10]. In the United States, 18.8% of MSM had decreased access to HIV testing and 5.6% had trouble getting HIV testing after the COVID-19 outbreak [11]. There are concerns that if MSM continue to engage in sexual behaviors while having problems accessing HIV testing and other HIV or sexually transmitted infection (STI) prevention services during the pandemic, there will be a surge in new HIV cases/STIs [12]. There is a dearth of studies investigating the impact of COVID-19 on HIV testing utilization among MSM in China. To the best of our knowledge, only 1 study has looked at the difficulties in accessing HIV services in general among Chinese MSM; difficulties were reported by 56.8% of the participants [13]. The magnitude of the impact of COVID-19 on HIV testing utilization among Chinese MSM or whether service utilization will rebound after the COVID-19 pandemic is under initial control is unclear. A knowledge gap hence exists.

Understanding the barriers to HIV testing utilization during the COVID-19 pandemic is important in order to inform service planning and intervention development. Previous studies have suggested that COVID-19 control measures increase structural barriers to accessing HIV testing due to the closure of facilities providing HIV testing services, shortage of medical staff providing HIV testing, suspension of public transportation, and lockdown/travel restrictions [8,13-16]. COVID-19 also exacerbated some perceived barriers to using HIV testing, such as the fear of going to hospitals because of COVID-19, concerns about COVID-19 infection or having close contact with patients with COVID-19 during HIV testing, and perceptions that health workers were reluctant to serve them during the pandemic [8,13-16]. These factors were considered by this study.

To address these knowledge gaps, we conducted a cross-sectional online survey among MSM in China. This study had 2 objectives. The first objective was to compare self-reported utilization of any type and a specific type of HIV testing in 3 different reference periods. The first period was before the COVID-19 outbreak (November 2019-January 2020), the second was after the outbreak and before the pandemic was under initial control (February-April 2020), while the third was after the pandemic was under initial control (May-July 2020). The second objective was to investigate factors associated with self-reported utilization of any type of HIV testing after the COVID-19 outbreak (February-July 2020).

Methods

Study Design

We conducted a cross-sectional online survey of 595 MSM in Shenzhen, China, during August-September 2020. Shenzhen is a major metropolitan city located in Guangdong Province in southern China, with a population of 13 million in 2020.

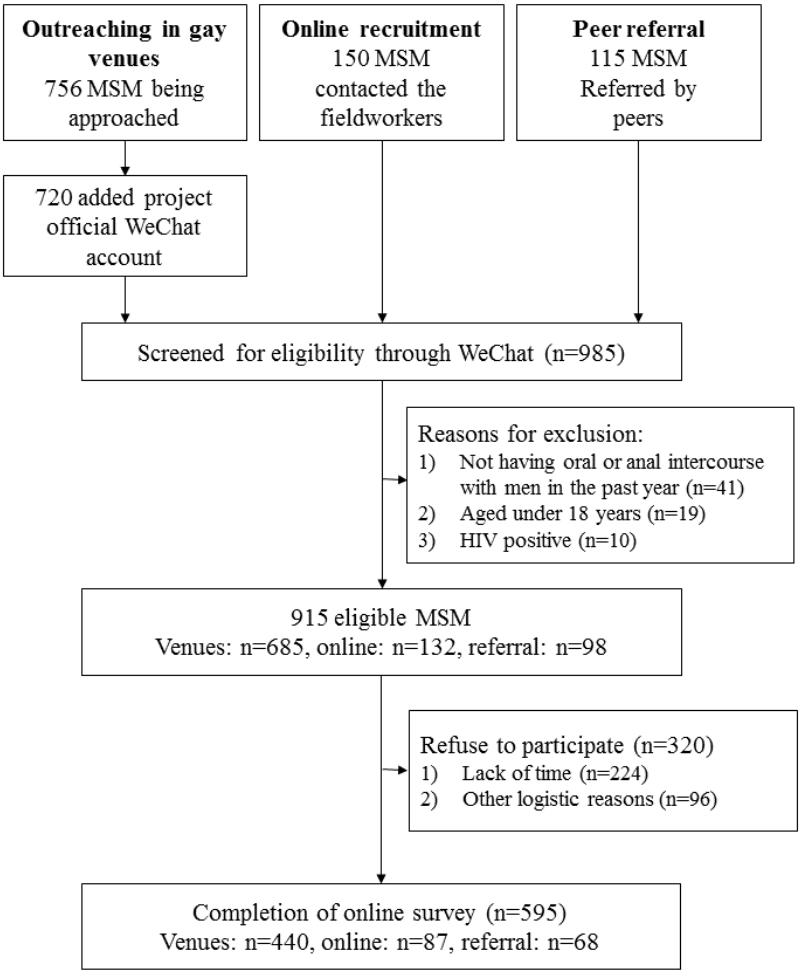
Participants and Data Collection

Participants (1) were Chinese-speaking men living in Shenzhen, (2) were aged at least 18 years, and (3) had oral or anal intercourse with at least 1 man in the past year. Those self-reporting to be HIV positive were excluded. Participants were recruited through multiple sources. Trained and experienced fieldworkers approached prospective participants in venues frequently visited by MSM (ie, bars, parks, and bathhouses) at different time slots on weekdays and weekends. The research team also conducted online outreaching by

periodically posting study information on Weibo and WeChat, 2 commonly used social media platforms in China. Recruitment was supplemented by peer referrals. Fieldworkers briefed prospective participants about the study details on-site or using telephone/live chat apps and invited them to create the project's official WeChat account. Through WeChat, fieldworkers screened the eligibility of prospective participants. Participants were assured that their identifiable information would be kept confidential, they had the right to discontinue participation in the study at any time, and their refusal or withdrawal from the study would not have any consequences. Participants signed an electronic consent form sent by WeChat. The fieldworkers approached 756 prospective participants in gay venues, 720 (95.2%) added the project official WeChat account, 685 (95.1%) were screened to be eligible through WeChat, 245 (35.8%) refused to participate, and 440 (64.2%) completed the online survey. Regarding online recruitment, 150 prospective participants contacted the fieldworkers, 132 (88%) were screened to be eligible through WeChat, 45 (34.1%) refused to participate, and 87 (65.9%) completed the survey. Of 115 prospective participants referred by peers, 98 (85.2%) were screened to be eligible through WeChat, 30 (30.6%) refused to participate and 68 (69.4%) completed the survey. A total of 595 participants completed this study. The main reasons for exclusion were (1) not having oral or anal intercourse with men in the past year (41/985, 4.2%), (2) being aged under 18 years (19/985, 1.9%), and (3) being HIV positive (10/985, 1%). The main reasons for refusals were lack of time and other logistic reasons. A flowchart of recruitment is shown in Figure 1.

We developed an online self-administered questionnaire using Questionnaire Star, a commonly used online survey platform in China. Quick response (QR) codes were generated and sent to the 595 participants through WeChat. The participants were asked to scan the QR code to complete the survey. Each mobile device was only allowed to access the online questionnaire once to avoid duplicate responses. The survey had 105 items (about 20 items per page for 5 pages), which took about 20 minutes to complete. The Questionnaire Star tool performed completeness checks before the questionnaire was submitted. The participants were able to review and change their responses through a Back button. An e-coupon of CNY 20 (US $2.97) was sent to the participants upon survey completion. All data were stored on the online server of Questionnaire Star and protected by a password. Only the corresponding author had access to the database.

Figure 1. Flowchart of subject recruitment. MSM: men who have sex with men.



Ethical Considerations

Ethics approval was obtained from the Longhua District Centers for Disease Control and Prevention (CDC; reference: 2021009).

Measurements

A panel consisting of 3 CDC staff, 2 public health researchers, a health psychologist, and 2 MSM volunteers was formed to develop the questionnaire used in this study. The questionnaire was pilot-tested among 10 MSM to assess clarity and readability. These 10 MSM did not participate in the actual survey. Based on their comments, the panel revised and finalized the questionnaire. The Chinese and English versions of the questionnaire are provided in Multimedia Appendix 1.

Background characteristics were collected, including age, relationship status, highest educational level attained, current employment status, monthly personal income, sexual orientation, and source of recruitment.

The dependent variable for this study was HIV testing utilization. In addition, 3 independent questions were used to assess whether participants performed a specific type of HIV testing (ie, HIV testing at community-based organizations [CBOs], public hospitals/the CDC, private hospitals, and other organizations in Shenzhen; HIV testing in a place other than Shenzhen; and home-based HIVST) in 3 reference periods. The first period was between November 2019 and January 2020. Soon after the China central government imposed a lockdown in Wuhan on January 23, 2020, Shenzhen initiated a tier 1 response (the highest level) to a major public health event on January 24, 2020 [17]. Therefore, the first reference period represented the time prior to the COVID-19 outbreak in China. The second period was between February and April 2020, after the lockdown in Wuhan was lifted in April 2020 and Shenzhen lowered its response level to tier 3 (the lowest level) in early May 2020 [17]. The second reference period hence represented the time after the COVID-19 outbreak and before the pandemic was under initial control in China. The last period was from May to July 2020, which represented the time after the COVID-19 pandemic was under initial control in China [17].

Independent variables included sexual risk behaviors, other HIV/STI prevention services, perceptions related to HIV testing, and structural barriers to HIV testing. Similar to measuring HIV testing behaviors, 3 independent questions were used to measure sexual risk behaviors and other HIV/STI prevention services in the 3 reference periods. The 4 different types of sexual risk behaviors assessed by the questionnaire were (1) condomless anal intercourse (CAI) with regular male sex partners (RPs), (2) CAI with nonregular male sex partners (NRPs), (3) CAI with male sex workers, and (4) sexualized drug use (SDU). An RP is defined as a stable boyfriend, while an NRP is defined as a man who is neither an RP nor a male sex worker. SDU is defined as the use of any of the following psychoactive substances before or during sexual intercourse: ketamine, methamphetamine, cocaine, cannabis, ecstasy, Dormicum/Halcion/Erimin 5/nonprescription hypnotic drugs, heroin, cough suppressant (not for curing cough), gamma-hydroxybutyric acid (GHB)/gamma-butyrolactone (GBL), 5-methocy-*N*,*N*-diisopropyltryptamine (Foxy), and mephedrone [18,19]. We created 4 variables comparing the presence of sexual risk behaviors before (period 1) and after (combined periods 2 and 3) the COVID-19 outbreak. The response categories of these variables were as follows: 1=no such behavior before or after the COVID-19 outbreak, 2=with such behavior only before the COVID-19 outbreak, 3=with such behavior both before and after the COVID-19 outbreak, and 4=with such behavior only after the COVID-19 outbreak.

The online survey also documented the participants' use of other STI testing, other HIV/STI prevention services (eg, receiving free condoms, receiving peer education or education pamphlets, and attending lectures or seminars), and preexposure prophylaxis (PrEP) after the COVID-19 outbreak.

We applied the theory of planned behavior (TPB) as the theoretical framework to select perceptions related to HIV testing after the COVID-19 outbreak [20]. The TPB postulates that willingness to adopt a health-related behavior is a strong predictor of actual behavior. To form such an intention, one would evaluate the pros and cons of the behavior (positive and negative attitudes), consider whether their significant others would support such behavior (perceived subjective norm), and appraise how much control one has over the behavior (perceived behavioral control) [20]. In this study, 1 item measured the participants' positive attitude toward HIV testing services during COVID-19 (ie, COVID-19 preventive measures taken by HIV testing service providers are effective); 2 other items measured some negative attitudes toward HIV testing services during COVID-19, such as the participants' concerns related to the risk of contracting COVID-19 during HIV testing and inconvenience of undergoing HIV testing during the pandemic; and 2 single items measured the perceived subjective norm (ie, people who are important to you would support you to undergo HIV testing after the COVID-19 outbreak) and perceived behavioral control (ie, whether to undergo HIV testing after the COVID-19 outbreak is completely under control). The response categories for the latter 5 items were 1=strongly disagree, 2=disagree, 3=neutral, 4=agree, and 5=strongly agree. In addition, 1 item measured the perceived risk of HIV infection comparing the participants' present situation with the situation before the COVID-19 outbreak ("When comparing your current situation versus the time before COVID-19, do you think your overall risk of HIV infection is higher, lower, or the same?"); the response categories were 1=much lower, 2=somewhat lower, 3=same, 4=somewhat higher, and 5=much higher.

The participants were also asked whether they adopted physical distancing after the COVID-19 outbreak (February-July 2020), including avoiding unnecessary travel and crowded places. Other structural barriers to utilizing HIV testing after the COVID-19 outbreak included whether HIV testing service providers were closed or had reduced their working hours and whether they had difficulty in obtaining HIVST kits and a history of home/centralized quarantine between February and July 2020.

Statistical Analysis

HIV testing utilization was compared using McNemar tests. Since 1 of our objectives was to investigate factors associated with HIV testing utilization after the COVID-19 outbreak, we

combined the utilization of any type of HIV testing in period 2 (February-April 2020) and period 3 (May-July 2020) and used it as the dependent variable in the subsequent analysis. First, associations between background characteristics and the dependent variable were analyzed using logistic regression models, and crude odds ratios (ORs) were obtained. After adjustment for those variables with $P<0.05$ in the univariate analysis, associations between independent variables of interest (HIV testing prior to the COVID-19 outbreak, other HIV/STI prevention service utilization after the COVID-19 outbreak, variables comparing the presence of sexual risk behaviors before and after the COVID-19 outbreak, perceptions related to HIV testing, and structural barriers to HIV testing after the COVID-19 outbreak) and the dependent variable were assessed by adjusted odds ratios (AORs). Each AOR was obtained by fitting a single logistic regression model, which involved 1 of the independent variables of interest and significant background variables. SPSS Statistics version 21.0 (IBM) was used for data analysis, with $P<.05$ considered statistically significant.

Results

Background Characteristics of the Participants

The majority of the participants were 18-30 years old (n=452, 75.9%), single (n=481, 80.8%), and employed full-time (n=433, 72.8%); had attained at least tertiary education (n=394, 66.2%), with a monthly personal income of CNY >=5000 (>=US$741.46) (n=346, 58.1%); see Table 1.

Table 1. Background characteristics of 595 MSM[a] participating in a cross-sectional survey from August to September 2020.

Characteristics	Participants, n (%)
Age (years)	
18-24	184 (30.9)
25-30	268 (45.0)
31-40	114 (19.2)
>40	29 (4.9)
Relationship status	
Single	481 (80.8)
Cohabiting with or married to a man	92 (15.5)
Cohabiting with or married to a woman	22 (3.7)
Highest educational level attained	
Senior high school or below	201 (33.8)
College or above	394 (66.2)
Current employment status	
Full-time	433 (72.8)
Part-time/unemployed/retired/student	162 (27.2)
Monthly personal income[b]	
CNY <3000 (<US $444.87)	87 (14.6)
CNY 3000-4999 (US $444.87-$741.31)	119 (20.0)
CNY 5000-6999 (US $741.46-$1037.89)	118 (19.8)
CNY 7000-9999 (US $1038.04-$1482.76)	99 (16.6)
CNY ≥10,000 (≥US $1482.91)	129 (21.7)
Refuse to disclose	43 (7.2)
Sexual orientation	
Homosexual	427 (71.8)
Bisexual	117 (19.7)
Heterosexual	18 (3.0)
Uncertain	33 (5.5)
Source of recruitment	
Outreach in gay venues	440 (73.9)
Online recruitment	87 (14.6)
Peer referral	68 (11.4)

[a]MSM: men who have sex with men.

[b]An exchange rate of CNY 1=US $0.15 has been used.

Frequency Distribution of Independent Variables

Relatively few participants (n=6-44, 1.0%-7.4%) reported the presence of sexual risk behaviors only after the COVID-19 outbreak (Table 2). The prevalence of sexual risk behaviors in different reference periods are shown in Multimedia Appendix 2. After the COVID-19 outbreak, 37-199 (6.2%-33.4%) participants used HIV/STI prevention services other than HIV testing (Table 3). Regarding perceptions related to HIV testing (Table 4), over half of the participants perceived their current risk of HIV infection was much/somewhat lower than that before COVID-19 (n=387, 65%) and agreed/strongly agreed that COVID-19 preventive measures taken by HIV testing service providers were effective (n=320, 53.7%). More than one-third of them had concerns related to COVID-19 infection during HIV testing (n=225, 37.9%) and the inconvenience of using HIV testing services during the pandemic (n=243, 40.8%). Regarding structural barriers to HIV testing, 58 (9.7%) and 63 (10.6%) participants reported that HIV testing service providers suspended and reduced their services, respectively, and 42 (7.1%) had difficulty in obtaining HIVST kits between February and July 2020 (Table 5).

Table 2. Frequency distribution of sexual risk behaviors before (November 2019-January 2020) and after (February-July 2020) the COVID-19 outbreak among 595 MSM[a] participating in a cross-sectional survey from August to September 2020.

Independent variables	Participants, n (%)
CAI[b] with RPs[c]	
No such behavior before or after the COVID-19 outbreak	427 (71.8)
With such behavior only before the COVID-19 outbreak	33 (5.5)
With such behavior both before and after the COVID-19 outbreak	91 (15.3)
With such behavior only after the COVID-19 outbreak	44 (7.4)
CAI with NRPs[d]	
No such behavior before or after the COVID-19 outbreak	509 (85.5)
With such behavior only before the COVID-19 outbreak	19 (3.2)
With such behavior both before and after the COVID-19 outbreak	35 (5.9)
With such behavior only after the COVID-19 outbreak	32 (5.4)
CAI with male sex workers	
No such behavior before or after the COVID-19 outbreak	576 (96.8)
With such behavior only before the COVID-19 outbreak	5 (0.8)
With such behavior both before and after the COVID-19 outbreak	8 (1.3)
With such behavior only after the COVID-19 outbreak	6 (1.0)
SDU[e]	
No such behavior before or after the COVID-19 outbreak	515 (86.6)
With such behavior only before the COVID-19 outbreak	13 (2.2)
With such behavior both before and after the COVID-19 outbreak	45 (7.6)
With such behavior only after the COVID-19 outbreak	22 (3.7)

[a]MSM: men who have sex with men.

[b]CAI: condomless anal intercourse.

[c]RP: regular male sex partner.

[d]NRP: nonregular male sex partner.

[e]SDU: sexualized drug use.

Table 3. Frequency distribution of HIV/STI[a] prevention service utilization after the COVID-19 outbreak (February-July 2020) among 595 MSM[b] participating in a cross-sectional survey from August to September 2020.

Independent variables	Participants, n (%)
Testing for other STIs	
No	373 (77.8)
Yes	132 (22.2)
Other HIV/STI prevention services (eg, receiving free condoms or peer education or education pamphlets, attending lectures or seminars)	
No	396 (66.6)
Yes	199 (33.4)
Use of PrEP[c] before CAI[d] with male sex workers	
No	558 (93.8)
Yes	37 (6.2)

[a]STI: sexually transmitted infection.

[b]MSM: men who have sex with men.

[c]PrEP: preexposure prophylaxis.

[d]CAI: condomless anal intercourse.

Table 4. Frequency distribution of perceptions related to HIV testing utilization after the COVID-19 outbreak among 595 MSM[a] participating in a cross-sectional survey from August to September 2020.

Independent variables	Participants, n (%)	Mean (SD)
Perceived risk of HIV infection comparing the present situation with the time before COVID-19		2.3 (1.3)
Much lower	218 (36.6)	N/A[b]
Somewhat lower	169 (28.4)	N/A
Same	31 (5.2)	N/A
Somewhat higher	143 (24.0)	N/A
Whether COVID-19 preventive measures taken by HIV testing services providers are effective		3.5 (1.1)
Strongly disagree	35 (5.9)	N/A
Disagree	57 (9.6)	N/A
Neutral	183 (30.8)	N/A
Agree	221 (37.1)	N/A
Strongly agree	99 (16.6)	N/A
Concern about COVID-19 infection when undergoing HIV testing		3.1 (1.3)
Strongly disagree	85 (14.3)	N/A
Disagree	90 (15.1)	N/A
Neutral	195 (32.8)	N/A
Agree	114 (19.2)	N/A
Strongly agree	111 (18.7)	N/A
Whether it is inconvenient to go to organizations providing HIV testing after the COVID-19 outbreak		3.3 (1.2)
Strongly disagree	59 (9.9)	N/A
Disagree	83 (13.9)	N/A
Neutral	210 (35.3)	N/A
Agree	124 (20.8)	N/A
Strongly agree	119 (20.0)	N/A
Whether people who are important to you support you to undergo HIV testing after the COVID-19 outbreak		4.0 (1.0)
Strongly disagree	28 (4.7)	N/A
Disagree	7 (1.2)	N/A
Neutral	135 (22.7)	N/A
Agree	212 (35.6)	N/A
Strongly agree	213 (35.8)	N/A
Whether to undergo HIV testing after the COVID-19 outbreak is completely under control		4.0 (1.0)
Strongly disagree	21 (3.5)	N/A
Disagree	14 (2.4)	N/A
Neutral	126 (21.2)	N/A
Agree	209 (35.1)	N/A
Strongly agree	225 (37.8)	N/A

[a]MSM: men who have sex with men.

[b]N/A: not applicable.

Table 5. Frequency distribution of structural barriers among 595 MSM[a] participating in a cross-sectional survey from August to September 2020.

Independent variables	Participants, n (%)
Avoiding unnecessary travel	
No	203 (34.1)
Yes	392 (65.9)
Avoiding crowded places	
No	181 (30.4)
Yes	414 (69.6)
HIV testing service providers suspending their services during February-July 2020	
No	537 (90.3)
Yes	58 (9.7)
HIV testing service providers reducing their service hours during February-July 2020	
No	532 (89.4)
Yes	63 (10.6)
Difficulty in obtaining HIVST[b] kits during February-July 2020	
No	553 (92.9)
Yes	42 (7.1)
History of home/centralized quarantine during February-July 2020	
No	504 (84.7)
Yes	91 (15.3)

[a]MSM: men who have sex with men.

[b]HIVST: HIV self-testing.

HIV Testing Utilization During Different Reference Periods

About half of the participants underwent any types of HIV testing between February and July 2020 (n=331, 55.6%). Compared to the time before the COVID-19 outbreak (period 1, November 2019-January 2020), a significantly lower proportion of the participants underwent any type of HIV testing between February and April 2020 (period 2 vs period 1: n=262 vs 363, 44.0% vs 61.0%, *P*<.001). The proportion of testers did not increase significantly after the pandemic was under initial control in China (period 3, May-July 2020; period 2 vs period 3: n=262 vs 277, 44.0% vs 46.6%, *P*=.21; period 3 vs period 1: n=277 vs 363, 46.6% vs 61.0%, *P*<.001). We observed similar changes in the utilization of HIV testing at CBOs in Shenzhen, at public hospitals/the CDC in Shenzhen, at other organizations in Shenzhen, and in places other than Shenzhen, as well as the utilization of HIVST. In addition, 331 (55.6%) participants had undergone any type of HIV testing after the COVID-19 outbreak (combined periods 2 and 3); see Table 6. Patterns of HIV testing utilization across the study period are also shown in Figure 2.

Table 6. HIV testing utilization during different reference periods among 595 MSM[a] participating in a cross-sectional survey from August to September 2020.

HIV testing locations	Participants who underwent testing, n (%)	Period 1[b] vs period 2[c], *P* value[d]	Period 2 vs period 3[e], *P* value[d]	Period 3 vs period 1, *P* value[d]
HIV testing at CBOs[f] in Shenzhen		<.001	.56	<.001
Period 1	72 (12.1)	N/A[g]	N/A	N/A
Period 2	41 (6.9)	N/A	N/A	N/A
Period 3	45 (7.6)	N/A	N/A	N/A
Combined periods 2 and 3	56 (9.4)	N/A	N/A	N/A
HIV testing at public hospitals or the CDC[h] in Shenzhen		<.001	.38	<.001
Period 1	137 (23.0)	N/A	N/A	N/A
Period 2	77 (12.9)	N/A	N/A	N/A
Period 3	85 (14.3)	N/A	N/A	N/A
Combined periods 2 and 3	113 (19.0)	N/A	N/A	N/A
HIV testing at private hospitals in Shenzhen		.08	.55	.33
Period 1	28 (4.7)	N/A	N/A	N/A
Period 2	20 (3.4)	N/A	N/A	N/A
Period 3	23 (3.9)	N/A	N/A	N/A
Combined periods 2 and 3	27 (4.5)	N/A	N/A	N/A
HIV testing at other organizations in Shenzhen		.002	.42	.05
Period 1	52 (8.7)	N/A	N/A	N/A
Period 2	34 (5.7)	N/A	N/A	N/A
Period 3	39 (6.6)	N/A	N/A	N/A
Combined periods 2 and 3	49 (8.2)	N/A	N/A	N/A
HIV testing in places other than Shenzhen		.002	.42	.05
Period 1	129 (21.7)	N/A	N/A	N/A
Period 2	76 (12.8)	N/A	N/A	N/A
Period 3	72 (12.1)	N/A	N/A	N/A
Combined periods 2 and 3	98 (16.5)	N/A	N/A	N/A
Home-based HIVST[i]		<.001	.83	<.001
Period 1	260 (43.7)	N/A	N/A	N/A
Period 2	200 (33.6)	N/A	N/A	N/A
Period 3	197 (33.1)	N/A	N/A	N/A
Combined periods 2 and 3	241 (40.5)	N/A	N/A	N/A
Any type of HIV testing		<.001	.21	<.001
Period 1	363 (61.0)	N/A	N/A	N/A
Period 2	262 (44.0)	N/A	N/A	N/A
Period 3	277 (46.6)	N/A	N/A	N/A
Combined periods 2 and 3	331 (55.6)	N/A	N/A	N/A

[a]MSM: men who have sex with men.

[b]Period 1: before the COVID-19 outbreak (November 2019-January 2020).

[c]Period 2: before COVID-19 was under initial control (February-April 2020).

[d]*P* values were obtained using McNemar tests.

[e]Period 3: after COVID-19 was under initial control (May-July 2020).

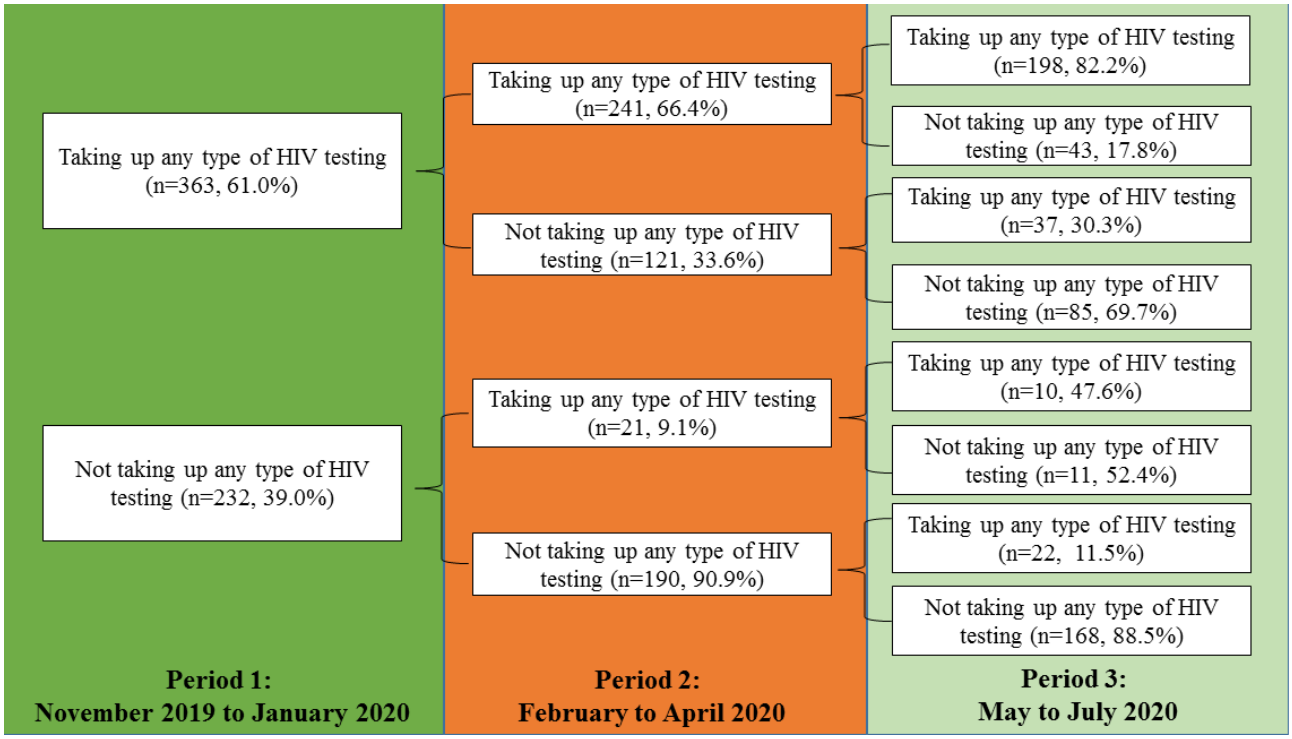
[f]CBO: community-based organization.

[g]N/A: not applicable.

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

[i]HIVST: HIV self-testing.

Figure 2. Patterns of HIV testing uptake in different reference periods.



Factors Associated With HIV Testing Utilization After the COVID-19 Outbreak (February-July 2020)

In univariate analysis, participants who cohabited with or were married to a woman and identified themselves as heterosexual were less likely to undergo any type of HIV testing between February and July 2020 (Table 7).

After adjusting for these significant background characteristics, CAI with RPs and SDU both before and after the COVID-19 outbreak were associated with higher utilization of HIV testing after the COVID-19 outbreak. CAI with RPs and NRPs only after the COVID-19 outbreak was also positively associated with the dependent variable. Regarding HIV/STI prevention service utilization, utilization of HIV testing services prior to the COVID-19 outbreak was associated with higher HIV testing utilization after the COVID-19 outbreak. Users of other STI testing, other HIV/STI prevention services, and PrEP after the COVID-19 outbreak were more likely to undergo any types of HIV testing in the same period.

The current perceived risk of HIV infection was higher than that before the COVID-19 outbreak (AOR 1.15, 95% CI 1.01-1.30, *P*=.03), and perceived COVID-19 preventive measures taken by HIV testing service providers to be effective (AOR 1.52, 95% CI 1.29-1.78, *P*<.001) and perceived higher behavioral control to undergo HIV testing after the COVID-19 outbreak (AOR 1.18, 95% CI 1.00-1.40, *P*=.048) were associated with higher HIV testing utilization between February and July 2020. COVID-19 infection during HIV testing (AOR 0.78, 95% CI 0.68-0.89, *P*<.001), avoiding crowded places (AOR 0.68, 95% CI 0.48-0.98, *P*=0.04), and HIV testing service providers reducing their working hours (AOR 0.59, 95% CI 0.48-0.98, *P*=0.046) were associated with lower HIV testing utilization during the same period (Table 8).

Table 7. Associations between background characteristics and utilizing any HIV testing after the COVID-19 outbreak (February-July 2020) among 595 MSM[a] participating in a cross-sectional survey from August to September 2020.

Characteristics	Prevalence of utilizing any HIV testing, n/N (%)	Crude OR[b] (95% CI)	*P* value
Age (years)			
18-24	94/184 (51.1)	1.0	N/A[c]
25-30	157/268 (58.6)	1.35 (0.93-1.98)	.12
31-40	60/114 (52.6)	1.06 (0.67-1.70)	.80
>40	20/29 (69.0)	2.13 (0.92-4.92)	.08
Relationship status			
Single	271/481 (56.3)	1.0	N/A
Cohabiting with or married to a man	54/92 (58.7)	1.10 (0.70-1.73)	.68
Cohabiting with or married to a woman	6/22 (27.3)	0.29 (0.11-0.76)	.01
Highest educational level attained			
Senior high school or below	105/201 (52.2)	1.0	N/A
College or above	226/394 (57.4)	1.23 (0.87-1.73)	.24
Employment status			
Full-time	246/433 (56.8)	1.0	N/A
Part-time/unemployed/retired/student	85/162 (52.5)	0.84 (0.58-1.21)	.34
Monthly personal income			
CNY <3000 (<US $444.87)	50/87 (57.5)	1.0	N/A
CNY 3000-4999 (US $444.87-$741.31)	60/119 (50.4)	0.75 (0.43-1.31)	.32
CNY 5000-6999 (US $741.46-$1037.89)	64/118 (54.2)	0.88 (0.50-1.53)	.65
CNY 7000-9999 (US $1038.04-$1482.76)	56/99 (56.6)	0.96 (0.65-1.72)	.90
CNY ≥10,000 (≥US $1482.91)	80/129 (62.0)	1.21 (0.69-2.10)	.50
Refuse to disclose	21/43 (48.8)	0.71 (0.34-1.47)	.35
Sexual orientation			
Homosexual	241/427 (56.4)	1.0	N/A
Bisexual	72/117 (61.5)	1.24 (0.81-1.88)	.32
Heterosexual	3/18 (16.7)	0.15 (0.04-0.54)	.004
Uncertain	15/33 (45.5)	0.64 (0.32-1.32)	.22
Source of recruitment			
Outreach in gay venues	247/440 (56.1)	1.0	N/A
Online recruitment	44/87 (50.6)	0.80 (0.50-1.27)	.34
Peer referral	40/68 (58.8)	1.12 (0.67-1.87)	.68

[a]MSM: men who have sex with men.

[b]OR: odds ratio.

[c]N/A: not applicable.

Table 8. Factors associated with utilizing any HIV testing after the COVID-19 outbreak (February-July 2020) among 595 MSM[a] participating in a cross-sectional survey from August to September 2020.

Factors	Crude OR[b] (95% CI)	*P* value	AOR[c] (95% CI)	*P* value
CAI[d] with RPs[e]				
No such behavior before or after the COVID-19 outbreak	1.0	N/A[f]	1.0	N/A
With such behavior only before the COVID-19 outbreak	1.71 (0.82-3.56)	.15	1.51 (0.72-3.17)	.28
With such behavior both before and after the COVID-19 outbreak	2.32 (1.42-3.77)	.001	2.15 (1.29-3.57)	.003
With such behavior only after the COVID-19 outbreak	2.09 (1.08-4.06)	.03	2.07 (1.06-4.07)	.03
CAI with NRPs[g]				
No such behavior before or after the COVID-19 outbreak	1.0	N/A	1.0	N/A
With such behavior only before the COVID-19 outbreak	0.63 (0.25-1.59)	.33	0.66 (0.25-1.70)	.39
With such behavior both before and after the COVID-19 outbreak	1.87 (0.91-3.93)	.09	1.83 (0.87-3.87)	.11
With such behavior only after the COVID-19 outbreak	3.75 (1.52-9.26)	.004	3.57 (1.43-8.89)	.01
CAI with male sex workers				
No such behavior before or after the COVID-19 outbreak	1.0	N/A	1.0	N/A
With such behavior only before the COVID-19 outbreak	3.18 (0.35-28.61)	.30	3.68 (0.40-34.19)	.25
With such behavior both before and after the COVID-19 outbreak	0.48 (0.11-2.01)	.31	0.46 (0.11-1.99)	.30
With such behavior only after the COVID-19 outbreak	0.79 (0.16-3.97)	.78	0.84 (0.16-4.34)	.84
SDU[h]				
No such behavior before or after the COVID-19 outbreak	1.0	N/A	1.0	N/A
With such behavior only before the COVID-19 outbreak	2.03 (0.62-6.66)	.25	1.91 (0.58-6.31)	.29
With such behavior both before and after the COVID-19 outbreak	3.15 (1.53-6.50)	.002	2.94 (1.41-6.06)	.004
With such behavior only after the COVID-19 outbreak	2.40 (0.93-6.23)	.07	2.49 (0.93-6.68)	.07
HIV/STI[i] prevention service utilization				
Utilizing any HIV testing from November 2019 to January 2021	11.05 (7.47-16.33)	<.001	10.75 (7.22-16.02)	<.001
Testing for other STIs after the COVID-19 outbreak (February-July 2020)	7.18 (4.23-12.19)	<.001	7.02 (4.10-12.02)	<.001
Other HIV/STI prevention services (eg, receiving free condoms or peer education or education pamphlets, attending lectures or seminars) after the COVID-19 outbreak (February-July 2020)	3.14 (2.17-4.55)	<.001	3.15 (2.16-4.60)	<.001
Use of PrEP[j] after the COVID-19 outbreak (February-July 2020)	3.66 (1.58-8.47)	.002	3.58 (1.54-8.34)	.002
Perceptions related to HIV testing utilization after the COVID-19 outbreak				
Perceived risk of HIV infection comparing the current situation with the time before COVID-19	1.15 (1.02-1.30)	.03	1.15 (1.01-1.30)	.03
COVID-19 preventive measures taken by HIV testing service providers are effective	1.55 (1.33-1.81)	<.001	1.52 (1.29-1.78)	<.001
Concern about COVID-19 infection when undergoing HIV testing	0.77 (0.68-0.88)	<.001	0.78 (0.68-0.89)	<.001
Whether it is inconvenient to go to organizations providing HIV testing after the COVID-19 outbreak	0.91 (0.80-1.04)	.16	0.88 (0.77-1.01)	.08
Whether people who are important to you support you to undergo HIV testing after the COVID-19 outbreak	1.05 (0.90-1.25)	.51	1.01 (0.86-1.19)	.91
Whether to undergo HIV testing after the COVID-19 outbreak is completely under control	1.21 (1.03-1.43)	.02	1.18 (1.00-1.40)	.048
Structural barriers				
Avoiding unnecessary travel	0.76 (0.54-1.07)	.12	0.77 (0.54-1.09)	.14
Avoiding crowded places	0.67 (0.47-0.95)	.02	0.68 (0.48-0.98)	.04

Factors	Crude OR[b] (95% CI)	*P* value	AOR[c] (95% CI)	*P* value
HIV testing service providers suspending their services during February-July 2020	0.58 (0.33-1.03)	.06	0.62 (0.35-1.10)	.12
HIV testing service providers reducing their service hours during February-July 2020	0.55 (0.31-0.96)	.04	0.59 (0.33-0.99)	.046
Difficulty in obtaining HIVST[k] kits during February-July 2020	0.68 (0.35-1.30)	.24	0.69 (0.36-1.34)	.28
History of home/centralized quarantine during February-July 2020	0.84 (0.53-1.32)	.84	0.87 (0.55-1.38)	.55

[a]MSM: men who have sex with men.

[b]OR: odds ratio.

[c]AOR adjusted odds ratio. The ORs were adjusted for significant background characteristics listed in Table 7 (ie, relationship status and sexual orientation).

[d]CAI: condomless anal intercourse.

[e]RP: regular male sex partner.

[f]N/A: not applicable.

[g]NRP: nonregular male sex partner.

[h]SDU: sexualized drug use.

[i]STI: sexually transmitted infection.

[j]PrEP: preexposure prophylaxis.

[k]HIVST: HIV self-testing.

Discussion

Principal Findings

To the best of our knowledge, this is 1 of the first studies investigating the impacts of the COVID-19 pandemic on HIV testing among MSM in China. A significant decline was observed in the utilization of facility-based HIV testing and HIVST comparing to the prepandemic era. The findings were similar to studies across countries [8-11,13]. A significant decline in sexual risk behaviors (CAI with RPs and NRPs) was also observed after the COVID-19 outbreak. Changes in sexual risk behaviors among MSM after the COVID-19 outbreak were mixed in the previous literature [21-27]. The level of sexual risk behaviors among our participants quickly rebounded to the prepandemic level after the COVID-19 pandemic was under initial control. This situation raised concerns about potential HIV/STI outbreaks among MSM in China in the postpandemic era. Currently, given the scale-up of COVID-19 vaccination, more countries are attempting to return to normal life. Our findings share some reference values for these countries regarding HIV prevention in the postpandemic era. After the control of the COVID-19 pandemic, local governments and service providers should rehire their personnel and resume their working hours for HIV prevention services. Given the implementation of physical distancing and the concerns about COVID-19 infection when using facility-based HIV testing, more efforts should be given to promote home-based HIVST with essential supporting services (eg, online counseling support and referral services for HIVST users) to mitigate the potential negative impacts caused by the pandemic.

Similar to previous findings, COVID-19 caused some structural barriers to accessing HIV testing [8,13-16]. During the pandemic, the Chinese government advocated physical distancing and recommended that people avoid unnecessary travel and crowded places [28,29]. In our study, about 70% of the participants reported avoiding crowded places after the COVID-19 outbreak. Avoiding crowded places was negatively associated with HIV testing utilization. Since facility-based HIV testing is usually provided by public hospitals, the CDC, and CBOs, it was likely that MSM would avoid these crowded places during the pandemic. About 10% of the participants reported that their HIV testing service providers reduced working hours during the pandemic, which was also a barrier. In China, public hospitals and the CDC reallocate some of the HIV prevention staff in order to implement COVID-19 prevention.

Our findings provide some empirical insights into service planning and intervention development. More attention should be given to MSM who cohabit with or are married to a woman or identify themselves as heterosexual, as in this study they reported lower HIV testing after the COVID-19 outbreak. Due to discrimination, MSM in China are sexual minorities and hidden in the population [30]. Some Chinese MSM marry a woman to conceal their homosexuality/same-sex behaviors and to deal with their parents' expectations [30]. Since HIV is a highly stigmatized disease in China, female sexual partners knowing about the MSM's HIV testing utilization might lead to some undesired consequences (eg, conflicts, exposure of homosexuality).

Use of HIV testing prior to the COVID-19 outbreak was associated with higher HIV testing utilization after the outbreak. Different health promotion strategies tailored to the needs of frequent and infrequent testers should be considered. Use of STI testing and other HIV/STI prevention services after the COVID-19 outbreak was also associated with higher HIV testing utilization during the same period. One explanation is that these services are usually performed simultaneously during HIV testing. COVID-19 did not have a significant impact on PrEP users, who reported higher HIV testing utilization, as they are required to undergo such tests every 3 months [31].

Maintaining or increasing sexual risk behaviors (CAI with RPs and NRPs, and SDU) after the COVID-19 outbreak was

significantly associated with higher HIV testing utilization during the same period. Participants might have perceived a lower risk of HIV infection due to the decline in sexual risk behaviors after the COVID-19 outbreak and hence perceived a lower need to undergo HIV testing. The perceived higher risk of HIV infection comparing to the prepandemic era was another facilitator of HIV testing utilization. However, although their sexual risk behaviors rebounded to the prepandemic level, more than 60% of the participants perceived their risk to be lower than the prepandemic level. Facilitating MSM to have an accurate HIV risk perception may be a useful strategy. A personalized HIV risk self-assessment tool may be helpful for MSM during the pandemic, which can be adapted from the HIV risk calculator developed by Chen and Dowdy [32].

Modifying perceptions related to HIV testing after the COVID-19 outbreak may also be useful. About 40% of the participants were concerned about COVID-19 infection when undergoing HIV testing. Such concern was associated with lower HIV testing utilization. Over half of the participants perceived COVID-19 preventive measures taken by HIV testing service providers to be effective. Such perception was a facilitator of HIV testing utilization. HIV testing service providers should make their COVID-19 preventive measures transparent to potential clients to reduce their concerns. The role of HIVST became more important during the COVID-19 pandemic. Previous studies have shown that the majority of MSM were willing to utilize HIVST during the social distancing period and that they preferred home delivery of HIVST kits and support of teleconsultation [33]. Recently, a novel HIVST service was implemented among Chinese MSM. A CBO sent a free HIVST kit through mail to users and provided real-time instructions and counseling through live chat apps, making the experience of HIVST similar to facility-based HIV testing. Such a service was effective in increasing HIV testing coverage and ensuring linkage to care [34,35]. This service could also improve perceived behavioral control to undergo HIV testing after the COVID-19 outbreak, which was another facilitator. Government organizations and CBOs in China should consider allocating more resources to implement HIVST services for MSM in the postpandemic era.

Limitations

This study had a few limitations. First, the cross-sectional study design could not adequately determine the magnitude of the impact of the COVID-19 pandemic and routine testing frequency on HIV testing utilization. However, we believe the impact of routine testing frequency would be limited. Sexually active MSM are recommended by the China CDC to undergo HIV testing every 3 months. In the presence of a window period, all people who receive a negative HIV testing result are also advised to test again 3 months afterward. In this study, the duration of each reference period was in line with the recommended interval of HIV testing for MSM.

Second, HIV testing, sexual risk behaviors, and other HIV/STI prevention service utilization in different reference periods were based on self-reported data, so recall bias existed. The participants were likely to overreport HIV testing or other HIV/STI prevention utilization and underreport sexual risk behaviors due to social desirability.

Third, participants were recruited by nonprobabilistic sampling in 1 Chinese city. Compared to other Chinese cities with a general or a lower economy, there are more organizations providing HIV testing services in Shenzhen. In addition, given the relatively high-income level of the people in Shenzhen, MSM living in the city would have lower financial barriers to using chargeable HIV testing services provided by private clinics or purchasing HIVST kits. Therefore, the findings of this study could not be applied to other Chinese cities with a general or a lower economy. The COVID-19 pandemic might have a greater impact on HIV testing services in other smaller or less developed Chinese cities.

Fourth, we were not able to obtain the characteristics of MSM who refused to participate in the study. The characteristics of those who refused to join the study might be different from the participants, so selection bias existed. The response rate was relatively high compared to online surveys on similar topics.

Fifth, the items were constructed for this study and were not validated by other studies. Moreover, we only obtained cross-sectional associations and could not establish causal relationships.

Conclusion

In sum, utilization of facility-based and home-based HIVST among Chinese MSM declined after the COVID-19 outbreak and did not increase after the pandemic was under initial control. Removing structural barriers to accessing HIV testing, caused by COVID-19; modifying perceptions related to HIV testing; and making use of HIVST might be useful strategies to improve HIV testing among MSM during the pandemic.

Acknowledgments

This study was funded by the High-Level Project of Medicine in Longhua, Shenzhen (HLPM201907020105) and the Key Discipline of Infectious Diseases Control and Prevention of Long Hua (Grant 2020-2014).

Conflicts of Interest

None declared.

Multimedia Appendix 1
Chinese and English versions of the survey questionnaire.
[DOCX File , 27 KB - publichealth_v8i5e30070_app1.docx]

Multimedia Appendix 2
Prevalence of sexual risk behaviors and other HIV or STI prevention service utilization. STI: sexually transmitted infection.
[DOCX File , 28 KB - publichealth_v8i5e30070_app2.docx]

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Abbreviations

AOR: adjusted odds ratio
CAI: condomless anal intercourse
CBO: community-based organization
CDC: Centers for Disease Control and Prevention

HIVST: HIV self-testing
MSM: men who have sex with men
NRP: nonregular male sex partner
OR: odds ratio
PrEP: preexposure prophylaxis
RP: regular male sex partner
SDU: sexualized drug use
STI: sexually transmitted infection
TPB: theory of planned behavior

Edited by T Sanchez; submitted 30.04.21; peer-reviewed by T Torres, X Zhang; comments to author 27.12.21; revised version received 02.03.22; accepted 27.04.22; published 25.05.22.

Please cite as:
Zhang KC, Fang Y, Cao H, Chen H, Hu T, Chen YQ, Zhou X, Wang Z
The Impacts of the COVID-19 Pandemic on HIV Testing Utilization Among Men Who Have Sex With Men in China: Cross-sectional Online Survey
JMIR Public Health Surveill 2022;8(5):e30070
URL: https://publichealth.jmir.org/2022/5/e30070
doi:10.2196/30070
PMID:35486811

Original Paper

The Effects of Internet Exposure on Sexual Risk Behavior Among Sexually Experienced Male College Students in China: Cross-sectional Study

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Abstract

Background: As a young subgroup, college students have become the main users of mobile social networks. Considering that people can indiscriminately access explicit sexual content on the internet, coupled with the increase of HIV infections in male college students, the role of the internet in meeting sexual partners and its correlation to risky sexual behavior has become an important topic.

Objective: The aim of this study is to explore the effects of internet exposure on sexual partners and sexual risk behavior among sexually experienced male college students.

Methods: An institution-based cross-sectional study design was used to collect data through a paper-based questionnaire administered to male college students recruited from colleges and gay organizations in Hangzhou, Zhejiang Province, China. A total of 1045 sexually experienced male students were incorporated in our analysis, with the following information collected: sociodemographic characteristics, sexual intercourse–related behaviors, and sexually transmitted disease (STD) knowledge. Mann-Whitney *U* and Kruskal-Wallis tests were used to examine differences regarding basic characteristics and sexual risk behaviors between male college students who meet sexual partners via the internet and those who do not. Sequential logistic regression models were employed to examine the influence of meeting sexual partners via the internet on risky sexual behaviors after controlling for other factors.

Results: The mean age of the sexually experienced male students was 21.6 (SD 2.0) years. The likelihood of risky sexual behavior was varied, yet it was the highest for those who aim to meet paid sexual partners (145/192, 75.5% to 19/22, 86.4%), followed by those seeking partners for love or romance (258/435, 59.3%). Compared to non-internet partner seekers, internet partner seekers tended to have more casual intercourse (292/542, 53.9% versus 51/503, 10.1%), paid intercourse (32/542, 5.9% versus 12/503, 2.4%), and intercourse with same-sex partners (349/542, 64.4% versus 41/503, 8.2%); they were also more likely to use psychoactive drugs (125/349, 35.8% versus 5/41, 12.2%) and have more than 2 partners. With the increase of HIV and STD knowledge, the probability of having unprotected intercourse decreased for non-internet partner seekers. However, it increased for internet partner seekers with a rising HIV knowledge score. Sequential logistic regression showed that meeting sexual partners on the internet was statistically associated with sexual risk behaviors with multiple sexual partners (odds ratio 4.434; $P<.001$).

Conclusions: Meeting sexual partners via the internet is a common behavior among sexually experienced male college students, and those who meet partners on the internet exhibited higher levels of risky sexual behaviors although they had sufficient HIV and STD knowledge; this is especially true for students who aimed to find partners for sexual intercourse. Thus, more attention should be paid to young adults to address the risky sexual behaviors that may contribute to STD spread among this population.

(JMIR Public Health Surveill 2022;8(5):e31847) doi:10.2196/31847

KEYWORDS

college males; internet exposure; sexual partners; risk behavior; HIV; MSM; social networks; students; sexually transmitted infections; public health

Introduction

With the development of information technology, China has entered the internet era. As of 2019, the number of internet users in China was 802 million, and there were up to 788 million mobile internet users [1]. The internet allows people with different cultures, from different regions to contact each other and can contain a diverse array of social beliefs, values, and subjects.

As a young subgroup, college students have become the main users of internet social networks. In 2016, a report on the internet behavior of Chinese teenagers released by the China Internet Network Information Center highlighted that young people aged 19-24 years accounted for the largest proportion of internet use, as high as 48.1% [2,3]. In addition, more than 90% of young people used mobile social networks, which far exceeded the overall level of internet users [2,3]. Moreover, meeting strangers has become one of the most popular mobile social functions for young college students [4,5]. For example, the "shake" mobile feature allows the user to add another user as a friend if they physically shake their mobile phones at the same time. With the characteristic of anonymity, the "drifting bottle" has also been popular among young students; it refers to the way that individuals can send drifting bottles to make friends without filling in real personal information. Another related mobile social function is called "find nearby people" and is based on the positioning of the user's mobile phone, allowing them to find nearby people whom they can befriend. Moreover, the use of some dating social media platforms (ie, Momo and Tantan) was up to 20% among college students, and the number of paying users for Momo alone increased to 11.6 million people in 2018 [6,7]. Indeed, exposure to the internet has some benefits for young people, for example, finding answers to sexual health questions, which can help to avoid the embarrassment they may encounter by visiting health providers in person [8,9]. Moreover, the internet is a powerful resource for young people who are at an age when experiencing many health-related issues can result in feelings of confusion, loneliness, or embarrassment [8-10]. Thus, the knowledge they gain from the internet is an important tool for health promotion and solving health-related problems. However, exposure to the internet may have many negative effects on young people, especially college students. For example, having intercourse with partners one meets on the internet increases the risk of HIV infection.

Indeed, the rates of HIV infection among young people have increased while the incidence of HIV has decreased among the whole population. For example, young people ages 15-24 years were found to account for 32% of newly infected cases and the number of young people living with HIV and AIDS has increased by more than 480,000 in the last 20 years [11,12]. In China, more worryingly, the prevalence of new HIV infections among college students has increased significantly, with an annual growth rate of 30%-50% in recent years [13]. In 2017, the number of newly diagnosed students was 3077, a number that is 10 times higher than it was 10 years ago, and nearly 10 HIV infections per day were reported among college students, especially among male students [14].

With societal and technological development, we now live in a pluralistic society where individuals face a variety of behavior choices. A pluralistic society not only permits various ways of sexual satisfaction but also presents the threat of STDs, especially for college students who are sexually active [15]. The emergence of the internet within the pluralistic society has also allowed for various ways to prevent the transmission of STDs. Moreover, as elaborated by risk society theory, hazards can be caused by the environment (ie, the internet) as well as individual factors, such as knowledge, behavior choices, and personal characteristics. Therefore, it is urgent to understand the risky sexual behaviors of individuals (ie, college students) within some environments to reduce the risk of acquiring STDs within society.

To achieve the 90-90-90 goals toward HIV elimination by 2030, it is urgent to strengthen prevention efforts among this emerging high-risk population [16]. Although some studies have been conducted regarding the use of the internet and risky sexual behaviors, most of them focused on the general population of students and men who have sex with men (MSM) [17]. Little research has been done focusing on sexually experienced young male college students, who are sexually active and the key population to target for preventing HIV spread. Under this background, we aim to explore the use of the internet for meeting sexual partners among sexually experienced male college students to provide evidence for effective interventions to reduce the likelihood of risky sexual behaviors and prevent the spread of HIV among young college students.

Methods

Ethics Approval

Consent to participate was obtained from each participant before data collection. We did not collect any personally identifiable information. The study protocol and consent procedure were approved by the Medical Ethics Committee of the Hangzhou Center for Disease Control and Prevention (20190712).

Participants

We used an institution-based cross-sectional study design to collect data from colleges and gay organizations located in Zhejiang Province, China. We chose these 2 sites for 2 reasons. First, the number of new HIV infections among college students has increased significantly in recent years. Second, this significant increase of new HIV infections has occurred mainly in male students as HIV disproportionately impacts MSM [14]. Therefore, we conducted the survey in the context of colleges and gay organizations to efficiently reach sexually experienced male students.

All college students who were studying in the 44 colleges between September 2020 and November 2020 were invited to participate in the investigation. The inclusion criteria for participants were (1) students who were studying in the 44 colleges and (2) male students. The exclusion criteria were (1) people who were not students studying in the colleges, (2) people under 18 years, (3) female students, (4) foreign students, and (5) students who did not want to participate in the investigation. However, only male students who had a sexual experience in the previous year were incorporated into the analysis, and these sexually experienced male students had experiences of ejaculation before. The sample size was calculated based on a 7.6% and 19% HIV diagnosis risk for men who did not meet sexual partners on the internet and men who did respectively [8] (α=.05), which requires at least 290 participants.

Finally, 1045 sexually experienced male students completed the questionnaire and were incorporated into our analysis.

Data Collection

A paper-based questionnaire was used to collect related data among male college students; it was pretested and then revised based on the pretest. The following information was collected from the participants: sociodemographic characteristics (eg, age, education, residence, and years in school), sexual intercourse–related information (eg, sexual orientation, age at first sexual intercourse, and condom use), sexual intercourse–related behaviors in the past 6 months (eg, commercial, homosexual, and casual sexual intercourse and psychoactive drug use) and HIV and sexually transmitted disease (STD) knowledge. Years in school represents how many years it has been since a participant attended college. HIV and STD knowledge mainly represents college males' understanding of the transmission routes and prevention methods for STDs such as HIV. HIV and STD knowledge was measured using the 18-item HIV Knowledge Questionnaire, which has been widely applied to HIV-related surveys in China and has been shown to have good validity [18], in addition to 4 questions measuring participants' knowledge of other STDs, issued by the Hangzhou Center for Disease Control and Prevention. Responses were recorded as "true," "false," or "don't know." If the answer was correct, a score of 1 was assigned; a score of 0 was assigned if the answer was incorrect or a response of "don't know" was provided. HIV and STD knowledge was measured by the total score, with a higher score indicating a higher level of HIV and STD knowledge.

Data Analysis

Sociodemographic data from the male college students was analyzed using descriptive statistics with frequency and percentage. Risky sexual behavior was defined as having unprotected intercourse with 1 or more partners. Mann-Whitney *U* and Kruskal-Wallis tests were used to examine the differences regarding basic characteristics and risky sexual behaviors between men who meet sexual partners on the internet and those who do not. Moreover, sequential logistic regression models were employed to determine the independent influence of meeting sexual partners on the internet on unprotected intercourse with 1, 2, or more sexual partners (dependent variable) after controlling for other factors (eg, psychoactive drug use during intercourse, HIV knowledge, age, stage of study, years in school, field of study, residence, sexual orientation, and age at first intercourse). If the odds ratio (OR) is greater than 1, having the exposure increases the odds of engaging in the sexual risk behavior. The exposure decreases the odds of the sexual risk behavior if the OR is less than 1. All data analyses were completed using the statistical software SPSS (version 23.0; IBM Corp). Variables with P<.05 were considered statistically significant.

Results

Table 1 shows the basic characteristics of male college students who had sexual experiences. The average age of male students who seek sexual partner(s) via the internet was 21.9 (SD 2.2) years, while it was 21.3 (SD 1.6) years for participants who do not seek sexual partners on the internet. Among men meeting partners on the internet, 73.6% (399/542) were studying for a bachelor's degree. Regarding sexual orientation, 60% (325/542) and 19.2% (104/542) of men meeting partners on the internet were homosexual and bisexual, respectively, and most (426/503, 84.7%) who did not meet partners on the internet were heterosexual (P<.001). In addition, 62% (336/542) of participants meeting partners on the internet had sexual intercourse for the first time before the age of 18 years; only 43.7% (220/503) of those who did not meet partners on the internet had sexual intercourse before the age of 18 years (P<.001).

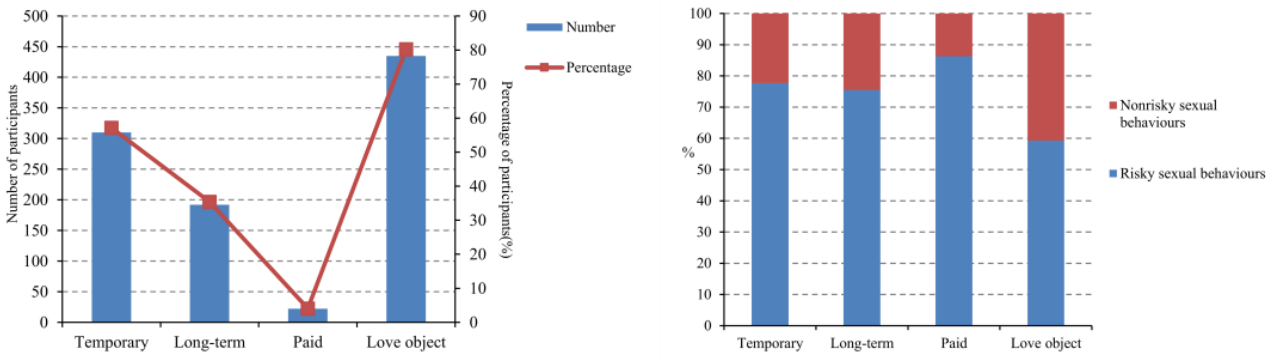
Regarding the aims of finding partners on the internet (Figure 1), 80.3% (435/542) of participants aimed to find love or a romantic relationship, 57.2% (310/542) sought a temporary sexual relationship or one-time sexual intercourse, 35.4% (192/542) sought a stable partner for intercourse, and 4.1% (22/542) sought paid sexual intercourse. In addition, it was found that the likelihood of risky sexual behavior varied, and the risk was the highest for those seeking paid sexual partners (19/22, 86.4%), followed by those seeking casual sexual relationships (241/310, 77.7%), long-term sexual relationships (145/192, 75.5%), and romantic partners (258/435, 59.3%).

Table 1. Characteristics of male college students by internet exposure.

Characteristic	Value			*P* value
	Total participants (N=1045)	Participants who met sexual partners on the internet (n=542)	Participants who did not meet sexual partners on the internet (n=503)	
Age in years, mean (SD)	21.6 (2.0)	21.9 (2.2)	21.3 (1.6)	<.001
Stage of study, n (%)				
Professional training	95 (9.1)	59 (10.9)	36 (7.2)	.07
Bachelor	830 (79.4)	399 (73.6)	431 (85.7)	
Master	100 (9.6)	69 (12.7)	31 (6.2)	
PhD	20 (1.9)	15 (2.8)	5 (1)	
Years in school, n (%)				
1	208 (22)	107 (19.7)	101 (20.1)	.007
2	308 (32.6)	144 (26.6)	164 (32.6)	
3	228 (24.2)	109 (20.1)	119 (23.7)	
4	176 (18.6)	114 (21.0)	62 (12.3)	
5	18 (1.9)	13 (2.4)	5 (1)	
≥6	6 (0.6)	4 (0.7)	2(0.4)	
Missing[a]	101 (9.7)	51 (9.4)	50 (9.9)	
Field of study, n (%)				
Non–health science	959 (91.8)	501 (92.4)	458 (91)	.42
Health science	86 (8.2)	41 (7.6)	45 (9)	
Residence, n (%)				
Urban	770 (73.7)	385 (71)	385 (76.5)	.04
Rural	275 (26.3)	157 (29)	118 (23.5)	
Sexual orientation, n (%)				
Heterosexual	539 (51.6)	113 (20.9)	426 (84.7)	<.001
Homosexual	372 (35.6)	325 (60)	47 (9.3)	
Bisexual	134 (12.8)	104 (19.2)	30 (6)	
Age at first sexual intercourse in years				
≤14	41 (3.9)	34 (6.3)	7 (1.4)	<.001
15-18	515 (49.3)	302 (55.7)	213 (42.4)	
19-22	465 (44.5)	194 (35.8)	271 (53.9)	
≥23	24 (2.3)	12 (2.2)	12 (2.4)	

[a]A total of 101 participants did not answer the questions regarding how many years of education they completed. Percentages are calculated based on the number of respondents who answered this category of questions.

Figure 1. The aims for finding partners online (A) and the related risk sexual behaviors (B) for male college students.



Risky sexual behaviors of male college students who sought partners on the internet and offline are shown in Table 2. Most (292/542, 53.9%) of the participants who met partners on the internet had a casual sexual relationship, and 64.4% (349/542) of them had more than 2 casual partners; this was only 10.1% (51/503) for non-internet partner seekers, and most (38/503, 74.5%) of them only had 1 sexual partner (*P*<.001). In addition, 5.9% (32/542) of internet partner seekers and 2.4% (12/503) of offline partner seekers had paid sexual partners respectively (*P*=.005). Those who sought partners on the internet also tended to have intercourse with other men (349/542, 64.4% versus 41/503, 8.2%) and more than 2 same-sex partners (214/349, 61.3% versus 6/39, 14.7%) compared to non-internet partner seekers (*P*<.001). Moreover, they also tended to use psychoactive drugs during intercourse with same-sex partners (125/349, 35.8% for internet partner seekers versus 5/41, 12.2% for offline partner seekers; *P*=.003).

The rate of sexual risk behaviors among male students who seek sexual partners through websites on the internet was the highest (40/49, 81.6%), followed by those seeking partners through software platforms (361/475, 76%) and social media (133/217, 61.3%). The differences were statistically significant (*P*<.001).

The probability of engaging in unprotected intercourse after meeting partners on the internet or offline related to HIV knowledge level is shown in Figure 2. With the increase in HIV knowledge, the probability of having unprotected intercourse was lower for those who seek sexual partners offline. However, for those who seek sexual partners on the internet, the probability rose with the increase of the HIV knowledge score.

As shown in Multimedia Appendix 1, among the factors influencing unprotected intercourse with 1 or more partners among male college students, meeting sexual partners via the internet was statistically associated with engaging in risky sexual behaviors with multiple sexual partners (OR 4.434; *P*<.001). Moreover, those who did not use psychoactive drugs during intercourse were also found to have a low likelihood of sexual risk behaviors (OR 0.102; *P*<.001).

Table 2. Sexual risk behaviors of male college students by internet exposure.

Behavior	Total participants (N=1045), n (%)	Participants who met sexual partners on the internet (n=542), n (%)	Participants who did not meet sexual partners on the internet (n=503), n (%)	*P* value
Protection at first intercourse				
Condom used	832 (79.6)	425 (78.4)	407 (80.9)	.32
No condom used	213 (20.4)	117 (21.6)	96 (19.1)	
Sexual experiences in the last 6 months				
Ever had intercourse with casual partner				
Yes	343 (32.8)	292 (53.9)	51 (10.1)	<.001
No	702 (67.2)	250 (46.1)	452 (89.9)	
Number of casual partners[a]				
1	142 (41.4)	104 (35.6)	38 (74.5)	<.001
2	71 (20.7)	64 (21.9)	7 (13.7)	
≥3	130 (37.9)	124 (42.5)	6 (11.8)	
Protection at last intercourse with casual partner[a]				
Condom used	308 (89.8)	264 (90.4)	44 (86.3)	.37
No condom used	35 (10.2)	28 (9.6)	7 (13.7)	
Ever had a paid sexual partner				
Yes	44 (4.2)	32 (5.9)	12 (2.4)	.005
No	1001 (95.8)	510 (94.1)	491 (97.6)	
Number of paid sexual partners[b]				
1	20 (45.5)	13 (40.6)	7 (58.3)	.37
2	14 (31.8)	11 (34.4)	3 (25.0)	
≥3	10 (22.7)	8 (25.0)	2 (16.7)	
Protection at last intercourse with paid partner[b]				
Condom used	35 (81.4)	25 (78.1)	10 (83.3)	.81
No condom used	9 (20.9)	7 (21.9)	2 (16.7)	
Ever had a same-sex partner				
Yes	390 (37.3)	349 (64.4)	41 (8.2)	<.001
No	655 (62.7)	193 (35.6)	462 (91.8)	
Condom use during intercourse with same-sex partner[c]				
Never	18 (4.6)	16 (4.6)	2 (4.9)	.10
Sometimes	81 (20.8)	68 (19.5)	13 (31.7)	
Always	291 (74.6)	265 (75.9)	26 (63.4)	
Number of same-sex partners[c]				
1	168 (43.3)	135 (38.7)	33 (80.5)	<.001
2	80 (20.6)	76 (21.8)	4 (9.8)	
≥3	140 (36)	138 (39.5)	2 (4.9)	
Ever had intercourse with same-sex partner while using psychoactive drugs[c]				
Yes	130 (33.3)	125 (35.8)	5 (12.2)	.003
No	260 (66.7)	224 (64.2)	36 (87.8)	

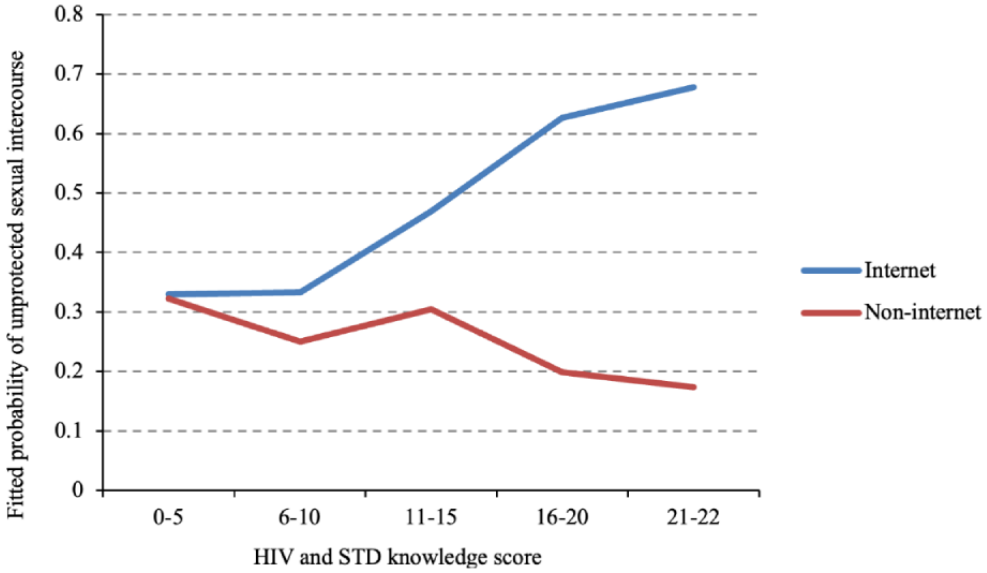
[a]n is equal to the number of participants who ever had intercourse with a casual partner within each group of participants. Percentages are calculated

accordingly.

[b]n is equal to the number of participants who ever had a paid sexual partner within each group of participants. Percentages are calculated accordingly.

[c]n is equal to the number of participants who ever had a same-sex partner within each group of participants. Percentages are calculated accordingly.

Figure 2. The fitted probability of engaging in unprotected sexual intercourse for male students who reported meeting sexual partners on the internet in the past 12 months and those who did not by HIV and sexually transmitted disease (STD) knowledge score.



Discussion

Principal Findings

It is well known that the internet is a popular venue for MSM to seek sexual partners; for example, previous research has found that 40% of MSM used the internet to seek sexual partners [19-22]. However, besides this high-risk population, most college students also use the internet to find sexual partners [23], and this proportion was 51.9% (542/1045) among the sexually active male college students in our study. This is because nowadays, the universal use of smartphones and laptops allows young adults to spend more time in private to establish social relationships, including sexual relationships [24]. In addition, using the internet to find sexual partners is considered relatively anonymous and has a lower perceived risk of social rejection for sexually active people, especially those belonging to marginalized groups [25]. Indeed, in our study, we found that 79.2% (429/542) of students seeking a partner on the internet were homosexual or bisexual. Thus, it is not surprising that the free and generally nondiscriminatory space of the internet has become an appealing place for male college students to find sexual partners. In addition, compared to previous research which found that 33% of young people met sexual partners via the internet, our results showed a higher prevalence (542/1045, 51.9%) [26-29]. This may be because the participants in our study were sexually experienced male college students rather than the male students in general, which may lead to a higher proportion of participants using the internet to meet sexual partners. After analyzing web-based venues for meeting sexual partners using anonymous software, we found Momo, Tantan, Blued, and Aloha are the most commonly used (470/542, 86.7%) by male students with a high probability of risky sexual behaviors. This implies the importance of health promotion campaigns and interventions through these platforms, which are being used to find partners, especially for young students. Moreover, evidence has shown that integrating HIV prevention interventions into dating apps for MSM allows for the targeting of individuals who exhibit markers of risk in their profiles [30,31].

Men who reported meeting sexual partners on the internet also reported a higher frequency of psychoactive drug use and unprotected sexual intercourse compared with men who did not meet their partners on the internet. This result was consistent with previous studies [32]. But the high proportion of MSM among the sexually experienced males in our study may also lead to a high observed proportion of those who use psychoactive drugs. Indeed, evidence has also shown that up to 70% of MSM used psychoactive drugs [32]. Moreover, in our study, the association between meeting sexual partners on the internet and risky sexual behaviors remained significant even after adjusting for sociodemographic covariates and other HIV-related factors. However, it is unclear whether using the internet to meet sexual partners is a risk factor in itself or whether high-risk young adults tend to exhibit their risky sexual behaviors by meeting partners anonymously on the internet. But the internet is certainly an important venue for seeking partners for young adults; thus, awareness campaigns are urgent to target young college students who have recently met a new sexual partner on the internet.

We also found that risky sexual behaviors are more strongly associated with the purpose of finding a partner on the internet. For example, the likelihood of risky sexual behaviors was almost 30%-50% higher for those who find partners for sexual intercourse rather than romantic reasons. A study in Norway also suggested that associations between high-risk sexual behavior and seeking partners on the internet are more likely to be due to the individual's aim for seeking partners using

social media rather than all the related high-risk behaviors [33]. To maintain and promote the health, including reproductive health, of young people, it is also important to target high-risk sexual behaviors among male college students, especially bisexual male students who may transmit STDs to both men and women [34,35]. Further, HIV and STD knowledge was found to be an effective measure against risky sexual behavior [36]. However, the probability of risky sexual behaviors actually increased with a higher level of HIV and STD knowledge among male students who meet partners on the internet. This may be because although most young men are mindful of the risks of sexual behaviors [37,38], they may not always be aware of the consequences of their own risk-taking. In addition, sensation-seeking and a lack of impulse control among these young adults may also increase their likelihood of engaging in risky sexual behaviors [39]. Moreover, young people tend to focus on the benefits rather than the risks associated with engaging in sexual behaviors with partners they meet on the internet [40]; this leads to them feeling less vulnerable to the negative consequences associated with these behaviors. This may remind us that focusing on traditional education through knowledge inculcation (eg, teaching students about HIV transmission routes or risk factors for STDs) among male college students is not effective enough to reduce the likelihood of risky sexual behaviors, especially for students meeting partners on the internet. Instead, enhancing their awareness of the negative consequences of risky sexual behaviors may be effective. For example, this approach may involve communicating the negative effects of risky sexual behaviors on life, study, work, and social communication by interviewing HIV-positive students in the form of a video to deter students from engaging in high-risk sexual behaviors to some extent. To avoid the transmission of STDs by individuals with latent infections who do not know their HIV status, it is vital to increase HIV testing among high-risk college students. Furthermore, considering the continued high prevalence of risky sexual behaviors among people diagnosed with HIV, especially in low- and middle-income countries [41], it is urgent to increase surveillance of positive cases to reduce HIV transmission among college students. Simultaneously, treatment as prevention has been shown to be an effective way to reduce HIV incidence; thus, improving pretest and posttest counselling to promote adherence to highly active antiretroviral therapy is also important for HIV prevention [42].

