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COVID-19 pandemics: Ethical, legal and social issues

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COVID-19 pandemics: Ethical, legal and social issues

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Table of contents

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Editorial: COVID-19 pandemics: Ethical, legal and social issues

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Editorial on the Research Topic
COVID-19 pandemics: Ethical, legal and social issues

Introduction

Assessing the ethical, legal, and social implications related to the numerous issues that have arisen in the short history of the virus is a hugely valuable effort that was the goal of this special Research Topic, especially as we are likely to experience additional pandemics or pandemic-like medical events in the foreseeable future. Indeed, on 23 July 2022, monkeypox was declared a global health emergency by the World Health Organization (WHO) (Titanji, 2022).

The numerous articles in this Research Topic are testament to the diversity of ethical, legal, and social implications (ELSI) raised by COVID and approaches proposed to address them. They relate to concerns regarding privacy (Beauvais and Maria Knoppers; Song et al.), uncertainty regarding the vaccine (Huang et al.; Kumar et al.; Sun et al.; Zigron et al.), and other prophylactic containment measures and tentative therapeutics (Maaravi et al.), triage guidelines (Merlo et al.) and government guidelines (Fargnoli et al.; Zakar et al.; Zewude et al.), and many more.

Lack of transparency and the lack of trust that this engenders regarding: 1) vaccine approvals by national healthcare authorities; 2) undisclosed contracts between governments and vaccine manufacturers; and 3) prioritization of vulnerable populations, were among the many drivers for vaccine hesitancy or worse in many countries (Qunaibi et al., 2021; Rosenthal and Cummings, 2021; Savoia et al., 2022). As such, among the most effective measures for building public trust in national vaccine drives is assuring clear and detailed transparency on these and other aspects (Cordero, 2021; Gurwitz, 2021; Strully et al., 2021). Although as we have seen with the pandemic and the rise of COVID related conspiracy theories, transparency does not always beget trust;

education, access to understandable information, and even good and directed marketing by healthcare stakeholders can all be important components in vaccine trust generation.

However, it is not just past instances relating to COVID vaccination at this intersection of science and society that carry challenging ethical, legal and social implications, but also the permanent or semi-permanent societal and even institutional changes that have been brought on by this pandemic, and that will also create future ELSI. As such, even as most societies have evolved significantly since the first outbreak of this virus, those changes still create issues that ought to be analyzed under the ELSI rubric.

Consider for example the extensive genetic testing infrastructure that has been set up at points of entry around the globe. Most countries have stopped conducting PCR tests on incoming travelers. Eventually all jurisdictions will no longer test for COVID-19 at their borders. At that point, ought we be concerned that this expensive technological infrastructure and their supporting organizational backbones will be repurposed to conduct other forms of genetic testing on incoming foreigners?

This isn't far-fetched. Recall the shuttle diplomacy that preceded the Russian invasion of Ukraine. The media often presented us with Russian President Vladimir Putin sitting at the head of a comically large table while in discussion with foreign leaders. International reporting confirmed that with foreign leaders unwilling to subject themselves to Russian COVID DNA testing, other appropriate social distancing methods had to be employed, hence the continued use of the long table. (John et al., 2022; Rose, 2022). These leaders were fearful that the Russian COVID testing apparatus was being repurposed such that genetic predispositions to diseases could be uncovered from the DNA of world leaders. (Hessel et al., 2012). Ought we not be concerned that other governments pursue this idea?

With DNA and RNA PCR testing costs continuing to plummet (The Global Genotyping Market size, 2022), it may become feasible for countries to test many of their incoming guests for a host of genetic preconditions scientifically proven, or otherwise, justifiable, or otherwise.

If this is the case, then we should work now to expand genetic privacy protection regimes, even as other areas of privacy are being whittled away (Dobbs, 2022). Thus, we should promote rules and regulations that limit what border officers can and cannot do with genetic information collected to detect an infectious disease, akin to the onerous regulations in place to prevent abuse of data collected through the FBI's CODIS system that employs genetics to identify individuals in the criminal justice system (34 U.S.C. 407 et seq). Notably, border control authorities in some countries are not forbidden from storing nasal swabs collected for COVID testing for undisclosed future purposes; these biosamples contain, in addition to viral RNAs, nasal epithelial cell DNA of tested individuals. These DNAs may yield tale-tell genetic and epigenomic information on individual lifestyles and disease risks, such as individual DNA methylation profiles (Cardenas et al., 2021).

Our privacy is not only at risk at the borders though. COVID has also brought extensive informative surveillance of wastewater as another tool to assess the level of COVID infections within a given population and the detection of emerging SARS-CoV-2 mutations in the community (Baker and Mallapaty, 2022). And like the potential to find alternative uses for COVID infrastructure, this technology has more recently been used to track Polio outbreaks. However, while the capacity to collect personal identifying information from the thousands of fragments of individual genomes in wastewater has not yet been demonstrated, we can sequence wastewater to track diseases and even drug usage, in particular in isolated communities (Lin et al., 2021). This information could be used to discriminate against historically discriminated minority groups unless we develop rules and regulations to monitor and direct the use of this powerful technology.

However, not all is bad. There are positive externalities resulting from the pandemic. Consider the potential for a drastic evolution in healthcare data sharing and prevention. Heretofore, the human response to such a global peril has been uncoordinated and slow, even as this is clearly not our first rodeo: the first documented human pandemic, the Antonine Plague, dates back almost 2000 years (Cunha et al., 2008).

Since then, medical knowledge and technologies have grown exponentially, and modern communication technologies have revolutionized human relations. Yet, even after two millennia, when COVID-19 struck, the world was again caught unprepared: news of the existence of the disease was slow to circulate; information about the virus, including data on its genetics, evolution, and characteristics of affected patients were unevenly shared (Schriml et al., 2020; Chiara et al., 2021). The results of clinical trials were complicated to obtain (Janiaud et al., 2021). This list of missed opportunities to streamline COVID-19 research, stimulate innovation, and improve our response to the pandemic is incomplete but is sufficient to illustrate our point: with the exception of rapid and open data sharing about newly emerging SARS-CoV-2 strains, the world's unsatisfactory response to COVID-19, in particular lack of coordination of containment measures on a global scale, is strongly related to a general incapacity to share a broad variety of data covering all aspects of the pandemic as well as research and development in this area.

A chain of important developments that should have prepared us for a public health challenge of this magnitude began unfolding in the middle of the 20th century. The creation of the WHO in 1948 and, the same year, the adoption in the Universal Declaration on Human Rights of Article 27 affirming the right of everyone to enjoy the benefits of scientific progress created both a legal foundation and an international organisation to advocate for health data sharing in a pandemic context (Knoppers et al., 2014). Other important

technical, political, and policy accomplishments ensued from these foundational efforts. To name only a few, these include the revision of the WHO International Health Regulations (IHR) to prevent, protect against, control, and provide a public health response to the international spread of disease (2005), the recognition of an international duty to register clinical trials (2008), the implementation of the GISAID database (2008) and the launch of the Public Health Alliance for Genomic Epidemiology (PHA4GE, 2019) (International, 2005; Krleža-Jerić and Lemmens, 2009; Shu and McCauley, 2017; Black et al., 2020). These initiatives and accomplishments are impressive, and viewed together with other similar realisations they would seem to indicate that we now possess both the regulations and infrastructures necessary to enable global data sharing for assuring public health. However, in practice the systematic, rapid implementation of international data sharing by national jurisdictions to help prevent COVID-19 was inconsistent at best (Kalia et al., 2021; Knyazev et al., 2022). Complicating the matter, there has been a lack of consensus over the choice of both data repositories and of the technical standards (Schriml et al., 2020; Griffiths et al., 2022). We believe a way forward is only possible if we can collectively overcome three major hurdles.

Need to agree on legally binding international regulations for pandemic preparedness

The current WHO system represented by the IHR has proven insufficient to ensure that national governments comply with their international data sharing responsibilities and reporting obligations (Gostin and Katz, 2016). The drafting of a new international instrument was agreed upon at a Special Session of the World Health Assembly that took place in the Spring 2022. Regulations containing pandemic specific extensive, well defined, responsibilities, meaningful sanctions and a transparent reporting system could foster the meaningful collaboration and accountability of state parties. An easier acceptance process makes international regulations' easier to adopt and more flexible than a treaty in case changes are warranted in the future (Knoppers et al., 2022). Beyond the addressing the responses of national governments, an additional non-binding protocol should address the role and duties of big pharma in times of pandemics. While it would be very challenging and time consuming to convince member states to bind pharmaceutical companies in their territory to specific international legal clauses, instead, using a system of reputational reward the names of companies meeting all requirements of the non-binding protocol, i.e., good corporate citizens, could be displayed on the WHO website. The treaty and protocol should consider the need to promote an interoperable data ecosystem covering all different stages of pandemic evolution, as well as for interim periods between outbreaks. A section of this treaty should provide the accommodations necessary to include lower-middle-income countries (LMIC) and vulnerable population groups as full partners. It goes without saying that representatives from these countries should be given a leading role in determining which accommodation(s) to include here.

Equity and solidarity

An important failure in data sharing for COVID-19 has been the general incapacity of national jurisdictions to engage LMIC countries and vulnerable population groups through enlisting their participation as active partners in international data sharing efforts (Pratt and Bull, 2021). The reluctance of these stakeholders is perfectly understandable given well-documented past abuses of developing countries and population groups by the research community, corrupt governments and big pharma (Haelewaters et al., 2021). A new arrangement grounded in solidarity and equity is required to address the uneven playing field currently prevailing. For example, as of summer 2022, COVAX has failed to reach its goal of providing COVID vaccine to many developing countries. Future agreements will need to address challenging topics such as benefit sharing for LMIC countries contributing data to research efforts, capacity building, timely access to innovation, intellectual property rights and waivers, additional protection for data from vulnerable minority groups, and a commitment not to present group data in ways that could be conducive to stigmatization and discrimination. A lesson must be learned from situations like that of South Africa who, after sharing information promptly on a new variant, faced stigmatization as a country and at the level of individual residents.

Ultimately concrete solution will need to be implemented to build LMIC countries' capacity to carry out effective pandemic surveillance and to develop their own data repository. The objective of this strategy is to provide necessary guarantees to obtain access to diverse representative data in terms of gender, ethnic and geographical origin, socio-economic status, etc. So that these data can be used for research to the benefit of the groups having contributed them as well as other populations.

A change of culture

A determining element of success of the global data sharing strategy we envision here will be the capacity of the WHO and other international organizations, NGOs, and policymakers to propagate an extensive and lasting change of culture towards data sharing. While investigators and data producers in some research fields such as informatics, bioinformatics, and large-scale genomic research have, to a large extent, embraced the open

science ethos and are developing incentives and standards to facilitate the process, the same cannot be said of other stakeholders involved in pandemic response. For example, national public health agencies and related departments, pharmaceutical companies, and researchers interested in the socio-economic determinants of health, are less familiar with data sharing requirements, or believe they have little to gain from participating in the process. Proper incentives, beyond the moral duty to contribute to the public good, are necessary to ensure significant buy-in to global data-sharing regulations. Similarly, processes to meaningfully identify and address instances of non-compliance to data sharing policies will need to be devised.

After over 2 years of the COVID-19 pandemic, with populations across the world having felt the negative impacts on population health of pressures on healthcare systems, restrictions on personal freedoms, international travel, and impacts on economic activities, there should be no excuse to further delay the adoption of pandemic data sharing regulations. Such regulations are clearly a necessity to ensure our response to emerging pandemics is well coordinated, meaningful and scientifically optimal. Considerations of equity and solidarity demand that we engage LMIC and other vulnerable groups early in this process to ensure such a framework will address their pandemic needs, not only those of G20 countries. Finally, to be truly effective, the regulations will need to trigger a broad, lasting culture change in favor of rapid data sharing for the benefit of humanity as a whole.

In summary, even as we head into the third year of this pandemic, there remains much to be learned, considered and dealt with, particularly in the areas relating to ethics, law and society. This Research Topic scratched only the surface of the myriad concerns, past, present and future. As we continue facing this global challenge, let us hope that debate and dialogue on these issues will result in policy reforms that will modernise and coordinate the global community capacity to respond to such public health crises in the future. Better harmonization of national public health policies during pandemics will help improve humanity's preparedness for the forthcoming climate change, already felt in Europe and North America in summer 2022.

Author contributions

DvG, DdG, and YJ each drafted a component of this editorial. All authors revised and edited the complete manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

From Dec. 2020 to April 2022, YJ was the Chair of the Data Sharing Committee for the Canadian Project CanCOGeN. This project was funded by Genome Canada. The committee was responsible for facilitating the responsible sharing of human and viral genomic sequences collected by the consortium with the research community.

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ORIGINAL RESEARCH
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United by Hope, Divided by Access: Country Mapping of COVID-19 Information Accessibility and Its Consequences on Pandemic Eradication

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Many government websites and mobile content are inaccessible for people with vision, hearing, cognitive, and motor impairments. The COVID-19 pandemic highlighted these disparities when health authority website information, critical in providing resources for curbing the spread of the virus, remained inaccessible for numerous disabled populations. The Web Content Accessibility Guidelines provide comparatively universally accepted guidelines for website accessibility. We utilized these parameters to examine the number of countries with or without accessible health authority websites. The resulting data indicate a dearth of countries with websites accessible for persons with disabilities. Methods of information dissemination must take into consideration individuals with disabilities, particularly in times of global health crises.

Keywords: accessibility, COVID-19, disabilility, information accessibility, global health, disability accessibility, website accessibility

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INTRODUCTION

The COVID-19 pandemic is challenging the boundaries of not only social behaviors and cultural institutions, but also the rapid and accurate dissemination of information. The containment of this epidemic has required stringent adherence to interpersonal behavioral modifications which are often developed and transmitted by national health authorities. Médecins Sans Frontières advocates for inclusive COVID-19 outreach and educational campaigns with the necessary accommodations specifically for people with disabilities (1). However, national health authority websites may lack website accommodations for people with vision, hearing, physical, or cognitive impairments. Because the COVID-19 pandemic has uniquely impacted communities affected by visual, hearing, cognitive, and motor impairments, minimizing the information gap between persons with and without disabilities is imperative for achieving global engagement in containing not only COVID-19, but also future pandemics (2). We sought to determine what percentage of national health

authority websites are fully accessible to people with disabilities according to Web Content Accessibility (WCAG 2.1) guidelines benchmarks (3). Our research demonstrates that only a small percentage of government health websites are fully accessible for people with disabilities.

According to the World Health Organization (WHO), an estimated 2.2 billion people suffer from vision impairment or blindness, while 466 million people have a disabling hearing loss (4, 5). Individuals with temporary or permanent motor or cognitive impairments also require accessibility modifications for proper interaction with websites. Inconsistent heading level and font size or color contrast of elements in webpages harbor barriers for proper interaction by visually impaired people. Likewise, alternative textual descriptions of visual elements on a page are essential for contextual understanding, in addition to proper interaction with text-to-speech engines. Lack of video content subtitles or transcripts present barriers to the hearing impaired. Compatibility with keyboard navigation, including skip linking in the backend of a website, is crucial to accommodate web navigation for people with motor impairment who interact with a single finger or with other motor gestures.

The Web Accessibility Initiative (WAI), launched and endorsed by the World Wide Web Consortium (W3C) (6), established a set of guidelines according to four accessibility principles: whether the website is Perceivable, Operable, Understandable, and Robust. An example for "perceivability" is whether a graphical table on a web page is able to be presented auditorily or via another method for a user while an example for "understandability" is whether a document contains a list of acronyms or initialisms to help the reader understand the abbreviations within the text. In this report, we used WAI guidelines to examine the accessibility of health authority websites worldwide.

MATERIALS AND METHODS

Each WCAG 2.1 principle has a set of testable criteria with a total number of 78 testable success criteria. Each success criteria is assigned to one of three conformance levels: A (lowest), AA (intermediate), and AAA (highest). The adherence to higher levels of conformance has been shown to improve accessibility for users with and without disabilities (7).

A panoply of web accessibility evaluation plug-ins was developed under open-source license for the systematic evaluation of website accessibility against the WCAG 2.1 criteria (3). A list of available tools are presented by the W3C website without an official recommendation for usage of one tool above another (8). These automated tools aim to complement the cardinal manual check of a website during the development process and throughout routine website updates to ensure maximal adherence to WCAG guidelines (8, 9). A comprehensive comparison between eight widely used accessibility evaluation tools highlights the strengths and weaknesses of each tool and recommends using more than one tool for optimal coverage of success criteria (10). In other words, while manual checks of websites by people can determine the usability of the website, automated applications can streamline the process and find hidden accessibility pitfalls within the webpages.

Hence, to test the accessibility of COVID-19 information disseminated through health authority websites, we utilized two independent accessibility evaluation engines including WAVE chrome extension (wave.webaim.org) and Accessibility Insights (accessibilityinsights.io), both of which have been described and utilized in previous literature (10, 11). The WAVE tool analyzes 180 checks according to two conformances level (152 level A; 28 level AA); whereas the Accessibility Insights tool analyzes 64 checks according to three conformances level (55 level A; 7 level AA; and 2 level AAA) (9). It must be noted that the weight of each error (e.g., minor, moderate, critical) is defined by the tool developer and thus may result in different impacts on the overall accessibility rank of the page results (10).

Due to the rapid growth of COVID-19 information and the frequent updates of health authorities' websites, which may influence the accessibility score at a given time point, the degree of accessibility of each website was evaluated at three different time points and the presented data refer to the following three consecutive days (5–7 April, 2020). The calculated number of errors of each health authority homepage augments the average number of errors in each test separately (WAVE and Accessibility Insights), with removal of redundant errors represented in both tests.

In addition to accessibility assessments, we tested each website for mobile usability in concordance to Google webmaster developer tools (developers.google.com). In this regard, previous studies have demonstrated that mobile-friendliness of a given website contributes not only to end user usability, but also for website visibility on search engine results (11, 12).

The list of health authorities' websites of 189 countries were drawn from The Geneva Foundation for Medical Education and Research (GFMER) (**Supplementary Table 1**) (13). Prior to accessibility evaluation, a manual check of each website on the list yielded 174 health authority websites. Websites of 15 countries were excluded due to an inability to load the site on the test server or when the official health authority homepage appeared as a social media page. This was a cross-sectional study concentrating on the accessibility of health authorities' websites' homepages (unit of analysis) providing health information and recommended public protective measures against COVID-19.

RESULTS

Only 4.7% of the countries examined had fully implemented the WAI accessibility guidelines: Italy, the Netherlands, Norway, Japan, Poland, South Korea, the United Kingdom, and the United States (**Figure 1**). In contrast, sites from the majority of countries continue to have accessibility errors that present significant barriers to people with disabilities around the world. Distribution of reported errors across all 174 tested health

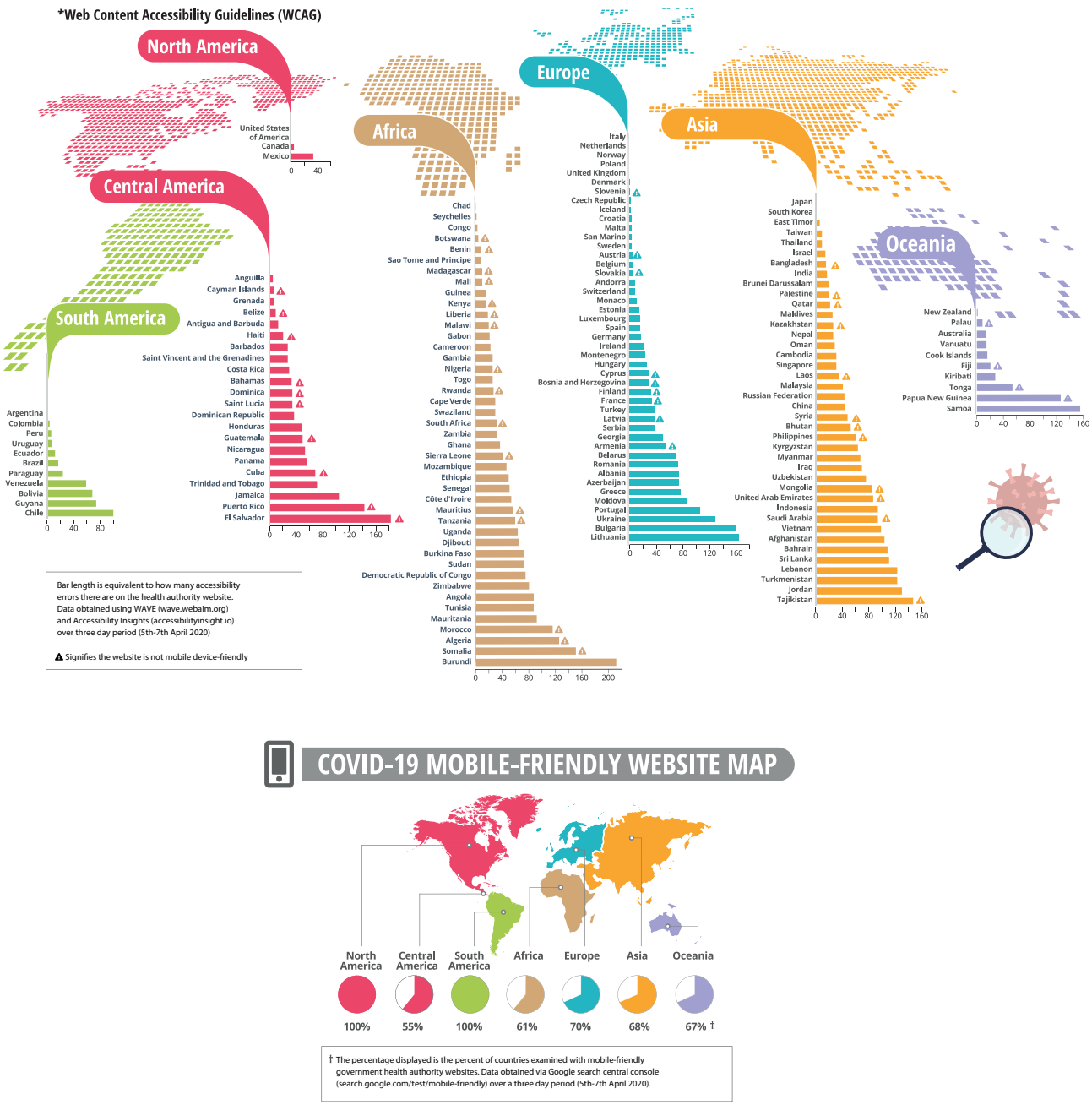

FIGURE 1 | Health authority websites of 174 countries worldwide, demonstrating accessibility errors and mobile friendly maps. The calculated number of errors of each health authority website augment the number of error results in each accessibility evaluation tool separately (WAVE and Accessibility Insights), following removal of redundant errors that are represented in both tests. Mobile computability check according to the Google web developer tool with either pass or fail results. All tests were performed on three consecutive days (5–7 April 2020).

authorities' homepages, according to WCAG conformance levels, reveals that 89% violate Level A criteria, while 11% of countries contain errors that violate higher levels of success criteria (AA and AAA). Inspection of the numbers of errors on all tested pages grouped by WCAG principles indicate that the most impacted principles are robustness (39%) and perceptibility (32%), as compared to operability (19%) and understandability (10%). While both error number, conformance, and principle distribution may be altered according to the selected assessment tools, the data collected signifies the insufficient implementation

of WCAG guidelines in the majority of health authority websites, rendering accessibility barriers to millions of people.

DISCUSSION

Reducing transmission of SARS-CoV-2 depends on tight adherence of the public to simple but challenging modifications in social and public behavior (14). Digital media provide numerous platforms to distribute essential information to the public through websites, social media, and instant messaging applications (15).