Conclusions

Our study suggests that most sexually experienced male college students engage in sexual behaviors with partners they meet on the internet. Those who met partners on the internet exhibited higher levels of risky sexual behaviors although they had sufficient HIV and STD knowledge, especially those who sought partners for intercourse. Therefore, it is urgent to offer support to help young male students better assess the risks of sexual behaviors on the internet, especially those who aim to find sexual partners. However, the traditional method of health education by spreading knowledge seems ineffective to reduce the likelihood of risky sexual behaviors, especially for students meeting partners on the internet. Instead, enhancing their awareness of the negative consequences (eg, conveying the negative effects on life) of risky sexual behaviors may be effective to deter these high-risk students to some extent. Moreover, it is vital to strengthen HIV testing among sexually experienced college students to avoid transmission by those with latent infections who do not know their HIV status.

Limitations

Our study has some limitations. First, considering the cross-sectional study design, the data can only provide an indication of the association between sexual partner–seeking on the internet and high-risk sexual behaviors. The causal relationship between these behaviors cannot be decided; that is, it is unclear whether meeting sexual partners via the internet is a risk in itself or whether high-risk young adults tend to exhibit their risky sexual behaviors by meeting partners anonymously on the internet. Second, due to the social desirability bias, the participants may have underreported related risk behaviors. Third, considering the sample consisted of sexually experienced male students and the study was conducted in the settings of colleges and gay organizations, the results cannot be generalized to the overall population of college students. Moreover, given the significant variation in cultures, economies, and traditions across China, data from one province are unlikely to be nationally representative. Furthermore, future studies should pay more attention to the effects of possible endogenous variables influencing high-risk sexual behaviors.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (project number 71904171), Zhejiang Provincial Soft Science Research Project (project number 2021C35015), China Medical Board (project number 20-391), Medical Health Science and Technology Project of Zhejiang Provincial Health Commission (project number 2020KY777), Social Development Project of Hangzhou Science and Technology Bureau (project number 20160533B51), and Class A project of Hangzhou Health and Family Planning Science and Technology Plan (project number 2018A81). The authors are grateful to all study participants for their valuable participation.

Data Availability

All the main data have been included in the results. Additional materials with details may be obtained from the corresponding author.

Authors' Contributions

JX conducted the literature review and data analysis and drafted the paper. YL was the co-first author. All authors contributed to the study's conception and design, interpretation of the data, and critical revisions of the paper. The authors all approved the final version of the manuscript for submission.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Sequential logistic regression predicting risk sex with 1 or more partners among male college students.
[DOCX File , 28 KB - publichealth_v8i5e31847_app1.docx]

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Abbreviations

MSM: men who have sex with men
OR: odds ratio
STD: sexually transmitted disease

Edited by Y Khader; submitted 07.07.21; peer-reviewed by P Zou, P Nguyen, A Benis, R Poluru; comments to author 28.08.21; revised version received 24.10.21; accepted 22.03.22; published 02.05.22.

Please cite as:
Xu J, Luo Y, Dong H, Zhao G
The Effects of Internet Exposure on Sexual Risk Behavior Among Sexually Experienced Male College Students in China: Cross-sectional Study
JMIR Public Health Surveill 2022;8(5):e31847
URL: https://publichealth.jmir.org/2022/5/e31847
doi:10.2196/31847
PMID:35499864

Original Paper

Prevalence and Associated Factors of Problematic Use of Smartphones Among Adults in Qassim, Saudi Arabia: Cross-sectional Survey

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Abstract

Background: The Kingdom of Saudi Arabia (KSA) ranks third globally in smartphone use. Smartphones have made many aspects of life easier. However, the overuse of smartphones is associated with physical and psychosocial problems.

Objective: The aim of this paper is to estimate the prevalence and associated factors of problematic use of smartphones among adults in the Qassim region of KSA.

Methods: We enrolled 715 participants using cluster random sampling for this cross-sectional survey. We assessed the problematic use of smartphones using the short version of the Smartphone Addiction Scale.

Results: We estimated the prevalence of problematic smartphone use among adults at 64% (453/708). Multivariable logistic regression analysis suggested that students are 3 times more likely to demonstrate problematic use compared with unemployed individuals (*P*=.03); adults using more than five apps are 2 times more likely to demonstrate problematic use compared to those using a maximum of three apps (*P*=.007). Protective factors against problematic smartphone use include using apps for academic (odds ratio [OR] 0.66; *P*=.04) or religious needs (OR 0.55; *P*=.007) and having a monthly family income of 5001-10,000 SAR (Saudi Riyal; US $1300-$2700; OR 0.46; *P*=.01) or 10,001-20,000 SAR (US $2700-$5400; OR 0.51; *P*=.03) compared to the <1501 SAR (US $400) income group.

Conclusions: We reported a very high prevalence of problematic use of smartphones in KSA. Considering its negative impact on physical and psychosocial health, public health programs should develop preventive strategies.

(JMIR Public Health Surveill 2022;8(5):e37451) doi:10.2196/37451

KEYWORDS

smartphone; smartphone addiction; problematic use of smartphones; mobile phone dependence; problematic use of mobile phones; Saudi Arabia; addiction; psychosocial; cross-sectional survey; psychological health; student; mental health

Introduction

Smartphones are considered the most used technological tool worldwide [1]. Smartphone addiction is a newly introduced term. The term is used by some due to the effects of overuse of smartphones on psychogenic illnesses and people's social lives [2], or due to resulting urges and drives for repeated use, use in dangerous situations, dependence, tolerance, withdrawal symptoms, and interruptions to one's work, social, and family life [3,4]. However, the conceptualization of smartphone overuse as an addiction remains controversial even among experts in this field [5]. Panova and Carbonell [2] argued that addiction is a disorder with severe effects on physical and psychological

health; while a behavior such as overuse of a smartphone may have a similar presentation to addiction, that does not mean it should be considered an addiction. They propose moving away from the addiction framework when studying technological behaviors and using, instead, terms such as "problematic use" to describe them [2]. Nevertheless, excessive and problematic use of smartphone negatively impacts people's lives, including their self-esteem [6]. The problematic use of a smartphone can be defined as "an inability to regulate one's use of the mobile phone, which eventually involves negative consequences in daily life (e.g. financial problems)" [7].

One review of studies around the world found a mean problematic smartphone use prevalence of 18.9%, with a higher prevalence among women, and a trend of decreasing prevalence after the age of 20 [8]. Studies in the Kingdom of Saudi Arabia (KSA) have shown that about one third to half of the smartphone users exhibit problematic use [9-11]. Another local study suggests that the problematic use of smartphones is associated with negative effects on sleep, energy level, mood, eating habits, weight, exercise, and academic performance [12]. However, these studies were conducted with young adults; hence, they cannot be generalized to a wider population group. In fact, most global research projects have studied problematic smartphone use or smartphone addiction only among young people [13]. Additionally, no such studies have been conducted in the Qassim region of KSA.

In this context, this study aims to estimate the prevalence of problematic smartphone use among an adult population aged 18-65 years in the Qassim region of KSA. We also explored whether factors such as demographics, app use, and reason for app use were associated with the problematic use of smartphones.

Methods

Study Design and Settings

We conducted a cross-sectional survey of adult residents of the Qassim region of KSA. We recruited our participants from the Qassim University and primary health care centers (PHC) in the Qassim region. Qassim, officially known as the Emirate of Al-Qassim, is an administrative province of KSA. It is located in the northern central part of the Kingdom and has an estimated 1.02 million people living in 65,000 square kilometers [14].

Recruitment

Male and female Saudi residents aged between 18 and 65 years were considered eligible for our study. We set an age cutoff due to limited access to residents older than 65 years. Individuals were excluded if they had any communicable respiratory illness or any other disease that made it difficult for them to participate in the study. We recruited participants from the Qassim University and PHC in the region using multistage cluster sampling. First, we developed a sampling frame comprising the primary sampling units—a list of Qassim University's 15 colleges situated on the main campus and a list of all PHC (N=158) in Qassim. We randomly selected 6 colleges and 52 PHC from the list. We calculated our sample size using the Epi Info, version 7 (Centers for Disease Control and Prevention). For a probability value of .05 and 50% expected prevalence, we needed 384 participants from each group—university and PHC.

Data collectors visited the colleges over a period of 2 months to randomly enroll students for the study. To recruit adults from the general population, our data collector invited every third adult patient or visitor entering the selected primary health care centers during 3 consecutive days each week. Data collection continued over a period of 3 months (between December 2019 and February 2020). We ended data collection after completing 715 interviews because of the COVID-19 lockdown measures, of which 708 (99%) were considered for analysis. Participants' characteristics are presented in Table 1.

Table 1. Sociodemographic characteristics of the participants (N=708).

Characteristics	Values
Gender, n (%)	
Male	325 (45.9)
Female	383 (54.1)
Age range (years), n (%)	
18-24	518 (73.2)
25-34	114 (16.1)
≥35	76 (10.7)
Mean, SD (years)	25.1 (8.5)
Median (years)	22.0
Marital status, n (%)	
Single	553 (78.4)
Married	152 (21.6)
Education, n (%)	
Primary	12 (1.7)
Intermediate-secondary	511 (72.4)
Higher diploma	88 (12.5)
Bachelor or higher	95 (13.5)
Occupation, n (%)	
Unemployed	64 (9.1)
Student	515 (72.9)
Employed	127 (18.0)
Monthly family income, n (%)	
1500 SAR (US $400) or less	96 (14.2)
1501-5000 SAR (US $400-$1300)	97 (14.3)
5001-10,000 SAR (US $1300-$2700)	188 (27.8)
10,001-20,000 SAR (US $2700-$5400)	203 (30.0)
>20,000 SAR (>US $5400)	93 (13.7)

Procedures

The structured questionnaire included demographic information and the short version of the Smartphone Addiction Scale (SAS-SV) [15]. Demographic information included participants' age, gender, educational level, marital status, current occupation, and income. The SAS-SV is a 10-item scale developed and validated in South Korea to measure smartphone addiction among adolescents [15]. Although we used the SAS-SV, we avoided the terminology "smartphone addiction" and used the terminology "problematic use of smartphones" instead, as explained in the introduction section.

Our questionnaire, including the SAS-SV, was translated into Arabic and reverse translated into English, and both were compared to ensure accuracy before starting data collection. Then, we carried out field testing with 24 Saudi adults to ensure that our questionnaire was understandable by our target population. The participants for field testing were purposively sampled to ensure diverse demographics for good representation of genders, income levels, education levels, and age groups. Field testing of the preliminary questionnaire was conducted by 2 male and 2 female medical students who were native Arabic speakers. Field testing was conducted in 3 phases of 8 interviews each, with the questionnaire undergoing revision after each phase. The final survey was conducted face-to-face by 6 male and 6 female final-year medical students who were trained to use the instrument.

Ethics Approval

All researchers completed the ethics course recommended by the local institutional review board. We received ethics approval from the Institutional Review Board of the Ministry of Health, Qassim region, Saudi Arabia (Approval No. 1378136-1440). All study participants received a detailed informed consent document that explained the purposes of the study and highlighted the topics, types of questions, and the time involved in the study. Confidentiality and anonymity of all information collected from the participants were maintained, and the

participants retained the right to refuse to answer specific questions or to opt out of the study at any time.

Statistical Analysis

Data entry and analyses were carried out using the SPSS version 20 (IBM Corp). To classify problematic smartphone use, we first computed participants' scores on each of the 10 SAS-SV items. Then, we used 31 and 33 as the male and female cutoff points, respectively, to determine problematic use [15]. We carried out descriptive analyses of sociodemographic and smartphone use characteristics, which were reported as percentages and frequencies. We conducted multivariable logistic regression analysis to investigate the factors associated with problematic smartphone use, reported as odds ratio (OR) with a 95% confidence interval. A *P* value of <.05 was considered statistically significant.

Results

We interviewed 715 adults aged 18 to 65 years. However, 7 (1%) participants were dropped from further analysis due to incomplete information. Table 1 presents participants' sociodemographic characteristics. Among the 708 participants, over half (n=383, 54%) were female; about three quarters (n=518, 73%) were aged between 18 and 24 years; over 78% (n=553) were single; 72.4% (n=511) had an intermediate-level education; 72.9% (n=515) were students; and 18% (n=127) were employed. Moreover, 193 (28.5%) participants had an average monthly family income of 5000 SAR (US $1300) or less, 188 (27.8%) had a monthly family income between 5001 SAR and 10,000 SAR (US $1300-$2700), while 203 (30%) had an income between 10,001 SAR and 20,000 SAR (US $2700-$5400).

Figure 1 presents the prevalence of problematic smartphone use in Qassim, KSA, by different sociodemographic groups. We estimated the overall prevalence at 64%. Among the income groups, the highest prevalence (n=96, 75%) was observed among the lowest monthly family income group (≤1500 SAR [US $400]). Prevalence among the single and married individuals was almost same (n=553, 63.2% and n=152, 64.2%, respectively). We observed a higher prevalence among employed adults (n=127, 67.7%) and students (n=515, 64.3%) compared with unemployed adults (n=64, 54.7%). Among the education groups, prevalence was lowest among the lowest education group (n=523, 62.5%) and highest among the highest education group (n=95, 68.4%). The prevalence of problematic smartphone use was higher among the 25-to-34-years age group (n=114, 69.3%) compared with the 18-to-24-years group (n=518, 63.1%) and the >34 years (n=76, 61.8%) age groups. Regarding gender, we found that men (n=325, 67.4%) had a higher prevalence of problematic smartphone use than women (n=383, 61.1%).

Figure 1. Prevalence of problematic use of smartphones among adults aged 18-65 years in Qassim, Kingdom of Saudi Arabia (cross-sectional survey, December 2019 to February 2020). SAR: Saudi Riyal.

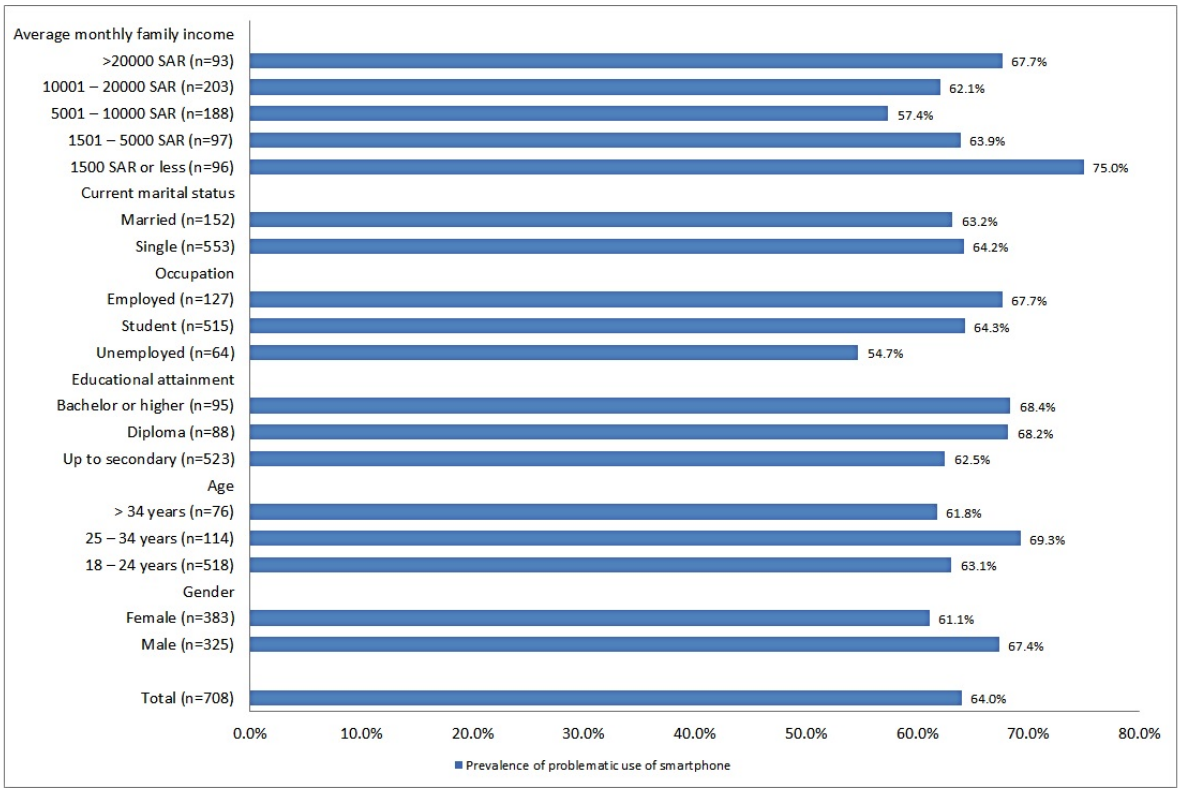

Table 2 presents characteristics of participants' smartphone use. Almost all of them had been using a smartphone for more than 3 years. A quarter (172/688, 25%) of them were using up to three smartphone apps, while the rest were using more than three apps, with 28.6% (197/688) using six or more apps regularly. Our participants' reasons for using smartphone apps included social networking (645/706, 91.4%), reading or listening to the news (424/706, 60.1%), watching movies or listening to music (392/706, 55.6%), academic/professional needs (260/706, 36.8%), searching for general knowledge

(223/706, 31.6%), playing games (214/706, 30.3%), religious needs (176/706, 24.9%), and watching sports (157/706, 22.2%).

Table 3 presents the factors associated with problematic smartphone use among adults in KSA. Among the sociodemographic variables, no statistically significant association was found between problematic smartphone use and gender, age, marital status, or educational attainment. The multivariable logistic regression analysis suggests that students were 3 times more likely to have problematic smartphone use than the unemployed (OR 2.99; *P*=.03). However, no statistically significant difference was observed between the unemployed and employed groups (*P*=.22). Our results also suggest that compared with individuals with an average monthly family income of 1500 SAR (US $400) or less, those with an income of 5001 SAR to 10,000 SAR (US $1300-$2700) and 10,001 SAR to 20,000 SAR (US $2700-$5400) were 54% (OR 0.46; *P*=.01) and 49% (OR 0.51; *P*=.03) more likely to have problematic smartphone use, respectively. However, no significant difference was observed between the lowest (<1500 SAR [US $400]) and highest (>20,000 SAR [US $5400]) income groups (*P*=*.50*).

Regarding characteristics of smartphone use, we found that compared with individuals who use 1 to 3 apps daily, users of more than 5 apps were 2 times more likely to have problematic smartphone use (OR 2.02; *P*=.007). Individuals who were using apps for academic or professional needs were 34% less likely to have problematic use (OR 0.66; *P*=.04), and individuals who were using the apps for religious purposes were 45% less likely to have problematic use (OR 0.55; *P*=.007) than those citing other reasons for use.

Table 2. Characteristics of participants' smartphone use in Qassim, KSA[a] (cross-sectional survey, December 2019-February 2020).

Smartphone use characteristics	Values, n (%)
Duration of use (n=705)	
Up to 3 years	14 (2.0)
>3 years	691 (98)
Apps used on an average day (n=688)	
1-3 apps	172 (25)
4-5 apps	319 (46.4)
>5 apps	197 (28.6)
Use app notifications (n=690)	
No	123 (17.8)
Yes	567 (82.2)
Reason for using apps	
To read or listen to news (n=706)	
No	282 (39.9)
Yes	424 (60.1)
Social networking (n=706)	
No	61 (8.6)
Yes	645 (91.4)
Academic or professional (n=706)	
No	446 (63.2)
Yes	260 (36.8)
Playing games (n=706)	
No	492 (69.7)
Yes	214 (30.3)
Watching sports (n=706)	
No	549 (77.8)
Yes	157 (22.2)
General knowledge (n=706)	
No	483 (68.4)
Yes	223 (31.6)
Religious (n=706)	
No	530 (75.1)
Yes	176 (24.9)
Watching movies/music (n=706)	
No	314 (44.5)
Yes	392 (55.5)

[a]KSA: Kingdom of Saud Arabia.

Table 3. Determinants of problematic smartphone use among adults (N=708) in Qassim, KSA[a] (cross-sectional survey, December 2019-February 2020).

Determinant (reference category)	*P* value	Odds ratio[b]	95% CI for odds ratio	
			Lower	Upper
Gender (male)				
Female	.55	0.89	0.61	1.30
Age (18-24 years)				
25-34 years	.14	2.06	0.79	5.36
>34 years	.22	1.98	0.67	5.87
Education (up to intermediate or secondary)				
Higher diploma	.29	1.41	0.75	2.68
Bachelor or above	.26	1.42	0.77	2.63
Occupation (unemployed)				
Student	.03	2.99	1.14	7.86
Employed	.22	1.61	0.75	3.45
Current marital status (single)				
Married	.88	0.95	0.47	1.92
Monthly family income (≤1500 SAR [US $400])				
1501-5000 SAR (US $400-$1300)	.27	0.68	0.35	1.34
5001-10,000 SAR (US $1300-$2700)	.01	0.46	0.25	0.83
10,001-20,000 SAR (US $2700-$5400)	.03	0.51	0.28	0.93
>20,000 SAR (US $5400)	.50	0.79	0.40	1.57
Use app notifications (no)				
Yes	.55	1.15	0.73	1.79
Number of apps used in an average day (1-3 apps)				
4-5 apps	.13	1.41	0.91	2.20
>5 apps	.007	2.02	1.21	3.35
Reasons for using apps				
Use apps to read or listen to news (no)				
Yes	.17	1.31	0.89	1.93
Use apps for social networking (no)				
Yes	.24	1.47	0.78	2.77
Use apps for academic or professional needs (no)				
Yes	.04	0.66	0.44	0.98
Use apps to play games (no)				
Yes	.28	1.25	0.83	1.89
Use apps to watch sports or games (no)				
Yes	.32	1.26	0.80	2.00
Use apps for general knowledge improvement (no)				
Yes	.06	0.68	0.45	1.02
Use apps for religious needs (no)				
Yes	.007	0.55	0.36	0.85
Use apps to watch movies or listen to music (no)				
Yes	.88	1.03	0.69	1.54

[a]KSA: Kingdom of Saud Arabia.

[b]Multivariable logistic regression analysis.

Discussion

Principal Findings

This study aimed to investigate the prevalence and associated factors of the problematic use of smartphones among adults aged 18-65 years in Qassim, KSA to reduce the gap in the literature. The majority of previous studies in this regard used exclusively college or university students [13]. We estimated a very high prevalence (64%) of problematic use of smartphone among this population groups. Determinants of the problematic use of smartphone include occupation, income, number of apps used, and reasons for using the apps.

We estimated the prevalence of problematic use of smartphones at 64% among adults aged 18 to 65 years in Qassim, KSA. This finding is in concordance with the findings reported by local studies conducted on university students, which were 71.9% [16] and 66% [10]. However, other local studies have shown smaller figures, for example 48% [17], 36.5% [11], and 19.1% [18]. A study that was conducted in 4 countries in the Middle East showed varying prevalence of problematic smartphone use: in Jordan, 59.8%; in KSA, 27.2%; in Sudan, 17.3%; and in Yemen, 8.6 % [19]. In other countries, studies have reported different figures: 38.9% in the United Kingdom [20], 38.5% in China [21], almost 30% in Malaysia [22], 21.5% in Belgium, and 12.5% in Spain [23].

Variation in prevalence could be affected by study design, sample size, or the scale used. Our study's high prevalence could be explained by the fact that Saudi Arabia's social media presence is one of the largest in the world. The large number of active social media users is mostly due to the high rate of smartphone ownership. With more than 84% of the population living in urbanized areas with very fast internet connections, it comes as no surprise that active social media users may number more than 25 million. According to reports from Hootsuite and We Are Social, Saudis are the largest group of active users on Instagram, Twitter, and Snapchat in the region [24].

Our results suggest that those with an average monthly family income of 5001 SAR (US $1300) to 20,000 SAR (US $5400) were less likely to have problematic smartphone use compared with people in the lower- or higher-income groups. In a study in China, the relationship of income with smartphone use was not clear [21]. However, a local Saudi study revealed a finding similar to ours and stated clearly that low-income individuals are more likely to have problematic smartphone use [17]. This is a difficult issue to explain. Could it be that poor people have fewer choices for entertainment or that lower-income students lack access to other information communication technologies [25]? Our participants with higher incomes also had a higher prevalence of problematic use. Zulkefly and Baharudin [26] concluded that students from higher-income families spent more time and money on their mobile phones.

Regarding characteristics related to smartphone use, we found that people using more than 5 apps were 2 times more likely to exhibit problematic smartphone use. A study in the United Kingdom showed that the use of social and communication apps significantly correlates with problematic smartphone use [27,28]. This could explain our finding because when using more than 5 apps, those apps will most likely include social media apps such as Snapchat and so on. In our study, we found that individuals who use apps for academic or professional or religious purposes were less likely to have problematic use.

In this study, there was no statistically significant association between problematic smartphone use and gender, age, marital status, or educational attainment. However, a multicenter study among Saudi university students showed that female students were more affected [18]. A study in Korea also reported that excessive use of smartphone and smartphone addiction–proneness is higher among females [6]. Furthermore, De-Sola Gutierrez et al [8] reported that all the studies included in their review indicated that women or girls have higher levels of dependence and problematic use than men or boys [8,29]. Our findings may differ because the older, married women included in our study were busy with other work, in contrast to the student groups who were the focus of many previous studies. We also used a higher problematic use cutoff point for women as suggested by the SAS-SV [15].

The relationship between marital status and problematic smartphone use is understudied as most previous research has focused on the young [8,13]. The only local study conducted among young adults (postgraduate medical residents) did not include marital status data [30].

With regard to age, other studies from different parts of the world have shown that the total time spent on cell phones decreases with age, with the highest times reported for people less than 20 years old. This is related to the decreased self-control found in this age group [8]. Our study did not include people younger than 18 years of age, but we found that students were 3 times more likely to have problematic smartphone use than the unemployed. One of the reasons for this high prevalence could be that educational material is now often available on the internet, and students may feel more comfortable using a smartphone to access them compared with using other devices.

In this study, there was no statistically significant difference between the unemployed and employed groups. Hence, time is seemingly not an issue for those with problematic smartphone use. In Spain, a study showed that unemployed individuals were more addicted to their smartphones than people in other employment categories [23], whereas in China, the relationship was not clear [21].

Study Limitations

Our study had some limitations, mainly in data collection; we depended on self-reported data, which could be a source of bias. Another limitation was that the SAS-SV scale is not validated for use in this culture. A third limitation was our sampling technique; although we employed systematic random sampling to recruit study participants, accessing them only from PHC

and one university in the Qassim region might have negatively affected representativeness.

Conclusions

The overall prevalence of problematic smartphone use was high among our study participants, and this problematic use was associated with being a student and using more than 5 apps. An average monthly family income of 5001 SAR (US $1300) to 20,000 SAR (US $5400) and using apps for academic or professional and religious purposes were found to have a protective effect against problematic smartphone use. Our findings have implications for future public health programs in KSA. Considering the high prevalence of problematic smartphone use among adults and its negative impact on physical and psychosocial health, public health programs should develop and implement appropriate preventive strategies. Further studies should focus on investigating the association between health-related quality of life and problematic use of smartphones.

Acknowledgments

The authors gratefully acknowledge Qassim University, represented by the Deanship of Scientific Research, on the financial support for this research under the number (grant med-2019-2-2-I-5437) during the academic year 2019.

Authors' Contributions

Conceptualization: AAM, IM, and MA; methodology: AAM and IM; formal analysis: IM; data curation, AAM, IM, and MA; writing—original draft preparation: AAM and IM; writing—review and editing: AAM and IM; visualization: IM; supervision: AAM and IM; project administration: AAM and MA; funding acquisition: AAM, IM, and MA. All authors have read and agreed to the published version of the manuscript. The authors thank Erin Strotheide for her editorial contributions to this work.

Conflicts of Interest

None declared.

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Abbreviations

KSA: Kingdom of Saudi Arabia
OR: odds ratio
PHC: primary health care centers
SAR: Saudi Riyal
SAS-SV: Smartphone Addiction Scale–Short Version

Edited by G Eysenbach; submitted 21.02.22; peer-reviewed by R Kabir, SL Lee, MM Abdul Kader Jilani; comments to author 15.03.22; revised version received 02.04.22; accepted 26.04.22; published 23.05.22.

Please cite as:
Al-Mohaimeed A, Alharbi M, Mahmud I
Prevalence and Associated Factors of Problematic Use of Smartphones Among Adults in Qassim, Saudi Arabia: Cross-sectional Survey
JMIR Public Health Surveill 2022;8(5):e37451
URL: https://publichealth.jmir.org/2022/5/e37451
doi:10.2196/37451
PMID:35604756

Original Paper

Factors Associated With Protective Mask-Wearing Behavior to Avoid COVID-19 Infection in China: Internet-Based Cross-sectional Study

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Abstract

Background: The novel coronavirus disease COVID-19 is likely to spread from person to person in close-contact settings. The Chinese Center for Disease Control and Prevention released a handbook on COVID-19, which introduced health information to the public, specifically related to wearing masks correctly and adopting preventive measures to avoid COVID-19 infection.

Objective: The aim of this study was to assess the level of mask knowledge, behavior related to mask usage, and major information channels used for obtaining mask- and COVID-19–related information in China.

Methods: An internet-based survey was conducted primarily using DingXiang Doctor WeChat public accounts. The data about mask knowledge and behavior were collected and analyzed. In addition to descriptive statistics, logistic regression was used to analyze significant risk factors contributing to protective mask behavior.

Results: Data were collected from a total of 10,304 respondents to the survey. More than half of the respondents were under 30 years old and nearly three-quarters were women. Over 80% of participants had a bachelor's degree or higher, and the largest proportion of respondents (n=4204, 40.80%) were employed as business/service workers. Over half of the study participants were married (n=5302, 51.46%). The findings revealed that 67.49% (6954/10,304) of the participants practiced protective mask behavior; 97.93% (10,091/10,304) believed that wearing masks is an effective protective measure against COVID-19; 96.85% (9979/10,304) chose a mask that has two or more layers of washable, breathable fabric; and 70.57% (7272/10,304) wore the masks correctly. Gender, age, occupation, and education level had significant effects on behavior, whereas marital status and the infection status of family members were not significantly related to mask-wearing behavior. In addition, WeChat public accounts (9227/10,304, 89.55%) were the most prominent source of obtaining health information for Chinese netizens after the outbreak of COVID-19.

Conclusions: This study elucidated that Chinese netizens' protective mask behavior is far lower than their mask-related knowledge. Improved information channels and adequate information on wearing masks are necessary to improve the public's protective mask behavior, particularly among men, the elderly, and people with less education.

(JMIR Public Health Surveill 2022;8(5):e32278) doi:10.2196/32278

KEYWORDS

COVID-19; internet-based; disease prevention; mask; knowledge; behavior

Introduction

The COVID-19 pandemic is considered a global public health emergency of serious concern [1-3]. The disease is caused by the novel coronavirus SARS-CoV-2. Due to its rapid spread, extremely harmful effects, and pathogenic complexity, the World Health Organization escalated the risk assessment of COVID-19 to "very high" [4]. By December 1, 2020, there were

44,579,298 cases and 1,494,630 deaths due to COVID-19 confirmed across the world [5].

The COVID-19 virus is highly infectious, which mainly spreads from person to person through respiratory droplets [4]. At the time of submission of this paper, target-specific drugs and vaccines were not yet available for protection against COVID-19. Hence, controlling the outbreak and taking proper measures to protect people became crucial. Among the control measures implemented, face masking has been shown to mitigate the transmission of SARS-CoV-2 by creating a physical barrier, making it one of the most efficient measures to prevent COVID-19 [6-8]. Although studies have found differences in the protective effect of different types of masks [7,8], the modeling predictions suggest that even the use of relatively ineffective masks can decrease community transmission of the virus relative to no masks [9]. China has taken the toughest measures to require the public to wear masks in public since the beginning of the outbreak in early 2020, mainly by restricting access to public places such as hospitals and shopping malls or prohibiting travel on public transport for nonmask-wearers. Even in a phase when the outbreak is gradually under control, face masks have become the new default social norm for the Chinese public.

From January 20, 2020, when person-to-person transmission was confirmed and widely known by the public [10], a wide-ranging, multilevel health education campaign against COVID-19 was carried out in China. Many promotional materials related to COVID-19 were compiled by health experts in China, such as the COVID-19 Guidelines for Public Protection (version 2) [11] and the guidebook on COVID-19 prevention [12]. The dissemination of the core content of these guidelines through the internet was perceived to be highly effective in setting up the desired health behavior and lifestyle to control the COVID-19 pandemic [13,14].

There are many major communication channels used to spread information on COVID-19 in China, such as WeChat, microblogs, television, radio, and other media outlets. Owing to the increased global access to the internet over the past decade, people have been more willing to acquire relevant knowledge over the internet [15] compared with the situation during the severe acute respiratory syndrome (SARS) outbreak in 2003 [16]. WeChat has grown into the largest and most influential social network in China, with 963 million active users [17]. It is possible for WeChat users to subscribe to the customer service from the WeChat public accounts and obtain specific information they desire. *DingXiang Doctor* is the most influential professional WeChat public account in the health field across China [18,19], which is effectively used to disseminate health information to the general population. Previous research in this field [20] has addressed the issue of Chinese netizens' effective access to desired COVID-19 information; however, there is a lack of further in-depth study on specific protective behavior. Therefore, the aim of this study was to describe Chinese netizens' behaviors related to wearing a mask and their relationship with internet content on mask-related information. We obtained representative data to assess the popularity of wearing masks through an in-depth analysis of data from an internet-based cross-sectional survey.

Methods

Participants

An internet-based cross-sectional survey was conducted from January 31 to February 2, 2020, at the beginning of the COVID-19 epidemic in China. A message stating "COVID-19, have you done enough to prevent it?" was created online with a link to the questionnaire. The target population for the survey was defined as all residents aged 15 years and above living in China. Participation in the study was purely voluntary, without any financial incentive.

Data Collection

The research tool used in the study was designed by health education experts from the Center for Disease Control and Prevention of Zhejiang Province. The survey contained four segments of 15 multiple-choice questions, including sociodemographic information (eg, gender, age, occupation, education level, marital status), infection status, COVID-19–related knowledge, and mastery of preventive measures (eg, mask wearing, hand washing). The questionnaire has been validated, demonstrating good reliability and validity [20]. The data were gathered using *DingXiang Doctor* WeChat public accounts.

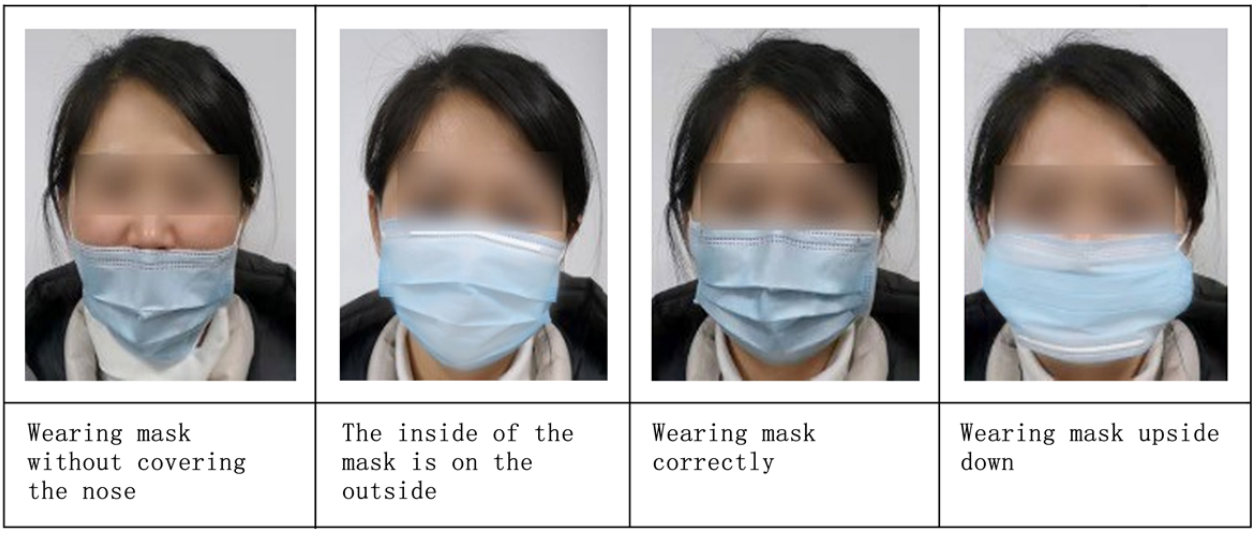
Measures

Protective Mask Behavior

Protective mask behavior was set as the dependent variable in this analysis, which was measured by asking the respondents on their perceptions of the protective effects of masks, their choice of mask type, and the way they wore the mask. Respondents were considered to be performing "protective mask behavior" if the responses to all three questions matched the statements: (1) "I believe that wearing a mask is effective to protect against COVID-19," (2) "I choose to wear a medical mask (two or more layers of washable, breathable fabric)," and (3) "I usually wear my mask as shown in the third image from the left" (Figure 1).

Relevant independent variables included in the analysis were obtained through self-report, comprising gender (male, female), age (15-20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years, 61 years or older), education level (primary or below, secondary, undergraduate, postgraduate or above), occupation (government institution staff, business/service worker, student, medical staff, homemaker, retired/unemployed), marital status (single/divorced/widowed, married), and COVID-19 infection status of family members (confirmed case/suspected case, close contact with a confirmed case, none of the above).

Figure 1. Images of the four ways of wearing masks used in the study.



Knowledge About COVID-19 Messages

The information channels that the participants used were assessed by asking the following question: "during the past 30 days, have you seen or received messages related to COVID-19 via the following channels?: (1) friends/relatives/colleagues, (2) websites, (3) WeChat public account, (4) microblogs, (5) WeChat, (6) news apps, (7) television/radio, (8) newspapers, (9) SMS text messages, (10) community outreach." The response options included "yes" and "no" to each category.

Patient and Public Involvement

The analyses were based on existing data of an internet-based cross-sectional survey. To our knowledge, no participants were involved in the design, recruitment, or conduct of the study. The research question and outcome measures of the study were determined by factors reported to be associated with protective mask behavior [21,22]. Thus, we could not disseminate the results to each participant; however, the results will be disseminated to the public through broadcasts and popular science articles.

Ethics

This study was approved by the Ethics Committee of the Zhejiang Provincial Center for Disease Control and Prevention (approval number: 2020-009). Informed consent was obtained from all participants before collecting their information. To protect the participants' confidentiality, we kept all data confidential and without any identifiers.

Statistical Analysis

SPSS version 18.0 was used for all analyses. Standard descriptive statistics were used to summarize demographic variables and other parameters that might be associated with protective mask behavior. Logistic regression was applied to determine the factors associated with protective mask behavior based on survey and self-report data. Two-sided *P* values <.05 were considered statistically significant.

Results

General Participant Characteristics

During the study period, a total of 590,000 *DingXiang Doctor* users visited the online page, 10,304 of whom responded to the survey. The sociodemographic characteristics are summarized in Table 1. Overall, the majority of respondents were women and slightly more than half were married. The age group with the highest proportion was 21-30 years, followed by 31-40 years, 41-50 years, 15-20 years, 51-60 years, and ≥60 years. Most of the respondents had an undergraduate degree, followed by postgraduate or above, secondary, and primary education or below. The majority of the respondents were employed as business/service workers, followed by medical staff, government institution staff, retired/unemployed, students, and homemakers. Less than 1% of the respondents had a confirmed/suspected case of COVID-19 in the family, and approximately 4% had close contact with a confirmed case (Table 1).

Table 1. Survey respondents' sociodemographic characteristics (N=10,304).

Sociodemographic characteristics	Respondents, n (%)
Gender	
Male	2670 (25.91)
Female	7634 (74.09)
Age (years)	
15-20	901 (8.74)
21-30	4830 (46.88)
31-40	2945 (28.58)
41-50	1141 (11.07)
51-60	403 (3.91)
>61	84 (0.82)
Education level	
Primary or below	526 (5.10)
Secondary	1117 (10.84)
Undergraduate	7219 (70.06)
Postgraduate or above	1442 (13.99)
Occupation	
Government institution staff	1729 (16.78)
Business/service worker	4204 (40.80)
Students	668 (6.48)
Medical staff	1894 (18.38)
Homemaker	202 (1.96)
Retired/unemployed	1607 (15.60)
Marital status	
Single/divorced/widowed	5002 (48.54)
Married	5302 (51.46)
COVID-19 infection status of family members	
Confirmed case/suspected case	70 (0.68)
Close contact with a confirmed case	360 (3.49)
None of the above	9874 (95.83)

Protective Mask Behavior

Table 2 shows the level of protective mask behavior by various sociodemographic factors. For instance, the majority (>65%) of the participants practiced protective mask behavior, and the great majority (>95%) believed that wearing a mask is effective protection against COVID-19 and chose a mask that has two or more layers of washable, breathable fabric. In addition, over 70% wore masks correctly (as shown in Figure 1). The percentage of practicing protective mask behavior varied with differences in gender, age, education, occupation, marital status, and infection status of family members. It was higher among women than men. Older respondents tended to have a lower level of protective mask behavior; even among the oldest age group (61 years or older), over 50% practiced this behavior. Education level was positively associated with protective mask behavior. Even among respondents with a primary education level or below, the majority practiced protective mask behavior. The highest protective behavior level was found in the business/service worker group, married group, and those with a positive infection status of family members relative to other corresponding categories.

Table 2. Distribution of respondents who practice protective mask behavior according to sociodemographic characteristics.

Sociodemographic characteristic	Believe that wearing a mask is effective protection against COVID-19, n (%)	Choose a mask that has two or more layers of washable, breathable fabric, n (%)	Wearing mask correctly, n (%)	Protective mask behavior[a], n (%)
Gender				
Male (n=2670)	2592 (97.08)	2578 (96.55)	1764 (66.07)	1663 (62.28)
Female (n=7634)	7499 (98.23)	7401 (96.95)	5508 (72.15)	5291 (69.31)
Age (years)				
15-20 (n=901)	886 (98.34)	865 (96.00)	629 (69.81)	606 (67.26)
21-30 (n=4830)	4726 (97.85)	4661 (96.50)	3496 (72.38)	3322 (68.78)
31-40 (n=2945)	2892 (98.20)	2880 (97.79)	2079 (70.59)	2005 (68.08)
41-50 (n=1141)	1113 (97.55)	1112 (97.46)	774 (67.84)	742 (65.03)
51-60 (n=403)	393 (97.52)	383 (95.04)	249 (61.79)	234 (58.06)
>61 (n=84)	81 (96.43)	78 (92.86)	45 (53.57)	45 (53.57)
Education level				
Primary or below (n=526)	511 (97.15)	505 (96.01)	339 (64.45)	324 (61.60)
Secondary (n=1117)	1092 (97.76)	1072 (95.97)	788 (70.550	747 (66.88)
Undergraduate (n=7219)	7069 (97.92)	7000 (96.97)	5121 (70.94)	4895 (67.81)
Postgraduate or above (n=1442)	1419 (98.40)	1402 (97.23)	1024 (71.01)	988 (68.52)
Occupation				
Government institution staff (n=1729)	1697 (98.15)	1687 (97.57)	1189 (68.77)	1149 (66.45)
Business/service worker (n=4204)	4109 (97.74)	4088 (97.24)	3037 (72.24)	2895 (68.86)
Students (n=668)	662 (99.10)	661 (98.95)	444 (66.47)	436 (65.27)
Medical staff (n=1894)	1852 (97.78)	1810 (95.56)	1350 (71.28)	1281 (67.63)
Homemaker (n=202)	198 (98.02)	192 (95.05)	131 (64.85)	123 (60.89)
Retired/unemployed (n=1607)	1573 (97.88)	1541 (95.89)	1121 (69.76)	1070 (66.58)
Marital status				
Single/divorced/widowed (n=5002)	4909 (98.14)	4817 (96.30)	3590 (71.77)	3421 (68.39)
Married (n=5302)	5182 (97.74)	5162 (97.36)	3682 (69.45)	3533 (66.64)
COVID-19 infection status of family members				
Confirmed case/suspected case (n=70)	68 (97.14)	66 (94.29)	49 (70.00)	46 (65.71)
Close contact with a confirmed case (n=360)	349 (96.94)	343 (95.28)	263 (73.06)	243 (67.50)
None of the above (n=9874)	9674 (97.97)	9570 (96.92)	6960 (70.49)	6665 (67.50)
Overall (N=10,304)	10,091 (97.93)	9979 (96.85)	7272 (70.57)	6954 (67.49)

[a]Calculated according to the number of respondents giving correct responses to the three questions.

Factors Associated With Protective Mask Behavior

A multivariate logistic analysis was performed on six factors (gender, age, education, occupation, marital status, and infection status of family members). Of these factors, gender, age, education, and occupation were significantly associated with the implementation of protective masking behavior, whereas marital status and infection status of family members did not show a significant association with the outcome. The findings showed that males were 73% more likely to have protective mask behavior compared to females. Compared to the ≥60 years age group, the proportion of respondents practicing protective mask behavior was higher in the age groups of 15-20 years, 21-30 years, 31-40 years, and 41-50 years, suggesting that the proportion of mask behavior decreases with age. People with secondary education and below were less likely to engage in protective masking behavior compared to those with higher education. In the occupational category, the business/service workers exhibited better mask behavior compared with the retired/unemployed class (see Table 3).

Table 3. Factors associated with protective mask behavior.

Covariate	OR[a] (95% CI)	*P* value
Gender		
Male	0.73 (0.66-0.88)	<.001
Female	Reference	—[b]
Age (years)		
15-20	2.03 (1.15-3.59)	.01
21-30	1.95 (1.14-3.34)	.01
31-40	1.91 (1.12-3.26)	.02
41-50	1.76 (1.03-3.02)	.04
51-60	1.24 (0.74-2.07)	.41
>61	Reference	—
Education level		
Primary or below	0.77 (0.62-0.97)	.02
Secondary	0.96 (0.81-1.15)	.69
Undergraduate	0.97 (0.86-1.10)	.66
Postgraduate or above	Reference	—
Occupation		
Government institution staff	1.02 (0.88-1.19)	.75
Business/service worker	1.16 (1.02-1.32)	.02
Students	0.96 (0.79-1.17)	.69
Medical staff	1.04 (0.87-1.24)	.70
Homemaker	1.27 (0.86-1.89)	.23
Retired/unemployed	Reference	—
Marital status		
Single/divorced/widowed	1.03 (0.91-1.15)	.67
Married	Reference	—
Infection status of family members		
Confirmed case/suspected case	0.90 (0.55-1.49)	.69
Close contact with a confirmed case	0.98 (0.78-1.22)	.83
None of the above	Reference	—

[a]OR: odds ratio.

[b]Not applicable.

Knowledge of Messages Against COVID-19

There were 10 major channels through which the public had seen messages against COVID-19, including (in descending order of popularity) WeChat public accounts, news apps, WeChat, television/radio, microblogs, friends/relatives/colleagues, websites, SMS, community outreach, and newspapers (Table 4). The education distribution indicated a step gradient; respondents with higher education used more information channels than others. The student community primarily received information from new media sources such as WeChat rather than through the traditional media such as television. Homemakers were more likely to obtain information from television/radio compared with other occupation groups.

Table 4. Information channels through which respondents obtain information about COVID-19.

Sociodemographic characteristics	Friends/ relatives/ colleagues, n (%)	Websites, n (%)	WeChat public account, n (%)	Microblogs, n (%)	WeChat, n (%)	News apps, n (%)	Television/radio, n (%)	Newspapers, n (%)	SMS, n (%)	Community outreach, n (%)
Gender										
Male (n=2670)	689 (25.81)	898 (33.63)	2355 (88.20)	954 (35.73)	1280 (47.94)	1529 (57.27)	1264 (47.34)	257 (9.63)	449 (16.82)	462 (17.30)
Female (n=7634)	2180 (28.56)	1780 (23.32)	6872 (90.02)	3605 (47.22)	3884 (50.88)	4219 (55.27)	3378 (44.25)	519 (6.80)	1333 (17.46)	1246 (16.32)
Age (years)										
<20 (n=901)	327 (36.29)	256 (28.41)	812 (90.12)	447 (49.61)	362 (40.18)	445 (49.39)	382 (42.40)	69 (7.66)	220 (24.42)	142 (15.76)
21-30 (n=4830)	1402 (29.03)	1132 (23.44)	4349 (90.04)	2770 (57.35)	2349 (48.63)	2565 (53.11)	2018 (41.78)	331 (6.85)	789 (16.34)	689 (14.27)
31-40 (n=2945)	745 (25.30)	757 (25.70)	2671 (90.70)	1019 (34.60)	1610 (54.67)	1709 (58.03)	1317 (44.72)	192 (6.52)	441 (14.97)	477 (16.20)
41-50 (n=1141)	287 (25.15)	384 (33.65)	980 (85.89)	250 (21.91)	619 (54.25)	732 (64.15)	599 (52.50)	122 (10.69)	235 (20.60)	290 (25.42)
51-60 (n=403)	90 (22.33)	127 (31.51)	343 (85.11)	66 (16.38)	179 (44.42)	250 (62.03)	267 (66.25)	53 (13.15)	81 (20.10)	96 (23.82)
> 61 (n=84)	18 (21.43)	22 (26.19)	72 (85.71)	7 (8.33)	45 (53.57)	47 (55.95)	59 (70.24)	9 (10.71)	16 (19.05)	14 (16.67)
Education level										
Primary or below (<9 years) (n=526)	168 (31.94)	121 (23.00)	434 (82.51)	120 (22.81)	218 (41.44)	313 (59.51)	252 (47.91)	43 (8.17)	122 (23.19)	104 (19.77)
Secondary (10-12 years) (n=1117)	318 (28.47)	333 (29.81)	975 (87.29)	400 (35.81)	484 (43.33)	719 (64.37)	528 (47.27)	87 (7.79)	271 (24.26)	227 (20.32)
Undergraduate (13-16 years) (n=7219)	1970 (27.29)	1866 (25.85)	6488 (89.87)	3423 (47.42)	3649 (50.55)	4028 (55.80)	3248 (44.99)	568 (7.87)	1230 (17.04)	1228 (17.01)
Postgraduate or above (> 16 years) (n=1442)	413 (28.64)	358 (24.83)	1330 (92.23)	616 (42.72)	813 (56.38)	688 (47.71)	614 (42.58)	78 (5.41)	159 (11.03)	149 (10.33)
Occupation										
Government institution staff (n=1729)	460 (26.60)	503 (29.09)	1583 (91.56)	700 (40.49)	966 (55.87)	1008 (58.30)	812 (46.96)	128 (7.40)	291 (16.83)	307 (17.76)
Business/service worker (n=4204)	1091 (25.95)	972 (23.12)	3795 (90.27)	1889 (44.93)	2139 (50.88)	2354 (55.99)	1890 (44.96)	283 (6.73)	638 (15.18)	642 (15.27)
Students (n=668)	226 (33.83)	247 (36.98)	551 (82.49)	238 (35.63)	403 (60.33)	439 (65.72)	328 (49.10)	110 (16.47)	166 (24.85)	193 (28.89)
Medical staff (n=1894)	617 (32.58)	515 (27.19)	1706 (90.07)	1059 (55.91)	797 (42.08)	871 (45.99)	807 (42.61)	144 (7.60)	376 (19.85)	245 (12.94)
Homemaker (n=202)	51 (25.25)	55 (27.23)	175 (86.63)	25 (12.38)	95 (47.03)	125 (61.88)	142 (70.30)	23 (11.39)	41 (20.30)	51 (25.25)
Retired/unemployed (n=1607)	424 (26.38)	386 (24.02)	1417 (88.18)	648 (40.32)	764 (47.54)	951 (59.18)	663 (41.26)	88 (5.48)	270 (16.80)	270 (16.80)
Marital status										
Single/divorced/widowed (n=5002)	1532 (30.63)	1234 (24.67)	4511 (90.18)	2824 (56.46)	2339 (46.76)	2527 (50.52)	2183 (43.64)	354 (7.08)	880 (17.59)	689 (13.77)
Married (n=5302)	1337 (25.22)	1444 (27.24)	4716 (88.95)	1735 (32.72)	2825 (53.28)	3221 (60.75)	2459 (46.38)	422 (7.96)	902 (17.01)	1019 (19.22)
COVID-19 infection status of family members										

Sociodemographic characteristics	Friends/ relatives/ colleagues, n (%)	Websites, n (%)	WeChat public account, n (%)	Microblogs, n (%)	WeChat, n (%)	News apps, n (%)	Television/radio, n (%)	Newspapers, n (%)	SMS, n (%)	Community outreach, n (%)
Confirmed case/suspected case (n=70)	22 (31.43)	20 (28.57)	61 (87.14)	35 (50.00)	44 (62.86)	37 (52.86)	25 (35.71)	5 (7.14)	17 (24.29)	10 (14.29)
Close contact with a confirmed case (n=360)	107 (29.72)	79 (21.94)	328 (91.11)	148 (41.11)	196 (54.44)	181 (50.28)	140 (38.89)	19 (5.28)	60 (16.67)	59 (16.39)
None of the above (n=9874)	2740 (27.75)	2579 (26.12)	8838 (89.51)	4376 (44.32)	4924 (49.87)	5530 (56.01)	4477 (45.34)	752 (7.62)	1705 (17.27)	1639 (16.60)
Overall (n=10,304)	2869 (27.84)	2678 (25.99)	9227 (89.55)	4559 (44.24)	5164 (50.12)	5748 (55.78)	4642 (45.05)	776 (7.53)	1782 (17.29)	1708 (16.58)

Discussion

Our study suggested that approximately two-thirds of the sampled population practiced protective mask behavior. The majority of respondents believed that wearing a mask was effective for protecting themselves from COVID-19; however, only approximately 70% of the respondents appeared to be wearing the mask correctly. There were many channels used for people to obtain COVID-19–related information; however, the WeChat public account was the most important channel for the respondents to obtain prevention knowledge about COVID-19.

From the results of this survey, 97.93% of Chinese netizens believed that wearing a mask was an effective protective measure against COVID-19, which was much higher than found in a previous study performed in Shanghai (45.7%) [23]. This phenomenon is possibly because the Chinese government and the relevant departments resorted to a variety of promotional work, disseminating information through various media [24] in early February in China. The information included requirements for wearing masks in a one-sided manner, but did not teach the public to specifically adopt the protective mask behavior. However, the limited depth of health-awareness information promoted to the public may have an effect on changing people's mask-wearing behavior to help control the COVID-19 pandemic. With the spread of the COVID-19 epidemic, the need for protective mask behavior was promoted through different major information channels [25].

Although we found that 97.93% of the respondents recognized the importance of wearing a mask for epidemic protection, only 67.49% of the Chinese netizens practiced protective mask behavior. In fact, the Chinese government enforces strict epidemic prevention measures, and face masks are required in all public places as well as indoor areas, which results in a very high rate of mask-wearing (99%) among the Chinese population [26]. In daily life, it is common to see masks being pulled to one side or resting on the chin without completely covering the nose and mouth. Obviously, wearing a mask prevents people from eating, communicating, and other regular activities involving the mouth, and also creates an uncomfortable feeling that could disrupt breathing. Nevertheless, there is no doubt that the use of masks remains the most cost-effective intervention to contain the COVID-19 pandemic [6]. Wearing masks incorrectly does not prevent the spread of the virus [27]. Therefore, based on the previous advocacy for people to carry out self-protection, we should strengthen the guidance on the details of protective measures, such as providing instructions for use in the mask packaging and using representative social media such as WeChat to disseminate more detailed videos on mask-wearing. In addition, in real-world settings, behavioral coaching can be carried out by relying on specific groups such as schools and companies, thereby improving the implementation and effectiveness of public health strategies. However, it is necessary to emphasize that the main body of self-protection is still the individual; thus, continuous publicity of epidemic prevention knowledge and health education for the public are still the most basic effective measures.

In addition, we found that protective mask behavior was significantly associated with gender, age, occupation, and education level for all respondents. These results are consistent with the findings obtained during past outbreaks of SARS and H1N1 influenza virus, where age, gender, and education level were also predictors of face mask usage [28-30]. We found that younger and more educated people showed a higher likelihood of practicing protective masking behavior. This could be due to the fact that these individuals usually spend more time online, and are able to understand relevant health information and implement self-protective behavior correctly. However, research has also suggested that the provision of more comprehensive instructions on mask usage is the strongest predictor of better compliance with mask-wearing, regardless of educational background [26]. This reminds us that it is necessary to provide highly accessible behavioral guidance information for all groups of people. In addition, a higher proportion of commercial/service workers practiced protective masking behaviors than the rest of the population, which could be attributed to the fact that these individuals typically require human contact during working hours and thus may be more concerned with self-protection against COVID-19. Gender differences were also evident, with men implementing protective mask behavior at a lower rate than women, which is consistent with the findings of another cross-national sample survey of face mask use [31]. Women are generally more health-conscious, and a previous study found that women are more anxious and worried about outbreaks than men [32], which leads to more effective self-protective behaviors.

In summary, men, the elderly, and people with less education should be the focus groups of health education on protective mask behavior, and all efforts need to be made to improve the protective mask behavior of the entire population.

With the rapid development of the internet, the way the public acquires health information has changed dramatically. This study found that accesses to health information has shifted from mass media such as television/radio and newspapers to the mobile internet, including WeChat public accounts, news apps, and Weibo. However, subgroups with different characteristics had completely different tendencies. Men appear to be more inclined to access information through websites. For students, WeChat and websites were the main information channels. Television/radio and newspapers, as traditional information channels, have less impact than previously [33]; however, the homemakers surveyed in this study still preferred to obtain information through these traditional channels. For the less educated, traditional interpersonal communication is more common. As such, we should take a cue from these findings to deliver more targeted health information to different groups of people. For instance, mobile users are usually younger and can be targeted with more interesting science videos; television/radio channels tend to include more family health information and preventive measures; and the traditional approach of community outreach can be used to raise awareness of protective mask behavior among the less educated or the elderly.

Within the context of the COVID-19 epidemic, this study relied on the internet to conduct the survey, which was user-friendly to implement and more accessible to a large sample size. However, there were a few limitations. First, the survey used data provided by the respondents' reports, which may be subject to recall bias and social desirability. Mask covering is a particular behavioral norm during the epidemic, and people tend to either intentionally or unintentionally omit or deny their own violations of the norm; thereby, the extent to which Chinese netizens master mask knowledge and behaviors may be overestimated. Second, protective mask behavior is relatively difficult to measure and inconsistently defined across studies; for example, some studies only consider face masks covering the mouth and nose and secured to the chin as good mask-wearing behavior [34]. On this basis, our study added consideration of personal beliefs as well as mask materials, which can reveal protective mask behavior more comprehensively to a certain extent. Nonetheless, the measurement of behavior is complex and further research is needed to improve the precision of the results.

In summary, an internet-based cross-sectional survey was employed to study the protective mask behavior of sampled respondents. The results showed that Chinese netizens' protective mask behavior was lower than their mask knowledge. Improved information channels and focused message content related to wearing a mask are necessary to improve the public's protective mask behavior, particularly among men, the elderly, and people with less education.

Acknowledgments

The authors would like to acknowledge the staff of the Ding Xiang Doctor WeChat platform for their role in data collection.

Conflicts of Interest

None declared.

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Abbreviations

SARS: severe acute respiratory syndrome

Edited by T Sanchez, A Mavragani; submitted 21.07.21; peer-reviewed by A Ren, A Tannoubi; comments to author 23.01.22; revised version received 11.02.22; accepted 27.04.22; published 26.05.22.

Please cite as:
Xu Y, Wu Q, Xu S, Zhao Y, Zhang X
Factors Associated With Protective Mask-Wearing Behavior to Avoid COVID-19 Infection in China: Internet-Based Cross-sectional Study
JMIR Public Health Surveill 2022;8(5):e32278
URL: https://publichealth.jmir.org/2022/5/e32278
doi:10.2196/32278
PMID:35486491

Original Paper

Identifying Cases of Shoulder Injury Related to Vaccine Administration (SIRVA) in the United States: Development and Validation of a Natural Language Processing Method

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Abstract

Background: Shoulder injury related to vaccine administration (SIRVA) accounts for more than half of all claims received by the National Vaccine Injury Compensation Program. However, due to the difficulty of finding SIRVA cases in large health care databases, population-based studies are scarce.

Objective: The goal of the research was to develop a natural language processing (NLP) method to identify SIRVA cases from clinical notes.

Methods: We conducted the study among members of a large integrated health care organization who were vaccinated between April 1, 2016, and December 31, 2017, and had subsequent diagnosis codes indicative of shoulder injury. Based on a training data set with a chart review reference standard of 164 cases, we developed an NLP algorithm to extract shoulder disorder information, including prior vaccination, anatomic location, temporality and causality. The algorithm identified 3 groups of positive SIRVA cases (definite, probable, and possible) based on the strength of evidence. We compared NLP results to a chart review reference standard of 100 vaccinated cases. We then applied the final automated NLP algorithm to a broader cohort of vaccinated persons with a shoulder injury diagnosis code and performed manual chart confirmation on a random sample of NLP-identified definite cases and all NLP-identified probable and possible cases.

Results: In the validation sample, the NLP algorithm had 100% accuracy for identifying 4 SIRVA cases and 96 cases without SIRVA. In the broader cohort of 53,585 vaccinations, the NLP algorithm identified 291 definite, 124 probable, and 52 possible SIRVA cases. The chart-confirmation rates for these groups were 95.5% (278/291), 67.7% (84/124), and 17.3% (9/52), respectively.

Conclusions: The algorithm performed with high sensitivity and reasonable specificity in identifying positive SIRVA cases. The NLP algorithm can potentially be used in future population-based studies to identify this rare adverse event, avoiding labor-intensive chart review validation.

(JMIR Public Health Surveill 2022;8(5):e30426) doi:10.2196/30426

KEYWORDS

health; informatics; shoulder injury related to vaccine administration; SIRVA; natural language processing; NLP; causal relation; temporal relation; pharmacovigilance; electronic health records; EHR; vaccine safety; artificial intelligence; big data; population health; real-world data; vaccines

Introduction

In 2017, shoulder injury related to vaccine administration (SIRVA) was officially added to the vaccine injury table by the National Vaccine Injury Compensation Program (VICP) [1-3]. The VICP defined SIRVA as shoulder pain and limited range of motion occurring after the administration of a vaccine intended for intramuscular administration in the upper arm. SIRVA is caused by an injury to the musculoskeletal structures of the shoulder (eg, tendons, ligaments, bursae). In 2019, the number of claims related to SIRVA rose to 55% of all claims received by VICP, which resulted in a payout of more than $200 million [4]. Meanwhile, there has been increasing debate on whether vaccination or vaccine can cause shoulder problems [5-7].

The debate is fueled by the lack of high-quality evidence from population-based studies [1,8-11]. Most SIRVA publications have been limited to case reports [12]. Based on reports filed in the Vaccine Adverse Event Reporting System (VAERS), one recent study examined cases of shoulder problems following influenza vaccine administration [13]. While VAERS data rely on spontaneous reporting and can be used for safety signal detection, comprehensive electronic medical record (EMR) data from integrated health care settings are better suited to calculate incidence rates, assess risk factors, or make causal inferences. One recent population-based study that used EMR data only examined one type of shoulder condition (subdeltoid bursitis) and one type of vaccination (influenza vaccine) [14].

Although EMR data provide unprecedented opportunities for research, much EMR data are stored as free text. Researchers frequently use manual chart review of medical records to acquire information that is not available from structured data in the EMR system. Because there are no defined diagnosis codes for SIRVA, SIRVA case identification and determination must be done by reviewing free-text clinical documents. Manual review is both costly and time consuming; this challenge is magnified with SIRVA. Because SIRVA occurs rarely, but shoulder problems are one of the most common musculoskeletal conditions, detecting SIRVA cases necessitates chart review of a significant number of medical records [11,14]. Compared with manual chart review of medical records, natural language processing (NLP) is more efficient and produces more consistent results [15,16]. For clinical research, NLP facilitates the identification and extraction of information unavailable or incomplete in structured data [17-19]. In vaccine safety studies, we have used NLP to identify 2 vaccine-related adverse events, anaphylaxis and local reaction [20,21]. Therefore, NLP has the potential to enable population-based SIRVA studies using EMR data.

Our objective was to develop an efficient SIRVA case-finding strategy using an NLP algorithm. We aimed to create and evaluate NLP components required for case identification, such as anatomic location, temporality, and causation. Furthermore, we sought to validate the SIRVA algorithm in a large, diverse vaccinated population.

Methods

Setting

This study was conducted at Kaiser Permanente Southern California (KPSC), an integrated health care system that provides prepaid comprehensive health care to more than 4.7 million racially, ethnically, and socioeconomically diverse members [22]. KPSC's EMR system stores medical information about sociodemographics, utilization, diagnoses, laboratory tests, pharmacy use, membership history, and vaccination. This study was performed using structured data and free-text clinical notes from the EMR.

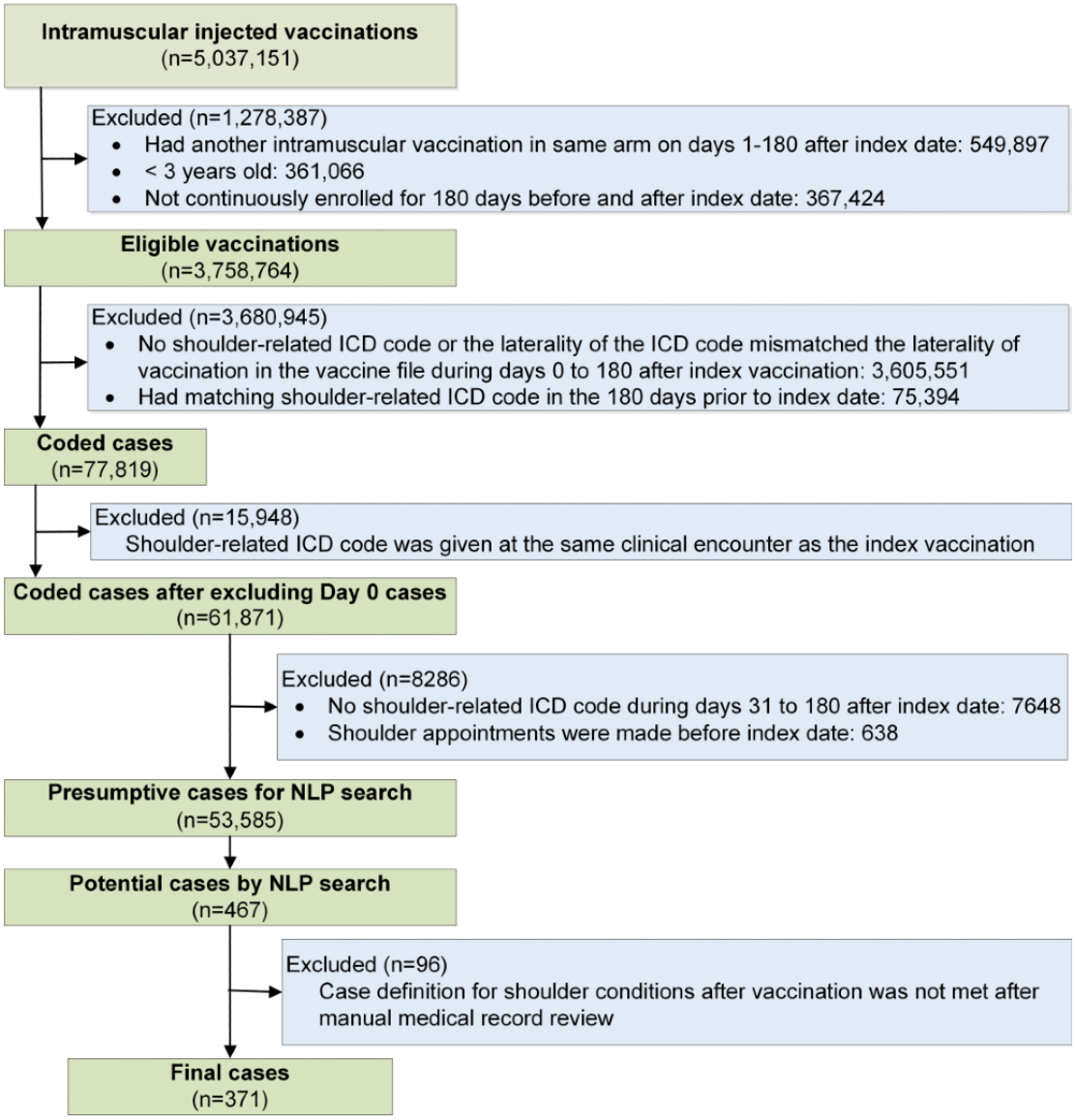
Vaccinated Population With Presumptive Shoulder Injury

The study was conducted among KPSC members aged 3 years or older who had at least 1 intramuscular vaccine administered in the arm between April 1, 2016, and December 31, 2017, within a KPSC facility (Figure 1). Each vaccination was specified by the members' unique identifier, the vaccination date (index date: ie, day 0), and the laterality of vaccination. Membership was required for 180 days before and after the index date.

Among the vaccinated population described above, we identified members with a presumptive shoulder injury using *International Classification of Diseases, 10th Revision, Clinical Modification* (ICD-10-CM) codes (Multimedia Appendix 1) within 180 days after the index date; the laterality of the shoulder injury code had to match that of the vaccination. We excluded vaccinations if the members had a shoulder-related visit or had a shoulder injury code within 180 days before the index date.

On day 0, members could have had clinical visits with preexisting shoulder conditions and subsequently receive vaccinations. To exclude these day 0 preexisting conditions, we required at least 2 encounters on day 0, of which at least 1 of the latter encounters had to be an urgent care, emergency department, or virtual visit (email, telephone, or video encounter). We sorted day 0 encounters by their timestamps. Day 0 encounters were excluded if the first encounter on day 0 had a shoulder injury code or if the encounter occurred before vaccination. In order to exclude vaccine-related local reactions, one of the most common adverse events occurring shortly after vaccination, a shoulder injury code also needed to appear during days 31 to 180 postvaccination.

Figure 1. Flowchart showing selection of eligible vaccinations with presumptive shoulder injuries, application of natural language processing algorithm, and shoulder injury related to vaccine administration (SIRVA) case confirmation results (index date is vaccination date). ICD: International Classification of Diseases, 10th Revision, Clinical Modification; NLP: natural language processing.