Due to the diversity of reporting sources and the harmful consequences of disinformation, governments often encourage the public to check local health authority websites frequently for regular updates (16). This demand requires the information on official websites to be accessible to as many citizens as possible. Unfortunately, individuals with the greatest need for timely and precise data may have the most difficulty accessing governmental material (17). Providing consistently high-quality government productions could also lead to a greater utilization of the Internet by persons with disabilities. Enhancing accessibility to government-sponsored resources could lead not only to immediate population benefits but could also promote the position of people with disabilities in the digital sphere through increased communication, global engagement, and visibility.

Despite remarkable technological advancements in recent history, for people with visual, hearing, motor and cognitive impairments, a seemingly simple website interaction can present a daunting challenge. Although internet access is still unavailable to approximately one-third of the world's population, the needs of all existing users must be accommodated to ensure equal benefits and access to essential health information. The growth and expansion of the Internet must therefore be accompanied by an equal development of sophisticated accessibility technologies, which would expand the usability of the web to individuals with disabilities. With over 2.2 billion people, worldwide, living with vision impairments, an undeniably large section of our society requires accommodations for regular interactions with digital media (3). Beyond the practical benefits of enhanced accessibility, promoting inclusivity for persons with disabilities contributes to an egalitarian society. Without underestimating the importance of accessibility implementation during normal times, the current COVID-19 pandemic now highlights just how important unhindered access to government websites is during a global health crisis.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

All authors contributed to the production of this manuscript and have approved the final version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2020.618337/full#supplementary-material

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BRIEF RESEARCH REPORT
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COVID-19 Vaccine Acceptance Among Dental Professionals Based on Employment Status During the Pandemic

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The COVID-19 pandemic spread rapidly across the globe, leading governments to impose prolonged lockdowns on both movement and commerce. Although lockdowns decrease the rates of novel infections, they can have devastating consequences on the economy and employment levels. One of the most severely affected sectors during this crisis has been dental medicine. Dental professionals are uniquely exposed to environments with high levels of occupational hazards, conferring additional risks of viral exposure and transmission. We analyzed 506 anonymous questionnaires completed by dentists and residents regarding acceptance of a future potential SARS-CoV-2 vaccine. Our results demonstrate a statistically significant correlation between the individual's unemployment rate and their willingness to inoculate with a SARS-CoV-2 vaccine when it becomes available. This information can be used to predict trends of vaccine acceptance or rejection based on economic burden during the COVID-19 pandemic by different sectors as part of the preparedness toward global vaccination programs.

Keywords: COVID-19, vaccine hesistancy, unemployment, SARS-CoV-2, vaccine

INTRODUCTION

Beginning late December 2019, the SARS-CoV-2 coronavirus spread rapidly worldwide, leaving in its wake devastating impacts on human mortality, social behaviors, economies, and healthcare systems. Long lockdown periods imposed by governments led to substantial operational obstructions of vast arrays of economic sectors including cultural institutions, restaurants, tourism, and travel, leading inevitably to soaring unemployment rates. Experts estimate that what has been seen so far is merely the tip of the iceberg, and only in many years will experts be able to assess the final consequences of the COVID-19 pandemic on the global economy. The International Labour Organization (ILO) announced on 15 June that 32% of the world's workers were living in countries with lockdown-related workplace closures for all but essential occupations (1). The ILO has coined the term "lockdown generation" to refer to youths particularly impacted by the global market depression which could, in its estimates, last a decade or longer (2).

One of the most acutely affected sectors has been dentistry and its related residencies. Dental professionals are uniquely exposed to environments with high levels of occupational hazards due to aerosols and oral fluids, conferring additional risks of viral exposure and transmission (3, 4). During the lockdown period in Israel between March 17th and April 19th, all elective procedures were postponed due to government order. The only treatments offered during the pandemic were those indicated for trauma, pain, head and neck infections, and malignant tumors, primarily performed by Oral and Maxillofacial (OMFS) surgeons and oral medicine specialists at hospitals. Minor first aid treatments have been performed in limited numbers of public and private dental clinics.

As an integral part of the fight against the COVID-19 pandemic, the World Health Organization (WHO) led the global effort in prevention, diagnosis, and treatment against this elusive pathogen. A simultaneously sustained race to discover an effective vaccine by more than 90 vaccine companies and over 100 countries is underway worldwide (5). Development of a vaccine appears to be the most promising means of restoring normalcy to civilian life and initiating economic rehabilitation. Nevertheless, SARS-Cov-2 vaccine's availability does not symbolize the end of the pandemic due to ongoing vaccine hesitancy and anti-vaccination movements (6). The WHO declared in 2019 that vaccine hesitancy is one of ten major threats to global health (7); echoing these fears, one recent study found 76% of SARS-Cov2 vaccine hesitancy is due to safety concerns (8).

The aim of our study was to evaluate the current vaccination compliance rate in correlation to unemployment among Israeli dentists, dental residents, and oral medicine specialists. The term "unemployment" in this paper refers to individuals willing but unable to work due to government-imposed workplace restrictions. The dental field can potentially reflect attitudes among other sectors, leading to a greater understanding of sentiments toward the vaccine and the development of plans to combat vaccine hesitancy. We distributed a multicenter anonymous questionnaire across Israel, asking if the dentist, resident, or specialist would agree to receive a SARS-CoV-2 vaccine once available. We analyzed the 506 responses based on occupation status in the lockdown period and willingness to vaccinate against SARS-Cov-2. All questionnaires were filled out during the mandatory quarantine period in Israel. We hypothesized that a higher rate of vaccine compliance would be observed among those who were unemployed at the time of the COVID-19 crisis.

STUDY DESIGN

Methods

As previously described (8), the study design and protocol were approved by the Research Ethics Committee of Galilee Medical Center and the web-based survey followed the American Association for Public Opinion Research (AAPOR) reporting guidelines. The survey was distributed during the lockdown period in Israel (March- April 2020) and data was collected from dentists, dental residents, and oral medicine specialists. The survey was distributed electronically via Qualtrics health care professionals via social networks and professional forums. Before filling out the survey questionnaire, each responder had to agree and sign for electronic informed consent, which was presented at the survey's introductory web page; additionally, the survey was anonymous to ensure the confidentiality of information. The survey consisted of a series of multi-choice questions and respondents were allowed to terminate the survey at any time point.

Data Collection

As previously described (8), demographic data were self-reported by the participants including gender (male or female), age (18–25, 26–30, 31–40, 41–50, 51–60, or >60 years) and geographic location. Specific questions asked whether the respondent is a specialist (e.g., oral medicine, orthodontics, OMFS, etc.) or general practitioner, whether he or she is a resident or practicing doctor, and place of work (hospital or private clinic). Questions regarding the status of employment during the COVID-19 crisis were included (e.g., working as usual, temporary unemployment, or lost job) though questions of religion or ethnicity were excluded. Participants were asked if they are willing to accept a future COVID-19 vaccination when it becomes available. To assess the willingness to inoculate with future SARS-CoV2 vaccine and correlation to unemployment status among dentistry healthcare sectors, we performed Chi-square and correlation tests in prism 8 software (Graphpad CA). Though the survey was not pretested, the number of respondents was sufficient to be statistically validated before initiating research.

RESULTS

According to our survey, the results demonstrate a statistically significant correlation between an individual's unemployment rate and their willingness to inoculate with the novel SARS-CoV-2 vaccine (**Figure 1**). An increase in the unemployment rate within the dental sector coincides with a rise in willingness for a SARS-CoV-2 vaccine while the converse, in which a decrease in unemployment results in a decreased willingness for inoculation, also occurs. While 50% (maxillofacial surgeons) of dental professionals are willing to receive a vaccine, over 50% of respondents for every other specialty are willing to be inoculated. The overall rate of acceptance for a COVID-19 vaccine, according to our survey, is 85%.

Of 506 respondents (57% females), 267 (53%) work as general practitioners; among them, 86% were unemployed during the lockdown period. One hundred and seven residents (21%) and 132 specialists (26%) responded to the questionnaire with variable unemployment rates depending on residency type. The mean respondent age was 36.3 for both sexes. The highest employment rate is observed among OMFS residents and specialists, 87% of whom continued to work during the COVID-19 lockdowns, work which can be attributed to mainly hospital-based operations. An interesting finding consistent with our observed trends finding is that the willingness to accept a COVID-19 vaccine among

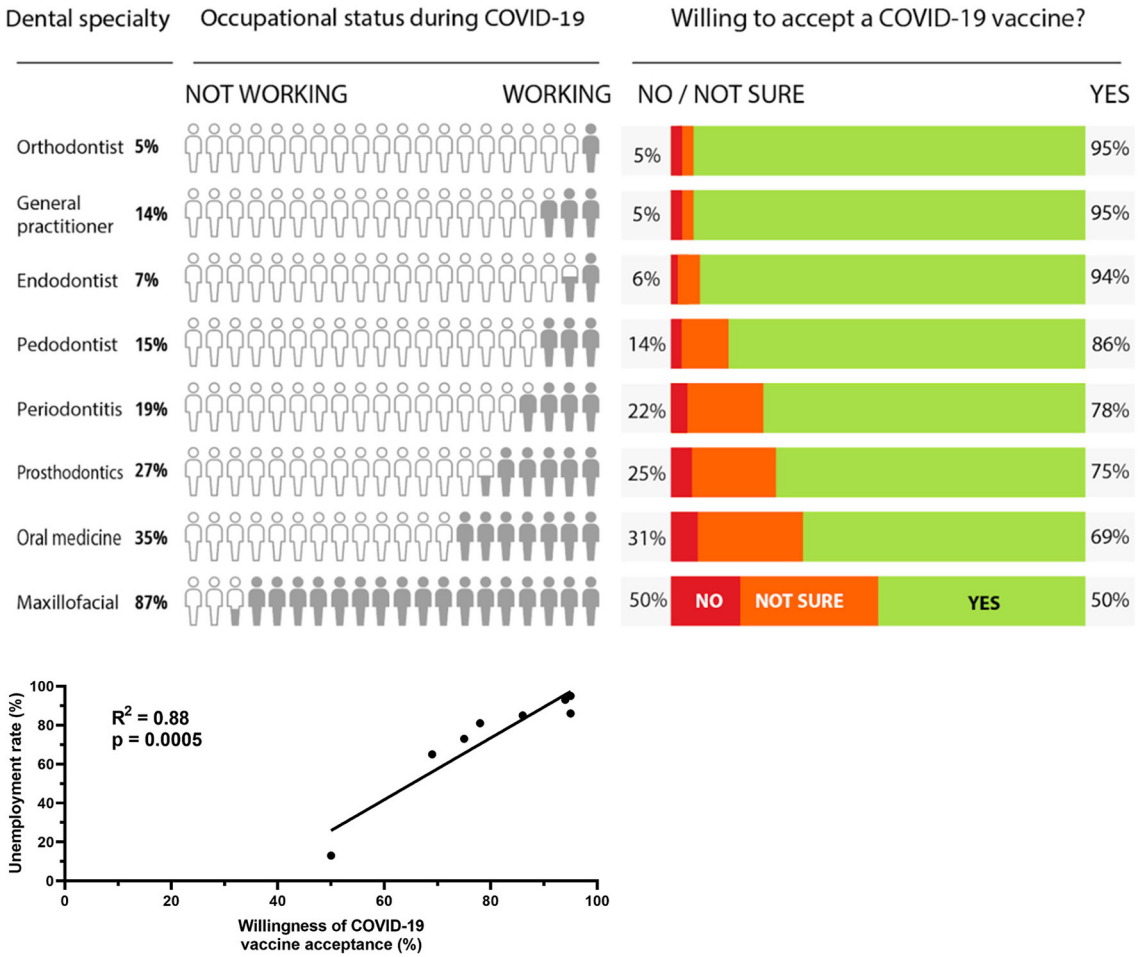

FIGURE 1 | We estimated the strength of the association between willingness of COVID-19 vaccine acceptance and unemployment rate by using Pearson's correlation coefficient ($r = 0.9414$). We used GraphPad Prism version 8.2.1 (GraphPad Software, La Jolla, CA, USA) for correlation analyses.

OMFS surgeons (residents and specialists) is the lowest (50%, $r = 0.9414$).

DISCUSSION

The current pandemic has brought about a new crisis in healthcare as the number of COVID-19-positive patients has risen dramatically worldwide. The signs and symptoms of SARS-CoV-2 were studied in tandem with the rapid development of a vaccine against this fatal disease. Global, sustained efforts have been undertaken by the WHO to limit the spread of infection and improve treatment protocols to decrease morbidity and mortality. The actions to contain the pandemic purchased time for development of effective and safe COVID-19 vaccines which as of the writing of this article are unreleased. Based on recently published research on the explanations for vaccine hesitancy, we hypothesized a correlation exists between unemployment and willingness to accept a SARS-CoV-2 vaccine. Like individuals working directly with COVID-19 patients, those who lost their jobs during the crisis may more acutely feel the impact of lockdowns and economic closures (8).

The future SARS-CoV-2 vaccine is considered by many countries as the last hope for protecting the population and economy against COVID-19 (9). Successful vaccines rely on high vaccine uptake among populations. However, recent evidence predicts an unsatisfactory acceptance rate of a COVID-19 vaccine in the general population. A survey among the general population in the United States in June 2020 suggests that only 50% of Americans are willing to get vaccinated once the vaccine is available (10). A survey in Europe, conducted in April 2020, predicts only a ∼70% acceptance rate for the future COVID-19 vaccine (11). A cross-sectional questionnaire of Israeli hospital workers during the lockdown recorded that 94% of healthcare workers within respiratory wards and COVID-19 departments plan to get a COVID-19 vaccine while, surprisingly, only 61% of the nurses working in non-COVID-19 departments

declare they will accept the future vaccine (12). This number is especially low when compared to the predicted acceptance rate of 75% among the general population in the same study. The date of survey enrollment may influence the public's opinion based on the extent of local health authority control on disease progression, the number of severely ill patients, and casualties (12).

Research on dentists' and dental students' acceptance of vaccinations has indicated incomplete compliance with recommended vaccinations across several countries. Research in Germany indicates there is low influenza vaccination compliance among German dental healthcare workers (13). Despite a robust understanding of the benefits of vaccination, ∼20% of Italian dental healthcare workers were not up to date on recommended vaccinations (14). Understanding the underlying concerns behind vaccine hesitancy, particularly among professionals who are highly educated as to the benefits of vaccination, may provide areas of approach and education for public, and global health experts.

Although restrictions and lockdown have been eased in many countries, the ongoing COVID-19 pandemic continues to be a significant burden on the economy and many unemployed individuals are trying, unsuccessfully, to return to the labor force. Because unemployment affects not only the economy but also has direct effects on psychological and social well-being of individuals and communities, experts estimate that the current wave of unemployment could raise global suicides by thousands (14, 15). Among dental professionals in particular, recent research in Italy has discovered a positive correlation between the COVID-19 shutdowns and increased levels of anxiety and career concerns (16). We sought to discover if there were merely a correlation or a substantial causative effect between unemployment among dental specialty workers and future COVID-19 vaccine acceptance. Dentistry is unique in that it is a private-sector workforce which, unlike most healthcare fields, was forced to discontinue non-essential operations in Israel, as well as in other countries, during the pandemic (17). This characteristic can allow extrapolations from questionnaires distributed to dentistry or dentistry-auxiliary employees regarding unemployment and vaccine willingness.

In the current article we hypothesized a possible explanation for low acceptance rates for the novel SARS-CoV-2 vaccine among dentistry workers. As shown here, unchanged employment status significantly correlates with reduced compliance to the novel SARS-CoV-2 vaccine. Although countries worldwide are attempting to manage the current crisis, the presented trends among the working population should alert governments and organizations about anticipated vaccination rates among their residents. Furthermore, the upcoming winter could present a colossal burden to the healthcare system due to the expected seasonality of respiratory viral infections, potentially once again leading governments to use lockdowns once again as tools of curbing the spread of COVID-19 (18). Historical perspectives indicate pandemic outbreaks occur in 10–50 years intervals, suggesting that a majority of the population will likely experience another pandemic in their lifetimes (19). In light of comparisons between the effects of the SARS-CoV-2 virus and the seasonal influenza virus, governments must pay close attention to employment as a factor in future campaigns to encourage vaccination.

Our results demonstrate a positive correlation between unemployment rate and willingness to receive a COVID-19 vaccine. Despite the small sample size of 506 respondents, the $r = 0.9414$ and low p-value indicate a significant and demonstrable correlation. Our research presents a unique influencing factor on vaccine hesitancy: employment rates. The results of over 500 dental and dentistry-adjacent respondents do indicate a positive correlation between the vaccine acceptance and unemployment. Our research furthers existing investigations into common factors between vaccine-hesitant individuals and identifies a statistically significant relationship between employment status in the current crisis and SARS-CoV-2 vaccine acceptance. High or low unemployment could be another examining tool to determine which professions and communities are at risk of vaccination hesitancy. While our paper excluded racial, ethnic, and religious characteristics and examines only self-identified Israeli dental professionals, stratification based on specific demographical criteria warrants future investigation. Further exploration of the attitudes of oral healthcare professionals globally toward a COVID-19 vaccine would likely be of broad research interest, as well. Moreover, our findings add to a growing body of research on vaccination among oral healthcare professionals. Close observation of professions with high rates of employment could potentially lead to early interventional, educational campaigns regarding the benefit of vaccines not only for the individual, but also for communities at large.

Limitations of our research include that our investigation is within a single country and that broader occupations were not included. Further research can and should delineate whether physicians working in private clinics, which may have been ordered to shut down except for essential services, vs. physicians in hospitals which were not shuttered, have differences in COVID-19 vaccine acceptance rates. Additionally, the explanations for differing vaccine acceptance rates among even one class of profession, such as physicians or dentists, must be clarified.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The study design and protocol were approved by the Research Ethics Committee of Galilee Medical Center and the web-based

survey followed the American Association for Public Opinion Research (AAPOR) reporting guidelines.

AUTHOR CONTRIBUTIONS

AZ, AAD, TS, TH, NM, NE, DR, FK, ES, HM, and SS were involved in the development of this manuscript and gave final approval before submission. All authors attest they meet the ICMJE criteria for authorship.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2021.618403/full#supplementary-material

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BRIEF RESEARCH REPORT
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"The Tragedy of the Commons": How Individualism and Collectivism Affected the Spread of the COVID-19 Pandemic

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Why did COVID-19 hit some countries harder than others? While this question is usually answered based on demographics (e. g., population age), health policy (e.g., quarantine), or economic factors, we argue that cultural variance across countries is just as crucial in understanding how susceptible a society is to the COVID-19 outbreak. To test this hypothesis, we first analyzed data collected across 69 countries and examined the relationship between culture and the impact of COVID. Next, we conducted two studies to validate our findings further and explore the mechanism at hand. As expected, we found that the more individualistic (vs. collectivistic) a country was, the more COVID-19 cases and mortalities it had. We also found that the more individualistic participants were, the higher the chances they would not adhere to epidemic prevention measures. These findings are important in understanding the spread of the pandemic, devising optimal exit strategies from lockdowns, and persuading the population to get the new vaccine against the virus.

Keywords: COVID-19, individualism–collectivism, Hofstede, the tragedy of the commons, public adherence

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INTRODUCTION

In just a few months since the first cases of COVID-19 were reported in China, SARS-CoV-2 has spread to almost all countries, infecting tens of millions, killing over a million and a half people, and undermining national and global economies (1). As the World Health Organization declared COVID-19 a pandemic and announced a global emergency (2), governments across the globe have issued numerous guidelines and measures to fight the spread and avoid catastrophic consequences. Some of the most common measures include reducing human contact through quarantine, isolation, and social distancing, as well as preventing infection through wearing masks, washing hands, and sterilizing surfaces (3).

To help policy-makers mitigate the pandemic, scientists and health organizations have been investigating different factors for contagion and prevention. One interesting question that has not been fully answered is the virus differential impact across various countries. Among the most commonly discussed factors for this variance are demographic and historical factors such as age, comorbidities of the population in different countries (4), and "countries" prior experience in dealing with such pandemics in recent years–e.g., Taiwan and the SARS epidemic in 2003 (5).

In the current article, we argue that cultural dimensions may also play a role in explaining the differential effect of the pandemic across countries and should therefore be taken into account when choosing the optimal measures needed to combat COVID-19 or similar pandemics in the future. Culture is defined as "the collective programming of the mind which distinguishes the members of one category of people from another" (6). Thus, population behavior and the psychological factors behind it may depend in part on a given country's culture (7). This may be crucial in understanding both COVID-19's spread and its mitigation–e.g., adhering to health authorities' guidelines such as social distancing or wearing masks (8). Indeed, a recent review (9) has identified several social and behavioral science insights—including cultural norms–that may support COVID-19 pandemic response, and called researchers to fill possible gaps urgently.

Here, we posit that the cultural aspect of Individualism vs. Collectivism is crucial in understanding the pandemic's global pattern (10). The individualism-collectivism continuum (11) describes the degree to which individuals in a given culture see themselves as independent—vs. interdependent—of the society they live in. It translates to individuals' self-concept of "I" or "we," which in turn, dictates how much they care for themselves and their immediate families only, as opposed to the entire community they live in, or—the larger whole.

Hardin's classic article "The Tragedy of the Commons" (12) offers a prediction for the difference between Individualistic vs. Collectivistic societies facing the pandemic. Hardin described a social dilemma where each decision-maker in a community is better off acting egocentrically. Still, if others acted likewise without concern for the cumulative impact on society, "the commons" are eventually destroyed. Indeed, subsequent literature (13) has indicated that people from different national cultures followed different decision-making schemas in such dilemmas that were dictated in part by their countries' individualistic vs. collectivistic approaches. It is relevant here, as fighting COVID-19 requires focusing on the common good [e.g., flattening the curve, (14)] more than on individualistic interests (e.g., going to work).

Interestingly, while common sense suggests that the spread of the virus will be more intensive in collectivistic societies due to their closer and more frequent social interactions, the combination of culture and Hardin's theory predict the opposite: the pandemic's impact will be greater in individualistic societies where people care less for the greater good. Thus, we hypothesized "The tragedy of individualistic societies" in facing COVID-19. Specifically, we argue and provide evidence across three studies that the spread of the pandemic and its consequences–in terms of cases and deaths—may be explained in part by the degree of societies' individualistic vs. collectivistic orientation in that the more individualistic a society is, the more it will be impacted by the pandemic.

STUDY 1

In Study 1, we investigated the relationship between the individualism-collectivism dimension using Hofstede's cultural dimension model and the number of COVID-19 cases and related deaths. This was done for all 69 countries, for which data was available in Hofstede's national culture survey (version 2015 12 08). The total population in these countries is 5.87 billion, representing 75% of the entire world population.

Methods

Information was retrieved from all databases used in Study 1 on April 21st, 2020. Hofstede's individualism score of national culture was retrieved from Hofstede's national culture survey (15). All COVID-19 related variables, i.e., number of Coronavirus cases, total tests per one million residents, and Coronavirus related deaths, were retrieved from the "Worldmeters" website, which presents constantly updating information about the SARS-CoV-2 (16). The number of days since the outbreak of Coronavirus disease in each country was calculated as the number of days since 100 people were diagnosed with the disease in the country (17). The information retrieved from this website was updated as of April 21st, 2020. The "Worldmeters" website is considered reliable and used by international agencies and academic research. Since much of the information regarding state demographic information in recent years was unavailable, with respect to each index, we used the most recent assessment that was available for the majority of the selected states in the sample (the year of the most recent assessment, i.e., the retrieved assessment, is in parenthesis). State population demographic information–i.e., percentage of population above 65, percentage of Urban Population (2018), Democracy index, Life expectancy at birth in years (2018), Population density (2018), GINI index (2016), percentage of the budget for healthcare (2017)–were all obtained from the World Bank website (18).