SIRVA Case Definition

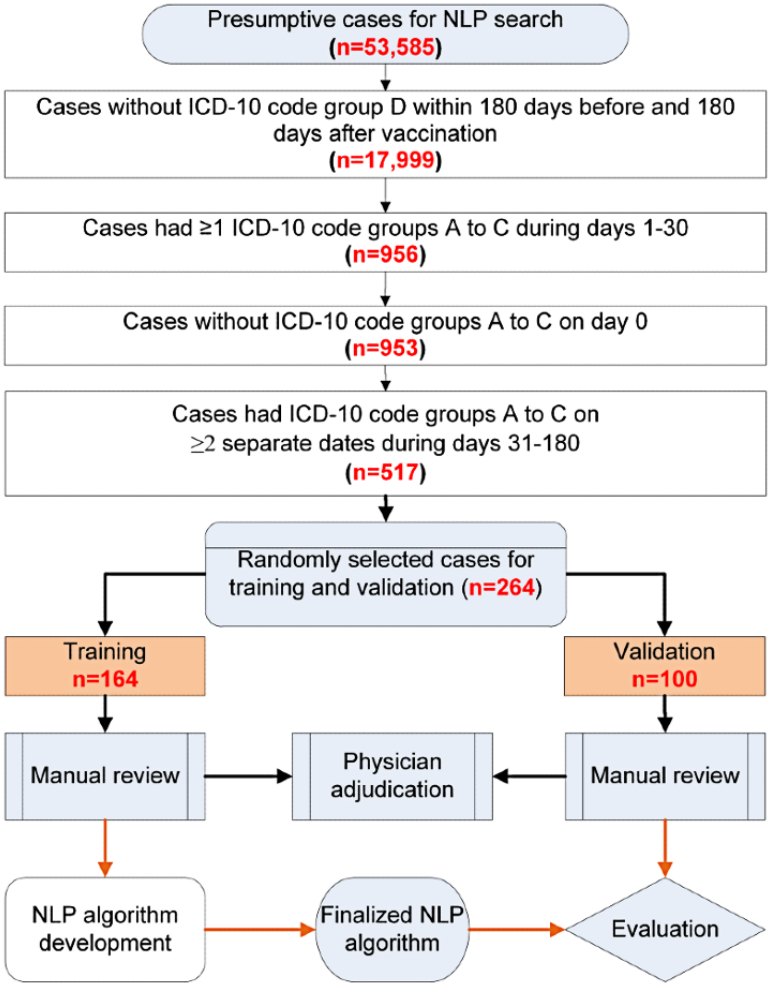
The VICP's SIRVA case definition was created for medicolegal purposes [3]. To meet this case definition, a vaccine recipient must manifest all of the following: (1) pain and reduced range of motion are limited to the shoulder in which the intramuscular vaccine was administered, (2) pain occurs within 48 hours of vaccination, (3) no history of pain, inflammation, or dysfunction of the affected shoulder prior to vaccination that would explain the alleged condition, (4) no other condition or abnormality is present that would explain the patient's symptoms, and (5) symptoms must last more than 6 months after vaccination [23].

Based on the VICP SIRVA case definition and other publications [1,8,13,14,24], we created a SIRVA case definition suitable for a population-based study using EMR data. A valid SIRVA case needed to meet 5 criteria: (1) damage to the shoulder region occurred and was confirmed by signs and symptoms (ie, pain, limited range of motion, weakness, and stiffness) and clinical diagnosis, (2) shoulder injury occurred in the same arm in which a vaccine was injected; (3) shoulder injury started within 7 days after vaccination, (4) vaccination was a possible cause of the shoulder injury and no other known causes were associated with the shoulder injury, and (5) shoulder injury lasted more than 30 days postvaccination.

Subpopulation for Training and Validation of NLP Algorithm

To increase the likelihood of including true SIRVA cases in the data sets used for training and validating the NLP algorithm, we applied additional criteria to the presumptive cases to define a subpopulation (n=517; Figure 2): (1) exclusion of cases with an external shoulder injury (eg, accident) code within 180 days before and 180 days after vaccination, (2) exclusion of cases with a shoulder injury code on day 0, (3) requirement of a shoulder injury code during days 1 to 30, and (4) requirement of a shoulder injury code on at least 2 different dates during days 31 to 180. The criteria were based on characteristics of chart-confirmed SIRVA cases from a prior study [14].

Figure 2. Flowchart to create data set for training and validation data sampling (group A: shoulder disorder diagnoses reported in shoulder injury related to vaccine administration [SIRVA] literature; group B: shoulder disorder diagnoses not previously reported in SIRVA literature; group C: shoulder symptom codes; group D: shoulder injury codes [ICD-10-CM chapter 19: Injury, poisoning and certain other consequences of external causes]). NLP: natural language processing; ICD-10: International Classification of Diseases, 10th Revision, Clinical Modification.



Training Data Set

From the substudy population described above, we selected a random sample for chart review. The NLP algorithm was built and refined based on incremental releases of training data [21]. In contrast to machine learning methods in which the model automatically updates its parameters based on training data, we manually created and updated the search queries based on training data. Once the NLP algorithm stabilized and achieved good performance, we stopped the training process. The final training dataset had 164 cases.

Validation Data Set

From the remaining cases in the substudy population (n=353), we randomly selected another 100 cases to form the validation dataset. The chart review results were used to evaluate the performance of the final NLP algorithm.

Manual Chart Review

We created a chart review form based on the SIRVA case definition. Chart abstractors reviewed the medical records and recorded information on the abstraction form (Multimedia Appendix 2) using the REDCap (Research Electronic Data Capture) system [25]. The abstraction form was derived from a previous study of subdeltoid bursitis after vaccination but was expanded to include other shoulder disorder diagnoses [14]. The chart abstraction and adjudication processes were similar to those used in past vaccine safety studies [14,21]. An ascertainment period of 180 days after vaccination was used for both NLP and chart abstraction, allowing members sufficient time to seek medical care [14]. A second person reviewed each completed abstraction form for quality. A KPSC physician adjudicated the potential cases according to the SIRVA case definition for cases in which the chart reviewers had difficulty making a final assessment.

NLP Terminology Development

NLP terminologies were derived from various data sources, including the clinical notes of the study participants, VAERS reports [26], ontologies (eg, Unified Medical Language System [27]), semantic lexicons (eg, WordNet [28]), and other online resources. We expanded the derived terminologies using various tools. We used Linguamatics I2E [29] to identify term variations including misspellings, morphological variants, and synonyms through I2E's synonym discovery capability. We used word-embedding methods (fastText [30] and GloVe [31]) to find related terms not necessarily limited to synonyms. For instance, NLTK and fastText (from the Gensim package [32])

were used to train subword embedding models. Because our main interest was to identify rare terms to enrich our terminologies, we trained skip-gram models in fastText. The trained model was used to identify similar terms based on their contexts. For instance, the word "injury" has similar terms with various semantic meanings including accident, fall, laceration, overuse, trip, and sprain.

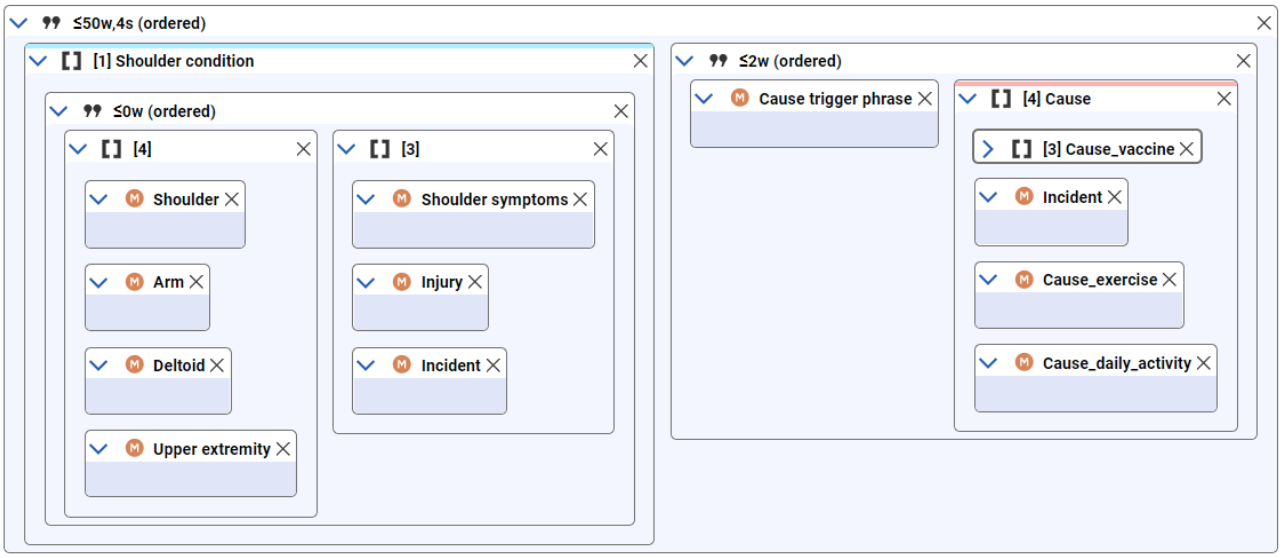
NLP Indexing

The preprocessing steps included section detection, sentence separation, and tokenization (that is, segmenting text into linguistic units such as words and punctuation). For each token, the indexing process added annotations for matched concepts and general linguistic entities (eg, lexical chunks like noun or verb phrases). Additional annotations captured linguistic variations such as wildcard, substring, spelling correction, and morphological variation.

NLP Search

We used a rule-based NLP algorithm for this study [15,21,33,34]. The NLP algorithm was developed to search each indexed note at different levels: section (eg, "past medical history"), intrasentence, and cross-sentence. A distance-based relationship detection algorithm was applied to relate terms to other terms based on the number of words or sentences between them, thereby associating shoulder injury with information on vaccination site, temporality, or causality (Figure 3). The relationship detection algorithm also allowed for terms to be specified as ordered or nested (eg, an inner relation is an element of an outer relation). We used negation algorithms similar to pyConText/NegEx [35] to identify negated, uncertain, and hypothetical statements. The relationship search identified 3 types of information associated with shoulder injury: anatomic, temporal, and causal.

Figure 3. Cross-sentence search query example. This query searches over a span of 4 sentences (4s in diagram) with a maximum number of 50 words (≤50w in diagram) in between query items. There are 2 nested relationship queries inside the outermost relationship search. The first query searches for shoulder conditions, and the second query searches for causality statement. We removed other contextual query items from diagram due to space limitations. w: week; s: sentence.



The anatomic site relationship algorithm extracted the body location and laterality of the shoulder injury. For example, "left" and "arm" were identified as the laterality and body location of the shoulder injury, respectively, in the sentence "Patient has persistent pain in his left arm."

The temporal relationship algorithm used linguistic terms, such as prepositions, to extract temporal relationships such as the onset date and duration associated with the vaccination event (eg, "for 2 months," "over the past 2 weeks," "since last Thursday"). Incomplete temporal information was inferred based on the note creation date. For example, dates with missing year information in clinical notes were assumed to occur near the note creation date. Additional details about the types of temporal expressions extracted by the NLP algorithm are available in Multimedia Appendix 3.

The causal relationship algorithm searched for possible causes of shoulder injury and classified them into 7 types (Table 1). The determination of causal relationships between cause and shoulder injury was made by lexical-syntactic rules based on more than 70 trigger terms (Multimedia Appendix 4). The terminologies for causes of shoulder injury other than vaccination are listed in Multimedia Appendix 5. Moreover, for each relationship search, we also extracted the vaccine name if available because multiple vaccines could be administered concomitantly or during follow-up.

Table 1. Types of causes associated with shoulder injuries.

Order	Type of cause	Description
1	Vaccination	Specific vaccine name or general vaccine terms
2	Accident	Accidents such as auto accident, fall, hit
3	Work	Work-related injury
4	Other medical conditions	Medical conditions that can cause shoulder injury such as arthritis or chest pain radiating to the shoulder
5	Exercise	Exercise or sports-related injury
6	Daily activity	Injuries occurred during other daily activities such as lifting groceries, overuse, or side sleeping
7	Unknown	Insidious or unknown cause

NLP Case Classification

The final classification was based on the case definition described in the section "SIRVA case definition" by integrating vaccine, anatomic location, temporality, and causality information. Because our algorithm emphasized sensitivity, we captured additional probable and possible cases identified by NLP with weaker evidence as defined by the following 3 criteria. First, the vaccination cause was identified only by cross-sentence causal relationship search. For example, shoulder injury and vaccination were described in separate sentences: "Patient requesting an appointment for evaluation for left arm pain. States experiencing pain × 1 month s/p flu vaccine." Second, vaccination was identified as a cause of shoulder injury 30 days or less after vaccination. Because causality was less likely to be documented when the visit date was further away from the onset date, vaccination may only be established as the cause of the shoulder injury within 30 days of vaccination, but not more than 30 days after vaccination. Third, the vaccine associated with shoulder injury documented in the clinical note did not match the vaccine recorded in the vaccination file. Positive cases that met the SIRVA case definition were further classified into 3 groups: definite if they met none of the 3 criteria; probable if they met only 1 of the 3 criteria; and possible if they met 2 or more of the 3 criteria.

NLP Algorithm Performance

We evaluated the NLP algorithm's accuracy in identifying SIRVA cases compared to the chart review reference standard in the validation dataset. We calculated sensitivity, specificity, positive predictive value, and negative predictive value and their 95% confidence intervals. Since the NLP algorithm could potentially be accurate in determining a case not to be SIRVA but based on an incorrect assessment of an individual component of the SIRVA case definition not being met, we also conducted an error analysis of cases in which there were discrepancies between the NLP algorithm and chart review for individual components of the case definition.

Application of NLP Algorithm to Study Population and Chart Confirmation

The final NLP algorithm was applied to the broader study population of vaccinated persons with presumptive shoulder injury (based on codes) to identify potential SIRVA cases. We performed manual chart confirmation on all NLP-identified cases and calculated chart confirmation rates and their 95% confidence intervals.

We assembled the final group of SIRVA cases based on the chart review results. We calculated the time between vaccination and the first visit for a shoulder disorder in these SIRVA cases. We also examined the vaccination-related temporal and causal statements in the clinical notes of these SIRVA cases.

Ethical Approval

The study was approved by the KPSC institutional review board (#4982), which waived the requirement for informed consent due to this being a data-only minimal risk study.

Results

Application of NLP Algorithm to Study Population

Out of 3,758,764 eligible vaccinations, we identified 77,819 records with a shoulder injury code (Figure 1). Among them, 16,048 had a code on day 0. After applying the day 0 inclusion criteria, the number of day 0 records remaining was 100. The NLP algorithm was applied to 53,585 cases with presumptive shoulder injury after vaccination.

Validation Results

The NLP algorithm achieved perfect accuracy (100%) in identifying the 4 SIRVA cases from the validation dataset (n=100). However, the small number of positive cases resulted in wide confidence intervals for sensitivity and positive predictive value (39.6%-100.0%). Meanwhile, the confidence intervals for specificity and negative predictive value remained narrow (95.2%-100.0%).

Discrepancies between the NLP algorithm and chart review were investigated by component (Table 2). For laterality, discrepancies were typically due to conflicting evidence or documentation errors in the clinical notes themselves. For temporality, the NLP algorithm incorrectly assigned symptom onset when performing cross-sentence searches and incorrectly assigned injury duration based on incorrect laterality or capture of a resolved shoulder injury.

For causality, the NLP algorithm missed causes such as daily activity and accident and incorrectly identified the cause as unknown. These mistakes, however, had no bearing on the causality classification of whether or not they were vaccine-related. Furthermore, because a confirmed case must meet all of the elements of the case definition, inaccuracy in 1

element may not affect the overall accuracy of the SIRVA case classification.

Table 2. Error analyses on the validation dataset.

	Clinical text examples and the causes of Natural Language Processing (NLP) errors
Error analysis on injury onset	
1	"She has chronic pain—neck, low back, B/L[a] shoulders. She has fibromyalgia and also fell a few weeks ago which worsened her back pain." NLP incorrectly associated the event ("fall") that occurred "a few weeks ago" with the shoulder problem when performing a cross-sentence search.
2	Prior condition reported on day 0 visit: "My left shoulder pain never went away despite still doing physical therapy and living on NSAIDs[b]. Now it is constant and much worse today." NLP incorrectly captured "today" as the shoulder pain onset date when performing a cross-sentence search.
Error analysis on injury duration	
3	On day 136, "States in past pain would travel to left shoulder causing numbness to left arm and lasting a few days but today denies any numbness." NLP incorrectly identified the injury duration based on a resolved shoulder symptom.
Error analysis on injury cause	
4	"...with 1 day of pain in the left arm and shoulder. Denies any injury. Did some lifting yesterday." NLP identified the cause as unknown, failing to identify the possible cause (daily activity).
5	"She has been working on the computer a lot. Overhead movement exacerbates the pain... No injury or trauma." NLP identified the cause as unknown, failing to identify the possible cause (daily activity).
6	"...who complains of left shoulder pain that started 3 weeks ago after vacuuming." NLP identified the cause as unknown, failing to identify the possible cause (daily activity).
7	"...likely subdeltoid bursitis and supraspinatus tendinopathy in the setting of DM[c] likely from acute movement with pain when getting IV[d] placed." NLP identified the cause as unknown, failing to identify the possible cause (accident).
8	"Patient reports left shoulder pain with movement; no trauma. Patient worked for years caring for young children and had to carry and lift them." NLP identified the cause as unknown, failing to identify the possible cause (daily activity).

[a]B/L: bilateral.

[b]NSAIDs: Nonsteroidal anti-inflammatory drugs.

[c]DM: diabetes mellitus.

[d]IV: intravenous.

NLP-Identified Potential SIRVA Cases

We applied the final NLP algorithm to the clinical notes of 53,585 presumptive shoulder injury cases. Among them, 99.9% (53,530/53,585) had at least 1 clinical note on days 0 to 180 after vaccination. The total number of clinical notes searched by NLP was 4,292,610. The average number of clinical notes per case was 80. The index size was around 50 gigabytes. The NLP algorithm identified shoulder injury in 46,086 records, and 96.5% of them had matched laterality compared to the vaccination files (Table 3). The NLP algorithm identified at least 1 cause for 55.0% (25,325/46,086) of the NLP-identified shoulder injury cases. The temporal relation search identified the onset date for 98.2% (45,252/46,086) of the NLP-identified shoulder injury cases. About 76.2% (35,135/46,086) of these NLP-identified shoulder injury cases had symptom duration of more than 30 days postvaccination. The number of potential SIRVA cases identified by the NLP algorithm was 467, classified into 291 definite, 124 probable, and 52 possible SIRVA cases.

Table 3. Number of cases identified by natural language processing (NLP) in the base study population (n=53,585).

Natural language processing–identified cases	n	%[a] (n=53,585)	%[b] (n=46,086)
Shoulder injury identified	46,086	86	—[c]
Anatomic site			
Laterality identified	44,488	83	96.5
Laterality mismatch	1220	2.3	2.6
Causality			
Cause identified[d]	25,325	47.3	55.0
Cause identified[e]	19,039	35.5	41.3
Temporality			
Onset identified	45,252	84.4	98.2
Symptom duration >30 days postvaccination	35,135	65.6	76.2
SIRVA[f] cases	467	0.9	1

[a]Percentage of cases among the number of cases with shoulder injury diagnosis code (n=53,585).

[b]Percentage of cases among the number of natural language processing–identified shoulder injury cases (n=46,086).

[c]Not applicable.

[d]Includes unknown cause stated in the clinical notes.

[e]Excludes unknown cause stated in the clinical notes.

[f]SIRVA: shoulder injury related to vaccine administration.

Final SIRVA Cases After Chart Review

We performed chart review on 467 NLP-identified SIRVA cases (Table 4). The chart confirmation rates were 95.5% (95% CI 92.5%-97.4%), 67.7% (95% CI 59.1%-75.3%), and 18.9% (95% CI 8.7%-30.8%) for the definite, probable, and possible groups, respectively. The final number of SIRVA cases was 371.

Among these 371 cases, the median times from vaccination to the first and last visit with a shoulder injury code were 43 days (IQR 21-79 days, range 0-180 days) and 127 days (IQR 77-162, range 31-180 days), respectively. The symptom onset occurred 2 or fewer days after vaccination in 93.5% (347/371) of cases and from 3 to 7 days after vaccination in 6.5% (24/371) of cases.

Most cases (355/371, 95.7%) had explicit temporal statements on symptom onset in relation to vaccination. Examples included "L shoulder pain that started the day she got a flu shot" and "Right shoulder pain and neck stiffness since immunizations." The symptom onset for the remaining cases (16/371, 4.3%) could be derived based on the date of clinical visit, symptom duration, and causality statement (eg, "Reports having R shoulder pain for last 2 months. Thought related to vaccine she received in R arm"). In 145 cases, there were explicit causal statements regarding the shoulder condition and the vaccination (eg, "status post vaccination—suspect rotator cuff irritation from vaccination itself"). Of those, 40 cases had mention of incorrect vaccine administration.

Table 4. Number of natural language processing–identified cases and chart-confirmed cases.

NLP[a]-identified group	NLP-identified	Chart confirmed	Confirmation rate (%)
Definite	291	278	95.5
Probable	124	84	67.7
Cross-sentence causality	64	46	71.9
Vaccination cause identified ≤30 days after vaccination	41	26	63.4
Vaccine mismatch	19	12	63.2
Possible	52	9	17.3
Total	467	371	79.4

[a]NLP: natural language processing.

Discussion

Principal Findings

SIRVA is a rare outcome after vaccination that does not have a specific diagnosis code, and it is impractical to conduct manual chart review to identify all SIRVA cases. We developed and validated an NLP algorithm to identify potential SIRVA cases with high accuracy. The only previous population-based study on SIRVA [14] was limited to shoulder bursitis after influenza vaccination. In that study, a random sample of 526 out of 1098 presumptive cases was chart reviewed to identify 12 subdeltoid bursitis cases attributed to vaccination. In this study, we included cases with all types of shoulder disorder diagnoses after vaccinations. Out of 53,585 presumptive cases, the NLP algorithm combined with manual chart review yielded 371 SIRVA cases. Among 3.8 million vaccinations, the rate of SIRVA in this study was around 1 per 10,000 vaccinations [12]. It should be noted that our SIRVA case definition was different from that of the VICP and other studies in terms of symptom onset, duration, and severity.

Although the NLP algorithm's overall accuracy was high, some challenges remained with the laterality component, despite the addition of laterality information in ICD-10-CM coding. First, descriptions of symptom location may not be precise. For example, the arm could refer to the region from the shoulder joint to the elbow joint (upper arm) or further down to the wrist. Second, the laterality recorded in the vaccine file or documented in the clinical notes could be incorrect. These issues must be considered when conducting studies using anatomic and laterality information.

There were several lessons learned from the temporality component of the NLP algorithm. First, there could be documentation of multiple onset dates during the 180 days after vaccination. Second, the disease onset information was more likely to be incomplete or inaccurate when the onset date was in the distant past, which could make it difficult to determine the onset date if the clinical visit date was further away from the vaccination date. In this study, to maximize sensitivity, any potential case with an onset falling within the predefined onset window satisfied the onset criteria.

In our study, the causality component worked reasonably well in identifying vaccination-related causality statements. Although the provider or patient may have stated that the shoulder injury was vaccination-related, such statements do not provide definitive proof of causality. Because shoulder symptoms could have an insidious onset with multiple contributing factors, it was difficult to draw definitive conclusions about cause and effect. To improve specificity, we excluded cases with nonvaccination causes of shoulder injury. However, it was still challenging to identify nonvaccination causes. First, there were numerous causes of shoulder injuries. Second, some of the causes could also be the treatment for the shoulder problem. For example, exercise could be both the cause and the therapy plan for shoulder injuries. Third, the cause of shoulder injury was often not mentioned in the clinical notes. In this study, the NLP algorithm could not identify the cause in about half of the cases. Last, the cause of shoulder injury was often not described in the same sentence as the shoulder symptom. The cross-sentence relationship search increased the sensitivity but decreased specificity. Causal relations have been studied extensively in the NLP field [36], but only a few studies focused on health-related causal relations and were conducted using Twitter messages [37] and literature [38-40]. One study extracted causal relations from clinical text using 3 causal key phrases (because, due to, and secondary to) and discontinuation key phrases to detect adverse drug reactions in ambulatory notes and achieved high specificity (98%) but low sensitivity (31%) and positive predictive value (45%) [41].

SIRVA-related shoulder symptoms are common for other acute or chronic medical conditions with many possible causes. Correctly integrating the NLP-identified laterality, temporality, and causality information is nontrivial. For the same patient, different clinical encounters could attribute the shoulder injury to different causes. In this study, we made patient-level classifications by using the information identified from all the components from all the notes. The combination of information across multiple notes increased the sensitivity of finding SIRVA cases but reduced the specificity since the NLP algorithm could misinterpret unrelated information extracted from multiple notes.

Because we tailored the NLP algorithm to emphasize sensitivity, the confirmation rates were low in the probable (67.7%) and possible (17.3%) groups. However, since SIRVA is a rare event, manual review of all the probable and possible cases was feasible in this study. In future studies, instead of categorizing the NLP output based on the strength of evidence, a machine learning model could be built on top of the NLP outputs [15] to further improve accuracy and develop thresholds. The SIRVA cases identified in this study could also serve as training data for a machine learning algorithm.

Limitations

This study had some potential limitations. We were unable to apply the algorithm to all the eligible vaccinations (n=3,758,764) due to time and resource restrictions. Our study population was limited to vaccinated cases with a diagnosis code for shoulder injury. However, loss of sensitivity is expected to be minimal since we used a comprehensive list of codes. Additionally, shoulder injuries can last a long time and are often accompanied by repeated visits. The 6-month lookback window used in this study may not have been sufficient to remove preexisting shoulder conditions. Failure to exclude prior shoulder conditions could reduce the specificity of the NLP algorithm. In our vaccine-related local reaction study [20], most people diagnosed with a presumptive code of interest on day 0 had symptom onset before vaccination. In this study, we excluded most cases with a shoulder injury code on day 0. Further research is needed to study the association between SIRVA and day 0 shoulder injury codes. Finally, because our method was tailored to this specific outcome after vaccination, its generalizability for use with other outcomes is unclear.

Conclusions

We developed and validated an NLP algorithm to identify potential SIRVA cases among vaccinated persons with presumptive shoulder injury. The algorithm achieved high

sensitivity and reasonable specificity. The NLP algorithm can potentially be used in future population-based studies to identify this rare adverse event, avoiding labor-intensive chart review validation.

Acknowledgments

We want to thank the following persons for their contributions to data collection and medical record abstraction: Anna Lawless, Bernadine Dizon, Claire Park, Jose Pio, Joy Gelfond, Karen Schenk, Kerresa Morrissette, Melena Taylor, Nancy Canul-Jauriga, and Radha Bathala. This study was funded under contract 200-2012-53580 through the Vaccine Safety Datalink from the Centers for Disease Control and Prevention (CDC). The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

Authors' Contributions

CZ, JD, LSS, CM, and SJJ contributed to conceptualizing the study and obtained the funding. CZ, I-LAL, SSK and DSR collected and analyzed the data. CZ designed and implemented the natural language processing algorithm. CZ drafted the initial manuscript. CZ, JD, LSS, WC, RAN provided critical revision of the article for important intellectual content. All authors reviewed and approved the final manuscript for publication.

Conflicts of Interest

LSS has received research support from GlaxoSmithKline, Dynavax, Seqirus, and Moderna for studies unrelated to this paper. LQ has received research support from GlaxoSmithKline, Moderna, and Dynavax for studies unrelated to this paper. All other authors report no conflicts of interest related to the submitted work.

Multimedia Appendix 1
International Classification of Diseases, 10th Revision, Clinical Modification code groups for identifying presumptive shoulder injury cases.
[DOCX File , 61 KB - publichealth_v8i5e30426_app1.docx]

Multimedia Appendix 2
Chart review abstraction form.
[DOCX File , 1106 KB - publichealth_v8i5e30426_app2.docx]

Multimedia Appendix 3
Sample extracted temporal expressions.
[DOCX File , 21 KB - publichealth_v8i5e30426_app3.docx]

Multimedia Appendix 4
Trigger phrases for identifying causal relationships.
[DOCX File , 25 KB - publichealth_v8i5e30426_app4.docx]

Multimedia Appendix 5
Terminology for causes of shoulder injury other than vaccination.
[DOCX File , 22 KB - publichealth_v8i5e30426_app5.docx]

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Abbreviations

CDC: Centers for Disease Control and Prevention
EMR: electronic medical record
KPSC: Kaiser Permanente Southern California
ICD-10-CM: International Classification of Diseases, 10th Revision, Clinical Modification
NLP: natural language processing
REDCap: Research Electronic Data Capture
SIRVA: shoulder injury related to vaccine administration
VAERS: Vaccine Adverse Event Reporting System
VICP: National Vaccine Injury Compensation Program

Edited by T Sanchez, A Mavragani; submitted 13.05.21; peer-reviewed by F Xie, W Zhang; comments to author 24.01.22; revised version received 22.02.22; accepted 26.04.22; published 24.05.22.

Please cite as:
Zheng C, Duffy J, Liu ILA, Sy LS, Navarro RA, Kim SS, Ryan DS, Chen W, Qian L, Mercado C, Jacobsen SJ
Identifying Cases of Shoulder Injury Related to Vaccine Administration (SIRVA) in the United States: Development and Validation of a Natural Language Processing Method
JMIR Public Health Surveill 2022;8(5):e30426
URL: https://publichealth.jmir.org/2022/5/e30426
doi:10.2196/30426
PMID:35608886

Corrigenda and Addenda

Correction: The Transition of Social Isolation and Related Psychological Factors in 2 Mild Lockdown Periods During the COVID-19 Pandemic in Japan: Longitudinal Survey Study

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Related Article:

Correction of: https://publichealth.jmir.org/2022/3/e32694

(JMIR Public Health Surveill 2022;8(5):e39498) doi:10.2196/39498

In “The Transition of Social Isolation and Related Psychological Factors in 2 Mild Lockdown Periods During the COVID-19 Pandemic in Japan: Longitudinal Survey Study” (JMIR Public Health Surveill 2022;8(3):e32694) the authors noted one error.

In Table 2 of the originally published article, the standard deviations of the PHQ-9 in phases 1 and 2 in the 'Persistent-SI' group were missed. The table was originally published as shown in Multimedia Appendix 1.

The 2 SD values were 5.93 and 6.07, respectively, and the corrected Table 2 is as follows:

Table 2. Differences and interactions between phases[a] and transition of SI[b] on different scales.

Phase	Mean score (SD)				Effect of phase			Effect of group			Interaction		
	No SI	Improved SI	Worsened SI	Persistent SI	*F* (*df*)	*P* value	η_G^2[c]	*F* (*df*)	*P* value	η_G^2	*F* (*df*)	*P* value	η_G^2
LSNS-6[d]													
1	16.84 (3.71)	7.89 (2.77)	14.58 (2.73)	5.50 (3.31)	15.18 (1, 7889)	<.001	0.000	8071.80 (3, 7889)	<.001	0.640	2046.36 (3, 7889)	<.001	0.066
2	16.46 (3.55)	14.56 (2.83)	7.81 (2.93)	5.21 (3.28)	N/A[e]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
UCLA-LS3[f]													
1	19.56 (4.67)	23.07 (4.61)	22.26 (4.55)	26.41 (5.20)	10.51 (1, 7889)	.001	0.000	1096.28 (3, 7889)	<.001	0.259	38.59 (3, 7889)	<.001	0.002
2	19.87 (4.86)	22.13 (4.76)	23.38 (4.59)	26.62 (5.33)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
K6[g]													
1	3.99 (4.38)	5.23 (5.37)	4.96 (4.88)	6.12 (5.77)	536.70 (1, 7889)	<.001	0.013	103.10 (3, 7889)	<.001	0.030	2.64 (3, 7889)	.048	0.000
2	2.63 (4.01)	3.37 (4.87)	3.68 (4.82)	4.71 (5.63)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
PHQ-9[h]													
1	3.05 (4.06)	4.41 (5.39)	4.19 (5.05)	5.53 (5.93)	168.90 (1, 7889)	<.001	0.004	126.46 (3, 7889)	<.001	0.038	2.32 (3, 7889)	.073	0.000
2	2.4 (3.89)	3.27 (5.19)	3.49 (4.88)	4.77 (6.07)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

[a]Phase 1: between May 11 and 12, 2020, in the final phase of the first state of emergency; phase 2: between February 24 and 28, 2021, in the final phase of the second state of emergency.

[b]SI: social isolation.

[c]η_G^2: 0.010, small; 0.060, medium; 0.140, large.

[d]LSNS-6: Lubben Social Network Scale (shortened version).

[e]N/A: not applicable.

[f]UCLA-LS3: University of California, Los Angeles (UCLA) Loneliness Scale, Version 3.

[g]K6: Kessler Psychological Distress Scale-6.

[h]PHQ-9: Patient Health Questionnaire-9.

The correction will appear in the online version of the paper on the JMIR Publications website on May 16, 2022, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

Multimedia Appendix 1

Original published version of "Table 2. Differences and interactions between phases[a] and transition of SI[b] on different scales." [DOCX File , 18 KB - publichealth_v8i5e39498_app1.docx]

Submitted 11.05.22; this is a non–peer-reviewed article;accepted 12.05.22; published 16.05.22.

Please cite as:
Sugaya N, Yamamoto T, Suzuki N, Uchiumi C
Correction: The Transition of Social Isolation and Related Psychological Factors in 2 Mild Lockdown Periods During the COVID-19 Pandemic in Japan: Longitudinal Survey Study
JMIR Public Health Surveill 2022;8(5):e39498
URL: https://publichealth.jmir.org/2022/5/e39498
doi:10.2196/39498
PMID:35576576

Original Paper

COVID-19 News and Its Association With the Mental Health of Sexual and Gender Minority Adults: Cross-sectional Study

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Abstract

Background: Sexual and gender minority (SGM; people whose sexual orientation is not heterosexual or whose gender identity varies from what is traditionally associated with the sex assigned to them at birth) people experience high rates of trauma and substantial disparities in anxiety and posttraumatic stress disorder (PTSD). Exposure to traumatic stressors such as news related to COVID-19 may be associated with symptoms of anxiety and PTSD.

Objective: This study aims to evaluate the relationship of COVID-19 news exposure with anxiety and PTSD symptoms in a sample of SGM adults in the United States.

Methods: Data were collected between March 23 and August 2, 2020, from The PRIDE Study, a national longitudinal cohort study of SGM people. Regression analyses were used to analyze the relationship between self-reported news exposure and symptoms of anxiety using the Generalized Anxiety Disorder-7 and symptoms of COVID-19–related PTSD using the Impact of Events Scale-Revised.

Results: Our sample included a total of 3079 SGM participants. Each unit increase in COVID-19–related news exposure was associated with greater anxiety symptoms (odds ratio 1.77, 95% CI 1.63-1.93; $P<.001$) and 1.93 greater odds of PTSD (95% CI 1.74-2.14; $P<.001$).

Conclusions: Our study found that COVID-19 news exposure was positively associated with greater symptoms of anxiety and PTSD among SGM people. This supports previous literature in other populations where greater news exposure was associated with poorer mental health. Further research is needed to determine the direction of this relationship and to evaluate for differences among SGM subgroups with multiple marginalized identities.

(JMIR Public Health Surveill 2022;8(5):e34710) doi:10.2196/34710

KEYWORDS

PTSD; posttraumatic stress disorder; anxiety; minority populations; vicarious trauma; tertiary trauma; COVID-19; pandemic; public health; sexual orientation; gender identity; mental health

Introduction

Since the World Health Organization declared COVID-19 a pandemic in March 2020 [1], there have been more than 6 million deaths and 456 million confirmed cases worldwide (as of March 2022) [2]. In addition to the impacts of COVID-19 on physical health, mental health may be affected by direct (eg, infection with COVID-19, the threat of infection, or the loss of a loved one) and indirect (eg, witnessing the illness or death of others worldwide) stressors associated with the illness. As the numbers of sick and dead are counted and described across news outlets, individuals are exposed to an ongoing threat. This ongoing, repeated threat is meaningfully different from most traumatic stressors that occur once in a singular moment in time. Further, the ongoing stressors associated with COVID-19 pose a significant threat to vulnerable communities who have disparate exposure to trauma and associated mental illness [3,4]. For example, sexual and gender minority (SGM) people (ie, people whose sexual orientation is not heterosexual or whose gender identity varies from that which is traditionally associated with their sex assigned at birth, respectively) are particularly at risk of both trauma and poor mental health outcomes. Unique mental health disparities observed among this population [5] include high rates of depression [6,7], anxiety [8], and posttraumatic stress disorder (PTSD) [4,9]. These existing disparities in mental health outcomes may contribute to increased vulnerability to COVID-19–related stress among SGM people, resulting in worse mental health outcomes.

Compared to the general US population, SGM people may experience a higher stress burden related to COVID-19 due to pre-existing complex social and structural vulnerability. For example, SGM people are vulnerable to economic instability, such as higher rates of unemployment and poverty when compared to the general population [10,11]. This economic instability has been intensified among SGM people during the COVID-19 pandemic [12], as demonstrated by high rates of unemployment or reduced employment (eg, decreased hours) [13,14], increased likelihood of having trouble paying for housing expenses, and reporting overall financial hardship [14]. These conditions prompted the Centers for Disease Control and Prevention to caution about the risk for disproportionate effects from the COVID-19 pandemic among SGM people [15]. Initial research findings examining the mental health of SGM people during the COVID-19 pandemic show greater symptoms of anxiety and depression reported by those who had *no* symptoms before the emergence of COVID-19 [16]. However, the effects of COVID-19 on SGM people when compared to the general population have yet to be reported and remain an obstacle due to a lack of standardized data collection regarding sexual orientation and gender identity [17,18].

Increased exposure to stressors, like COVID-19, drives some individuals to engage with news and online information resources [19,20]. In a recent report, 74% of SGM individuals reported increased attentiveness to the news in response to COVID-19, compared to 68% of the general population; 60% of SGM participants indicated that they have "conducted their own research on the virus" compared to 45% of the general US population [14]. Increased engagement with COVID-19–related news may affect mental health outcomes by increasing exposure to traumatizing information or experiences. For example, those exposed to news during the COVID-19 pandemic experienced greater anxiety in relation to news exposure [21].

Public health experts have described the need to study COVID-19's impact on the health of marginalized populations including SGM people [22,23]. Therefore, the purpose of this study was to investigate the relationship between COVID-19 news exposure (ie, time spent accessing COVID-19–related news resources) and symptoms of anxiety and PTSD among SGM individuals. We hypothesized that greater COVID-19 news exposure would be associated with greater symptoms of anxiety and, separately, that COVID-19 news exposure would be associated with greater symptoms of PTSD.

Methods

Participants and Procedures

Data were collected from the Coronavirus Impact Survey within The PRIDE Study, a longitudinal cohort study of SGM adults in the United States [24]. Eligible participants for The PRIDE Study meet the following inclusion criteria: identify as lesbian, gay, bisexual, transgender, queer, or another sexual or gender minority; are 18 years or older; reside in the United States or its territories; and are able to read and understand English. Participants are consented and enrolled through The PRIDE Study digital research platform. Participants in The PRIDE Study were recruited through multiple methods including through PRIDEnet Community Partners consisting of health, community, and other SGM-serving organizations within the United States; online through direct recruitment and advertising on social media and other venues; and in person at lesbian, gay, bisexual, transgender, queer community events. Further details about The PRIDE Study can be found elsewhere [24,25]. Data for the Coronavirus Impact Survey were collected from The PRIDE Study participants during the window of March 23 to August 2, 2020. Demographic items were merged from previous participant data within The PRIDE Study (eg, Annual Questionnaires).

Ethics Approval

This study was approved by the institutional review boards of Stanford University (IRB-63400) and the University of California, San Francisco (IRB 18-26982).

Measures

Demographics

Demographics measured included age, race/ethnicity, gender identity, sexual orientation, and the highest level of education completed. Participants could endorse all races or ethnicities

that applied to them with a select-all-that-apply variable (ie, American Indian or Alaskan Native; Asian; Black, African American, or African; Hispanic, Latino, or Spanish; Middle Eastern or North African; Native Hawaiian or other Pacific Islander; White; and "none of these categories fully describes me"). Gender was measured by mutually exclusive categories in which participants self-selected the term that was most closely aligned with their gender identity (ie, cisgender woman, cisgender man, nonbinary, transgender man, transgender woman, or another gender identity). Sexual orientation was measured using mutually exclusive categories in which the participant self-selected the term that was most closely aligned with their sexual orientation (ie, asexual/demi/gray-ace, bi/pansexual, gay/lesbian, queer, straight/heterosexual, or another sexual orientation). Participants were included if they completed the Coronavirus Impact Survey items (ie, news exposure variable, the Generalized Anxiety Disorder 7 [GAD7], and the Impact of Events Scale-Revised [IES-R] scale; N=3079).

Symptoms of Anxiety

The GAD7 was developed to measure general anxiety disorder symptom severity [26]. Each of the seven items are measured on a four-point Likert-type scale where 0 indicates "not at all" and 3 indicates "nearly every day" regarding symptoms experienced during the past 2 weeks. The items are then summed and provide a range from 0 to 21 (α=.92). Diagnostic cutoff scores were applied to create an ordinal variable for our analyses (<5=no diagnosis of anxiety, 5-9=mild symptoms of anxiety, 10-14=moderate symptoms of anxiety, >14=severe symptoms of anxiety) [26].

Symptoms of Posttraumatic Stress

The IES-R was developed to measure PTSD symptom severity [27]. The IES-R is a self-report scale where participants indicated whether they experienced each item in the past 7 days within the context of COVID-19 experiences, defined as "hearing news about the virus, hearing about the experiences of others, having your own experience with symptoms, caregiving for someone with symptoms, or other experience related to the novel coronavirus." Participants could respond to each of the 22 items using a Likert-type scale where 0 indicated "not at all" and 4 indicated "extremely" (α=.93). These items were summed and were dichotomized based on the diagnostic cutoff values where scores greater than 22 indicate presence of PTSD [27].

COVID-19 News Exposure

Participants were asked "How many hours a day do you watch or read the news for information about the novel coronavirus?" and provided a free-text box to report their estimation of time spent (in hours) engaging with COVID-19 news. Participants who answered fewer than 0 hours or greater than 24 hours were dropped from the final analysis (n=6). The variable was recoded as a four-level ordinal variable: less than 1 hour, 1 to less than 2 hours, 2 to 3 hours, and greater than 3 hours [21].

Analysis

Descriptive statistics examined demographic variables within the total sample. The distributions of all variables were examined for outliers and missing data, which were dropped from the analyses (n=28). An ordinal logistic regression was used to evaluate the direct effects of news exposure with the GAD7 ordinal categories while covarying race/ethnicity, age, education, sexual orientation, and gender identity in the first model. In the second model, a logistic regression was used to evaluate the direct effects of news exposure with the IES-R dichotomous outcome (presence or absence of symptoms) while covarying race/ethnicity, age, education, sexual orientation, and gender identity. All analyses were run using STATA 15 (Statacorp) [28]. Standardized and unstandardized regression coefficients were compared with the alpha set at $P<.05$ (2-tailed).

Results

Sample Characteristics

Our sample included a total of 3079 SGM participants with a median age of 32.3 years (IQR 25.9-44.5 years; Table 1). Cisgender men comprised 27.8% (n=782) of our sample, 34.3% (n=965) were cisgender women, 18.5% (n=520) were nonbinary, 11.4% (n=322) were transgender men, 4.9% (n=965) were transgender women, and 3.2% (n=90) reported that their gender was not listed. Among the sample, 70.3% (n=2165) described their race or ethnicity as only White, 4.4% (*n*=135) described themselves as Hispanic/Latino/a, 3.6% (n=112) as Asian, 2.9% (n=89) as Black, and the remaining sample as additional races or ethnicities. A total of 24.4% (n=751) were multiracial. Our sample was highly educated: 42% (n=1292) indicated that they completed a graduate degree and 35% (n=1078) completed a 2- or 4-year college degree.

Table 1. Characteristics of The PRIDE Study's Coronavirus Impact Survey (March 23 to August 2, 2020) sample (N=3079).

Variable	Value
Age (years), mean (SD)	36.7 (14.3)
Race/ethnicity[a], n (%)	
American Indian/Alaska Native	75 (2.44)
Asian	112 (3.64)
Black/African American/African	89 (2.89)
Latino/a/Hispanic	135 (4.38)
Middle Eastern/North African	27 (0.88)
Multiracial	752 (24.42)
Native Hawaiian/Asian Pacific Islander	6 (0.19)
White	2408 (78.21)
A racial/ethnic identity not listed	29 (0.94)
Gender identity, n (%)	
Cisgender man	782 (27.8)
Cisgender woman	965 (34.3)
Nonbinary	520 (18.5)
Transgender man	322 (11.4)
Transgender woman	137 (4.9)
A gender identity not listed	90 (3.2)
Sexual orientation, n (%)	
Asexual/demisexual/gray-ace	262 (8.5)
Bisexual/pansexual	865 (28.0)
Gay/lesbian	1580 (51.4)
Queer	344 (11.2)
Straight/heterosexual	21 (0.7)
Another sexual orientation	7 (0.2)
Education level, n (%)	
Less than high school	18 (0.6)
High school graduate, GED[b], or some college	691 (22.4)
College degree (2 or 4 years)	1078 (34.9)
Graduate degree	1292 (42.0)

[a]Participants could select all options that applied.

[b]GED: General Educational Development.

COVID-19 News Exposure and Anxiety Symptoms

Within our sample, 42% (n=1293) had mild anxiety symptoms, 34% (n=1047) had moderate anxiety symptoms, and 9% (n=277) had severe anxiety symptoms. The median GAD7 score was 8 (IQR 4-14). Each unit increase in COVID-19–related news exposure was associated with greater anxiety symptoms (odds ratio 1.77, 95% CI 1.63-1.93; $P<.001$; ie, GAD7; see Table 2 for full results).

Multimedia Appendix 1, Table S1 reflects the results of all variables of interest as well as indicator variables that were covaried. Figure 1 shows the relationship between COVID-19–related news exposure and anxiety symptoms for each of the different news categories.

Table 2. Results from ordinal logistic regression (GAD7) and logistic regression (IES-R) models that evaluated the relationship between COVID-19 news exposure and symptoms of anxiety (GAD7) and posttraumatic stress disorder (IES-R).

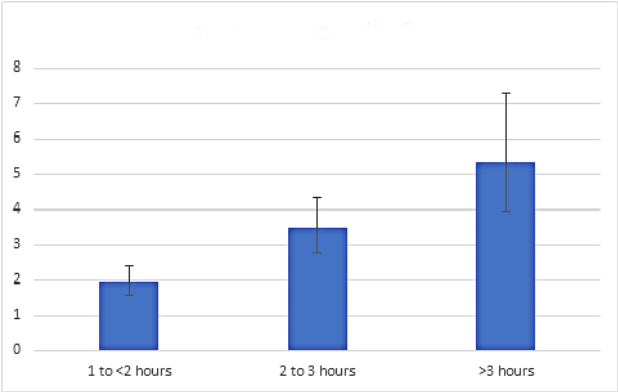
Model[a]	Odds ratio (SE)	95% CI	*z*	*P* value
COVID-19 news exposure and GAD7[b]	1.77 (0.08)	1.63-1.93	12.92	<.001
COVID-19 news exposure and IES-R[c]	1.93 (0.10)	1.74-2.14	12.48	<.001

[a]All models included the following covariates: age, education, sexual orientation, gender identity, and race/ethnicity.

[b]GAD7: Generalized Anxiety Disorder-7.

[c]IES-R: Impact of Events Scale-Revised.

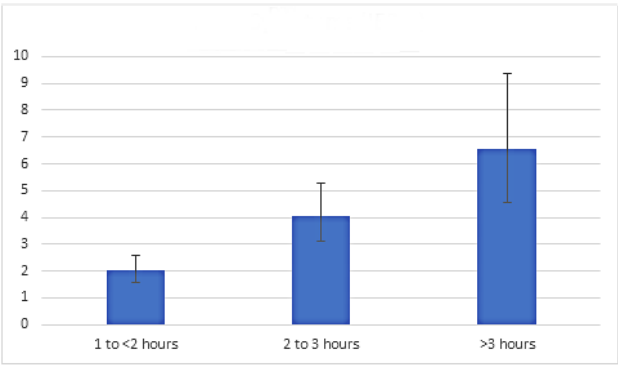
Figure 1. Odds of greater anxiety symptoms (GAD) with each level of COVID-19–related news exposure. GAD7: Generalized Anxiety Disorder-7.



COVID-19 News Exposure and PTSD

A total of 57% (n=1755) of our sample met the threshold for presence of PTSD (score >22). The median of the IES-R score was 25 (IQR 15-37). Each unit increase in COVID-19–related news exposure was associated with 1.93 greater odds (95% CI 1.74-2.14; *P*<.001) of PTSD (ie, IES-R; see Table 2 for full results). Multimedia Appendix 1, Table S2 reflects the results of all variables of interest as well as indicator variables that were covaried. Figure 2 shows the relationship between COVID-19–related news exposure and PTSD for each of the different news conditions.

Figure 2. Odds of greater PTSD symptoms (IES-R) with each level of COVID-19–related news exposure. IES-R: Impact of Events Scale-Revised; PTSD: posttraumatic stress disorder.



Discussion

Principal Findings

This study suggests that COVID-19–related news exposure is positively associated with greater anxiety and PTSD symptom severity among SGM people, consistent with previous findings within the general population [29-31]. Previous studies among the general population examined the impact of COVID-19–related media consumption on mental health, showing increased symptoms of anxiety and depression (particularly among those who were not symptomatic prior to the pandemic) [21,32,33]. This study extends this work to SGM populations, showing that COVID-19–related news exposure is substantially associated with greater symptoms of anxiety and PTSD.

It is important to note that these findings are correlational and, therefore, cannot establish directional causality. Nonetheless our study and others have found a correlation between COVID-19–related news exposure and mental health outcomes. For example, a recent study found that higher levels of anxiety at the start of the US pandemic were associated with greater time spent online [34], a frequent source of news, and time on

smartphones accessing news sources [35]. A longitudinal study of participants with previously diagnosed PTSD reported greater news exposure, which was associated with greater symptoms of PTSD [36]. One explanation for our findings is that people with high anxiety or PTSD symptoms before the pandemic may be more likely to engage with COVID-19–related news, possibly to seek reassurance and cope with uncertainty. SGM individuals in our sample who engaged more with COVID-19–related news media (ie, as a reassurance-seeking behavior) may have higher baseline levels of anxiety or PTSD. Excessive reassurance-seeking behaviors prospectively predict symptoms of anxiety disorders, even when controlling for trait anxiety and intolerance of uncertainty [37]. Therefore, it is also possible that, even if news exposure was higher among those with greater trait anxiety, engagement with news may still have had an amplifying effect on anxiety symptoms. Longitudinal data from the pandemic where baseline anxiety is collected in addition to measures of news engagement could disentangle this relationship; however, a lack of systematic sexual orientation and gender identity measurement in large public data sets creates a significant barrier [38,39]. We do know that in a longitudinal study with a convenience sample of SGM people, worsening mental health symptoms such as depression, suicidality, and anxiety from April 2020, the start of US lockdown in some states, and at a 5-month follow up were observed [40]. Another study found that SGM people had worse depressive symptoms during the pandemic when compared to their pre–COVID-19 baseline depressive symptoms [16]. Within our sample, 85% of participants had at least mild anxiety symptoms at the time of data collection, whereas symptoms of anxiety in the general population between August 2020 to February 2021 were estimated to be 41.5% [41].

Social support is associated with improved mental health, while feelings of loneliness are associated with worse mental health symptoms [42]. COVID-19 has reduced in-person gatherings where people may seek engagement and support from others [43], leading to greater social media and online interaction. It also increases the potential for one to be exposed to COVID-19–related news [44]. Social media has been a source of misinformation throughout the COVID-19 pandemic [45,46], which may contribute to increased symptoms of anxiety. During the COVID-19 pandemic, SGM people reported lower social support compared to their cisgender heterosexual peers [13]. Virtual engagement may be sought as a substitute for in-person gatherings; however, social media use was positively correlated with symptoms of anxiety [47] and PTSD [48]. Therefore, changes in social support may offer one possible explanation for the deleterious impacts of COVID-19–related news exposure on mental health—particularly among already-marginalized communities such as SGM people.

Implications of This Study

COVID-19 poses considerable risk to physical health, but the associated mental health risks are still emerging. Further evaluation of news exposure among populations with known mental health disparities is needed to address potential areas of increased psychological risk among individuals exhibiting symptoms, or worsening symptoms, of anxiety or PTSD. Investigation into the directionality of the relationship between COVID-19–related news exposure, anxiety, and PTSD symptoms is needed to identify possible mechanisms as well as opportunities for targeted interventions.

Strengths, Limitations, and Future Directions

COVID-19 has presented us with unprecedented challenges globally, ranging from impacts to physical health to broad-reaching economic impacts. Our study expands on the emerging knowledge surrounding COVID-19 and its relationship to the mental health of SGM people. Our study illuminates how even indirect exposure to COVID-19 news was associated with mental health outcomes. Further, it points to the potential impacts on SGM people, a population for whom mental health disparities have been consistently observed. This offers opportunities for intervention where either news access can be altered or interventions to support mental health can be introduced. Further, we form these inferences based on a large sample of SGM people, who are frequently absent from analyses on traumatic events and associated mental health outcomes. However, there are several limitations to this study. This sample was obtained by convenience sampling, also limiting its representation of the broader SGM population and comparison to the general population. For example, our sample was highly educated with 42% (n=1292) of our sample reporting that they have a graduate degree. This varies from what is known about the education level of the broader SGM population, of whom 13% of SGM are estimated to have a graduate degree [49,50]. Self-report measurement may have resulted in social desirability bias with responses that are not representative of objective events. Our measure of news exposure did not differentiate between types of news; therefore, we were not able to determine how much of this time was spent on social media, direct from news agencies, or offline news sources (eg, traditional print media) that could impact the findings [30]. These sources of news may be related to our findings although participants may not include them in their time estimation based on whether or not participants perceive the source as news (eg, time spent on social media). Further, we cannot be sure whether the number of hours reported by participants was accurate; this is partially a function of the use of a free text entry for time as opposed to other methods for participant responses (eg, response choices provided in ranges). This results in some participants being dropped for responding with a number of hours greater than the possible 24 or less than 0 (n=6); however, this is a small number of the overall sample and unlikely to have impacted our findings. A certain level of bias is expected as to the meaning of exact, yet unlikely numbers (eg, 20 hours) are lost. Underlying health conditions that increase risk of COVID-19 complications could impact our findings as fear or concern of one's health could increase anxiety, symptoms, or PTSD. Another important limitation to acknowledge is that while our sample includes diverse lived experiences (eg, sexual orientation, gender identity, race, and ethnicity), we do not address the way in which these social positions intersect and how that power differential may affect mental health outcomes and the way COVID-19–related news may be accessed and internalized. As recent reports have shown, the effects of COVID-19 have been disproportionate among people of color and certain SGM groups [13,51]. Future

work in this area should involve mixed methods research so that qualitative data can contextualize these experiences [52].

Future work is needed in several areas. Analysis that differentiates the types of news consumption and whether there are differences in their relationship with anxiety and PTSD would help to identify more specific recommendations for protective mental health behaviors. Further, considering the important role of social support and how social media is both a source of social support but also a common news source necessitates further work. Along these lines, future studies should examine the relationships between problematic smartphone use and mental health symptoms—particularly within marginalized populations. A recent report indicated that the association between reassurance-seeking behaviors and problematic smartphone use may be a key mechanism in the maintenance of anxiety and depression [37,53]. Additionally, examination of baseline anxiety and PTSD symptoms would help determine if some groups are more at risk of worsening mental health outcomes than others.

Conclusions

This study expands the available evidence supporting an association between news exposure and symptoms of anxiety and PTSD during the COVID-19 pandemic by identifying this relationship among a sample of SGM people. Opportunities exist for clinicians working with individuals to identify possible coping strategies, limit news and social media consumption, refer to safe means of social support, or incorporate psychoeducation about media consumption to reduce the accompanying stress caused by news exposure. As causality cannot be inferred from our findings, evaluation of systems of mental health access for existing anxiety and PTSD symptoms are necessary to ensure continuity of care. Further research exploring the effectiveness of online or social media community-based support and its role as a potential moderator between news stressor exposure and mental health symptoms is needed.

Conflicts of Interest

MRL has consulted for Hims Inc (2019 to present) and Folx Inc (2020). JO-M has consulted for Sage Therapeutics (May 2017) in a 1-day advisory board, Ibis Reproductive Health (a non–for-profit research group March 2017 to May 2018), Folx Inc (2020 to present), and Hims Inc (2019 to present). None of these roles present a conflict of interest with this work as described here. No other authors have conflicts of interest to disclose.

Multimedia Appendix 1
Supplementary tables.
[DOCX File , 20 KB - publichealth_v8i5e34710_app1.docx]

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Abbreviations

GAD7: Generalized Anxiety Disorder 7
IES-R: Impact of Events Scale-Revised
PTSD: posttraumatic stress disorder
SGM: sexual and gender minority

Edited by T Sanchez, A Mavragani; submitted 04.11.21; peer-reviewed by S Moore, N Nekliudov; comments to author 22.01.22; revised version received 14.03.22; accepted 27.04.22; published 30.05.22.

Please cite as:
Clark KD, Lunn MR, Sherman ADF, Bosley HG, Lubensky ME, Obedin-Maliver J, Dastur Z, Flentje A
COVID-19 News and Its Association With the Mental Health of Sexual and Gender Minority Adults: Cross-sectional Study
JMIR Public Health Surveill 2022;8(5):e34710
URL: https://publichealth.jmir.org/2022/5/e34710
doi:10.2196/34710
PMID:35486805

Original Paper

The Effect of a Web-Based Cervical Cancer Survivor's Story on Parents' Behavior and Willingness to Consider Human Papillomavirus Vaccination for Daughters: Randomized Controlled Trial

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Abstract

Background: Providing adequate information to parents who have children eligible for human papillomavirus (HPV) vaccination is essential to overcoming vaccine hesitancy in Japan, where the government recommendation has been suspended. However, prior trials assessing the effect of brief educational tools have shown only limited effects on increasing the willingness of parents to vaccinate their daughters.

Objective: The aim of this trial is to assess the effect of a cervical cancer survivor's story on the willingness of parents to get HPV vaccination for their daughters.

Methods: In this double-blinded, randomized controlled trial (RCT) implemented online, we enrolled 2175 participants aged 30-59 years in March 2020 via a webpage and provided them with a questionnaire related to the following aspects: awareness regarding HPV infection and HPV vaccination, and willingness for HPV vaccination. Participants were randomly assigned (1:1) to see a short film on a cervical cancer survivor or nothing, stratified by sex (male vs female) and willingness for HPV vaccination prior to randomization (yes vs no). The primary endpoint was the rate of parents who agreed for HPV vaccination for their daughters. The secondary endpoint was the rate of parents who agreed for HPV vaccination for their daughters and the HPV vaccination rate at 3 months. The risk ratio (RR) was used to assess the interventional effect.

Results: Of 2175 participants, 1266 (58.2%) were men and 909 (41.8%) were women. A total of 191 (8.8%) participants were willing to consider HPV vaccination prior to randomization. Only 339 (15.6%) participants were aware of the benefits of HPV vaccination. In contrast, 562 (25.8%) participants were aware of the adverse events of HPV vaccination. Although only 476 (21.9%) of the respondents displayed a willingness to vaccinate their daughters for HPV, there were 7.5% more respondents in the intervention group with this willingness immediately after watching the short film (RR 1.41, 95% CI 1.20-1.66). In a subanalysis, the willingness in males to vaccinate daughters was significantly higher in the intervention group (RR 1.50, 95% CI 1.25-1.81); however, such a difference was not observed among females (RR 1.21, 95% CI 0.88-1.66). In the follow-up survey at 3 months, 1807 (83.1%) participants responded. Of these, 149 (8.2%) responded that they had had their daughters receive vaccination during

the 3 months, even though we could not see the effect of the intervention: 77 (7.9%) in the intervention group and 72 (8.7%) in the control group.

Conclusions: A cervical cancer survivor's story increases immediate willingness to consider HPV vaccination, but the effect does not last for 3 months. Furthermore, this narrative approach to parents does not increase vaccination rates in children eligible for HPV vaccination.

Trial Registration: UMIN Clinical Trials Registry UMIN000039273; https://tinyurl.com/bdzjp4yf

(JMIR Public Health Surveill 2022;8(5):e34715) doi:10.2196/34715

KEYWORDS

human papilloma virus vaccination; vaccination; vaccine; vaccine hesitancy; cancer survivor; narrative story; web based; randomized controlled trial; RCT; HPV; human papilloma virus; virus; hesitancy; cancer; willingness; behavior; parent

Introduction

Background

To eliminate cervical cancer, the World Health Organization (WHO) set a future goal that 90% of girls worldwide would be vaccinated for the human papillomavirus (HPV) by the age of 15 years, by the year 2030 [1]. In fact, a number of countries with high vaccination coverage have already achieved an immunization rate of 90% or higher in this target population [1]. In Japan, due to the suspension of proactive government recommendations since 2013, most people have been hesitant to get the HPV vaccination [2-4]. As a result, the vaccination rate of the target population has been estimated to be below 1% [5,6]. The incidence of HPV vaccination has been changing in recent years, with quadruple the number of HPV vaccination doses supplied in the first 3 months of 2021 compared to the same period 4 years ago [7]. Although the trend in the HPV vaccination rate seems to have been increasing in Japan, it is still important to find better ways to promote HPV vaccination—not only in Japan but also in other countries that have not accomplished the 90% vaccination goal. Furthermore, given that the nationwide proactive recommendation of HPV vaccination for girls aged 11-16 years resumed in April 2022 in Japan [8], it should be necessary to find effective ways to promote the vaccination rate.

In many countries, vaccine hesitancy is a crucial public health issue that governments continue to struggle with [9,10]. Vaccine hesitancy is usually based on perceived safety concerns associated with receiving the vaccines. In Japan, the repeated broadcast of adverse events, which are regarded as functional disorders, has discouraged many individuals from getting their daughters vaccinated [2,5,11]. In the United States, the HPV vaccination rate has risen to around 50% among vaccine-eligible adolescents, with vaccine hesitancy as a main source of the ongoing problem [12]. It has been demonstrated that the most frequent reason for hesitancy stems from people's concerns regarding safety and adverse effects [12]. As social media continues to become a major source for public health information, it has become increasingly difficult to filter out wrong and inaccurate information.

Providing brief scientific information regarding HPV vaccination through websites has been shown to be an effective way of disseminating the importance of vaccination [4], with the potential to change people's sentiments toward vaccination for their children. Our previous randomized controlled trial (RCT) showed that the brief education material significantly increased the number of people willing to consider HPV vaccination for their children; however, the effect was seen only in the men's cohort [4]. The reason for this was thought to be that more negative attitudes toward HPV vaccination existed among women compared to men, which could then affect women's attitudes. The difference in the effectiveness of educational interventions between sexes was a notable outcome. Therefore, there is a need to assess whether other educational approaches can change women's willingness to consider HPV vaccination for their daughters.

Goal of the Study

The aim of this study is to assess whether a cervical cancer survivor's story could change parents' minds about HPV vaccination. We plan to build up the theory of a better way to change people's minds and behaviors to overcome vaccine hesitancy. Little is known about evidence-based interventions promoting the prevention of HPV, so this trial could provide a novel insight into digital educational methods for promoting disease prevention through vaccination to the general public.

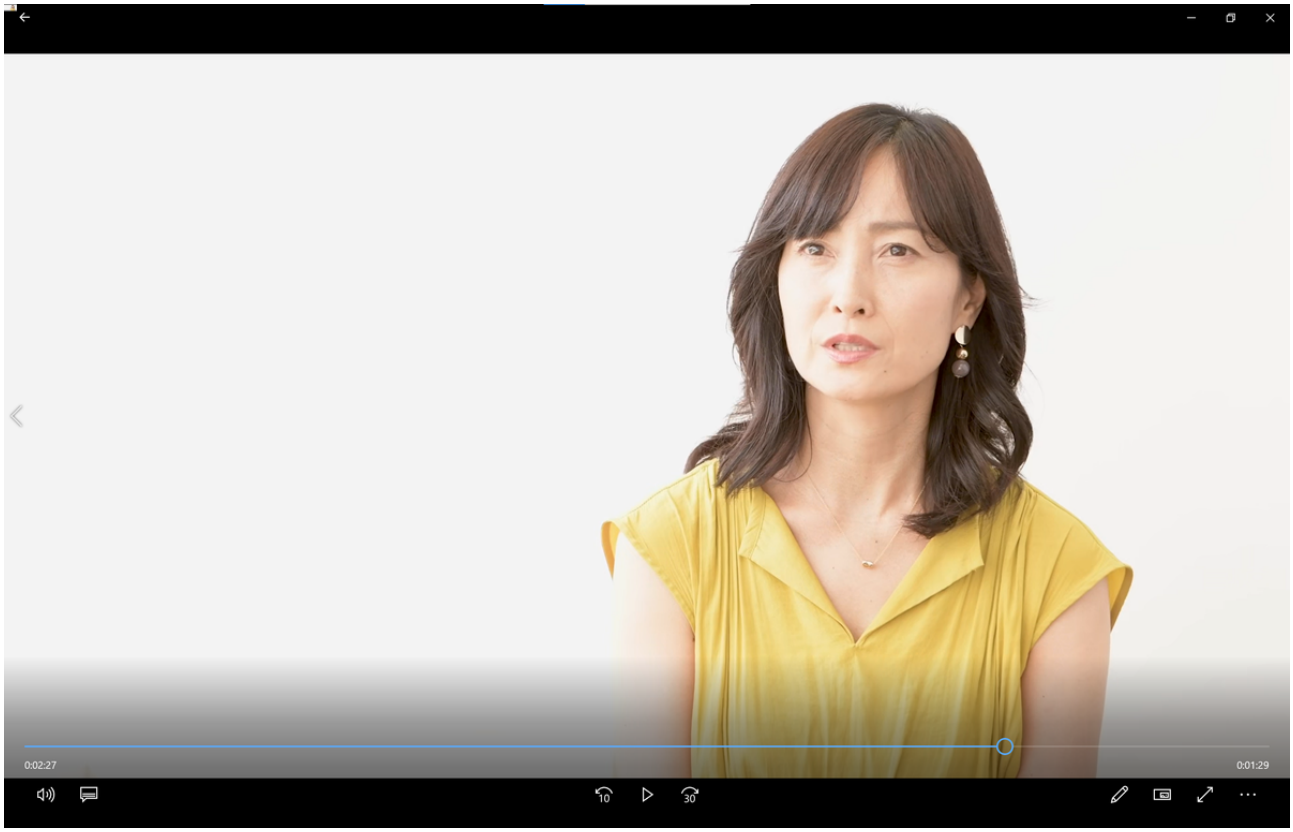
Methods

Study Design and Participants

A total of 2175 participants were recruited in March 2020 via a webpage dedicated to this trial. These were registered members of the research panel owned by NTT Com Online Marketing Solutions Corporation (Tokyo, Japan) and used for consumer satisfaction, marketing, and academic research [13]. More than 53,000 people in Japan have registered on this research panel based on their applications [14]. The eligible participants were aged between 30 and 59 years and had at least 1 daughter between sixth-grade elementary (11 and 12 years of age) and third-grade high school (17 and 18 years of age). The parents who had their daughters vaccinated against HPV were not allowed to join this study. The first survey was conducted on March 19-30, 2020, while the 3-month follow-up survey was conducted on June 26-July 6, 2020. Participants were recruited until the target sample size was reached after considering a dropout rate of approximately 30%-40% for the 3-month follow-up. Each participant responded to an identical willingness questionnaire. However, only participants in the intervention group watched a short film on a cancer survivor (as displayed in Figure 1 and Multimedia Appendix 1) prior to taking the

survey; participants who were assigned to the control group could choose to watch the short film after all questionnaires, including a follow-up questionnaire, were completed. The full process of this trial was implemented online. The primary endpoint was the rate of parents who have willingness to vaccinate their daughters against HPV. The secondary endpoint was the HPV vaccination rate at a 3-month follow-up and awareness regarding the prevention of cervical cancer.

Figure 1. Short film on Yoko Matsuda, a cervical cancer survivor.



Information Prior to Randomization

Basic information about the benefits and adverse effects of HPV vaccination was impartially provided to all participants on a 2-slide handout prior to randomization, with the aim of sharing scientific nonnarrative information. On the first slide, the perceptions of the Japanese Ministry of Health, Labour and Welfare (MHLW) regarding adverse effects after receiving HPV vaccination was provided [3]. The following 3 points were shared:

- "Most vaccinated people experience pain and swelling on the arm where the shot is given."
- "Severe adverse effects, such as unspecified body pain and sudden loss of strength, are rarely reported and are thought to be due to a functional disorder with unknown specific cause."
- "Healthcare providers can access information on the website of MHLW regarding individuals who received the shot and developed continuous adverse effects."

On the second slide, 3 points regarding cervical cancer and HPV vaccination were provided:

- "In Japan, approximately 10,000 people a year are diagnosed with cervical cancer, while about 3,000 people die annually."
- "Many developed countries recommend HPV vaccination in adolescence as a national prevention program."
- "The HPV vaccine, which the World Health Organization (WHO) reports to be safe, can lead to the prevention of 70% of cervical cancers and other HPV-related cancers (e.g., oropharyngeal cancer, oral cancer, vulval cancer, and anal cancer)."

Intervention

In this study, a 4-minute-long short film was used as the intervention. In this film, a cervical cancer survivor who had undergone radical hysterectomy with bilateral salpingo-oophorectomy and pelvic lymphadenectomy talked about her experience—from the beginning of the diagnosis to the sequelae of first-line therapy. She was a singer, songwriter, and actress in Japan. Seven messages were inserted as subtitles throughout her talk. The added subtitles were as follows:

- "She was diagnosed with cervical cancer at 31 years old."
- "In Japan, approximately 10,000 people a year are diagnosed with cervical cancer and about 3,000 people die annually."
- "Undergoing surgery wasn't the end of suffering."
- "The burden of cervical cancer was greater than expected and is relatively seen in younger ages."
- "Cervical cancer can be prevented by HPV vaccination and Pap smears."
- "A lot of children have lost their chance to prevent cervical cancer in Japan."
- "Why don't we take action for our children's future?"

We did not use any psychosocial theoretical frameworks to manipulate the participants' mindset or behavior. The short film was produced by Ideas and Effects, Ltd., and supervised by the first author (YS) and the last author (EM), for use in educational campaigns.

Randomization

Participants were randomly assigned (1:1) to each group using a web-based randomization procedure. The randomization with minimization was stratified by sex (female/mother and male/father) and willingness toward HPV vaccination prior to randomization (yes or no). Randomization was performed using the web research system of the NTT Data Institute of Management Consulting, Inc. The participants and investigators were double-blinded to the study distribution. Once the upper limit of each stratum was reached, new participants could not be added to the web system. This ensured a uniform distribution of stratification factors. In the intervention group, we provided the narrative short film prior to answering questions related to the willingness to prevent HPV, following consent for the online study.

Questionnaire

The participant demographics included sex (male/father and female/mother), age group (thirties, forties, fifties), willingness to use HPV vaccination prior to randomization (yes or no), marital status, number of children, education, household income, and tobacco use. The individual background information already existed in the research panel database prior to our study, except for the level of willingness to use the HPV vaccine. Information regarding the HPV vaccination history of respondents and a previous Papanicolaou (Pap) test for female participants was also collected for this study. In total, data of marital status, household income, and education level were collected from 1550 participants.

The participants completed a 7-item awareness questionnaire to determine HPV awareness as background information. They were instructed to answer either "Yes, I have heard of it" or "I haven't heard of it" for each question. We defined those who answered "I haven't heard of it" for all questions as the no-awareness group, whereas those who answered "Yes, I have heard of it" for at least 1 question were defined as the normal-awareness group.

The awareness questions (AQs) were as follows:

- AQ 1. It is possible to detect both cancer and precancerous lesions through cervical cancer screening.
- AQ 2. Sexual experience is associated with HPV infection.
- AQ 3. Cervical cancer screening is necessary for women even after vaccination.
- AQ 4. I have heard of the benefits of the HPV vaccine.
- AQ 5. I have heard of the adverse events associated with the HPV vaccine.
- AQ 6. HPV can cause anal cancer and oropharyngeal cancer in males, other than cervical cancer in women.
- AQ 7. HPV vaccination is included in the national immunization program (routine vaccination schedule) and publicly funded for children from sixth-grade elementary school students to first-grade high school students (12-16 years of age). However, the MHLW suspended a proactive recommendation for HPV vaccination due to the suspicious relationship between the vaccine and unspecific chronic pain.

The willingness questions (WQs) after the intervention were as follows:

- WQ 1. Would you consider getting your daughter vaccinated against HPV? (Yes/No/I'm not sure)
- WQ 2. Would you consider undergoing a Pap smear? If male, would you want your family member or partner to undergo a smear test? (Yes/No/I'm not sure)
- WQ 3. Do you think the HPV vaccination program should be actively recommended by the government? (Yes/No/I'm not sure)
- WQ 4. Do you plan to inform family members, friends, or others about cervical cancer prevention and screening (through Instagram, Facebook, LINE, Twitter, TikTok, etc)? (Yes/No/I'm not sure)
- WQ 5. Are you going to make an appointment for HPV vaccination for your daughter as soon as possible? (Yes/No)

The follow-up questions (FQs) after 3 months were as follows:

- FQ 1. Has your daughter been vaccinated against HPV after the first-round questionnaire? (Yes/Only an appointment/No)

Participants who answered "No" were subsequently tasked to answer the following items:

- FQ 1'. Would you consider getting your daughter vaccinated against HPV? (Yes/No/I'm not sure)

FQs 2-5 were identical to WQs 2-5.