Results and Discussion

We first conducted two simple correlations analyses to examine the association between Hofstede's Individualism score with the number of COVID-19 cases and COVID-19 related deaths. The correlations between Hofstede's Individualism score and the number of COVID-19 cases ($r = 0.49$, $p < 0.001$), and COVID-19 related deaths were highly significant ($r = 0.48$, $p < 0.001$). To compare countries with similar economic or ideological backgrounds, we then examined the association between those same variables only among the 36 OECD countries (used in our original sample). We found a similar yet nearing significant pattern of correlations between Hofstede's Individualism score and the number of COVID-19 cases among the sample of OECD countries (see Supplementary Materials; $r = 0.29$, $p = 0.09$). We also found the same pattern of correlations between Hofstede's Individualism score and the number of COVID-19 deaths among the sample of OECD countries (see **Figure 1**; $r = 0.35$, $p = 0.040$).

We then conducted the same correlations analyses on the complete sample while controlling for eight relevant variables, i.e., days since outbreak of the pandemic, percentage of population over 65, democracy index, Gini index, percentage of the budget for health care, life expectancy, population density and total COVID-19 tests per million. Both the correlation between Hofstede's Individualism score with the number of COVID-19 cases ($r = 0.34$, $p = 0.028$), and the correlation between Hofstede's Individualism score with the number of COVID-19 related

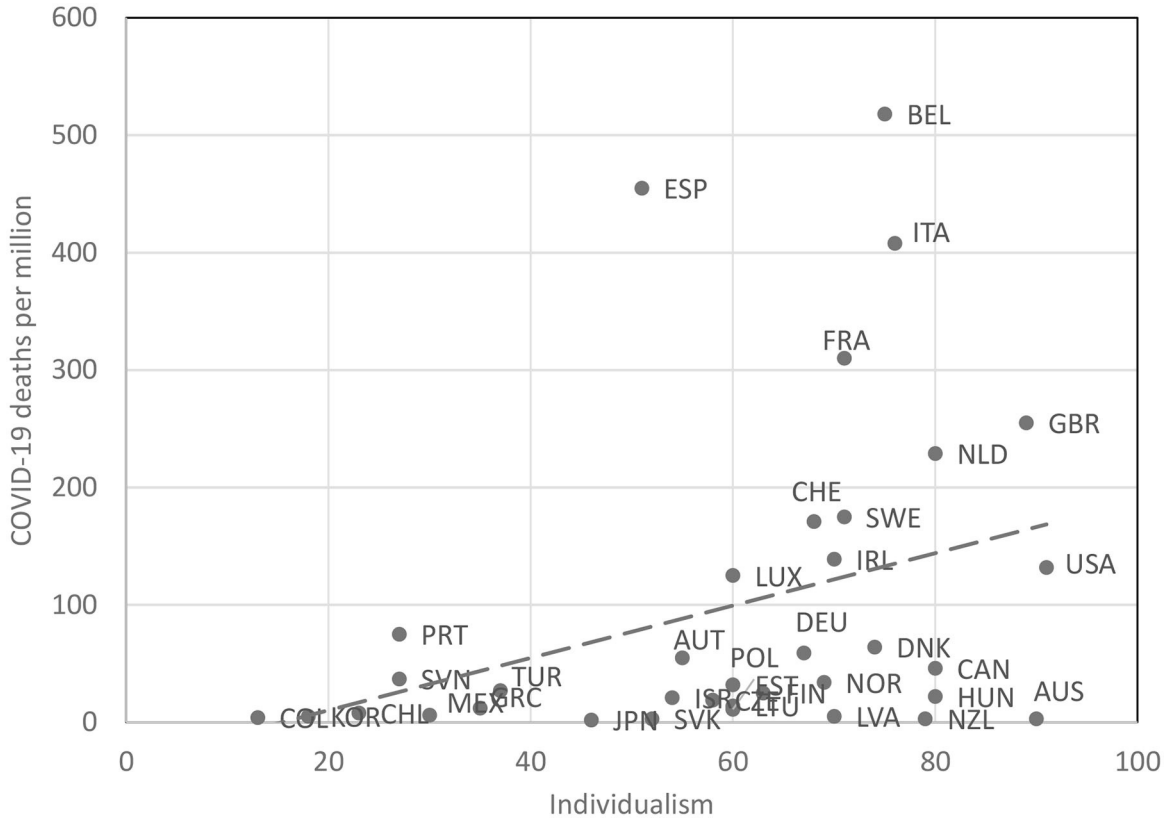

FIGURE 1 | The relationship between countries' individualism score and COVID-19 deaths within a given country for OECD countries (for country codes see Supplementary Materials; Study 1).

deaths were significant when we controlled for the variables mentioned above ($r = 0.33$, $p = 0.036$). Taken together, these results suggest that, indeed, the more individualistic a society is, the more it suffers from COVID-19 related cases and deaths.

STUDY 2

In Study 2, we investigated the possible mechanism for the above pattern. We picked Israel since the country scored 54 on Hofstede's individualism-collectivism model, which is approximately the mid-range of the 69 countries (6-91).

Methods

Sample

Our sample consisted of 327 Israelis [49.8% women: Mage (mean age) = 44.44, SD = 14.28]. Participants were contacted via a large Israeli online survey company (iPanel) and asked to participate in exchange for monetary compensation. Most participants (98.2%) defined themselves as Jews. The rest of the participants defined themselves as either Muslim (0.6%), Christians (0.3%), Druze (0.3%), or religionless (0.6%; for additional information, see Supplementary Materials).

Procedure

We investigated a serial mediation model with four levels: people's norms of individualism vs. collectivism, their collectivistic attitudes, their COVID-19 planned behavior (19), and their COVID relevant decision-making. We assessed individuals' collective orientation (norms) using a measure of individual-collective primacy (20), which entailed 7-item to which people responded on a 1 (highly disagree) to 7 (highly agree) response scale ($\alpha = 0.59$). One additional item used in the original scale was omitted as it reduced the reliability of the full scale (i.e., *"In most cases, to cooperate with someone whose ability is lower than yours is not as desirable as doing the thing on your own"*). Participants attitudes were assessed using two items ($r = 0.25$, $p < 0.001$) regarding individual vs. collective orientation (i.e., *"It is best to quarantine the entire population to save those who are at risk (such as the elderly)"*; *"Concern for the environment is more important than concern for the needs of the individual"*). Planned behavior of adherence to COVID-19-related guidelines was assessed using five statements ($\alpha = 0.89$) such as: "I intend to strictly make sure to wear a mask." Finally, participants' decision making was assessed by choosing one of four masks to buy. Participants read that all four masks were identical in terms of the wearer's safety, but they differed in cost (about 0.75, about 1.5, about 3, about 6 USD per

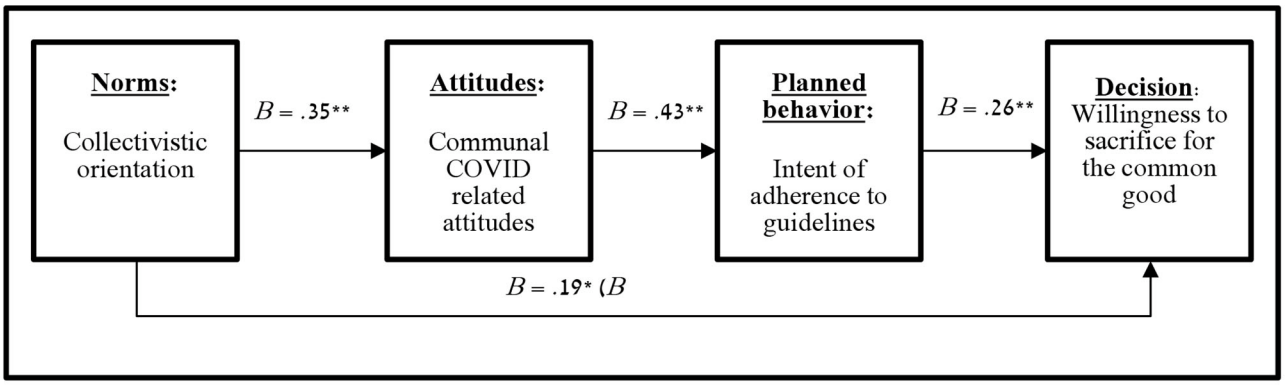

FIGURE 2 | Serial mediation model of collectivism norms, collective attitudes, COVID-19 planned behavior, and relevant decision-making (Study 2). *$p < 0.05$, **$p < 0.01$.

unit) and the level of protection to other people they will come in contact with (low, mediocre, good, and excellent). All relevant scales are reported here, and the full scales are available in the Supplementary Materials.

Results and Discussion

We conducted a serial mediation which employed Hayes' (2018 version 3.3;21) PROCESS bootstrapping command (model 6: 5,000 iterations) (21). The effect of each level in the serial mediation was indeed significant (see **Figure 2**), and the total effect of collectivistic orientation on willingness to make a financial sacrifice for the common good was significant (B = 0.19, SE = 0.08, $p = 0.021$, CI 95% [0.03, 0.36]). The model revealed a full mediation as the direct effect turned insignificant when the indirect path was presented (B = 0.10, SE = 0.08, $p = 0.240$, CI 95% [−0.06, 0.26]). We also found an indirect effect of collectivistic orientation on willingness to sacrifice for the common good via both communal COVID related attitudes and intent of adherence to guidelines (B = 04, SE = 0.02, CI 95% [0.01, 0.08]; total indirect effect: B = 0.10, SE = 0.03, CI 95% [0.04, 0.17]).

The results of Study 2 indicate that collectivistic orientation is associated with willingness to sacrifice for the common good by promoting the protection of one's environment from being infected via communal COVID related attitudes and intent of adherence to COVID health guidelines. The results correspond with the findings of Study 1. These results point to a possible mechanism that may explain the link between collectivistic culture with the number of COVID related cases and, therefore, also deaths found at the state level.

STUDY 3

Study 3 was designed to further establish the relations between collectivistic orientation and adherence to health guidelines using different measures among a different sample population. While Study 2 was held in Israel with a sample compiled of mainly Jews, Study 3 was held among American participants.

Methods

Sample

Our sample consisted of 121 American participants (73.6% women; Mage = 27.00, SD = 7.46). Participants were contacted via a large online survey platform ("Prolific") and were asked to participate in the survey for monetary compensation. Of the participants, the majority (76.9%) were White, and the rest were Black or African American (8.3%), Asian (9.1%), Hispanic or Latino (2.5%), Arab (0.8%), and Multiracial (2.5%). Religion wise, over a quarter of participants were Christians (27.3%), and the rest were Jewish (0.8%), Muslim (6.6%), Hindu (1.7%), Buddhist (1.7%). The rest of the participants defined themselves as Agnostic, Atheist, or Other (62%).

Procedure

Here, collectivistic orientation was assessed using three relevant indices: Social-Value orientation (SVO), Perspective-taking (PT), and Empathic concern (EC). SVO was operationalized as the sum of prosocial choices made in a nine-item SVO scale (22). The SVO scale included scenarios in which one has to choose a resource allocation between oneself and another player: equal distribution (prosocial), maximizing one's profit, or maximizing the gap ($\alpha = 0.83$). A particular example might be (self, other): 480-480, 540-480, and 480-80. Perspective-taking (PT) and Empathic concern (EC) were assessed on a 7-point scale using the sum of participant's responses to 7 items each (23). Among the perspective-taking items was: *"When I'm upset at someone, I usually try to 'put myself in his shoes' for a while"* ($\alpha = 0.82$). Among the empathic concern items was "*When I see people being taken advantage of, I feel kind of protective toward them"* ($\alpha = 0.80$). Finally, guideline adherence was assessed by using a single statement: *"Since the COVID-19 eruption, I have been very strict about following the instructions (staying at home, reducing contact with people as much as possible)."*

Results and Discussion

We tested the correlations among the various manifestations of collectivistic orientation (SVO, PT and EC) to guidelines adherence and found significant correlations. SVO ($r = 0.21$, p

$= 0.022$), PT ($r = 0.34$, $p < 0.001$), and EC ($r = 0.31$, $p = 0.001$), were all positively correlated with guidelines adherence.

In Study 3, we replicated the association between collectivistic orientation and guideline adherence by using other measures evaluating collectivistic orientation (not used in Study 2). We had also used an American sample vs. the Israeli sample used in Study 2. The sample was a random (not representative) sample of Prolific participants, which entailed a relatively young and mostly female participants. The correlations found in Study 3 are small to moderate; however, they indicate an effect that may not be of large proportions but is of great importance as it affects the number of human lives lost in the pandemic. Despite the non-representative sample and the moderate size of the correlations, since the results suit the results found in Studies 1 and 2, while using different measures and sample study 3 adds credence to the general argument of this paper.

DISCUSSION

Some countries suffer a devastatingly high COVID-19 related death toll while others are less affected (4). One cultural aspect that may explain the disparity in fatalities among different countries is the public cooperation and willingness to sacrifice to support the common good and adhere to health guidelines (24). In three studies, we found a tie between individualism (vs. collectivism) to epidemic prevention measures at the personal level (Studies 2 and 3) and a relation between countries' individualism (vs. collectivism) and the mortality rate they suffered at the societal level (Study 1). It is important to note that despite the overall trend we found in Study 1, there may be country-specific differences in the underlying mechanisms that should be further explored moving forward.

The research described in this paper has two main implications. First, for scientists and practitioners examining social aspects of the pandemic, our results suggest that despite the virus outbreak being a global phenomenon, different countries and cultures may react differently to it. Thus, research insight and policy formulation should be treated in a case-by-case manner based on culture, and overarching global generalization should be avoided.

The second implication is that leaders should try to foster a more collectivistic mindset among their constituents regarding promoting safe conduct during the current pandemic or future ones. For example, when trying to promote safe behavior during the pandemic, New York's Governor Andrew Cuomo was quoted saying: "Yeah it's your life do whatever you want, but you are now responsible for my life.… We started saying, It's not about me it's about we." (25). Alternatively, in cases where the individualistic tendencies are deeply rooted, it might be better to stress the individual benefits of safe conduct and vaccination instead of making the case of collectivistic social responsibility (26). Notably, both approaches should be further investigated to avoid a "boomerang effect," where counterproductive results might occur, when psychological interventions imply negative social connotations and threaten one's positive self-image (27).

Furthermore, as COVID-19 vaccines have been recently approved, governments and health authorities are now facing a new challenge, namely: people who are reluctant to take the new vaccines out of fear or as part of the anti-vaccine movement (28). Indeed, it seems that even the devastating impact of the COVID-19 pandemic has not convinced those who oppose vaccination (29). Research has pointed to differences in acceptance rates of COVID-19 vaccines across different countries (30). Thus, messages that speak to ones' responsibility toward the community might be more effective within collectivistic communities. Within individualistic societies, on the other hand, self-protection messages should be considered.

To conclude, we argue that cultural variance across countries is just as crucial in understanding adherence to epidemic prevention measures and, therefore, how susceptible a society is to the COVID-19 outbreak. These are initial indications of one mechanism that may explain the disparity of the death toll brought on different cultures by COVID-19.

DATA AVAILABILITY STATEMENT

All data is available in the main text or as part of the datasets. The datasets generated for this study can be found in the OSF website https://osf.io/8jw2g/?view_only=f7933c6632c84fe383c822b354918fc9.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The Institutional Review Board, IDC Herzliya Adelson School of Entrepreneurship. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

YM: study design, data interpretation, writing, figures, and literature search. AL: study design, data interpretation, and writing. TG: data collection, data analysis, writing results, and figures. DC: data collection, data analysis, and writing results. SS: data collection and data analysis. All authors contributed to the article and approved the submitted version.

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Coming Out to Play: Privacy, Data Protection, Children's Health, and COVID-19 Research

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The COVID-19 pandemic has underscored the need for new ways of thinking about data protection. This is especially so in the case of health research with children. The responsible use of children's data plays a key role in promoting children's well-being and securing their right to health and to privacy. In this article, we contend that a contextual approach that appropriately balances children's legal and moral rights and interests is needed when thinking about data protection issues with children. We examine three issues in health research through a child-focused lens: consent to data processing, data retention, and data protection impact assessments. We show that these issues present distinctive concerns for children and that the *General Data Protection Regulation* provides few bright-line rules. We contend that there is an opportunity for creative approaches to children's data protection when child-specific principles, such as the best interests of the child and the child's right to be heard, are put into dialogue with the structure and logic of data protection law.

Keywords: children, data protection, privacy, health research, pediatrics, research ethics

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INTRODUCTION

It is axiomatic that children are vulnerable. Without fully formed cognitive capacities and the lack of life experience, children need help from their parents, civil society, and the State to look after their best interests. During the COVID-19 pandemic, their vulnerability as a group and as individuals has only increased. Threats to the biological existence of citizens have necessitated the use of State power to change daily social life. In the face of such changes, it is nevertheless regrettable that the rights and interests of children have been largely ignored. Indeed, for today's children, there is a certain irony to current circumstances. By and large, children and adolescents are actually less *biologically* vulnerable to COVID-19, being spared the worst effects of the disease. Yet, where such legal and political power is leveraged in response to adult biological vulnerability, children may be pawns, owing to their political vulnerability (Larcher and Brierley, 2020).

With the COVID-19 pandemic, we are at the apex of the collection, use, and disclosure of data about children. In this article, we contend that the new ways of thinking about data protection issues with children in the health research context are overdue. We first outline the opportunities and challenges of children's data. They are at once indispensable for the promotion of children's rights and interests and yet pose risks to their well-being if improperly used. We then examine children's rights to privacy and data protection under the *Convention on the Rights of the Child* (CRC; 1989) and the *General Data Protection Regulation* (GDPR; 2016). We contend that the lack of clear, child-specific provisions means that a highly contextual approach must be taken to understand the relationship of children's privacy to health research. As such, we examine three specific issues for children and COVID-19 research: consent, data retention, and data protection impact assessments. Each of these three issues presents a delicate balancing exercise with few bright-line rules. As such, we conclude by calling for increased attention to the data protection needs of children in health research.

CHILDREN'S DATA: OPPORTUNITIES AND CHALLENGES

During the pandemic, children's lives have been transformed. Many are attending school virtually – logging on for most of the day to interact with their classmates and teachers. Even for children who are going to school in person, the management of their education has shifted dramatically. As with other infectious disease outbreaks, contact tracing is frequently used, revealing potentially sensitive information about children's interactions with others, especially in the case of adolescents (Berman et al., 2020). It is still lively debated whether school openings are responsible for increased incidents of COVID-19 among children and adolescents, with some arguing that children are not the super spreaders many had initially worried about (Munro and Faust, 2020), and others contending that children play a key role in community transmission (Hyde, 2020). Irrespective of the validity of either hypothesis, when schools are open, consideration must be given to the allocation and prioritization of COVID-19 testing (Mathew, 2020; Pettit et al., 2020), which again generate additional data about the health status of children and their families.

Turning to the health research context, there is a wide array of questions regarding the effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on children. This ranges from concerns regarding the multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19 (Consiglio et al., 2020; Jiang et al., 2020; Jones et al., 2020; Verdoni et al., 2020) to the involvement of children in clinical trials for vaccines (Anderson et al., 2020), which would eventually include on-going Phase IV monitoring (Nell, 2018), to the psychosocial toll social distancing and stay-at-home orders have had on children (Cardenas et al., 2020). This is to say nothing of the need to develop therapeutics, improve treatment protocols, and other applications of clinical knowledge in a way that attends to the specific physiological needs of children. Meeting this challenge of pandemic proportions requires the broad sharing of data among international research teams in ways that ensure children's rights and interests are furthered and that public trust is maintained.

Big data presents both challenges and opportunities for children (Berman and Albright, 2017; Almog and Franco, 2020). Children's rights and interests may be furthered through sophisticated analyses of data across domains – from clinical to environmental to educational. In the health context, big data in the form of -omics data has begun to show success in the stratification of sick children (Ding et al., 2019). The Committee on the Rights of the Child has encouraged States to conduct research with children "to learn about their health challenges, developmental needs, and expectations as a contribution to the design of effective interventions and health programs" (United Nations Committee on the Rights of the Child, 2013a). The Committee further opines that data concerning key health problems and health determinants should be collected through routine health information systems and through research (United Nations Committee on the Rights of the Child, 2013a).

At the same time, data may be used against children's rights and interests through profiling, targeted advertising, and unjustified discrimination. And concerns about children's data are growing. Parents worry about who has access to data about their children and for which purposes such data may be used (Barassi, 2020). Sociological research suggests that concerns regarding who can share what with whom are shared by both parents (Barassi, 2020; Cino and Vandini, 2020) and children (Sarkadi et al., 2020). A growing body of scholarship highlighting the potential dangers of using children's data in ways that are not in children's best interests accompanies these sentiments. Zuboff (2019), for example, has warned of the pitfalls of immersing children in environments that are designed to harvest data and help to shape future consumption behaviors.

CHILDREN'S PRIVACY: SOURCES

Against this data-rich backdrop, the privacy interests of children have been hitherto underdeveloped. Enshrined in the CRC, the child's right to privacy provides children with a right to informational privacy, as well as giving the family a sphere of decisional privacy (United Nations General Assembly, 1989). Only in the past decade or so, with the advent of social networks and other platforms that heavily rely on personal data, have children's privacy interests garnered much interest (Dowty, 2008; Shmueli and Blecher-Prigat, 2011). The majority of scholarship and normative guidance on the topic of children's data protection consequently have been aimed at attending to the multifaceted issues such websites present (Milkaite and Lievens, 2019). For example, the GDPR includes a special consent regime for social networking websites. Otherwise, the regulation is mostly silent on the specific issues children's data pose, other than its express recognition that children are vulnerable. The COVID-19 pandemic has, however, spawned further research into the children's privacy issues related to contact tracing and other public health surveillance

technologies (Berman et al., 2020). Children's privacy in health research remains nevertheless little researched.

BEST INTERESTS OF THE CHILD

As a structuring principle for *all* children's rights (United Nations Committee on the Rights of the Child, 2013b), the best interests of the child standard (BIC) is central to delimiting the child's right to data protection. The BIC demands that, in all decisions concerning a child, their best interests are a primary consideration (United Nations General Assembly, 1989). That the BIC is *a* rather than *the* primary consideration means that it is not an overriding concern in all matters, i.e., it may be departed from in certain circumstances.

Despite not being children's rights instruments *per se*, the BIC is further secured under the *European Convention of Human Rights* (ECHR; Council of Europe, 1950; European Court of Human Rights (First Section), 2007) and the *Charter of Fundamental Rights of the European Union* (CFREU; European Union, 2012). Under the ECHR, the BIC assists in the elaboration of the rights, where children are involved (Hubert-Dias, 2014). The CFREU expressly incorporates the BIC, specifying that it is a primary consideration, "in all actions relating to children, whether taken by public authorities or private institutions" (European Union, 2012, Art 24). The inclusion of the BIC in both the ECHR and CFREU is not a mere formality. The GDPR, as an elaboration of the rights to private life and to data protection under the ECHR and CFREU, uses these rights and obligations as its framework (Kuner et al., 2020). In the context of children's data, guidance from the Article 29 Data Protection Working Part (A29 DPWP) expressly recognizes that, "the core legal principle [for data processing and beyond] is that of the best interest of the child" (Article 29 Data Protection Working Party, 2009, p. 4).

The BIC imposes an obligation on decision-makers – be they parents, policymakers, ethicists, lawyers, researchers, and others – to engage in a reasoned decision process (Eekelaar and Tobin, 2019). After having determined the best interest, any decisions to depart from what the BIC requires must be justified. The BIC further acts as an aid in interpreting and implementing the panoply of rights and obligations to which the CRC gives rise (Hammarberg, 2011). In this vein, the Committee on the Rights of the Child has recommended that the BIC guide all actions and decisions by the government concerning legislation, court decisions, administrative decisions, and projects, programs, and services that have an impact on children (United Nations Committee on the Rights of the Child, 2009). This approach requires taking into consideration a broad spectrum of factors that affect the well-being of the child (United Nations Committee on the Rights of the Child, 2013b).