Participants who answered "Yes" or "Only an appointment" in FQ 1 were tasked to answered only FQs 2-4.

Statistical Analysis

The chi-square (χ^2) test, Student *t* test, and risk ratio (RR) were used for statistical analyses of background characteristics, baseline knowledge level, and primary/secondary outcomes. The background characteristics and baseline knowledge between both groups were not significantly different, so we did not adjust the present variables. All statistical analyses were performed using SPSS Statistics version 28 (IBM). The sample size was calculated as 80% power to detect a 10% effect in the intervention group (increased from 25% in the control group to 35% in the intervention group) with a 2-sided *P* value of .05. Statistical significance was set as less than .05. The hypothetical baseline willingness rate was determined based on our previous studies; 23.6% of participants who were provided with information regarding the benefit of HPV vaccination considered getting their daughter vaccinated [4]. The sample size was calculated as 784 (392 vs 392), and the effect of the intervention estimated a 10% increase after 3 months. We set the target number of participants recruited at 3 times the calculated sample size because the web-research company estimated the follow-up rate to be 30%-40% at 3 months after the initial survey.

Ethical Considerations and Funding

The trial protocol was approved by the institutional research ethics committee of the Yokohama City University School of Medicine (B200109003). The trial registration number was UMIN000039273. We received research funding from the Japan Agency for Medical Research and Development (Grant 19ck0106369h0003). The website construction and web-based survey were outsourced to the NTT Data Institute of Management Consulting, Inc. The participants received JPY 25 (~US $0.23) and an additional JPY 5 (~US $0.045) if they joined the follow-up survey.

Results

Analysis of Participant Demographics

A total of 2175 participants were recruited. Stratifying factors, such as sex and willingness to undergo HPV vaccination prior to randomization, were evenly allocated (Multimedia Appendix 1). The retention rates at the 3-month follow up survey were 89.6% (976/1089) in the intervention group and 76.5% (831/1086) in the control group. The following variables did not demonstrate significant differences between the intervention and control groups: age group, marital status, number of children, number of daughters, education, household income, and tobacco use (Table 1).

Table 1. Characteristics and baseline knowledge level of the participants recruited via a website before intervention (March 19-30, 2020).

Characteristics and baseline knowledge	Total (N=2175)	Intervention (N=1089)	Control (N=1086)	*P* value[a]
Sex, n (%)				
Male (father)	1266 (58.2)	633 (58.1)	633 (58.3)	N/A[b]
Female (mother)	909 (41.8)	456 (41.9)	453 (41.7)	.94
Age (years), n (%)				
30-39	138 (6.3)	76 (7.0)	62 (5.7)	N/A
40-49	1306 (60.0)	629 (57.8)	677 (62.3)	N/A
50-59	731 (33.6)	384 (35.3)	347 (32.0)	.08
Marital status, n (%)[c]				
Married	1439 (92.8)	734 (93.1)	705 (92.5)	N/A
Unmarried	111 (7.2)	54 (6.9)	57 (7.5)	.31
Number of children, n (%)				
1	899 (41.3)	457 (42.0)	442 (40.7)	N/A
2	1048 (48.2)	521 (47.8)	527 (48.5)	N/A
3	209 (9.6)	104 (9.6)	105 (9.7)	N/A
4	19 (0.9)	7 (0.6)	12 (1.1)	.82
Number of daughters, n (%)				
1	1651 (75.9)	818 (75.1)	833 (76.7)	N/A
2	482 (22.2)	255 (23.4)	227 (20.9)	N/A
3	38 (1.7)	16 (1.5)	22 (2.0)	N/A
4	4 (0.2)	0	4 (0.4)	.15
Education, n (%)[c]				
Less than high school graduate	21 (1.4)	7 (0.9)	14 (1.8)	N/A
High school graduate	355 (22.9)	189 (24.0)	166 (21.8)	N/A
More than high school graduate	1174 (75.7)	592 (75.1)	582 (76.4)	.203
Household income (million JPY/year)[c,d], mean (SD)	7.41 (4.68)	7.50 (5.43)	7.32 (3.74)	.44
Willingness for HPV[e] vaccination before randomization, n (%)				
Yes	191 (8.8)	97 (8.9)	94 (8.7)	N/A
No	1984 (91.2)	992 (91.1)	992 (91.3)	.84
Tobacco use, n (%)				
Smoker	563 (25.9)	285 (26.2)	278 (25.6)	N/A
Nonsmoker	1069 (49.1)	549 (50.4)	520 (47.9)	N/A
Previous smoker	543 (25.0)	255 (23.4)	288 (26.5)	.24
Awareness level from AQs[f] 1-7, n (%)				
No awareness	1017 (46.8)	507 (46.6)	510 (47.0)	N/A
Normal awareness	1158 (53.2)	582 (53.4)	576 (53.0)	.85
AQ 1 (possibility to find both cancer and precancerous lesions through cervical cancer screening), n (%)				
Already known	591 (27.2)	303 (27.8)	288 (26.5)	N/A
Not known	1584 (72.8)	786 (72.2)	798 (73.5)	.49
AQ 2 (association of sexual experience with HPV infection), n (%)				
Already known	834 (38.3)	412 (37.8)	422 (39.6)	N/A
Not known	1341 (61.7)	677 (62.2)	644 (60.4)	.62

Characteristics and baseline knowledge	Total (N=2175)	Intervention (N=1089)	Control (N=1086)	*P* value[a]
AQ 3 (cervical cancer screening necessary for women even after vaccination), n (%)				
Already known	387 (17.8)	188 (17.3)	199 (18.3)	N/A
Not known	1788 (82.2)	901 (82.7)	887 (81.7)	.52
AQ 4 (effectiveness associated with HPV vaccination), n (%)				
Already known	339 (15.6)	164 (15.1)	175 (16.1)	N/A
Not known	1836 (84.4)	925 (84.9)	911 (83.9)	.498
AQ 5 (adverse events associated with HPV vaccination), n (%)				
Already known	562 (25.8)	269 (24.7)	293 (27.0)	N/A
Not known	1613 (74.2)	820 (75.3)	793 (73.0)	.23
AQ 6 (HPV can cause anal cancer and oropharyngeal cancer in males, other than cervical cancer in women), n (%)				
Already known	339 (15.6)	164 (15.1)	175 (16.1)	N/A
Not known	1836 (84.4)	925 (84.9)	911 (83.9)	.498
AQ 7 (national immunization program of HPV vaccine and suspension of the proactive recommendation from the Japanese government), n (%)				
Already known	448 (20.6)	228 (20.9)	220 (20.3)	N/A
Not known	1727 (79.4)	861 (79.1)	866 (79.7)	.696
Last Pap[g] test[h], n (%)				
<2 years	468 (51.5)	235 (51.5)	233 (51.4)	N/A
2-5 years	95 (10.5)	46 (10.1)	49 (10.8)	N/A
>5 years	153 (16.8)	77 (16.9)	76 (16.8)	N/A
Never	179 (19.7)	91 (20.0)	88 (19.4)	N/A
Unknown	14 (1.5)	7 (1.5)	7 (1.5)	.87
HPV vaccination[h], n (%)				
Already vaccinated	11 (1.2)	7 (1.5)	4 (0.9)	N/A
Not yet vaccinated	837 (92.1)	420 (92.1)	417 (92.1)	N/A
Unknown	61 (6.7)	29 (6.4)	32 (7.1)	.81

[a]*P* values were estimated using chi-square and Student *t* tests.

[b]N/A: not applicable.

[c]Only participants who provided background information about marital status, educational level, and household income (n=1550, 71.3%).

[d]JPY 110=US $1 USD.

[e]HPV: human papillomavirus.

[f]AQ: awareness question.

[g]Pap: Papanicolaou.

[h]Only female participants (n=909, 41.8%).

Baseline Awareness of HPV and Prevention of Cervical Cancer

For AQ1 to AQ7 on HPV and HPV awareness, there were no significant differences in the recognition rates across all 7 questions between the intervention and control groups (Table 1). Only 339 (15.6%) parents were aware of the effectiveness of HPV vaccination (AQ4), while 562 (25.8%) were aware of the adverse effects (AQ5). The highest awareness rate was seen in the question about the causal relationship between sexual experience and HPV (AQ2; n=834, 38.3%). Among women, there was no significant difference in the pattern of the Pap test and HPV vaccination between the 2 groups.

Willingness to Vaccinate Daughters and Other Areas of HPV Vaccination Awareness

Only 476 (21.9%) parents displayed a positive attitude toward HPV vaccination for their daughters (WQ 1). Compared to parents in the control group, an additional 7.5% parents responded affirmatively in the intervention group (279/1089 vs 197/1086, 25.6% vs 18.1%; RR 1.41, 95% CI 1.20-1.66); see Table 2. Affirmative attitudes toward other areas, such as undergoing a pap smear (RR 1.14, 95% CI 1.05-1.24), desiring the recommendation from the government (RR 1.36, 95% CI 1.29-1.55), and disseminating HPV vaccination information to

someone by social media (RR 1.41, 95% CI 1.20-1.66), were also higher in the intervention group (Table 2).

Table 2. Comparison of attitudes and willingness toward HPV[a] vaccination for the prevention of cervical cancer after intervention from the web survey between the intervention group and the control group (March 19-30, 2020).

Responses to WQs[b]	Total (N=2175), n (%)	Intervention (N=1089), n (%)	Control (N=1086), n (%)	Yes vs other RR[c] (95% CI)	*P* value[d]
WQ 1. Would you consider getting your daughter vaccinated against HPV?					
Yes	476 (21.9)	279 (25.6)	197 (18.1)	1.41 (1.20-1.66)	<.001
No	500 (23.0)	200 (18.4)	300 (27.6)	N/A[e]	N/A
I'm not sure	1199 (55.1)	610 (56.0)	589 (54.2)	N/A	N/A
WQ 2. Would you consider undergoing a Pap[f] smear? If male, would you want your family member or partner to undergo a smear test?					
Yes	1066 (49.0)	569 (52.2)	497 (45.8)	1.14 (1.05-1.24)	.003
No	357 (16.4)	153 (14.0)	204 (18.8)	N/A	N/A
I'm not sure	752 (34.6)	367 (33.7)	385 (35.5)	N/A	N/A
WQ 3. Do you think the HPV vaccination program should be actively recommended by the government?					
Yes	626 (28.8)	361 (33.1)	265 (24.4)	1.36 (1.29-1.55)	<.001
No	371 (17.1)	156 (14.3)	215 (19.8)	N/A	N/A
I'm not sure	1178 (54.2)	572 (52.5)	606 (55.8)	N/A	N/A
WQ 4. Do you plan to inform family members, friends, or others about cervical cancer prevention and screening (through Instagram, Facebook, LINE, Twitter, TikTok, etc)?					
Yes	481 (22.1)	282 (25.9)	199 (18.3)	1.41 (1.20-1.66)	<.001
No	797 (36.6)	357 (32.8)	440 (40.5)	N/A	N/A
I'm not sure	897 (41.2)	450 (41.3)	447 (41.2)	N/A	N/A
WQ 5. Are you going to make an appointment for HPV vaccination for your daughter as soon as possible?					
Yes	497 (22.9)	298 (27.4)	199 (18.3)	1.49 (1.27-1.75)	<.001
No	1678 (77.1)	791 (72.6)	887 (81.7)	N/A	N/A

[a]HPV: human papillomavirus.

[b]WQ: willingness question.

[c]RR: risk ratio.

[d]*P* values were estimated using the chi-square test. If Bonferroni correction was applied, the threshold of significance level was adjusted to .05/5=.01, which showed the *P* values in this table were still significantly low.

[e]N/A: not applicable.

[f]Pap: Papanicolaou.

Sex-wise Attitudes Toward HPV Vaccination and Awareness Regarding the Prevention of Cervical Cancer

The comparison of attitudes toward HPV vaccination and awareness regarding the prevention of cervical cancer according to sex are shown in Table 3.

Differences between sexes were identified in all questions. Fathers were more likely to have an affirmative attitude toward HPV vaccination for their daughters in the intervention group (fathers: RR 1.50, 95% CI 1.25-1.81; mothers: RR 1.21, 95% CI 0.88-1.66). Additionally, fathers in the intervention group were more likely to have affirmative attitudes regarding other areas of awareness, such as undergoing a Pap smear, desiring the recommendation from the government, and disseminating HPV vaccination information to someone by social media (Table 3). In an overall comparison between fathers and mothers irrespective of the short-film intervention, the willingness to consider HPV vaccination for daughters was significantly higher in fathers than in mothers (n=343, 27.1%, vs n=133, 14.6%, *P*<.001).

In addition, 650 (71.5%) of 909 mothers knew at least 1 of the items regarding HPV vaccination, while only 508 (40.1%) of 1266 fathers were aware of at least 1 item (Multimedia Appendix 2). However, in the subgroup analysis by awareness level, the intervention increased the willingness to consider HPV vaccination for their daughters in both awareness level groups: 6.0% increase (RR 1.27, 95% CI 1.04-1.55) in the normal-awareness group and 9.2% increase (RR 1.69, 95% CI 1.28-2.22) in the no-awareness group (data not shown).

Table 3. Sex-wise comparison of attitudes and willingness toward HPV[a] vaccination for the prevention of cervical cancer after intervention from the web survey (March 19-30, 2020).

Responses to WQs[b]	Mothers (N=909)					Fathers (N=1266)				
	Total, n (%)	Intervention (N=456), n (%)	Control (N=453), n (%)	Yes vs other RR[c] (95% CI)	Yes vs other *P* value[d]	Total, n (%)	Intervention (N=633), n (%)	Control (N=633), n (%)	Yes vs other RR[c] (95% CI)	Yes vs other *P* value[d]
WQ 1. Would you consider getting your daughter vaccinated against HPV?										
Yes	133 (14.6)	73 (16.0)	60 (13.2)	1.21 (0.88-1.66)	.24	343 (27.1)	206 (32.5)	137 (21.6)	1.50 (1.25-1.81)	<.001
No	286 (31.5)	110 (24.1)	176 (38.9)	N/A[e]	N/A	214 (16.9)	90 (14.2)	124 (19.6)	N/A	N/A
I'm not sure	490 (53.9)	273 (59.9)	217 (47.9)	N/A	N/A	709 (56.0)	337 (53.2)	372 (58.8)	N/A	N/A
WQ 2. Would you consider undergoing a Pap[f] smear? If male, would you want your family member or partner to undergo a smear test?										
Yes	523 (57.5)	262 (57.5)	261 (57.6)	1.00 (0.89-1.12)	.96	543 (42.9)	307 (48.5)	236 (37.3)	1.30 (1.14-1.48)	<.001
No	160 (17.6)	73 (16.0)	87 (19.2)	N/A	N/A	197 (15.6)	80 (12.6)	117 (18.5)	N/A	N/A
I'm not sure	226 (24.9)	121 (26.5)	105 (23.2)	N/A	N/A	526 (41.5)	246 (38.9)	280 (44.2)	N/A	N/A
WQ 3. Do you think the HPV vaccination program should be actively recommended by the government?										
Yes	167 (18.4)	93 (20.4)	74 (16.3)	1.25 (0.95-1.65)	.114	459 (36.3)	268 (42.3)	191 (30.2)	1.40 (1.21-1.63)	<.001
No	200 (22.0)	81 (17.8)	119 (26.3)	N/A	N/A	171 (13.5)	75 (11.8)	96 (15.2)	N/A	N/A
I'm not sure	542 (59.6)	282 (61.8)	260 (57.4)	N/A	N/A	636 (50.2)	290 (45.8)	346 (54.7)	N/A	N/A
WQ 4. Do you plan to inform family members, friends, or others about cervical cancer prevention and screening (through Instagram, Facebook, LINE, Twitter, TikTok, etc)?										
Yes	213 (23.4)	119 (26.1)	94 (20.8)	1.26 (0.99-1.59)	.06	268 (21.2)	163 (25.8)	105 (16.6)	1.55 (1.25-1.93)	<.001
No	349 (38.4)	148 (32.5)	201 (44.4)	N/A	N/A	448 (35.4)	209 (33.0)	239 (37.8)	N/A	N/A
I'm not sure	347 (38.2)	189 (41.5)	158 (34.9)	N/A	N/A	550 (43.4)	261 (41.2)	289 (45.7)	N/A	N/A
WQ 5. Are you going to make an appointment for HPV vaccination for your daughter as soon as possible?										
Yes	147 (16.2)	83 (18.2)	64 (14.1)	1.29 (0.96-1.74)	.095	350 (27.6)	215 (34.0)	135 (21.3)	1.59 (1.32-1.92)	<.001
No	762 (83.8)	373 (81.8)	389 (85.9)	N/A	N/A	916 (72.4)	418 (66.0)	498 (78.7)	N/A	N/A

[a]HPV: human papillomavirus.

[b]WQ: willingness question.

[c]RR: risk ratio.

[d]*P* values were estimated using the chi-square test. If Bonferroni correction was applied, the threshold of significance level was adjusted to .05/10=.005, which showed the *P* values in this table were still significantly low.

[e]N/A: not applicable.

[f]Pap: Papanicolaou.

Follow-Up Survey After 3 Months

At the follow-up survey after 3 months, 368 (16.9%) parents did not answer the online survey (Figure 1). The remaining 1807 (83.1%) parents were provided with a follow-up questionnaire. The results of the follow-up survey are presented in Table 4. A total of 149 (8.2%) parents responded that their daughters were vaccinated in the past 3 months. However, there was no difference in the vaccination rate in both groups: 77 (7.9%) in the intervention group versus 72 (8.7%) in the control group (RR 0.88, 95% CI 0.66-1.18). Among those who answered that they did not let their daughters get vaccinated (n=1638, 75.3%), only 124 (7.6%) of the parents displayed a positive attitude toward HPV vaccination for their daughters (FQ 1'). Regarding this question, the effect of the short film on willingness to consider HPV vaccination was not observed

(8.0% in the intervention group vs 7.1% in the control group, *P*=0.497). We could not find any effect of the intervention on the subsequent 4 questions (FQs 2-5), although the effect was seen in the first survey.

Table 4. Comparison of attitudes, willingness, and behaviors toward HPV[a] vaccination for the prevention of cervical cancer at the 3-month follow-up from the web survey between the intervention group and the control group (June 26-July 6, 2020).

Responses to FQs[b]	Total (N=1807), n (%)	Intervention (N=976), n (%)	Control (N=831), n (%)	Yes vs other RR[c] (95% CI)	*P* value[d]
FQ 1. Has your daughter been vaccinated after the first-round questionnaire?					
Vaccinated	149 (8.2)	77 (7.9)	72 (8.7)	0.88 (0.66-1.18)	.39
Only an appointment	20 (1.1)	9 (0.9)	11 (1.3)	N/A[e]	N/A
Nothing	1638 (90.6)	890 (91.2)	748 (90.0)	N/A	N/A
FQ 1'. Would you consider getting your daughter vaccinated against HPV?[f]					
Yes	124 (7.6)	71 (8.0)	53 (7.1)	1.13 (0.80-1.59)	.497
No	424 (25.9)	228 (25.6)	196 (26.2)	N/A	N/A
I'm not sure	1090 (66.5)	591 (66.4)	499 (66.7)	N/A	N/A
FQ 2. Would you consider undergoing a Pap[g] smear? If male, would you want your family member or partner to undergo a smear test?					
Yes	852 (47.1)	466 (47.7)	386 (46.5)	1.03 (0.93-1.13)	.582
No	327 (18.1)	163 (16.7)	164 (19.7)	N/A	N/A
I'm not sure	628 (34.8)	347 (35.6)	281 (33.8)	N/A	N/A
FQ 3. Do you think the HPV vaccination program should be actively recommended by the government?					
Yes	362 (20.0)	196 (20.1)	166 (20.0)	1.01 (0.84-1.21)	.96
No	362 (20.0)	193 (19.8)	169 (20.3)	N/A	N/A
I'm not sure	1083 (59.9)	587 (60.1)	496 (59.7)	N/A	N/A
FQ 4. Do you plan to inform family members, friends, or others about cervical cancer prevention and screening (through Instagram, Facebook, LINE, Twitter, TikTok, etc)?					
Yes	314 (17.4)	174 (17.8)	140 (16.8)	1.06 (0.86-1.30)	.583
No	743 (41.1)	389 (39.9)	354 (42.6)	N/A	N/A
I'm not sure	750 (41.5)	413 (42.3)	337 (40.6)	N/A	N/A
FQ 5. Are you going to make an appointment for HPV vaccination for your daughter as soon as possible?[f]					
Yes	204 (12.5)	111 (12.5)	93 (12.4)	1.00 (0.78-1.30)	.98
No	1434 (87.5)	779 (87.5)	655 (87.6)	N/A	N/A

[a]HPV: human papillomavirus.

[b]FQ: follow-up question.

[c]RR: risk ratio.

[d]*P* values were estimated using the chi-square test.

[e]N/A: not applicable.

[f]Asked only to participants who answered no in FQ 1.

[g]Pap: Papanicolaou.

Discussion

Principal Findings

This web-based RCT showed that showing a 4-minute-long film on the story of a patient with cervical cancer increases parents' willingness to consider HPV vaccination for their daughters. Furthermore, the willingness to undergo cervical cancer–screening tests and to disseminate HPV vaccination–related information about what they saw and felt also increased in the intervention group. These effects were observed in the fathers' cohort but not in the mothers' cohort. This result was similar to our prior RCT, which showed that a brief educational tool using the importance of HPV vaccination increases the willingness to consider the vaccination for their daughters and sons [4]. The noteworthy point is that both brief material based on medical evidence and a short film based on a cervical cancer survivor's story positively affect only men. In contrast, the story of a cancer patient did not change the parents'

behavior toward HPV vaccination, and 3 months later, the parents' willingness toward vaccination was not sustained. Even the mothers' personal experiences of cervical cancer were not a sufficient factor in increasing their children's vaccination rate [15], so it seems cogent that a cancer survivor's story does not impact parents' behavior regarding their daughters' vaccination against HPV.

Similar to the prior RCT, a possible reason the educational intervention was more effective among men could be that women had more existing awareness about HPV and HPV vaccination and had more negative sentiments against HPV vaccination (Multimedia Appendix 2). In fact, there was a significant difference between fathers and mothers in the awareness level of HPV vaccination. However, we found that the intervention increased the willingness to consider HPV vaccination for their daughters irrespective of awareness level. Thus, our trial indicated that sex differences may be a significant factor in the decision-making of HPV vaccination for daughters. Although several studies have described the mothers' hesitancy to get their children vaccinated against COVID-19 as a potential factor for a lower vaccination rate [16], little is known about parents' sex differences affecting the likelihood of HPV vaccination for their children. Even if the awareness level is not a factor influencing their willingness, there might be a difference between fathers and mothers regarding anxiety or the decision-making process. We need to consider measuring this sort of index to examine possible factors affecting the gender difference toward HPV vaccination.

In the follow-up survey, we did not find a significant intervention effect on HPV vaccination for the participants' daughters. There may be some reason for this. First, this awareness change happened to just 1 parent. The decision-making process with another parent or daughter would be needed to take an action for vaccination. Therefore, this type of indirect intervention could have some limitations in its impact. Surprisingly, a total of 8.2% of the participants had their daughters vaccinated after participation in this trial, which was higher than the general HPV vaccination rate in Japan at the time of the study [5,6]. The information we provided, including that given prior to randomization and awareness questions, might have changed their attitudes and behaviors. The information including general facts addressing safety concerns and the benefits regarding HPV vaccination could reduce the participants' hesitancy [17]. Moreover, the effect of intervention was not present anymore 3 months later, implying that this particular intervention may be limited in sustaining one's attitudes toward HPV vaccination over a period of time. We did not limit the participants' access to any resources, such as health care providers and health information from various media. This possibly reduced the effect of the intervention.

Although face-to-face educational approaches with parents might be an effective way to improve awareness and understanding of the vaccination [18], we need to increasingly utilize the online approach according to the rapid growth in the share of social media users worldwide [19]. Abundant information regarding health issues is provided and disseminated mainly through social media [20]. Furthermore, information based on public health facts and misinformation based on no-scientific theory, provaccine posts, and antivaccine posts is mixed [21-23]. The problem is that antivaccine information has a tendency to be created by individuals who do not have a medical background, while the information still sounds plausible for many people [19]. In some countries, including Japan, some European countries, and the Unites States, nationwide vaccine hesitancy in regard to HPV vaccination was seen to be caused by online and offline dissemination of misleading beliefs [2,4,5,24-27]. Although many researchers know that 1 of the main causes of vaccine hesitancy may be information overload and misinformation, which is also called an "infodemic" [28,29], medical professionals should also provide information about HPV vaccination to the public as a reliable information resource and keep encouraging parents to get their children vaccinated [27]. Additionally, a national scale approach that is coordinated among health care providers, parents, media, and policy makers should be utilized to combat disinformation and misinformation regarding vaccines [24,30].

Twitter [23,31,32], Instagram [21], and Facebook [32-34] have been proposed as promising educational methods in the past 5 years; however, little is still known about the best specific way to mitigate vaccine hesitancy for HPV vaccination [35-37]. A study reported that using social media to promote health behavior leads to a significant improvement in behavioral change [38]. For instance, in the United States, the use of social media has grown in the past decade [39]; therefore, it might be a great platform to educate people about HPV vaccination–related information. The data also shows the rate of use by age and sex [39]. A strategy by age or sex based on the theory of social marketing [2,40] will be valuable if we proceed with a campaign of HPV vaccination based on the results of studies like ours [4], although social media could lead to parents' vaccine hesitancy [16,30]. As a systematic review suggested, the identified strategy should be carefully tailored according to specific populations [37], considering the pros and cons of social media.

Limitations

Although this study displayed a promising effect on overcoming vaccine hesitancy, we need to consider several limitations. First, the cohort of the specified internet survey population used in this study may have some selection bias. The cohort has a higher educational background and is wealthier than the general Japanese population; approximately JPY 5.16 million is the average household income [41]. Additionally, the gender imbalance in this study's population needs to be considered as another selection bias.

Second, interventions using this kind of awareness material are usually not universal, that is, the effect may vary when other materials are used. In particular, the effect might change depending on the individuals in the film, the content of the anecdotes, and the length of the film.

Third, although this trial was designed to assess the sustainability of awareness change and concrete behavior for HPV vaccination, we could not incorporate the actual vaccination records into our research. Therefore, the reported vaccination rate might be different from the actual vaccination rate.

Fourth, there was some potential social desirability bias that affected the effectiveness of the intervention at the first survey; on the contrary, the effect could not be seen in the follow-up survey. We have to take a look at the effectiveness of the film, considering the existence of a bias away from null.

Given that this trial implemented under the suspension of proactive recommendation by the Japanese government, we have a tentative plan to conduct the same trial after resuming the national vaccination program. In addition, there were potential negative impacts in the study period, which was carried out during the COVID-19 pandemic. A lockdown was not declared in Japan during the study period; however, a portion of participants might have refrained from going to the hospital for nonurgent vaccination.

Conclusion

Inference of the Study Findings

This study demonstrated a positive immediate effect on the willingness for HPV vaccination in parents who have daughters, following intervention using a short film on cervical cancer, especially among fathers. Such an approach is promising for overcoming the hesitancy toward HPV vaccination. Additionally, this RCT showed the importance of the father's role in improving the HPV vaccination rate and overcoming vaccine hesitancy.

Impact of the Findings

An anecdotal cervical cancer survivor's story increases the willingness of Japanese parents to consider HPV vaccination for their daughters. However, this type of intervention might not sustain their motivation months afterward.

Acknowledgments

The authors would like to thank the members of the research group affiliated with Niigata University, Osaka University, and Yokohama City University for their cooperation. We would like to thank Editage for English language editing. We also deeply thank the NTT Data Institute of Management Consulting, Inc. (Tokyo, Japan), especially Yoshiyuki Ogawa and Fumihiro Takayama for their dedication in this trial. In addition, we offer our sincerest thanks to Yoko Matsuda for sharing her personal experience as a cervical cancer survivor to highlight the importance of preventing HPV.

Authors' Contributions

YS was responsible for the study conceptualization, data collection, statistical analysis, interpretation, and writing. AS, YU, MS, TE, AM, JDW, and EM reviewed and edited the manuscript. YU, MS, TE, and EM contributed to funding acquisition.

Conflicts of Interest

JDW reports research funding from Merck Sharp & Dohme Corp. EM received grants and lecture fees from Merck Sharp & Dohme Corp and Chugai Pharmaceutical Co, Ltd. EM also received honoraria from Takeda Pharmaceutical Co, Ltd. and AstraZeneca plc.

Multimedia Appendix 1
Flow diagram of the study.
[PPTX File , 43 KB - publichealth_v8i5e34715_app1.pptx]

Multimedia Appendix 2
Characteristics and knowledge level between father and mother.
[DOCX File , 18 KB - publichealth_v8i5e34715_app2.docx]

Multimedia Appendix 3
CONSORT-eHEALTH checklist (V 1.6.1).
[PDF File (Adobe PDF File), 8199 KB - publichealth_v8i5e34715_app3.pdf]

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Abbreviations

AQ: awareness question
FQ: follow-up question
HPV: human papillomavirus
MHLW: Ministry of Health, Labour and Welfare
Pap: Papanicolaou
RCT: randomized controlled trial
RR: risk ratio
WQ: willingness question

Edited by T Sanchez; submitted 04.11.21; peer-reviewed by R Mpofu, L Guo; comments to author 06.01.22; revised version received 25.02.22; accepted 12.04.22; published 25.05.22.

Please cite as:
Suzuki Y, Sukegawa A, Ueda Y, Sekine M, Enomoto T, Melamed A, Wright JD, Miyagi E
The Effect of a Web-Based Cervical Cancer Survivor's Story on Parents' Behavior and Willingness to Consider Human Papillomavirus Vaccination for Daughters: Randomized Controlled Trial
JMIR Public Health Surveill 2022;8(5):e34715
URL: https://publichealth.jmir.org/2022/5/e34715
doi:10.2196/34715
PMID:35421848

Original Paper

Factors Associated With COVID-19 Death in the United States: Cohort Study

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Abstract

Background: Since the initial COVID-19 cases were identified in the United States in February 2020, the United States has experienced a high incidence of the disease. Understanding the risk factors for severe outcomes identifies the most vulnerable populations and helps in decision-making.

Objective: This study aims to assess the factors associated with COVID-19–related deaths from a large, national, individual-level data set.

Methods: A cohort study was conducted using data from the Optum de-identified COVID-19 electronic health record (EHR) data set; 1,271,033 adult participants were observed from February 1, 2020, to August 31, 2020, until their deaths due to COVID-19, deaths due to other reasons, or the end of the study. Cox proportional hazards models were constructed to evaluate the risks for each patient characteristic.

Results: A total of 1,271,033 participants (age: mean 52.6, SD 17.9 years; male: 507,574/1,271,033, 39.93%) were included in the study, and 3315 (0.26%) deaths were attributed to COVID-19. Factors associated with COVID-19–related death included older age (≥80 vs 50-59 years old: hazard ratio [HR] 13.28, 95% CI 11.46-15.39), male sex (HR 1.68, 95% CI 1.57-1.80), obesity (BMI ≥40 vs <30 kg/m_2: HR 1.71, 95% CI 1.50-1.96), race (Hispanic White, African American, Asian vs non-Hispanic White: HR 2.46, 95% CI 2.01-3.02; HR 2.27, 95% CI 2.06-2.50; HR 2.06, 95% CI 1.65-2.57), region (South, Northeast, Midwest vs West: HR 1.62, 95% CI 1.33-1.98; HR 2.50, 95% CI 2.06-3.03; HR 1.35, 95% CI 1.11-1.64), chronic respiratory disease (HR 1.21, 95% CI 1.12-1.32), cardiac disease (HR 1.10, 95% CI 1.01-1.19), diabetes (HR 1.92, 95% CI 1.75-2.10), recent diagnosis of lung cancer (HR 1.70, 95% CI 1.14-2.55), severely reduced kidney function (HR 1.92, 95% CI 1.69-2.19), stroke or dementia (HR 1.25, 95% CI 1.15-1.36), other neurological diseases (HR 1.77, 95% CI 1.59-1.98), organ transplant (HR 1.35, 95% CI 1.09-1.67), and other immunosuppressive conditions (HR 1.21, 95% CI 1.01-1.46).

Conclusions: This is one of the largest national cohort studies in the United States; we identified several patient characteristics associated with COVID-19–related deaths, and the results can serve as the basis for policy making. The study also offered directions for future studies, including the effect of other socioeconomic factors on the increased risk for minority groups.

(JMIR Public Health Surveill 2022;8(5):e29343) doi:10.2196/29343

KEYWORDS

COVID-19; risk factors; survival analysis; cohort studies; EHR data

Introduction

The COVID-19 pandemic has brought an unprecedented crisis in global public health since it first appeared in late 2019. By the end of 2020, 19,943,605 confirmed cases and 344,497 deaths were reported in the United States [1], which was the largest number of any country in the world. Although based on a short observation period or within a single geographical region, reports and studies from the early stage of the pandemic revealed high hospitalization and mortality rates [2-4]. Identifying prognostic factors can help determine patients at the highest risk for poor outcomes and focus interventions accordingly.

Many studies have been conducted on this topic in the United States. For example, a study of 2215 adult COVID-19 patients admitted to intensive care units showed that patients older than 80 years had a much higher risk of COVID-19–related death. Men also were at an increased risk [5]. Similar findings also were reported from a study involving 64,781 patients treated in 592 US hospitals during April and May 2020 [6]. Pre-existing conditions including obesity, coronary artery disease, cancer, liver or kidney dysfunction, neurological disorder, diabetes, and dementia were each associated with raised risks of a severe outcome [5,6]. Although many studies have explored the linkage between patient characteristics and COVID-19 death, most of them involved limited sample sizes and relatively short time spans. Recently, a large cohort study of 1,926,526 patients with 174,568 COVID-19 confirmed cases from the National COVID Cohort Collaborative (N3C), a centralized national data resource, reported that age, male sex, liver disease, dementia, African American and Asian race, and obesity were associated with poor outcomes [7]. There is a scarcity of studies using large national data similar to the N3C cohort in the United States to provide accurate and reliable findings.

In 2020, a UK team used National Health Service data to build the OpenSAFELY platform and to conduct a cohort study of 17 million people to investigate factors associated with COVID-19–related deaths in England [8]. The findings showed that people over 80 years old had a 20 times higher risk compared with those aged 50-59 years (hazard ratio [HR] 20.6, 95% CI 18.7-22.68). Men had slightly higher risk than women (HR 1.59, 95% CI 1.53-1.65). Minority groups, including mixed-race, South Asian, and Black people, were at higher risks than White people. In addition, obesity and most comorbidities, including cardiac, pulmonary, kidney disease, and malignancies, were all associated with higher risks of COVID-19–related deaths.

To understand whether these factors proposed in the OpenSAFELY study, including age, sex, and other comorbidities, were also linked to higher risks of COVID-19–related deaths among the US population during the similar time window, we conducted a study that expands upon the UK study through the analysis of the Optum de-identified COVID-19 electronic health record (EHR) data set and compared findings with the aforementioned N3C cohort with over 1 million patient records between February 1, 2020, and August 31, 2020, in the United States.

Methods

Study Design

This study was designed to replicate the UK OpenSAFELY [8] study within the constraints of the available data. We conducted a cohort study using data from the Optum de-identified COVID-19 EHR data set. The study started on February 1, 2020, which was the earliest date Optum began compiling the COVID-19 data. The date was 10 days after the first COVID-19 confirmed case and several weeks before the first reported COVID-19–related death in the United States. The study ended on August 31, 2020, which was the latest accessible record released by Optum by the time the study was performed. In the primary analysis, all eligible participants were included in the study regardless of their SARS-CoV-2 test results (the full cohort) to assess risks among the general population. For the analysis among COVID-19 patients, a subset of patients was extracted from the full cohort with at least one lab-confirmed polymerase chain reaction (PCR)–positive SARS-CoV-2 test result or with diagnosis code U07.1 or B97.29 between February 1, 2020, and August 17, 2020 (the date was chosen 2 weeks before the study ended to allow the outcome to fully develop). No randomization was conducted. No investigator was involved in the outcome assessment.

Data Source

The Optum COVID-19 data set was provided by Optum to the University of Texas (UT) Center for Health Care Data, University of Texas Health Science Center (UTHealth) School of Public Health, and UTHealth School of Biomedical Informatics (SBMI) Data Service. The data set accessed throughout the study was locally hosted by SBMI. It comprised longitudinal EHR data derived from a network of health care provider organizations across the United States. The data were certified as de-identified by an independent statistical expert following Health Insurance Portability and Accountability Act statistical de-identification rules and managed according to Optum customer data use agreements. Clinical and other medical administrative data were obtained from both inpatient and ambulatory EHRs, practice management systems, and numerous other internal systems. Information was processed, normalized, and standardized across the continuum of care from both acute inpatient stays and outpatient visits. Optum data elements included demographics, medications prescribed and administered, lab results, vital signs, other observable measurements, clinical and inpatient stay administrative data, and coded diagnoses and procedures.

All authors were authorized to access the Optum COVID-19 data set and were compliant with the data use agreements.

Study Population and Observation Period

Considering many of the risk factors investigated in this study are chronic health conditions that are more commonly present

in adult patients, the study population included only adult men and women aged 18 years or older on or before February 1, 2020. To be included in the study, participants must have had at least 1 year of prior observation before the study start date in order to adequately capture their baseline characteristics. Participants also were required to have EHRs for the prior year to be considered eligible for inclusion. In addition, participants with missing demographics, including sex, age, and region, were excluded from the study. Eligible participants were followed from February 1, 2020, until their deaths due to COVID-19, deaths due to other causes, or the end of the study (August 31, 2020). The Optum data set used in this study was delivered on September 3, 2020, which contained some death data for early September. However, we elected to end the study period a few days earlier to account for possible delays in data delivery.

Ethical Considerations

Data for this study were provided by Optum and remain on the servers of the Biomedical Informatics Group-the Analytics Research Center, SBMI, UTHealth. No individually identifiable information was provided, and no participants were contacted by the investigators directly. The secondary analysis of this de-identified data was approved by the Committee for the Protection of Human Subjects, University of Texas Health Science Center at Houston (the UTHSC-H institutional review board) under protocol HSC-SBMI-20-1194.

Outcome

The outcome of interest was COVID-19–related deaths. All non-COVID-19–related deaths or surviving patients were censored at the time of death or the end of the study, respectively. Due to the de-identification of data, only the death year and month were available. Neither the exact death day nor the cause of death was provided. We, therefore, used an indirect way to define COVID-19–related deaths: If the month of a patient's last COVID-19 diagnosis (International Classification of Diseases [ICD]-10 codes U07.1 on or after February 1, 2020, or ICD-10 codes B97.29 on or after February 20, 2020) matched or was within 1 month after the death month and any of the other most recent recorded dates (hospital discharge date, health service encounter date, diagnosis date, lab test ordered date, prescription date, and medical procedure date) was the same as or within 1 month after the death month, the patient was considered to have experienced a COVID-19–related death. The extra 1-month window was included to account for the possible delay of data entry. For example, if a patient had a positive COVID-19 diagnosis on April 4 and died in April, with any of the aforementioned dates falling in April, the patient was considered to have died from COVID-19. However, if the patient had a positive diagnosis in February but died in April, the patient would be considered to have died from other causes. To determine the death day, we defined the most recent recorded date among the aforementioned dates that matched the death month as the presumptive date of death. For those without matching records on the death month, the presumptive date of death was set to the 15th of the death month as the midpoint of possible death dates.

Covariates

Potential risk factors and their categorizations in this study generally followed those used in the OpenSAFELY study [8]. Age was grouped into 6 categories: 18-39, 40-49, 50-59, 60-69, 70-79, and 80 years old. BMI was obtained either directly from the recorded BMI values or calculated from weight measurements within the past 10 years and restricted to those taken when the patient was over 16 years old. Obesity was determined according to BMI value, using cut-offs from the US Centers for Disease Control and Prevention: <30 kg/m^2, not obese; ≥30 and <35 kg/m^2, class I obesity; ≥35 and <40 kg/m^2, class II obesity; ≥40 kg/m^2, class III obesity [9]. Smoking status was grouped into never, former, and current smokers. The Optum data set had race and ethnicity recorded separately. Race included African American, Asian, Caucasian, and other/unknown. Ethnicity included Hispanic, non-Hispanic, or unknown. Due to the fact that Hispanic African American and Hispanic Asian together accounted for only 0.3% of the study population, we treated them simply as African American and Asian, respectively. Caucasian was divided into Hispanic or non-Hispanic White. For Caucasian with unknown ethnicity, we categorized them as unknown race/ethnicity. Consequently, the race/ethnicity variable in the data set was grouped into non-Hispanic White, Hispanic White, African American, and Asian. The regions included West, South, Northeast, and Midwest according to the US Census Bureau.

Based on glycated hemoglobin (HbA_{1C}) measured within the past 15 months, diabetes was grouped into uncontrolled (HbA_{1C} ≥58 mmol/mol), controlled (HbA_{1C} <58 mmol/mol), or without recent HbA_{1C} records. Cancers were grouped based on the first diagnosis date (<1 year, ≥1 year). The most recent creatinine value was used to calculate estimated glomerular filtration rate (eGFR) according to the CKD-EPI equation [10]. Since this equation adjusts for race, eGFR was not calculated for patients without race and was considered missing. Reduced kidney function was grouped into eGFR <30 or 30 ≤ eGFR < 60 mL/min/1.73 m^2. Chronic respiratory disease other than asthma included chronic obstructive pulmonary disease, bronchiectasis, cystic fibrosis, and interstitial lung fibrosis. Cardiac disease included ischemic heart disease and congestive heart failure. Hypertension or high blood pressure was defined as either a prior diagnosis of hypertension or most recent systolic or diastolic blood pressure ≥140 mm Hg or ≥90 mm Hg, respectively. Chronic liver disease included chronic viral hepatitis, cirrhosis, and primary genetic liver disease. Stroke or dementia included hemorrhagic stroke and dementia that were related to cardiovascular etiology. Besides stroke or dementia, other neurological diseases included motor neuron disease, myasthenia gravis, multiple sclerosis, Parkinson disease, cerebral palsy, quadriplegia or hemiplegia, and progressive cerebellar disease. Organ transplant included both solid organ and bone marrow transplant. Autoimmune disease indicated rheumatoid arthritis, systemic lupus erythematosus, and psoriasis. Other immunosuppressive conditions included HIV, permanent immunodeficiency ever diagnosed, as well as aplastic anemia and temporary immunodeficiency diagnosed within the last year.

Information on patients' comorbidities was obtained by the diagnosis codes in their health care records. The coding system in the Optum COVID-19 data set included ICD-9, ICD-10, and SNOMED CT. To best recapitulate the disease groups as in the OpenSAFELY study, we used the SNOMED code lists provided on the OpenSAFELY website [11] and mapped them to ICD-9/ICD-10 codes using mapping tools from the Unified Medical Language System [12]. The Clinical Classifications Software from the Agency for Healthcare Research and Quality was also used to obtain ICD-9/ICD-10 codes for disease groups where available [13]. All SNOMED CT and ICD-9/ICD-10 codes were compared to the final code lists released by the UK OpenSAFELY platform and were manually curated to match our disease definitions. Decisions on every code list were documented and were reviewed by physicians.

Statistical Analysis

All statistical analyses mirrored the UK OpenSAFELY study [8], and most of their Stata codes were reused with minor modifications to suit our data set. The Kaplan-Meier method was used to estimate the cumulative incidence of COVID-19–related deaths by age groups and sex. A univariable Cox proportional hazards model was fit for each potential risk factor and was adjusted for age and sex (age-sex adjusted models), with age modeled using a restricted cubic spline. A separate sex-adjusted univariable Cox model for age groups was fitted to show the HRs for different age categories. All the factors including age, sex, obesity, smoking status, region, diabetes, hematological malignancy, lung cancer, other cancers, reduced kidney function, asthma, respiratory disease, chronic cardiac disease, hypertension, liver disease, stroke or dementia, other neurological diseases, organ transplant, rheumatoid arthritis/lupus/psoriasis, and other immunosuppressive conditions were then fit in 1 multivariable Cox proportional hazards model (fully adjusted model). Similarly, age was fit using a restricted cubic spline, and a separate fully adjusted model for age groups was refitted. The proportional hazards assumption was explored by testing for the non-zero slopes of the scaled Schoenfeld residuals for each factor. The Breslow method was used to handle ties, and all the time scales used in the survival analysis were measured in days. Estimated HRs and their 95% CIs are reported for both age-sex adjusted models, as well as the fully adjusted model.

In the primary analysis, participants with missing BMI, smoking status, and eGFR were considered to be non-obese, be never-smokers, and have normal kidney function based on the assumption that having these characteristics were more likely to be captured. A sensitivity analysis was conducted using participants with complete records for these factors only. The differences in HRs were compared with the primary analysis. Due to around 18% of participants without a recorded race, it was not included in the primary model, and its HR was separately obtained by fitting a Cox model using observations with known race. This race-adjusted model, together with other covariates, was presented in another sensitivity analysis to assess the impact of including race on all other factors.

C-statistics were calculated to show the model's discriminative performance. Due to the computational limits, this was done by randomly sampling 2000 observations from both with and without the event of interest. The process was repeated 10 times, and the average was taken as the estimate of the C-statistic. Weights were applied to the calculation [14]. All *P* values shown here are 2-sided.

Data management was performed in SQL, Python 3.6.10, and R 3.6. All statistical analyses were conducted using Stata/IC 16.1.

Results

Among 1,848,463 individuals in the original sample, exclusions were made for the following reasons: lack of a complete year of information prior to February 2020 (378,031/1,848,463, 20.45%), inconsistent or missing information on death (57,443/1,848,463, 3.11%), age less than 18 years (99,064/1,848,463, 5.36%), and missing information on age, sex, or geographic region (42,892/1,848,463, 2.32%), leaving an analytic sample of 1,271,033 persons who were tested for COVID-19 between February 1, 2020, and August 31, 2020 (Figure 1). Among them, 3315 deaths were attributed to COVID-19 by the end of the study. A summary of patient characteristics is shown in Table 1. Certain characteristics had missing information for a proportion of the 1,271,033 persons: BMI, 100,237 (7.89%); smoking status, 88,006 (6.92%); race, 225,881 (17.77%); blood pressure, 79,142 (6.23%); and creatinine, 326,787 (25.71%).

Kaplan-Meier curves showed that men had a higher cumulative probability of death from COVID-19 in every age group compared with women. In addition, mortality rose as age increased for both sexes (Figure 2).

The HR of COVID-19 deaths for each characteristic is shown in Figure 3 and Table 2.

In this study, except when reporting the HRs for age groups (fit as a categorical variable), age was otherwise modeled as a restricted cubic spline. With that approach, the relationship between log HRs and age was approximately log-linear (Figure 4). The risks of COVID-19–related death increased in older age groups. In people over 80 years old, the risk was around 13 times that in those aged 50-59 years (reference group). Our results also showed that men had a higher risk of COVID-19–related death compared with women. The minority groups (Hispanic White, African American, and Asian) also had elevated risks compared with non-Hispanic Whites, with HRs ranging from 2.06 (Asians) to 2.46 (Hispanic Whites) in the fully adjusted model. People who lived in the Northeast had the highest HR of 2.50 (2.06-3.03).

The risk increased with rising BMI. Patients with diabetes showed elevated risks. However, well-controlled diabetes (HbA_{1c} <58 mmol/mol during the past 15 months) diminished the risk to 1.11 (1.00-1.23) compared with that of 1.67 (1.46-1.91) in patients with poorer diabetic control or 1.92 (1.75-2.10) in those without recent assessment of control. Other chronic conditions including cardiac disease, severely reduced kidney function (eGFR <30 mL/min/1.73 m^2), chronic respiratory disease, stroke or dementia, other neurological

diseases, organ transplant, and other immunosuppressive conditions were associated with elevated risks of COVID-19–related death. The effects of hematological and lung cancers were investigated separately from other cancers due to their direct impact on the immune system and the sites of the COVID-19 infection, respectively. Other cancers did not increase the risk, whereas having lung cancer diagnosed within the prior year raised the risk of COVID-19–related death. Patients diagnosed with hematological cancer within the prior year had a higher but statistically nonsignificant risk elevation.

Neither former nor current smokers had elevated risks of COVID-19–related death. Instead, the risks were significantly lower compared with nonsmokers. Participants with hypertension showed higher risk in the age-sex adjusted univariable model. However, the HR lost statistical significance when other covariates were included. To investigate which factors contributed to this reduction, we included other variables one at a time to the model containing age, sex, and hypertension. We found that obesity, diabetes, and cardiac disease were primarily responsible for the diminished association. Including these 3 factors in the age-sex adjusted hypertension model reduced the HR for hypertension from 1.30 to 1.03 (0.93-1.14). Similarly, the apparent impact of chronic liver disease was decreased with the adjustment for diabetes. Asthma and autoimmune diseases did not show increased risks of COVID-19–related death in either the age-sex adjusted model or the fully adjusted model.

Figure 1. Flowchart for defining the study population in the United States between February 1, 2020, and August 31, 2020.

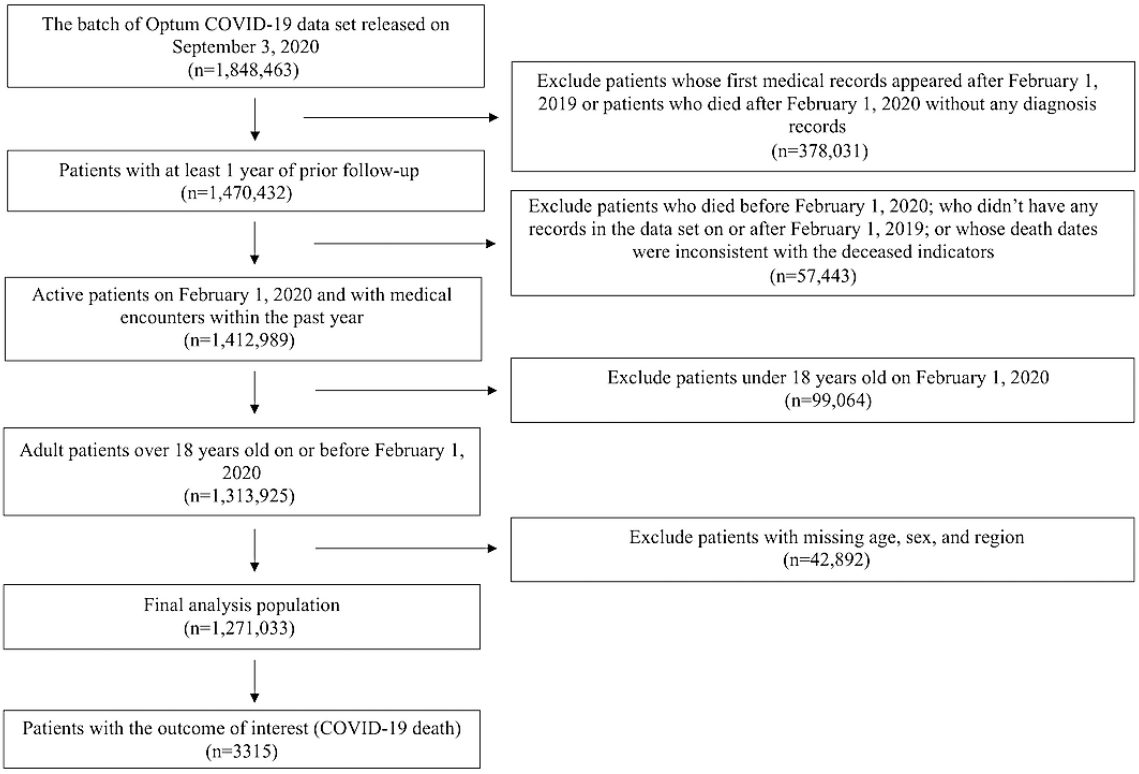


Table 1. Characteristics of the overall adult study population and COVID-19 fatalities in the United States between February 1, 2020, and August 31, 2020.

Characteristic	Overall sample (N=1,271,033), n (%)	Number of COVID-19–related deaths (n=3315), n (%)
Age (years)		
18-39	348,372 (27.41)	46 (0.01)
40-49	188,305 (14.82)	96 (0.05)
50-59	248,913 (19.58)	246 (0.10)
60-69	248,017 (19.51)	578 (0.23)
70-79	151,866 (11.95)	869 (0.57)
≥80	85,560 (6.73)	1480 (1.73)
Sex		
Female	763,459 (60.07)	1472 (0.19)
Male	507,574 (39.93)	1843 (0.36)
BMI (kg/m^2)		
<18.5	16,190 (1.27)	62 (0.38)
18.5-24.9	283,597 (22.31)	682 (0.24)
25-29.9	356,721 (28.07)	910 (0.26)
30-34.9 (obesity class I)	257,837 (20.29)	658 (0.26)
35-39.9 (obesity class II)	138,765 (10.92)	320 (0.23)
≥40 (obesity class III)	117,686 (9.26)	278 (0.24)
Missing	100,237 (7.89)	405 (0.40)
Smoking		
Never	262,320 (20.64)	574 (0.22)
Former	727,211 (57.21)	2163 (0.30)
Current	193,496 (15.22)	236 (0.12)
Missing	88,006 (6.92)	342 (0.39)
Race/ethnicity		
Non-Hispanic White	837,195 (65.87)	1933 (0.23)
Hispanic White	30,582 (2.41)	99 (0.32)
African American	147,830 (11.63)	564 (0.38)
Asian	29,545 (2.32)	85 (0.29)
Missing	225,881 (17.77)	634 (0.28)
Region		
West	100,986 (7.95)	112 (0.11)
South	225,884 (17.77)	664 (0.29)
Northeast	389,344 (30.63)	1449 (0.37)
Midwest	554,819 (43.65)	1090 (0.20)
Blood pressure		
Normal[a]	373,078 (29.35)	661 (0.18)
Elevated[b]	184,987 (14.55)	487 (0.26)
High, stage I[c]	467,196 (36.76)	1064 (0.23)
High, stage II[d]	166,630 (13.11)	788 (0.47)
Missing	79,142 (6.23)	315 (0.40)

Characteristic	Overall sample (N=1,271,033), n (%)	Number of COVID-19–related deaths (n=3315), n (%)
High blood pressure/hypertension		
Yes	650,425 (51.17)	2738 (0.42)
No	620,608 (48.83)	577 (0.09)
Chronic respiratory disease		
Yes	170,033 (13.38)	1017 (0.60)
No	1,101,000 (86.62)	2298 (0.21)
Asthma		
Yes	208,254 (16.38)	422 (0.20)
No	1,062,779 (83.62)	2893 (0.27)
Cardiac disease		
Yes	215,816 (16.98)	1583 (0.73)
No	1,055,217 (83.02)	1732 (0.16)
Diabetes		
HbA_{1c}[e] <58 mmol/mol	105,697 (8.32)	497 (0.47)
HbA_{1c} ≥58 mmol/mol	49,193 (3.87)	267 (0.54)
No recent[f] HbA_{1c} value	86,896 (6.84)	699 (0.80)
Not diabetic	1,029,247 (80.98)	1852 (0.18)
Other cancer (excluding hematological and lung cancer)		
Diagnosed <1 year	30,835 (2.43)	85 (0.28)
Diagnosed ≥1 year	137,456 (10.81)	467 (0.34)
Never	1,102,742 (86.76)	2763 (0.25)
Hematological cancer		
Diagnosed <1 year	4681 (0.37)	30 (0.64)
Diagnosed ≥1 year	17,873 (1.41)	98 (0.55)
Never	1,248,479 (98.23)	3187 (0.26)
Lung cancer		
Diagnosed <1 year	2927 (0.23)	24 (0.82)
Diagnosed ≥1 year	7419 (0.58)	41 (0.55)
Never	1,260,687 (99.19)	3250 (0.26)
eGFR[g] (mL/min/1.73 m^2)[h]		
≥60	823,048 (64.75)	1378 (0.17)
45-59.9	71,698 (5.64)	499 (0.70)
30-44.9	30,453 (2.40)	361 (1.19)
15-29.9	11,007 (0.87)	172 (1.56)
<15	8040 (0.63)	119 (1.48)
Missing	326,787 (25.71)	786 (0.24)
Chronic liver disease		
Yes	90,213 (7.10)	265 (0.29)
No	1,180,820 (92.90)	3050 (0.26)
Stroke or dementia		
Yes	104,876 (8.25)	913 (0.87)
No	1,166,157 (91.75)	2402 (0.21)

Characteristic	Overall sample (N=1,271,033), n (%)	Number of COVID-19–related deaths (n=3315), n (%)
Other neurological diseases		
Yes	41,187 (3.24)	391 (0.95)
No	1,229,846 (96.76)	2924 (0.24)
Organ transplant		
Yes	12,429 (0.98)	95 (0.76)
No	1,258,604 (99.02)	3220 (0.26)
RA[i], SLE[j], or psoriasis		
Yes	65,387 (5.14)	188 (0.29)
No	1,205,646 (94.86)	3127 (0.26)
Other immunosuppressive condition		
Yes	31,005 (2.44)	127 (0.41)
No	1,240,028 (97.56)	3188 (0.26)

[a]Systolic blood pressure <120 mm Hg; diastolic blood pressure <80 mm Hg.

[b]Systolic blood pressure ≥120 and ≤129 mm Hg; diastolic blood pressure <80.

[c]Systolic blood pressure ≥130 and ≤139 mm Hg; diastolic blood pressure ≥80 and ≤89 mm Hg.

[d]Systolic blood pressure ≥140 or diastolic blood pressure ≥90.

[e]HbA_{1c}: glycated hemoglobin.

[f]HbA_{1c} value within 15 months before February 1, 2020.

[g]eGFR: estimated glomerular filtration rate.

[h]Calculated from the creatinine value.

[i]RA: rheumatoid arthritis.

[j]SLE: systemic lupus erythematosus.

Figure 2. Kaplan-Meier cumulative probability of death due to COVID-19 for (A) women and (B) men.

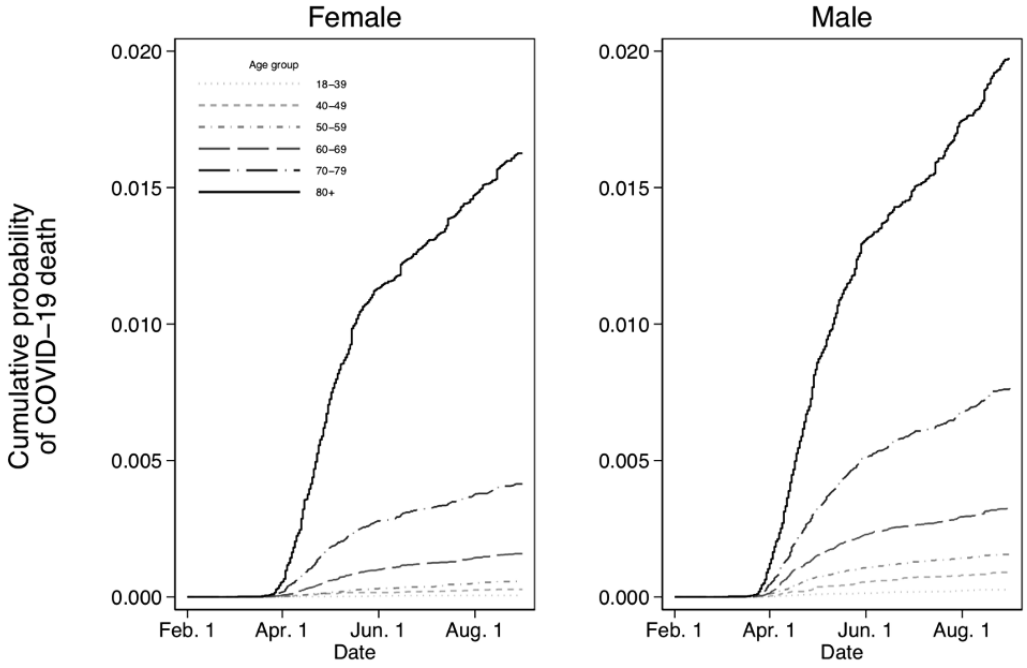


Figure 3. Forest plot showing hazard ratios for each risk factor from the fully adjusted Cox proportional hazards model (n=1,271,033). The values for race were separately ascertained by fitting a Cox proportional hazards model using only those with known race (n=1,045,152) and adjusted for all other covariates. eGFR: estimated glomerular filtration rate.

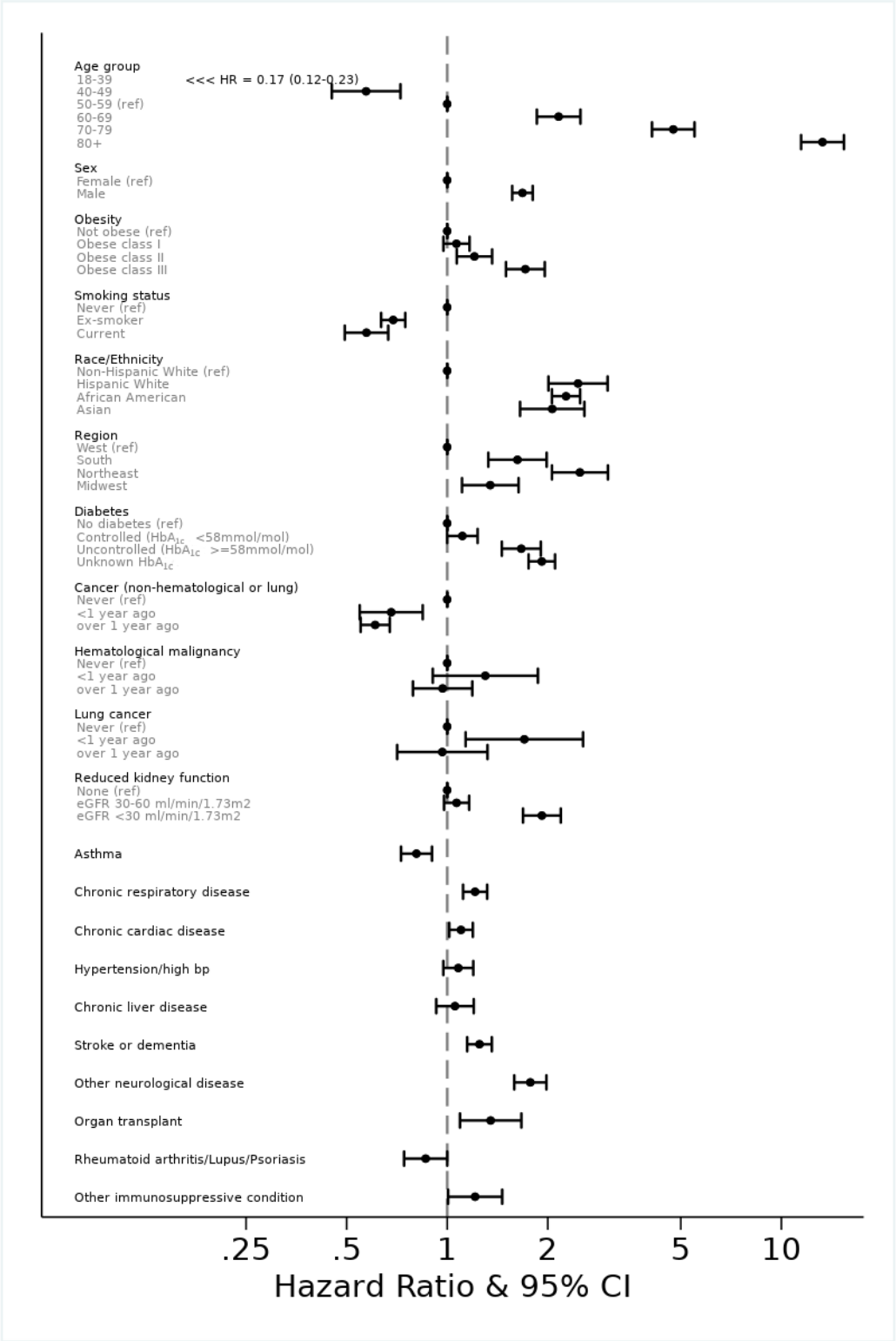


Table 2. Adjusted hazard ratios (HRs) for COVID-19–related death for each patient characteristic.

Characteristic	Age-sex adjusted model[a], HR (95% CI)	Fully adjusted model (primary analysis)[b], HR (95% CI)
Age[c] (years)		
18-39	0.14 (0.10-0.19)	0.17 (0.12-0.23)
40-49	0.53 (0.42-0.67)	0.57 (0.45-0.72)
50-59	1.00 (ref[d])	1.00 (ref)
60-69	2.32 (2.00-2.69)	2.15 (1.85-2.50)
70-79	5.70 (4.95-6.57)	4.75 (4.10-5.50)
≥80	18.00 (15.73-20.60)	13.28 (11.46-15.39)
Sex		
Female	1.00 (ref)	1.00 (ref)
Male	1.68 (1.57-1.80)	1.68 (1.57-1.80)
Obesity		
Not obese	1.00 (ref)	1.00 (ref)
Class I (BMI 30-34.9 kg/m^2)	1.07 (0.98-1.17)	1.07 (0.97-1.17)
Class II (BMI 35-39.9 kg/m^2)	1.25 (1.11-1.41)	1.21 (1.07-1.36)
Class III (BMI ≥40 kg/m^2)	1.83 (1.61-2.09)	1.71 (1.50-1.96)
Smoking		
Never	1.00 (ref)	1.00 (ref)
Former	0.76 (0.70-0.82)	0.69 (0.63-0.75)
Current	0.64 (0.55-0.73)	0.57 (0.49-0.67)
Race/ethnicity		
Non-Hispanic White	1.00 (ref)	1.00 (ref)
Hispanic White	2.76 (2.25-3.38)	2.46 (2.01-3.02)
African American	2.65 (2.41-2.91)	2.27 (2.06-2.50)
Asian	2.30 (1.85-2.85)	2.06 (1.65-2.57)
Region		
West	1.00 (ref)	1.00 (ref)
South	1.85 (1.52-2.27)	1.62 (1.33-1.98)
Northeast	2.63 (2.17-3.18)	2.50 (2.06-3.03)
Midwest	1.49 (1.23-1.81)	1.35 (1.11-1.64)
High blood pressure/hypertension	1.30 (1.18-1.42)	1.08 (0.97-1.20)
Chronic respiratory disease	1.25 (1.16-1.35)	1.21 (1.12-1.32)
Asthma	0.90 (0.81-1.00)	0.81 (0.73-0.90)
Cardiac disease	1.34 (1.24-1.44)	1.10 (1.01-1.19)
Diabetes		
HbA_{1c}[e] <58 mmol/mol	1.28 (1.16-1.41)	1.11 (1.00-1.23)
HbA_{1c} ≥58 mmol/mol	1.99 (1.75-2.26)	1.67 (1.46-1.91)
No recent[f] HbA_{1c} value	2.19 (2.01-2.39)	1.92 (1.75-2.10)
Other cancer (excluding hematological and lung cancer)		
Diagnosed <1 year	0.71 (0.58-0.89)	0.68 (0.55-0.84)
Diagnosed ≥1 year	0.65 (0.59-0.72)	0.61 (0.55-0.67)

Characteristic	Age-sex adjusted model[a], HR (95% CI)	Fully adjusted model (primary analysis)[b], HR (95% CI)
Hematological cancer		
Diagnosed <1 year	1.36 (0.95-1.94)	1.30 (0.91-1.87)
Diagnosed ≥1 year	1.02 (0.83-1.25)	0.97 (0.79-1.19)
Lung cancer		
Diagnosed <1 year	1.61 (1.08-2.40)	1.70 (1.14-2.55)
Diagnosed ≥1 year	0.92 (0.68-1.25)	0.97 (0.71-1.32)
Reduced kidney function[g]		
eGFR[h] 30-60 mL/min[1]/1.73 m^2	1.12 (1.03-1.22)	1.07 (0.98-1.16)
eGFR <30 mL/min[1]/1.73 m^2	2.35 (2.07-2.66)	1.92 (1.69-2.19)
Chronic liver disease	1.19 (1.05-1.35)	1.05 (0.93-1.20)
Stroke or dementia	1.44 (1.33-1.56)	1.25 (1.15-1.36)
Other neurological diseases	1.92 (1.72-2.13)	1.77 (1.59-1.98)
Organ transplant	1.66 (1.35-2.03)	1.35 (1.09-1.67)
RA[i], SLE[j], or psoriasis	0.89 (0.77-1.03)	0.86 (0.74-1.00)
Other immunosuppressive condition	1.35 (1.13-1.62)	1.21 (1.01-1.46)

[a]Univariable Cox proportional hazards model adjusted for age and sex.

[b]Multivariable Cox proportional hazards model containing all covariates other than race; hazard ratios for race were obtained from a separate model using only observations with known race. Missing BMI, smoking status, and estimated glomerular filtration rate (eGFR) were considered to be nonobese, never smokers, and with normal kidney function.

[c]For all models, age was modeled as a restricted cubic spline except for age groups.

[d]ref: reference level.

[e]HBA_{1c}: glycated hemoglobin.

[f]HbA_{1c} values within 15 months before February 1, 2020.

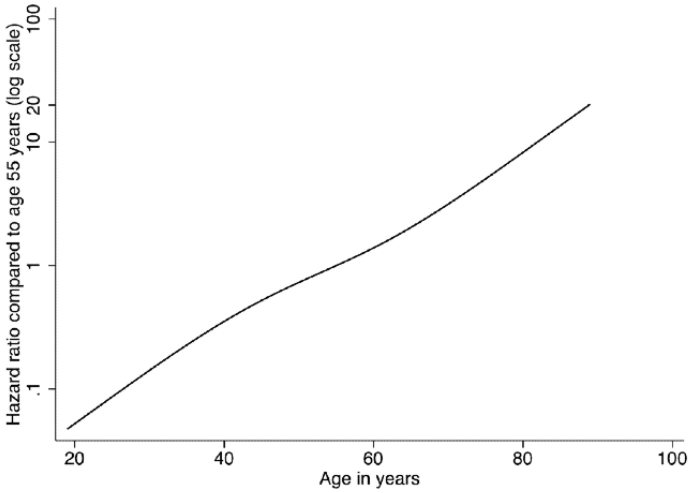
[g]Calculated from the creatinine value.

[h]eGFR: estimated glomerular filtration rate

[i]RA: rheumatoid arthritis.

[j]SLE: systemic lupus erythematosus.

Figure 4. Log-linear relationship between log hazard ratios and age, which was fitted using a restricted cubic spline with 4 knots. The plot was obtained from the fully adjusted model (excluding race) by setting all covariates other than age to the respective reference levels.



In the primary analysis, all the eligible participants were included regardless of SARS-CoV-2 test results. To investigate if the risk factors for death among persons with COVID-19 differed from mortality in the overall cohort, separate Cox proportional hazard models using only the lab-confirmed COVID-19 cases were fit (Figure 5 and Tables 3 and 4). Most of the findings did not differ greatly from the full cohort analysis. The lower risks among current smokers and persons

with other cancers diagnosed within 1 year seen in the primary analysis, however, were eliminated. In addition, the magnitudes of the risk elevations for minority groups were reduced among the COVID-19 patients.

Figure 5. Forest plot showing the hazard ratios (HRs) for each risk factor from the fully adjusted Cox proportional hazards model among COVID-19 patients (n=116,426). The values for race were separately ascertained by fitting a Cox proportional hazards model using only those with known race (n=89,027) and adjusted for all other covariates. The number of COVID-19–related deaths is slightly different from the full cohort (3136 among COVID-19 patients vs 3315 among the full cohort) due to failing or censoring on the same day as being diagnosed with COVID-19. eGFR: estimated glomerular filtration rate.

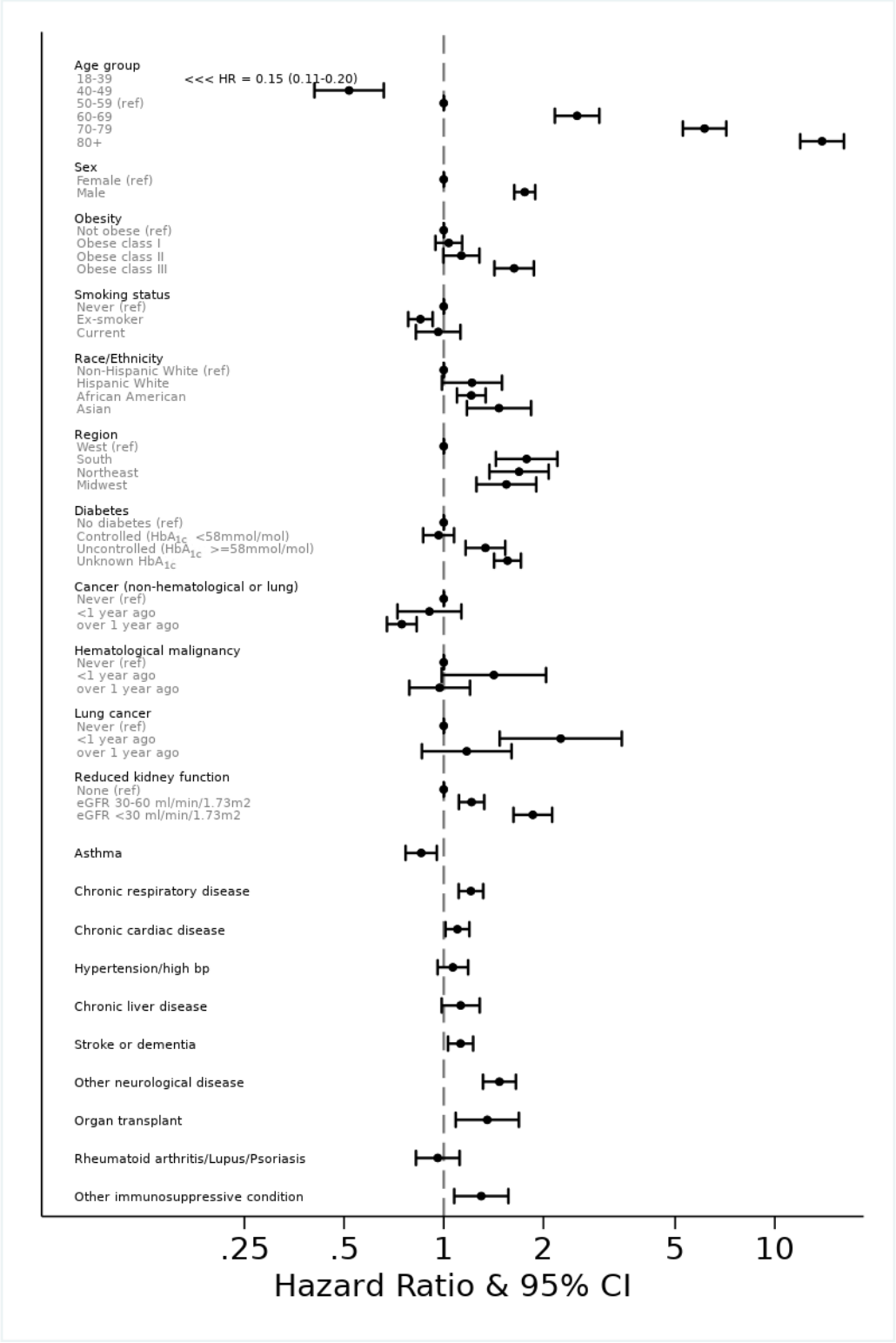


Table 3. Characteristics of the subpopulation of COVID-19–confirmed cases.

Characteristic	Overall sample (n=116,426), n (%)	Number of COVID-19–related deaths (n=3136[a]), n (%)
Age (years)		
18-39	35,207 (30.24)	43 (0.12)
40-49	19,344 (16.61)	93 (0.48)
50-59	22,968 (19.73)	233 (1.01)
60-69	19,409 (16.67)	548 (2.82)
70-79	10,949 (9.40)	827 (7.55)
≥80	8549 (7.34)	1392 (16.28)
Sex		
Female	67,953 (58.37)	1388 (2.04)
Male	48,473 (41.63)	1748 (3.61)
BMI (kg/m^2)		
<18.5	1142 (0.98)	58 (5.08)
18.5-24.9	22,891 (19.66)	650 (2.84)
25-29.9	31,680 (27.21)	869 (2.74)
30-34.9 (obesity class I)	24,232 (20.81)	621 (2.56)
35-39.9 (obesity class II)	13,543 (11.63)	303 (2.24)
≥40 (obesity class III)	11,752 (10.09)	266 (2.26)
Missing	11,186 (9.61)	369 (3.30)
Smoking		
Never	29,452 (25.30)	553 (1.88)
Former	66,351 (56.99)	2053 (3.09)
Current	10,917 (9.38)	218 (2.00)
Missing	9706 (8.34)	312 (3.21)
Race/ethnicity		
Non-Hispanic White	59,162 (50.82)	1833 (3.10)
Hispanic White	5351 (4.60)	96 (1.79)
African American	21,176 (18.19)	536 (2.53)
Asian	3338 (2.87)	83 (2.49)
Missing	27,399 (23.53)	588 (2.15)
Region		
West	9941 (8.54)	98 (0.99)
South	19,490 (16.74)	633 (3.25)
Northeast	41,808 (35.91)	1381 (3.30)
Midwest	45,187 (38.81)	1024 (2.27)
Blood pressure		
Normal[b]	33,932 (29.14)	628 (1.85)
Elevated[c]	16,512 (14.18)	463 (2.80)
High, stage I[d]	42,219 (36.26)	1024 (2.43)
High, stage II[e]	15,406 (13.23)	734 (4.76)
Missing	8357 (7.18)	287 (3.43)
High blood pressure/hypertension		

Characteristic	Overall sample (n=116,426), n (%)	Number of COVID-19–related deaths (n=3136[a]), n (%)
Yes	57,048 (49.00)	2599 (4.56)
No	59,378 (51.00)	537 (0.90)
Chronic respiratory disease		
Yes	13,007 (11.17)	966 (7.43)
No	103,419 (88.83)	2170 (2.10)
Asthma		
Yes	17,140 (14.72)	407 (2.37)
No	99,286 (85.28)	2729 (2.75)
Cardiac disease		
Yes	18,035 (15.49)	1497 (8.30)
No	98,391 (84.51)	1639 (1.67)
Diabetes		
HbA_{1c}[f] <58 mmol/mol	9822 (8.44)	476 (4.85)
HbA_{1c} ≥58 mmol/mol	5207 (4.47)	251 (4.82)
No recent[g] HbA_{1c} value	8879 (7.63)	661 (7.44)
Not diabetic	92,518 (79.47)	1748 (1.89)
Other cancer (excluding hematological and lung cancer)		
Diagnosed <1 year	2294 (1.97)	82 (3.57)
Diagnosed ≥1 year	10,791 (9.27)	453 (4.20)
Never	103,341 (88.76)	2601 (2.52)
Hematological cancer		
Diagnosed <1 year	395 (0.34)	30 (7.59)
Diagnosed ≥1 year	1433 (1.23)	92 (6.42)
Never	114,598 (98.43)	3014 (2.63)
Lung cancer		
Diagnosed <1 year	170 (0.15)	22 (12.94)
Diagnosed ≥1 year	506 (0.43)	41 (8.10)
Never	115,750 (99.42)	3073 (2.65)
eGFR[h] (mL/min/1.73 m^2)[i]		
≥60	67,744 (58.29)	1317 (1.94)
45-59.9	5574 (4.79)	479 (8.59)
30-44.9	2497 (2.14)	340 (13.62)
15-29.9	1003 (0.86)	159 (15.85)
<15	888 (0.76)	113 (12.73)
Missing	38,720 (33.26)	728 (1.88)
Chronic liver disease		
Yes	7367 (6.33)	256 (3.47)
No	109,059 (93.67)	2880 (2.64)
Stroke or dementia		
Yes	9311 (8.00)	866 (9.30)
No	107,115 (92.00)	2270 (2.12)
Other neurological diseases		

Characteristic	Overall sample (n=116,426), n (%)	Number of COVID-19–related deaths (n=3136[a]), n (%)
Yes	3887 (3.34)	368 (9.47)
No	112,539 (96.66)	2768 (2.46)
Organ transplant		
Yes	1090 (0.94)	90 (8.26)
No	115,336 (99.06)	3046 (2.64)
RA[j], SLE[k], or psoriasis		
Yes	4989 (4.29)	181 (3.63)
No	111,437 (95.71)	2955 (2.65)
Other immunosuppressive condition		
Yes	2528 (2.17)	126 (4.98)
No	113,898 (97.83)	3010 (2.64)

[a]179 deaths were excluded, compared with the full cohort, due to failing or censoring on the same day as being diagnosed with COVID-19.

[b]Systolic blood pressure <120 mm Hg; diastolic blood pressure <80 mm Hg.

[c]Systolic blood pressure ≥120 and ≤129 mm Hg; diastolic blood pressure <80.

[d]Systolic blood pressure ≥130 and ≤139 mm Hg; diastolic blood pressure ≥80 and ≤89 mm Hg.

[e]Systolic blood pressure ≥140 or diastolic blood pressure ≥90.

[f]HbA_{1c}: glycated hemoglobin.

[g]HbA_{1c} value within 15 months before February 1, 2020.

[h]eGFR: estimated glomerular filtration rate.

[i]Calculated from the creatinine value.

[j]RA: rheumatoid arthritis.

[k]SLE: systemic lupus erythematosus.

Table 4. Adjusted hazard ratios (HRs) for COVID-19–related death among COVID-19–confirmed cases.

Characteristic	Age-sex adjusted model[a], HR (95% CI)	Fully adjusted model[b], HR (95% CI)
Age[c] (years)		
18-39	0.13 (0.09-0.17)	0.15 (0.11-0.20)
40-49	0.49 (0.38-0.62)	0.52 (0.41-0.66)
50-59	1.00 (ref[d])	1.00 (ref)
60-69	2.76 (2.37-3.22)	2.53 (2.17-2.95)
70-79	7.62 (6.59-8.81)	6.13 (5.28-7.13)
≥80	18.51 (16.11-21.26)	13.89 (11.93-16.17)
Sex		
Female	1.00 (ref)	1.00 (ref)
Male	1.76 (1.64-1.88)	1.76 (1.63-1.89)
Obesity		
Not obese	1.00 (ref)	1.00 (ref)
Class I (BMI 30-34.9 kg/m^2)	1.05 (0.96-1.15)	1.04 (0.94-1.14)
Class II (BMI 35-39.9 kg/m^2)	1.20 (1.06-1.36)	1.13 (1.00-1.28)
Class III (BMI ≥40 kg/m^2)	1.79 (1.57-2.05)	1.63 (1.42-1.87)
Smoking		
Never	1.00 (ref)	1.00 (ref)
Former	0.98 (0.90-1.06)	0.85 (0.78-0.93)
Current	1.15 (0.99-1.33)	0.96 (0.82-1.12)
Race/ethnicity		
Non-Hispanic White	1.00 (ref)	1.00 (ref)
Hispanic White	1.30 (1.06-1.59)	1.22 (0.99-1.50)
African American	1.31 (1.19-1.44)	1.21 (1.10-1.34)
Asian	1.35 (1.08-1.69)	1.47 (1.17-1.84)
Region		
West	1.00 (ref)	1.00 (ref)
South	2.00 (1.62-2.48)	1.78 (1.44-2.20)
Northeast	1.77 (1.44-2.17)	1.69 (1.37-2.07)
Midwest	1.68 (1.36-2.07)	1.55 (1.26-1.90)
High blood pressure/hypertension	1.35 (1.22-1.48)	1.07 (0.96-1.18)
Chronic respiratory disease	1.34 (1.24-1.45)	1.21 (1.11-1.32)
Asthma	0.97 (0.87-1.08)	0.86 (0.77-0.95)
Cardiac disease	1.35 (1.25-1.45)	1.10 (1.01-1.19)
Diabetes		
HbA_{1c}[e] <58 mmol/mol	1.16 (1.05-1.28)	0.96 (0.87-1.07)
HbA_{1c} ≥58 mmol/mol	1.63 (1.43-1.86)	1.34 (1.16-1.53)
No recent[f] HbA_{1c} value	1.80 (1.64-1.97)	1.56 (1.42-1.71)
Other cancer (excluding hematological and lung cancer)		
Diagnosed <1 year	0.94 (0.75-1.17)	0.91 (0.72-1.13)
Diagnosed ≥1 year	0.80 (0.73-0.89)	0.75 (0.67-0.83)

Characteristic	Age-sex adjusted model[a], HR (95% CI)	Fully adjusted model[b], HR (95% CI)
Hematological cancer		
Diagnosed <1 year	1.57 (1.10-2.25)	1.42 (0.99-2.04)
Diagnosed ≥1 year	1.04 (0.84-1.28)	0.97 (0.79-1.20)
Lung cancer		
Diagnosed <1 year	2.41 (1.58-3.67)	2.26 (1.48-3.45)
Diagnosed ≥1 year	1.19 (0.87-1.62)	1.17 (0.86-1.60)
Reduced kidney function[g]		
eGFR[h] 30-60 mL/min/1.73 m^2	1.29 (1.18-1.41)	1.21 (1.11-1.33)
eGFR <30 mL/min/1.73 m^2	2.22 (1.95-2.53)	1.86 (1.62-2.13)
Chronic liver disease	1.28 (1.13-1.46)	1.13 (0.99-1.28)
Stroke or dementia	1.33 (1.23-1.45)	1.12 (1.03-1.23)
Other neurological diseases	1.61 (1.44-1.80)	1.47 (1.31-1.65)
Organ transplant	1.73 (1.40-2.13)	1.35 (1.09-1.69)
RA[i], SLE[j], or psoriasis	1.02 (0.88-1.18)	0.96 (0.82-1.12)
Other immunosuppressive condition	1.52 (1.27-1.82)	1.30 (1.08-1.57)

[a]Univariable Cox proportional hazard model adjusted for age and sex.

[b]Multivariable Cox proportional hazards model containing all covariates other than race; hazard ratios for race were obtained from a separate model using only observations with known race. Missing BMI, smoking status, and estimated glomerular filtration rate (eGFR) were considered to be nonobese, never smokers, and with normal kidney function.

[c]For all models, age was modeled as a restricted cubic spline except for age groups.

[d]ref: reference level.

[e]HbA_{1c}: glycated hemoglobin.

[f]HbA_{1c} values within 15 months before February 1, 2020.

[g]Calculated from the creatinine value.

[h]eGFR: estimated glomerular filtration rate

[i]RA: rheumatoid arthritis.

[j]SLE: systemic lupus erythematosus.

In the primary analysis, participants with missing BMI, smoking status, and eGFR were treated as non-obese, never-smoker, and normal kidney function. To determine whether this affected the results, we fit a separate Cox proportional hazard model using only the participants with complete information on all 3 factors. The HRs were similar to those from the primary analysis, suggesting robustness of the model to missing values (Table 5).

Similarly, due to about 18% of the participants missing a designation of race, the primary multivariable model did not include race. The HRs reported in the primary analysis (Table 2) for race were obtained by a separate Cox proportional hazard model using complete records of race/ethnicity only. HRs for other factors in this model were very similar to those obtained from the primary analysis, suggesting that including race/ethnicity did not alter the model meaningfully (Table 5). The proportional hazards assumption violation was detected for some variables in the primary model (P<.001). Checking the plots of the scaled Schoenfeld residuals versus time, however, revealed no non-zero slopes in any of the factors. The apparent violation of the proportional hazards assumption, therefore, could be due to the large sample size of the study. The C-statistic of the primary model was 0.87, demonstrating a satisfactory discriminative ability in identifying the risks of COVID-19–related death.

Table 5. Sensitivity analyses for the Cox proportional hazards model under various conditions.

Characteristic	Primary analysis (n=1,271,033), HR[a,b] (95% CI)	Cases complete with BMI, smoking status, and eGFR[c] (n=906,359), HR[b] (95% CI)	Cases complete with race/ethnicity (n=1,045,152), HR[b] (95% CI)
Number of outcomes, n	3315	2342	2681
Age[d] (years)			
18-39	0.17 (0.12-0.23)	0.24 (0.16-0.37)	0.15 (0.10-0.23)
40-49	0.57 (0.45-0.72)	0.56 (0.41-0.77)	0.53 (0.40-0.71)
50-59	1.00 (ref[e])	1.00 (ref)	1.00 (ref)
60-69	2.15 (1.85-2.50)	1.96 (1.63-2.37)	2.27 (1.91-2.71)
70-79	4.75 (4.10-5.50)	4.28 (3.56-5.15)	5.32 (4.48-6.30)
≥80	13.28 (11.46-15.39)	12.11 (10.05-14.59)	15.88 (13.37-18.86)
Sex			
Female	1.00 (ref)	1.00 (ref)	1.00 (ref)
Male	1.68 (1.57-1.80)	1.56 (1.43-1.69)	1.73 (1.60-1.87)
Obesity			
Not obese	1.00 (ref)	1.00 (ref)	1.00 (ref)
Class I (BMI 30-34.9 kg/m^2)	1.07 (0.97-1.17)	1.08 (0.97-1.20)	1.02 (0.92-1.13)
Class II (BMI 35-39.9 kg/m^2)	1.21 (1.07-1.36)	1.20 (1.04-1.38)	1.23 (1.07-1.41)
Class III (BMI ≥40 kg/m^2)	1.71 (1.50-1.96)	1.68 (1.44-1.96)	1.75 (1.51-2.03)
Smoking			
Never	1.00 (ref)	1.00 (ref)	1.00 (ref)
Former	0.69 (0.63-0.75)	0.85 (0.75-0.95)	0.75 (0.68-0.82)
Current	0.57 (0.49-0.67)	0.72 (0.60-0.86)	0.62 (0.53-0.74)
Race/ethnicity			
Non-Hispanic White	1.00 (ref)	1.00 (ref)	1.00 (ref)
Hispanic White	2.46 (2.01-3.02)	2.72 (2.19-3.37)	2.46 (2.01-3.02)
African American	2.27 (2.06-2.50)	2.20 (1.97-2.45)	2.27 (2.06-2.50)
Asian	2.06 (1.65-2.57)	2.04 (1.58-2.64)	2.06 (1.65-2.57)
Region			
West	1.00 (ref)	1.00 (ref)	1.00 (ref)
South	1.62 (1.33-1.98)	1.95 (1.49-2.56)	1.51 (1.14-2.01)
Northeast	2.50 (2.06-3.03)	2.92 (2.24-3.80)	2.26 (1.71-3.00)
Midwest	1.35 (1.11-1.64)	1.64 (1.26-2.13)	1.30 (0.98-1.72)
High blood pressure/hypertension	1.08 (0.97-1.20)	1.31 (1.13-1.53)	1.05 (0.93-1.18)
Chronic respiratory disease	1.21 (1.12-1.32)	1.23 (1.12-1.35)	1.23 (1.12-1.35)
Asthma	0.81 (0.73-0.90)	0.82 (0.73-0.92)	0.81 (0.72-0.90)
Cardiac disease	1.10 (1.01-1.19)	1.20 (1.09-1.32)	1.14 (1.04-1.25)
Diabetes			
HbA_{1c}[f] <58 mmol/mol	1.11 (1.00-1.23)	1.11 (0.99-1.24)	0.98 (0.88-1.11)
HbA_{1c} ≥58 mmol/mol	1.67 (1.46-1.91)	1.63 (1.40-1.89)	1.44 (1.24-1.67)
No recent[g] HbA_{1c} value	1.92 (1.75-2.10)	1.85 (1.66-2.07)	1.64 (1.48-1.81)
Other cancer (excluding hematological and lung cancer)			

Characteristic	Primary analysis (n=1,271,033), HR[a,b] (95% CI)	Cases complete with BMI, smoking status, and eGFR[c] (n=906,359), HR[b] (95% CI)	Cases complete with race/ethnicity (n=1,045,152), HR[b] (95% CI)
Diagnosed <1 year	0.68 (0.55-0.84)	0.72 (0.57-0.92)	0.73 (0.57-0.92)
Diagnosed ≥1 year	0.61 (0.55-0.67)	0.63 (0.56-0.70)	0.62 (0.56-0.69)
Hematological cancer			
Diagnosed <1 year	1.30 (0.91-1.87)	1.45 (0.99-2.12)	1.32 (0.89-1.96)
Diagnosed ≥1 year	0.97 (0.79-1.19)	1.07 (0.86-1.32)	1.06 (0.86-1.31)
Lung cancer			
Diagnosed <1 year	1.70 (1.14-2.55)	1.91 (1.26-2.88)	1.63 (1.05-2.54)
Diagnosed ≥1 year	0.97 (0.71-1.32)	0.91 (0.64-1.28)	1.05 (0.76-1.45)
Reduced kidney function[h]			
eGFR 30-60 mL/min/1.73 m^2	1.07 (0.98-1.16)	1.21 (1.10-1.33)	1.17 (1.07-1.28)
eGFR 30 mL/min/1.73 m^2	1.92 (1.69-2.19)	2.15 (1.87-2.47)	1.93 (1.68-2.21)
Chronic liver disease	1.05 (0.93-1.20)	1.14 (0.99-1.31)	1.11 (0.96-1.27)
Stroke/ dementia	1.25 (1.15-1.36)	1.32 (1.20-1.45)	1.29 (1.18-1.41)
Other neurological diseases	1.77 (1.59-1.98)	1.75 (1.55-1.98)	1.82 (1.61-2.05)
Organ transplant	1.35 (1.09-1.67)	1.25 (1.00-1.58)	1.25 (0.99-1.58)
RA[i], SLE[j], or psoriasis	0.86 (0.74-1.00)	0.89 (0.76-1.05)	0.87 (0.74-1.03)
Other immunosuppressive condition	1.21 (1.01-1.46)	1.17 (0.96-1.44)	1.13 (0.92-1.38)

[a]HR: hazard ratio.

[b]Fully adjusted HR.

[c]eGFR: estimated glomerular filtration rate.

[d]For all models, age was modeled as a restricted cubic spline except for age groups.

[e]ref: reference level.

[f]HbA_{1c}: glycated hemoglobin.

[g]HbA_{1c} values within 15 months before February 1, 2020.

[h]Calculated from the creatinine value.

[i]RA: rheumatoid arthritis.

[j]SLE: systemic lupus erythematosus.

Discussion

Principal Findings

This study, using individual-level EHR data from a large population, is one of the largest cohort studies published on this topic in the United States. The results are complementary to those reported from the N3C—the largest US-based cohort to date.

The inclusion of all populations in the primary analysis may raise the doubt of assessing risks for being infected and for death after infection. Our analysis among COVID-19 patients eliminates the concern by showing no apparent differences between the 2 groups.

Our results regarding increasing risks for demographic factors and comorbidities were consistent with various studies [2,6,8,15,16]. In either the full cohort or the COVID-19–positive cases, the risks for the minority groups only reduced slightly in the fully adjusted models compared with the age-sex adjusted models. This was similar to the OpenSAFELY study, in which including other covariates only explained a small portion of the risks expressed by race/ethnicity. This suggested that other socioeconomic factors, such as income, education, housing, and occupation, could play critical roles.

The elevated risk observed in the Northeast was likely due to the fact that, at the earliest stage of the pandemic, it was the disease hot zone where hospital capacity was stretched and evidence-based disease management protocols were not yet developed. Studies that have investigated the relationship between smoking and COVID-19 prevalence or mortality have generated conflicting results. Some suggested that smoking was not associated with COVID-19 [17,18], while others reported that smoking could lead up to twice the risk of COVID-19–related death [19]. Our results from the full or COVID-19–positive cohorts did not support any increased risks associated with smoking. Lower risks of current and prior smokers were observed in the full cohort, but this might be attributable to smokers perceiving that their risks were higher

and thus moderating their risk of viral exposure, rather than to any effect of smoking per se. Studies designed to specially assess the impact of smoking are required to draw a more definitive conclusion.

Many studies have reported a higher risk of severe outcomes of COVID-19 in cancer patients [5,8,20-22]. When examined by cancer types, however, studies in Italy and China showed that lung cancer and hematological malignancies had statistically higher risks of COVID-19–related death, while others did not [20,23]. Our results for cancer were comparable to these findings in which lung cancers and hematological malignancies showed elevated risks, although the HR for hematological malignancies was not statistically significant. Asthma was not associated with an increased risk of COVID-19–related death in this study, which confirms other reports [24,25]. We attempted to stratify asthma based on recent use of oral corticosteroids (OCS) as a proxy for severity, but the limited number of participants (n=333 for recent use of OCS) did not allow a precise estimate.

The prevalence of the comorbidities examined in our study was slightly higher than the National Health Interview Survey 2017 data, as shown in a recent study on a similar topic [26]. This was expected since the present sample was drawn from persons who perceived their risk of COVID-19 to be sufficiently high to warrant testing. A prior report from the Optum COVID-19 data set, although based upon differences in sampling dates and inclusion criteria, yielded similar prevalence estimates to this analysis [27].

Limitations

The current study has some important limitations that must be considered. Unlike the UK's National Health Service, the fragmented health care system in the United States limits the ability to aggregate health records for the general US population. Patients switching to different insurance companies or providers may experience gaps in their electronic medical records, and those without health insurance are much less likely to be seen by the providers contributing to this cohort. The geographic distribution of the participating providers also can affect the representativeness of this sample.

To correctly capture patients' baseline health conditions, we imposed the restriction that only participants with at least 1 year of prior health care engagement were eligible to be included in this study. However, this approach may introduce some selection biases. Those who did not meet this criterion may have different outcomes from COVID-19 infection and therefore, could reduce the generalizability of our study findings.

To protect the identities of individual patients, the exact death date and the cause of death were not included in the data set. Although we have developed a reasonable criterion to define the 2 features (see the Methods section), misestimations are still possible, impacting the risk assessments. In addition, at the early stage of the pandemic, testing and diagnosis coding standards were not fully established, so some persons with COVID-19 may not have been detected. Such misclassification, to the extent that it occurred, would tend to be random and only serve to reduce the associations that were observed.

Conclusion

Identifying patient characteristics associated with increased risks of COVID-19–related death has been an important topic since the start of the pandemic. Using over 1 million patient EHRs to conduct a large cohort survival analysis, we found that age, gender, race, region, and comorbidities including obesity, diabetes, recently diagnosed lung cancer, reduced kidney function, chronic respiratory disease, cardiac disease, stroke or dementia, other neurological diseases, organ transplant, and other immunosuppressive conditions were associated with elevated risks of COVID-19–related death, while smoking, other cancers, asthma, and certain autoimmune diseases were not. Our large and geographically diversified individual-level data provide comprehensive and reliable results on this topic. This study can also serve as a foundation for future policy making about the protection of vulnerable populations, the distribution of vaccines, and other considerations.

Acknowledgments

XJ is a Cancer Prevention & Research Institute of Texas (CPRIT) Scholar in Cancer Research (RR180012), and he was supported in part by a Christopher Sarofim Family Professorship; University of Texas (UT) Stars award; University of Texas Health Science Center (UTHealth) startup; the National Institutes of Health (NIH) under award numbers R01AG066749, R01AG066749-S1, and U01TR002062; and the National Science Foundation (NSF) RAPID #2027790.

We would like to thank Optum for providing the data for this study and J Young for coordinating between UTHealth and Optum. We also thank L Chen for data preprocessing.

Authors' Contributions

UIC and XJ designed the study. UIC conducted all the data cleaning and statistical analyses and wrote the initial manuscript. UIC, RG, and XD performed the disease groupings. HX and TMK provided technical support and comments. XJ supervised the overall project. All authors reviewed and approved the final manuscript.

Conflicts of Interest

None declared.

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Abbreviations

eGFR: estimated glomerular filtration rate
EHR: electronic health record
HbA_{1C}: glycated hemoglobin
HR: hazard ratio
ICD: International Classification of Diseases
N3C: National COVID Cohort Collaborative
NIH: National Institutes of Health
NSF: National Science Foundation
OCS: oral corticosteroids
PCR: polymerase chain reaction
SBMI: School of Biomedical Informatics
UT: University of Texas
UTHealth: University of Texas Health Science Center

Edited by T Sanchez; submitted 02.04.21; peer-reviewed by J Wu, M Zheng; comments to author 30.08.21; revised version received 21.11.21; accepted 01.04.22; published 12.05.22.

Please cite as:
Chen UI, Xu H, Krause TM, Greenberg R, Dong X, Jiang X
Factors Associated With COVID-19 Death in the United States: Cohort Study
JMIR Public Health Surveill 2022;8(5):e29343
URL: https://publichealth.jmir.org/2022/5/e29343
doi:10.2196/29343
PMID:35377319

Original Paper

COVID-19 Vaccination and Public Health Countermeasures on Variants of Concern in Canada: Evidence From a Spatial Hierarchical Cluster Analysis

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Abstract

Background: There is mounting evidence that the third wave of COVID-19 incidence is declining, yet variants of concern (VOCs) continue to present public health challenges in Canada. The emergence of VOCs has sparked debate on how to effectively control their impacts on the Canadian population.

Objective: Provincial and territorial governments have implemented a wide range of policy measures to protect residents against community transmission of COVID-19, but research examining the specific impact of policy countermeasures on the VOCs in Canada is needed. Our study objective was to identify provinces with disproportionate prevalence of VOCs relative to COVID-19 mitigation efforts in provinces and territories in Canada.

Methods: We analyzed publicly available provincial- and territorial-level data on the prevalence of VOCs in relation to mitigating factors, summarized in 3 measures: (1) strength of public health countermeasures (stringency index), (2) the extent to which people moved about outside their homes (mobility index), and (3) the proportion of the provincial or territorial population that was fully vaccinated (vaccine uptake). Using spatial agglomerative hierarchical cluster analysis (unsupervised machine learning), provinces and territories were grouped into clusters by stringency index, mobility index, and full vaccine uptake. The Kruskal-Wallis test was used to compare the prevalence of VOCs (Alpha, or B.1.1.7; Beta, or B.1.351; Gamma, or P.1; and Delta, or B.1.617.2 variants) across the clusters.

Results: We identified 3 clusters of vaccine uptake and countermeasures. Cluster 1 consisted of the 3 Canadian territories and was characterized by a higher degree of vaccine deployment and fewer countermeasures. Cluster 2 (located in Central Canada and the Atlantic region) was typified by lower levels of vaccine deployment and moderate countermeasures. The third cluster, which consisted of provinces in the Pacific region, Central Canada, and the Prairies, exhibited moderate vaccine deployment but stronger countermeasures. The overall and variant-specific prevalences were significantly different across the clusters.

Conclusions: This “up to the point” analysis found that implementation of COVID-19 public health measures, including the mass vaccination of populations, is key to controlling VOC prevalence rates in Canada. As of June 15, 2021, the third wave of COVID-19 in Canada is declining, and those provinces and territories that had implemented more comprehensive public health measures showed lower VOC prevalence. Public health authorities and governments need to continue to communicate the importance of sociobehavioural preventive measures, even as populations in Canada continue to receive their primary and booster doses of vaccines.

(JMIR Public Health Surveill 2022;8(5):e31968) doi:10.2196/31968

KEYWORDS

COVID-19; variants of concern; stringency index; mobility index; vaccination coverage; machine learning; Canada

Introduction

Background

The devastating impacts of COVID-19 cannot be overemphasized. With an estimated 423 million cases and 6 million deaths (as of February 21, 2022) worldwide [1], the pandemic is one of the worst in human history. In Canada alone, about 3.2 million people, representing 8.4% of residents, have been infected with COVID-19 [2]. Canada's case fatality rate for COVID-19 is 1.1% (ie, 36,000 deaths) [2].

At the time our analyses were performed (June 15, 2021, when the third wave was waning), there were 3 forces in "tension": vaccine uptake, newly emerging variants of COVID-19, and calls to "re-open the economy." Since then, the emergence and spread of additional variants of concern (VOCs) and the expansion of vaccination campaigns have changed the complexion of the pandemic. Variants, as expected, have added complexity to the nature of COVID-19. At the same time, following a slow start to vaccination rollouts, vaccine uptake has been increasing in Canada, and many provinces and territories, who are largely responsible for vaccination and public health policy in Canada's decentralized federation, have become eager to relax public health countermeasures. However, public health experts remain uneasy about variant-led surges and outbreaks and are calling for the reapplication of some measures.

As of February 21, 2022, 5 phylogenetic VOCs declared by the World Health Organization are being tracked in Canada. The Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), and Omicron (B.1.1.529) variants, first detected in the United Kingdom, South Africa, Brazil, India, and South Africa, respectively, are spreading in Canada and the rest of the world [3]. Canada confirmed its first cases of the Alpha variant in a couple from Toronto who had contact with a traveler from the United Kingdom on December 26, 2020 [3]. The Beta variant was first reported in Alberta on January 8, 2021 [3]. The Gamma variant was first confirmed in Ontario in an international traveler from Brazil on February 8, 2021 [3]. On April 4, 2021, the Delta variant was first reported in British Columbia [3]. The latest variant (Omicron) was first detected in Ontario from 2 travelers from Nigeria on November 28, 2021 [3].

Although much still remains to be learned about the epidemiology, diagnosis, management, and sequalae of these 5 VOCs, using the data available at the time of analysis, we sought to understand the spread of VOCs in Canada and how they might be held in check by vaccine uptake and public health countermeasures. Although lab-based research and modeling have shown the need to combine public health countermeasures with vaccination to achieve epidemic control [4,5], there has been a paucity of population-level studies to assess the effects of nonpharmaceutical public health measures on VOCs. In a mathematical model of COVID-19 transmission in New York City, public countermeasures such as mask wearing and social distancing were shown to have immediate impact on the epidemic [5]. The synergistic effects of vaccination and public countermeasures in reducing new COVID-19 cases cannot be overemphasized [5]. Alpha and Delta variants are more transmissible than the initial strains of the virus, but the Gamma, Beta, and Delta variants hugely impact vaccine effectiveness. A major concern is the continuous genetic evolution of the virus, which complicates reopening plans across Canada. Although studies are underway to determine the degree of virulence of Omicron variants, it is believed that a subvariant known as BA.2 is more contagious than its predecessor, BA.1, and currently dominating in Canada [6].

Objectives

This "up to the point" analysis of VOCs in Canada (ie, during the downward trajectory of the third wave) examines (1) clustering patterns of COVID-19 mitigation efforts and (2) cluster differences in the prevalence of COVID-19 VOCs in Canada. In doing so, it aimed to provide insights into the differences in the subnational responses to inform ongoing policy and public health interventions at the provincial and territorial levels of government.

Methods

Ethics Approval

This analysis centered on publicly available data with no identifiable information about the people studied. Therefore, research ethics board approval was not required for this study.

Data Sources

We analyzed provincial- and territorial-level data on COVID-19 VOCs in Canada along with data on COVID-19 mitigating strategies from publicly available data sources. Our outcome variable—prevalence of VOCs by type and total—was estimated as the proportion of cases with VOC per 1 million population as of June 15, 2021. The cumulative number of VOC cases for Alpha, Beta, Gamma, and Delta variants was extracted from a COVID-19 VOC tracker in Canada [7]. Populations at risk were predefined as the first quarter, 2021, provincial population estimates obtained from Statistics Canada [8]. Our independent variables—vaccine uptake (the percentage of each provincial or territorial population fully vaccinated against COVID-19), policy response (stringency index—see the following paragraphs for more details), and behavioral changes (mobility index) were mapped with the VOC prevalence outcome. These mitigating factors were selected based on growing evidence that uptake of primary series of vaccination (2 doses) [9-15], reduction in human mobility [16-18], and social distancing policies [19,20] are effective in curtailing community transmission of COVID-19.

During the study period, 3 COVID-19 vaccines (ie, AstraZeneca, Moderna, and Pfizer-BioNTech) were authorized and in use in vaccination campaigns in Canada. Full vaccination coverage

rates were retrieved from the COVID-19 Tracker Canada [21]. As opposed to first dose (ie, partial immunization) rates, full vaccination (2 doses) rates were analyzed in this study because complete vaccination is widely believed to offer greater protection than partial vaccination in slowing down COVID-19 transmission, hospitalizations, disease sequalae, and fatalities [22].

The stringency index is a composite score generated by the researchers at the University of Oxford to document how the governments' coronavirus responses are changing around the world and over time. The metric is an additive score of 9 indicators (ie, school and workplace closures, restrictions on public transport, cancellation of public events and gatherings, stay-at-home policies, travel restrictions, public information campaigns, testing policies, contact tracing, and masking), measured on an ordinal scale, and rescaled to vary from 0 to 100. The lowest possible score is 0 (mildest), and the highest score is 100 (strictest). The policy index was publicly available at the Oxford COVID-19 Government Response Tracker (OxCGRT) website [23]. The constituent variables used in generating the stringency index are summarized in Multimedia Appendix 1. It should be noted that the stringency index is not a measure of effectiveness of government policies in response to COVID-19 but rather a measure of the degree to which and the comprehensiveness of governmental response. To account for the changing patterns of COVID-19 containment policies, average stringency indices for the period of January 1, 2021, to June 15, 2021 were reported.

To assess individuals' compliance with government stringency measures (especially reduction in human movement to slow the spread of the virus), we obtained mobility reports from Google LLC [24]. Recent infodemiological and infoveillance studies [25-29] have utilized mobility reports from Google [24] to observe changes in the movement of people to places designed as high risk based on relative frequency, time, and duration of visits during the pandemic. The technical details of data aggregation and anonymization procedures have been fully described by Aktay et al [30]. Through Google Map's location history feature, daily anonymized data on people's movement to places such as retail and recreation, grocery stores and pharmacies, parks, transit stations, workplaces, and residential areas were collected from smartphones and compared to the baseline 5-week prepandemic period (January 3, 2020, to February 6, 2020). Due to privacy issues, Google could not provide information on the inter- or intraprovincial and territorial movement [30]. Also, in a bid to ensure additional privacy protections, a metric for a given place is discarded when the counts of the opted-in Google users are less than 100 people or the geographical area is less than 30 km^2 [30]. As deemed useful by public health researchers to make critical decisions about COVID-19, the Google community mobility reports help provide insights into how busy certain places are and, thus, the extent to which individuals are engaging in social distancing [30].

To determine mobility patterns across the provinces and territories, we estimated the average number of visits to each category of place (eg, park or workplace) between January 1, 2021, and June 15, 2021. The average of the mobility patterns across the entire study period was estimated to account for changes in movement due to weather and holidays, as well as any within-province variations of public health countermeasures. Using the first component of principal component analysis (PCA), the dimensions of the 6 variables that measured changes in movement of people relative to the pre-COVID era were reduced with the singular value decomposition method and z-score transformation (ie, mean of 0 and variance of 1). The first component (interpreted as the mobility index) explained 60% of the total variance, and its eigenvalue was 3.60. The first component had positive loadings on residential areas (0.47) and parks (0.36), but negative loadings on workplace (–0.5), transit stations (–0.49), grocery stores (–0.11), and retail or recreational centers (–0.39). For each variable, a positive loading suggests a higher mobility index, and negative loading indicates a lower mobility index.

Statistical Analysis

Descriptive statistics were generated. We conducted a spatial agglomerative hierarchical cluster analysis (unsupervised machine learning) to detect clusters of spatial (dis)similarities in COVID-19 mitigating factors in GeoDa version 1.18 software [31]. Furthermore, we determined differences in prevalence of VOCs across the clusters. A symmetrical distance-based weight matrix with an optimal arc distance of 7000 km was generated. After many calibrations, single-linkage clustering with an Euclidean distance function and geometric centroid weight of 1 was considered appropriate and used.

A spatial hierarchical cluster analysis was performed using the mitigating factors (ie, vaccine uptake, public health countermeasures, and mobility). With the single linkage, intercluster distance was determined by the closest distance between the observations (ie, closest neighbor clustering). The first step was to transform the independent variables using z-score standardization since they were in different scales. Z-score standardization is an important preprocessing step for a machine learning algorithm, which involves rescaling the features to have a normal distribution. Data standardization before PCA has been shown to outperform an unscaled data set [32]. In an attempt to select the number of clusters that provided the best fit (distinct clustering), we used a stopping rule—the Duda-Hart index. We selected groups with the highest Duda-Hart index (0.6) and lowest pseudo T-squared (4.4). The stopping rule corresponds to the 3 clusters reported.

The Kruskal-Wallis equality-of-population rank test was used to determine the differences in the prevalence of VOCs among the clusters using Stata version 17.0 software [33]. A rank-based nonparametric test was used because the sample size is small (ie, 11 provinces and territories). Post hoc pairwise (posteriori) comparisons of the clusters were performed with the Dunn test; false detection rates were minimized by using Benjamini-Hochberg adjustment. The statistical significance was set at 2-sided $P<.05$. To visualize the relationships between the prevalence of VOCs, vaccine uptake, and countermeasures, bivariate choropleth maps were generated in QGIS version 3.12.1 software [34]. The bivariate maps were based on a quantile classification (ie, tertile); see Figures 1-3. As shown,

the 3x3 2D color palette density becomes progressively darker as it moves from lower to higher tertiles and highlights the differences in relative position of features. The tertile classification is based on the sample distribution. We report the observed value ranges for each tertile classification.

Results

Descriptive Statistics

Table 1 shows the distribution of COVID-19 VOCs in Canada. As of June 15, 2021, when our analysis was performed, 4 VOCs (Alpha, B.1.1.7; Beta, B.1.351; Gamma, P.1; and Delta, B.1.617.2) had been identified, for a prevalence of 6157.5 per 1 million population and 16.7% of all cases. Nova Scotia reported the lowest, at 89.9 per 1 million population, to Alberta the highest, at 10,848.1 per 1 million population. At 91.4% of all VOCs, the Alpha variant was the predominant strain in Canada. The Gamma variant accounted for 6.5%, Beta variant for 0.8%, and Delta variant for 0.8% of the mutant strains. Although Alberta and Ontario had a higher prevalence of the Alpha variant, lower prevalence of this strain was observed in Yukon and Nova Scotia. The prevalence of the Beta variant was highest in Ontario, followed by Quebec. The Gamma and Delta variants were more common in British Columbia and Alberta.

Compared with the baseline (January 3, 2020-February 6, 2020), mobility related to home or residential areas increased by 12.7% between January 1, 2021, and June 15, 2021, among Canadians. On average, movement of people to parks and outdoor spaces increased by 38.8%; however, in Prince Edward Island, it decreased (average trend=–45%). Overall, mobility related to visits to grocery or pharmacy stores decreased by 4.6% across Canada but increased in Nova Scotia (by 2.6%), British Columbia (2.5%), and Saskatchewan (1.9%). Across Canada, movement related to public transport stations decreased by 56.5%, retail and recreational centers by 29.4%, and workplaces by 31.3%. The average national stringency index for COVID-19 was 73.6% (lowest in Yukon at 47.2% and highest in Ontario at 90.7%). The Canadian population fully vaccinated against COVID-19 was 13.8% (lowest in Newfoundland and Labrador at 5.7% and highest in Yukon at 61.6%).

Table 1. Geographic-specific distribution of COVID-19 variants of concern in Canada, June 15, 2021 (per 1,000,000 population).

Location	Overall	Alpha B.1.1.7	Beta B.1.351	Gamma P.1	Delta B.1.617.2
Nunavut	532.9	532.9	0	0	0
Newfoundland and Labrador	374.68	359.31	11.53	1.92	1.92
Prince Edward Island	175.2	162.68	0	0	12.51
Nova Scotia	89.85	74.53	12.25	1.02	2.04
New Brunswick	236.55	230.16	5.11	1.28	0
Quebec	900.43	791.63	47.81	56.9	4.08
Ontario	9919.34	9530.06	77.06	280.38	31.85
Manitoba	4597.61	4371.68	32.59	120.21	73.14
Saskatchewan	5461.34	5200.06	8.48	195.96	56.84
Alberta	10,848.11	10,122.95	35.16	609.52	80.47
British Columbia	3626.21	1963.5	26.2	1465.35	171.16
Yukon	189.61	71.10	0	118.51	0
Northwest Territories	1705.96	1683.8	0	22.16	0
Canada (overall)	6157.47	5655.01	50.33	401.75	50.38

Spatial Hierarchical Clustering

Cluster analysis with the single-linkage method identified 3 cluster profiles of VOC prevalence, vaccine uptake, public health countermeasures, and mobility among Canadian provinces or territories (see Table 2). The clusters were significantly different from one another in their average prevalence of COVID-19 variant cases and variant-specific prevalence, vaccine uptake, and public health countermeasures (see Table 2). Multimedia Appendix 2 shows the frequency distribution of the variables after Benjamini-Hochberg correction for post hoc pairwise comparisons.

Yukon, Northwest Territories, and Nunavut—the first cluster—had a moderate prevalence of VOCs, high vaccine uptake (fully vaccinated), and low countermeasures. The 4 Atlantic provinces, New Brunswick, Newfoundland and Labrador, Nova Scotia, Prince Edward Island, and Quebec—the second cluster—had a low prevalence of VOCs, low vaccine uptake (fully vaccinated), moderate mobility, and moderate countermeasures. The 4 western provinces, British Columbia, Alberta, Saskatchewan, and Manitoba, along with Ontario—the third cluster—showed a high prevalence of VOCs, moderate vaccine uptake, high mobility, and high countermeasures.

Table 2. Characteristics of clusters from spatial hierarchical clustering analysis of mitigating factors.

Characteristics	All clusters (n=13)	Cluster 1: YT[a], NT[b], NU[c] (n=3)	Cluster 2: NB[d], NL[e], NS[f], PE[g], QC[h] (n=5)	Cluster 3: AB[i], BC[j], MB[k], ON[l], SK[m] (n=5)	*P* value[n]
Variants of concern (cases per 1 million population), median (IQR)					
All (B.1.1.7, B.1.351, P.1, and B.1.617.2)	900.43 (236.55 to 4597.61)	532.9 (189.61 to 1705.96)	236.55 (175.20 to 374.68)	5461.33 (4597.61 to 9919.34)	.01
Only Alpha B.1.1.7	791.63 (230.16 to 4371.68)	532.9 (71.1 to 1683.8)	230.16 (162.68 to 359.31)	5200.06 (4371.68 to 9530.06)	.01
Only Beta B.1.351	11.53 (0 to 32.59)	0	11.53 (5.11 to 12.25)	32.59 (26.20 to 35.16)	.04
Only Gamma P.1	56.9 (1.28 to 195.96)	22.16 (0 to 118.51)	1.28 (1.02 to 1.92)	280.38 (195.96 to 609.52)	.01
Only Delta B.1.617.2	4.08 (0 to 56.84)	0	2.04 (1.92 to 4.08)	73.14 (56.84 to 80.47)	.007
2-dose vaccine coverage (%), median (IQR)	13.83 (10.85 to 18.89)	58.53 (40.39 to 61.56)	10.49 (5.67 to 10.85)	15.85 (13.83 to 17.98)	_[o]
Stringency index (%), mean (SD)	67.411 (11.41)	58.49 (9.78)	68.61 (10.09)	71.57 (12.55)	_[o]
Mobility index (z-score change), median (IQR)	0.41 (–1.04 to 1.25)	–2.09 (–3.22 to –1.04)	0.41 (–1.04 to 0.7)	1.25 (1.19 to 1.31)	_[o]

[a]YT: Yukon.

[b]NT: Northwest Territories.

[c]NU: Nunavut.

[d]NB: New Brunswick.

[e]NL: Newfoundland and Labrador.

[f]NS: Nova Scotia.

[g]PE: Prince Edward Island.

[h]QC: Quebec.

[i]AB: Alberta.

[j]BC: British Columbia.

[k]MB: Manitoba.

[l]ON: Ontario.

[m]SK: Saskatchewan.

[n]Intercluster differences assessed with the Kruskal-Wallis test.

[o]Analyses of the differences in vaccine coverage, stringency index, and mobility index across the clusters were not conducted because they contributed to the cluster analysis. Probabilistic assessment of the differences of these 3 variables across the clusters, therefore, was inappropriate.

Cluster Profile 1 (Yukon, Northwest Territories, and Nunavut; 23% of Variance): Moderate Prevalence of VOCs, High Vaccine, Low Stringency, and Low Mobility

Compared with the other clusters, the Northwest Territories, Nunavut, and Yukon were characterized by a moderate prevalence of aggregated VOCs and the Alpha variant (533 per 1 million population) and the Gamma variant (22 per 1 million population). It is important to note that the Beta and Delta variants had not been identified in the 3 territories of cluster 1. In addition, cluster 1 had the highest proportion of Canadians who had received 2 doses of COVID-19 vaccines (58.5%), lowest mobility index (–2.1), and lowest stringency index (58.5%).

Cluster Profile 2 (New Brunswick, Newfoundland and Labrador, Nova Scotia, Prince Edward Island, and Quebec; 38.46% of Variance): Low Prevalence of VOCs, Low Vaccination, Moderate Stringency, and Moderate Mobility

Compared with the other clusters, cluster 2 was characterized by the lowest prevalence of aggregated VOCs (237 per 1 million population), the Alpha variant (230 per 1 million population), and the Gamma variant (1 per 1 million population). However, it had relatively moderate levels of the Beta (12 per 1 million population) and Delta (2 per 1 million population) variants. In addition, cluster 2 had the lowest full vaccination coverage rates (10.5%), a moderate mobility index (0.4), and a moderate stringency index (68.6%).

Cluster Profile 3 (Alberta, British Columbia, Manitoba, Ontario, and Saskatchewan; 38.46% of Variance): High Prevalence of VOCs, Moderate Vaccination, High Stringency, and High Mobility

Compared with the other clusters, cluster 3 had the highest prevalence of VOCs (5461 per 1 million population) and variant-specific prevalences—Alpha (5200 per 1 million

population), Beta (33 per 1 million population), Gamma (280 per 1 million population), and Delta (73 per 1 million population). Also, cluster 3 had moderate fully vaccinated coverage rates (15.9%), the highest mobility index (1.3), and the highest stringency index (71.6%).

COVID-19 Variants of Concern and Vaccine Uptake

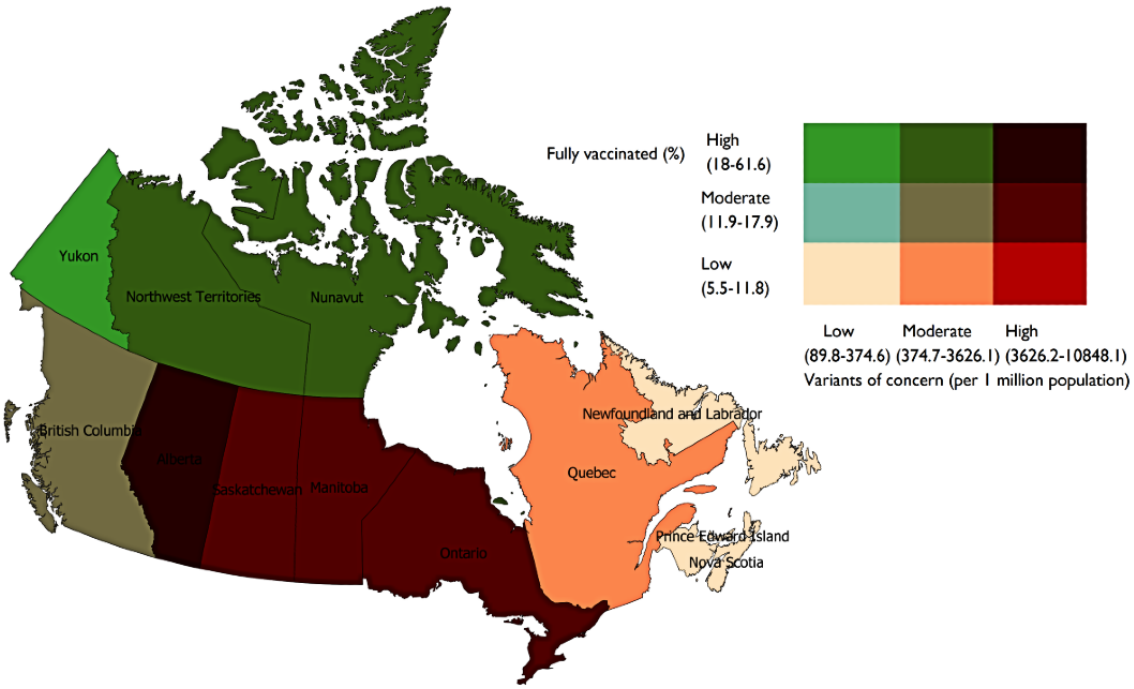
Figure 1 shows the distribution of VOCs and the proportion of Canadians who received the complete schedule of COVID-19 vaccine by province. Provinces shown in the darkest color (towards the top right in the legend in map) have relatively high VOC prevalences and high vaccination rates; those in the lightest color (bottom left) have low VOC prevalences and low vaccination rates.

Of all provinces and territories, Alberta was classified as having a marginally higher vaccine rate and high VOC prevalence: 18.9% of people fully vaccinated and VOC prevalence of 10,848 per 1 million population. Ontario (9919 per 1 million population), Saskatchewan (5461 per 1 million population), and Manitoba (4598 per 1 million population) had the high prevalences of VOCs and relatively moderate vaccine uptake rates (Ontario: 13.8%; Manitoba: 15.9%; and Saskatchewan: 18%).

At the opposite end, meaning low VOC prevalences and low vaccine rates, the Atlantic provinces with low VOC prevalences and low vaccine rates were Nova Scotia (VOC prevalence of 90 per 1 million population and 5.6% vaccine rate), Prince Edward Island (175 per 1 million population and 10.9%), New Brunswick (237 per 1 million population and 10.5%), and Newfoundland and Labrador (374 per 1 million population and 5.7%).

Québec and British Columbia had moderate VOC prevalences and vaccine uptake rates (Quebec, VOC prevalence of 900 per 1 million population and vaccine rate of 11.9%, and British Columbia, VOC prevalence of 3626 per 1 million population and vaccine rate of 12.8%). Yukon had a low prevalence of VOCs (190 per 1 million population) and high vaccine rate (41.6%), followed by the Northwest Territories (1706 per 1 million population and 58.53%) and Nunavut (533 per 1 million population and 40.4%).

Figure 1. Association between variants of concern and 2 doses of COVID-19 vaccine in Canada as of June 15, 2021.



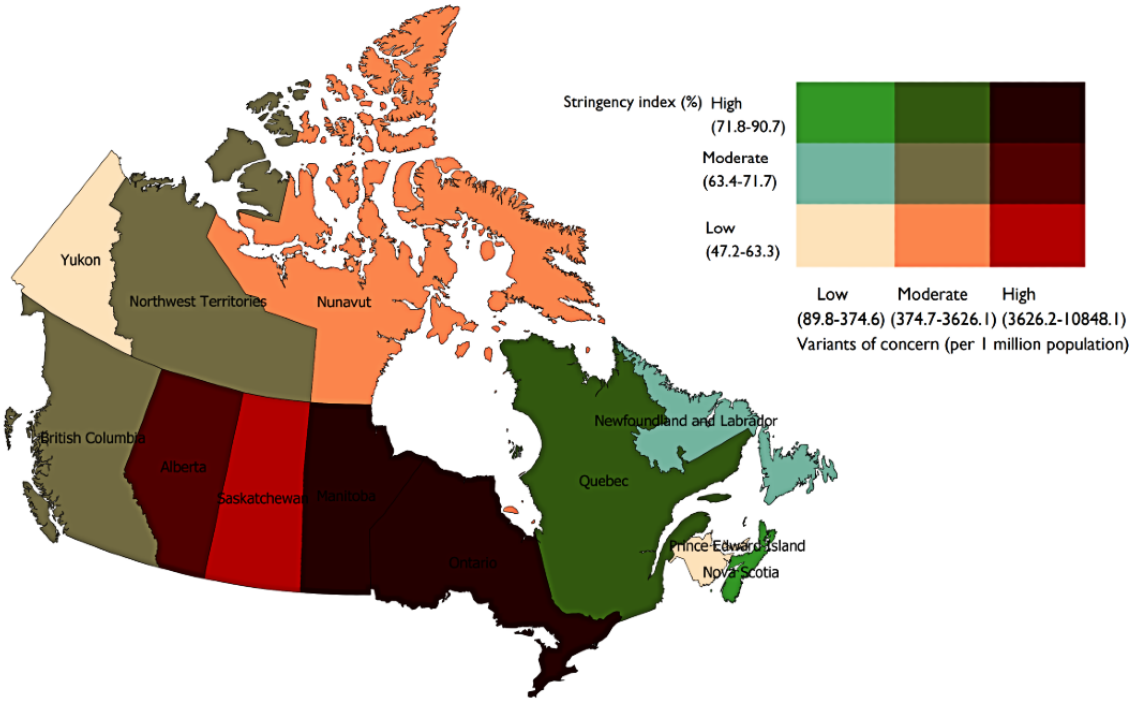
COVID-19 Variants of Concern and Public Health Countermeasures

Figure 2 shows the relationship between the prevalence of VOCs and government stringency measures to curb COVID-19. The provinces of Ontario and Manitoba showed higher prevalences of VOCs (9919 and 4598 per 1 million population, respectively) and high scores on the stringency index—Ontario: 90.7% and Manitoba: 75.9%. Saskatchewan recorded a higher prevalence of VOCs (5461 per 1 million population) and lower stringency (57.9%). Alberta had a high prevalence of VOCs (10,848 per 1 million population) and moderate stringency (68.5%).

The province of Quebec had a moderate level of VOC prevalence (900 per 1 million population) with high stringency (73.2%). British Columbia and Northwest Territories had moderate prevalences of VOCs (3626 per 1 million population and 1706 per 1 million population, respectively) and moderate levels of stringency—British Columbia: 64.8% and Northwest Territories: 64.8%.

At the low end of VOC prevalence, Yukon, Prince Edward Island, and New Brunswick had lower stringency—Yukon: 47.2%; Prince Edward Island: 58.3%; and New Brunswick: 58.3%. Nova Scotia reported a lower prevalence of VOCs (90 per 1 million population) and relatively higher stringency (81.5%), and Newfoundland and Labrador had a lower prevalence of VOCs, at 374 per 1 million population, and moderate stringency, at 71.8%.

Figure 2. Association between variants of concerns and stringency measures in Canada as of June 15, 2021.



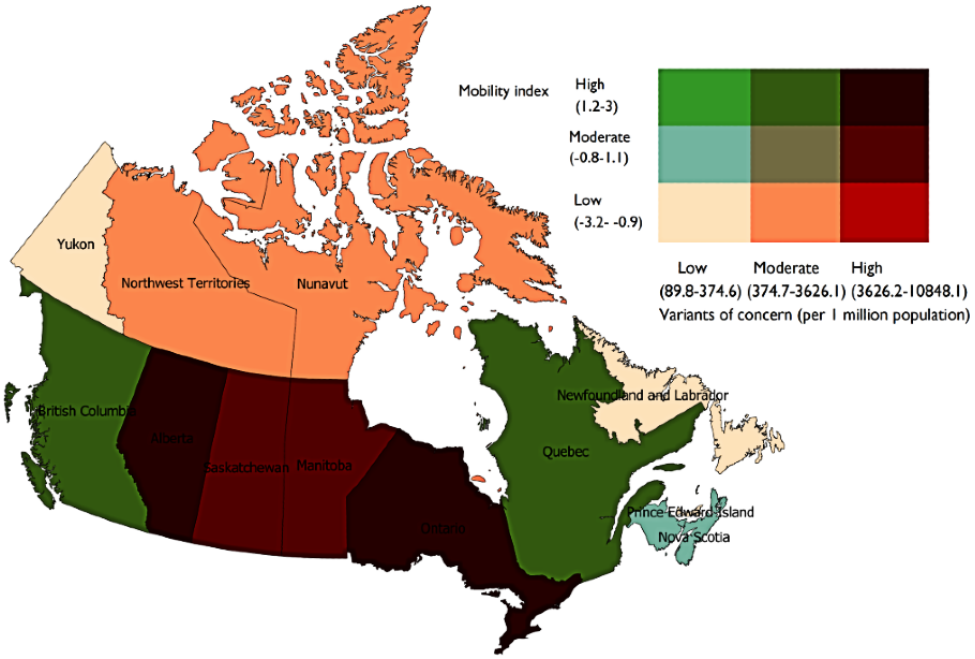
COVID-19 Variants of Concern and Mobility Index

Figure 3 presents the association between the prevalence of VOCs and changes in movement of people in relation to the beginning of the pandemic (mobility index). Among the provinces reporting higher VOC prevalences, populations in Ontario and Alberta showed higher mobility indices—Ontario: 3.0 and Alberta: 1.3. In this higher-prevalence VOC group, Manitoba and Saskatchewan populations had moderate mobility indices—1.2 and 0.2, respectively.

Among the provinces and territories reporting moderate VOC prevalences, Quebec and British Columbia recorded higher mobility indices—Quebec: 2.1 and British Columbia: 1.3—while Northwest Territories (–1.0) and Nunavut (–3.2) had lower mobility indices.

Two of the 4 Atlantic provinces, Prince Edward Island and Newfoundland and Labrador, and Yukon recorded low VOC prevalences and low mobility indices—Prince Edward Island at –2.7, Newfoundland and Labrador at –1.0, and Yukon at –2.1. Nova Scotia and New Brunswick recorded low prevalences of VOCs and moderate mobility, at 0.7 and 0.4, respectively.

Figure 3. Association between variants of concern and mobility index in Canada as of June 15, 2021.



Discussion

Principal Findings

This study shows markedly elevated prevalence of COVID-19 VOCs in Canada and wide geographical variation across the provinces and territories. We observed that the provinces in cluster 3—the Pacific region, Central Canada, and the Prairie provinces—were hot spots of VOCs as determined by the highest cluster-level prevalence of aggregated and variant-specific VOCs. We also observed that there was "north-south" disparity between the territories and the provinces in the prevalence of variant-specific VOCs, vaccine coverage, and public health countermeasures.

As with most COVID-19 research, this study sought to understand the disease as it is unfolding: specifically, COVID-19 VOCs in Canadian provinces and territories. By June 15, 2021, the daily new case rates in all Canadian provinces and territories were declining, indicating the resolution phase of the third wave of the epidemic curve. Many provinces set in motion plans to relax public health countermeasures, relying on vaccination rates as the criterion for reopening. At the same time, however, there was since-validated concern that the VOCs, in particular the Delta variant, could trigger widespread outbreaks, especially among the unvaccinated or partially vaccinated.

Across Canadian provinces and territories, we have shown a pattern of VOC spread, vaccine uptake (both doses), and policy countermeasures that can be profiled in 3 clusters. The first cluster, comprising all 3 Canadian territories, is characterized by moderate VOC prevalence, higher degree of vaccine uptake, and lesser degree of governmental countermeasures. The second cluster, comprising the Atlantic provinces of Nova Scotia, Prince Edward Island, Newfoundland and Labrador, and New Brunswick, along with the province of Quebec, is characterized by low VOC prevalence, low vaccine uptake, and moderate stringency of countermeasures. The third cluster, comprising Ontario, Manitoba, Saskatchewan, Alberta, and British Columbia, is characterized by high prevalence of VOCs, moderate vaccine uptake, and more stringent countermeasures. Strikingly, intercluster disparity in the prevalence of VOCs is more evident for cluster 3, making the provinces in that group VOC hot spots.

As governments across Canada continue to enact plans for easing public health countermeasures, there is concern that provinces and territories need to have much higher rates of vaccination with both primary and booster doses. Although per capita case rates are declining across Canada, there has been a recent increase in the highly transmissible VOCs, Delta and Omicron, in provinces [35,36]. These recent regional outbreaks were seen mostly among unvaccinated people [37].

As Canadian health officials strive to get as many people vaccinated within the shortest time possible, policy countermeasures may need to be further calibrated depending on the local spread of VOCs and vaccine hesitancy and refusals [38,39]. There have been several alarms raised that the B.A2 subtype of Omicron variant could become dominant if an insufficient proportion of the population did not complete the full COVID-19 primary vaccination regimen and receive booster doses [13]. In a past study conducted in Scotland, the first dose was shown not to confer complete immunity against the emerging variants versus the Alpha variant; however, full vaccination (2 doses) combined with booster shots improves immune effectiveness [38]. Our present study confirms that, in the postvaccine period in Canada (ie, December 2020), vaccination coverage rates are uneven across the country.

At least three strains of VOC with different transmission risks and responses to COVID-19 vaccines were concomitantly identified in more than half of the provinces. Like in the United States [15], in the first quarter of 2021, the dominant variant in Canada was the Alpha variant. According to Davies et al [14], the Alpha variant had a high reproductive number (43%-90%). However, a more worrying observation during the study period was the identification of 2 highly virulent variants (Beta and Delta) in 77% of the provinces. Due to the key mutations at E484K and K417N receptor-binding sites of the spike proteins for Beta [10-13] and L452R receptors for Delta [40], both variants are capable of escaping recognition by neutralizing antibodies (nAbs), thus evading both natural and vaccine-induced immunity. Also, T478K is not well recognized as responsible for immune evasion for Delta variants and may, like N501Y, be more relevant for angiotensin-converting enzyme 2 (ACE2) binding; however, additional mutations at K417N have been reported for the Delta variant [41]. Given the relatively high prevalence of the Gamma variant in some provinces or territories (ie, British Columbia, Alberta, Ontario, Saskatchewan, Manitoba, and Yukon), the Gamma variant also evades the immune system (but less so than the Beta variant) through a significant change in an nAb epitope (E484K and K417T).

This observation has far-reaching consequences on health outcomes and prolongation of the epidemic due to new infections. Considering the high prevalence of Beta, Gamma, Delta, and Omicron variants in some provinces (ie, Ontario, Quebec, Alberta, British Columbia, Saskatchewan, and Manitoba), stakeholders should continue to emphasize 2-dose vaccine uptake combined with booster shots and maintenance of public health countermeasures such as mask wearing and social distancing. Although the structural and operational barriers to vaccination (eg, vaccine stock shortages, long wait times, and vaccine refusal or hesitancy) need to be tackled, people must be adequately sensitized to complete the second and booster doses to offer full population protection against the VOCs (especially Beta, Gamma, Delta, and Omicron), thereby reducing future risk of new variants.

The discordance between VOC prevalence and stringency measures warrants cautious interpretation. Our analysis could not show whether the relaxation of countermeasures in the territories of Canada was informed by declining COVID-19 cases and progressive vaccine rollout, or vice versa. This inverse relationship, which is quite possible, means the timing of implementation of polices in relation to the changing epidemiological contexts of the pandemic is important. The degree of social compliance with government stringency measures might also depend on seasonality effects. Stringency measures may reduce COVID-19 incidence not only directly,

for example, by reducing mobility, exposure, and public circulation but also indirectly through weather on mobility patterns [18,42]. Although we attempted to reduce the effect of weather by taking the average of mobility indices from January 2021 to June 2021, there might be some residual effects because of the varying daily temperatures across the provinces and territories. In our study, we observed low mobility index and stringency index in the territories, in contrast to the provinces.

At the time of conducting this study, no comprehensive time series data were easily available for Canada. Further investigation with time series will shed more light on the observed phenomenon. However, we could establish that successful immunization campaigns and reducing human mobility in the territories in northern Canada have played a role in lowering VOC cases. Fast tracking second-dose vaccination not only is key to return to normalcy but also has been shown in previous studies [14,43] to curtail transmission of COVID-19 variants.

Our results noted some spatial outliers (ie, discordant areas) for the relationship between the selected public health measures and VOCs in Ontario and in the Canadian Prairie provinces. To optimize public health impacts, these provinces need to revisit some of their approaches and reprioritize specific interventions. It is also noteworthy to further examine the intraprovincial variations between the public health measures and patterns of VOCs for the spatial outliers.

Strengths and Limitations

The novelty of this study is that no known published study has described spatial clusters based on VOCs, vaccination coverage, and public health measures for Canadian jurisdictions. Overall, this study contributes to the current information needs to guide stakeholders on preventive measures to curtail VOCs during subsequent waves of the COVID-19 pandemic. Specifically, evidence from this study could serve as a comparison point for informing interventions for future variant-driven outbreaks and surges. Also, the bivariate choropleth map eased readability of spatial patterns, compared with proportional symbol maps. This study has some limitations. The recommendations for administration of different vaccine products (eg, messenger ribonucleic acid [mRNA]–based, viral vector–based) have been quite fluid in Canada; we have not taken into consideration the spatial associations between different vaccine products and VOCs. Further research is needed to specifically assess the geographical patterns of vaccine products and VOCs, especially for the Beta, Gamma, Delta and Omicron variants. As mentioned, this is an ongoing information need, rather than a one-time project.

The biggest limitation, however, is the time lag and the uneven testing, detecting, and sequencing efforts to identify VOCs in Canada. Whole genomic sequencing (WGS) efforts to identify VOCs by large volumes are currently lagging in Canada. Also, there is selection bias of the samples that are sent for sequencing. The provinces and territories have different criteria for sending samples for sequencing, which could delay detection and bias the proportion of VOCs associated with the Beta and Gamma variants. For example, in Ontario, the WGS was triggered from quantitative polymerase chain reaction (qPCR) testing for E48K. The samples with the E48K mutations were prioritized for WGS. However, in May 2021, the WGS algorithm changed to randomly selected sampling of 10% positives, with the proportion then increasing to 50% and now to all positives. This calls for new and rapid detection methods for VOCs even as Canada continues to fully vaccinate its populations. Also, there is possibility of systematic bias in the Google mobility index being underestimated among people without smartphones, who opted-out of the Google's location history feature, or who had poor internet connection (especially in the territories). Due to how the mobility patterns were captured by Google LLC—geographical jurisdiction—it is challenging to delineate international travels and interprovincial and territorial mobility.

Conclusions

This study found that COVID-19 VOCs in Canadian provinces and territories, to date, show discernible geographical clustering patterns: The territories recorded low VOC prevalences, Atlantic provinces and Quebec recorded moderate VOC prevalences, and the Western provinces and Ontario recorded high VOC prevalences. A fuller picture of VOC emerges when its prevalence is correlated with the proportions of populations having received 2 doses of vaccines, governmental countermeasures, and mobility. The implementation of COVID-19 public health measures including mass full vaccination of populations are key to controlling VOC prevalence rates in Canada. Surveillance of VOCs should continue across Canada, while accelerating the rollout of second and booster doses of vaccines. Achieving a balance in relation to lifting and relaxation of public health countermeasures and full-dose vaccine coverage is prudent to preempt any VOC-driven COVID-19 surges.

Acknowledgments

The authors would like to acknowledge the valuable feedback on previous drafts provided by colleagues in the Canadian Institutes of Health Research (CIHR) Coronavirus Variants Rapid Response Network (CoVaRR-Net), specifically Dr Anne-Claude Gingras (Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, Sinai Health and Department of Molecular Genetics, University of Toronto) and Dr Marc-Andre Langlois (Director of the University of Ottawa Biocontainment Facility and Department of Biochemistry, Microbiology and Immunology, University of Ottawa).

This work is supported by a CIHR Coronavirus Variants Rapid Response Network grant, FRN# 175622 (nominated principal applicant: Marc-Andre Langlois; co-applicants include NM, CN, and CAC).

Data Availability

Data on the cumulative number of variant of concern (VOC) cases can be downloaded from CTV News COVID-19 variants of concern tracker [7], and vaccine coverage rates are available at the COVID-19 Vaccination Tracker [21]. Provincial- and territorial-level population estimates are available from Statistics Canada [8]. The stringency index can be obtained at the Oxford COVID-19 Government Response Tracker (OxCGRT) website [23]. The mobility reports can be downloaded from Google LLC [24]. Researchers who require access to the study data can contact the corresponding author for further information.

Authors' Contributions

The corresponding author and supervisor for this study is NM. NM and DAA were responsible for the conception and development of the study. DAA extracted and completed the statistical analysis of the data. DAA drafted the manuscript, and NM, CAC, CN, and WNM revised the manuscript for important intellectual content. All the authors approved the final version for publication and agreed to be accountable for the work.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Description of variables.
[DOCX File , 18 KB - publichealth_v8i5e31968_app1.docx]

Multimedia Appendix 2
Post-hoc pairwise comparison of the clusters.
[DOCX File , 18 KB - publichealth_v8i5e31968_app2.docx]

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Abbreviations

ACE2: angiotensin-converting enzyme 2
CIHR: Canadian Institutes of Health Research
CoVaRR-Net: CIHR Coronavirus Variants Rapid Response Network
mRNA: messenger ribonucleic acid
nAbs: neutralizing antibodies
OxCGRT: Oxford COVID-19 Government Response Tracker
PCA: principal component analysis
qPCR: quantitative polymerase chain reaction
VOC: variant of concern
WGS: whole genomic sequencing

Edited by T Sanchez, A Mavragani; submitted 12.07.21; peer-reviewed by L Nweke, J Park; comments to author 02.02.22; revised version received 23.02.22; accepted 26.04.22; published 31.05.22.

Please cite as:
Adeyinka DA, Neudorf C, Camillo CA, Marks WN, Muhajarine N
COVID-19 Vaccination and Public Health Countermeasures on Variants of Concern in Canada: Evidence From a Spatial Hierarchical Cluster Analysis
JMIR Public Health Surveill 2022;8(5):e31968
URL: https://publichealth.jmir.org/2022/5/e31968
doi:10.2196/31968
PMID:35486447

Original Paper

Individual-Level Evaluation of the Exposure Notification Cascade in the SwissCovid Digital Proximity Tracing App: Observational Study

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Abstract

Background: Digital proximity tracing (DPT) aims to complement manual contact tracing (MCT) in identifying exposed contacts and preventing further transmission of SARS-CoV-2 in the population. Although several DPT apps, including SwissCovid, have shown to have promising effects on mitigating the pandemic, several challenges have impeded them from fully achieving the desired results. A key question now relates to how the effectiveness of DPT can be improved, which requires a better understanding of factors influencing its processes.