Of particular import for COVID-19 research, the obligation for the BIC to be a primary consideration in all matters affecting a child includes the promotion of their health and welfare interests. In the context of research, this means that, under the broad WHO definition of "health," their general physical and psychological well-being must be taken into account (World Health Organization, 2020). This nexus between the BIC and the inclusion of children in research as a population with specific developmental needs is accentuated in public health as there are additional implications for their future health as adults. This is all the more true when one considers that public health is founded on an ethos of supporting a public good (Upshur, 2002), which in a pandemic should include children as a vulnerable population.

The BIC also, however, acts a protective factor for research involving children. The collective societal interest in COVID-19-related does not negate the duty to ensure that any participation in research be in an individual child's best interests or that of children of the same age or condition (World Medical Association, 2013). For example, the Committee on the Rights of the Child has stressed that the BIC requires anyone undertaking research involving child-participants to follow international ethical guidelines (United Nations Committee on the Rights of the Child, 2013a). More concretely, the Committee states categorically that the BIC "shall always prevail over the interest of general society or scientific advancement" (United Nations Committee on the Rights of the Child, 2013a, p. 85).

SPECIFIC ISSUES REGARDING CHILDREN'S DATA PROTECTION AND HEALTH RESEARCH

As a general proposition, then, the child's right to data protection and to have their interest be a primary consideration is always at play. Without specific norms regarding how these rights are to be reconciled in the context of health research, we propose to look at the data protection issues that three aspects of COVID-19-related research with children present: consent, data retention, and data protection impact assessments.

Consent

Even during a pandemic, informed ethical consent is a *sine qua non* of ethical research involving human participants. Where data processing is concerned, however, the GDPR provides various other legal bases by which personal data may be processed. Indeed, consent as a legal basis may not be appropriate in many forms of health research because of the power imbalance between the researcher-controller and the participant-data subject. Clinical trials with sick participants are one potential case (European Data Protection Board, 2019). The increased vulnerability of research with sick children only intensifies this imbalance that negates the freely given aspect of consent. If possible, scientific research related to COVID-19 may find it easier to rely upon a public interest basis for certain processing (Becker et al., 2020).

Beyond power imbalances, the complex nature of contemporary big data biomedical research stretches what one can reasonably expect data subjects to understand to give consent, especially in the case of children. This position can be inscribed in larger debates regarding the insufficiency of consent in the context of very complex data processing activities whose consequences on the data subject's interests are difficult, if not possible, to

understand (Weigend, 2017). If a competent adult hypothetically may struggle to understand the nature of processing and its consequences, conveying this to children is even more difficult. Despite these consent issues, some EU Member States have gone in the opposite direction. Ireland, for example, requires consent to be the legal basis for data processing for health research, unless certain conditions are met (Republic of Ireland, 2018).

The additional physical risks that COVID-19 creates also present difficulty, whether doing research with children or adults (Largent et al., 2020). Physical enrolment, the taking of biosamples, and other such tasks increase the risk of exposure to SARS-CoV-2. There are multiple models for mitigating these risks, such as opt-out with notification (Knoppers et al., 2020). These models may not satisfy the narrow notion of GDPR consent because, among other things, an affirmative act is required (European Data Protection Board, 2020b). Choosing another legal basis for data processing may then help to minimize contact and exposure to risk.

Findings ways to solicit the child's views and give effect to them in these circumstances must be carefully considered. Parents or other legally authorized representatives exercise rights on behalf of children, and thus are the only ones who may give a legally valid consent, saving a judicial order specifying otherwise. There is, however, a dynamic process between children and parents in giving effect to a child's burgeoning autonomy. Under the CRC, children have a right to be heard (United Nations General Assembly, 1989). Giving effect to this right requires that there be opportunity for the child to make their views known and that any decisions be justified in light of these views.

So-called "mature minor" doctrines are aimed at giving effect to a child's views when they understand the nature and consequences of a procedure and the procedure is viewed to be in that child's best interests (Appellate Committee of the House of Lords, 1985; Dalpé et al., 2019). Some have argued that the mature minor doctrine should be transposed into the data protection context for children (Buitelaar, 2018). However, transposing such a contextually specific doctrine to health research, and to data processing more generally, raises more questions than answers (Taylor et al., 2017). Clinical decision-making implies a different range of considerations than in health research and in data processing, e.g., the expectation that the procedure is likely to confer health benefits upon the patient, clinical procedures involve a child's physical integrity, etc.

To take the child's autonomy seriously, it has been suggested that data controllers have ongoing, transparent engagement with the child data subjects (Taylor et al., 2017). Such an approach may be particularly well suited for biobanking and other such longitudinal studies. For research projects with shorter timescales and less resources for participant engagement, this could pose challenges. A project webpage that includes age-appropriate consent and assent materials may go a long way to ensuring that parents and children are sufficiently engaged.

Data Retention (Storage)

The diverse array of host genomic and phenotypic data collected during the course of COVID-19-related research may be met with an uncertain future. The EDPB's own guidelines for scientific research during the COVID-19 pandemic state categorically that "storage periods (timelines) shall be set and must be proportionate" (European Data Protection Board, 2020a, p. 13). Paradoxically, however, we note that the GDPR is clear on this point: personal data used exclusively for research purposes may be kept indefinitely, provided that there are appropriate safeguards in place (Bovenberg et al., 2020). Any secondary use would then be limited to other scientific research studies (or for archiving in the public interest and historical research or statistical purposes). Although this does not confer unfettered discretion on researcher-controllers, it should allow for undefined storage periods in the case of data that are either difficult to generate or even impossible to generate again because they represent the child's health indicators at a given moment in time.

Children, again, hypothetically pose specific issues. And, perhaps unsurprisingly, the EDPB's COVID-19 scientific research guidelines are silent on this point. Due to the physiological changes that children undergo, it is more likely that certain health data represent unique points in time and cannot be replicated. This justification must be weighed against the potential risks that continued storage presents to the children-data subjects. Depending on the research type and the data generated, this may include discrimination, embarrassment, or other social stigma in the case of a data breach. In other words, utility must confront vulnerability.

Taking the BIC seriously as regards data retention would suggest that less data be retained, unless retention can be justified to serve an objective or interest that supersedes the child's best interests. Given that the A29 DPWP has taken an expansive approach to the notion of data subject interests that goes beyond legal interests, ethical principles, and concerns may also hypothetically feature in the analysis (Article 29 Data Protection Working Party, 2014). This approach could accommodate non-legal notions such as the child's moral "right to an open future" (Feinberg, 1980).

The child's moral right to an open future is a complex consideration for data storage, and indeed data processing writ large. At its core, the right calls for parents to conserve certain decisions for children when such decisions may be made autonomously by the child. This would seem to militate against data retention. Nevertheless, autonomy may still work with data retention. Providing the child with, and facilitating the exercise of, the ability to opt-out at the age of majority, discussed below, may also be seen as compatible with the child's moral right to an open future. The moral right to an open future should, in our estimation, also feature as a concern of data minimization, thus decreasing risks to child data subjects.

Assuming that data are retained: the numerous research studies involving children and COVID-19 will eventually have to confront another reality: what happens with data when the child-participants reach the age of majority? According to A29 DPWP guidance, where consent is the legal basis for processing, it is unlikely that the parental consent alone will be sufficient to justify continued processing once the child reaches the age of majority (Article 29 Data Protection Working Party, 2009).

Where consent is not the legal basis relied upon, the issue is very open textured. In keeping with the core principles of transparency and accountability, controller-researchers should strive, at a minimum, to notify participants about their data and the research when they reach the age of majority and provide the opportunity for opt-out. This allows the newly emancipated participants the ability to decide what is done with their data in a way that strikes a balance with the enduring interest in health research. Such an approach further coheres with the choice within the GDPR to include a right to object, for instances, where consent is not the legal basis for processing.

Data Protection Impact Assessments

At every turn thus far, we have advocated for a balancing exercise when it comes to the contextual nature of children's data protection in the health context. Whether issues relate to giving due respect to the child's best interests, child and parental autonomy, or data retention, child-data subjects present distinct concerns for which few bright-line norms exist. Indeed, analyzing what the broad spectrum of rights secured under the CRC requires in any context implicates a weighing exercise.

One particularly germane tool for this weighing exercise is a data protection impact assessment (DPIA; van der Hof and Lievens, 2018). DPIAs are a tool to analyze the scope and effects of data processing, where processing is "likely to result in a high risk to the rights and freedoms of natural persons." DPIAs present the opportunity for controller-researchers to carefully examine the risks that inhere to data processing throughout its lifecycle and to then implement safeguards to reduce or eliminate such risks. Because DPIAs are meant to be conducted from the point-of-view of the data subject (Article 29 Data Protection Working Party, 2017), they lend themselves to engaging with children to understand the risks certain scientific data processing tasks may pose to their interests.

As a tool that is meant to be updated as processing operations change, it can be updated in response to the evolving capacities of children for longitudinal studies. Making the DPIAs available to parents and child-participants would do much to further transparency, accountability, and trust. In the case of presenting a DPIA to children, it should be tailored to their level of understanding (Lievens and Verdoodt, 2018). If properly done, a DPIA may be useful for seeking informed consent to research (ethics consent), or for even teaching children (and parents) about the risks and benefits of data processing and how the researcher-controller is keeping their data secure, helping to create the "tripartite relationship of mutual trust between patients, families and health care teams" that pediatric data sharing requires (Rahimzadeh et al., 2018, p. 477).

CONCLUSION

The COVID-19 pandemic has put our normative frameworks to the test in many regards. For children's rights, perhaps the most difficult has been ensuring that these rights and the interests that ground them are taken into account when it comes to crafting public health measures. Beyond immediate public health concerns, we have seen a phenomenal expansion of children's digital footprints. Although much of this has happened outside of the health research context through changes, such as online schooling and increased reliance on digital technologies for socializing, the changes emphasize the need to think more about children's right to data protection and its interaction with other children's rights, in particular the right to health. Science may be able to bring the pandemic to an end, but it cannot answer important normative questions such as those that relate to children's data.

We have striven to canvas issues with a pragmatic lens to real-world issues that COVID-19 research with children may present. Yet, we have seen that there is little authoritative guidance regarding data protection law and its application to children. On the one hand, this is an opportunity; the silence of norms invites creative thinking and flexibility for researcher-controllers and policymakers. On the other hand, researcher-controllers are forced to confront potentially difficult choices to which even the best of intentions may not quickly provide an answer. At minimum, though, the need to take into account children's best interests and to provide reasoned justification in a transparent manner are central to any effective approach to children's data protection. Further elucidating issues related to children's data protection as regards their health data should be a central concern of scholars, researchers, policy makers, and clinicians alike.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

MB and BK conceived the article. MB conducted the research and drafting in consultation with BK. All authors contributed to the article and approved the submitted version.

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Will Healthcare Workers Accept a COVID-19 Vaccine When It Becomes Available? A Cross-Sectional Study in China

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Objective: The Coronavirus disease 2019 (COVID-19) vaccine is currently available. This timely survey was conducted to provide insight into on the willingness of healthcare workers (HCWs)to receive the vaccine and determine the influencing factors.

Methods: This was a cross-sectional online survey. An online questionnaire was provided to all participants and they were asked if they would accept a free vaccine. The questionnaire gathered general demographic information, and included the General Health Questionnaire (GHQ-12); Myers-Briggs Type Indicator questionnaire (MBTI); Depression, Anxiety, and Stress Scales (DASS-21); and the 12-item Short Form Health Survey (SF-12). The data were collected automatically and electronically. Univariate analysis was done between all the variables and our dependent variable. Multivariable logistic regression models were employed to examine and identify the associations between the acceptance of the COVID-19 vaccine with the associated variables.

Results: We collected 505 complete answers. The participants included 269 nurses (53.27%), 206 clinicians (40.79%), 15 administrative staff (2.97%), and 15 other staff (2.97%). Of these, 76.63% declared they would accept the vaccine. The major barriers were concerns about safety, effectiveness, and the rapid mutation in the virus. Moreover, four factors were significantly associated with the willingness to receive the vaccine: (a) "understanding of the vaccine" (odds ratio (OR):2.322; 95% confidence interval [CI]: 1.355 to 3.979); (b) "worried about experiencing COVID-19" (OR 1.987; 95% CI: 1.197–3.298); (c) "flu vaccination in 2020" (OR 4.730; 95% CI: 2.285 to 9.794); and (d) "living with elderly individuals" (OR 1.928; 95% CI: 1.074–3.462).

Conclusions: During the vaccination period, there was still hesitation in receiving the vaccine. The results will provide a rationale for the design of future vaccination campaigns and education efforts concerning the vaccine.

Keywords: COVID-19, vaccine, healthcare workers, vaccination, acceptance

INTRODUCTION

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is currently the most urgent public emergency, which has attracted huge global attention. As of January 24, 2021, there have been a total of 99,152,664 confirmed cases, besides, 71,230,238 have recovered and 2,125,084 deaths have resulted all over the world. In China alone, there are official reports of 99,931 confirmed cases and 4,810 deaths as of January 24, 2021 (1). The pandemic has brought the danger of deaths from the epidemiologic contagion. Although drugs have been used to treat severe COVID-19 patients (2–5) and many policies have been in place to stop the spread of the virus, COVID-19 has continued to spread rapidly throughout the world. Therefore, vaccines for COVID-19 are considered an effective weapon to prevent the spread of the infection.

COVID-19 vaccines are finally becoming available, but uptake of any COVID-19 vaccine is an important challenge to address. A global survey found that 71.5% people would be very or somewhat likely to take a COVID-19 vaccine (6). One survey from July 2020 estimated that one-third or more of the United States (U.S). Population would decline COVID-19 vaccination (7). A cross-sectional study in Indonesia found that only 67.0% would like to be vaccinated if the effectiveness was 50% (8). A nationwide online survey in China from June 2020 revealed that 56.4% would be willing to receive the vaccine, with a definite yes intent of 28.7% (9). For medical institutions that are the main battlefield against the epidemic, protecting healthcare wokers (HCWs) against COVID-19 is crucial and some countries, including China have begun to carry out the mass vaccination campaign targeted at the highest risk groups including HCWs since December 2020 (10–12).

A cross-sectional study to assess the attitude of HCWs toward COVID-19 vaccination in U.S found that 36% of respondents were willing to take the vaccine when it became available while 56% were not sure or would wait to review more data (10). And a similar survey in Saudi Arabia revealed that 50.52% of HCWs were willing to have the COVID-19 vaccine (13). These investigations indicated that there is still some hesitation about vaccination when the vaccine become available, which could potentially blunt the potential of the vaccine in protecting long-term care residents.

Because HCWs are planned to be candidates for early vaccination and the role of HCWs becomes particularly important in advising patients and communities, and as well as through role modeling behavior. In this study, we assessed the acceptance of COVID-19 vaccine of HCWs in Third People's Hospital Of Chengdu in China and conducted a comparative analysis to examine what factors influence vaccination intentions. This study aimed to provide useful information to government and non-government organizations for taking the necessary steps toward a successful vaccination program.

MATERIALS AND METHODS

Study Participants

A cross-sectional study was performed using the social media platform-based (WeChat) survey program, "Questionnaire Star," between January 4 and 6, 2021. Participation was voluntary and the responses were anonymous. We included questionnaires from all HCWs from the Third People's Hospital of Chengdu (Sichuan, China). Those who agreed to participate in our study provided informed consent on the survey platform and later received a photo of a QR Code. They participated in the questionnaire by scanning this QR code. The exclusion criteria were as follows: (a) participants under 18 years old or over 59 years of age, (b) participants that were not HCWs in our hospital, and (c) participants that did not complete the assessment.

Questionnaire and Data Collection

Before initiating the formal study, we first consulted psychologists working at our institution. The final questionnaire included an assessment of demographics (such as sex, age, education level, current position, marital status, children), the General Health Questionnaire (GHQ-12) (14–16), Myers-Briggs Type Indicator questionnaire (MBTI) (17–19),Depression, Anxiety, and Stress Scales (DASS-21) (20–23),and the 12-item Short Form Health Survey (SF-12) (24–27). This study was approved by the Ethics Committee of Third People's Hospital of Chengdu (【2021】-S-51), and all responders provided written informed consent before participating in this study. The survey lasted 3 days and ended on the day of vaccination. Incomplete questionnaires were eliminated electronically to ensure only full datasets were acquired. The data were collected through an online survey platform and the responses to the questionnaires were automatically encoded and organized by the "Questionnaire Star," to avoid errors caused by manual entry. Finally, we exported the data to spreadsheets. The data were saved in both text format and numeric form.

Description of the GHQ-12, MBTI, DASS-21, and SF-12

GHQ-12 is widely used in many studies to identify common psychiatric conditions (14, 15). According to the World Health Organization (WHO) guidelines, the GHQ-12 questionnaire is frequently used with the 0-0-1-1 scoring method where the first two and last two choices are scored as 0 and 1 points, respectively, leading to a total score ranging between 0 and 12 points. We used 3 points as the cut-off value, where 3 points or more suggested a mental health problem (16), the higher the score, the more significant the mental problem.

MBTI was developed to enable researchers to measure Jung's psychological types (17). It can measure Jung's three personality dimensions Extroversion/Introversion (E/I), Sensation/Intuition (S/N), and Thinking/Feeling (T/F), and also a dimension proposed by Myers, namely judging (J)/perceiving (P). MBTI is also frequently used to assess someone's personality (18, 19). In this study, we mainly discussed whether E/I or T/F would affect the vaccination intentions.

The DASS-21 is a popular measure of mental health (20, 21), and with its 21 items (7 items for each subscale) and three dimensions with similar psychometric properties is based on the tripartite model of depression, anxiety, and stress. Each 7-item subscale is rated on a 4-point Likert scale ranging from 0 (Did not apply to me at all) to 3 (Applied to me very much). Higher scores represent greater symptomology (22, 23).

The SF-12 has been used to investigate the quality of life (24, 25) and includes the Physical Component Summary (PCS) and Mental Component Summary (MCS) (26). The SF-12 physical (PCS-12) and mental (MCS-12) component summary scales were scored with reference to a formula (27). As it was particularly tedious to calculate the MCS and PCS singularly by individual items, we developed an EXCEL formula using Visual Basic for Applications(VBA)to process this data to avoid errors. The MCS and PCS scores ranged from 0 to 100, the higher the score, the better the quality of life.

Statistical Analysis

All statistical analyses were performed using the SPSS 23.0 for Windows software package and the statistical significance level was set at a $p \leq 0.05$. Descriptive statistics for the demographics and general health state of the medical staff were reported as the mean, standard deviation (SD), number (n), and percentage. Univariate analysis were done between all the variables and our dependent variable. Multivariable logistic regression models were employed to examine and identify the factors associated with the acceptance of COVID-19 vaccine.

RESULTS

Demographic Characteristics

In this study, we collected a total of 505 responses, including 114 males (22.57%) and 391 females (77.43%).The participants included 206 clinicians (40.79%), 269 nurses (53.27%), 15 administrative staff (2.97%), and 15 other staff (2.97%). Of these, 97.42% had an educational level of bachelor's degree and above, 59.21% were married, 51.68% had at least one child, and 54.65% were living with an elderly individual. Of the participants, 61.19% (309) were extroverted. The demographic data are shown in **Table 1**.

Acceptance of COVID-19 Vaccine and the Major Obstacles

Of the 505 respondents, 387 (76.63%) were willing to receive vaccination and 118 (23.37%) were not. We listed six possible factors. The top three reasons concerned safety, efficacy, and the rapid mutation of the virus (**Figure 1**).

Variables Associated With the Acceptance of the COVID-19 Vaccine

For the univariate analysis (**Table 1**), we divided participants into two groups according to whether they were willing to be vaccinated, namely those who would accept a vaccine were put into group 1, while the remainder were placed in the second group. There were significant differences based on respondents living with elderly individuals, prior flu vaccination, understanding of the vaccine, worries of developing COVID-19, and the effects of COVID-19. Results of the group comparisons are displayed in **Table 1**. The results showed that individuals willing to receive a vaccine were more likely to be living with an elderly individual ($\chi^2 = 4.911$, $p = 0.034$), had a higher demand for flu vaccine ($\chi^2 = 21.491$, $p = 0.000$), were more worried about infection ($\chi^2 = 7.162$; $p = 0.010$), had a better understanding of the vaccine ($\chi^2 = 12.691$; $p = 0.001$), and believed COVID-19 had a greater impact on their lives ($\chi^2 = 14.805$; $p = 0.002$). However, there were no significant differences in terms of sex, age, occupation, educational level, marital status, personality, or physical and mental health status. Nonetheless, we found that men seemed to more likely accept a vaccine than women (81.58 vs. 75.19%), and the willingness to receive vaccination gradually decreased with the increase in educational level. According to the survey, we also found that clinicians and nurses seemed more hesitant to receive a vaccine compared with administrative and other staff members.

The Multivariable logistic regression regarding the factors that are associated with the willingness to be vaccinated is presented in **Table 2**.We found that four factors were significantly associated with the willingness to receive the vaccine: (a) "understanding of the vaccine"; (b) "worried about experiencing COVID-19"; (c) "flu vaccination in 2020" and (d) "living with elderly individuals." Those who knew more about the vaccine properties were twice as likely to accept a COVID-19 vaccine, OR: 2.322; 95%CI: 1.355, 3.979, $p = 0.002$. In addition, those with high perceived risk to be infected had almost twice the odds of vaccine psychology compared to those with no perceived risk to be infected (OR: 1.987; 95%CI: 1.197, 3.298, $p = 0.008$). Those who get a Flu vaccine in 2020 were more likely to accept the vaccine compared to those who did not, with the OR: 4.730 (95%CI: 2.285,9.794, $p = 0.000$).Those living with elderly individuals had 1.928 times greater odds of accepting the vaccine compared to those who were not, OR: 1.928; 95%CI: 1.074, 3.462, $p = 0.028$. Those with a bachelor's degree were more likely to accept the vaccine compared to those with a Junior/senior school degree (OR: 2.353; 95%CI: (1.135, 4.880, $p = 0.021$). Those who thought the COVID-19 had severe effect on their lives were less likely to receive the vaccine than those who thought it had no effect (OR: 0.277; 95%CI:(0.084,0.913, $p = 0.035$).

DISCUSSION

Since the COVID-19 vaccine gradually become reality, some studies were conducted to assess acceptance of a COVID-19 vaccine (6–9). But most surveys have focused on the general population. In fact, since January 2021, our government has given priority to carry out the mass vaccination campaign targeted at the highest risk groups including HCWs, which also have happened in other countries (10–12). There are some studies showing that HCWs can themselves be vaccine hesitant and their hesitancy levels can thus impact hesitancy and aversion to receiving the vaccine among the general public (28–30). Therefore, we selected HCWs for this study. To the best of our knowledge, this cross-sectional study conducted during the early phase of the COVID-19 vaccination program is the first study evaluating the acceptance of a COVID-19 vaccine among healthcare wokers in China. In this study, we reported the proportion of HCWs willing to be vaccinated for COVID-19, and identified factors associated with acceptance of the vaccine. Our findings can be used to guide future projections of vaccine uptake.

TABLE 1 | Univariate analysis showing factors associated with acceptance of a COVID-19 vaccine ($n = 505$).