Objective: In this study, we aim to provide a detailed examination of the exposure notification (EN) cascade and to evaluate potential contextual influences for successful receipt of an EN and subsequent actions taken by cases and contacts in different exposure settings.

Methods: We used data from 285 pairs of SARS-CoV-2-infected cases and their contacts within an observational cohort study of cases and contacts identified by MCT and enrolled between August 6, 2020, and January 17, 2021, in the canton of Zurich, Switzerland. We surveyed participants with electronic questionnaires. Data were summarized descriptively and stratified by exposure setting.

Results: We found that only 79 (58.5%) of 135 contacts using the SwissCovid app whose corresponding cases reported to have triggered the EN also received one. Of these, 18 (22.8%) received the EN before MCT. Compared to those receiving an EN after MCT (61/79, 77.2%), we observed that a higher proportion of contacts receiving an EN before MCT were exposed in nonhousehold settings (11/18, 61.1%, vs 34/61, 55.7%) and their corresponding cases had more frequently reported mild-to-moderate symptoms (14/18, 77.8%, vs 42/61, 68.9%). Of the 18 contacts receiving an EN before MCT, 14 (77.8%) took recommended measures: 12 (66.7%) were tested for SARS-CoV-2, and 7 (38.9%) called the SwissCovid Infoline. In nonhousehold settings, the proportion of contacts taking preventive actions after receiving an EN was higher compared to same-household settings (82%, vs 67%). In addition, 1 (9%) of 11 ENs received in the nonhousehold setting before MCT led to the identification of a SARS-CoV-2-infected case by prompting the contact to get tested. This corresponds to 1 in 85 exposures of a contact to a case in a nonhousehold setting, in which both were app users and the case triggered the EN.

Conclusions: Our descriptive evaluation of the DPT notification cascade provides further evidence that DPT is an important complementary tool in pandemic mitigation, especially in nonhousehold exposure settings. However, the effect of DPT apps can only be exerted if code generation processes are efficient and exposed contacts are willing to undertake preventive actions. This highlights the need to focus efforts on keeping barriers to efficient code generation as low as possible and promoting not only app adoption but also compliance with the recommended measures upon an EN.

Trial Registration: International Standard Randomised Controlled Trial Number Registry 14990068; https://doi.org/10.1186/ISRCTN14990068

(JMIR Public Health Surveill 2022;8(5):e35653) doi:10.2196/35653

KEYWORDS

digital proximity tracing; contact tracing; SwissCovid; mobile app; COVID-19; SARS-CoV-2; epidemiology; public health; tracking; surveillance; app; mHealth; evaluation; exposure; notification; observational

Introduction

Digital proximity tracing (DPT) has been utilized by several countries as a complementary tool to enhance the effectiveness of manual contact tracing (MCT) in interrupting SARS-CoV-2 transmission chains [1-4]. Findings from population-level evaluations of the National Health Service (NHS) COVID-19 app in the United Kingdom [5] and the Corona-Warn-App in Germany [6] based on app monitoring and SARS-CoV-2 incidence data suggest that DPT exerted an important contribution to the identification of infected cases in the respective countries. Similarly, population-level data and simulations for the Swiss canton of Zurich suggest that exposure notifications (ENs) of the SwissCovid DPT app triggered voluntary quarantine recommendations in the equivalent of 5% of all contacts placed in mandatory quarantine after identification by MCT [7]. Furthermore, recent findings from the roll-out of a DPT app in Norway revealed that at least 11% of the identified contacts were exposed by a chance encounter and thus could have been missed by MCT [8]. However, despite these promising findings, early expectations regarding the role of these apps in preventing SARS-CoV-2 transmission have not been completely fulfilled [9]. This raises the key question of how the effectiveness of DPT could be improved further, which requires a better understanding of the factors influencing DPT processes.

A main determinant for DPT effectiveness is app adoption in the population [1,5]. However, many countries have struggled with relatively low uptake rates, impeding the apps from reaching their full potential [10-15]. Multiple studies have also shown differences in uptake across population subgroups relating to sociodemographic and behavioral factors, such as health and digital literacy, motivation, and trust in the government or science [12,15-18]. Yet, app adoption is not the only determinant for DPT effectiveness, and sociodemographic and behavioral factors are likely insufficient to explain further observed shortcomings along the DPT notification cascade [19-21]. For example, Salathé et al [20] found that only 2 (67%) of 3 upload authorization codes (ie, codes issued to the SARS-CoV-2-infected cases who should enter them into the app to warn their exposed contacts) were eventually uploaded [20]. Furthermore, individual-level data from an online panel comprising approximately 2000 individuals from Switzerland suggest that only 3 (75%) of 4 exposed contacts undertook the recommended actions after receiving an EN [22]. Such findings are concerning since DPT effectiveness is built on the premise that users (ie, cases after receiving the upload authorization code or contacts after receiving the EN) will undertake the necessary actions to prevent further transmission. In this context, we recently highlighted the importance of the exposure setting in prompting individuals to undertake recommended actions after receiving an EN in a study of cases and contacts identified by MCT in the canton of Zurich [23]. We found that receipt of ENs was associated with a faster time until the start of quarantine when the transmission risk occurred in nonhousehold settings, while there was no effect on time to quarantine in same-household exposure settings, where information flows are bound to be faster.

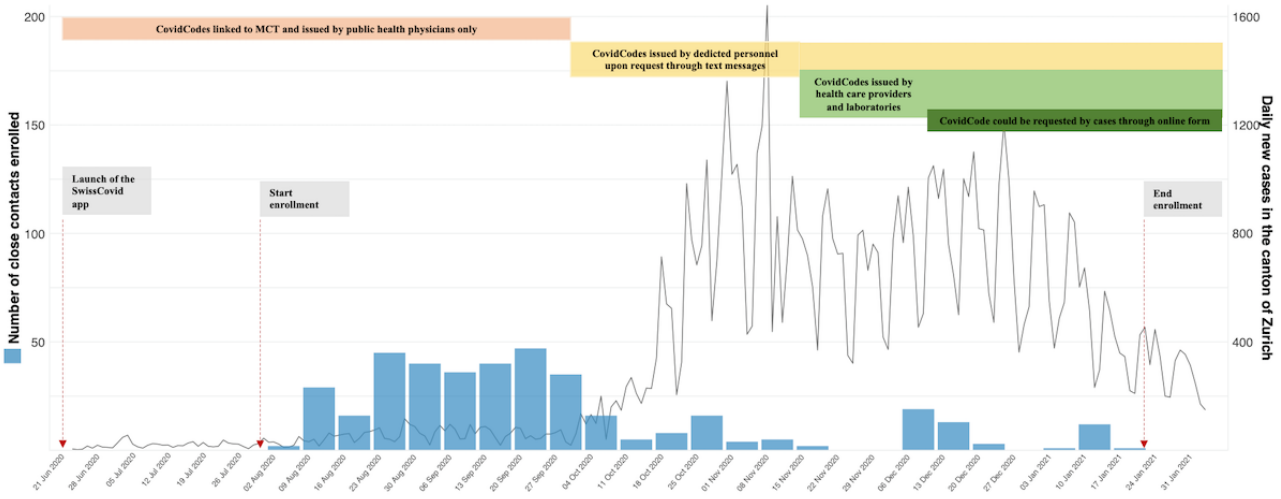
In this study, we aim to extend these previous analyses to evaluate potential contextual factors influencing the receipt of ENs and users' subsequent actions. Our analysis leverages data from confirmed case-contact pairs identified by MCT and enrolled in the Zurich SARS-CoV-2 Cohort study, which enabled us to recreate individual-level EN cascades and to study the exposure context and subsequent actions taken along the cascade. Specifically, we examine (1) the proportion of cases and contacts who fulfilled the necessary steps along the notification cascade in different exposure settings, (2) case and contact characteristics that may be associated with receipt of ENs by contacts, and (3) the type of and adherence to recommended actions among contacts who received an EN.

Methods

Pandemic Context

This study was conducted in Zurich, Switzerland, and analyzes data from August 6, 2020, to January 17, 2021. During the beginning of this time frame, the SARS-CoV-2 incidence in Switzerland was relatively low but steadily rising (Figure 1) [24]. At the beginning of October 2020, daily incidence sharply increased and MCT, as well as other services, such as SARS-CoV-2 testing, quickly reached capacity limits. Although relatively swift measures were undertaken to analyze and mitigate bottlenecks, their effects on reducing case numbers only materialized at the end of November 2020.

Figure 1. Study enrollment and events relating to key changes in processes related to DCT and MCT. DCT: digital contact tracing; MCT: manual contact tracing.



The SwissCovid Digital Proximity Tracing App

Switzerland was among the first to launch a DPT app in June 2020 to support MCT in reducing the spread of the virus. The SwissCovid app is based on a privacy-preserving design and uses a notification cascade involving multiple sequential steps and actions taken by infected cases and their proximity contacts [2,7,21]. Upon receipt of a positive SARS-CoV-2 test, app users can request an upload authorization code (CovidCode) and enter it in the app. This triggers an EN to contacts who were within a proximity radius of less than 1.5 m for at least 15 min during the time of infectivity of the case. Therefore, an uninterrupted information flow along the notification cascade requires 3 conditions to be fulfilled: (1) cases and contacts need to be app users, (2) cases must have received and uploaded the code to trigger an EN, and (3) contacts must receive the EN. Furthermore, DPT only has an effect on preventing transmission if exposed contacts are willing to undertake the recommended preventive actions after receiving the EN. Notified contacts are thus strongly encouraged to call the SwissCovid Infoline (or, since December 2020, to complete a web form) and to get tested and enter self-quarantine, if indicated. However, these measures are not mandatory and are merely recommended by the health authorities. This stands in contrast to MCT, where quarantine and testing are mandated.

Study Design and Participants

This study is based on data from the Zurich SARS-CoV-2 Cohort study, a prospective, case-ascertained study of 1106 individuals infected with SARS-CoV-2 (cases) and 395 of their contacts. A detailed description of the study design, its inclusion criteria, and its procedures are reported elsewhere [23]. In brief, all cases and their contacts in the canton of Zurich were identified through mandatory laboratory reporting and routine MCT by the Cantonal Department of Health and invited if they were ≥18 years old, residing in the canton of Zurich, had sufficient knowledge of the German language, and were able to follow the study procedures. After identification of eligible cases and contacts, we performed a daily random sampling of both participant populations. The sampling of cases was stratified by age, whereas contacts were randomly sampled in clusters based on the corresponding case. Sampled individuals were then invited to participate in the study.

In this study, we analyzed data from known pairs of cases and contacts. An anonymized paired data set allowing the cross-linkage of cases and corresponding contacts in the study was obtained from MCT at the Department of Health. We included only pairs for which both the case and the contact were enrolled in the study and provided data for this analysis.

Ethical Considerations

Informed consent was obtained from all participants agreeing to participate in the study. The study protocol was approved by the responsible ethics committee of the canton of Zurich (BASEC 2020-01739) and was prospectively registered on the International Standard Randomised Controlled Trial Number Registry (ISRCTN14990068) [25].

Data Collection

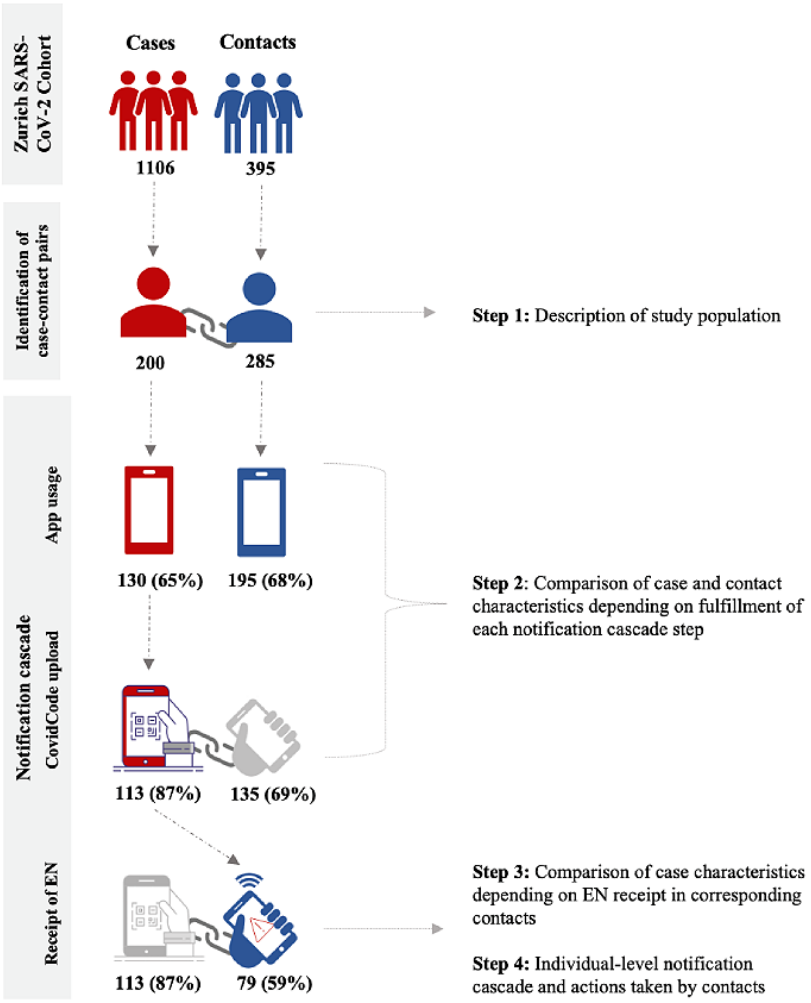
Upon enrollment, both cases and contacts completed an electronic questionnaire. For cases, information collected included sociodemographics, date of SARS-CoV-2 testing, COVID-19-related symptoms, and details regarding the suspected SARS-CoV-2 transmission event. Questionnaires for contacts included sociodemographics, presence and severity of symptoms, and details regarding the relevant exposure event (ie, setting, date, and duration). Both questionnaires included questions concerning the use of SwissCovid, including the receipt and uploading of CovidCodes by cases, as well as any ENs received by contacts. Contacts were additionally followed up at the end of quarantine, and results of any SARS-CoV-2 testing during that time were recorded. All study data were collected and managed using the Research Electronic Data Capture system (REDCap, Vanderbilt University) [26,27].

Statistical Analysis

The analytical steps are outlined in Figure 2. In the first step, we described the participant characteristics, including the setting in which the risk exposure occurred. In the second step, we

descriptively analyzed the characteristics of cases and contacts by whether they fulfilled the necessary conditions in the notification cascade (ie, app usage among cases and contacts, cases uploading a CovidCode vs those not uploading it, and contacts receiving an EN before or after MCT vs those not receiving it). In the third step, we examined whether there were differences in the characteristics of the cases who uploaded a CovidCode and whose corresponding contacts received an EN before or after MCT. In the last step, we examined the individual-level notification cascade and the preventive actions taken by the contacts after receipt of the EN (ie, uploading the CovidCode, calling the SwissCovid Infoline, entering quarantine, or undergoing SARS-CoV-2 testing).

Figure 2. Description of the analytical steps of the study. EN: exposure notification.



We presented the results for the study population overall and stratified by exposure setting as reported by the contact (ie, same-household, nonhousehold, and unknown settings). We additionally reviewed the contacts' free-text responses regarding their steps taken after receiving the EN. Responses were thematically coded and descriptively analyzed based on their context. We reported continuous variables as medians with IQRs and categorical variables as frequencies and percentages. All analyses were performed using R version 4.0.3 (R Core Team) [28].

Results

Description of Cases and Contacts

We identified 285 case-contact pairs within the study time frame in which both the case and the contact were enrolled in the study (n=200 cases and n=285 corresponding contacts, with a median of 1 contact per case, IQR 1-2, maximum 8). Analysis was limited to these case-contact pairs. Details of the full enrollment process of cases and contacts in the study are provided in Multimedia Appendix 1.

The median age of cases and contacts was 41 and 43 years, respectively (Table 1). Of 200 cases, 91 (45.5%) and of 285 contacts, 146 (51.2%) were female. Both populations were similar with respect to education level, employment status, Swiss nationality, and the presence of at least 1 medical comorbidity. Within case-contact pairs, the exposure occurred within the same household in 113 (39.6%) pairs and in a nonhousehold setting in 162 (56.8%) pairs, and the setting was unknown to the contacts in 8 (2.8%) pairs.

Table 1. Baseline characteristics of cases and contacts from 285 case-contact pairs in the Zurich SARS-CoV-2 Cohort study.

Characteristics	Cases (N=200)	Contacts (N=285)
Age in years, median (IQR)	41 (30-57)	43 (30-57)
Sex, n (%)		
Female	91 (45.5)	146 (51.2)
Male	109 (54.5)	139 (48.8)
Education, n (%)		
Mandatory school	9 (4.5)	12 (4.2)
Vocational training/baccalaureate	82 (41)	98 (34.4)
Technical college or university studies	108 (54)	174 (61)
Missing	1 (0.5)	1 (0.4)
Employment status, n (%)		
Employed	151 (75.5)	217 (76.1)
Student	13 (6.5)	28 (9.8)
Unemployed/retired	35 (17.5)	39 (13.7)
Missing	1 (0.5)	1 (0.4)
Monthly household income,[a] n (%)		
<CHF 6000 (<US $6060)	57 (28.5)	90 (31.6)
CHF 6000-12,000 (US $6060-US $12,120)	86 (43)	113 (39.6)
>CHF 12,000 (>US $12,120)	49 (24.5)	68 (23.9)
Missing	8 (4)	14 (4.9)
Number of household members, median (IQR)	2 (1-3)	2 (1-3)
Missing data on household members, n (%)	4 (2)	3 (1)
Nationality, n (%)		
Swiss	173 (86.5)	255 (89.5)
Non-Swiss	27 (13.5)	30 (10.5)
Chronic medical conditions, n (%)		
At least 1 self-reported comorbid condition	45 (22.5)	60 (21.1)
Missing	3 (1.5)	7 (2.5)
Presence of COVID-19 related symptoms, n (%)	171 (85.5)	46 (16.1)
Missing	0	23 (8.1)
COVID-19 symptom severity, n (%)		
Asymptomatic	29 (14.5)	N/A[b]
Mild to moderate	138 (69)	N/A
Severe to very severe	32 (16)	N/A
Missing	1 (0.5)	N/A
Hospitalized due to COVID-19, n (%)	2 (1)	N/A
Same-household exposure setting, n (%)	15 (7.5)	113 (39.6)
Nonhousehold exposure setting, n (%)		
Private setting[c]	32 (16)	78 (27.4)
Workplace	16 (8)	33 (11.6)
Public space[d]	27 (13.5)	41 (14.4)
Health care facility	1 (0.5)	0

Characteristics	Cases (N=200)	Contacts (N=285)
School/university	1 (0.5)	6 (2.1)
Other	2 (1)	4 (1.4)
Unknown setting	105 (52.5)	8 (2.8)
Missing	1 (0.5)	2 (0.7)
Country in which the exposure occurred, n (%)		
Switzerland	87 (43.5)	268 (94)
Abroad	8 (4)	4 (1.4)
Unknown	105 (52.5)	8 (2.8)
Missing	0	5 (1.8)
SwissCovid app use, n (%)		
App nonuser	69 (34.5)	88 (30.9)
App user	130 (65)	195 (68.4)
Missing	1 (0.5)	2 (0.7)

[a]A currency exchange rate of CHF 1 = US $1.01 was applied.

[b]N/A: not applicable (information relating to symptom severity and hospitalization related to COVID-19 only collected for cases).

[c]Settings such as friends' apartments, private vehicles, private gatherings, or events.

[d]Settings such as restaurants, bars, shops, concerts, public transport, or religious gatherings.

Comparison of Case and Contact Characteristics Depending on Fulfillment of Each Notification Cascade Step

Overall, 130 (65%) of 200 cases and 195 (68.4%) of 285 contacts were app users. Both cases and contacts who were app nonusers were, on average, older, and a lower proportion had a technical college or university degree, were employed, and were Swiss nationals compared to app users (Multimedia Appendix 2). There were no relevant differences between cases and contacts who used the app and those who did not in terms of their respective exposure setting, relation to the case, or country of exposure (Table 2).

Of the 130 cases who were app users, 122 (93.8%) received a CovidCode, of which 113 (92.6%) uploaded the code into the app (Table 2 and Multimedia Appendix 3). A comparison between cases uploading the code and those not uploading the code was hindered by the low number of cases not uploading the code (n=8, 6.6%). However, no relevant differences between the 2 groups were observed (Multimedia Appendix 2).

The 113 cases uploading the code were linked to 135 (69.2%) of 195 contacts using the app (Table 2). Within these 135 case-contact pairs, 79 (58.5%) of contacts received an EN through the app. Of these, 18 (22.8%) received an EN before and 61 (77.2%) after MCT. Contacts receiving an EN before MCT were more frequently exposed through nonhousehold or unknown settings compared to those receiving an EN after MCT (12/18, 66.7%, vs 34/61, 55.7%). Furthermore, the proportion of contacts whose corresponding case was a family member or a partner was lower among those receiving an EN before MCT compared to those receiving an EN after MCT (8/18, 44.4%, vs 34/61, 55.7%). Those receiving the EN before MCT were also older, on average; more frequently male (12/18, 66.7%, vs 29/61, 47.5%), and more frequently unemployed or retired (6/18, 33%, vs 4/61, 6.6%) compared to those receiving the EN after MCT (Multimedia Appendix 3). The 52 (18.2%) of 285 contacts who did not receive an EN were more often exposed in their workplace (n=11, 21.1%, vs n=1, 5.6%, receiving an EN before MCT and n=3, 4.9%, receiving an EN after MCT) and non-Swiss nationals (7/52, 13.5%, vs 0/18, 0%, and 4/61, 6.6%, respectively). We found similar results when analyzing data from all contacts (ie, not restricted to only those whose exposure case reported uploading the code); see Multimedia Appendices 4 and 5.

Table 2. COVID-19-related characteristics of cases (N=200) and contacts (N=285) for key steps along the notification cascade.

Characteristics	Cases[a]				Contacts[a]				
	App nonuser (N=69)	App user (N=130)	Code not uploaded (N=8)	Code uploaded (N=113)	App nonuser (N=88)	App user (N=195)	EN[b] before MCT[c] (N=18)	EN after MCT (N=61)	No EN (N=52)
Household exposure setting, n (%)	8 (11.6)	7 (5.4)	0	5 (4.4)	41 (46.6)	71 (36.4)	6 (33.3)	27 (44.3)	15 (28.8)
Nonhousehold exposure setting, n (%)	27 (39.1)	51 (39.2)	3 (37.5)	46 (40.7)	45 (51.1)	117 (60)	11 (61.1)	34 (55.7)	37 (71.2)
Private setting[d]	9 (13)	22 (16.9)	2 (25)	20 (17.7)	26 (29.5)	52 (26.7)	4 (22.2)	16 (26.2)	13 (25)
Workplace	6 (8.6)	10 (7.7)	1 (12.5)	9 (8)	10 (11.4)	23 (11.8)	1 (5.6)	3 (4.9)	11 (21.2)
Public space[e]	9 (13)	18 (13.9)	0	17 (15)	6 (6.8)	35 (17.9)	4 (22.2)	14 (23)	10 (19.2)
School/university	1 (1.5)	0	0	0	1 (1.1)	5 (2.6)	2 (11.1)	1 (1.6)	2 (3.9)
Health care facility	1 (1.5)	0	0	0	0	0	0	0	0
Other	1 (1.5)	1 (0.7)	0	0	2 (2.3)	2 (1)	0	0	1 (1.9)
Unknown setting	34 (49.3)	71 (54.7)	4 (50)	62 (54.9)	2 (2.3)	6 (3.1)	1 (5.6)	0	0
Missing	0	1 (0.7)	1 (12.5)	0	0	1 (0.5)	0	0	0
Country in which the exposure occurred, n (%)									
Switzerland	32 (46.4)	54 (41.5)	4 (50)	46 (40.7)	86 (97.7)	182 (93.3)	17 (94.4)	60 (98.4)	51 (98.1)
Abroad	3 (4.3)	5 (3.9)	0	5 (4.4)	0	4 (2.1)	0	1 (1.6)	1 (1.9)
Unknown country	34 (49.3)	71 (54.6)	4 (50)	62 (54.9)	2 (2.3)	7 (3.6)	1 (5.6)	0	0
Missing	0	0	0	0	0	2 (1)	0	0	0
Relation of participant with SARS-CoV-2 infected individual, n (%)									
Family/partner	8 (11.6)	10 (7.7)	1 (12.5)	7 (6.2)	48 (54.5)	90 (46.1)	8 (44.4)	34 (55.8)	19 (36.6)
Friend/acquaintance	14 (20.3)	22 (16.9)	1 (12.5)	19 (16.8)	20 (22.7)	59 (30.3)	6 (33.3)	17 (27.9)	18 (34.6)
Coworker	3 (4.3)	8 (6.2)	1 (12.5)	7 (6.2)	10 (11.4)	29 (14.9)	2 (11.1)	6 (9.8)	11 (21.2)
Customer/business partner	2 (2.9)	2 (1.5)	0	2 (1.8)	2 (2.3)	2 (1)	0	0	2 (3.8)
Patient	1 (1.5)	0	0	0	0	0	0	0	0
Other	7 (10.1)	15 (11.5)	0	15 (13.3)	6 (6.8)	7 (3.6)	1 (5.6)	3 (4.9)	2 (3.8)
Case unknown	34 (49.3)	71 (54.6)	4 (50)	62 (54.8)	2 (2.3)	6 (3.1)	1 (5.6)	0	0
Missing	0	2	1 (12.5)	1 (0.9)	0	2 (1)	0	1 (1.6)	0
COVID-19 related symptoms and self-reported severity,[f] n (%)									
Asymptomatic	9 (13)	19 (14.6)	0	16 (14.1)	N/A[g]	N/A	N/A	N/A	N/A
Mild to moderate	47 (68.1)	91 (70)	6 (75)	82 (72.6)	N/A	N/A	N/A	N/A	N/A
Severe to very severe	12 (17.4)	20 (15.4)	2 (25)	15 (13.3)	N/A	N/A	N/A	N/A	N/A
Missing	1 (1.5)	0	0	0	N/A	N/A	N/A	N/A	N/A
COVID-19 related symptoms and self-reported severity of exposure case, n (%)									
Asymptomatic	N/A	N/A	N/A	N/A	N/A	N/A	3 (16.7)	10 (16.3)	8 (15.4)
Mild to moderate	N/A	N/A	N/A	N/A	N/A	N/A	14 (77.8)	42 (68.9)	35 (67.3)
Severe to very severe	N/A	N/A	N/A	N/A	N/A	N/A	1 (5.5)	9 (14.8)	9 (17.3)
Missing	N/A	N/A	N/A	N/A	N/A	N/A	0	0	0

[a]Missing information from 1 case on app use, 1 case on code upload, 2 contacts on app use, and 4 contacts on receipt of an EN.

[b]EN: exposure notification.

[c]MCT: manual contact tracing.

[d]Settings such as friends' apartments, private vehicles, private gatherings, or events.

[e]Settings such as restaurants, bars, shops, concerts, public transport, or religious gatherings.

[f]Information relating to COVID-19 symptom severity was only collected in case questionnaires.

[g]N/A: not applicable.

Comparison of Case Characteristics Depending on EN Receipt by Corresponding Contacts

In a further step, we analyzed whether there were differences in the characteristics of cases, depending on whether their corresponding contacts received the notification, before or after MCT (n=135, 69.2%; Table 2 and Multimedia Appendix 6). Overall, cases corresponding to contacts who received the EN before MCT more frequently reported having mild-to-moderate symptoms (14/18, 77.8%, vs 42/61, 68.9%) compared to cases corresponding to contacts who received the EN after MCT. Meanwhile, cases corresponding to contacts who received the EN after MCT more frequently reported having been severely or very severely affected by COVID-19 compared to those corresponding to contacts who received the EN before MCT. When analyzing case characteristics across the different exposure contexts, cases corresponding to contacts receiving an EN before MCT in the same-household setting more frequently reported being asymptomatic (2/6, 33.3%, vs 5/27, 18.5%) or having severe-to-very-severe symptoms (1/6, 16.7%, vs 1/27, 3.7%) compared to those receiving an EN after MCT (Multimedia Appendix 7). We observed similar distributions of disease severity among nonhousehold case-contact pairs as well as those with unknown exposure setting. Cases corresponding to contacts not receiving an EN generally had comparable characteristics to cases corresponding to contacts who received an EN after MCT.

Individual-Level Notification Cascade and Actions Taken by Contacts

Figures 3 and 4 present the sequence of events occurring along the notification cascade and the actions taken by the contacts in case-contact pairs. Figure 3 illustrates 162 case-contact pairs (n=117, 72.2%, pairs who are app users) with exposure in a nonhousehold setting, while Figure 4 shows 113 case-contact pairs (n=71, 62.8%, pairs who are app users) in a same-household setting. Multimedia Appendix 8 presents the sequence of events among the 8 pairs where the exposure setting was unknown to the contact.

In *nonhousehold case-contact pairs*, 71 (70.3%) cases and 117 (72.2%) contacts were app users. Almost all cases received a CovidCode, and 63 (94%) of 67 uploaded the received code, thereby triggering an EN. Of the 85 contacts linked to cases that uploaded the CovidCode, only 45 (53%) also received the EN, of which 11 (24%) received it before MCT. Of these 11 contacts who received the EN before MCT, 5 (45%) called the SwissCovid Infoline and a total of 9 (82%) underwent SARS-CoV-2 testing. Of these 9 individuals, 1 (11%) subsequently tested positive for SARS-CoV-2 infection. Of the 34 individuals who received an EN after MCT, the majority (n=27, 79%) did not undertake any steps as they were already in quarantine. However, 6 (18%) called the SwissCovid Infoline or responsible public health physicians and 1 (3%) reported directly seeking SARS-CoV-2 testing. Of the 37 individuals who did not receive a notification, 33 (89%) were tested for SARS-CoV-2, and 2 (6%) of them tested positive.

In *same-household case-contact pairs*, 48 (92%) of 52 cases using SwissCovid received and uploaded a CovidCode, triggering an EN in 33 (69%) of the 48 corresponding contacts using the app. Of these, 6 (18%) received the EN before MCT, and 4 (67%) reported taking recommended actions, such as undergoing testing (n=3, 75%) and calling the SwissCovid Infoline (n=1, 25%) after EN receipt. Most of those who were notified by the app after MCT (n=23, 86%) did not take any additional actions, as they were already in quarantine, and some (n=4, 17%) were also tested for SARS-CoV-2. Meanwhile, 4 (14%) undertook recommended actions after EN receipt, such as calling the SwissCovid Infoline (n=2, 50%) and seeking testing (n=2, 50%). Of those who did not receive a notification, 14 (93%) underwent SARS-CoV-2 testing, of which 1 (7%) person tested positive.

Of the 8 case-contact pairs in which the *exposure setting was unknown* to the contact, only 3 (38%) reported to be app users. Of these, 2 (67%) received and uploaded a CovidCode, triggering an EN in 1 (50%) corresponding contact, after which this contact called the SwissCovid Infoline (Multimedia Appendix 8).

Figure 3. Notification cascade and preventive actions taken upon EN receipt among nonhousehold case-contact pairs (N=162, including 101, 62.3%, unique cases; *missing data on notification status in 3, 1.9%, individuals). EN: exposure notification; MCT: manual contact tracing.

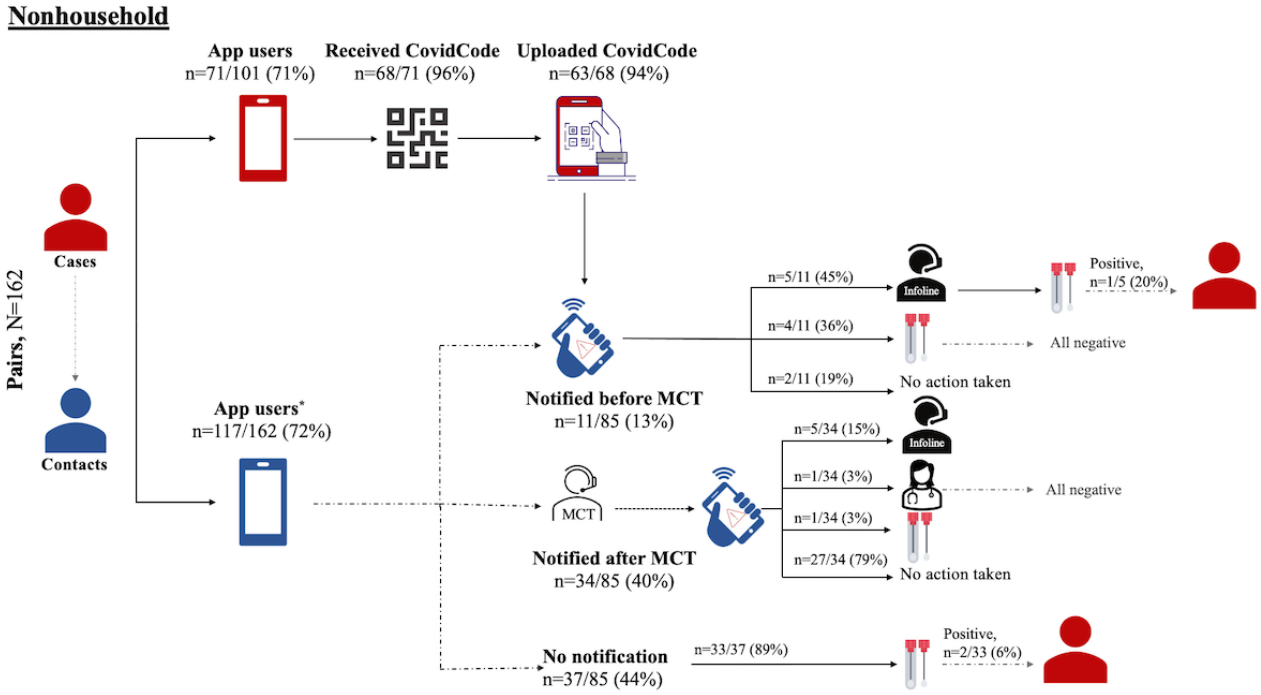
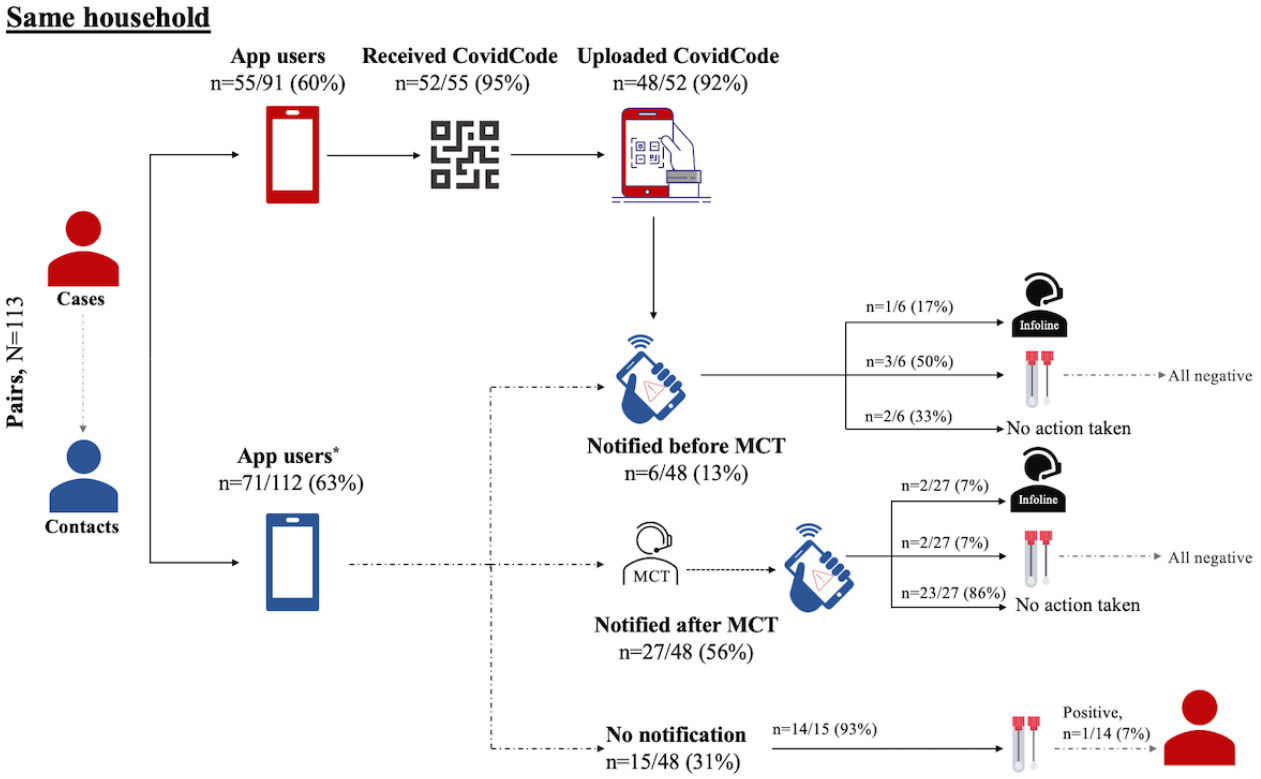


Figure 4. Notification cascade and recommended actions taken upon EN receipt among same-household case-contact pairs (n=113 pairs, including 91, 80.5%, unique cases; *missing data on app use in 3, 2.7%, individuals). EN: exposure notification; MCT: manual contact tracing.



Discussion

Principal Findings

We previously found that receipt of SwissCovid ENs was associated with earlier time to quarantine among nonhousehold contacts [23]. Here, we provide more granular data that allow a detailed assessment of the events and actions taken along the notification cascade among 285 case-contact pairs. We further interpret our results, considering the contextual changes to DPT and MCT processes over the course of the study, with the aim to provide insights that support the further optimization of current and future implementations of DPT.

The success of any DPT app strongly relies on a well-functioning EN cascade to identify and warn exposed contacts in a timely manner, as well as on the actions taken by these contacts. Our analysis suggests that a substantial proportion of ENs were not received in a timely manner and the received ENs did not always trigger the desired response in contacts. Specifically, our individual-level reconstruction of EN cascades in case-contact pairs suggests that only 79 (58.5%) of 135 exposed contacts received an EN. This finding is noteworthy because the preconditions for an EN were present in all 135 pairs (ie, both cases and contacts were app users and cases had triggered the ENs by uploading the required CovidCodes). However, we cannot exclude that some cases may have falsely reported to have uploaded the upload authorization code due to social desirability bias or that they had not yet downloaded the app at the time of the exposure and may have actually downloaded it and uploaded the code after being tested or developing symptoms. In such cases, their exposed contacts, who were identified by MCT, would not receive an EN. Furthermore, it is also possible that the risk exposure identified through MCT was not captured by the Bluetooth Low Energy signal–based technology for technical reasons (ie, proximity period too short, distance too high, diverging definition of duration or proximity by the device compared to MCT, or potential technical failures of DPT app processes) or because the devices were not carried by both individuals at the time of risk exposure. Further investigations into addressing the reasons of this gap (eg, technical improvements or education of the public on the appropriate use of the app) are required to optimize DPT performance.

Among exposed contacts who received an EN, only 18 (23%) of 79 received the EN before they were reached by MCT. These numbers should be interpreted in the light of the broader study context. The participants were enrolled in a period during which the incidence of SARS-CoV-2 was steeply rising (Figure 1). Because the issuance of CovidCodes was initially delegated to MCT personnel, the increasing workload experienced by MCT during this period also affected the timeliness of CovidCode issuance and led to cascade delays. Conversely, MCT was still relatively fast in some instances during that time (eg, if contacts were easily identifiable and contactable), thus diminishing the relative speed advantage of DPT. Our previous analysis conducted within the same cohort suggested a speed advantage of EN in nonhousehold settings but not in same-household exposure situations [23]. However, future investigations should strive to capture EN cascade steps in an even greater timely resolution. On a positive note, the majority (n=14, 77.8%) of those receiving an EN before MCT undertook recommended measures, such as seeking SARS-CoV-2 testing (n=12, 66.7%) or calling the SwissCovid Infoline (n=7, 38.9%). Similarly, another Swiss study also found that 76% of EN-notified contacts undertook a recommended action [22]. These findings stand in contrast to an experimental study from Spain, which found that only 10% of the notified contacts acted upon EN receipt by calling a designated infoline [29]. Although this low proportion could be related to the awareness of the participants about the experimental nature of that study, the inaction of contacts raised concerns about the effectiveness of the app in preventing secondary transmission. These findings emphasize the importance of having public information campaigns to increase the awareness of DPT apps. These campaigns should not only focus on highlighting the importance of using the app but also focus on adherence to the recommended actions.

We additionally examined whether case and exposure characteristics also varied noticeably by EN receipt status. Two findings, although based on limited sample sizes, may be helpful to obtain a better understanding of the notification cascade. First, contacts with workplace risk exposures seemed to be somewhat less likely to receive an EN. Only 4 (27%) of 15 individuals exposed at the workplace received a notification, as opposed to 41 (61%) of 67 for other nonhousehold exposure settings (ie, private and public spaces and schools**)**. Although coworkers may share the same workspace, the proximity or exposure time may still not reach the necessary thresholds to trigger an EN. Nevertheless, coworkers may still be identified as close contacts by MCT. Second, we found that cases whose corresponding contacts received an EN before MCT had more frequently stated having mild-to-moderate symptoms, while the cases of those receiving it after MCT more frequently mentioned severe-to-very-severe symptoms. Thus, the presence of severe symptoms could have potentially led to a delay in the uploading of CovidCodes (eg, because the case felt too ill). In those situations, allowing the possibility for proxies to swiftly trigger ENs may be considered.

In addition, we explored whether the exposure context may influence the timing of the receipt of ENs in relation to MCT as well as adherence of the contacts to recommended actions. We noted that compared to same-household settings, a higher proportion of contacts exposed in a nonhousehold setting received an EN before MCT and undertook at least 1 recommended action after receiving the EN. These actions included SARS-CoV-2 testing, with 1 (9%) of 11 received ENs having led to the identification of a SARS-CoV-2-infected case in the nonhousehold setting. Some same-household contacts also reported to have taken preventive actions after EN receipt, which may point toward a reinforcing effect of the DPT app. Current guidance on the recommended steps after receiving an EN from the SwissCovid app does not make a distinction between possible exposure settings. However, it may be worthwhile considering providing SwissCovid users with more targeted information and recommendations. For example, different recommendations could be issued for contacts knowingly exposed in household settings or through their

infected partner and for contacts knowingly exposed in the nonhousehold setting or contacts with an unknown exposure context.

Limitations

Our findings should be interpreted considering potential limitations and changes that occurred during the study period. First, study recruitment was restricted to exposed contacts identified by MCT. One advantage of DPT is to notify contacts who would otherwise be missed by MCT. This potential advantage could not be assessed within our study due to the MCT-based recruitment of study participants, thus allowing our study to only provide a partial picture of DPT effectiveness. Second, several changes to MCT and DPT processes occurred during the course of study enrollment, which may have limited the interpretation of our results (Figure 1). Upload authorization codes were initially issued by MCT personnel, and delays in receiving CovidCodes or ENs were reported during that time. This was followed by a sharp increase in case numbers in October-December 2020, during which MCT reached its capacity limits. During this period, the enrollment of contacts in the study was severely affected and had to be paused, since MCT was unable to trace an important proportion of contacts. Although a potential advantage of DPT is to compensate when MCT is overwhelmed, this setting could also not be explored due to the setup of the study. Furthermore, during that same period, several changes to CovidCode generation and MCT processes were implemented. From November 2020, the issuing of CovidCodes was improved through simplified code generation processes and by allowing laboratories and health care providers to issue the codes. Starting in December 2020, a digitally assisted form of MCT using web forms was implemented, through which cases self-reported their contacts, including contact information. At the same time, the issuance of CovidCodes was linked to the completion of the web form by the case. Although this was being implemented, the Department of Health did not have access to close contacts' information for a certain time, which further affected our recruitment processes. In addition, we only enrolled contacts who were reached by MCT and who were still in quarantine upon first contact with our study team. In consequence, we may have missed those who were reached late or not at all by MCT and thus are most likely to have an advantage through DPT. Finally, we could not conduct any statistical analyses due to the limited sample size. However, although the findings of this study may not carry a strong statistical weight, they provide a unique observational account of the potential effects of a DPT app.

All these changes and their implications for our study may have likely led to an underestimation of the effects of SwissCovid. Conversely, some selection may have also occurred, and participants included in the study may reflect populations with higher health literacy, which may also be more likely to comply with the recommended actions and undertake preventive actions after being notified by the DPT app. Nevertheless, our results are broadly consistent with a population-based assessment of actions taken by SwissCovid app users receiving an EN in which 76% of app users took at least 1 preventive action after EN [22].

Conclusion

In conclusion, our study provides further evidence that DPT apps can have an impact on the control of SARS-CoV-2 transmission. The detailed evaluation along each step of the DPT notification cascade within case-contact pairs demonstrates that app notifications and preventive actions taken by exposed contacts can indeed contribute to the prevention of further infections. Meanwhile, our results also show that timely compliance with the recommended measures is key for the app to exert its desired effects. It is thus important that public health messaging be targeted not just at app uptake but also for compliance with recommendations and that barriers for rapid issuance of upload authorization codes and preventive actions, such as testing and quarantine, be kept as low as possible. Further evidence collected in unknown exposure settings or times during which MCT reaches capacity limits would be desirable to judge additional contributions of DPT that could not be assessed in this study. Based on current data, DPT appears to be a relevant complementary tool in mitigating the current pandemic, while notification cascade processes and compliance are crucial determinants for its real-world effects.

Acknowledgments

The Zurich SARS-CoV-2 Cohort study is part of the Corona Immunitas research program, coordinated by the Swiss School of Public Health (SSPH+) and funded through SSPH+ fundraising, including funding by the Swiss Federal Office of Public Health, the cantons of Switzerland (Basel, Vaud, and Zurich), private funders (ethical guidelines for funding stated by SSPH+ were respected), and institutional funds of the participating universities. Additional funding specific to this study was provided by the Swiss Federal Office of Public Health, the Department of Health of the canton of Zurich, and the University of Zurich Foundation. TB received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant (Agreement 801076) through the SSPH+ Global PhD Fellowship Programme in Public Health Sciences (GlobalP3HS) of the Swiss School of Public Health. Study funders had no role in the study design, data collection, analysis, interpretation, or writing of this report. The authors would like to thank the study administration team and the study participants for their dedicated contribution to this research project.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Study enrollment and populations in the Zurich SARS-CoV-2 Cohort study.
[DOCX File , 94 KB - publichealth_v8i5e35653_app1.docx]

Multimedia Appendix 2
Sociodemographic characteristics of cases and contacts for key steps along the notification cascade.
[DOCX File , 23 KB - publichealth_v8i5e35653_app2.docx]

Multimedia Appendix 3
Reasons for not uploading the CovidCodes by cases who are app users and received a code.
[DOCX File , 16 KB - publichealth_v8i5e35653_app3.docx]

Multimedia Appendix 4
COVID-19 characteristics of all contacts who are app users stratified by receipt of exposure notification (regardless of whether the case uploaded the code, N=195).
[DOCX File , 19 KB - publichealth_v8i5e35653_app4.docx]

Multimedia Appendix 5
Sociodemographic characteristics of all contacts who are app users stratified by receipt of exposure notification (regardless of whether the case uploaded the code, N=195).
[DOCX File , 19 KB - publichealth_v8i5e35653_app5.docx]

Multimedia Appendix 6
Sociodemographic characteristics of cases corresponding to contacts whose exposure case uploaded a CovidCode, stratified by notification status.
[DOCX File , 17 KB - publichealth_v8i5e35653_app6.docx]

Multimedia Appendix 7
Characteristics of cases corresponding to contacts whose exposure case uploaded a CovidCode, stratified by notification status and exposure setting of the contact.
[DOCX File , 23 KB - publichealth_v8i5e35653_app7.docx]

Multimedia Appendix 8
Notification cascade and preventive actions taken upon exposure notification among case-contact pairs in which the exposure setting was unknown to the exposed contact (n=8).
[DOCX File , 213 KB - publichealth_v8i5e35653_app8.docx]

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Abbreviations

DPT: digital proximity tracing
EN: exposure notification
MCT: manual contact tracing

Edited by T Sanchez, A Mavragani; submitted 12.12.21; peer-reviewed by M Clarysse, S Rostam Niakan Kalhori; comments to author 24.01.22; revised version received 03.02.22; accepted 26.04.22; published 19.05.22.

Please cite as:
Ballouz T, Menges D, Aschmann HE, Jung R, Domenghino A, Fehr JS, Puhan MA, von Wyl V
Individual-Level Evaluation of the Exposure Notification Cascade in the SwissCovid Digital Proximity Tracing App: Observational Study
JMIR Public Health Surveill 2022;8(5):e35653
URL: https://publichealth.jmir.org/2022/5/e35653
doi:10.2196/35653
PMID:35476726

Original Paper

Changes in Parental Attitudes Toward COVID-19 Vaccination and Routine Childhood Vaccination During the COVID-19 Pandemic: Repeated Cross-sectional Survey Study

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Abstract

Background: It was reported that one in four parents were hesitant about vaccinating their children in China. Previous studies have revealed a declining trend in the vaccine willingness rate in China. There is a need to monitor the level of parental vaccine hesitancy toward routine childhood vaccination and hesitancy toward the COVID-19 vaccine during the ongoing COVID-19 pandemic.

Objective: This study aims to assess changes in trends of parental attitudes toward routine childhood vaccines and COVID-19 vaccinations across different time periods in China.

Methods: Three waves of cross-sectional surveys were conducted on parents residing in Wuxi City in Jiangsu Province, China from September to October 2020, February to March 2021, and May to June 2021. Participants were recruited from immunization clinics. Chi-square tests were used to compare the results of the three surveys, controlling for sociodemographic factors. Binary and multivariable logistic regression analysis was used to examine factors related to parental vaccine hesitancy and COVID-19 vaccine willingness.

Results: Overall, 2881, 1038, and 1183 participants were included in the survey's three waves. Using the Vaccine Hesitancy Scale, 7.8% (225/2881), 15.1% (157/1038), and 5.5% (65/1183) of parents showed hesitancy to childhood vaccination (P<.001), and 59.3% (1709/2881), 64.6% (671/1038), and 92% (1088/1183) of parents agreed to receive a COVID-19 vaccine themselves in the first, second, and third surveys, respectively (P<.001). In all three surveys, "concerns about vaccine safety and side effects" was the most common reason for refusal.

Conclusions: There has been an increasing acceptance of COVID-19 vaccination in Wuxi City, China. Effective interventions are needed to mitigate public concerns about vaccine safety.

(JMIR Public Health Surveill 2022;8(5):e33235) doi:10.2196/33235

KEYWORDS

childhood vaccination; COVID-19 vaccine; vaccine hesitancy; repeated cross-section survey

Introduction

Vaccination is considered one of the most successful interventions in disease prevention. Annually, it prevents 2 to 3 million deaths from vaccine-preventable diseases (VPDs), including diphtheria, tetanus, pertussis, influenza, and measles [1]. However, vaccine hesitancy, which refers to delaying or refusing vaccines, threatens the success of vaccination and is among the most important current global health concerns [2,3]. Parental hesitancy to childhood vaccines can decrease vaccination coverage among children; moreover, numerous VPDs continue to spread because of low vaccine uptake. For example, the Asia-Pacific region reported 63,483 pertussis cases in 2019 [4], and EU countries reported 148,279 measles cases from 2010 to 2019 [5].

Surveys on parental childhood vaccine hesitancy have been conducted globally since 2011 [6]. According to a national survey in the United States, one in five parents showed hesitation toward childhood vaccinations from 2018 to 2019 [7]. A 2018 survey of 5736 samples conducted in 18 European countries showed that the hesitancy rate among parents ranged from 9% (Portugal) to 42% (Israel) [8]. A 2020 survey conducted in Peru reported a vaccine hesitancy rate among parents of approximately 10% [9].

In China in 2017, VPDs were reported in 280,315 children and adolescents [10]. In addition, a study conducted in 2015 in Zhejiang Province, China reported that one in four parents were hesitant about vaccinating their children [11]. This data suggests a need to address parental vaccine hesitancy toward routine childhood vaccines in China. Specifically, there is a need to monitor both children's immunization coverage and the level of parental vaccine hesitancy.

During the ongoing COVID-19 pandemic, hesitancy toward the COVID-19 vaccine is a substantial concern. Subsequently, there have been worldwide surveys on the acceptability of COVID-19 vaccines, revealing widely varying levels of acceptability across countries [12,13]. A meta-analysis of 38 studies including 81,173 individuals showed that the acceptance rate ranged from 94.31% (Malaysia) to 43.38% (Greece) [13].

Since March 2020, numerous Chinese studies have been conducted on COVID-19 vaccination willingness [14-18]. These data demonstrate that the willingness rate in China varied between 52.2% and 83.8%, and that the changing trend in willingness rates warrants monitoring. One repeated cross-sectional study and two longitudinal studies have revealed a declining trend in the vaccine willingness rate in China [19-21]; this could substantially impede efforts to contain COVID-19, especially with the rise of Delta and other variants. However, most of these studies were performed before the COVID-19 vaccine rollout in China [14-21]. A cohort study conducted in the United States reported increased vaccine acceptability after the vaccination program commenced [22]. Therefore, the acceptability of vaccines needs to be reassessed in China, especially after the COVID-19 vaccine's rollout. As of August 18, the cumulative number of COVID-19 vaccines administered in mainland China exceeded 1.9 billion [23]. Furthermore, vaccine policies and strategies in China have evolved, bolstering the need to monitor public reactions toward COVID-19 vaccination regularly.

Our study aimed to assess changes in the level of parental vaccine hesitancy toward routine childhood vaccines and public acceptance of COVID-19 vaccines at different times in China, especially after their rollout. Specifically, we aimed to examine the reasons for accepting or refusing the COVID-19 vaccine across various time intervals. In addition, we examined changes in both the number of administered COVID-19 vaccine doses and the vaccination strategies in the first half of 2021 to assess actual vaccination decisions in Wuxi City in Jiangsu Province.

Methods

Study Design and Participants

We conducted three waves of cross-sectional surveys in Wuxi City (total population: 6.59 million in 2018), located in Eastern China, from September 21 to October 17, 2020; February 9 to March 13, 2021; and May 24 to June 10, 2021. The three surveyed periods corresponded with three stages of COVID-19 vaccine development and rollout: COVID-19 vaccine trials (first survey), before mass COVID-19 vaccination (second survey), and during mass COVID-19 vaccination (third survey). We recruited participants from 6 immunization clinics across the city. The selection method of vaccination clinics has been previously described by Wang et al [24]. The sample size was calculated as  ; 90% COVID-19 vaccination willingness rate (P) [14], 2.5% precision (d), and 5% type I error (α); the final size was 959 participants.

An informed consent form and a self-administered questionnaire were distributed to the parents of all children treated at the selected vaccination clinics during the survey periods. Parents were informed about the study purpose and anonymization of the investigation. Paper-form questionnaires were used during the first survey period, while online questionnaires were used during the second and third survey periods. The online questionnaire was created and distributed through the Wenjuanxing website. The participants accessed and completed the questionnaire by scanning a QR code (2D barcode). All potential participants were assured that participation in the research was voluntary and that they would be free to discontinue participation at any time.

The inclusion criteria included the father or mother being with the child (aged ≤6 years), and when both parents visited the clinic simultaneously, the one who self-identified as the child's primary caregiver completed the questionnaire. The exclusion criteria included the father or mother being younger than 18 years and parents having mental illnesses.

Ethics Approval

Wuxi Center for Disease Control and Prevention Ethics Committee approved the surveys (2020No10).

Measures and Data Collection

The questionnaire comprised three parts: sociodemographic characteristics, parental vaccine hesitancy, and willingness to receive COVID-19 vaccination. The first survey comprised questions regarding sociodemographic characteristics, including the participant's age, sex, educational level, annual household income, and health care occupation status. The subsequent surveys added four additional questions regarding the number of people in residence, contacts per day, self-reported health, and influenza vaccination status in the last season. These questions were all specific to participants. The questions regarding parental vaccine hesitancy toward routine childhood vaccines referred to the 10-item Vaccine Hesitancy Scale (VHS) developed by the Strategic Advisory Group of Experts [25]. The 10-item VHS has been used in numerous countries with acceptable reliability and validity [26-28]. We used a 5-point scale (strongly disagree: 1; disagree: 2; neither agree nor disagree: 3; agree: 4; or strongly agree: 5) for responses to each VHS item.

During the vaccine trial period, one question, "If the COVID-19 vaccine was available, will you vaccinate yourself?" was used to measure the participants' willingness to accept a COVID-19 vaccination (responses: "yes," "not sure," and "no"). The next question asked for specific reasons for acceptance or refusal (If "yes," "why?" or if "no/not sure," "why?"). The other two surveys replaced this question with "Will you vaccinate against COVID-19 for yourself?" as the COVID-19 vaccine had become available in China in January 2021. Other options were also added to the survey for answers regarding the reasons for accepting or refusing a COVID-19 vaccination. These questionnaires are provided in Multimedia Appendix 1.

COVID-19 vaccination records were derived from the information management system for COVID-19 vaccines to assess actual vaccination decisions. Furthermore, governmental vaccination strategies were obtained from the official websites of relevant health authorities (Multimedia Appendix 2).

Statistical Analysis

All analyses were performed using R software (R Foundation for Statistical Computing). Categorical variables are expressed using frequencies and percentages while continuous variables are presented as means and SDs.

We calculated the VHS score using the participants' responses to the 10 items [24], with a lower score indicating a higher hesitancy level. Parental vaccine hesitancy to routine childhood vaccines was classified as either low or high hesitancy (VHS score>30 and ≤30, respectively). Regarding the analyses of COVID-19 vaccination willingness, "no" and "not sure" responses were combined into a "refusal" response. Samples from the second and third surveys were directly standardized according to the age, gender, and medical occupation status distribution of the sample from the first survey to ensure comparability of the findings across all surveys [19]. Intersurvey comparisons were performed using the chi-square or Fisher exact test. A two-sided P value <.05 was considered statistically significant. Pairwise comparisons among groups were performed with Bonferroni correction.

Binary logistic regression analysis was used to examine factors related to parental vaccine hesitancy and COVID-19 vaccine willingness. Outcome variables included parental vaccine hesitancy and COVID-19 vaccine willingness. Independent variables included sex, age, educational level, annual household income, health care occupation status, number of people in residence, number of contacts per day, self-reported health, and influenza vaccination status in the last season. Regression analyses included data from the second and third surveys as some important variables (including influenza vaccination experience) were not queried in the first survey. The variables with P<.10 in the univariate regression model were included in the multivariable regression model. A 95% CI for the crude odds ratio was derived from univariate analysis. A 95% CI for the adjusted odds ratios (AORs) was derived from multivariable analyses. A two-sided P<.05 in the multivariable analyses was considered significant.

Results

Sociodemographic Characteristics of the Participants

Overall, 2881 (response rate 79.9%), 1038 (response rate 78.7%), and 1183 (response rate 79.3%) participants were included in the first, second, and third surveys, respectively (Table 1). The average ages of the responders in the first, second, and third surveys were 31.36 (SD 4.38), 33.36 (SD 4.74), and 32.12 (SD 5.49) years, respectively. In the first, second, and third surveys, 69.5% (2001/2881), 89.1% (925/1038), and 82.9% (980/1183) of participants, respectively, had an education level of college (or equivalent) or above. Additionally, 22.1% (229/1038) and 20.9% (247/1183) of participants in the second and third surveys, respectively, reported receiving an influenza vaccination in the last season.

Table 1. Participant's sociodemographics in three cross-section surveys.

Variables	COVID-19 vaccine trials period (September to October 2020; n=2881)	Premass COVID-19 vaccination period (February to March 2021; n=1038)	Ongoing mass COVID-19 vaccination period (May to June 2021; n=1183)
Sex, n (%)			
Women	2146 (74.5)	699 (67.3)	680 (57.5)
Men	735 (25.5)	339 (32.7)	503 (42.5)
Age (years), mean (SD)	31.36 (4.38)	33.36 (4.74)	32.12 (5.49)
Age group (years), n (%)			
<26	248 (8.6)	32 (3.1)	116 (9.8)
26-30	1086 (37.7)	239 (23)	365 (30.9)
31-35	1112 (38.6)	475 (45.8)	418 (35.3)
36-40	356 (12.4)	216 (20.8)	201 (17.0)
≥41	79 (2.7)	76 (7.3)	83 (7.0)
Educational level, n (%)			
Junior high school or below	338 (11.7)	21 (2.0)	40 (3.4)
High school graduate or equivalent	542 (18.8)	92 (8.9)	163 (13.8)
College or equivalent	1791 (62.2)	755 (72.7)	880 (74.4)
Master's diploma or above	210 (7.3)	170 (16.4)	100 (8.5)
Annual household income (RMB; US $), n (%)			
<50,000 (<7669)	206 (7.2)	53 (5.1)	79 (6.7)
50,000 to <100,000 (7669 to <15,337)	850 (29.5)	264 (25.4)	348 (29.4)
100,000 to <150,000 (15,337 to <23,006)	754 (26.2)	277 (26.7)	304 (25.7)
≥150,000 (≥23,006)	1071 (37.2)	444 (42.8)	452 (38.2)
Health care occupation, n (%)			
Yes	181 (6.3)	449 (43.3)	287 (24.3)
No	2700 (93.7)	589 (56.7)	896 (75.7)
Number of people in residence, n (%)			
1	—[a]	31 (3.0)	26 (2.2)
2-5	—	902 (86.9)	1003 (84.8)
≥6	—	105 (10.1)	154 (13.0)
Number of contacts per day, n (%)			
1-10	—	544 (52.4)	544 (45.2)
11-20	—	251 (24.2)	251 (28.2)
≥21	—	243 (23.4)	243 (26.5)
Self-reported health, n (%)			
Very good	—	378 (36.4)	204 (17.2)
Good	—	507 (48.8)	517 (43.7)
Fair	—	150 (14.5)	420 (35.5)
Poor	—	1 (0.1)	28 (2.4)
Very poor	—	2 (0.2)	14 (1.2)
Influenza vaccination in the last season, n (%)			
No	—	809 (77.9)	936 (79.1)
Yes	—	229 (22.1)	247 (20.9)

[a]These items were not queried about in the first questionnaire.

Parental Vaccine Hesitancy and COVID-19 Vaccination Willingness

In Multimedia Appendix 3 and Multimedia Appendix 4, Figure S1, the rate of high hesitancy toward childhood vaccines was 7.8% (225/2881), 17.8% (157/1038), and 5.5% (65/1183) in the COVID-19 vaccine trial, premass COVID-19 vaccination, and ongoing mass COVID-19 vaccination periods, respectively. The COVID-19 vaccination willingness was 59.3% (1709/2881), 64.6% (671/1038), and 92% (1088/1183) in the COVID-19 vaccine trial, premass COVID-19 vaccination, and ongoing mass COVID-19 vaccination periods, respectively. The willingness rate continuously increased and was the highest in the third survey. There were significant intersurvey differences in the "high hesitancy toward childhood vaccination" rate and COVID-19 vaccination willingness (P<.001 and P<.001, respectively).

Administered COVID-19 Vaccine Doses in Wuxi City

As shown in Multimedia Appendix 4, Figure S2, the cumulative number of administered COVID-19 vaccines in Wuxi City exceeded 10 million doses by July 2021. The vaccination strategy varied over time. During the early period (between January and March), a select population was vaccinated against COVID-19. From June, vaccines were administered to people 18 years and older.

Factors Associated With Parental Vaccine Hesitancy

Sex and self-reported health status were associated with parental vaccine hesitancy (Table 2 and Multimedia Appendix 4, Figure S3). Compared with women, men were more likely to show hesitancy (AOR 1.372, 95% CI 1.028-1.832). Compared with participants who reported having very good health, those who reported only good health were less likely to be hesitant about childhood vaccines (AOR 0.549, 95% CI 0.399-0.755).

Table 2. Univariable factors associated with parental vaccine hesitancy to routine childhood vaccine and COVID-19 vaccine willingness.

Variables	Parental vaccine hesitancy to routine childhood vaccine[a]		COVID-19 vaccine willingness[b]	
	COR[c] (95% CI)	*P* value	COR (95% CI)	*P* value
Sex (female as reference)				
Male	1.260 (0.959-1.654)	.10	1.906 (1.498-2.425)	<.001
Age group (years; <26 as reference)				
26-30	0.995 (0.558-1.775)	.99	0.543 (0.295-1.000)	.05
31-35	0.834 (0.473-1.470)	.53	0.356 (0.197-0.644)	.001
36-40	1.253 (0.694-2.264)	.45	0.382 (0.206-0.708)	.002
≥41	1.187 (0.590-2.389)	.63	0.516 (0.253-1.051)	.07
Educational level (junior high school or below as reference)				
High school graduate or equivalent	1.493 (0.554-4.023)	.43	1.373 (0.558-3.379)	.49
College or equivalent	1.266 (0.500-3.204)	.62	0.579 (0.261-1.286)	.18
Master's diploma or above	1.779 (0.669-4.731)	.25	0.337 (0.147-0.774)	.01
Annual household income (RMB; US $; <50,000 [<7669] as reference)				
50,000 to <100,000 (7669 to <15,337)	0.888 (0.504-1.564)	.68	1.383 (0.833-2.296)	.21
100,000 to <150,000 (15,337 to <23,006)	0.693 (0.388-1.239)	.22	1.053 (0.639-1.736)	.84
≥150,000 (≥23,006)	0.812 (0.468-1.409)	.46	0.725 (0.45-1.167)	.19
Health care occupation (no as reference)				
Yes	1.447 (1.099-1.905)	.008	1.262 (0.997-1.598)	.05
Number of people in residence (1 as reference)				
2-5	0.545 (0.271-1.096)	.09	1.059 (0.543-2.065)	.87
≥6	0.616 (0.282-1.345)	.22	1.271 (0.608-2.659)	.52
Number of contacts per day (1-10 as reference)				
11-20	0.764 (0.548-1.066)	.11	1.397 (1.073-1.819)	.01
≥21	0.791 (0.565-1.106)	.17	1.664 (1.257-2.202)	<.001
Self-reported health (very good as reference)				
Good	0.453 (0.332-0.617)	<.001	0.724 (0.550-0.954)	.02
Fair	0.454 (0.315-0.655)	<.001	0.778 (0.570-1.062)	.11
Poor	0.790 (0.269-2.321)	.67	0.461 (0.198-1.075)	.07
Very poor	0.706 (0.158-3.154)	.65	0.762 (0.213-2.728)	.68
Influenza vaccination in the last season (no as reference)				
Yes	0.918 (0.657-1.282)	.62	5.764 (3.702-8.974)	<.001
Survey (second survey as reference)				
Third survey	0.304 (0.226-0.409)	<.001	6.118 (4.712-7.944)	<.001

[a]For parental vaccine hesitancy, "high-hesitant" was used as the reference.

[b]For COVID-19 vaccination willingness, "yes" was used as the reference.

[c]COR: crude odds ratio.

Factors Associated With COVID-19 Vaccination Willingness

Table 2 and Multimedia Appendix 4, Figure S3 show that sex, educational level, participants' health care occupation status, number of contacts per day, self-reported health status, and influenza vaccination history were associated with COVID-19 vaccination willingness. Participants in health care occupations were more likely to accept COVID-19 vaccinations (AOR 1.853, 95% CI 1.397-2.457). Compared with participants who reported that they were in very good health, those who reported good, fair, poor, or very poor health were more likely to refuse COVID-19 vaccination. Influenza vaccination in the last season

was positively associated with willingness to receive COVID-19 vaccination (AOR 5.564, 95% CI 3.372-8.531).

Reasons for Accepting or Refusing Vaccination Against COVID-19

In all three surveys, "Protect all the people you are around" was the most frequent reason stated for accepting the COVID-19 vaccine (Multimedia Appendix 4, Figure S4). Further, in all three surveys, "Concern about vaccine safety and side effects" was the most frequent reason for refusing COVID-19 vaccination. The second most frequent reasons for refusing COVID-19 vaccination were "doubt the vaccine effectiveness," "no professional gave me a detailed introduction to the vaccine," and "vaccination contraindications" in the first, second, and third surveys, respectively.

Discussion

Principal Findings

Our findings demonstrate that public attitudes toward routine childhood vaccines and the COVID-19 vaccine specifically varied across time. One in seven parents showed hesitancy toward routine childhood vaccines between February and March 2021. COVID-19 vaccination willingness showed a significantly increasing trend in Wuxi, China, from 59.3% to 92% (P<.001). In all three surveys, the most common reasons for parents' accepting and refusing COVID-19 vaccines for themselves were "protecting all the people you are around" and "concern about vaccine's safety and side effects," respectively.

COVID-19 vaccine acceptability (>90%) was higher during the ongoing mass COVID-19 vaccination period than seen in other studies (varied between 52.2% and 83.8%) [14-18]. Moreover, the reported values were higher than those in most countries worldwide [13,29]. The vaccination willingness rate was estimated as 80.3% (95% CI 74.9%-85.6%) across low- and middle-income countries [29]. Consistent with previous findings [22], there was an upward trend (P<.001) in COVID-19 vaccine acceptability in Wuxi City, especially after the vaccine rollout. The willingness rate in the United States was estimated to increase from 54% to 65% between October 2020 and March 2021 [22]. However, one cohort study in England and Wales showed that the willingness rate decreased from 56% to 52% between December 2020 and February 2021 [30].

The cumulative number of administered COVID-19 vaccines to adults in Wuxi City exceeded 10 million doses by July 2021. A series of national and local interventions have been implemented to improve public acceptance of the COVID-19 vaccine. Specifically, the Chinese government has organized numerous press conferences to clarify the efficacy, safety, and importance of COVID-19 vaccines [31,32]. In addition, the attitudes and practices toward COVID-19 vaccination of China's top public health influencers, including Dr Nanshan Zhong, a nationally famous scientist, were widely referred to as part of vaccine communications [33]. Local governments also produced slogans and short videos to promote vaccine acceptance [32].

Sex, education attainment, participants' health care occupation status, number of contacts per day, self-reported health status, and influenza vaccination history were associated with parents' COVID-19 vaccination acceptance for themselves. Health care workers (HCWs) constitute an important population, and HCWs have a higher risk of COVID-19 infection [34]. Moreover, HCWs are crucially involved in vaccination recommendations and administration [35-37]. Consistent with the findings from the systematic review, influenza vaccination in the last season was a strong positive predictor of COVID-19 vaccination [13]. The number of people in residence was not associated with parental vaccine hesitancy and COVID-19 vaccination willingness. Some participants, who tended to belong to single-parent families or divorced families, lived alone. Their child might live with their grandparents instead of their parents because a single father or mother could not care for their child due to work. Because of the necessity of signing informed consent before a child's vaccination and grandparents who were not literate, the father or mother would accompany the child to clinics for vaccinations.

Consistent with previous studies [12,13,29], the most common reasons for refusal were concerns about safety and side effects. A systematic review reported that the rate of adverse events after COVID-19 vaccination was close to that of other routine vaccines [38]. The allergic reaction rate was approximately 2 cases per million doses for inactivated vaccines. For RNA vaccines, the rate of allergic reactions was approximately 2 to 5 cases per million doses [38]. There is a need to educate the public on the safety of the COVID-19 vaccine. Moreover, emerging SARS-CoV-2 variants have posed a threat to global immunity recently. COVID-19 breakthrough infections have been reported in vaccine recipients [39]. The emergence of breakthrough infections could cause public distrust in the COVID-19 vaccine. Surveillance of vaccine confidence regarding the influence of breakthrough infection events should be rapidly performed to allow specific responses to public concerns.

Additionally, to our knowledge, this is the first repeated cross-sectional study to assess changes in parental vaccine hesitancy toward routine childhood vaccines. There were significant intersurvey differences with large fluctuations; the hesitancy rate was the highest in the second survey (between February and March 2021). Our data identified a sudden increase in parental hesitancy toward routine childhood vaccines between February and March, immediately prior to the introduction of the mass COVID-19 vaccination policy.

Limitations

Our study has several limitations. First, our choice of study design and sampling method might impede the generalizability of our findings as the surveys were performed in vaccination clinics in Wuxi City. In China, children must uptake a series of mandatory vaccinations before school entry [26]. Children who did not receive all of these vaccines were not allowed to go to school [26]. Hence, parents need to bring their children to the immunization clinics. We believe the representation of participants recruited from immunization clinics might be acceptable. However, the surveying in immunization clinics was still likely to cause a selection bias. Meanwhile, the self-selection bias in the surveys could not be ignored because

parents showing concerns about vaccines were not likely to respond and complete the questionnaires. These parents might be more hesitant about childhood vaccinations. There is a need for a more rigorous study design (cohort study) and representative populations to provide more robust evidence. Second, findings regarding intersurvey comparisons should be interpreted cautiously because of differences in sociodemographic characteristics. To ensure intersurvey comparability of the results, we applied direct standardization. However, there were other factors that were not adjusted in the standardization, such as influenza vaccination history, that may produce a bias. However, we believe that these unstandardized factors would not influence the results significantly because the distributions of demographic characteristics in different surveys was approximated. Third, responses to questionnaires might be affected by complex factors, including recall bias and social desirability bias. Some factors associated with parental vaccine hesitancy, including marital status and child's age, need to be explored further. Fourth, the methods for completing the questionnaire (via paper or the internet) differed across the surveys, leading to different responses. Fifth, we did not determine the causal relationship between vaccine hesitancy and health authority policies. More efforts should be made in further studies to investigate this link.

Conclusion

In Wuxi City, China, three cross-sectional surveys revealed that 1 in 7 parents showed hesitancy toward routine childhood vaccines between February and March 2021. The acceptability of COVID-19 vaccines showed an increasing trend, especially after they became available (>90%). The cumulative number of administered COVID-19 vaccines to adults in Wuxi City has exceeded 10 million doses by July 2021. In all three survey waves, "concerns about vaccine safety and side effects" were the most common reason for refusal. Effective interventions need to be taken to mitigate public concerns about vaccine safety.

Acknowledgments

Supported by the Wuxi City Technology Development Fund (N20191007); Postgraduate Research & Practice Innovation Program of Jiangsu Province (KYCX20_0153); the Fundamental Research Funds for the Central Universities (3225002102D); Public Health Research Center of Jiangnan University (JUPH201845); and AIR@InnoHK administered by Innovation and Technology Commission. The funder/sponsor did not participate in the work.

Authors' Contributions

QW, SX, HJ, SZ, and LL conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. QW, SX, LY, YH, TC, NS, ML, YY, and CL designed the data collection instruments and collected data. QW and SX carried out the initial analyses. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Questionnaires.
[DOCX File , 23 KB - publichealth_v8i5e33235_app1.docx]

Multimedia Appendix 2
Official websites of relevant health authorities.
[DOCX File , 15 KB - publichealth_v8i5e33235_app2.docx]

Multimedia Appendix 3
Participants' vaccine hesitancy and COVID-19 vaccination willingness in three cross-section studies.
[DOCX File , 17 KB - publichealth_v8i5e33235_app3.docx]

Multimedia Appendix 4
Supplementary figures.
[DOCX File , 990 KB - publichealth_v8i5e33235_app4.docx]

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Abbreviations

AOR: adjusted odds ratio
HCW: health care worker
VHS: Vaccine Hesitancy Scale
VPD: vaccine-preventable disease

Edited by T Sanchez, A Mavragani; submitted 02.09.21; peer-reviewed by M Noushad, J Park; comments to author 24.01.22; revised version received 02.03.22; accepted 26.04.22; published 13.05.22.

Please cite as:
Wang Q, Xiu S, Yang L, Han Y, Cui T, Shi N, Liu M, Yi Y, Liu C, Wang X, Yang G, Ji L, Zhou W, Jin H, Zhen S, Lin L
Changes in Parental Attitudes Toward COVID-19 Vaccination and Routine Childhood Vaccination During the COVID-19 Pandemic: Repeated Cross-sectional Survey Study
JMIR Public Health Surveill 2022;8(5):e33235
URL: https://publichealth.jmir.org/2022/5/e33235
doi:10.2196/33235
PMID:35486516

Original Paper

The Effectiveness of Pfizer-BioNTech and Oxford-AstraZeneca Vaccines to Prevent Severe COVID-19 in Costa Rica: Nationwide, Ecological Study of Hospitalization Prevalence

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Abstract

Background: The Costa Rican COVID-19 vaccination program has used Pfizer-BioNTech and Oxford-AstraZeneca vaccines. Real-world estimates of the effectiveness of these vaccines to prevent hospitalizations range from 90%-98% for two doses and from 70%-91% for a single dose. Almost all of these estimates predate the Delta variant.

Objective: The aim of this study is to estimate the dose-dependent effectiveness of COVID-19 vaccines to prevent severe illness in real-world conditions in Costa Rica, after the Delta variant became dominant.

Methods: This observational study is a secondary analysis of hospitalization prevalence. The sample is all 3.67 million adult residents living in Costa Rica by mid-2021. The study is based on public aggregated data of 5978 COVID-19–related hospital records from September 14, 2021, to October 20, 2021, and 6.1 million vaccination doses administered to determine hospitalization prevalence by dose-specific vaccination status. The intervention retrospectively evaluated is vaccination with Pfizer-BioNTech (78%) and Oxford-AstraZeneca (22%). The main outcome studied is being hospitalized.

Results: Vaccine effectiveness against hospitalization (VEH) was estimated as 93.4% (95% CI 93.0-93.9) for complete vaccination and 76.7% (95% CI 75.0-78.3) for single-dose vaccination among adults of all ages. VEH was lower and more uncertain among older adults aged ≥58 years: 92% (95% CI 91%-93%) for those who had received full vaccination and 64% (95% CI 58%-69%) for those who had received partial vaccination. Single-dose VEH declined over time during the study period, especially in the older age group. Estimates were sensitive to possible errors in the population count used to determine the residual number of unvaccinated people when vaccine coverage is high.

Conclusions: The Costa Rican COVID-19 vaccination program that administered Pfizer-BioNTech and Oxford-AstraZeneca vaccines seems to be highly effective at preventing COVID-19–related hospitalization after the Delta variant became dominant. Even a single dose seems to provide some degree of protection, which is good news for people whose second dose of the Pfizer-BioNTech vaccine was postponed several weeks to more rapidly increase the number of people vaccinated with a first dose. Timely monitoring of vaccine effectiveness is important to detect eventual failures and motivate the public to get vaccinated by providing information regarding the effectiveness of the vaccines.

(JMIR Public Health Surveill 2022;8(5):e35054) doi:10.2196/35054

KEYWORDS

COVID-19; vaccine; effectiveness; hospitalization; epidemiology; prevention; severity; Costa Rica; observational; prevalence; real-world; virus; variant; policy; monitoring; surveillance

Introduction

Concerns regarding the possible lack of effectiveness of a single dose of COVID-19 vaccine arose with the emergence of the Delta variant, a more contagious variant of COVID-19. In Costa Rica, COVID-19 cases caused by the Delta variant increased from 11% of new infections in the last week of June 2021 to 55% of new infections in the first week of August and to 100% in the last week of September 2021 (Instituto Costarricense de Investigación y Enseñanza en Nutrición y Salud [INCIENSA], unpublished data). In the same period, the incidence of COVID-19 increased from 288 to 445 daily cases per million population, despite the rapid increase in the proportion of vaccinated people from 32% on June 28, 2021, to 66% on September 27, 2021 [1].

The universal public health care system of Costa Rica, which is provided by the Costa Rican Social Security Fund (CCSS, acronym in the Spanish language), has been the single source of COVID-19 vaccination in the country. The CCSS uses two vaccines, the messenger RNA vaccine from Pfizer-BioNTech and the adenovirus vector vaccine from Oxford-AstraZeneca. By October 20, 2021, approximately 85% of the 3.7 million adult residents had been vaccinated with at least one dose and 59% with two doses [2]. Older adults aged ≥58 years received only the Pfizer-BioNTech vaccine; among older adults, 87% received the two doses with a 3-week interval and 13% with an 8- to 12-week interval. Among adults <58 years of age, 77% received the Pfizer-BioNTech vaccine and 23% received the Oxford-AstraZeneca vaccine, mostly with an 8- to 12-week interval between doses. The Costa Rican vaccination program had a strong initial focus on older adults (aged ≥58 years, as defined by the government). By June 1, 2021, more than 80% of the population in this age group had been vaccinated compared to 17% in the 40-57 years age group and 7% in the 20-39 years age group. Due to this initial focus on older adults, the proportion of older adults with more than a 6-month period after their second dose was growing rapidly during the study period, from 2% on September 14, 2021, to 24% on October 20, 2021.

At the time of this study, the literature reported the following real-world estimates (based on observational studies rather than randomized trials) of COVID-19 vaccine effectiveness against hospitalization (VEH). The 2-dose Pfizer-BioNTech VEH was 97% in Israel [3], 98% in Ontario, Canada, in a vaccination program that had primarily allocated Pfizer-BioNTech vaccine (77%) [4], 91% in the United States in the first 4 months after full vaccination [5], 90% in California when 93% of COVID-19 cases were caused by the Delta variant [6], and 90% in Qatar according to a preprint study on only Delta variant cases [7]. The highest VEH estimates (in Israel and Ontario) were obtained before the emergence of the Delta variant.

Single-dose VEH estimates were 70% in the Ontario vaccination program, which mostly used the Pfizer-BioNTech vaccine [4], 80% in England for both Pfizer-BioNTech and Oxford-AstraZeneca vaccines [8], and 91% and 88% in Scotland for Pfizer-BioNTech and Oxford-AstraZeneca vaccines, respectively [9]. All these estimates predated the Delta variant.

The objective of this study was to estimate the dose-dependent effectiveness of COVID-19 vaccines to prevent severe cases of COVID-19, as measured by the prevalence of hospitalizations, in a middle-income country (Costa Rica). These estimates were based on secondary analysis of COVID-19–related hospitalized individuals from September 14 to October 20, 2021.

Methods

Study Design

This observational, nationwide study used a cross-sectional prevalence design. The study performed secondary analysis of official statistics and reports. It compared the COVID-19–related hospitalization prevalence among the unvaccinated population with the prevalence among the semivaccinated and fully vaccinated populations at 6 time points, each 1 week apart, from September 14 to October 20, 2021.

Data

The VEH estimates used three sources of data:

1. A series of weekly reports presented by the Department of Health Statistics to the Board of Directors of the CCSS (unpublished data), which is the most important information. These reports show the distribution by vaccination status of COVID-19–related hospitalizations by the ages of patients. CCSS officers linked the databases of hospitalizations and vaccinations to determine the vaccination status of hospitalized individuals and some demographic characteristics such as age and sex. For 2% of the hospital records, the vaccination status was not established.
2. The time series of the number of first and second doses of the COVID-19 vaccines administered (6.1 million by October 20, 2021) according to population age groups as reported weekly by the CCSS [2]. These data were used to estimate the nationwide populations of semivaccinated and fully vaccinated individuals by age group at the 6 time points of the study. No adjustments were made for changes in demographics (no vaccinated individual died, out-migrated, or changed age bracket) in these populations since the impact of these changes is small considering the short study period.
3. The mid-2021 nationwide population estimate by the National Institute of Statistics and Censuses (INEC) [10]. This estimate was used to determine the residual group of unvaccinated individuals, who represented the control group in the analysis. It was assumed that there were no changes in the population from the date of the estimate to the study dates.

Variables

The outcome variable was “being hospitalized due to COVID-19.”

The intervention variables were the two vaccination statuses as defined by the CCSS:

1. Partially or semivaccinated individuals: 15 or more days after the first dose and either less than 15 days after the second dose or no second dose.

2. Fully vaccinated individuals: 15 or more days since the second dose.

All analyses were stratified according to three age groups: 20-39, 40-57, and ≥58 years. These age brackets were defined in the priority calendar of the national vaccination program.

Statistical Methods

VEH is an epidemiological measure of relative risk reduction. Therefore, it was estimated as one minus the hospitalization prevalence ratio of vaccinated to unvaccinated populations.

Given the strong confounding effects of age, the Mantel-Haenzel technique was used to aggregate the age-specific estimates into a summary indicator for the entire adult population [11]. No imputations were made for the 2% of hospitalizations that had missing data, which were assumed to be randomly distributed. Estimates were obtained using Stata 17 statistical software (version 17; StataCorp LLC) and its "epitab" commands [12].

Although the number of vaccinated persons is a direct count of administered vaccines, the number of unvaccinated persons was an indirect estimate of the residual: population minus the number of vaccinated people. Errors in the population estimate would therefore overestimate or underestimate the number of unvaccinated individuals. A sensitivity analysis was performed to assess the impact of this potential error on the VEH.

Ethics Statement

This study is a secondary analysis of aggregated public data and as such does not need clearance or permissions from an ethics committee.

Results

Participants

Overall, the study included data of 3.67 million individuals, the entire adult population of Costa Rica. Of this population, 47% were in the younger group, 31% in the intermediate group, and 22% in the older group. The number of hospital records assessed in the 6 time periods was 5978, excluding 138 records with missing information. Table 1 shows the data used in the study, namely the number of participants (the population) and COVID-19–related hospitalizations. The table also shows the resulting prevalence proportions.

The highest rates of hospitalization occurred among older unvaccinated individuals, with a prevalence of 3537-4765 per million people. The lowest rates of hospitalization occurred among fully vaccinated younger adults, with prevalence ranging from 7-32 per million people, approximately 400 times lower than unvaccinated older adults. Hospitalization prevalence increased with age and was substantially higher among unvaccinated individuals. Over time, the prevalence proportions reflected the fact that COVID-19 cases in Costa Rica had reached their peak at the beginning of September, followed by a peak in hospitalizations 2 weeks later [13].

Table 1. Population, number of COVID-19–related hospitalized people, and hospitalization prevalence by vaccination status and age at 6 points in time, using data from Costa Rica.

Date and vaccination status	Age 20-39 years			Age 40-57 years			Age ≥58 years		
	N-pop[a]	N-hosp[b]	Prev[c]	N-pop	N-hosp	Prev	N-pop	N-hosp	Prev
September 14, 2021									
Total	1,732,200	249	144	1,124,100	476	423	817,400	476	582
No	602,453	189	314	243,809	302	1239	63,883	302	4727
Semi	944,645	54	57	593,039	147	248	20,660	147	7115
Fully	185,102	6	32	287,252	27	94	732,857	27	37
September 22, 2021									
Total	1,732,200	255	147	1,124,100	428	381	817,400	428	524
No	596,169	204	342	240,656	302	1255	63,374	302	4765
Semi	824,275	42	51	458,855	91	198	16,322	91	5575
Fully	311,756	9	29	424,589	35	82	737,704	35	47
September 29, 2021									
Total	1,732,200	239	138	1,124,100	409	364	817,400	409	500
No	551,141	180	327	224,643	287	1278	62,052	287	4625
Semi	790,324	54	68	355,344	84	236	14,192	84	5919
Fully	390,735	5	13	544,113	38	70	741,156	38	51
October 6, 2021									
Total	1,732,200	233	135	1,124,100	377	335	817,400	377	461
No	469,731	165	351	195,425	250	1279	58,864	250	4247
Semi	740,414	57	77	263,446	80	304	14,829	80	5395
Fully	522,055	11	21	665,229	47	71	743,707	47	63
October 13, 2021									
Total	1,732,200	196	113	1,124,100	312	278	817,400	312	382
No	387,924	130	335	164,113	194	1182	53,971	194	3595
Semi	724,720	57	79	227,889	79	347	17,645	79	4477
Fully	619,556	9	15	732,098	39	53	745,784	39	52
October 20, 2021									
Total	1,732,200	159	92	1,124,100	232	206	817,400	416	509
No	354,165	108	305	150,857	146	968	51,176	181	3537
Semi	704,530	46	65	208,980	52	249	18,588	31	1668
Fully	673,505	5	7	764,263	34	44	747,636	204	273
Pooled (averages)									
Total	1,732,200	222	128	1,124,100	372	331	817,400	403	493
No	493,597	163	330	203,251	247	1214	58,887	253	4291
Semi	788,151	52	66	351,259	89	253	17,039	85	5008
Fully	450,452	8	17	569,591	37	64	741,474	65	88

[a]N-pop: population.

[b]N-hosp: number of COVID-19–related hospitalized people.

[c]Prev: hospitalization prevalence per 1 million population.

Vaccine Effectiveness

As stated previously, VEH was estimated by comparing the prevalence of COVID-19 hospitalizations in the partially or fully vaccinated group to that in the unvaccinated group. Figure 1 shows all VEH estimates with 95% CIs.

The VEH for full vaccination ranges between 0.90 and 0.98 in the 3 age groups and 6 time points, with a statistically significant ascending time trend in the youngest group. In contrast, the VEH for partial vaccination significantly declined during the study period, especially in the older age group. The average weekly decline is 0.01, 0.02, and 0.05 in the 3 age groups, respectively. The partial vaccination effectiveness estimates ranged from 0.52-0.77 among older adults and from 0.71-0.84 among the other adult groups. Estimates of VEH for partial vaccination are substantially less precise than that for full vaccination, as shown by the wider confidence interval, especially in the older adult group.

Table 2 shows the summary indicators of VEH obtained after pooling the data from the 6 observed time periods. These estimates represent the status of the COVID-19 vaccination effort in early October 2021 in Costa Rica. The age-adjusted estimates for all adults suggest a VEH of 93.4% (95% CI 93.0-93.9) for the full vaccination schedule of 2 doses and 77% (95% CI 75.0-78.3) for partial vaccination with 1 dose. Older adults showed slightly lower VEH for full vaccination (92%, 95% CI 91.4-92.5) and substantially lower VEH for partial vaccination (64%, 95% CI 57.5-69.4) compared to the other age groups. The majority of the COVID-19 hospitalizations were probably caused by the Delta variant, which was dominant at the time of the study according to the Costa Rican genomic tracking system of the variants of concern (INCIENSA, unpublished data).

Figure 1. COVID-19 VEH estimates and their 95% CIs by age group and cross-section date, in Costa Rica, September and October 2021. VEH: vaccine effectiveness against hospitalization.

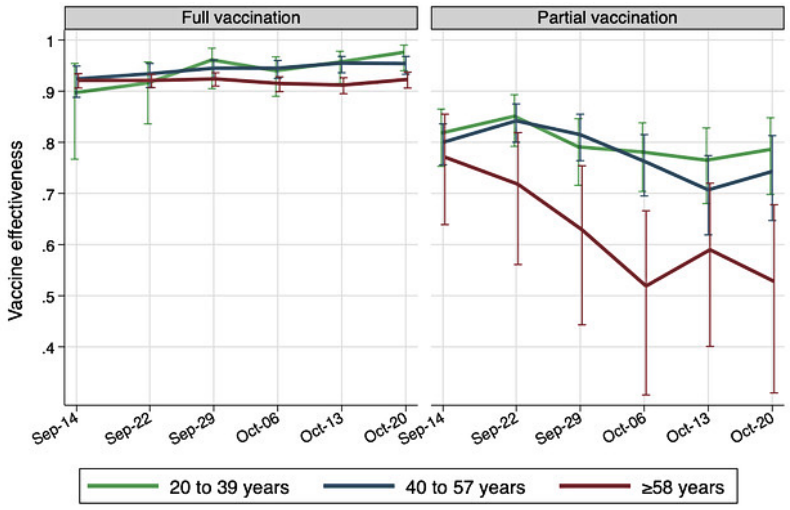


Table 2. Vaccine effectiveness against hospitalization for full and partial COVID-19 vaccination and relative risk of the unvaccinated being hospitalized by age group in Costa Rica in October 2021.

Age groups	Full vaccination	Partial vaccination
Vaccine effectiveness against hospitalization (95% CI)		
20-39 years	0.949 (0.932-0.963)	0.801 (0.774-0.825)
39-57 years	0.947 (0.939-0.954)	0.792 (0.770-0.811
≥58 years	0.920 (0.914-0.925)	0.639 (0.575-0.694
All ≥20 years, crude	0.806 (0.795-0.816)	0.835 (0.824-0.846)
All ≥20 years, age adjusted[a]	0.934 (0.930-0.939)	0.767 (0.750-0.783)
Relative risk of hospitalization of the unvaccinated (95% CI)		
20-39 years	19.8 (14.7-26.7)	5.0 (4.4-5.7)
39-57 years	18.9 (16.4-21.7)	4.8 (4.3-5.3)
≥58 years	12.5 (11.6-13.4)	2.8 (2.4-3.3)
All ≥20 years, crude	5.1 (4.9-5.4)	6.1 (5.7-6.5)
All ≥20 years, age adjusted[a]	15.3 (14.2-16.4)	4.3 (4.0-4.6)

[a]Mantel-Haenzel estimate.

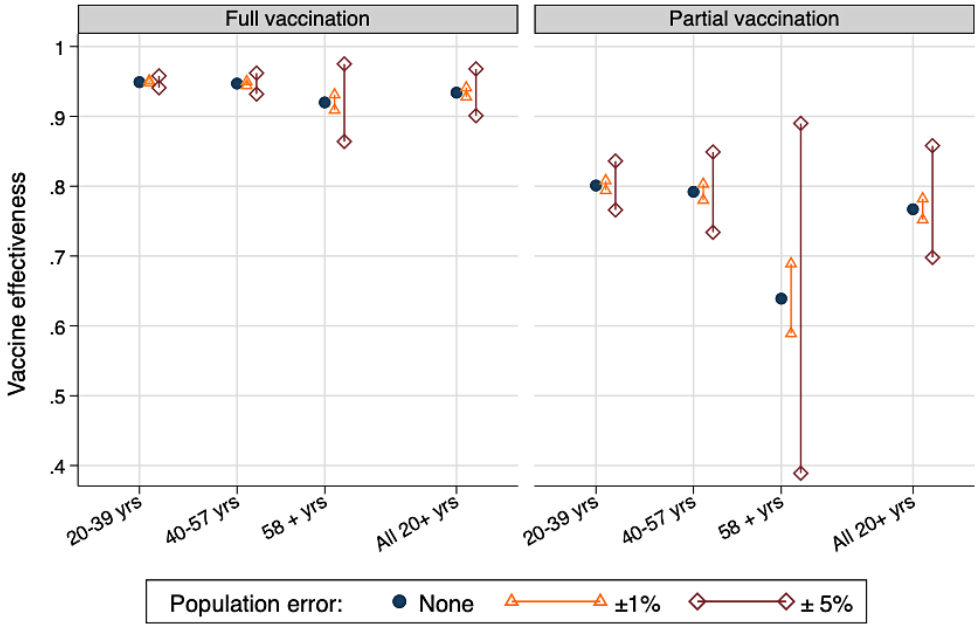
Another metric for demonstrating vaccine effectiveness is by comparing the risk of being hospitalized between the unvaccinated and vaccinated, as reported in the second half of Table 2. These metrics may be more meaningful for laypeople. Table 2 shows that risk of hospitalization in the unvaccinated was 15.3 (95% CI 14.2-16.4) times higher than that in the fully vaccinated and 4.3 (95% CI 4.0-4.6) times higher than that in the partially vaccinated.

There were significant differences between the crude and age-adjusted estimates for the entire adult population (Table 2). Age was a significant confounder in these data. Older individuals had a much higher risk of being hospitalized and were more likely to be fully vaccinated than other adults. These two associations meant that for the all-age estimate, the crude VEH was substantially lower in the older adult group than in the other age groups and, thus, lower than its real magnitude, which was estimated by the simple method proposed by Mantel and Haenzel [11] in 1959 (ie, as a weighted average of age-specific figures). The crude all-age VEH for full vaccination was 81% compared to 93% when the age was adjusted.

Sensitivity Analysis

Figure 2 summarizes the sensitivity of VEH estimates to possible errors in the population data used as input. Errors of plus or minus 1% in the population input would bias the VEH estimates by less than 0.01 except in partially vaccinated older adults, where a change of 0.05 would occur. Larger errors of plus or minus 5% in the population input would alter the VEH by 0.02 in the two younger groups and would strongly bias the estimate between 0.04 and 0.27 for the partially vaccinated. VEH estimates for older adults appear especially sensitive to errors in the population data, which originates from the very high vaccination coverage reached by this age group: approximately 90% fully and 3% partially vaccinated at the end of the study period. Small errors in population inputs substantially amplify the residual estimates of unvaccinated individuals when vaccine coverage is high.

Figure 2. Sensitivity of estimates of vaccine effectiveness against hospitalization to possible errors in the population number used as input.



Discussion

Principal Findings

COVID-19 vaccine effectiveness to prevent severe illness, as identified by the prevalence of hospitalizations, is 93% for the complete vaccination scheme of 2 doses in the adult population of Costa Rica. Among the subgroup of adults aged ≥58 years, VEH was slightly lower (92%) than that in the other subgroups. The corresponding VEH estimates for 1 dose were 77% for all adults and 64% for the older subgroup. Costa Rica uses two COVID-19 vaccines, Pfizer-BioNTech (78% of the vaccines administered) and Oxford-AstraZeneca (22% of the vaccines administered) [2]. The estimates in this article largely reflect vaccine effectiveness against the Delta variant since it was the dominant variant in the country during the study period (INCIENSA, unpublished data).

The high VEH for the single dose showed a statistically significant decline in time trend by 0.01 or 0.02 per week in adults aged 20-57 years and 0.05 per week in the older age group. It is important to note that the decline in the VEH did not occur for full vaccination. If it was caused by the spread of the Delta variant or by depletion of the immunity provided by the vaccine, the decline should have also occurred among the fully vaccinated. A plausible explanation is that the partially vaccinated may have comprised two types of people: those who are in the group temporarily while waiting for the second shot and those who intentionally avoid the second shot and behave less carefully to avoid contagion. The VEH decline might reflect an increased share of the second subgroup as complete vaccination coverage approaches 100%.

Comparison With Prior Studies

This study's estimate of 93% VEH for 2 doses of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines is within

the 90%-98% range of previous real-world estimates obtained in Israel, Ontario, the United States, California, and Qatar [3-7]. Only the studies performed in California and Qatar reported that most of the sample population had the Delta variant, as reported in this study.

The 77% VEH for a single dose of the vaccines is also within the range of 70%-91% found by studies performed in Ontario, England, and Scotland [4,8,9]. However, these previous estimates predated the Delta variant. This Costa Rican estimate is thus the first study that has reported that the Delta variant did not substantially reduce the effectiveness of a single dose of either the Pfizer-BioNTech or Oxford-AstraZeneca vaccine to prevent hospitalization. Costa Rican adults aged ≥58 years received only the Pfizer-BioNTech vaccine, while the vaccine mix for the remaining adults was 77% Pfizer-BioNTech and 23% Oxford-AstraZeneca at the time of this study.

Strengths

A strength of this observational study is that it shows the effectiveness of COVID-19 vaccines in the real-world conditions of a middle-income country, which is beyond the hypercontrolled conditions of clinical trials. Further strengths include that this study reports on the vaccines' effectiveness after the Delta variant became dominant and on the dose-specific effectiveness of the vaccines.

The secondary analysis of existing aggregated data in this study is an inexpensive design that can be broadly used to produce quick estimates for timely monitoring of vaccine effectiveness.

Being a nationwide study based on the entire adult population, it is free of issues regarding sampling bias and random errors derived from small sample sizes.

The outcome variable used in this study, being hospitalized due to COVID-19–related conditions, is a definite count that is mostly free of classification errors. A threat to its validity as a measure of severe COVID-19 infections could occur if some people have poor access to hospital care. However, this is not the case in the universal health care system of Costa Rica.

The statistics of dose-specific vaccinated people are probably accurate since the sole provider of vaccines in the country digitally records real-time information of every single vaccine administered. The database for this information is also used for inventory control purposes and for providing digital vaccination certificates to the population. If there were widespread errors, they would certainly be noticed by these other uses of the data.

Limitations

This observational study has the well-known limitations of nonrandomized, nonblinded trials including selection biases, such as the early vaccination of older people in Costa Rica (which biased the crude VEH estimates, as shown in this study), and other confounders such as the risk-taking behavior modification of some individuals after vaccination. The VEH estimates in this study should be interpreted as associations between vaccination status and hospitalization rather than the true causal effects of vaccination.

Being a study based on aggregated data, instead of microdata, it does not offer an opportunity to understand how differences at an individual level can contribute to VEH or can bias the VEH estimate. Potential errors derived from this limitation are sometimes called "ecological fallacy."

A more specific limitation of the method used in this study is that it requires high-quality data of the population count to obtain a valid estimate of the number of unvaccinated individuals. Errors in the population count affect the calculation of the number of people who have not been vaccinated, especially as the vaccination coverage approaches 100%, as is the case for older adults in Costa Rica. However, it must be noted that Costa Rica is considered to have accurate demographic data [14].

The lack of specific results for each brand of vaccine used in Costa Rica, as well as the lack of estimates of the vaccines' effectiveness at preventing COVID-19, may also be limitations of the interpretation of these study results.

Conclusions

The Costa Rican vaccination program, based on the Pfizer-BioNTech and Oxford-AstraZeneca vaccines, was highly effective at preventing COVID-19–related hospitalizations even after the Delta variant became dominant. Completing the 2-dose scheme clearly provides more protection than that provided by a single dose, and this result must always be the goal of vaccination policies. However, the data also show that even a single dose appears to provide some protection against the Delta variant, which is good news for people whose second dose of the Pfizer-BioNTech vaccine was postponed several weeks to more quickly increase the number of people who received a first dose.

Timely monitoring of vaccine effectiveness appears feasible with procedures that are analogous to those used in this study. It is important to continue the monitoring of vaccine effectiveness to detect eventual failures in the vaccination program and motivate the public by showing that vaccinations are having an impact.

Acknowledgments

The author thanks Susana López Delgado, a statistician at the Caja Costarricense de Seguro Social (CCSS), for providing the official reports with the aggregated data on COVID-19–related hospitalizations by vaccination status.

Conflicts of Interest

None declared.

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Abbreviations

CCSS: Costa Rican Social Security Fund (Caja Costarricense de Seguro Social)
INCIENSA: Instituto Costarricense de Investigación y Enseñanza en Nutrición y Salud
INEC: National Institute of Statistics and Censuses (Instituto Nacional de Estadística y Censos)
RR: relative risk
VEH: vaccine effectiveness against hospitalization

Edited by T Sanchez, A Mavragani; submitted 19.11.21; peer-reviewed by S Governor, C Shah; comments to author 25.01.22; revised version received 31.01.22; accepted 26.04.22; published 20.05.22.

Please cite as:
Rosero-Bixby L
The Effectiveness of Pfizer-BioNTech and Oxford-AstraZeneca Vaccines to Prevent Severe COVID-19 in Costa Rica: Nationwide, Ecological Study of Hospitalization Prevalence
JMIR Public Health Surveill 2022;8(5):e35054
URL: https://publichealth.jmir.org/2022/5/e35054
doi:10.2196/35054
PMID:35483079

Original Paper

Risk Factors Associated With SARS-CoV-2 Breakthrough Infections in Fully mRNA-Vaccinated Individuals: Retrospective Analysis

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Abstract

Background: COVID-19 messenger RNA (mRNA) vaccines have demonstrated efficacy and effectiveness in preventing symptomatic COVID-19, while being relatively safe in trial studies. However, vaccine breakthrough infections have been reported.

Objective: This study aims to identify risk factors associated with COVID-19 breakthrough infections among fully mRNA-vaccinated individuals.

Methods: We conducted a series of observational retrospective analyses using the electronic health records (EHRs) of the Columbia University Irving Medical Center/New York Presbyterian (CUIMC/NYP) up to September 21, 2021. New York City (NYC) adult residences with at least 1 polymerase chain reaction (PCR) record were included in this analysis. Poisson regression was performed to assess the association between the breakthrough infection rate in vaccinated individuals and multiple risk factors—including vaccine brand, demographics, and underlying conditions—while adjusting for calendar month, prior number of visits, and observational days in the EHR.

Results: The overall estimated breakthrough infection rate was 0.16 (95% CI 0.14-0.18). Individuals who were vaccinated with Pfizer/BNT162b2 (incidence rate ratio [IRR] against Moderna/mRNA-1273=1.66, 95% CI 1.17-2.35) were male (IRR against female=1.47, 95% CI 1.11-1.94) and had compromised immune systems (IRR=1.48, 95% CI 1.09-2.00) were at the highest risk for breakthrough infections. Among all underlying conditions, those with primary immunodeficiency, a history of organ transplant, an active tumor, use of immunosuppressant medications, or Alzheimer disease were at the highest risk.

Conclusions: Although we found both mRNA vaccines were effective, Moderna/mRNA-1273 had a lower incidence rate of breakthrough infections. Immunocompromised and male individuals were among the highest risk groups experiencing breakthrough infections. Given the rapidly changing nature of the SARS-CoV-2 pandemic, continued monitoring and a generalizable analysis pipeline are warranted to inform quick updates on vaccine effectiveness in real time.

(JMIR Public Health Surveill 2022;8(5):e35311) doi:10.2196/35311

KEYWORDS

COVID-19; medical informatics; real-word evidence; vaccination; electronic health records

Introduction

The ongoing global COVID-19 pandemic has infected hundreds of millions of people worldwide, imposing a tremendous burden on the global health care system. COVID-19 vaccines are currently the best defense against the rapidly evolving SARS-CoV-2, having demonstrated efficacy in preventing symptomatic COVID-19, while being relatively safe in trial studies [1-3]. In addition to the clinical trial studies, multiple studies have been conducted to confirm vaccine effectiveness using real-world observational data as well [4-9]. As of March 2022, over 200 million individuals in the United States had been fully vaccinated [10].

The Centers for Disease Control and Prevention (CDC) has reported vaccine breakthrough infections, defined as a fully vaccinated person getting infected with COVID-19 [11]. SARS-CoV-2 reinfection and vaccine breakthrough have now been frequently reported [12-17]. Newer variants of concern that now account for the majority of infections worldwide, including delta (B.1.617.2) and omicron (B.1.1.529), have also increased transmissibility and increased rates of vaccine breakthrough compared to older variants [18,19]. Given the concerns about vaccine breakthrough infections [20], studies have been conducted to confirm vaccine breakthrough infections with SARS-CoV-2 variants using genome sequencing [16] and to investigate clinical characteristics of the vaccine breakthrough infections [21-23]. Early reports have found breakthrough infections more often occur in individuals with solid organ transplants [24-27], obesity [28], hypertension [29], diabetes [29,30], congestive heart failure [29,31], chronic kidney disease (CKD) [22,32], lung diseases [33], dementia [34], and cancer [22,35-37]. Here, we retrospectively analyzed electronic health records (EHRs) from the Columbia University Irving Medical Center/New York Presbyterian (CUIMC/NYP) up to September 21, 2021, to systematically identify risk factors associated with breakthrough infections among fully messenger RNA (mRNA)–vaccinated individuals.

Methods

Ethical Considerations

The study adhered to the principles set out in the Declaration of Helsinki, with informed consent obtained from all participants. The Columbia University Health Sciences Institutional Review Board (IRB) reviewed and approved the study (IRB AAAR3954). The analysis in this study was conducted on the deidentified data.

Study Design and Population

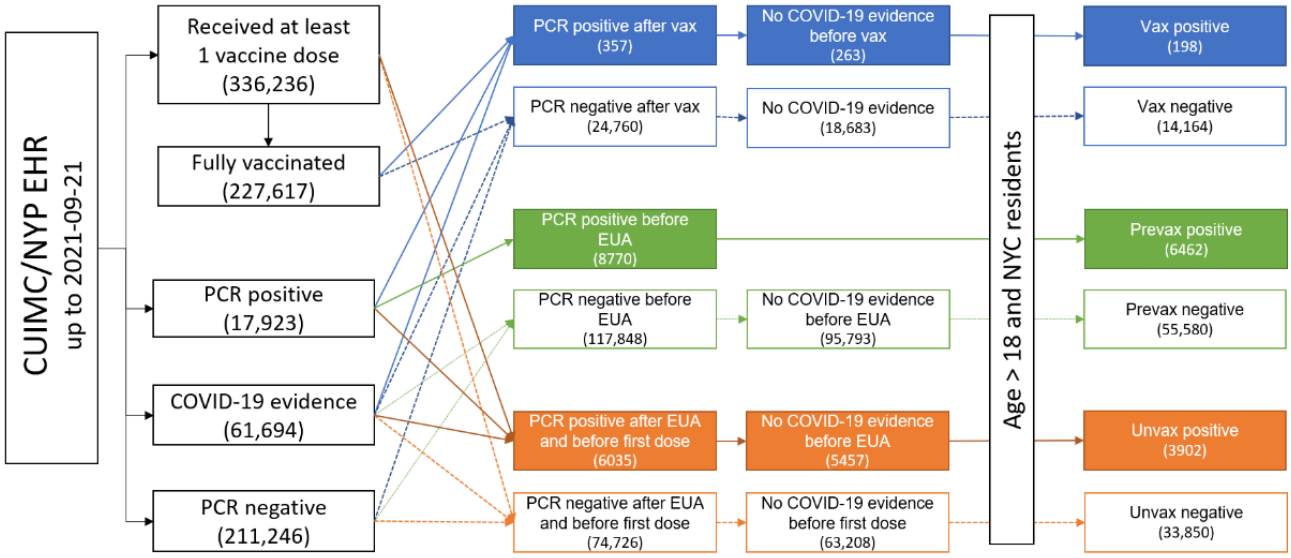
We used EHR data obtained from the NYP/CUIMC data warehouse. The NYP/CUIMC is a quaternary care academic medical center that includes an academic hospital, a children's hospital, and a community-based hospital serving a diverse patient population in northern Manhattan, New York City (NYC). EHR data were collected and stored in the data warehouse during routine clinical care at the CUIMC/NYP. The EHR data were converted to the Observational Medical Outcomes Partnership (OMOP) common data model (CDM) version 5.0 [38]. All data involved in this analysis were collected up to September 21, 2021, which captured the B.1.1.7 (alpha; January 2021-June 2021) and B.1.617.2 (delta; June 2021-December 2021) variant waves but did not include data from the B.1.1.529 (omicron; December 2021-present) wave [39]. Due to the insufficient sample size of individuals vaccinated with non-mRNA vaccines, and the different mechanisms between the mRNA vaccine and adenovector vaccines (such as Johnson & Johnson) [40], we only investigated breakthrough infections in the fully mRNA-vaccinated individuals.

Cohort Definition

Individuals over the age of 18 years who resided in NYC were included in this study. OMOP concepts related to vaccines were used to identify vaccinated individuals who received 2 doses of Pfizer/BNT162b2 or Moderna/mRNA-1273. To minimize potential bias resulting from missing vaccination records, vaccines records in our data warehouse were obtained from both CUIMC EHR data and the NYC vaccine registry. We required individuals to complete their 2-dose administration with a time interval of 20-23 days for Pfizer/BNT162b2 and 27-31 days for Moderna/mRNA-1273; individuals with 2 doses with 14 days of available follow-up after their second dose were considered fully vaccinated. Individuals who received doses from more than 1 manufacturer or only received 1 vaccine dose were excluded. We defined COVID-19-positive cases by using the OMOP measurement concepts and corresponding value concepts related to detect positive RNA using polymerase chain reaction (PCR). Individuals with at least 1 positive SARS-CoV-2 PCR test were flagged as COVID-19 positive. To balance the cofounding between positive cases and negative cases, we adopted a test-negative design—only individuals with at least 1 negative PCR test were included as COVID-19-negative cases. To reduce the potential false positives in the negative cohort, we additionally established stringent criteria to further exclude individuals with any evidence of a prior SARS-CoV-2 infection: (1) a positive SARS-CoV-2 PCR test, (2) a positive SARS-CoV-2 antibody test, or (3) a concept indicating SARS-CoV-2 infection. The details of OMOP concepts used for the cohort definition are available in Multimedia Appendix 1.

Based on the vaccine and SARS-CoV-2 status, we then constructed 6 cohorts based on evidence of COVID-19 breakthrough infection (ie, positive or negative) and vaccination status (ie Vax, Prevax, and Unvax), as shown in Figure 1. For example, "Vax positive" is a collection of individuals who were vaccinated but later experienced breakthrough infections. The vaccination status was classified into "Vax" (those who were fully vaccinated), "Prevax" (those during a period when vaccines were unavailable), and "Unvax" (those who were not vaccinated during the period when vaccines were available). Individuals who were in the Prevax infection–negative cohort could also be in a Vax cohort later. Of note, if an individual receives a first dose for vaccination, that individual exits the Unvax cohort (and may later become part of a Vax cohort if fully vaccinated). More details about the cohort definitions can be found in the Results section.

Figure 1. Cohort construction diagram and study overview. Vaccines records were obtained from both CUIMC EHR data and the NYC vaccine registry. Only fully vaccinated individuals with mRNA vaccines were included. Individuals with a positive SARS-CoV-2 PCR test, a positive SARS-CoV-2 antibody test, or a concept indicating a SARS-CoV-2 infection in the condition table were flagged as having evidence of SARS-CoV-2 infection. No COVID-19 evidence was required before entering the cohort for positive individuals and before exiting the cohort for negative individuals. Only age >18 years and NYC residents were included in this analysis. "Vax": individuals 14 days after receiving their second doses were considered fully vaccinated; "EUA": the date on which the first dose of the vaccine was administrated (ie, December 11, 2021); "first dose": the date on which the individual was administrated their first (including Johnson & Johnson) vaccine dose (or the end of the study if a vaccine was not ever administrated). CUIMC/NYP: Columbia University Irving Medical Center/New York Presbyterian; EHR: electronic health record; EUA: Emergency Use Authorization; mRNA: messenger RNA; NYC: New York City; PCR: polymerase chain reaction.



Feature Extraction

For each cohort, we extracted individuals' demographic data, including age, gender, ethnicity, and race. For the vaccinated cohorts, the vaccine brand and corresponding administration dates were also extracted. To approximate the available observation time, we extracted the total number of prior EHR visits and days of observation periods between clinical encounters for each individual. We extracted all previous condition and drug concepts from the *condition_era* and *drug_era* tables. To avoid extracting condition/drug concepts potentially caused by the SARS-CoV-2 infection itself, we added a 90-day washout period (ie, ignore all the concepts within the 90-day window prior to the PCR test regardless of its result). To identify individuals who might have compromised immune systems, we compiled a list of conditions and drugs, including active solid tumors and hematologic malignancies (within 2 years), solid-organ or hematopoietic stem cell transplant, primary immunodeficiencies, HIV infection, immunosuppressive therapies (eg, cancer chemotherapeutic agents, certain biologic agents, rituximab), and CKD [41]; see Multimedia Appendices 2 and 3. Individuals could fall into multiple immunocompromised subgroups. To adjust for the caseload in NYC, a 7-day rolling average of cases was applied [42].

Identifying Risk Factors Associated With Breakthrough Infections

We compared the Vax-positive and Vax-negative cohorts to identify potential risk factors associated with breakthrough infections (Multimedia Appendix 4). The entry date was defined as the fully vaccinated date, and individuals were then followed until the first positive PCR date (or the end of the study for Vax-negative individuals). For each risk factor (eg, vaccine brand, demographics, immunocompromised status), a univariate Poisson regression was fit to assess the incidence rate ratio (IRR; ie, breakthrough per 1000 person-days) against the reference status. To minimize potential bias resulting from daily caseload, viral mutations, and EHR data quality, the Poisson regression was adjusted for (1) the total number of observation days in the EHR before the entry date, (2) the total number of visits in the EHR before the entry date, and (3) the calendar month of the PCR test date. We further applied a non-hypothesis-driven approach to uniformly evaluate the risk effect for each historical condition and drug by fitting a univariate Poisson regression with similar adjustment. Condition and drug concepts significantly associated with the breakthrough infections were identified as a <.05 Bonferroni-adjusted *P* value [43].

Evaluation of Vaccine Effectiveness in Fully Vaccinated Individuals in Preventing Infection by Comparing Vaccinated Individuals With Pre- and Unvaccinated Individuals

For the Vax cohorts, the entry date was defined similarly to the entry date for the risk factor analysis. For the Unvax cohorts, the entry date was defined as January 18, 2021 (14 days after the first individual received their second dose at the CUIMC/NYP), and individuals were then followed up until the first positive PCR test (latest for negative individuals) or the date when they received their first dose, whichever came first (Multimedia Appendix 5). We 1:1-matched vaccinated individuals to unvaccinated individuals using a nearest-neighbor search based on (1) observation days, (2) visit count, (3) calendar week of the PCR test (earliest positive PCR or latest negative PCR), (4) demographics (eg, gender, age, race,

ethnicity), and (5) immunocompromised status (binary). The IRRs for the vaccine were estimated via Poisson regressions.

As shown in Multimedia Appendix 6, we further identified 1:1-matched individuals in the Prevax cohort based on the same covariates, except for the calendar week of the PCR test, which was replaced by the 7-day rolling average of cases in NYC at the PCR testing date. Given the difficulty in identifying an appropriate entry date for the prevaccinated cohort, we applied a case-control design to calculate the odds ratio (OR) of contracting COVID-19 infection between the Vax cohort and the Prevax cohort using logistic regressions.

Results

Cohort Characteristics

Table 1 provides baseline characteristics of the 6 cohorts (note: some individuals are in multiple cohorts at different times). For the Vax-positive (ie, breakthrough) cohort, the median age was 60 years (IQR 40.7-75.4). Of 198 individuals in the Vax-positive cohort, 156 (78.8%) received Pfizer/BNT162b2, while 42 (21.2%) received Moderna/mRNA-1273. In addition, 65 (45.5%) had underlying immunocompromised conditions, and 120 (60.6%) of the patients with breakthrough infections were hospitalized. In general, PCR-positive individuals had a higher number of prior visits and observational days compared to unvaccinated individuals. For later analyses, we used a matching strategy to balance the covariates between the cohorts.

The overall estimated breakthrough infection rate was 0.16 (95% CI 0.14-0.18). Table 2 summarizes risk factors associated with breakthrough infections. We found a significantly higher incidence rate in vaccinated males than in females (IRR=1.47, 95% CI 1.11-1.94). We did not find any significant change in the incidence rate associated with other demographics, though Black individuals are likely to have a higher incidence rate and Asian individuals are likely to have a lower incidence rate. However, given the large portion of unknown race/ethnicity in the EHRs, our study was unable to estimate this association with meaningful accuracy. There was a significantly higher rate of breakthrough infections among those vaccinated with Pfizer/BNT162b2 compared to Moderna/mRNA-1273 (adjusted IRR=1.66, 95% CI 1.17-2.35). An immunocompromised state was significantly associated with a higher incidence rate among the vaccinated (adjusted IRR=1.48, 95% CI 1.09-2.00). Those with primary immunodeficiency, a history of organ transplant, an active tumor, and use of immunosuppressant medications were at the highest risk.

For the underlying conditions and drug usage analysis, a total of 1359 and 536 unique candidate conditions and drugs were available for investigation, respectively. Concepts needed a minimum of 100 individuals to be considered. Table 3 summarizes the top 10 breakthrough infection-associated condition and drug concepts. In addition to previously known conditions and drugs related to immunocompromised status (eg, immunodeficiency disorder, valganciclovir), we found that prior conditions and drugs related to pulmonary disease (eg, postinflammatory pulmonary fibrosis, albuterol) were also among those significantly associated with an increased breakthrough infection rate. The full list of associated conditions and drug concepts is provided in Multimedia Appendices 2 and 3.

We analyzed the protective effect of vaccination in the Vax cohort using 2 matched Prevax and Unvax cohorts. When comparing the Vax cohort with the Prevax cohort, the risk of COVID-19 infection in vaccinated individuals was significantly lower (adjusted OR 0.12, 95% CI 0.10-0.13), which was also the case when stratifying by age, gender, and immunocompromised status (Table 4). Similarly, we found a significant reduction in the incidence rate (adjusted IRR=0.42, 95% CI 0.36-0.49) when comparing the Vax cohort with the Unvax cohort (Table 5); similar observations were found across age, gender, and immunocompromised status subgroups.

Table 1. Baseline characteristics of the individuals in 6 cohorts (prematched).

Characteristics	Vax cohort		Unvax cohort		Prevax cohort	
	Vax positive[a] (N=198)	Vax negative[b] (N=14,164)	Unvax positive[c] (N=3902)	Unvax negative[d] (N=33,850)	Prevax positive[e] (N=6462)	Prevax negative[f] (N=55,580)
Entry date	Full vaccinated date	Full vaccinated date	January 18, 2021	January 18, 2021	January 1, 2020	January 1, 2020
End date	September 21, 2021	End of the study	Vaccination date or September 21, 2021	Vaccination date or September 21, 2021	December 10, 2020	December 10, 2020
Previous visit counts, mean (SD)	80 (124.75)	65.7 (121.91)	64 (121.15)	44.4 (91.4)	70.6 (127.86)	45.2 (95.1)
Observational days, mean (SD)	5470 (3909.61)	5425.2 (3843.99)	5940.6 (4045.09)	4999.3 (3799.28)	5942.1 (3978.71)	4932.6 (3672.63)
Age (years), n (%)						
18-39	53 (26.8)	2995 (21.1)	1249 (32)	13,151 (38.9)	1401 (21.7)	19,074 (34.3)
40-59	42 (21.2)	3611 (25.5)	1167 (29.9)	10,363 (30.6)	1760 (27.2)	15,454 (27.8)
60-79	71 (35.9)	5547 (39.2)	1078 (27.6)	7836 (23.1)	2298 (35.6)	15,782 (28.4)
>=80	32 (16.2)	2011 (14.2)	408 (10.5)	2500 (7.4)	1003 (15.5)	5270 (9.5)
Gender, n (%)						
Female	110 (55.6)	9010 (63.6)	2199 (56.4)	21,065 (62.2)	3293 (51)	34,563 (62.2)
Male	88 (44.4)	5153 (36.4)	1702 (43.6)	12,765 (37.7)	3168 (49)	21,009 (37.8)
Unknown/other	N/A[g]	1 (0)	1 (0)	20 (0.1)	1 (0)	8 (0)
Race, n (%)						
Asian	3 (1.5)	545 (3.8)	73 (1.9)	804 (2.4)	132 (2)	2021 (3.6)
Black	30 (15.2)	1851 (13.1)	831 (21.3)	7046 (20.8)	1231 (19)	9218 (16.6)
White	88 (44.4)	6325 (44.7)	887 (22.7)	9740 (28.8)	1779 (27.5)	20,816 (37.5)
Unknown/other	77 (38.9)	5443 (38.4)	2111 (54.1)	16,260 (48)	3320 (51.4)	23,525 (42.3)
Ethnicity, n (%)						
Hispanic or Latino	58 (29.3)	3932 (27.8)	1840 (47.2)	12,081 (35.7)	2823 (43.7)	15,018 (27)
Not Hispanic or Latino	101 (51)	7571 (53.5)	1339 (34.3)	14,512 (42.9)	2224 (34.4)	27,194 (48.9)
Unknown/other	39 (19.7)	2661 (18.8)	723 (18.5)	7257 (21.4)	1415 (21.9)	13368 (24.1)
Vaccine brand, n (%)						
Moderna/mRNA[h]-1273	42 (21.2)	4626 (32.7)	N/A	N/A	N/A	N/A
Pfizer/BNT162b2	156 (78.8)	9538 (67.3)	N/A	N/A	N/A	N/A
Immunocompromised[i], n (%)						
Solid tumor	46 (23.2)	2354 (16.6)	274 (7)	2826 (8.3)	629 (9.7)	6702 (12.1)
CKD[j]	28 (14.1)	1486 (10.5)	364 (9.3)	2124 (6.3)	910 (14.1)	4098 (7.4)
HIV	9 (4.5)	478 (3.4)	114 (2.9)	982 (2.9)	190 (2.9)	1603 (2.9)
On immunosuppressive therapy	13 (6.6)	362 (2.6)	74 (1.9)	616 (1.8)	156 (2.4)	1248 (2.2)
Immunodeficiency disorders	49 (24.7)	2545 (18)	370 (9.5)	3124 (9.2)	759 (11.7)	6660 (12)
Organ transplant	10 (5.1)	366 (2.6)	108 (2.8)	610 (1.8)	244 (3.8)	1288 (2.3)
None	108 (54.5)	9031 (63.8)	3072 (78.7)	26,835 (79.3)	4641 (71.8)	41,150 (74)

[a]Individuals with a positive PCR[k] test after full vaccination and without evidence of SARS-CoV-2 infection before full vaccination.

[b]Individuals with a negative PCR test after full vaccination and without evidence of SARS-CoV-2 infection at any time in their records.

[c]Individuals with a positive PCR test after the entry date and before administration of a first vaccination dose (if ever administrated), while having no evidence of SARS-CoV-2 infection before the entry date.

[d]Individuals with a negative PCR test after the entry date and before administration of a first vaccination dose (if ever administrated), while having no evidence of SARS-CoV-2 infection before the entry date.

[e]Individuals with a positive PCR test before the vaccination period.

[f]Individuals with a negative PCR test and without any evidence of SARS-CoV-2 infection before the vaccination period.

[g]N/A: not applicable.

[h]mRNA: messenger RNA.

[i]These are not mutually exclusive (except for the “None” category).

[j]CKD: chronic kidney disease.

[k]PCR: polymerase chain reaction.

Table 2. Risk factors associated with the breakthrough case rate in the CUIMC/NYP[a].

Risk factors	Infection rate (95% CI) per 1000 person-days	IRR[b] (95% CI)[c]	*P* value	Adjusted IRR (95% CI)[d]	*P* value adjusted
Overall	0.16 (0.14-0.18)	N/A[e]	N/A	N/A	N/A
Age (years)					
18-39	0.19 (0.15-0.25)	Reference	Reference	N/A	N/A
40-59	0.14 (0.10-0.19)	0.77 (0.51-1.17)	.22	N/A	N/A
60-79	0.15 (0.11-0.19)	0.98 (0.66-1.47)	.93	N/A	N/A
>=80	0.16 (0.11-0.23)	1.16 (0.70-1.91)	.56	N/A	N/A
Gender					
Female	0.14 (0.11-0.17)	Reference	Reference	N/A	N/A
Male	0.19 (0.16-0.24)	1.47 (1.11-1.94)	.01	N/A	N/A
Race					
Asian	0.06 (0.01-0.18)	Reference	Reference	N/A	N/A
Black	0.19 (0.13-0.27)	3.25 (0.99-10.70)	.05	N/A	N/A
White	0.15 (0.12-0.19)	2.90 (0.91-9.19)	.071	N/A	N/A
Unknown/other	0.17 (0.13-0.21)	2.88 (0.91-9.18)	.073	N/A	N/A
Ethnicity					
Hispanic or Latino	0.18 (0.13-0.23)	Reference	Reference	N/A	N/A
Not Hispanic or Latino	0.15 (0.12-0.18)	0.85 (0.60-1.21)	.37	N/A	N/A
Unknown/other	0.17 (0.12-0.23)	0.91 (0.60-1.40)	.68	N/A	N/A
Vaccine brand					
Moderna/mRNA[f]-1273	0.10 (0.07-0.14)	Reference	Reference	Reference	Reference
Pfizer/BNT162b2	0.19 (0.16-0.22)	1.65 (1.17-2.33)	.005	1.66 (1.17-2.35)[g]	.004
Immune system					
Not immunocompromised	0.14 (0.11-0.17)	Reference	Reference	Reference	Reference
Is immunocompromised	0.19 (0.15-0.24)	1.49 (1.10-2.00)	.009	1.48 (1.09-2.00)	.011
Active tumor	0.22 (0.16-0.29)	1.57 (1.11-2.21)	.01	1.56 (1.10-2.2)	.012
CKD[h]	0.2 (0.13-0.29)	1.35 (0.89-2.07)	.16	1.33 (0.86-2.06)	.19
HIV	0.21 (0.10-0.40)	1.24 (0.63-2.44)	.54	1.25 (0.63-2.47)	.52
On immunosuppressed therapy	0.21 (0.16-0.28)	1.46 (1.03-2.05)	.03	1.45 (1.03-2.04)	.03
Primary immunodeficiency	0.4 (0.21-0.68)	2.55 (1.41-4.60)	.002	2.53 (1.40-4.58)	.002
Organ transplant	0.31 (0.15-0.57)	1.9 (0.98-3.71)	.059	1.9 (0.98-3.71)	.058

[a]CUIMC/NYP: Columbia University Irving Medical Center/New York Presbyterian.

[b]IRR: incidence rate ratio.

[c]Adjusted for number of visits, days of previous observation, and calendar month of the PCR[i] test result.

[d]Adjusted for number of visits, days of previous observation, calendar month of the PCR test result, and age at the last vaccine dose.

[e]N/A: not applicable.

[f]mRNA: messenger RNA.

[g]Adjusted for number of visits, days of previous observation, calendar month of the PCR test result, age at the last vaccine dose, and whether the immune system is compromised.

[h]CKD: chronic kidney disease.

[i]PCR: polymerase chain reaction.

Table 3. Top 10 (ranked by *P* value) condition and drug concepts associated with breakthrough cases in the Vax cohort in the CUIMC/NYP[a].

OMOP[b] concept ID[c]	IRR[d] (95% CI)[e]	*P* value	Condition name
Conditions			
315831	4.07 (2.07-7.99)	<.001	Chronic pulmonary heart disease
4228361	2.60 (1.56-4.33)	<.001	Asteatosis cutis
433740	3.62 (1.81-7.22)	<.001	Immunodeficiency disorder
253797	3.34 (1.69-6.59)	<.001	Postinflammatory pulmonary fibrosis
4177206	3.84 (1.78-8.28)	.001	Tubulointerstitial nephritis
378419	3.50 (1.68-7.28)	.001	Alzheimer disease
257315	2.97 (1.05-5.87)	.002	Bacterial pneumonia
4170770	2.45 (1.39-4.32)	.002	Epidermoid cyst
443729	2.78 (1.45-5.36)	.002	Peripheral circulatory disorder due to type 2 diabetes mellitus
44782747	3.62 (1.58-8.27)	.002	Acute deep venous thrombosis of femoral vein
Drugs			
1703063	4.33 (1.92-9.76)	<.001	Valganciclovir
715997	2.91 (1.50-5.65)	.002	Donepezil
1325608	3.62 (1.54-8.49)	.003	Pegfilgrastim
19008339	3.27 (1.42-7.53)	.005	Vitamin A
1317640	3.18 (1.40-7.24)	.006	Telmisartan
1154343	1.56 (1.13-2.15)	.007	Albuterol
40239216	3.01 (1.32-6.86)	.009	Linagliptin
1341927	2.21 (1.21-4.02)	.01	Enalapril
1149196	1.93 (1.17-3.17)	.01	Cetirizine
19003999	2.77 (1.27-6.04)	.01	Mycophenolate mofetil

[a]CUIMC/NYP: Columbia University Irving Medical Center/New York Presbyterian.

[b]OMOP: Observational Medical Outcomes Partnership.

[c]Only concepts that occurred in more than 100 individuals were included in this analysis.

[d]IRR: incidence rate ratio.

[e]Poisson regression was fitted for each variable with adjustment for age, number of visits, and observational days.

Table 4. Vaccine effectiveness against SARS-CoV-2 infection comparing the Vax cohort with a matched Prevax cohort before December 11, 2020.

Characteristics	Prevax/Vax[a], n (%)	Prevalence (Precax/Vax), n (%)	OR[b] (95% CI)[c]	Adjusted OR (95% CI)[d]
Overall	14,362 (100)/14,362 (100)	1556 (100)/198 (100)	0.12 (0.10-0.13)	0.12 (0.10-0.14)
Age (years)				
18-39	2997 (20.9)/3048 (21.2)	206 (13.2)/53 (26.8)	0.24 (0.18-0.32)	0.25 (0.18-0.34)
40-59	3788 (26.4)/3653 (25.5)	338 (21.7)/42 (21.2)	0.12 (0.09-0.16)	0.12 (0.09-0.17)
60-79	5218 (36.3)/5618 (39.1)	636 (40.9)/71 (35.8)	0.09 (0.07-0.12)	0.09 (0.07-0.12)
>=80	2359 (16.4)/2043 (14.2)	376 (24.2)/32 (16.2)	0.08 (0.06-0.12)	0.08 (0.06-0.12)
Gender				
Male	5142 (35.8)/5241 (36.5)	702 (45.1)/88 (44.4)	0.11(0.09-0.14)	0.11 (0.09-0.14)
Female	9220 (64.2)/9120 (63.5)	854 (54.9)/110 (55.6)	0.12 (0.10-0.15)	0.12 (0.10-0.15)
Is immunocompromised				
True	5287 (36.8)/5223 (36.4)	642 (41.3)/90 (45.5)	0.13 (0.10-0.16)	0.13 (0.10-0.16)
False	9075 (63.2)/9139 (63.6)	914 (58.7)/108 (54.5)	0.11 (0.09-0.13)	0.11 (0.09-0.13)

[a]Each cohort contained 14,362 individuals in total because of 1:1 matching; matching was based on previous visit counts, observational days, demographics, underlying immune conditions, and the NYC[e] 7-day rolling average of COVID-19 cases on the PCR[f] test date.

[b]OR: odds ratio.

[c]OR obtained by fitting a univariate logistic regression between the Vax cohort and a matched Prevax cohort.

[d]OR obtained by fitting a logistics regression adjusted for the previous number of visits and observational days.

[e]NYC: New York City.

[f]PCR: polymerase chain reaction.

Table 5. Vaccine effectiveness against SARS-CoV-2 infection comparing the Vax cohort with a matched Unvax cohort after June 18, 2021.

Characteristics	Unvax/Vax[a], n (%)	Incidence rate/1000 person-days (Unvax/Vax)	IRR[b] (95% CI)[c]	Adjusted IRR (95% CI)[d]
Overall	14,362 (100)/14,362 (100)	0.37/0.16	0.42 (0.36-0.49)	0.41 (0.35-0.48)
Age (years)				
18-39	3748 (26.1)/3048 (21.2)	0.32/0.2	0.63 (0.46-0.85)	0.64 (0.47-0.87)
40-59	4216 (29.4)/3653 (25.4)	0.37/0.14	0.38 (0.28-0.53)	0.38 (0.27-0.52)
60-79	4548 (31.7)/5618 (39.1)	0.39/0.15	0.37 (0.28-0.48)	0.35 (0.27-0.46)
>=80	1850 (12.9)/2043 (14.2)	0.47/0.16	0.34 (0.23-0.50)	0.31 (0.21-0.46)
Gender				
Male	5272 (36.7)/5241 (36.5)	0.4/0.19	0.49 (0.39-0.62)	0.48 (0.38-0.61)
Female	9089 (63.3)/9120 (63.5)	0.36/0.14	0.38 (0.31-0.47)	0.37 (0.30-0.45)
Is immunocompromised				
True	4079 (28.4)/5223 (36.4)	0.41/0.19	0.47 (0.37-0.59)	0.43 (0.34-0.55)
False	10,283 (71.6)/9139 (63.6)	0.36/0.14	0.38 (0.31-0.47)	0.38 (0.31-0.46)

[a]Each cohort contained 14,362 individuals in total because of 1:1 matching; matching was based on previous visit counts, observational days, demographics, underlying immune conditions, and the NYC[e] 7-day rolling average of COVID-19 cases on the PCR[f] test date.

[b]IRR: incidence rate ratio.

[c]IRR obtained by fitting a univariate Poisson regression between the Vax cohort and a matched Unvax cohort.

[d]IRR obtained by fitting a Poisson regression adjusted for the previous number of visits and observational days.

[e]NYC: New York City.

[f]PCR: polymerase chain reaction.

Discussion

Principal Findings

By comparing the breakthrough cohort (ie, Vax positive) against the no-breakthrough cohort (ie, Vax negative), we found a number of medical commodities were associated with an increased risk of breakthrough infection. First, we found that immunosuppressive therapy is associated with higher rates of breakthrough infection. Individuals with active tumors also had higher rates of breakthrough infection, suggesting that the effects of active malignancy or chemotherapy lead to a reduced immune response. There was a statistically not significant increase in individuals with a history of tumors, suggesting that individuals whose cancers are in remission are more similar to the average population in terms of immune response. Our findings are in line with prior studies of solid organ transplant recipients who have shown weaker immune responses in patients who are immunosuppressed and undergo vaccination against COVID-19 [44,45]. For example, valganciclovir is a drug used commonly to prevent cytomegalovirus disease after solid organ transplantation [46], and we found it was significantly associated with the increased risk of breakthrough infection, indicating individuals who underwent solid organ transplant were among those at high risk of breakthrough infections. We also observed an increased risk of infection in individuals with prior lung infection. A potential explanation is the microbiome changes within the lung that play a key role in the initiation and progression of COVID-19 [47,48]. In addition, studies have shown that patients with COVID-19 and preexisting interstitial lung disease (ILD) had a poorer prognosis [49,50], which highlights the importance of staying vigilant and continued use of personal protective and social measures, even with vaccination among those individuals. Furthermore, in individuals with Alzheimer disease who were vaccinated, there was an increased risk of infection, which might be due to their frailty and medical vulnerability, and nonadherence to infection control measures, such as physical distancing [51]. This is also confirmed by the finding that donepezil is a high-risk factor, which is used to treat confusion (dementia) related to Alzheimer disease [52]. We did not find a significantly increased risk of breakthrough infection in individuals with CKD. An ongoing study (the Renal Patients COVID-19 Vaccination Immune Response [RECOVAC-IR] study) aims to provide further guidance regarding the efficacy of vaccines in patients with CKD or whether other measures, such as booster vaccinations, are required [53].

Although our findings reaffirmed the high protection of mRNA vaccines against COVID-19 infection, we found that Moderna/mRNA-1273 had an overall higher effectiveness in preventing SARS-CoV-2 infections. A previous high-quality prospective study [54] involving 3975 individuals observed through April 2021 demonstrated similar vaccine effectiveness between the mRNA vaccines, but it was underpowered and did not perform statistical analysis. A more recent Mayo Clinic study of data collected through July 2021 [55] was consistent with our findings despite differences in cohort definitions and geography. Another recent study comparing the SARS-CoV-2 antibody response following vaccination similarly found higher antibody titers in participants vaccinated with mRNA-1273 compared with those vaccinated with Pfizer/BNT162b258. A more recent meta-analysis study of data collected through September 2021 showed that the estimated long-term vaccine effectiveness for COVID-19 hospitalization was 85.4% (95% CI 84.8%-86.0%) with the Pfizer/BNT162b2 vaccine and 89.8% (95% CI 89.2%-90.4%) with Moderna/mRNA-1273. Additional studies should be considered to provide further guidance on effectiveness differences between vaccine brands and booster shot prioritization. Although individuals with immunosuppressed disorders are at higher risk of developing breakthrough infection, the adjusted IRR in immunocompromised individuals is 0.43 (95% CI 0.34-0.55), supporting the conclusion that vaccination can still greatly reduce the infection rate among this subgroup [56]. Our study supports the current policies recommending that immunocompromised individuals receive booster doses [57].

It is important to provide constant public health surveillance of vaccine protection. By leveraging EHR data from various health systems, we can provide more robust and generalizable evidence of vaccine effectiveness. Unfortunately, it is not always easy to aggregate the medical data from multiple institutions due to Health Insurance Portability and Accountability Act of 1996 (HIPPA) constrains. Therefore, we developed an entirely CDM-based analysis pipeline, making it easily transferable to dozens of other health care databases compatible with it [58]. We have provided our OMOP-compatible analysis pipeline on the GitHub repository [59]. Other institutions that have implemented their OMOP instance can download the code and easily replicate the analysis using their own institution's OMOP instance and share the evidence in a timely manner.

Limitations

Given the high level of missingness typically found in EHR data, it is challenging to estimate the absolute incidence rate of breakthrough infections. In our study, the incidence rate among the vaccinated cohort was estimated to be 0.16 per 1000 person-days. This potentially overestimates the incidence rate (particularly in comparison to 0.031 in Israel's national surveillance data [60], ~0.01 in the original Pfizer/BNT162b2 and Moderna/mRNA-1273 trials [1,2]) because we imposed a criterion to only include those who have at least 1 PCR test available, which is also called test-negative design [61]. If we remove this requirement, the incidence rate among the vaccinated cohort becomes ~0.007 per 1000 person-days. However, this is an underestimation of the true rate because some of the SARS-CoV-2-infected individuals might have been tested elsewhere or not at all. In addition, despite adopting a test-negative design, we were still unable to confirm whether negative cases were truly negative (eg, tested positive elsewhere). Similarly, some patients may be incorrectly labeled as unvaccinated if their vaccinations took place outside of NYC or the NYP health system, which could lower effectiveness estimations. However, our main focus in this study was to identify the risk subgroups at increased risk of breakthrough infections, and a cofounding-aligned comparative design can achieve this goal by matching the patient's demographics and their tendency in seeking health care in our medical center.

Another limitation of this study is we could not stratify breakthrough infections by variant type due to limitations in testing data. Our study used the EHR data collected through September 2021, which covers periods where the B.1.1.7 (alpha) and B.1.617.2 (delta) variants were prevalent. Our findings cannot be generalized to other newly emerged variants of concerns, including B.1.1.529 (omicron) for which the existing mRNA vaccines may have differing effectiveness. However, this is not unique to our study, as the pandemic has often evolved faster than high-quality analyses can be performed. Even a recent systematic review of the efficacy and effectiveness of the COVID-19 vaccines published in January 2022 included only papers before April 2021 (the data collected in those papers can be from even earlier). The conflict between the speed of scientific publication and the rapid evolution of the pandemic remains a significant challenge for the overall research community.

Finally, the CUIMC/NYP is an academic medical center in NYC, which might not represent the general American population or other potential patient groups of interest. In particular, the overall population in our study is sicker than the general population, as evidenced by the high rate of comorbidities and older age of our patient cohort.

Conclusion

We performed a retrospective analysis to investigate risk factors contributing to COVID-19 breakthrough infections among vaccinated individuals. We found those who are male, immunocompromised, or have preexisting pulmonary disease are at a higher risk of COVID-19 breakthrough infection. Although both vaccines are highly effective in preventing SARS-CoV-2 infection, Moderna/mRNA-1273 is associated with a lower risk of breakthrough infection than Pfizer/BNT162b2. Multiple medical institutions' data are warranted to better link the PCR test results and vaccination information. Those with an OMOP instance of their data can reapply our analysis to check the robustness of our results [59].

Acknowledgments

This study was supported by the National Library of Medicine/the National Human Genomic Research Institute (Grant R01LM012895-03S1), and additional support was provided by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health (Awards 5UM1AI069470-14, U01CK0000592, K23AI150378, and L30AI133789 to JZ).

Conflicts of Interest

None declared.

Multimedia Appendix 1
The details of OMOP concepts used for cohort definition. OMOP: Observational Medical Outcomes Partnership.
[XLSX File (Microsoft Excel File), 4340 KB - publichealth_v8i5e35311_app1.xlsx]

Multimedia Appendix 2
The full list of breakthrough-associated condition concepts.
[XLSX File (Microsoft Excel File), 127 KB - publichealth_v8i5e35311_app2.xlsx]

Multimedia Appendix 3
The full list of breakthrough-associated drug concepts.
[XLSX File (Microsoft Excel File), 4348 KB - publichealth_v8i5e35311_app3.xlsx]

Multimedia Appendix 4
Study design in identifying risk factors for breakthrough events by comparing PCR-positive cases and PCR-negative cases among vaccinated individuals. PCR: Polymerase Chain Reaction.
[PDF File (Adobe PDF File), 74 KB - publichealth_v8i5e35311_app4.pdf]

Multimedia Appendix 5
Study design in assessing vaccine effectiveness by comparing a vaccinated cohort and a matched unvaccinated cohort.
[PDF File (Adobe PDF File), 69 KB - publichealth_v8i5e35311_app5.pdf]

Multimedia Appendix 6
Study design in assessing vaccine effectiveness by comparing a vaccinated cohort and a matched prevaccinated cohort.
[PDF File (Adobe PDF File), 66 KB - publichealth_v8i5e35311_app6.pdf]

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Abbreviations

CDC: Centers for Disease Control and Prevention
CDM: Common Data Model
CKD: chronic kidney disease
CUIMC/NYP: Columbia University Irving Medical Center/New York Presbyterian
EHR: electronic health record
IRR: incidence rate ratio
mRNA: messenger RNA
NYC: New York City
OMOP: Observational Medical Outcomes Partnership
OR: odds ratio
PCR: polymerase chain reaction

Edited by T Sanchez, A Mavragani; submitted 02.12.21; peer-reviewed by K Lutrick, S Modi; comments to author 18.03.22; revised version received 29.03.22; accepted 27.04.22; published 24.05.22.

Please cite as:
Liu C, Lee J, Ta C, Soroush A, Rogers JR, Kim JH, Natarajan K, Zucker J, Perl Y, Weng C
Risk Factors Associated With SARS-CoV-2 Breakthrough Infections in Fully mRNA-Vaccinated Individuals: Retrospective Analysis
JMIR Public Health Surveill 2022;8(5):e35311
URL: https://publichealth.jmir.org/2022/5/e35311
doi:10.2196/35311
PMID:35486806

Original Paper

Artificial Intelligence–Enabled Social Media Analysis for Pharmacovigilance of COVID-19 Vaccinations in the United Kingdom: Observational Study

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Abstract

Background: The rollout of vaccines for COVID-19 in the United Kingdom started in December 2020. Uptake has been high, and there has been a subsequent reduction in infections, hospitalizations, and deaths among vaccinated individuals. However, vaccine hesitancy remains a concern, in particular relating to adverse effects following immunization (AEFIs). Social media analysis has the potential to inform policy makers about AEFIs being discussed by the public as well as public attitudes toward the national immunization campaign.