Variables	*n* (505) Frequency (%)	Group1 (*n* = 387) Frequency (%)	Group2 (*n* = 118) Frequency (%)	*χ2/t*	*P*-value
Sex					
Male	114(22.57)	93 (81.58)	21 (18.42)	2.011	0.168
Female	391(77.43)	294 (75.19)	97 (24.81)		
Age *(Mean ± SD)*	505	32.35 ± 8.98	32.71 ± 7.90	−0.395	0.693
Weight (KG) *(Mean ± SD)*	505	58.11 ± 11.16	56.99 ± 8.32	1.006	0.315
Height (cm) *(Mean ± SD)*	505	162.75 ± 7.06	162.68 ± 5.48	0.108	0.914
Occupation					
Clinician	206(40.79)	158 (76.70)	48 (23.30)	5.269	0.261
Nurse	269(53.27)	202 (75.09)	67 (24.91)		
Administration	15(2.97)	14 (93.33)	1 (6.66)		
Others	15(2.97)	13 (86.67)	2 (13.33)		
Education					
Junior/senior school*(R)*	13(2.58)	11 (84.62)	2 (15.38)	4.131	0.248
Bachelor	412(81.58)	321 (77.91)	91 (22.10)		
Postgraduate	80(15.84)	55 (68.75)	25 (31.25)		
Marital status					
Married	299(59.21)	225 (75.25)	74 (24.75)	0.783	0.394
Single	206(40.79)	162 (78.64)	44 (21.36)		
Children					
Yes	261(51.68)	201 (77.01)	60 (22.99)	0.043	0.916
No	244(48.32)	186 (76.23)	58 (23.77)		
Living with elderly individuals					
Yes	276(54.65)	222 (80.43)	54 (19.56)	4.911	0.034*
No	229(45.35)	165 (72.05)	64 (27.95)		
Flu vaccination in 2020					
Yes	124(24.55)	114 (91.93)	10 (8.06)	21.491	0.000*
No	381(75.45)	273 (71.65)	108 (28.35)		
Worried about experiencing COVID-19					
Yes	334(66.14)	268 (80.24)	66 (19.76)	7.162	0.010*
No	171(33.86)	119 (69.59)	52 (30.41)		
Understanding of the vaccine					
Yes	401(79.41)	321 (80.05)	80 (19.95)	12.691	0.001*
No	104(20.59)	66 (63.46)	38 (36.54)		
Effect of COVID-19					
Not at all	265(52.48)	213 (80.38)	52 (19.62)	14.805	0.002*
Mild	160(31.68)	121 (75.63)	39 (24.38)		
Moderate	50(9.90)	28 (56.00)	22 (44.00)		
Severe	30(5.94)	25 (83.33)	5 (16.66)		
GHQ-12					
≥3	29(5.74)	20 (68.97)	9 (31.03)	1.010	0.365
<3	476(94.3)	367 (77.10)	109 (22.90)		
MBTI (I/E)					
Introvert	309(61.19)	237 (76.70)	72 (23.30)	0.002	1.000
Extrovert	196(38.81)	150 (76.53)	46 (23.47)		
MBTI (T/F)					
Thinking	266(52.67)	206 (77.44)	60 (22.56)	0.206	0.674
Feeling	239(47.33)	181 (75.73)	58 (24.26)		
Depression*(Mean ± SD)*	505	3.52 ± 3.99	3.45 ± 3.98	0.174	0.862
Anxiety*(Mean ± SD)*	505	3.73 ± 3.78	3.53 ± 3.57	0.510	0.611
Stress*(Mean ± SD)*	505	4.95 ± 4.45	4.81 ± 4.46	0.300	0.764
PCS *(Mean ± SD)*	505	52.34 ± 5.44	51.53 ± 6.81	1.329	0.184
MCS *(Mean ± SD)*	505	50.76 ± 8.57	50.33 ± 9.10	0.466	0.641

*$p < 0.05$.

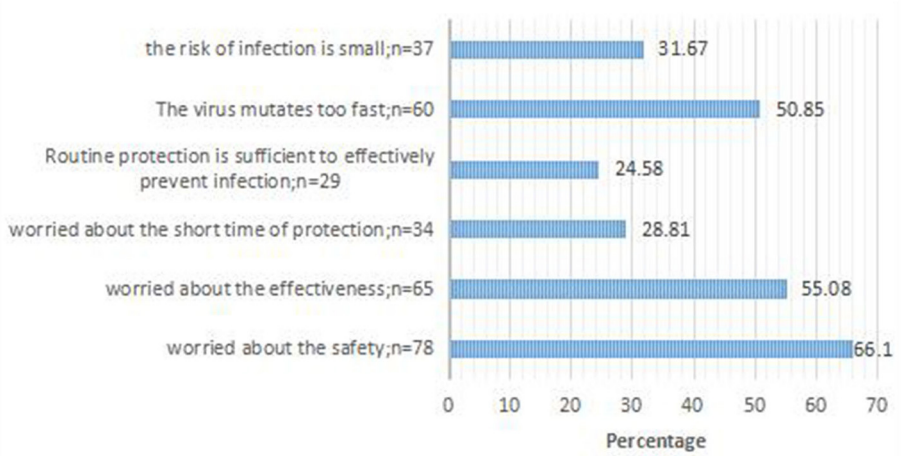

FIGURE 1 | Reason for COVID-19 vaccine hesitancy; response for 118 participants who said they would refuse the COVID-19 vaccine.

In our study, three quarters of HCWs were willing to be vaccinated. The vaccination acceptance rate was higher compared to the similar studies conducted in Saudi Arabia and U.S (10). But the remarkable thing is we conducted our research in Chengdu while the other studies conducted in the whole country. In this study, only a quarter of respondents refused the COVID-19 vaccine. The major obstacles to accepting vaccination were concerns about side effects, the efficacy of the vaccine, and the potential for mutation of the virus, which were similar to the concerns raised in previous studies (31). These concerns are not surprising given the rapidity of vaccine development and its protective efficacy is still uncertain. Hence, public health intervention programs that focus on increasing the perception of the benefits of vaccination are needed. It is more important to improve the effectiveness and safety of the vaccine during the manufacturing process. We also found that some individuals who were not willing to vaccinate expressed optimism about the epidemic. This may have been a result of the effective control of the COVD-19 outbreak in our country. During the outbreak of the epidemic, Karaoke Television (KTV), bars, movie venues, and other businesses were closed, crowds were prohibited, workers were encouraged to hold online meetings, all individuals were required to reduce visits to relatives and friends during the Spring Festival, and were required to wear a facemask outdoors. This study did not take into consideration the cost of vaccination as a variable in the statistical analysis, because vaccines were freely available in China (32). In addition, the number of injections was not included in the analysis in this study because vaccines both nationally and abroad currently require two injections (33). Nonetheless, there may be additional reasons for an individual's refusal to vaccinate, which warrant future investigation.

Our study indicated that having more comprehensive knowledge about the vaccine might have contributed to them being more willing to accept the vaccine compared to those who had less information about the vaccine's properties. This suggested that greater education efforts about the vaccine should be considered to increase public confidence in vaccination. Additionally, our analysis also found that those who perceived themselves to be at risk for COVID-19 infection were more likely to accept the vaccine. Shekhar et al. (10) also reported similar findings in their HCWs population survey for COVID-19 vaccine uptake. Further, our study revealed that living with elderly individuals were associated with stronger intention to be vaccinated against COVID-19 though other studies have not included this factor. It is well-known that elderly individuals are more vulnerable to infectious diseases because of the considerable decline in the number of T-cells, which play an important role in identifying and reacting continuously to growing pathogens such as viral infections (34) which may have led staff members who are living with elderly individuals to accept the vaccine more readily in order not to transmit the virus to their family members. In addition, it is important to highlight that who had received flu vaccination in 2020 was a significant predictor of a definite willingness to be vaccinated for COVID-19 vaccination,as also suggested by Ameerah et al. (13).This may be in part due to the fact that they had already benefited from the experience of being vaccinated, and were also more likely to be more knowledgeable about the vaccine than others, and thus had a better understanding of its safety and side effects. We also found that those with a bachelor's degree were more likely to accept the vaccine compared to those with a Junior/senior school degree and those who thought the COVID-19 had severe effect on their lives were less likely to receive the vaccine than those who thought it had no effect, but it should be noted that there is a big difference in numbers between the two groups which could generate statistical error.

While prior work has explored the demographic and social underpinnings of decisions to receive a COVID-19 (6–8, 10, 13), little is known about how the physical and mental health state of people are associated with this choice. In fact, there have been some studies on the psychology of flu vaccination and those studies found that a sense of fear\conspiratorial thinking were

TABLE 2 | Multivariable logistic regression analyses showing factors associated with acceptance of a COVID-19 vaccine ($n = 505$).

Variables	OR	95% CI	*p*-value
Sex			
Male*(R)*	1		
Female	0.761	0.398–1.457	0.410
Age *(Mean ± SD)*	0.977	0.940–1.016	0.241
Occupation			
Clinician*(R)*	1		
Nurse	0.472	0.070–3.192	0.442
Administrative staff	0.270	0.040–1.804	0.177
Others	0.858	0.052–14.267	0.915
Education			
Junior/senior school*(R)*	1		
Bachelor	3.699	0.511–26.750	0.195
Postgraduate	2.353	1.135–4.880	0.021*
Marital status			
Married *(R)*	1		
Single	1.442	0.637–3.265	0.380
Children			
Yes*(R)*	1		
No	0.506	0.207–1.233	0.134
Living with elderly individuals			
No*(R)*	1		
Yes	1.928	1.074–3.462	0.028*
Flu vaccination in 2020			
No*(R)*	1		
Yes	4.730	2.285–9.794	0.000*
Worried about experiencing COVID-19			
No*(R)* Yes	1		
	1.987	1.197–3.298	0.008*
Understanding of the vaccine			
No*(R)*	1		
Yes	2.322	1.355–3.979	0.002*
Effect of COVID-19			
Not at all*(R)*	1		
Mild	0.834	0.276–2.523	0.748
Moderate	0.591	0.193–1.812	0.358
Severe	0.277	0.084–0.913	0.035*
GHQ score			
<3*(R)*	1		
≥3	1.712	0.640–4.581	0.284
MBTI (I/E)			
Extroversion*(R)*	1		
Introversion	1.159	0.706–1.902	0.560
MBTI (T/F)			
Thinking*(R)*	1		
Feeling	0.848	0.524–1.374	0.504
Depression	0.988	0.880–1.110	0.840
Anxiety	1.020	0.897–1.160	0.764
Stress	1.028	0.923–1.145	0.611
PCS	1.041	0.996–1.087	0.074
MCS	1.009	0.978–1.041	0.580

associated with vaccination (35, 36).In this study, we included in the questionnaire international scales to value general health state and personality of HCWs and we found that personality and physical and mental health status did not differ significantly between those willing to be vaccinated and those who were not. This indicated that the attitude toward vaccines is rational. If there is sufficient evidence provided to prove the effectiveness and safety of the vaccine, it is believed that the number of people willing to be vaccinated will increase significantly. This approach will help the government to successfully implement the prevention and control measures of COVID-19 and lay the foundation for the establishment of herd immunity.

A major strength of our study is that this study is the first study evaluating the acceptance of a COVID-19 vaccine among HCWs in China. In addition, we evaluated general health state and personality of responders to investigate if their physical and mental health state and personality would influence their hesitance to vaccination. These results indicated that the attitude toward vaccines is rational.

This study has a few limitations. First, our study employed an electronic questionnaire to collect data instead of a face-to-face questionnaire and is on a voluntary basis, resulting in sampling bias and uncontrolled conditions during the completion of the questionnaire. Moreover, the sample size was relatively small, thus the results should be considered preliminary and descriptive. Another limitation is that this study was conducted at a specific timepoint during the pandemic, and the results will likely change given the control of the spread of the virus and the development of a vaccine. Thus, further follow-up studies using qualitative and quantitative methods are necessary. Future studies will investigate whether and how propaganda and education can help HCWs to reduce their concerns about the vaccine. Furthermore, future studies should follow-up with the antibody test results of the HCWs who received the vaccine, and the protective effect of the vaccine.

CONCLUSIONS

During the vaccination period, there was still hesitation in receiving the vaccine and specific concerns regarding COVID-19 vaccine are prevalent. In addition, willingness to be vaccinated was significantly associated with a better understanding of the vaccine's properties, perceived risk of COVID-19, prior flu vaccination in 2020, and living with elderly individuals. This study will help the government to better understand the social issues surrounding willingness for vaccination, and will improve publicity and education programs concerning the vaccine. In addition, the findings can provide a rationale for the design of future vaccination campaigns.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

This study was approved by the Ethics Committee of Third People's Hospital of Chengdu, and all responders provided written informed consent before participating in this study.

AUTHOR CONTRIBUTIONS

YS, TX, XC, and MC conceived and designed the questionnaire. TX, XC, PW, and JZ recruited participants. YS, TX, and HD analyzed the data. YS wrote and revised the paper. All the authors have approved the manuscript and agreed with submission to your esteemed journal.

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"Live and Let Die": What We Learned From US Healthcare and What Seems to Be Valid in the COVID-19 Pandemic

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In 2020, the USA experienced an extreme situation in which medical professionals had to answer essential medical ethics questions regarding rationing and prioritization. In Germany and Switzerland, the vast majority of people, with or without work, are covered by health insurance, especially in the less affluent classes. Scenes like those in New York toward the end of April, where seriously ill people were being turned away from hospitals, were completely unimaginable. European medicine has learnt a great deal from its US counterpart: both the modern US hospital system and the basic assumptions of US medical ethics have been copied on the other side of the Atlantic. The pandemic shows that US medicine not only has to suspend ethical principles due to the particular situation (e.g., triage) but that some ethical principles can hardly be observed in other situations, as the healthcare system hardly allows this.

During one of its peaks in the ongoing COVID-19 pandemic, for instance in New York City, the wide gulf between the ideals of US medical ethics and the reality of the enormous disparities in the US health system became obvious to a worldwide audience. This has been the case for not only medical ethics but also the US hospital system, which for decades has set the tone worldwide. What do US medical ethics and US hospital construction concretely offer that would help in the context of this pandemic and of a wider future in the sense of enfolding something that is already a prominent part of the US health system? When US President Donald Trump visited a mask factory in Arizona on May 5, 2020, the public relations department selected the song "Live and Let Die" by the band Guns N' Roses as the background music (1). It does not refer to the ethical measures of rationing and prioritization that are currently prevalent in the US healthcare system when we look at the global significance of American medical ethics and the US hospital system in recent decades.

In 2020, most parts of the world experienced an extreme situation in which medical professionals had to answer essential medical ethics questions regarding rationing and prioritization. Some countries, such as Germany, Switzerland, and the USA, had a medically favorable starting position when the pandemic began. Medical supplies and hospital equipment were in such good order that rationing and prioritization in connection with the pandemic has so far only occurred in rare cases (2). However, there was a considerable difference between those countries. Meanwhile we heard about a lot of patients who could not be treated due to a lack of health insurance coverage (3). At present, it is precisely the southern states that are affected, where many people do not have insurance (4, 5). Elsewhere, this situation is impossible: for instance, in Germany and Switzerland, the vast majority of people, with or without work, are covered by health insurance, especially in the less affluent classes. Scenes like those in New York toward the end of April, where seriously ill people were being turned away from hospitals, were completely unimaginable. It was incomprehensible to think that this could happen in the USA, a country that has always set an example to those of us who work, research, and teach as medical ethicists and historians (6). But it should come as no surprise,

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because the reality is this problem has always existed in the US healthcare system, but now it has become more apparent in the context of the pandemic. The contradiction with medical ethics is also more apparent here, as it has now become clear to the entire world for the first time.

More than 40 years ago, two US medical ethicists, Beauchamp and Childress (7), first published their four principles under the title *Principles of Biomedical Ethics*. Both probably taught the four basic assumptions to their students in such a prayer-mill-like canon that they called it the "Georgetown Mantra": respect for *autonomy*, *non-maleficence*, *beneficence*, and *justice*. The Georgetown Mantra became the most influential text for the development of the discipline of medical ethics, not only in the USA, but also around the world. In recent years, research in ethics has been searching for answers to this question of humane healthcare with the help of the Georgetown Mantra: can the patient maintain self-determination in the absence of health insurance coverage, especially in times of a pandemic? How do I come to a decision in a triage situation? Do I fulfill my duty of care as a hospital employee? Do I not harm the patient? Is there social justice in answering a medical–ethical dilemma? In most university hospitals, this mantra is an integral part of medical education. However, also many current examples from the USA show medical ethicists from Europe that US medicine in particular is finding it difficult at present to recognize two of the most widely replicated principles developed at Georgetown University. In the following, we would like to explain some current examples based on the mantra:

- *Beneficence*: At the beginning of the 20th century, medical awareness in the USA grew for a holistic treatment of diseases and especially for a functional optimization of inpatient facilities for diagnostics and care (8). This required adequate structures within the hospital. Closer cooperation of physicians within one hospital was the only logical solution. In Rochester (Minnesota), William Worrall Mayo was the first to establish a large community hospital where numerous specialists could work together under one roof. Doctors should become team workers and no longer be individual rulers in their specialist clinics. The new Mayo Clinic, opened in 1914, received worldwide attention (9). Several architects oriented themselves to the coordinated diagnostic and therapeutic processes in this clinic. The Mayo Clinic not only revolutionized the US hospital system, but it also became an export hit.

  The system was adopted in Europe, even though it took time to be established: in 1958, the US architect Arthur Q. Davis was only able to achieve the first prototypical (public) hospital building in accordance with the Mayo system in West Berlin thanks to the idealistic and financial support of the US State Department (10). Until the opening of the new Berlin Medical Center 50 years ago in 1969, German chief physicians had never known "teamwork" carried out on such a scale (10). And again, a US model of *beneficence* was adapted in Europe and began its triumphal march.
- *Justice:* The question of social justice, which in the Georgetown Mantra is actually the central fourth element of any basic medical–ethical consideration, (11) had to be completely ignored, particularly in the USA: Beauchamp and Childress' principle demands fair distribution of healthcare administration, capacities, and resources; that is, equal cases should be treated equally. Some COVID-19 patients in the USA often have poor or no health insurance coverage, and a large proportion of them belong to a less affluent class (4, 5). This is despite the fact that intensive care unit (ICU) bed capacity in the USA at 29.7 (12) [like Germany's at 38.7 (13)] is one of the highest per-capita numbers in the world, far more than many other European countries (Sweden at 5.8 and the UK at 6.6) (14).

  In Sweden, in principle, every resident is covered by state health insurance through income tax; even people who do not pay taxes, however, are entitled to medical care (15). In the UK, everyone who is a resident is automatically insured through the National Health Service (NHS). There are no health insurance contributions there. Everyone who does not work is also insured as long as they are registered as a resident. Public healthcare for the entire population is financed by taxpayers' money (doctors and nurses are directly employed by the NHS), so that almost all medical services are free of charge for all residents (except drugs and dental services) (16).

  In Germany, every employer must pay regular contributions to health insurance companies based on income (there are standard legal insurance and private insurance with better benefits for self-employed or people with higher income). These health insurances then reimburse services that are insured in the event of illness. Unemployed persons are insured through the employment office. There is an insurance obligation. Uninsured people exist but are fairly rare (17).
- *Non-maleficence*: When US President Trump visited that mask factory in Arizona, "Live and Let Die," which many found cynical in view of the simultaneous situation in many US states, can also be seen as a metaphor for a current medical–ethical question. For years, in almost all countries of the world, medical ethics has been discussing the questions of rationing and prioritization in the face of scarcity of funds in the healthcare system (18).
- *Autonomy*: There would certainly be other examples to show that basic principles of medical ethics according to Beauchamp and Childress cannot be fulfilled in the USA at present: the fact that ventilation was initially applied in such a way that no critical perspective of the negative consequences was considered contradicts this approach. There might also be COVID-19 patients who prefer palliative therapy.

European medicine has learnt a great deal from its US counterpart: both the modern US hospital system and the basic assumptions of US medical ethics have been copied on the other side of the Atlantic. Both Beauchamp and Childress as well as Franklin, Mayo, and Davis were not only pioneers for the healthcare system in the USA but have had far-reaching significance in the history of hospitals and ethics of medicine in Europe to this day.

But at this point, an appeal should be made again based on the ongoing experience of the COVID-19 pandemic for a fair hospital system closely following Franklin's and Mayo's models and the ideas in the Georgetown Mantra.

The normal ethical principles are replaced by triage. The pandemic shows that US medicine not only has to suspend ethical principles due to the particular situation (e.g., triage) but that some ethical principles can hardly be observed in other situations, as the healthcare system hardly allows this. With this text, we want to launch a discussion as to why so many achievements, which were once established by US university ethics and which are taught worldwide in order to make even better use of the achievements of the US hospital system, have fallen into oblivion in the USA today.

AUTHOR CONTRIBUTIONS

AJ focused on the history and hospital system and MW on the ethical assessment.

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Ethical Considerations for Unblinding and Vaccinating COVID-19 Vaccine Trial Placebo Group Participants

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INTRODUCTION

The Pfizer-BioNTech, Moderna, and Johnson & Johnson COVID-19 vaccinations have been approved under "Emergency Use Authorization" by the United States Food and Drug Administration (FDA). Other vaccines, such as the Sputnik V and AstraZeneca vaccines, have begun to be distributed in other nations around the world after the publication of promising efficacy results. Multiple more vaccine candidates are likely to follow, which will still require safety and efficacy testing. As vaccines have been distributed in a tiered fashion to the public, there has been discussion and disagreement regarding the matter of vaccination of placebo groups from the past or upcoming trials (1). It has been argued that only trial participants (placebo group) who would be otherwise offered the vaccine outside of the trial [i.e., high risk participants or healthcare workers (HCWs)] should be unblinded and given the vaccine, while all other participants should remain blinded (2, 3). We argue that, once proven efficacious, vaccine makers and researchers have an ethical obligation to unblind the placebo groups of COVID-19 vaccine trials and offer them vaccine, based on the four principles of medical ethics.

NON-MALEFICENCE AND AUTONOMY

The first two principles to consider are non-maleficence and autonomy. The blinded placebo group is at increased risk of COVID-19 due to two main factors: participant behavior changes and the accelerated spread and morbidity of COVID-19. The first factor is related to non-maleficence, while the second invokes the principle of autonomy. Non-maleficence, or the obligation to not cause harm, must be considered, as keeping placebo groups blinded may put them at a higher risk of harm. As part of a blinded study, participants were likely informed that they should maintain all of the same safety precautions as if they are not vaccinated. However, participants who received placebo may change their behavior, either intentionally or unintentionally, and relax precautions as a result of the published efficacy results of the vaccines. This issue could be further compounded by the constantly changing guidelines for vaccinated and unvaccinated persons by federal agencies such as the US Centers for Disease Control and Prevention (CDC) and a lack of additional guidance from trial investigators. Previous research has demonstrated that humans change their short-term behavior to interact with more people after receiving a vaccine that is known to be effective (4). It was found that in the 48 h after receiving a flu vaccine, the average number of people with which study participants interacted doubled in comparison to their interactions in the previous 48 h. While the authors speculate that this effect may be due to viral antigen exposure, they also hypothesize that it could be due to the feeling

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of protection or invincibility elicited by vaccination. As an additional concerning factor, the development of virus variants in certain parts of the world with more aggressive transmissibility has further increased the potential harm of remaining unvaccinated (5). Thus, false reassurance and change of behavior could theoretically put placebo participants, who believe they were vaccinated, at a higher risk for contracting COVID-19, a harm which could be mitigated by unblinding them.

Second, the placebo group agreed to some risk when they consented to their involvement in the study. This is in accordance with the principle of autonomy, which requires that patients should fully understand the risks and benefits of any procedure prior to consent. It can be ethically acceptable to allow research participants to experience some risks in order to collect scientific or socially valuable data, even once a vaccine has been proven effective (1). However, in this case of the approved vaccines, the potential of this data collection is not more valuable than the risk to participants (i.e., acquiring COVID-19 infection and potentially death) and the public (i.e., an individual becomes a carrier and passes the virus to others) if participants are kept blinded. The risk of being unvaccinated has increased significantly since trials began: the spread of COVID-19 has overwhelmed the healthcare systems of many countries, the true morbidity of the virus has become more apparent, and increasingly transmissible variants have emerged. Therefore, the level of risk to which the participants originally agreed no longer applies, and the prior assessment of the incurred risks is no longer valid. Therefore, keeping the placebo group unblinded does not respect the principle of non-maleficence nor autonomy.

BENEFICENCE AND JUSTICE

The second set of principles to consider is beneficence and justice. The primary arguments for keeping the placebo group blinded include the ongoing collection of research data and public health gains, which draw upon beneficence, providing a treatment with the intention of doing good, and justice, the obligation for fair distribution of a treatment. We argue that vaccinating current placebo groups and strategically planning future trials can respect both principles to a greater extent.

The collection of long-term safety data is of paramount importance to ensure the safety and efficacy of the vaccines. However, there are already risks to the validity of ongoing data collection if trials continue as planned now that the efficacy data has been made public (6). Participants are beginning to drop out of trials if their status is not revealed, if they are antibody-negative, and/or they have the potential to be vaccinated through other means (7, 8). High-risk patients who do become eligible through other sources are likely to leave first, which could bias long-term safety and efficacy results. Investigators are also ethically bound by "Good Clinical Practice" guidelines to inform trial participants about information that may change their willingness to participate in the trial, that is, the published efficacy results and the availability of vaccine to the general public, which may lead to further drop-out rates (9). By being offered a vaccine when provided with this information, placebo participants would be more likely to remain enrolled in a trial, and additional long-term data could be collected by monitoring them for 1–2 years after they receive the vaccine. There would now be different cohorts of participants that received a vaccine at different times of year with exposure to virus variants, which may be able to provide helpful information about vaccine efficacy. There are multiple options available to continue to collect valuable research data in current trials while allowing placebo group vaccination, including conducting an "intent-to-continue" subgroup analysis, or adjusting to a crossover or open label design (2, 9). In addition, there may be an opportunity to recruit individuals who do not want to receive vaccine as a placebo group. While this will not allow for a true blinded and randomized comparison, it may still be possible to accrue valuable long-term data about vaccine efficacy through these suggested changes. In addition, other designs could be considered for new studies to be conducted in parallel, such as non-inferiority trials or human challenge trials (10). Vaccinating the placebo group maximizes individual and societal benefit, as it directly benefits the participants who receive vaccine and indirectly benefits the general population by keeping participants engaged in the trial and allowing for longer-term data collection even after vaccines have been preliminarily proved to be efficacious.

The second concern regarding public health gains appeals to both beneficence and justice, as it is argued that vaccine should be allocated in a tiered system in order of greatest need, which will overall improve public health. Those against vaccinating placebo groups have stated that vaccinating placebo group individuals (who are not front-line HCWs, elderly or individuals with comorbidities) would reduce public health gains (2). We agree that HCWs should be prioritized first in situations where there is a scarcity of vaccine. However, many countries have already been able to vaccinate most HCWs and are moving on to other tiers of distribution. Moreover, many individuals (both HCWs and members of the general public) do not intend to get the vaccine, and vaccine is at risk of going to waste (11, 12). In countries where vaccine is not yet available to the general public, we believe that the placebo group should be given priority in the next tier of vaccine distribution, above their respective risk group in the general population. In early 2021, both Pfizer and Moderna began to offer participants the option to become unblinded and receive the vaccine (13, 14). By vaccinating placebo groups publicly, we could further improve perception of vaccination in the public eye, which may potentially lead to greater vaccine acceptance and improved public health gains.

Undoubtedly, placebo groups are an important tool in evidence-based medicine. In certain circumstances, it may still be ethical to use a placebo group in COVID-19 vaccine trials. An expert group assembled by the World Health Organization (WHO) identified characteristics that establish when the use of a placebo group at the onset of a vaccine is acceptable (i.e., when no safe vaccine is available, and the vaccine will benefit the population in which it will be tested) and when it is not (i.e., when a safe and effective vaccine exists and is currently available, and risks to participants of delaying the vaccine cannot be mitigated) (15). In the case of COVID-19 vaccine trials, there

is an opportunity to continue to run randomized controlled trials (RCTs) with placebo groups while simultaneously increasing the overall number of vaccinated persons by planning and executing vaccine trials in low- and middle-income countries (LMICs) that currently have limited or no vaccine access. Many LMICs have had limited access to currently approved COVID-19 vaccines, both due to cost and a lack of appropriate infrastructure to store and distribute vaccines (16, 17). By focusing on expanding trials of approved vaccines and experimental vaccines to LMICs, vaccine manufacturers and researchers will still be able to collect valuable data while providing the most good for the largest number of people. There are important ethical considerations to address while running vaccine trials in LMICs, namely ensuring that the placebo group is truly justified in that context and that local stakeholders are involved (15). As long as these issues are appropriately addressed, COVID-19 vaccine trials in LMICs may be conducted in accordance with the principles of both beneficence and justice.

CONCLUSIONS

As COVID-19 vaccine trials continue and efficacy results are published, it will become increasingly more difficult and ethically fraught to maintain a valid placebo group, especially in high-income countries. By unblinding and vaccinating placebo participants regardless of distribution tier, researchers have the opportunity to address all four of the primary bioethical principles: beneficence, non-maleficence, autonomy, and justice. Consequently, the need for placebo groups may be satisfied in future trials in LMICs, which will allow for additional gains in the pursuit of beneficence, justice, and health for all.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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REVIEW
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Appraisal of China's Response to the Outbreak of COVID-19 in Comparison With SARS

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Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2, was first reported in Wuhan, China, in December 2019 and has since become a pandemic. The COVID-19 containment measures were comparable to those used with severe acute respiratory syndrome (SARS), although these were stricter and more organized, and were initiated earlier and on a larger scale. Based on the lessons learned from SARS, the Chinese government acted aggressively in response to COVID-19, through a unified and effective commanding system, using law-based and science-driven strategies, and coordinated deployment of medical resources. Additionally, the application of high-tech measures, traditional Chinese medicine, and hierarchical medical systems also played an important role in control measures. Despite the remarkable performance, the initial delay in response suggests that the coordination between public health and medical services, reserve and coordination of emergency materials, and capacity for disease control and prevention need to be strengthened.

Keywords: infectious disease control, COVID-19, SARS, control measures, outbreak

INTRODUCTION

In December 2019, a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), emerged in Wuhan, China. By December 21, 2020, the number of COVID-19 cases worldwide reached 75,704,857 with 1,690,061 deaths.

As the first country affected by COVID-19, local outbreaks have been largely contained in mainland China. The prompt and decisive response to COVID-19 in China was hailed as an extraordinary achievement by the World Health Organization (WHO) and "bought time" for the development of an effective vaccine and implementation of other measures in response to COVID-19 (1). Dr. Tedros praised China for its transparency, data sharing, and quick response (2).

Adopting a similar approach as the response to SARS, COVID-19 was mainly contained through traditional public health interventions, such as case detection and isolation, close contact tracing and quarantining, social distancing, screening of travelers, implementation of infection prevention guidelines, and enhanced infection control in healthcare settings. In contrast to SARS, the total

number of COVID-19 cases is much higher due to the inherent difficulties in identifying and counting mild and asymptomatic cases (3). The objective of this review is to explore how China has responded to the challenges presented by COVID-19 and what new lessons have been learned from the COVID-19 response.

METHOD

We based our review on reports (international and domestic), official documents, and published work. We searched the Web of Science, PubMed, and China Knowledge Resource Integrated Database for articles, books, and reports published from 2003 onwards. In addition, official websites of the Chinese government, National Health commission of China, and Chinese Centre for Disease Control and Prevention (CDC) were searched for information, official documents, and guidelines. The Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) and other information issued by the WHO served as additional sources. We restricted our search to works published in English or Chinese and used the following search terms: "control measures," "containment measures," "public health measures," "response," "SARS," "COVID-19 or 2019-nCOV," "China," and combinations of these terms. The date of the last search was February 25, 2021. Moreover, a book published by the Chinese CDC in 2003, "Compilation of literature on prevention and control technology and integrated management of SARS," provided evidence regarding important moments during the SARS epidemic.

RESULTS

Table 1 summarize the timeline of outbreaks and control measures implemented during the outbreaks of SARS and COVID-19 in mainland China. This shows that although similar containment measures were applied during the two outbreaks, these were initiated at a later stage and on a smaller scale during the SARS outbreak. **Figures 1**, **2** more intuitively show the difference in response speed between COVID-19 and SARS. During the SARS outbreak, state-level control measures were not implemented until February 2003. It was only after a second outbreak in Beijing in April 2003 that a nationwide response began. In stark contrast, the Chinese government initiated large-scale and forceful control measures within 2 months of the COVID-19 epidemic. The following six control categories were analyzed to explore what had changed since the 2003 SARS outbreak, and how exactly have these changes had an effect with respect to the response to COVID-19, regardless of whether these changes were an improvement or setback.

Abbreviations: COVID-19, coronavirus disease 2019; WHO, World Health Organization; SARS, severe acute respiratory syndrome; JPCM, Joint Prevention and Control Mechanism; MOH, Ministry of Health; NHC, National Health Commission; HCWs, health care workers; AI, artificial intelligence; TCM, traditional Chinese medicine; SHI, Social Health Insurance; NHSA, National Healthcare Security Administration.

Organizational and Administrative Measures

Joint Prevention and Control Mechanism

A unified and effective command system is a prerequisite for the effective and orderly implementation of prevention and control measures (4). In response to the SARS and COVID-19 outbreaks, the Chinese central government set up task forces to coordinate national infection control efforts, although response timelines varied widely. The national "SARS control and prevention headquarters" was set up only when the outbreak affected Beijing (5), by which time the infection had spread to 26 provinces in China (6). The lack of coordination in the early stages of the SARS outbreak led to extensive spread. Based on the earlier experience of SARS outbreak, as soon as human-to-human transmission was identified, the State Council established a Joint Prevention and Control Mechanism (JPCM) composed of 32 ministries (7). A central leading group on epidemic response and a central steering group stationed in Wuhan were established on January 25, 2020, with Prime Minister Li Keqiang as the leader and Vice-Premier Sun Chunlan as the frontline leader. Furthermore, President Xi Jinping personally presided over China's epidemic response to COVID-19, which greatly increased the commitment of and leadership from the government to respond to public health emergencies (1).

Emergency Response

During the SARS outbreak, China had no legal mechanism to directly oversee public health emergencies (8). On May 12, 2003, the State Council promulgated the "Regulations on Public Health Emergencies," which stipulates the responsibilities that governments at all levels and medical institutions should assume at various stages of public health emergencies (9). In 2006, the government issued the "National General Guideline on Public Health Emergencies" to standardize the process of dealing with public health emergencies, which divided the public health emergencies into four levels (10). In accordance with the above laws, the Chinese CDC initiated Level 2 and Level 1 emergency responses on January 6 and January 15, respectively (11). As of January 25, 2020, 30 provinces in mainland China initiated a Level 1 emergency response (7), meaning the Stata Council has unified command of emergency response.

Notifiable Infectious Disease Management

Both SARS and COVID-19 were added to the list of notifiable infectious diseases. While SARS took nearly 5 months to be considered a statutory infectious disease, COVID-19 was defined as a Class B notifiable disease in 43 days (12); Subsequently, it was managed as a Class A infectious disease. This means that SARS and COVID-19 were required to be managed using the prevention and control measures of Class A infectious diseases, such as mandatory reporting and isolation of confirmed and suspected cases (13). COVID-19 was also defined as a quarantinable communicable disease to control international spread (14).

TABLE 1 | Summary of the main control measures implemented during SARS and COVID-19, by date of onset (if available).

	COVID-19	SARS
Date of onset	8 December 2019	16 November 2002
Number of cases reported	90.655 (Mainland, by 29 April 2021)[a]	5.327 in mainland China
Control measures	**Days since onset (Date)**	**Days since onset (Date)**
Organizational and administrative measures		
Joint prevention and control mechanism	44 days (21 January 2020)	N/A
Joint leading group	48 days (25 January 2020)	158 days (25 April 2003)
Emergency response	Level 2: 29 days (6 January 2020) Level 1: 38 days (15 January 2020)	N/A
Notifiable infectious disease management	43 days (January 20, 2020)	143 days (8 April 2003)
Reporting		
Public notification	23 days (31 December 2019)	138 days (3 April 2003); Guangdong-86 days (10 February 2003)
Mandatory reporting	43 days (20 January 2020)	143 days (8 April 2003); Guangdong−79 days (3 February 2003)
Notifying the WHO	26 days (3 January 2020)	87 days (11 February 2003)
Case detection and contact tracing		
Blocking transmission	24 days (1 January 2020)	N/A
Protocol for diagnosis and treatment	38 days (15 January 2020)	149 days (14 April 2003); Guangdong-68 days (23 January 2003)
Rapid detection technology	27 days (4 January 2020)	151 days (16 April 2003)
Case detection and isolation	43 days (20 January 2020)	143 days (8 April 2003); Guangdong 77 days (1–3 February 2003)
Contact tracing and quarantine	38 days (15 January 2020)	
Contact tracing		Guangdong- 77 days (early February 2003); Beijing-144 days (9 April 2003)
Quarantine		Guangdong- 131 days (27 March 2003); Beijing 156 days (21 April 2003)
Travel-related measures		
Travel restrictions	46 days (23 January 2020)	N/A
Entrance and exit screening	43 days (20 January 2020)	157 days (22 April 2003)
Community containment measures		
Decreasing social interaction	49 days (26 January 2020)	158 days (23 April 2003)
Community access control	49 days (26 January 2020)	Only in very few communities
Hospital containment measures		
Strict infection control	57 days (3 February 2020)	169 days (4 May 2003)
Establishing separate triage facilities		
Triage in CHCs or Fever Clinics	47days (24 January 2020)	152 days (17 April 2003)
Designated hospital	43 days (20 January 2020)	156 days (21 April 2003)[b]
New hospital	Huoshenshan 58 days (4 February 2020) Leishenshan 62 days (8 February 2020)	Xiaotangshan 166 days (1 May 2003)
Makeshift hospitals	59 days (5 February 2020)	N/A

[a] *Data from the website of National Health commission of China: http://www.nhc.gov.cn/xcs/yqtb/202104/80fb5915f82049f4abf53293804382a2.shtml. (accessed April 30, 2021).*
[b] *http://news.sina.com.cn/c/2003-04-21/20201008906.shtml.*

Reporting

Public Notification

On February 10, 2003, the Guangdong Ministry of Health (MOH) held a press conference to announce an outbreak of atypical pneumonia (6, 15). This took place 87 days after the first identified case of SARS and, at this point, 218 cases had been detected in Guangdong (6). Prior to this and for the month following the announcement, the SARS epidemic went largely unnoticed, likely resulting in many avoidable cases (16)[1]. Based on earlier experience and more recent advances in the public health system, on December 31, 2019, 27 cases of pneumonia of unknown etiology were publicly reported by the Wuhan NHC for the first time (3). Notification of the COVID-19 outbreak to the public, which occurred ∼23 days from the COVID-19 onset, occurred more rapidly than in the earlier SARS outbreak. Official daily disease information was released on January 21, 2020. The JPCM held a daily press conference to share the latest news with the public from January 27 (7).

Mandatory Reporting

In China's Guangdong Province, reporting of cases of atypical pneumonia using a standard case definition and reporting form became mandatory from February 3, 2003 (17). At the beginning of the spread of SARS, due to the lack of transparent reporting system, information regarding the outbreak was not clear; it took

[1] Summary of SARS prevention and control work[EB/OL] http://www.gov.cn/test/2005-06/28/content_10716.htm.

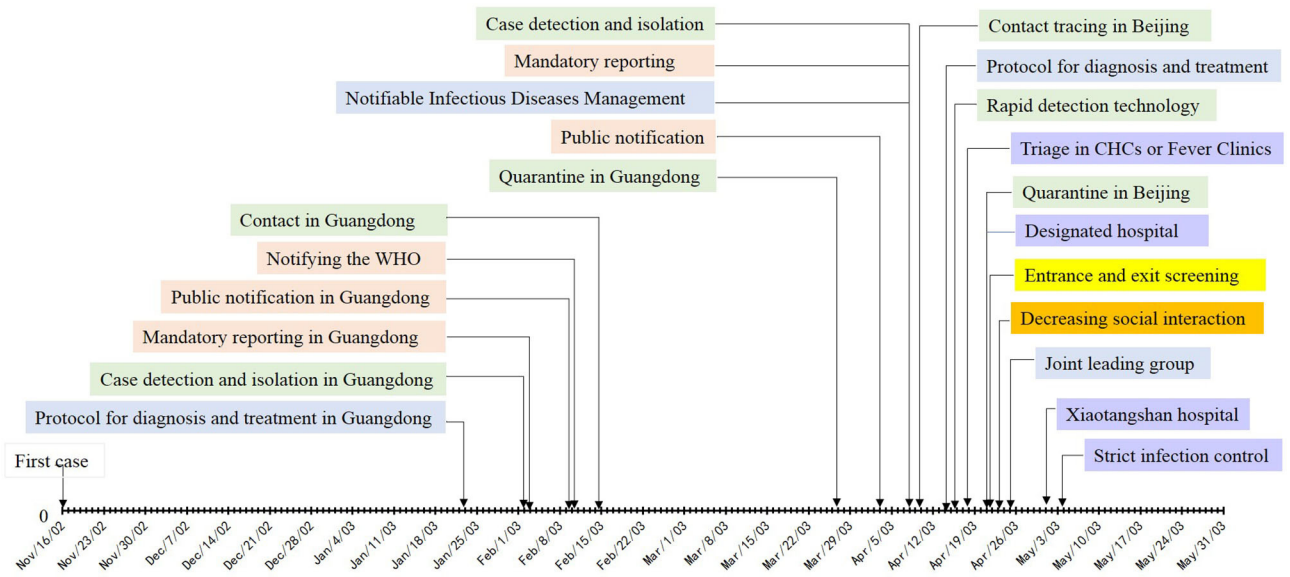

FIGURE 1 | Timeline of control measures implemented in SARS.

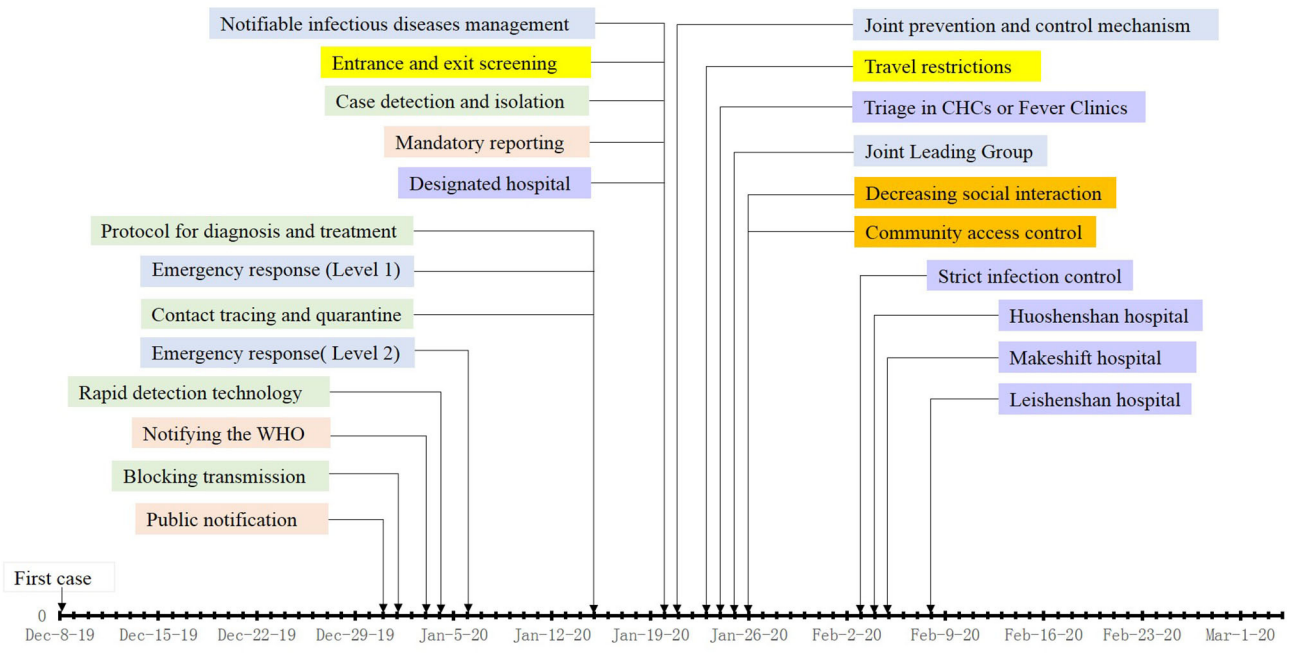

FIGURE 2 | Timeline of control measures implemented in COVID-19.

8–9 days for a detected case to be reported and 3–4 days for a hospitalized case to be reported, seriously affecting the ability to implement timely control measures (18). After SARS was included in the statutory report of infectious diseases on April 8, 2003, health authorities in all provinces were required to collect and report all probable cases and deaths using a standardized case report form (19). To avoid previous errors, the Reporting Regulations for Public Health Emergencies and Communicable Diseases Surveillance was issued in November 2003, clearly set out the required information and time limits for the reporting of infectious disease outbreaks and epidemics (20). Mandatory reporting of COVID-19 has been in place since the introduction of notifiable infectious disease management in January 20, 2020 (21). This involves reporting of all suspected cases, confirmed

cases, and asymptomatic infected individuals *via* a web-based reporting system within 2 h of diagnosis. Violating reporting rules or concealing information is punishable according to law (22).

Notifying the WHO

The MOH and CDC notified the WHO about the SARS outbreak on February 11, 2003, 3 months after the first case was reported, when 300 cases and five deaths had already occurred (3). One month later in March 12, 2003, when the number of cases reached ∼800 in mainland China (23), the WHO issued global alerts (4, 23). The WHO was notified of COVID-19 on January 3, 2020 (24). At this point, there were only 27 known cases and zero deaths (3). The WHO shared the detailed information and issued a Disease Outbreak News report on January 5, and then declared COVID-19 a Public Health Emergency of International Concern on January 30, 2020. The WHO expressed its satisfaction with the swift and effective information sharing by China (25) as this greatly helped in coordinating international resources to address emerging problems.

Case Detection and Contact Tracing

Controlling Sources of Infection

On January 1, 2020, the government shut down the probable infection source, Huanan Seafood Wholesale Market, as links between infected individuals and the market were found in most of the 41 laboratory-confirmed cases (3, 26). The 4Es, consisting of early detection, early reporting, early isolation, and early treatment, were subsequently implemented nationwide and greatly contributed to controlling the spread of disease (7). In contrast, the palm civet was not removed from the markets until it was identified as a reservoir in the SARS outbreak (26).

Case Detection and Isolation

Case detection and isolation is an effective measure to limit community transmission of infectious disease. By April 16, 5 months after the first case was identified, rapid detection technology had been developed that could provide results within 2 h of testing. Due to the lack of accurate guidelines and detection technology in the early stage of the SARS epidemic, 709 cases occurred in healthcare workers (HCWs) (19). Following significant progress, on 4 January 2020, 4 days after isolating the virus specimen, the Chinese CDC successfully developed polymerase chain reaction diagnostic reagents that were used for the detection and diagnosis of suspected COVID-19 cases in Wuhan on January 11 (11). To avoid missed detection, the NHC updated the diagnostic criteria to include suspected cases in Hubei with imaging features of pneumonia (27).