Objective: We sought to assess the frequency and nature of AEFI-related mentions on social media in the United Kingdom and to provide insights on public sentiments toward COVID-19 vaccines.

Methods: We extracted and analyzed over 121,406 relevant Twitter and Facebook posts, from December 8, 2020, to April 30, 2021. These were thematically filtered using a 2-step approach, initially using COVID-19–related keywords and then using vaccine- and manufacturer-related keywords. We identified AEFI-related keywords and modeled their word frequency to monitor their trends over 2-week periods. We also adapted and utilized our recently developed hybrid ensemble model, which combines state-of-the-art lexicon rule–based and deep learning–based approaches, to analyze sentiment trends relating to the main vaccines available in the United Kingdom.

Results: Our COVID-19 AEFI search strategy identified 46,762 unique Facebook posts by 14,346 users and 74,644 tweets (excluding retweets) by 36,446 users over the 4-month period. We identified an increasing trend in the number of mentions for each AEFI on social media over the study period. The most frequent AEFI mentions were found to be symptoms related to appetite (n=79,132, 14%), allergy (n=53,924, 9%), injection site (n=56,152, 10%), and clots (n=43,907, 8%). We also found some rarely reported AEFIs such as Bell palsy (n=11,909, 2%) and Guillain-Barre syndrome (n=9576, 2%) being discussed as frequently as more well-known side effects like headache (n=10,641, 2%), fever (n=12,707, 2%), and diarrhea (n=16,559, 3%). Overall, we found public sentiment toward vaccines and their manufacturers to be largely positive (58%), with a near equal split between negative (22%) and neutral (19%) sentiments. The sentiment trend was relatively steady over time and had minor variations, likely based on political and regulatory announcements and debates.

Conclusions: The most frequently discussed COVID-19 AEFIs on social media were found to be broadly consistent with those reported in the literature and by government pharmacovigilance. We also detected potential safety signals from our analysis that have been detected elsewhere and are currently being investigated. As such, we believe our findings support the use of social media analysis to provide a complementary data source to conventional knowledge sources being used for pharmacovigilance purposes.

(JMIR Public Health Surveill 2022;8(5):e32543) doi:10.2196/32543

KEYWORDS

COVID-19; artificial intelligence; deep learning; Facebook; health informatics; natural language processing; public health; sentiment analysis; social media; Twitter; infodemiology; vaccination

Introduction

A number of vaccines for SARS-CoV-2 infection have been developed, found to be effective, and are now being rolled out at unprecedented speed and scale across the world. A major component of vaccine deployment strategies should be the use of robust surveillance systems to monitor for adverse effects following immunization (AEFIs) [1]. This is particularly important given the persisting concerns around vaccine hesitancy and that new vaccine technologies are being employed for the first time [2].

Postlicensure monitoring of AEFIs primarily consists of passive surveillance, whereby reports of AEFIs are collected and statistically analyzed by regulators (eg, Vaccine Adverse Event Reporting System in the United States and Yellow Card in the United Kingdom), and also in epidemiological studies [3]. However, there has recently been growing interest in exploring the use of social media data to supplement traditional pharmacovigilance methods [4]. These techniques could be particularly beneficial in low- and middle-income countries given their underdeveloped vaccine safety surveillance systems [5,6].

Recent studies have highlighted the potential of artificial intelligence–enabled social media analysis to complement conventional assessment methods, such as public surveys, and inform governments and institutions on public attitudes [7-9]. Social media analysis has yet to be used to explore commonly reported AEFIs with a vaccine against SARS-CoV-2 infection, which could help to identify potential safety signals not being identified elsewhere (eg, rarely reported side effects). Sentiment analysis can be useful to gauge public opinion around topics of interest, and peaks and valleys on sentiment trend graphs could inform deliberations on sensitivity analyses conducted prior to studies.

In this study, we aimed to assess the frequency and nature of COVID-19 AEFI-related mentions on social media and analyze public sentiment toward vaccines in the United Kingdom.

Methods

Data Sources

We used data from two of the most popular and representative social media platforms, namely, Facebook and Twitter. Facebook posts were obtained from CrowdTangle, and tweets were obtained from the COVID-19 Twitter Dataset (using a publicly available Twitter Application Processing Interface) [10,11]. We extracted English-language Facebook posts and tweets, posted in the United Kingdom from December 8, 2020 (the start of the United Kingdom's COVID-19 vaccination campaign), to April 30, 2021, and thematically filtered these using a 2-step approach. The initial filter used predefined COVID-19–related keywords, and the resulting data set was used to assess COVID-19 AEFI-related mentions. The second filter used vaccine-related keywords, and this subset of data was used to analyze public sentiment toward vaccines and their manufacturers. A geographical filter for the United Kingdom was also applied across the data set (see Multimedia Appendix 1 for a detailed search strategy) [7].

Vaccine AEFI Search Strategy

Our vaccine adverse effect search strategy was informed by AEFI reports received by the Yellow Card scheme and the Vaccine Adverse Event Reporting System, the national passive surveillance pharmacovigilance systems of the United Kingdom and the United States, respectively (see Multimedia Appendix 1 for a detailed search strategy). The frequency of grouped AEFI mentions was calculated and plotted. The output combined results from the Facebook and Twitter data sets (which had the "initial" filter applied) and represented them using horizontal stacked bar charts. The distribution of user posts was also obtained using descriptive statistics and density distribution plots.

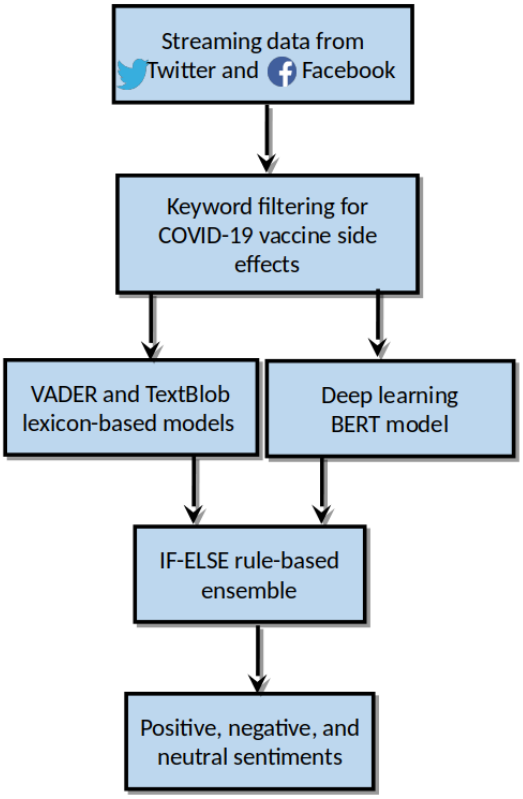
Hybrid Ensemble Model

We also adapted and utilized our recently developed hybrid ensemble model (Figure 1), which combines state-of-the-art lexicon rule–based and deep learning–based approaches, to analyze sentiment trends relating to the main vaccines and their manufacturers since their rollout in the United Kingdom. Sentiment trend graphs were plotted, and average sentiment was calculated.

Our hybrid ensemble model utilized weighted averaging of the VADER (Valence Aware Dictionary for Sentiment Reasoning) and TextBlob lexicon-based models, resulting in the following weights: VADER × 0.45 + TextBlob × 0.55. A higher weight of 0.55 was assigned to TextBlob as it demonstrated marginally better accuracy compared to VADER for classifying positive sentiment. The averaged output was combined with the BERT (Bidirectional Encoder Representations from Transformers) deep learning model with the help of rule-based constructs. The lexicon models performed better for positive sentiments, and the BERT model provided better performance for neutral and

negative sentiments. Therefore, they were combined through IF-ELSE rule-based programming constructs. If the output of lexicon-based weighted averaging was positive, then the IF-ELSE rules chose a positive output as the final output of the ensemble; otherwise, for neutral and negative sentiments, the output of the BERT model was preferred as the final ensemble output sentiment.

Figure 1. Hybrid ensemble sentiment analysis framework. BERT: Bidirectional Encoder Representations from Transformers; VADER: Valence Aware Dictionary for Sentiment Reasoning.



Ethical Considerations

The data analyzed in this study were completely in the public domain, and no ethical review was necessary. A thorough assessment of the study's privacy risk to individuals was conducted to ensure compliance with the General Data Protection Regulation. We also complied with best practices for user protection. Nonpublic material was not included in our data set. We did not share any posts or quotes from individuals, or names or locations of users that are not public organizations or entities.

Results

Our COVID-19 AEFI search strategy identified 46,762 unique Facebook posts by 14,346 users and 74,644 tweets (excluding retweets) by 36,446 users over the 4-month period. This corresponded to an average of 3.26 (SD 6.40) posts per user on Facebook and 2.01 (SD 1.76) posts per user on Twitter. Density distribution plots showed the log-normal distributions of posts per user for both platforms (see Figures S1 and S2 in Multimedia Appendix 1).

Figure 2 shows the frequency of grouped AEFI mentions across Facebook and Twitter, divided into 2-week periods (see a detailed breakdown in Multimedia Appendix 1: Table S1, Figures S3 and S4). We identified an increasing number of mentions for each AEFI on social media over the period of study. The most frequent mentions were found to be symptoms related to appetite change (n=79,132, 14%), allergy (n=53,924, 9%), diarrhea (n=16,559, 3%), fever (n=12,707, 2%), headache (n=10,641, 2%), injection site (n=56,152, 10%), and clots (n=43,907, 8%) (see Table S1 in Multimedia Appendix 1). Less commonly mentioned AEFIs included Bell palsy (n=11,909, 2%) and Guillain-Barre syndrome (n=9576, 2%).

Figure 3 shows the average weekly public sentiment on Twitter and Facebook. Overall, we found public sentiment toward vaccines to be largely positive (58%), with negative (22%) and neutral (19%) sentiment nearly equally split. The sentiment trend was relatively steady over time and had minor variations, likely based on political and regulatory announcements and debates.

Figure 2. Stacked bar graph showing the number of mentions of each COVID-19 vaccine side effect over time on both Facebook and Twitter in the United Kingdom from December 2020 to April 2021.

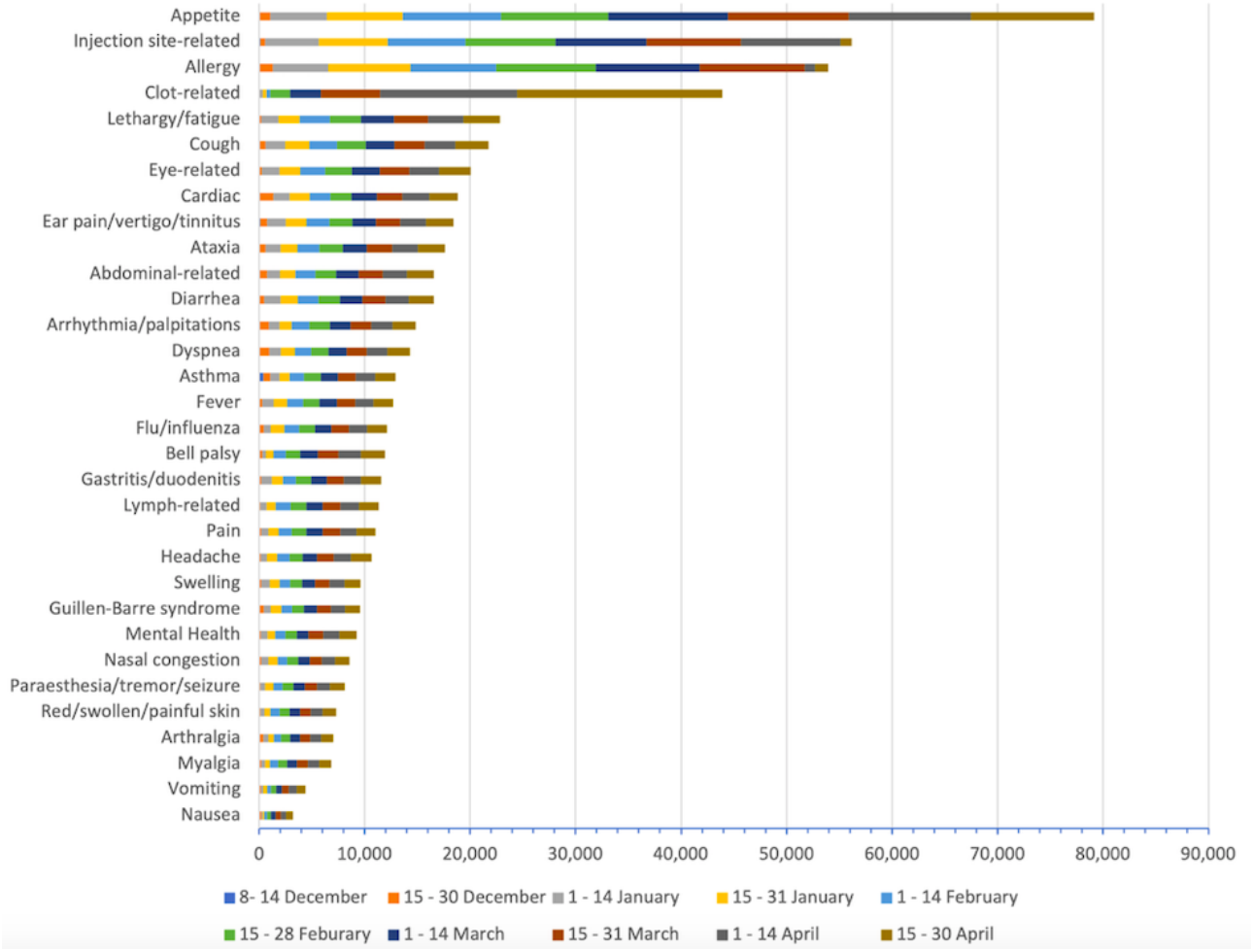
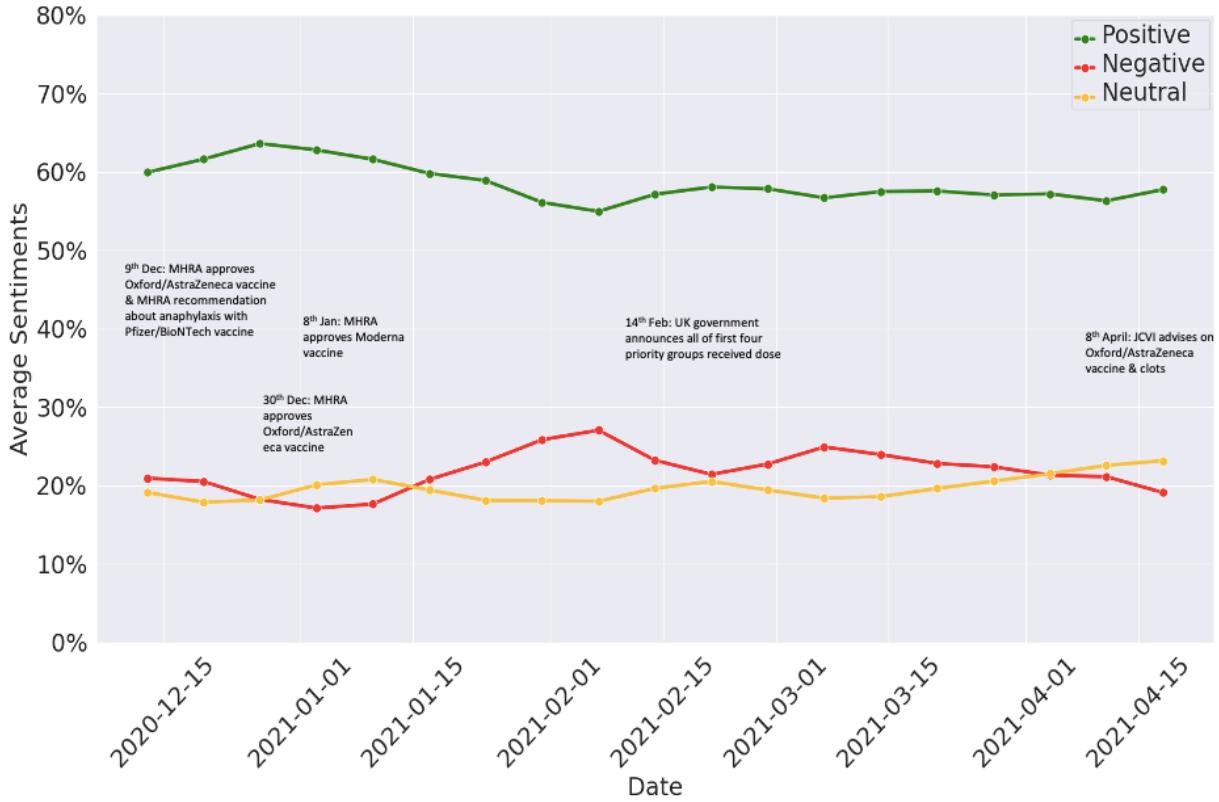


Figure 3. Average weekly public sentiments on COVID-19 vaccines on Facebook and Twitter in the United Kingdom from December 2020 to April 2021 with annotations of some key events. JCVI: Joint Committee on Vaccination and Immunisation; MHRA: Medicines and Healthcare Products Regulatory Agency.



Discussion

Principal Findings

We have identified and extracted a substantial number of social media posts relating to vaccines and possible AEFIs in the United Kingdom. Our analysis showed an increasing trend in the number of AEFI mentions over time and revealed that both established adverse events (eg, headaches and clots) and those still under investigation (eg, Bell palsy and Guillain-Barre syndrome) were being discussed.

The most frequently mentioned symptoms were broadly found to be similar to those most frequently reported in the Yellow Card system [12]. For example, the most commonly reported AEFI on Yellow Card was related to injection-site reactions and generalized symptoms (eg, fever, headache, lethargy, muscle ache, flu, vomit, nausea), which in our analysis accounted for 10% and 13% of the mentions, respectively. The number of clot-related AEFI mentions increased 2-fold from the end of March to mid-April, and approximately 2-fold again until the end of April, which correlates with the significant press coverage of reports in March 2021 on blood clots being associated with the Oxford-AstraZeneca vaccine [13]. In a recent study, the most common systemic side effects were found to be headache and fatigue, and the most common localized side effect was injection site–related pain, redness, or swelling [14]. The latter is consistent with our findings, where injection site pain or redness (n=56,152, 10%) was one of the most commonly mentioned AEFIs. It is interesting to note that we found more rarely reported AEFIs, such as Bell palsy, Guillain-Barre syndrome, and appetite changes, being discussed as frequently as more well-known side effects, such as headache, fever, and diarrhea. This can be useful for governments and institutions to detect potential safety signals and could enable further exploration of public perceptions toward rarer side effects and consideration of educational campaigns and interventions.

Public sentiment toward vaccines over the course of the vaccination rollout campaign has on the whole been consistently positive. This is in line with the successful uptake of vaccinations in the United Kingdom and important government and political announcements (examples can be found annotated in Figure 3). These findings indicate the potential for social media analysis to complement traditional surveys, both by informing their design and also corroborating findings [15].

Overall, this work has confirmed the opportunity for social media analysis to provide insights into public sentiments and complement more established pharmacovigilance efforts. It is important to note that we did not aim to identify new side effects; our objective was rather to monitor trends relating to currently reported ones. The trends identified can be useful for public health policy makers to identify which symptoms are being discussed most frequently. Further analysis can then be carried out on social media, alongside traditional surveys, to explore public perception relating to specific AEFIs.

Strengths and Limitations

Our study is the first to assess trends in the number of AEFI mentions on both Facebook and Twitter. It employed our novel ensemble-based approach to analyze public sentiment toward vaccines over the course of the vaccination drive and has

provided important insights into the number of posts relating to vaccines and AEFIs, trends in the number of AEFI mentions, and public sentiment toward vaccinations. Our AEFIs were informed by the Yellow Card system, and our keywords for filtering were informed by clinicians and a literature search. Our novel ensemble-based approach has been shown to robustly identify public sentiment over a period of time, for example, toward vaccinations and apps [8,9].

It is important to consider the limitations of our study to define challenges and inform future work. Social media users are by and large not representative of the wider UK population (eg, younger, wealthier, higher level of education); the age factor, in this case, is particularly significant given that the majority of COVID-19 vaccinations within the United Kingdom so far has been given to older age groups [8,9]. The selection bias from social media can be mitigated by using it as a complementary data source to conventional knowledge sources and by ensuring any search terms used to filter data sets are defined appropriately.

Another limitation is that it is difficult to ascertain which posts are specific to those who had received the vaccine (making them less useful if studying side-effect experiences) and would require deeper semantic and linked analysis with external trustworthy data sources, such as surveys and electronic health records. In addition, a proportion of social media users are known to be more vocal than others, which can skew study findings. Descriptive statistics and density plots of the distribution of user posts can therefore be useful to help contextualize findings (as was done in our study), while social network analysis could help identify clusters of users on a large scale.

Our study was also limited by its relatively small sample size, due to a stringent search strategy, restricting tweets to those with geotags and the use of the COVID-19 Twitter Dataset. We combined our results for Facebook and Twitter to mitigate this. For future work, we propose obtaining Academic Research access from Twitter and hydrating tweets at a large scale using an optimized search strategy. While this would be more time and labor intensive, it will provide more flexibility in the scope and breadth of tweets, as the data set would not be prefiltered for COVID-19. We also did not carry out any further manual labeling of social media posts to further train our ensemble-based model for extracting public sentiment due to resource limitations (however, it was trained in a previous study [8] to assess sentiment toward vaccines). Lastly, misinformation and fake news remain open challenges for social media analysis. Social media platforms have their own mechanisms to help tackle this issue; however, for future work, researchers can utilize techniques, such as social network analysis, to identify and remove clusters of users from their data sets.

Conclusion

In summary, our work has shown it is possible to identify and interrogate large volumes of social media posts using our novel ensemble-based approach to generate insights into public sentiments toward vaccines and AEFIs. These can help develop a complementary data source to the conventional knowledge sources that are being used for pharmacovigilance purposes. In the future, governments and institutions should consider the opportunity to use social media analyses to aid pharmacovigilance efforts.

Acknowledgments

This work was supported by the Chief Scientist Office of the Scottish Government under its COVID-19 priority research program (COV/NAP/20/07). AS was supported by BREATHE - The Health Data Research Hub for Respiratory Health (MC_PC_19004), funded by the UK Research and Innovation Industrial Strategy Challenge Fund and delivered through Health Data Research UK. AH was supported by Engineering and Physical Sciences Research Council grants (EP/T021063/1, EP/T024917/1) from the Government of the United Kingdom.

Data Availability

We have made the code and data used for data extraction and analysis openly available on GitHub [16].

Conflicts of Interest

AS is a member of the chief medical officer's COVID-19 Advisory Group of the Scottish Government and the Government of the United Kingdom's New and Emerging Respiratory Virus Threats Risk Stratification Subgroup. The views expressed are those of the authors and do not represent the views of the Scottish or UK Governments.

Multimedia Appendix 1
Detailed search strategy and results.
[DOCX File , 358 KB - publichealth_v8i5e32543_app1.docx]

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Abbreviations

AEFI: adverse effect following immunization
BERT: Bidirectional Encoder Representations from Transformers
VADER: Valence Aware Dictionary for Sentiment Reasoning

Edited by T Sanchez; submitted 02.08.21; peer-reviewed by A Louren, L Huangfu, T Ntalindwa, P Li; comments to author 26.08.21; revised version received 03.11.21; accepted 08.02.22; published 27.05.22.

Please cite as:
Hussain Z, Sheikh Z, Tahir A, Dashtipour K, Gogate M, Sheikh A, Hussain A
Artificial Intelligence–Enabled Social Media Analysis for Pharmacovigilance of COVID-19 Vaccinations in the United Kingdom: Observational Study
JMIR Public Health Surveill 2022;8(5):e32543
URL: https://publichealth.jmir.org/2022/5/e32543
doi:10.2196/32543
PMID:35144240

Original Paper

The Efficacy of a Brief, Altruism-Eliciting Video Intervention in Enhancing COVID-19 Vaccination Intentions Among a Population-Based Sample of Younger Adults: Randomized Controlled Trial

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Abstract

Background: High COVID-19 vaccine uptake is crucial to containing the pandemic and reducing hospitalizations and deaths. Younger adults (aged 20-39 years) have demonstrated lower levels of vaccine uptake compared to older adults, while being more likely to transmit the virus due to a higher number of social contacts. Consequently, this age group has been identified by public health authorities as a key target for vaccine uptake. Previous research has demonstrated that altruistic messaging and motivation is associated with vaccine acceptance.

Objective: This study had 2 objectives: (1) to evaluate the within-group efficacy of an altruism-eliciting short, animated video intervention in increasing COVID-19 vaccination intentions amongst unvaccinated Canadian younger adults and (2) to examine the video's efficacy compared to a text-based intervention focused exclusively on non-vaccine-related COVID-19 preventive health measures.

Methods: Using a web-based survey in a pre-post randomized control trial (RCT) design, we recruited Canadians aged 20-39 years who were not yet vaccinated against COVID-19 and randomized them in a 1:1 ratio to receive either the video intervention or an active text control. The video intervention was developed by our team in collaboration with a digital media company. The measurement of COVID-19 vaccination intentions before and after completing their assigned intervention was informed by the multistage Precaution Adoption Process Model (PAPM). The McNemar chi-square test was performed to evaluate within-group changes of vaccine intentions. Exact tests of symmetry using pairwise McNemar tests were applied to evaluate changes in multistaged intentions. Between-group vaccine intentions were assessed using the Pearson chi-square test postintervention.

Results: Analyses were performed on 1373 participants (n=686, 50%, in the video arm, n=687, 50%, in the text arm). Within-group results for the video intervention arm showed that there was a significant change in the intention to receive the vaccine (χ^2_1=20.55,

P<.001). The between-group difference in postintervention intentions (χ^2_3=1.70, *P*=.64) was not significant. When administered the video intervention, we found that participants who had not thought about or were undecided about receiving a COVID-19 vaccine were more amenable to change than participants who had already decided not to vaccinate.

Conclusions: Although the video intervention was limited in its effect on those who had firmly decided not to vaccinate, our study demonstrates that prosocial and altruistic messages could increase COVID-19 vaccine uptake, especially when targeted to younger adults who are undecided or unengaged regarding vaccination. This might indicate that altruistic messaging provides a "push" for those who are tentative toward, or removed from, the decision to receive the vaccine. The results of our study could also be applied to more current COVID-19 vaccination recommendations (eg, booster shots) and for other vaccine-preventable diseases.

Trial Registration: ClinicalTrials.gov NCT04960228; https://clinicaltrials.gov/ct2/show/NCT04960228

(JMIR Public Health Surveill 2022;8(5):e37328) doi:10.2196/37328

KEYWORDS

COVID-19; vaccination; altruism; prosocial motives; video intervention; randomized controlled trial; younger adults; vaccine hesitancy; public health; youth; digital intervention; health intervention; health promotion; web survey; digital health; online health; health information

Introduction

SARS-CoV-2 has caused the greatest pandemic of our lifetime. At the time of writing, the virus had infected 251 million people and killed over 5 million worldwide [1]. To contain the COVID-19 pandemic, governments have recommended and mandated preventive health measures, such as physical distancing, mask wearing, and restrictions on indoor and outdoor gatherings. Although these measures have been instrumental in reducing virus transmission and the burden on the health care system, they have also had severe impacts on the economy and individual well-being [2-4].

Following a rapid mobilization and development process, COVID-19 vaccination was introduced in late 2020, and widespread vaccination has since been encouraged for the general population. In Canada, vaccinating against COVID-19 has likely saved 476,000 lives [5]. Compared to those who are vaccinated, unvaccinated individuals make up a disproportionally higher percentage of infection cases (61.9% vs 38.1%), hospitalizations (77.3% vs 22.7%), and deaths (74.6% vs 25.4%) [6]. Further, there is evidence that vaccination has helped reduce virus transmission [7].

Vaccine hesitancy, which refers to a set of attitudes and beliefs that may lead to delay or refusal of 1 or more vaccines despite their availability [8,9], poses a significant threat to achieving sufficient COVID-19 vaccination rates to mitigate the pandemic. Younger age has been associated with vaccine hesitancy [10-14]. Additionally, younger adults often experience mild or asymptomatic infections [15,16] and are more socially active. In Canada, this age group also demonstrates lower adherence to other preventive health measures (eg, social distancing) [17,18]. Thus, younger adults play an important role in virus transmission. To protect the Canadian population at large, it is important to ensure adequate vaccine uptake amongst younger adults.

Although providing basic vaccine education to the population is critical, research has shown that correcting vaccine misinformation and refuting vaccine myths are largely ineffective in enhancing vaccine intentions [19]. This resistance may be attributable in part to confirmation bias. Studies have shown that vaccine-hesitant individuals are less receptive to new information that disconfirms their beliefs [19,20]. Additionally, vaccine hesitancy cannot be understood as a total refusal or acceptance of vaccination but rather as a continuum. Individuals in different stages of vaccine decision-making have different attitudes and beliefs toward vaccination [21,22]. Therefore, the efficacy of interventions designed to address vaccine hesitancy might be moderated by the set of attitudes, beliefs, and cognitions a specific individual has toward vaccination.

A novel and promising approach is to develop interventions that elicit altruism, that is, intentional and voluntary action in which the primary goal is to increase the welfare of another person [23,24]. Previous hypothetical and laboratory game studies have found that altruistic messages can increase vaccination intentions [25-27] or demonstrated that altruistic motives were related to self-reports of actual vaccine intentions or behaviors. However, few studies have experimentally elicited altruism to examine its impact on vaccine intentions [28,29], and none have used a video-based intervention. Younger adults have lower concerns of hospitalization and mortality than older adults [30] and thus may perceive receiving a COVID-19 vaccine as less personally beneficial. To increase vaccination intentions and uptake amongst this age group, it could be more effective to highlight messages of altruism and the protection of others rather than oneself [12,31].

Considering the need to address hesitancy toward COVID-19 vaccination amongst younger adults, the aim of this study was to evaluate the efficacy of a short video intervention eliciting altruistic motives for vaccination. Understanding the effectiveness of altruism-based messaging could inform public health communications targeting COVID-19 vaccine uptake in this age group. The specific objectives were to estimate (1) pre- to postintervention change of COVID-19 vaccine intentions and (2) between-group COVID-19 vaccine intentions postintervention.

Methods

Trial Design

We used a 2-arm parallel randomized pre-post design. Participants in a web-based survey were randomly allocated in a 1:1 ratio to the video-based intervention or the active control arm consisting of a text-based intervention. The study was designed to detect a significant pre-post increase in COVID-19 vaccine intentions in the video intervention group and the superiority of the video intervention compared to the text intervention in eliciting pro-COVID-19 vaccine intentions. We used the Consolidated Standards of Reporting Trials (CONSORT) statement to report the results [32].

Participants and Study Setting

Participants from all Canadian provinces or territories who met following eligibility criteria were enrolled in the study: (1) not vaccinated for COVID-19, (2) age range of 20-39 years, (3) Canadian resident, and (4) willing to complete the survey in either English or French. To ensure a balanced participation in the study and informed by the Canadian Census data, we used quota sampling for the primary language spoken at home (80% Anglophones, 20% Francophones); biological sex (50% males, 50% females), annual total income before taxes of all members of the household before the pandemic (50% more than CA $75,000 [US $58,563.80], 50% less than CA $75,000), and population density (80% urban, 20% rural). During data collection (July 30-September 13, 2021), the daily incidence of COVID-19 was rising, signaling the emergence of the fourth pandemic wave in Canada that reached its peak mid-September, when about 4300 new daily cases were reported nationwide. In this period, about one-third of daily cases were reported in Canadians aged 20-39 years and the estimated daily COVID-19 incidence in this age group reached 1500 (35% of total daily cases) [33]. In Canada, our target population became eligible for COVID-19 vaccination in April-May 2021, although provincial rollout varied widely. Therefore, as of April 17, 2021, the national cumulative percentage of individuals aged 20-39 years who received at least 1 COVID-19 vaccine dose was only about 9%. Vaccine uptake increased sharply in the upcoming months and the cumulative percentage of individuals in this age group who received at least one dose reached about 62% by June 5th, 2021. During data collection, the estimated national vaccine coverage (at least 1 dose) in individuals aged 20-39 years increased from about 72% at the start to 78% [34]. In this period that corresponded with the beginning of the academic year, extensive public health interventions (eg, messages distributed through media) aiming at increasing vaccine uptake were ongoing and vaccination mandates were beginning to be implemented in some jurisdictions (eg, Quebec).

Study Procedures

Data collection was carried out by Dynata, an international online market research company with experience in programing surveys and collecting data for universities and companies in various fields (eg, public health, politics). Dynata used a combination of recruitment methods (eg, its own website, direct emails, ads on social media) to recruit participants. At the beginning of the survey, we checked whether participants' electronic device (the survey could be completed on a smartphone, computer, or tablet) had adequate video and sound capabilities to complete the survey. After providing electronic consent, participants deemed eligible to participate were randomly allocated to 1 of the 16 strata based on the 4 quota sampling criteria (ie, primary language, biological sex, income, and population density; see Multimedia Appendix 1 for details). Within each stratum, a random concept picker approach was used to ensure a 1:1 allocation. Correspondingly, the first participant of a pair was randomly allocated to the intervention or the control arm and the second participant to the opposite arm. If a participant did not finish the survey (incomplete data), that place in the pair was allocated to the next participant. Thus, the quota in each stratum was filled in pairs and ensured a balanced group allocation throughout the data collection period.

After randomization, participants completed the remaining baseline sociodemographic questionnaire and provided their intentions to receive a COVID-19 vaccine. Then, they participated in the intervention (watched a short video eliciting altruism motives) or read a text related to general hygiene and preventive measures (active control group). All participants were prompted that attention check questions would follow. Those who did not correctly identify the names of the video characters were offered the possibility to watch the video a second time. Those who decided to watch the video again but still answered incorrectly were terminated. The video could be paused but not skipped or muted. Participants could not continue the survey until the video had been played entirely. In the active control arm, the sequence of information sections was randomized (to control for bias attributable to presentation order) and participants could neither skip sections nor progress to the next section until 10 seconds had elapsed to encourage careful reading. After each section, participants answered an attention check question asking them to identify a measure that was not mentioned in the section they had just read. Participants who answered all 3 attention check questions incorrectly were terminated.

Immediately after completing the intervention, we reassessed their intentions to receive a COVID-19 vaccine. Subsequently, participants answered additional questions (offered after the second assessment of vaccine intentions to avoid response bias), which included flu vaccination status, health care professional status, smoking history, and measures of altruism, empathy, and psychological distress. Only participants who provided complete survey data were retained in the final database. Participants were compensated by Dynata according to the reward system in which points are earned that can be later redeemed for company rewards (eg, Amazon, Starbucks).

Interventions

Video Intervention

Because mobile streaming is highly popular in our target age group [35], we decided to use a video-based intervention to maximize its acceptability and minimize study attrition. The development of the intervention was informed by a literature review conducted by our team showing that eliciting prosocial motives (altruism) can increase vaccine intentions. Accordingly, the messaging was framed around the concept of social benefit

of vaccination by emphasizing the importance of indirectly protecting the health of vulnerable individuals who either cannot receive the vaccine (eg, children under the age of 5 years) or might develop an insufficient immune response (eg elderly, immunocompromised) [36-41]. Moreover, protecting children and the elderly and providing details about negative health outcomes caused by infection were found to elicit empathy and altruism and increase vaccine acceptability in young adults [28,42,43]. Because narratives represent an essential component of human communication and their use has been recommended for health behavior change interventions [44], we used this approach to emphasize the importance of receiving the vaccine for protecting others. Finally, we drew a parallel between the collective benefits of having a public health system and the social benefits of being adequately vaccinated.

The development of the intervention unfolded in following phases: First, we developed the script to focus on 3 characters with different COVID-19 vulnerability profiles (ie, John, 82 years old, vaccinated but at risk because of his age; Simon, 4 years old, not eligible for vaccination at the time of the study; and Marie, 32 years old, at risk of infection because of the immunosuppressive effects of chemotherapy). Subsequently, an initial storyboard was created by Akufen (a Montreal-based media design company), which was further refined and produced in video format. Adjustments were made based on the feedback received from 5 young adults (aged 20-39 years who had not yet received the COVID-19 vaccine) who viewed the video and participated in a focus group in June 2021. The final animated character video was 2 minutes 47 seconds in length. (Click to view the videos in English [45] or French [46]). All narration was completed by an experienced, fully bilingual professional narrator.

Text Intervention

Consistent with the widespread use of public health messaging campaigns during the pandemic focusing on promoting preventive health behaviors, we decided to include an active instead of a placebo control group. We developed the text-based intervention by selecting *non-vaccine-related* preventive health behavior recommendations disseminated through the Public Health Agency of Canada's website [47]. The text-based intervention was limited to about 450 words to ensure a reading time similar to the duration of the video-based intervention. Recommendations were divided into 3 sections: travel restrictions (eg, mandatory COVID-19 testing, mandatory isolation), general hygiene (eg, handwashing, mask wearing), and physical distancing (eg, avoiding closed spaces, maintaining a physical distance of 2 m from people outside of your household). See Multimedia Appendix 2 for the text intervention and attention check questions.

Measures

Baseline Sociodemographics

Baseline sociodemographics included continuous (ie, age) and categorical (province or territory, ethnicity, self-perceived visible minority [yes/no], gender identity, identification as a parent [yes/no], language spoken at home [English, French, other], postsecondary education attainment [yes/no], and income [CA $10,000 increments]) variables. Variables with a small cell count for some categories were recategorized. Provinces or territories were recategorized into Western, Central, and Eastern Canada. The 9 categories used by Statistics Canada to measure self-reported ethnic origins [48] were recategorized into North American Aboriginal, other North American (eg, Canadian, American), European, Asian, and other (ie, Caribbean, Latin, Central and South American, African, dual/mixed ethnicities, and uninterpretable open-ended responses). We used multiple validated categories [49] to measure gender identity that captures men and women's socially constructed roles, identities, and behaviors and retained for analyses 3 categories: male, female, and gender diverse (ie, transgender male/trans man/female-to-male, transgender female/trans woman/male-to-female, genderqueer, neither exclusively male nor female, other [open ended], and prefer not to answer).

Main Outcome

Based on the World Health Organization (WHO) Strategic Advisory Group of Experts on Immunization (SAGE) Working Group definition, vaccine hesitancy is considered on a continuum, which implies that using a binary (yes/no) would not allow for a precise, nuanced understanding of where individuals are in their vaccination decision-making process. Therefore, to measure COVID-19 vaccine intentions, we used a stage-based model of health decision-making, the Precaution Adoption Process Model (PAPM) [50]. Informed by the PAPM, we asked participants, "Which of the following best describes your thoughts about a COVID-19 vaccine?" and allowed participants to place themselves in 1 of 4 nominal intention stages: (1) *unengaged* ("At this moment, I have not thought about receiving the COVID-19 vaccine."), (2) *undecided* ("At this moment, I am undecided about receiving the COVID-19 vaccine."), (3) *decided not* ("At this moment, I do NOT want to receive the COVID-19 vaccine."), and (4) *decided to* ("At this moment, I do want to receive the COVID-19 vaccine.").

Additional Measures

Additional measures included following dichotomous (yes/no) variables: identification as a caregiver for an elderly person, identification as a health care professional, receiving a COVID-19 test, influence of religion on health decisions, and seasonal influenza vaccine uptake in the past 12 months. Smoking history was captured by 3 categories: *never smoked*, *smoked in the past but not anymore*, and *currently a smoker*. Vaccination uptake of all recommended vaccines since birth was captured by 3 categories: *all vaccines*, *some vaccines*, and *no vaccines*. The validated 6-point-item (*excellent* to *very poor*) measure of self-perceived health status [51] was dichotomized into *excellent or very good* and *good or less*. Empathy was assessed using the validated 16-item Toronto Empathy Questionnaire (TEQ) [52]. Psychological distress was assessed using the validated 6-item Kessler Psychological Distress Scale (K6) [53]. Altruism was assessed using the validated 5-item altruism subscale from the Prosocial Tendencies Measure (PTM) [54].

Sample Size

To calculate the required sample size for the within-participant change in vaccine hesitancy (ie, pre- to postintervention), we used survey data that showed that in January/February 2021, approximately 40% of Canadians aged 20-39 years were hesitant toward a COVID-19 vaccine (ie, don't know yet or would refuse vaccination) [55,56]. Estimating a 5% decrease in hesitancy in the intervention group and a correlation of about 0.4 between paired observations, the intervention group required a sample size of 907 pairs for detecting a 5% change in marginal proportions at a power of 80% and 2-sided significance of 5% [57]. To detect a 5% superiority of the video intervention in increasing vaccine intentions compared to the active control group at a power of 80%, we estimated a required sample per group of about 1300 participants. Considering a 1:1 allocation, the total sample required for this study was approximately 2600 participants (2×1300=2600).

Data Analysis

Data Cleaning

Using data-cleaning techniques to identify careless responses is recommended for internet-based surveys as inattentive responses represent a threat to data validity [58]. We used 2 methods to identify careless responses using the database received from Dynata. First, amongst both the video and text groups, we excluded participants who spent less than 273 seconds or more than 2401 seconds on the survey (lowest and highest 5% of time spent on the survey compared to the mean, 699 seconds). Next, we used responses to the TEQ to identify straight-liners (ie, exhibited no variance in their responses across scale items) and excluded them from subsequent analyses. We chose this scale because it included reverse-coded items, thereby making it highly unlikely that a participant would provide the same response for all items.

Statistical Analyses

For baseline sociodemographics, we calculated proportions and means (and SD) and used the Pearson chi-square test and the Welch 2-sample *t* test to evaluate whether the 2 study groups differed significantly. At baseline and postintervention and for each of the study groups, we calculated the proportion of participants in each of the 4 PAPM intention stages (ie, *unengaged*, *undecided*, *decided not*, and *decided to*). For each study group, we calculated the pre- to posttransitions in intentions to receive the COVID-19 vaccine. To estimate the pre- to postintervention change in vaccine intentions, we used a binary outcome (ie, "intenders" corresponding to the stage *decided to* and "nonintenders" that included stages *unengaged*, *undecided*, and *decided not*) and the McNemar chi-square test. To estimate pre-post changes in PAPM intention stages, we conducted exact tests of symmetry (4×4 contingency tables) that comprise pairwise McNemar tests (using the *nominalSymmetryTest* function available in the R package *rcompanion*) [59]. We reported adjusted *P* values for multiple comparisons (Benjamini and Hochberg method), odds ratios (ORs), and the Cohen g effect size that was interpreted as small (0.05 to <0.15), medium (0.15 to <0.25), or large (≥0.25). For each study group, we used the significant transitions between vaccine intention stage pairs for calculating the total number of participants who changed toward increased vaccination intentions (eg, from *undecided* to *decided to*) and estimated the between-group difference using the chi-square 2-sample test for equality of proportions. To estimate the between-group difference in vaccine intentions, the Pearson chi-square Test was conducted on postintervention vaccine intentions using the 4-stage PAPM outcome.

Additional Analyses

Using the same analysis approach, we performed 2 subgroup analyses that included (1) all participants who answered the postintervention COVID-19 vaccine intentions question and participants who were initially removed during data cleaning (N=1654) and (2) all participants who were randomly allocated to the study groups and who answered the preintervention COVID-19 vaccine intentions question (N=2089, intention-to-treat approach). In addition, for both subgroups, we performed exploratory between-group analyses and operationalized the vaccine intention outcome in 2 different ways: (1) baseline (preintervention) vaccine intentions in the text group and postintervention intentions in the video group and (2) postintervention vaccine intentions in the text group and baseline intentions in the video group.

All statistical analyses were conducted using R v. 4.0.5 (R Core Team) [60].

Ethical Considerations

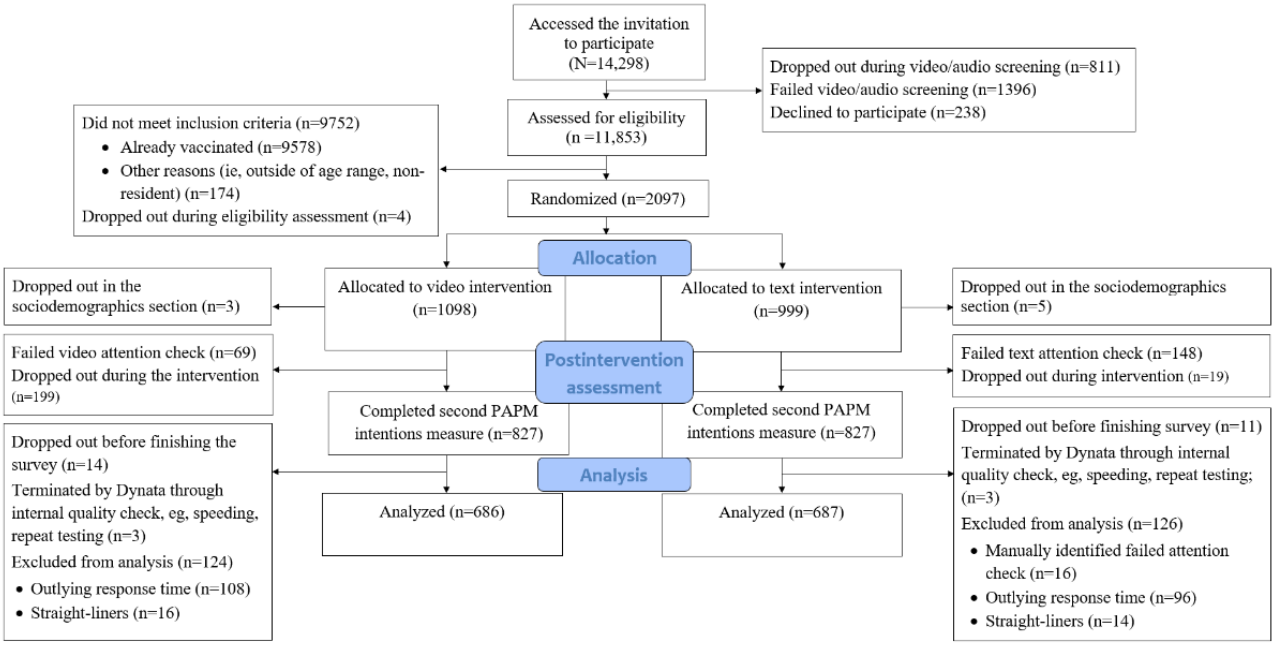
The study was approved by the Research Ethics Board of the Integrated Health and Social Services University Network for West-Central Montreal (CIUSSS West-Central Montreal; Project ID #2021-2732).

Results

Participant Flow

Of 14,298 participants in the target age group who accessed the invitation to participate, 11,853 (82.9%) were assessed for eligibility, of whom 2097 (17.7%) were eligible (n=9578, 80.8%, were excluded because they were already vaccinated against COVID-19; n=174, 1.5%, did not meet other inclusion criteria; and n=4, 0.03%, dropped out) and were randomly allocated to the study arms: 1654 (78.9%) completed the postintervention assessment, and 1373 (65.5%; ie, 686, 50%, and 687, 50%, in the video and text intervention arms, respectively) were included in the analyses. See Figure 1.

Figure 1. CONSORT diagram. CONSORT: Consolidated Standards of Reporting Trials; PAPM: Precaution Adoption Process Model.



Recruitment Dates and Reasons for Stopping the Trial

Data collection took place from July 30 to September 13, 2021. At about 5 weeks into data collection, daily recruitment significantly declined. The main barrier was the relative low proportion (about 22%) of eligible participants (ie, unvaccinated in the age group of 20-39 years). We conducted preliminary analyses using a total sample of 1346 participants (673, 50%, per group) and found that the number of observations ensured 80% power to detect a 5% pre-post change in vaccine intentions. Preliminary analyses showed a difference of about 2% as opposed to the expected between-group difference of 5% in vaccine intentions that we had anticipated. To reach a similar level of power would have required about 5500 participants per group (ie, an increase of 4200 from our initial sample calculations) to detect a statistically significant superiority of the video intervention. Reaching the new sample size target would not have been feasible due to time and budget considerations, and we decided to stop data collection.

Baseline Data

The sample consisted of slightly more females (n=740, 53.9%), the mean age was 30.7 years, the majority used English as the primary language at home (n=1122, 81.7%), most reported a total gross household income in the year preceding the pandemic of less than CA $75,000 (US $58563.80, n=848, 61.8%), and most resided in an urban area (n=1067, 77.7%). None of the sociodemographic characteristics differed significantly between the study groups (see Table 1 and Multimedia Appendix 3 for additional subgroup analyses). In the video group, 86 (12.5%) intended to receive the vaccine, 292 (42.6%) were decided against vaccination, 234 (34.1%) were undecided, and 74 (10.8%) had not thought about receiving the COVID-19 vaccine (ie, *unengaged*). Participants allocated to the active control group (text intervention) reported similar vaccine intentions, and the difference between groups was not statistically significant: χ^2_3=1.62, *P*=.65; see Table 2.

Table 1. Sociodemographic variables.

Characteristics	Total (N=1373)	Video group (N=686)	Text group (N=687)	Between-group difference[a] *P* value
Age, mean (SD)	30.7 (5.3)	30.7 (5.4)	30.7 (5.3)	.94
Sex, n (%)				.98
Male	633 (46.1)	316 (46.1)	317 (46.1)	—[b]
Female	740 (53.9)	370 (53.9)	370 (53.9)	—
Gender, n (%)				.98
Man	626 (45.6)	311 (45.3)	315 (45.9)	—
Woman	721 (52.5)	362 (52.8)	359 (52.3)	—
Gender diverse	26 (1.9)	13 (1.9)	13 (0.4)	—
Canadian region, n (%)				.08
Western	451 (32.8)	225 (32.8)	226 (32.9)	—
East	105 (7.7)	40 (5.8)	65 (9.5)	—
Central	813 (59.2)	419 (61.1)	394 (57.3)	—
Territories	4 (0.3)	2 (0.3)	2 (0.3)	—
Place of residence, n (%)				.43
Rural	306 (22.3)	159 (23.2)	147 (21.4)	—
Urban	1067 (77.7)	527 (76.8)	540 (78.6)	—
Self-perceived visible minority, n (%)				.05
Yes	401 (29.2)	217 (31.6)	184 (26.8)	—
No	972 (70.8)	469 (68.4)	503 (73.2)	—
Language spoken at home, n (%)				.46
English	1122 (81.7)	561 (81.8)	561 (81.7)	—
French	203 (14.8)	105 (15.3)	98 (14.2)	—
Other	48 (3.5)	20 (2.9)	28 (4.1)	—
Education (any postsecondary), n (%)				.63
Yes	858 (62.5)	433 (63.1)	425 (61.9)	—
No	515 (37.5)	253 (36.9)	262 (38.1)	—
Income (CA $)[c], n (%)				.56
<19,999 (US $15,616.20)[d]	149 (10.9)	72 (10.5)	77 (11.2)	—
20,000-39,999 (US $15,617-$31,233.20)	253 (18.4)	136 (19.8)	117 (17.0)	—
40,000-59,999 (US $31,224-$46,850.20)	227 (16.5)	113 (16.5)	114 (16.6)	—
60,000-79,999 (US $46,851-$62,467.20)	217 (15.8)	109 (15.9)	108 (15.7)	—
80,000-99,999 (US $62,468-$78,084.20)	188 (13.7)	82 (12.0)	106 (15.5)	—
>100,000 (US $78,085)	288 (21.0)	148 (21.5)	140 (20.4)	—
Prefer not to answer	51 (3.7)	26 (3.8)	25 (3.6)	—
Ethnicity, n (%)				.31
North American Aboriginal	107 (7.8)	62 (9.0)	45 (6.6)	—
Other North American	637 (46.4)	303 (44.2)	334 (48.6)	—
European	320 (23.3)	160 (23.3)	160 (23.3)	—
Asian	98 (7.1)	51 (7.4)	47 (6.8)	—
Other	211 (15.4)	110 (16.0)	101 (14.7)	—

Characteristics	Total (N=1373)	Video group (N=686)	Text group (N=687)	Between-group difference[a] *P* value
Identification as a parent, n (%)				.89
Yes	697 (50.8)	347 (50.6)	350 (50.9)	—[b]
No	676 (49.2)	339 (49.4)	337 (49.1)	—

[a]Chi-square or *t* test.

[b]—: not applicable.

[c]Of 1373 participants, 848 (61.8%) and 525 (38.2%) reported an annual income before taxes of all members of the household before the pandemic of <CA $75,000 and ≥CA $75,000, respectively. The between-group difference in proportions was not significant (*P*=.48).

[d]An exchange rate of CA $1=US $0.78 has been applied.

Table 2. Number of participants by PAPM[a] vaccine intention stage and intervention group at baseline and postintervention (N=1373).

Group	Unengaged	Undecided	Decided not	Decided to	Total	Between-group difference[b] *P* value
Baseline, n (%)						.65
Video	74 (10.8)	234 (34.1)	292 (42.6)	86 (12.5)	686 (50.0)	—[c]
Text	73 (10.6)	255 (37.1)	272 (39.6)	87 (12.7)	687 (50.0)	—
Postintervention, n (%)						.64
Video	54 (7.9)	236 (34.4)	277 (40.4)	119 (17.3)	686 (50.0)	—
Text	47 (6.8)	249 (36.2)	285 (41.5)	106 (15.4)	687 (50.0)	—

[a]PAPM: Precaution Adoption Process Model.

[b]Chi-square test.

[c]—: not applicable.

Outcomes

In the video group, 43 (6.3%) participants changed from nonintenders at baseline (ie, *unengaged*, *undecided*, or *decided not*) to vaccine intenders (ie, *decided to*) postintervention and 10 (1.5%) participants changed from vaccine intenders at baseline to nonintenders postintervention. The McNemar test was significant (χ^2_1=20.55, *P*<.001). In the active control (text) group, 24 (3.5%) participants changed from nonintenders at baseline to vaccine intenders postintervention and 5 (0.7%) participants changed from vaccine intenders at baseline to nonintenders postintervention. Unexpectedly, the McNemar test was also significant (χ^2_1=12.45, *P*<.001).

In the video group, we found a statistically significant change from *decided not* at baseline to *undecided* postintervention (n=28, 4.1%; *P*=.02, OR 2.8, Cohen g=.24), from *undecided* to *decided to* (n=29, 4.2%; *P*<.001, OR 5.8, Cohen g=.35), and from *unengaged* to *decided to* (n=10, 1.5%; *P*=.03, OR 10, Cohen g=.41). In total, in the video group, 67 significant changes toward increased vaccination intentions were observed (see Figure 2 for a visual representation of PAPM stage transitions from baseline to postintervention in the video group and Tables S1 and S2 in Multimedia Appendix 4).

In the text group, we found a statistically significant change from *unengaged* at baseline to *decided not* postintervention (denoting a change toward decreased vaccine intentions; n=14, 2%; *P*=.02, OR 7, Cohen g=.38) and from *undecided* to *decided to* (n=16, 2.3%; *P*=.01, OR 8, Cohen g=.39). In other words, in the text group, 14 (2%) participants moved toward decreased intentions and 16 (2.3%) participants moved toward increased vaccination intentions (see Figure 3 for a visual representation of PAPM stage transitions from baseline to postintervention in the text group and Tables S1 and S3 in Multimedia Appendix 4). We found a significant difference between those who changed toward increased vaccine intentions in the video group (n=67, 9.77%) compared to the text group (n=16, 2.33%): χ^2_1=33.43, *P*<.001.

Postintervention, in the video group, 119 (17.3%) intended to receive the vaccine, 277 (40.4%) were decided against vaccination, 236 (34.4%) were undecided, and 54 (7.9%) reported being unengaged. In the text group, 106 (15.4%) intended to receive the vaccine, 285 (41.5%) were decided against vaccination, 249 (36.2%) were undecided, and 47 (6.8%) reported being unengaged. The between-group difference in vaccine intentions was not significant: χ^2_3=1.70, *P*=.64.

Results of additional subgroup analyses did not significantly differ from per protocol analyses (see Multimedia Appendix 5). The only difference consisted in the loss of statistical significance of the transition from *unengaged* to *decided to* in the video group (see Table S2 in Multimedia Appendix 5) that could be explained by 2 additional participants who transitioned from *decided to* at baseline to *unengaged* postintervention. Since one cannot change from *decided to* get the vaccine to *unengaged*, this was an artifact introduced by careless responding.

Results of exploratory analyses provided a signal that the video intervention was superior to the text intervention as the between-group difference in vaccine intentions was significant when using preintervention intentions in the text group and postintervention intentions in the video group (χ^2_1=5.90, *P*=.02) and not significant when using preintervention intentions in the video group and postintervention intentions in the text group (χ^2_1=2.39, *P*=.12); see Tables S10 and S11 in Multimedia Appendix 5. The same results were obtained using samples comprising 1654 (all completers of the second vaccination intention assessment; see Tables S5 and S6 in Multimedia Appendix 5) and 2089 (intention-to-treat) participants (see Tables S8 and S9 in Multimedia Appendix 5).

Figure 2. PAPM stage transitions from T1 (baseline) to T2 (postintervention) in the video group (N=686). OR: odds ratio; PAPM: Precaution Adoption Process Model. Green arrows show significant transitions toward increased and red arrows toward decreased vaccination intentions. Gray arrows show nonsignificant transitions between stages..

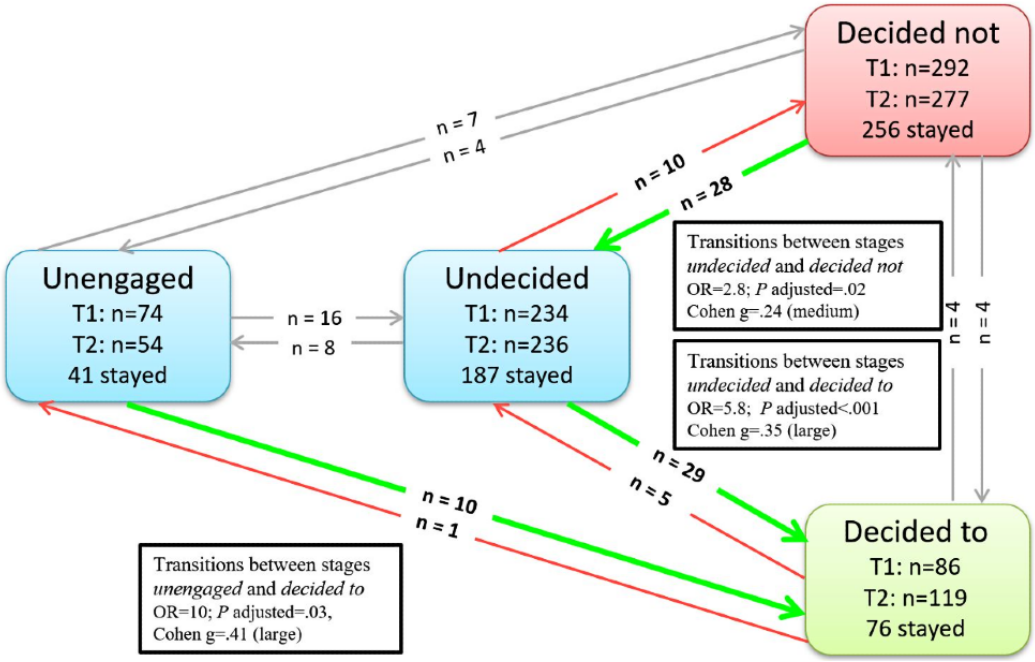
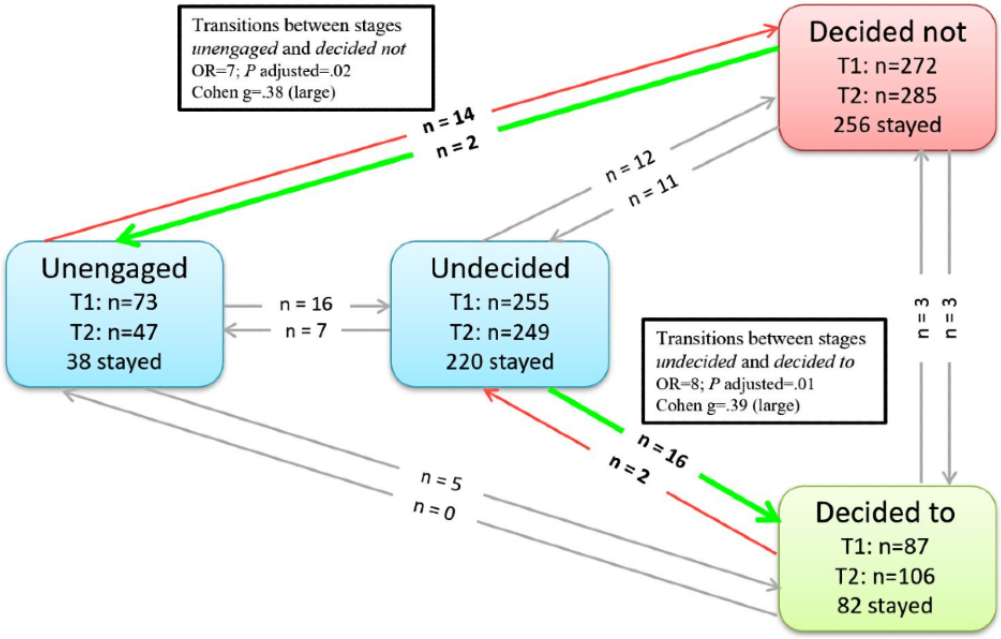


Figure 3. PAPM stage transitions from T1 (baseline) to T2 (postintervention) in the text group (N=687). OR: odds ratio; PAPM: Precaution Adoption Process Model. Green arrows show significant transitions toward increased and red arrows toward decreased vaccination intentions. Gray arrows show nonsignificant transitions between stages.



Discussion

Principal Findings

To the best of our knowledge, this is the first population-based study that examined the effect of a video-based intervention eliciting prosocial (altruistic) motives on intentions to receive the COVID-19 vaccine in younger Canadian adults. We used a pre-post and randomized control trial (RCT) study design and recruited a national sample of unvaccinated 20-39-year-old Canadians who participated in a web-based survey between July and September 2021 in the context of the fourth COVID-19 pandemic wave. Our study had 2 specific objectives: (1) to estimate pre- to postintervention vaccine intention changes in participants who were randomly allocated to the video intervention or the text-based intervention that provided non-vaccine-related preventive health measures and (2) to estimate between-group vaccine intentions postintervention.

Comparison With Prior Work

First, we found that the video intervention was effective in changing vaccine intentions and that 4.8% more participants intended to receive the vaccine postintervention. The size of the effect is consistent with results of the experimental study conducted by Li et al [28], who studied 3952 participants (median age range 31-40 years) from 8 countries (China, France, Japan, United Kingdom, United States, Israel, Brazil, and South Africa) who participated in an internet survey in 2013 before the start of the flu season at the time. They reported a 6% absolute increase in intentions to receive the influenza vaccine in participants who were exposed to prosocial (altruism) messages [28]. Understanding the evolving context in which our study was conducted could explain the modest (4.8%) increase in vaccine intentions. At the time of data collection (July 30-September 13, 2021), about 3 months had elapsed since adults 20-39 years old became eligible to receive the COVID-19 vaccine in Canada. Three-quarters of them had received at least 1 dose [34]. In surveys conducted before the start of vaccination, approximately 40% of our target population was vaccine hesitant compared to 87% who reported vaccine hesitancy in our analyzed sample who are more resistant to vaccination. Therefore, it is possible that had this study been conducted 2 months earlier, our results would have shown a higher increase in pre- to postintervention vaccine intentions. Surprisingly, vaccine intentions also significantly increased in the group that received information about nonvaccine preventive measures in text format, although the effect was smaller than that in the video group, as only 2.7% reported higher vaccine intentions postintervention. Because we used a vaccine-neutral intervention in the active control group, it is possible that the increase represents social desirability. Since we did not measure social desirability, it is possible this bias was also present in the video intervention group as the video depicted vaccination as a social benefit.

Using the theoretical PAPM to inform the measurement of vaccine intentions, we found a more nuanced understanding of pre- to postintervention change in vaccine intentions. Our results show that significantly more participants who watched the video changed toward a more advanced vaccine decision stage than participants in the text group. In both groups, we found that individuals who had not thought about receiving the vaccine (*unengaged*) and those who were *undecided* were more likely to change their intentions to *decided to* vaccinate compared to those who reported being *decided not* at baseline, and this effect was more pronounced in the video group. This pattern of decision-making changes aligns with our previous findings from a longitudinal study evaluating human papillomavirus (HPV) vaccine intention change over a 9-month period in parents of 9-16-year-old boys and girls [22]. In that study, we demonstrated that parents who were *unengaged* or *undecided* at baseline were more likely to increase their HPV vaccine acceptability over time and deemed "flexible hesitant" (ie, changed to *decided to* vaccinate or vaccinated their child). This was in contradistinction with parents who were initially in the *decided not* stage and remained *decided not* over time, whom we deemed as "rigid hesitant" [22]. Therefore, investigating vaccine hesitancy as a binary outcome does not convey the nuances of movement in vaccine intention stages. For individuals who are "flexible hesitant," viewing messages that highlight altruism may provide the necessary "push" to move toward adoption stages of accepting the vaccine. This could reflect behavioral nudging, in which promoting the positive impacts of a behavior without changing incentives or forbidding negative options can have a substantial impact on the behavior [61,62]. A recent systematic review by Reñosa et al [63] found that nudging messages that invoked emotional affect, such as storytelling and dramatic narratives, can improve vaccine confidence and uptake. In addition, Wood and Schulman (2021) [64] suggested that apathy toward vaccination, a characteristic that might contribute to someone being *unengaged*, could be addressed with peripheral, emotional messaging to motivate behavior change. Interestingly, in the video group, significantly more people moved from *decided not* to *undecided*, suggesting that the evocation of concern for others (altruism) may prompt even "rigid" hesitant individuals to reflect and rethink their decision.

Although pre-post analyses showed that the video intervention was effective in increasing vaccine intentions, between-group analyses did not confirm our hypothesis that watching the video would result in statistically significant higher intentions compared to reading non-vaccine-related information. Two factors may have contributed to this outcome: (1) The unexpected 2.7% increase in vaccine intentions in the active control group that reduced the hypothesized 5% between-group difference, and (2) the higher-than-expected vaccine hesitancy in our sample (which comprised ~40% "rigid hesitant" compared to ~10% found in 2 population-based studies conducted by our team that investigated HPV vaccine hesitancy [21,65]) that could have attenuated the effect of the video on vaccine intentions because "rigid hesitant" are less amenable to changes in intentions.

Although achieving statistical significance for the between-group difference would have sent a strong signal related to the efficacy of the video intervention, we believe that our study can inform future research using interventions that elicit prosocial motives to increase COVID-19 vaccine intentions. For example, interventions could be adapted to include other forms of prosocial motivations, such as collectivism (the practice

of prioritizing a group over individuals within the group) [66]. Previous research has shown that collectivism is associated with COVID-19 vaccine acceptance [12,67], while individualism (ie, emphasis on the autonomous individual) is associated with COVID-19 vaccine hesitancy [68]. Therefore, to override feelings of personal invulnerability to COVID-19 in countries that are more individualistic than collectivistic (eg, Canada, the United States), messages that promote community well-being, highlight shared goals, and induce feelings of interdependence should be used to encourage COVID-19 vaccination [69]. Importantly, the design of our intervention aligns well with the recommendations for animated, video-based health communication interventions published by Adam et al [70] in 2021. Our intervention used a narrative approach, was well adapted to the Canadian cultural context as it was available in English and French, used characters of different ages and ethnic backgrounds, used appealing colors that ensured an optimal contrast independent of the size of the screen, included the voice of a narrator with experience in media communications, and had a length aligned with the recommend optimal length of around 2.5 minutes [70].

Limitations

The main limitations derive from the premature termination of the study dictated by barriers in participant recruitment and by lower-than-anticipated COVID-19 vaccine hesitancy in the population of interest. As the target sample size was not reached, the sampling quotas used to match Canadian Census data deviated from the planned quotas and we included 3.9% more females, 2.3% more participants residing in rural areas, 5.2% less Francophones, and 11.8% less participants with annual total income before taxes of all members of the household before the pandemic of CA $75,000 (US $58,563.80). Although between-group differences were not significant, these differences in sociodemographics could impede the generalizability of the results to the Canadian population. The high proportion of participants who were in the *decided not* to vaccinate stage could have diminished our ability to prove the superiority of the video intervention in increasing vaccine intentions. Additionally, the use of an active control group could have diminished our capacity to prove the statistical superiority of the video intervention, perhaps due to social desirability. Finally, follow-up 3-6 months later would have allowed us to evaluate the translation of increased vaccine intentions into actual vaccine uptake.

Conclusion

Using a web-survey and a pre-post and RCT study design, we showed that a brief video eliciting prosocial (altruism) motives increased COVID-19 vaccine intentions of Canadians aged 20-39 years, especially among those who were less engaged in the decision to vaccinate or were undecided. As web streaming is highly popular among younger adults, using short videos is an efficient modality to disseminate public health messages. The effect of the new intervention on increasing intentions was modest, but delivering messages that elicit prosocial motives to vaccinate to a large population could increase vaccine intentions in a significant number of individuals and assist in reaching vaccination targets and curbing the effect of the pandemic. As vaccine hesitancy is complex, it is likely that a multifaceted messaging approach that includes the benefits of vaccination for the community would be beneficial, especially in societies where individual values prevail over collective values. Our intervention could be adapted to align with the latest COVID-19 immunization recommendations (eg, boosters) or to increase vaccine intentions for other preventable diseases.

Acknowledgments

This study was supported by a grant from the McGill Interdisciplinary Initiative in Infection and Immunity (MI4). The study was also partially supported by a supplementary grant from the Canadian Immunization Research Network (CIRN). OT is supported by the Canadian Institutes of Health Research (CIHR)-Frederick Banting and Charles Best Doctoral award (Award FBD-170837) outside the submitted work.

The authors warmly thank the media design company Akufen for producing and Laurie Blanchette for narrating the video, as well as our focus group participants.

Conflicts of Interest

Within the past 5 years, GZ has served as a consultant to Merck (regarding human papillomavirus [HPV] vaccination), Pfizer (regarding meningococcal vaccination), and Sanofi Pasteur (regarding adolescent vaccination). GZ also has served on advisory boards for Merck (regarding HPV vaccination) and Moderna (regarding COVID-19 vaccination). The other authors declare no conflicts of interest.

Multimedia Appendix 1
Strata.
[DOCX File , 109 KB - publichealth_v8i5e37328_app1.docx]

Multimedia Appendix 2
Text intervention.
[DOCX File , 18 KB - publichealth_v8i5e37328_app2.docx]

Multimedia Appendix 3
Sociodemographics subgroups.
[DOCX File , 34 KB - publichealth_v8i5e37328_app3.docx]

Multimedia Appendix 4
Results tables.
[DOCX File , 18 KB - publichealth_v8i5e37328_app4.docx]

Multimedia Appendix 5
Additional analyses.
[DOCX File , 31 KB - publichealth_v8i5e37328_app5.docx]

Multimedia Appendix 6
CONSORT-eHEALTH checklist (V 1.6.1).
[PDF File (Adobe PDF File), 363 KB - publichealth_v8i5e37328_app6.pdf]

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Abbreviations

CONSORT: Consolidated Standards of Reporting Trials
HPV: human papillomavirus
K_6: 6-item Kessler Psychological Distress Scale
OR: odds ratio
PTM: prosocial tendencies measure
PAPM: Precaution Adoption Process Model
RCT: randomized control trial
TEQ: Toronto Empathy Questionnaire

Edited by T Sanchez, A Mavragani, G Eysenbach; submitted 15.02.22; peer-reviewed by J Bishop, J Johnston; comments to author 13.04.22; revised version received 28.04.22; accepted 07.05.22; published 30.05.22.

Please cite as:
Zhu P, Tatar O, Griffin-Mathieu G, Perez S, Haward B, Zimet G, Tunis M, Dubé È, Rosberger Z
The Efficacy of a Brief, Altruism-Eliciting Video Intervention in Enhancing COVID-19 Vaccination Intentions Among a Population-Based Sample of Younger Adults: Randomized Controlled Trial
JMIR Public Health Surveill 2022;8(5):e37328
URL: https://publichealth.jmir.org/2022/5/e37328
doi:10.2196/37328
PMID:35544437

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