For early case detection, it is necessary to provide accurate case definition and diagnostic protocols for hospitals, in addition to rapid detection technology. On April 3, 2003, almost 5 months after the first SARS case was detected, the Chinese CDC officially released the diagnostic criteria and treatment protocols for SARS on a nationwide scale (19). Actually, Guangdong authorities developed and implemented treatment and control guidelines as early as January 2003, and these were praised by the WHO as a "model for the rest of China or maybe for the rest of the world;" (4) however, these guidelines were not promptly or fully shared with other provinces in China or other countries (28). Taking into account the inadequate response to SARS, the National Health Commission (NHC) issued the first edition of the Diagnosis and Treatment Protocol for COVID-19 on January 15, 2020, only 12 days after the WHO had been notified about the new virus. By March 4, the Protocol was updated to the seventh edition (**Table 2**), as knowledge of the virus and experience in the diagnosis and treatment of COVID-19 accumulated.

During the SARS outbreak, cases in Guangdong were required to isolate from the beginning of February 2003 (17). However, in Beijing, isolation of cases was not commenced until SARS was included as a statutory infectious disease on April 8 (19). However, Wuhan isolated confirmed and suspected COVID-19 cases from January 20, 2020, according to the Law of the People's Republic of China on prevention and control of infectious diseases (2).

Contact Tracing and Quarantine

During the SARS outbreak, contact tracing and quarantine activities were mainly initiated in the epidemic areas, Guangdong in early February, and Beijing in early April (17). Beijing quarantined close contacts individually and in groups from 21 April, 2003 (19), among which 12,000 people were quarantined in completely sealing off hospitals, construction sites, residential buildings, and universities (29). COVID-19 is contagious during its incubation period and, accordingly, a stricter and more extensive quarantine of contacts was implemented. Since the first edition of the Prevention and Control Protocol for COVID-19 was issued on January 15, 2020, all close contacts were under medical observation at home or at designated places (e.g., hotels), with no permission to undertake unnecessary outdoor activities. Many provinces quarantined all returnees from Hubei province for 14 days, even if they had no contact with any confirmed cases (30). New technologies such as big data and artificial intelligence (AI) have been applied to strengthen contact tracing and the management of priority populations (1). For example, the fellow traveler inquiry system was used to check whether passengers had a history of traveling with any confirmed cases so that close contacts could be identified or self-reported. With the increase in cluster outbreaks, many provinces no longer quarantined close contacts at home but placed them in dedicated sites for medical observation (31).

Travel-Related Measures

Travel Restrictions

Due to the travel season peaking during the Spring Festival holiday in China, travel restrictions during the COVID-19 outbreak were more stringent and extensive than those for SARS. On January 23, all transportation networks to and from Wuhan were shut down, including railway stations, airports, and bus stations. Subway and bus services in Wuhan were also suspended (32). By January 25, restrictions were expanded to other cities in Hubei Province, prevented the virus from spreading outside Hubei. Although there were stricter requirements for travel to and from the affected areas during SARS (22), there were no control as stringent as city-level lockdowns.

TABLE 2 | Comparisons of seven editions of Diagnosis and treatment Protocol for COVID-19.

Edition	Date	Revisions
Edition 1–2	January 15–16	–
Edition 3	January 22	Epidemiology- History of travel to or residence in Wuhan and its surrounding areas, or in other communities where cases have been reported within 14 days prior to the onset of the Disease; or in contact with novel coronavirus infected people (with positive results for the nucleic acid test) within 14 days prior to the onset of the disease. Clinical performance- Fever, fatigue and dry cough were the main performance. Some patients may not have fever Diagnostic criteria- The COVID-19 is highly homologous with the known gene sequence if the nucleic acid positive Refined treatment plan.
Edition 4	January 27	Epidemiology-Add clinical classification
Edition 5	February 4	Epidemiology-The infection source was COVID-19 patients and asymptomatic infectious. Clinical performance-Added severe and mild patient symptoms. Diagnostic criteria-Different treatment between Hubei Province and other provinces except Hubei Province 1. Treatment-Added "no effective antiviral therapy has been confirmed at present" and "people with condition can conduct cytokines detection"
Edition 6	February 18	Epidemiology-Added the possibility of aerosol transmission. Diagnostic criteria- canceled the difference between Hubei Province and other provinces, which can be divided into "suspected cases" and "confirmed cases." Treatment-Added trail drugs and divide TCM plan
Edition 7	March 3	Epidemiology- Novel coronavirus can be isolated in feces and urine, attention should be paid to feces or urine contaminated environment that may lead to aerosol or contact. Clinical performance- Added the description of clinical manifestations of pregnant women and children and serological test. Diagnostic criteria- Make explanation of "clustering disease" in epidemiology and modify the content "Lymphocyte count decreased" in clinical manifestation s to "lymphocyte count was normal or decreased."

Entrance and Exit Screening

In the early stages of the SARS epidemic, there were no clear travel advice or precautions. On April 12, 2003, 147 days after the onset of the SARS outbreak, the former Ministry of Health (MOH) and five other departments jointly issued a notice to begin travel-related measures to prevent and the spread of SARS by means of transport (33). From April 22, 2003, all arriving and departing passengers were required to submit health declaration cards and undergo temperature checks. During the COVID-19 outbreak, through continuous improvement of the legal system, travel-related measures, such as temperature checks and healthcare declarations, were implemented at transportation hubs on January 20, 2020, by which time few cases had been confirmed outside Wuhan (34). Meanwhile, the JPCM published guidelines recommending the use of masks on public transport and providing advice on the disinfection of transportation depots (35).

Community Containment Measures

Decreasing Social Interaction

Measures aimed at increasing social distance were implemented in epidemic areas during the SARS outbreak; these were applied nationwide during the COVID-19 epidemic. From April 24, 2003, schools and public places were closed in Beijing (19). Meanwhile, 22 (32%) of the 68 universities in Beijing canceled classes and allowed limited visits (19). The COVID-19 outbreak coincided with the Spring Festival holiday, the most popular time for Chinese family gatherings and public entertainment. To avoid cluster transmission, the Spring Festival holiday has been extended to 10 days on January 26, 2020 (36). Subsequently, the Ministry of Education issued a postponement notice of the new academic semester on January 27 (37). Meanwhile, the JPCM advised people to stay at home; canceled large mass gatherings, such as lantern shows during the Lantern Festival; and closed public places, such as libraries, cinemas, shopping malls, and parks.

Community Access Control

During the SARS outbreak, closed-off community management was mainly implemented in areas where extensive unexplained community transmission was suspected (38). During COVID-19, community containment was implemented as soon as the first cases of COVID-19 were found outside of Wuhan on January 15 (7). From January 26, 2020, the day after the Spring Festival, strict access control to all communities and villages was initiated. With the community as the basic unit, China conducted nationwide grid management to ensure 4 earlies (7). The population was urged to check and report their temperature to their community grid staff and employers at least once a day. Thermal scanning at the point of entrance to the community was implemented in almost every community, not just in those where community transmission was suspected.

Hospital Containment Measures

Strict Infection Control

On May 4, 2003, the MOH developed detailed SARS infection control guidelines for both hospitals and HCWs and conducted special infection control training courses for HCWs. Beginning on April 18, prior to the MOH's announcement, 62,363 health care workers in Beijing underwent training on the management of patients with SARS, infection control, and the use of PPE through in-person courses, videotapes, and printed materials

(19). However, the training activities seemed to have been supplied too late. By May 2, 2003, 778 SARS cases were identified as nosocomial infections, accounting for over 20% of the total 3,799 cases (19). In light of the previous experience with SARS, the NHC issued guidelines for infection control and prevention techniques and the use of PPE in medical facilities in the early stages of the COVID-19 outbreak (39). Furthermore, medical institutions across the country enforced an emergency pre-examination triage system on February 3, 2020. Many hospitals launched online consultations, set up emergency isolation areas in general wards, and tightened visitation to prevent the infection of other patients (31).

Establishing Separate Triage Facilities

A hierarchical treatment system was established for both SARS and COVID outbreaks, comprising fever clinics, designated hospitals, and new specialized hospitals for patient triage, isolation, and treatment. On April 17, 2003, 123 fever clinics were established in all secondary and tertiary hospitals in Beijing (19). On April 27, all patients with SARS were placed together in designated hospital wards (19). A new 1000-bed SARS hospital, Xiaotangshan Hospital, was opened on May 1 (40).

Unlike SARS, primary medical institutions played an important role in the triage of COVID-19. Of the 203 Community Health Centers in Wuhan, 199 were designated for COVID-19 screening and triage on January 24 (41). After the SARS outbreak, the former MOH required all hospitals above level II to regularly set up infectious diseases departments that included fever clinics, which were separate from other patient care areas and staffed by trained personnel (42). As the epicenter of infection, Wuhan released a list of the first group of designated hospitals with fever clinics on January 20 (41). Huoshenshan Hospital and Leishenshan Hospital, which are mainly used for treating severe patients, started to treat patients on February 4 and February 8, respectively (41). In addition, public places were transformed into makeshift hospitals starting on February 5 to isolate and treat many patients with mild disease. In total, 16 makeshift hospitals treated over 12,000 patients in Wuhan (43).

DISCUSSION

Evidence from previous studies indicates that strong political commitment and a centrally coordinated response were the most important factors underlying the control of SARS in mainland China (44). Although there were effective containment guidelines at the time of SARS, the government's hesitation resulted in a nationwide outbreak of SARS in China. Following the disastrous experience of SARS, the Chinese government acted aggressively during the COVID-19 outbreak, implementing decisive measures, such as a cordon sanitaire around Wuhan, restriction of mass gatherings, and prolonged holidays. Previous studies have shown that the drastic control measures implemented in China substantially mitigated the spread of COVID-19 (45). These measures should be properly recognized as the situation may have been worse if these measures had not been implemented to respond to COVID-19 during a period of general population mobility in China. There were both improvements and new lessons in disease prevention and control.

Achievements

Law-Based Strategies

After the SARS outbreak, the central government revised the law on the control of infectious diseases in March 2004.The revision provides instructions to respond to infectious disease outbreaks, improve the reporting of infectious diseases, implement interventions to control disease spread, provide clinical services, fund the control of infectious diseases (46). In 2007, the Emergency Response Law of the People's Republic of China was issued and further stipulated the establishment of an emergency management system that urged unified leadership, comprehensive coordination, categorized management, graded responsibility, and territorial management (47). As a result, the government's response to the COVID-19 outbreak was organized and transparent.

Implementing the National Reporting System (NRS)

On April 1, 2004, the MOH implemented the world's largest Internet-based communicable-disease reporting system, which was jointly funded by the central government (250 million CNY) and local governments (480 million CNY). This system addressed the delays and incomplete reporting of communicable diseases, which were most evident during the SARS epidemic when governmental authorities could not quickly assess the extent of the epidemic. Up to April 2014, all CDCs at different levels, 98% of health facilities at and above the county level, and 94% of township-level health facilities reported the country's 39 notifiable diseases through this system (48). The mean length of time to report from a county-level health facility to the central level was reduced from 29 days to 1 day (49). COVID-19 was integrated into the system on January 24, 2020 (50), and official figures were published daily, which provided governments and their respective departments with an up-to-date understanding of the situation, allowing evidence-based changes in their control measures (7). De facto, the daily report delivered correct and timely information to the public, which prevented mass panic and helped the public protect themselves (51).

Strengthening CDC Systems

The Chinese government has devoted substantial resources to developing a new CDC system after SARS (52). This was re-formed in 2006 into a four-level (i.e., central, provincial, city, and township) disease control and prevention as well as health surveillance system. There has been substantial investment in public health infrastructure, such as new buildings, improvements in internet connectivity, and the purchase of advanced equipment (16). By 2012, CDCs across China had received 93 billion and 8 million CNY, which increased by 516.8% during the decade. There was an annual expenditure of 2.7 million CNY for the prevention program, which increased by 821.4% over the same period (53). Significant improvements in the capacity of public health personnel have been achieved in the workforce-development program through the Field Epidemiology Training Program.

Highlights

Extensive Use of Traditional Chinese Medicine

The combination of traditional Chinese medicine (TCM) and Western Medicine (WM) was extensively employed for the treatment of both SARS and COVID-19. At the time of SARS epidemic, 58.27% of the clinically confirmed patients with SARS received TCM treatment in China, with apparent curative effect (54). On March 6, 2020 at the State Council Press Conference, Yu Yanhong, a member of the Central Leadership Group, made the following statement: "The fact that most of the 50,000 cured patients have adopted TCM, fully proves that the integrative TCM/WM has a remarkable effect" (30). Based on the curative effects of TCM in patients with COVID-19, dozens of provinces have published COVID-19-related prevention and treatment guidance for TCM (31). TCM was used in over 99.93% of cases in the makeshift hospitals in Wuhan (41).

A Hierarchical Medical System Helped to Control the Outbreak

All suspected cases were first screened, classified, and located in the community. Highly suspected cases were then transferred to fever clinics for further medical examination, while quarantine and isolation at home was imposed for other cases. Patients with severe symptoms were transferred to specialized hospitals. This triage process reduced the risk of cross-infection and reduced the pressure on COVID-19-designated hospitals.

Application of High-Tech Measures

Many forms of eHealth services have been implemented during the COVID-19 outbreak, such as online outpatient services, online COVID-19-related consultations, and AI doctors. In addition to medical services, some services used health QR codes, such as health condition checks and community entrance passes, during the outbreak (51). After the initial outbreak between December 2019 and March 2020, smaller-scale resurgences occurred in Beijing and Heilongjiang, among other places (55). Targeted "test-trace-isolate" strategies was adopted during these resurgences. Big data and AI technology played a role in the determination of population mobility, the conduct of epidemiological research, and the tracing close contacts (1, 43, 51).

Challenges

Initial Delay in Information-Sharing

In December 2019, some hospitals reported cases of unexplained pneumonia to the Wuhan Health Committee. However, it was not until January 14, 2020 that a surveillance system for COVID-19 was integrated with an internet-based infectious disease reporting system (50). However, some blame the convoluted process for reporting cases and the lack of practitioner training for the spread of misinformation in the early stages of the outbreak (25).

Disconnection Between Disease Prevention and Treatment

The CDC in China is classified as a public institution that has no authority with respect to public affairs, including public health emergencies. In addition to the lack of decision-making authority, the CDC in China failed to cooperate with the medical system. CDC professionals are only allowed to have licenses for public health practitioners, which forbids the issuing of prescriptions and conducting clinical work, while clinical practitioners are allowed to diagnose and prescribe; however, they lack experience in infectious disease testing, investigation, and reporting. This disconnect between public health and clinical practitioners from these two systems resulted in neglect and failure in containing the outbreak at an early stage.

Urgent Work Needed to Strengthen Disease Control and Prevention System

China was applauded for its progress in improving the disease prevention system since the SARS outbreak; however, in 2012 the follow-up reform that changed the CDC into a non-profit public institute resulted in cutbacks in both personnel number and income. Statistics show that the brain drain from different levels of CDC greatly increased between 2009 and 2017. The number of public health personnel dropped by 4.1% (56). Meanwhile, township CDC staff appear to be inadequately qualified, with only 10.7% of personnel having senior titles and only 25% of personnel holding a bachelor's degree or above (53). In addition to the lack of professional staff, there was a shortage of equipment. Only 20% of provincial CDCs were equipped with a minimum number of Standard-A hardware (56). Consequently, the CDC failed to fulfill its mission during this outbreak.

CONCLUSIONS

As the first country to experience both the SARS and COVID-19 epidemics, attention was garnered by the public health system in China and interventions were taken to improve it. The SARS outbreak clearly highlighted weaknesses of the public health system and emergency management system. Therefore, once the outbreak ended, the government prioritized strengthening of the CDC systems, improving the legal system, and implementing an internet-based communicable-disease reporting system. Based on the lessons learned from tackling SARS, the COVID-19 containment measures were stricter and more organized, and were initiated earlier and on a larger scale than those used with SARS. Although China has made great progress, as can be seen in its response to COVID-19 in comparison with that to SARS, some exposed weaknesses suggest that further efforts should be made to improve the capacity of the disease prevention and control systems. First, the CDC's staffing, equipment and financial support should be ensured. Second, the CDC's integration with medical institutions regarding disease prevention and treatment should be strengthened. Third, the information sharing mechanism between regions and departments should be improved.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

This study was approved by Academic Research Ethics Committee of school of public health, Shandong University.

AUTHOR CONTRIBUTIONS

SL and WC are responsible for the overall design of the review and analysis of the paper. JL wrote the first draft of the manuscript and contributed to the production of the figures. ZW produced **Table 1**, contributed to the literature review, and analysis of the paper. WF and JZ contributed to the figures and literature review. WC edited the manuscript and contributed to the overall interpretation of the findings. ZL edited the manuscript and contributed to the literature review and analysis. All authors contributed to the literature review, data gathering and analyses, and comments on the manuscript.

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BRIEF RESEARCH REPORT
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Age and Gender Disparities in Adverse Events Following COVID-19 Vaccination: Real-World Evidence Based on Big Data for Risk Management

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Background: Two coronavirus disease 2019 (COVID-19) vaccines have received emergency use authorizations in the U.S. However, the safety of these vaccines in the real-world remains unknown.

Methods: We reviewed adverse events (AEs) following COVID-19 vaccination among adults in the Vaccine Adverse Event Reporting System (VAERS) from December 14, 2020, through January 22, 2021. We compared the top 10 AEs, serious AEs, along with office and emergency room (ER) visits by age (18–64 years, ≥65 years) and gender (female, male).

Results: There were age and gender disparities among adults with AEs following COVID-19 vaccination. Compared to younger adults aged between 18 and 64 years, older adults were more likely to report serious AEs, death, permanent disability, and hospitalization. Males were more likely to report serious AEs, death, and hospitalization compared to females.

Conclusions: COVID-19 vaccines are generally safe but possible age and gender disparities in reported AEs may exist.

Keywords: vaccine adverse event reporting system, COVID-19, mRNA vaccines, real-world data, real-world study

BACKGROUND

The coronavirus disease 2019 (COVID-19) pandemic has caused more than 20 million cases and more than 400,000 deaths in the U.S (1). As two COVID-19 vaccines have received emergency use authorizations from the Food and Drug Administration (FDA), there is a hope of ending the pandemic (2–4). Unlike conventionally developed inactivated vaccines, the new type of mRNA vaccines were never marketed before and were expedited with limited clinical trial data, which has raised concerns over their safety (3–5).

Most recently, the Norwegian Medicines Agency (NOMA) reported 29 deaths in older adults occurred shortly after the administration of mRNA COVID-19 vaccines (6), indicating that there may be age disparities in serious AEs and death following COVID-19 vaccination. Therefore, understanding the safety of such vaccines in the real-world (RW) settings

is urgently needed. Furthermore, it remains unknown if mRNA vaccines are associated with possible age and gender disparities, as previously reported in a systematic review of disparities in seasonal influenza vaccines (7).

By using national data from Vaccine Adverse Event Reporting System (VAERS), we report the characteristics of AEs and possible age and gender disparities following COVID-19 vaccination.

METHODS

This study used data from VAERS, which is a national post-marketing spontaneous surveillance program for vaccine safety (8, 9). VAERS is co-administered by the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) (8, 9), and it collects information on AEs of vaccines after administration from patients, healthcare providers, vaccine manufacturers, and others (9, 10). AE symptoms in VAERS are coded using the Medical Dictionary for Regulatory Activities (MedDRA), which is a clinically validated, internationally standardized terminology (9, 10). Since June 30, 2017, VAERS labeled a person to have "serious AEs" if any of the following is reported: death, life-threatening illness, hospitalization, existing hospitalization prolonged, permanent disability, and congenital anomaly or birth defect (9–11). VAERS also collects information on office visits and emergency room (ER) visits (11). This study was reviewed and approved by the University of South Carolina Institutional Review Board. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

We reviewed the characteristics of adults aged 18 years or older who reported AEs following COVID-19 vaccination in VAERS from December 14, 2020, through January 22, 2021. Proportional reporting rate per 1,000 people of top 10 reported AEs, serious AEs, and their subtypes (death, life-threatening illness, hospitalization, and permanent disability) were generated along with office and ER visits. We did not report congenital anomaly or birth defect because it occurs only in pregnant women, and there were only a few cases in the VAERS during the study period. To identify possible age and gender disparities in the AEs following COVID-19 vaccination, two strategies were implemented. First, we investigated age- and gender-specific proportional reporting rates for Top 10 AEs, serious AEs and the subtypes following vaccine use. The proportional reporting rate was calculated as the number of a given AE divided by the number of total AE reports following COVID-19 vaccination multiplying 1,000 to report the incident number of the given AE per 1,000 reports. Second, we used a logistic regression model controlling for onset intervals, doses, vaccine manufacturers, and administration types for adjusted odds ratios (AORs) with 95% confidence intervals.

RESULTS

More younger adults aged between 18 and 64 years reported AEs following COVID-19 vaccination compared to the older adults aged 65 years or older (**Table 1**). Meanwhile, more females reported AEs than males. Most of the AEs reported occurred within 1 week following the first dose of administration. More AE reports came from the Pfizer-BioNTech's vaccine. Approximately 10% of the reports were serious, and ∼2% involved death. More than 5% of the reports involved hospitalization, more than 10% involved office visits, and more than 20% involved ER visits. The top 10 AEs following COVID-19 vaccination were non-serious, including headache, fatigue, dizziness, chills, pyrexia, nausea, pain, injection site pain, pain in extremity, and dyspnoea.

In older adults aged 65 years or older, several serious AEs, including death and dyspnoea were among the top 10 AEs but were not in the younger group between 18 years and 64 years (**Figure 1A**). The proportional reporting rate of serious AEs and

TABLE 1 | Characteristics of adults with VAERS reports following COVID-19 vaccination ($N = 8,976$).

Characteristics	*N*	%
Age		
18–64 years	8,207	91.4
65+ years	769	8.6
Gender		
Female	7,033	78.6
Male	1,914	21.4
Onset interval		
0 day	5,353	61.0
1–7 days	3,145	35.9
8–14 days	179	2.0
≥15 days	93	1.1
Dose		
1st dose	7,300	95.9
2nd doses	314	4.1
Manufacture		
Pfizer-BioNTech	6,964	77.6
Moderna	2,009	22.4
Series reports	1,155	11.8
Death	266	2.7
Life-threatening illness	265	2.7
Permanent Disability	101	1.0
Hospitalizations	698	7.1
Office visits	1,194	12.2
ER visits	1,998	20.4
Top 10 AEs		
Headache	1,977	22.0
Fatigue	1,464	16.3
Dizziness	1,370	15.3
Chills	1,320	14.7
Pyrexia	1,307	14.6
Nausea	1,305	14.5
Pain	1,239	13.8
Injection site pain	904	10.1
Pain in extremity	783	8.7
Dyspnoea	663	7.4

ER, Emergency room; AE, Adverse event.

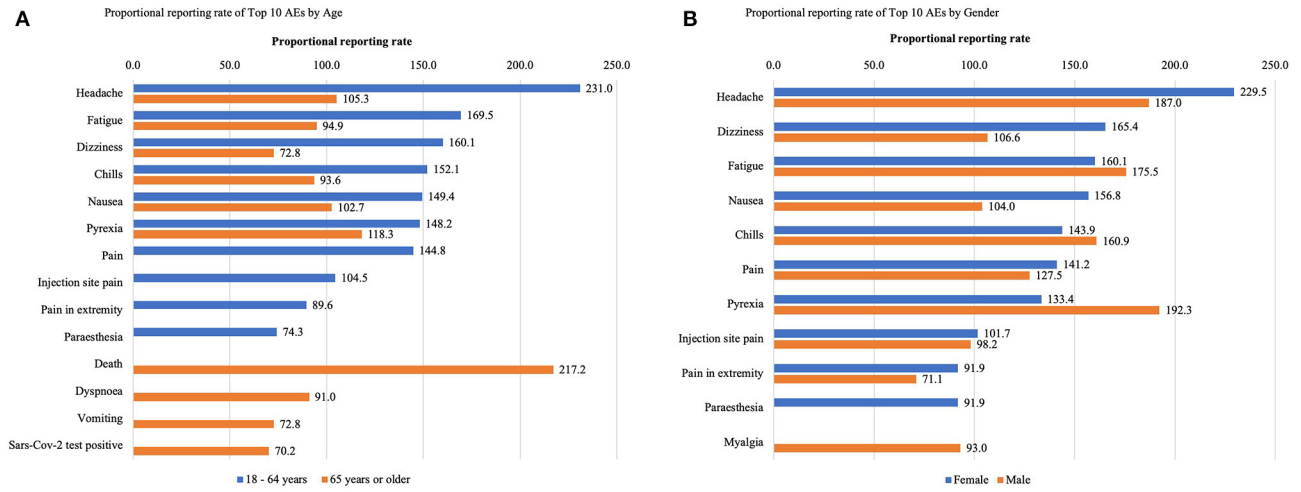

FIGURE 1 | The proportional reporting rate per 1,000 people of the top 10 AEs by **(A)** age and **(B)** gender among adults who had AEs following COVID-19 vaccination. AEs, Adverse events; COVID-19, Corona virus disease 2019; VAERS, Vaccine Adverse Event Reporting System.

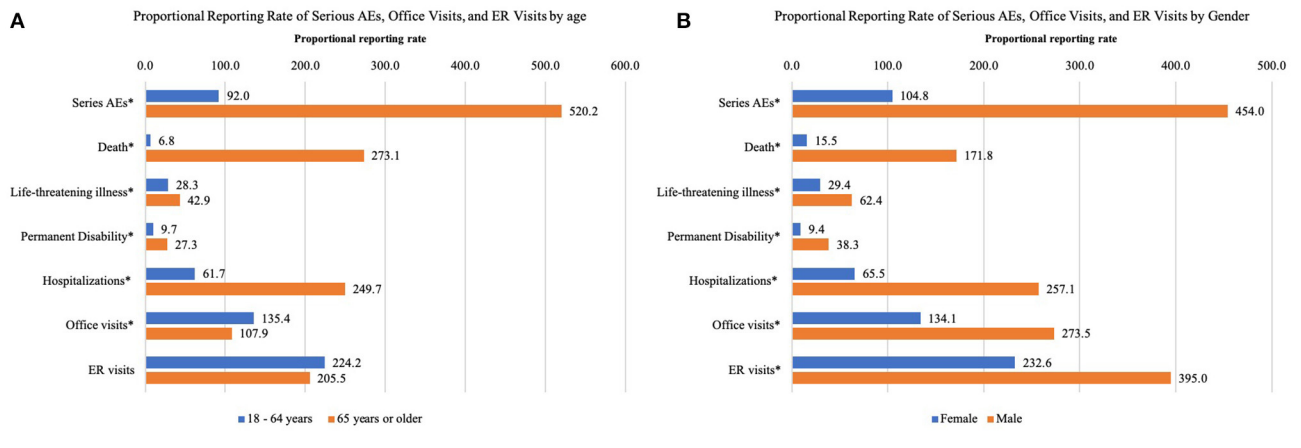

FIGURE 2 | The proportional reporting rate per 1,000 people of serious AEs, office visits, and ER visits by **(A)** age, and **(B)** gender among adults who had AEs following COVID-19 vaccination. Hospitalizations include hospitalization and existing hospitalization prolonged. ER, Emergency room. *Significant at 0.05 confidence level.

the subtypes were significantly higher in older adults than in younger adults, with the exception of ER visits (**Figure 2A**). As for gender, the top 10 AEs following COVID-19 vaccination were similar between males and females (**Figure 1B**). However, the proportional reporting rate of serious AE reports and their subtypes, along with office and ER visits, were significantly higher in males than in females (**Figure 2B**).

Results of logistic regression models (**Figures 3A,B**) showed that compared to younger adults, older adults were more likely to report serious AEs (AOR: 6.26; 95% CI: 5.00–7.84), death (AOR: 19.99; 95% CI: 13.29–30.07), permanent disability (AOR: 2.08; 95% CI: 1.07–4.04), and hospitalization (AOR: 2.96; 95% CI: 2.28–3.85). Besides, compared to females, males were more likely to report serious AEs (AOR: 1.50; 95% CI: 1.25–1.80), death (AOR: 3.31; 95% CI: 2.28–4.82), and hospitalization (AOR: 1.32; 95% CI: 1.08–1.1.63).

DISCUSSION

This study is the first safety report on age and gender disparities of COVID-19 vaccines based on national safety data. We found that the most frequent AEs following COVID-19 vaccination were non-serious, and most of the AEs occurred within 1 week of the administration. Moreover, more than 20% of adults who reported AEs following COVID-19 vaccination had ER visits, and ∼7% of them involved hospitalization. Age disparities were found in the top 10 AEs, as well as serious AEs and their subtypes, which were not reported in the previous RCTs. Our results indicate that several serious AEs (e.g., death) and new development of COVID-19 infection (measured by SARS-COV-2 test positive following vaccination) are among the top 10 AEs in older adults, but not in the younger population aged between 18 and 64 years. These

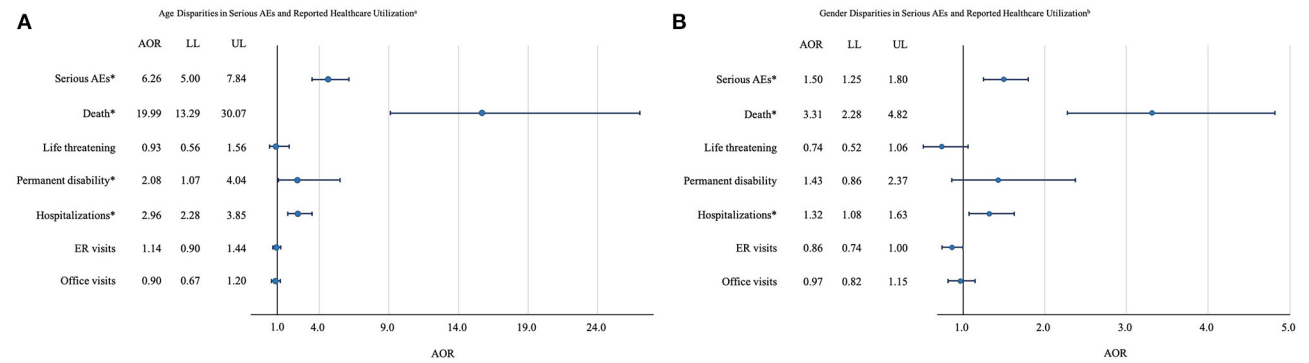

FIGURE 3 | (A) Age disparities and **(B)** gender disparities in serious AEs, ER visits, and office visits among adults who had AEs following COVID-19 vaccination in VAERS. The circle represents the point estimate of AOR. The length of the line represents the 95% CI of the AOR. Hospitalizations include hospitalization and existing hospitalization prolonged. AEs, Adverse events; AOR, Adjusted odds ratio; LL, Lower limit; UL, Upper limit; CI, Confidence interval; ER, Emergency room; COVID-19, Coronavirus disease 2019; VAERS, Vaccine Adverse Event Reporting System; [a]Adults aged 65 years or older vs. adults aged between 18 and 65 years. [b]Males vs. females. *Significant at 0.05 confidence level.

results suggest that older frail adults have a higher proportional reporting rate of serious AEs and a lower rate of office visits, and that males have a higher proportional reporting rate of serious AEs, as well as office and ER visits compared with females.

Logistic regression to compare serious AEs, office visits, and ER visits among adults who had AE following COVID-19 vaccination showed age and gender disparities. The AOR of death of older adults was 19.99 compared to the younger group of 18 and 64 years. Compared with the commonly used approaches of crude reporting odds ratios and crude proportional reporting ratios for surveillance data, using logistic regressions could control for possible confounding factors (12). Results show that older adults were more likely to report serious AEs, death, permanent disability, and hospitalization compared to the younger counterparts. The higher prevalence of death in the older population might be associated with their higher all-cause death rates (13). These older adults are often frail people with serious underlying health conditions and users of medications and polypharmacy (13). Certain vaccine-disease and vaccine-drug interactions might have contributed to or have worsened the outcomes of these older frail adults. However, considering the higher prevalence of serious AEs and death following COVID-19 vaccination, caution should be used when vaccinating older adults to prevent possible fatal events and serious AEs.

Our results show that more females report AEs following COVID-19 vaccination compared to males. In addition, males are more likely to have serious AEs, hospitalizations, and death. However, in 2019, the unadjusted OR of all-cause mortality of males compared with females was 1.12, which shows males have a higher mortality rate in the general population (14). Thus, additional studies are warranted to determine if vaccines pose additional mortality risks for males.

Our results are consistent with age and gender disparities in AEs reported in influenza vaccines. According to a systematic review based on 46 studies, a higher rate of AEs following immunization was reported in females compared with males (7). Also, a study based on two phase three trials reported that compared to younger adults aged between 18 and 64 years, older adults aged 65 years or older had a higher incidence of serious adverse events and deaths following either quadrivalent virus-like particle vaccination or quadrivalent inactivated vaccination (15).

Age and gender disparities in the safety of COVID-19 vaccines found in our study might be related to the different immune responses by different age and gender groups. Males and females have different immune responses to antigens, and there are differences in innate and adaptive immune responses (16). According to Bouman et al., there is a relative suppression of the cellular immune response of the specific immune system in males as compared with females (17). Evidence also shows that compared to the younger population, the older population has a lower ability to establish an effective response to vaccination (18). Specifically, a study by Müller et al. found that there was a lower frequency of neutralizing antibodies in the older population following BNT162b2 vaccination compared to the younger population (19). Different immune responses by different age and gender groups might relate to the strength of immunity so that there were age and gender disparities in AEs following COVID-19 vaccination (20).

However, our study had several limitations. First, as of January 22, 2021, the majority of the vaccination population (82.6%) completed only the first dose by the time of the study (21, 22). The second dose might pose different AEs risks and data are currently limited in the VAERS. Second, it has been a short time since the vaccines were approved for use and the long-term effects remain unknown. Finally, due to the lack of data in the original dataset, there were only a few confounding factors available for adjustment in the regression models. Therefore, we were not able to control for other potential confounding factors, and no causality could be drawn in this study. No prior research on COVID-19 vaccines was able to control for confounding factors, and this study provides evidence for possible age and gender disparities on important safety measures after controlling for potential confounding factors.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. The data can be found at: https://vaers.hhs.gov/.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the University of South Carolina Institutional Review Board. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

XX, BJ, and ZL: concept and design. XX: acquisition, analysis, and interpretation of data. XX, JY, ML, and ZL: drafting of the manuscript. XX, JY, ML, BJ, and ZL: critical revision of the manuscript for important intellectual content. XX: statistical analysis. ZL: administrative, technical, material support, and supervision. All authors contributed to the article and approved the submitted version.

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Sociocultural Challenges in the Implementation of COVID-19 Public Health Measures: Results From a Qualitative Study in Punjab, Pakistan

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Informed public health measures are crucial to curb the COVID-19 pandemic. The sociocultural context is important to understand the success or failure of implementing public health measures. This study explores the social and behavioral response to COVID-19 and unveils challenges in the implementation of related public health measures in Pakistan. Within this qualitative study, we conducted 34 telephonic/online in-depth interviews with youths, adults, elderly people, and healthcare professionals in the Punjab province of Pakistan. Framework analysis was used for data analysis. People's poor understanding about COVID-19 and the need for preventive measures were the major challenge in implementing public health preventive strategies. Study participants reported that the lockdown strategy increased poverty and unemployment. People's poor living conditions and living environment compelled them not to follow social distancing and restricting themselves to home. Additionally, an underdeveloped healthcare system was one of the major challenges for Pakistan. The culture of denial in Pakistan related to the epidemiology of COVID-19 was an important challenge within the implementation of public health preventive measures. It is extremely important that public health experts and social scientists work together to understand the contextual sociocultural factors which shape behaviors associated with the spread of a pandemic.

Keywords: COVID-19, corona, SARS-CoV-2, public health, Pakistan, social behavior

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INTRODUCTION

Coronavirus disease 19 (COVID-19) is a disease caused by infection with a coronavirus. It was first reported in the Wuhan province of China in December 2019. Within a few months, the virus had spread across the world. On January 30, 2020, the World Health Organization (WHO) declared the outbreak to be a public health emergency of international concern (1), and later, on March 11, 2020, announced that COVID-19 was a pandemic (2). According to the WHO COVID-19 Dashboard, there have been about 111 million confirmed COVID-19 cases reported worldwide by February, 2021 (3).

Global experiences and growth patterns of the pandemic clearly indicate that COVID-19 is directly linked to social behaviors and socioeconomic inequalities (4). Social construction of health and illness in any society plays a significant role in health-seeking behavior. Knowledge or awareness of the risks associated with any disease significantly influence what preventive measures people adopt or refuse to adopt. In this paper, we draw on Graham's theoretical paradigm of disease development that emphasizes the contextualization of an epidemic within the social situations in which it occurs (5). Focusing on Pakistan, our research highlights sociocultural factors that exacerbate the spread of COVID-19 and associated risks in the local context. However, their contribution is usually undermined while designing and implementing public health measures. This study emphasizes that timely understanding of social behaviors associated with the spread of an epidemic can help to frame an effective public health strategy.

Although, no country in the world is immune to coronavirus, it is more difficult to combat the pandemic in countries like Pakistan due to social and cultural factors that exacerbate the public health risks (6). This is exemplified in an article published in the New York Times on March 26, 2020. It highlighted that in order to combat the spread of COVID-19 in Pakistan, one needs to counteract political and economic instability and rigid social behaviors that further aggravate challenges for the country (7). Having already a weak public healthcare system struggling to manage the routine health issues in Pakistan, the only option to avoid a health crisis is to adopt a proactive approach to control the spread of the pandemic.

The first case of COVID-19 was detected in Pakistan on February 26, 2020. As of February 20, 2021, the number has risen to 570,000 confirmed cases, including 12,563 deaths (8). Although, the Pakistani government is making serious efforts to enhance its COVID-19 testing capacity, many tend to believe that the actual number of cases could be much higher. Initially, only a very limited number of people had been tested–mainly those who had already shown some symptoms (9–12). Some private laboratories and hospitals also offered COVID-19 testing services, but those were very expensive for the individuals. The low testing rate in Pakistan potentially hindered the ability of the government to assess the real magnitude of the disease in the country (9, 12).

Based on international research and experiences so far, WHO has emphasized some basic preventive measures against the disease, including acquiring awareness about the disease, keeping social distancing, frequent handwashing, and seeking early medical advice in case of any associated symptoms. While these public health measures seem very basic and simple to prevent the spread of coronavirus disease, their meticulous implementation depends on an individual's ability to understand the mechanism of transmission and spread of virus.

Due to diverse local cultural beliefs about illness and various sources of knowledge, population subgroups have varying health risk perceptions, and many do not consider COVID-19 as a serious public health risk in Pakistan (7, 11, 13). A survey conducted in Pakistan assessed the knowledge and practices of people about COVID-19. It shows that people have a limited understanding of COVID-19, especially related to symptoms associated with the disease. Furthermore, gender was slightly associated with the knowledge about the disease (14). Another study showed significant differences in the knowledge and practice of preventive measures related to COVID-19. However, despite having knowledge about the disease, people did not practice preventive measures (15). Moreover, a majority of the people surveyed were of the opinion that government and opposition were not on the same page in the fight against COVID-19. More than half of the study population out of 212 respondents had misconceptions about COVID-19 (15). Therefore, it becomes imperative that public health awareness strategies should counter the myths and misperceptions associated with the pandemic and provide appropriate knowledge.

It should be noted that in developing countries, such as Pakistan, people's perceptions about disease causation are influenced by the supernatural model of disease causation which is quite different from the invisible and complex philosophy of germ theory of disease causation propounded by the biomedical model (7, 13). As a result, people may not comprehensively understand the disease causation, especially related to infectious diseases, which adversely affects their health-seeking behaviors, and adoption of preventive measures (7, 13). In such a plural setup, confusion and misunderstandings arise to implement the basic preventive measures suggested by WHO. Given this backdrop, sociocultural factors in a society are very important to understand the success or failure of the implementation of preventive public health measures. Cultural and societal norms need special consideration for the acceptability and feasibility of public health measures. Drawing upon in-depth interviews with the general public, including youths, adults, elderly people, and healthcare professionals in the Punjab province of Pakistan, this study explores the social and behavioral response to coronavirus and unveils challenges in the implementation of COVID-19 public health measures. We argue for sociocultural-informed public health measures to curb COVID-19. We opine that it is extremely important to understand the contextual sociocultural factors that shape behaviors associated with the spread of the pandemic in order to design and implement preventive strategies that could work effectively in the local context. Moreover, only a better understanding of the contextual sociocultural factors can help to change the behaviors of the people.

METHODS

We conducted an exploratory qualitative study based on in-depth interviews. Study participants were drawn from diverse age groups assuming that they had different kinds of experiences and perceptions regarding the implementation of various public health measures in the province of Punjab, Pakistan. Punjab is the largest province of Pakistan comprising 52% of the total population of Pakistan. Another reason for the selection of participants from Punjab was that it has had the highest number of COVID-19 diagnosed cases before the time of data collection. We included participants from the general public (young: 18–25

years, adult: 26–60 years, and elderly: >60 years) and healthcare professionals who had had experience of dealing with COVID-19 cases in healthcare facilities. Thirty-four study participants (seven interviews within each age group of the general public and 13 interviews with healthcare professionals) were recruited from the cities of Lahore, Rawalpindi, Faisalabad, and Sialkot, which had the highest number of cases in the province of Punjab, in July 2020.

Participants belonging to the general public were recruited through purposive sampling technique. It helped us to select participants with diverse characteristics such as from a wide geographic area (from different cities), from different age groups, and having varied experiences with the COVID-19 pandemic. Being part of the academic community, researchers had good contacts with the professors in universities within the study areas. The study participants were approached through these contacts in each city. These contact persons introduced the study to their respective community through WhatsApp and/or mobile numbers and asked for their willingness to participate in the study. They shared the Skype IDs, Zoom links and/or WhatsApp numbers of willing participants with the first and third author. For the selection of healthcare professionals, a list containing contact information of these professionals was obtained from the Punjab Healthcare Department. Four healthcare professionals from each study area were selected through purposive sampling in the study; three interviews were incomplete, so these were not included in the analysis. Because it was not possible to conduct face-to-face interviews during the lockdown, telephone- or online-based in-depth interviews *via* WhatsApp, Skype or Zoom were held with these participants at their convenient time and day. The interviews were conducted during a 3-week time period in August 2020.

A semi-structured in-depth interview guide was used for the data collection (**Supplementary File 1**). The guide was developed for this study based on a literature review on the topic and the expert opinion of two healthcare professionals and social scientists was sought. Study participants were first asked about their knowledge related to COVID-19 and its routes of transmission. They were also asked about COVID-19 preventive strategies and further probed about maintaining social distancing and its benefits and demerits, handwashing practices, and the use of face masks. Further, questions were asked about the perceived effectiveness of lockdown as a preventive strategy and its effects on the society. Furthermore, we included questions regarding problems the study participants experienced while observing public health measures in their households, their neighborhoods, and social spaces. Probing questions were added to ask about social and cultural factors. In addition, we asked what the interviewees thought about the challenges of implementing COVID-19 strategies. There were also questions about fake news regarding COVID-19 and fear- and anxiety-related factors.

Interviews were performed in the national language, i.e., Urdu. Each interview lasted between 60 and 80 min. All interviews were audio-recorded and notes were taken during the interviews. All the audio-recorded data were transcribed verbatim and translated into English. After translation, the data were read independently and carefully by three researchers multiple times. The data were analyzed by using the framework method, because it is a systematic approach to analyze data collected from diverse groups of people such as healthcare professionals, patients and lay people (16). After multiple reading, meaningful statements and codes were extracted which were grouped together into categories and themes were formulated. The three researchers then met to compare the themes and conflicting opinions were resolved after thorough discussion on the contents of the themes. A spreadsheet was used to develop a framework matrix.

The study protocol was reviewed and approved by the Institutional Review Board, University of the Punjab. Informed consent was taken using telephone consent script from all study participants before the start of the interviews.

RESULTS

Out of 34 study participants, 21 belonging to the general public, out of which, 15 (71.4%) were males and six (28.6%) were females. Four (19%) participants had no formal schooling, 11 (52.4%) had up to 12 years education and 6 (28.6%) had university education. Thirteen (61.9%) participants had a monthly family income <75,000 Pakistan Rupees (PKR) (1 US$ = 161 PKR), 5 (23.8%) between 76,000 and 100,000 PKR and 3 (14.3%) had more than 100,000 PKR (**Table 1**). Out of 13 healthcare professionals, nine (69.2%) were medical practitioners and four (30.8%) were public health experts; four (30.7%) were <35 and nine (69.3%) were 35 years old and older; seven (53.8%) were males and six (46.2%) were females (**Table 1**).

A total of eight themes have been identified from the data analysis, which are described in detail below and exemplified with quotations from the interviewees.

Poor Literacy and Understanding of Disease

All study participants highlighted that people's understanding of COVID-19 is limited due to poor literacy and a lack of education – particularly in rural areas. The findings show that it was difficult for people to understand the need for social isolation, especially for people who had rigid religious beliefs. This was the reason that the spread of the coronavirus in Pakistan started from clusters such as congregations at the time of religious events. One of the study participants who was employed as a general physician in a public hospital stated:

> "Many of the cases which are asymptomatic or reported with mild illness at hospitals did not follow medical guidelines and protective and preventive measures. This resulted in increased local transmission of COVID-19 to their families and relatives."

One young male study participant with 12 years of education said:

> "I cannot say 'no' to my friends when they shake hands with me and hug me. I feel embarrassed if I show reluctance."

TABLE 1 | Socio-demographic characteristics of the study participants ($n = 34$).

Characteristics	*n*	%
Group of study participants		
General public (GP)	21	61.8
Healthcare professionals (HCPs)	13	38.2
Gender of GP participants		
Male	15	71.4
Female	6	28.6
Gender of HCPs		
Male	7	53.8
Female	6	46.2
Age of GP participants (in years)		
18–20	1	4.8
21–22	2	9.5
23–25	4	19.0
26–35	2	9.5
36–45	2	9.5
46–60	3	14.3
61–65	4	19.0
>65	3	14.4
Age of HCPs (in years)		
≤35	4	30.7
>35	9	69.3
Education of GP participants		
No formal schooling	4	19.0
1–8 years of schooling	4	19.0
9–12 years of schooling	7	33.4
13–14 years of schooling	2	9.6
>14 years of schooling	4	19.0
Monthly income of GP (in Pakistan rupees)		
<30,000	4	19.0
30,001–75,000	9	42.9
75,001–100,000	5	23.8
>100,000	3	14.3
Type of HCPs		
Medical practitioners	9	69.2
Public health experts	4	30.8
Duration of work experience of HCPs (in years)		
≤10	3	23.1
>10	10	76.9

In addition, the awareness of the severity of disease among study participants from the general public was limited. A healthcare professional (public health expert) reported:

> "Many people are not aware of the disease severity. They could not understand how it could be a serious disease if they only have mild symptoms."

Furthermore, another healthcare physician said:

> "People do not know about the significance of social distancing [. . .]. They think this is against their culture if they are not meeting people."

Another medical doctor claimed:

> "If people do not think it [referring to COVID-19] is a real threat, they will not modify their behavior. So, the first thing is to make them realize that COVID-19 is a serious disease."

A female public health expert added:

> "Our people have very casual attitudes toward COVID-19. This is the reason that we are receiving a large number of cases nowadays."

A majority of the healthcare professionals were of the view that the culture of ignorance and not taking the COVID-19 seriously would accelerate the spread of the virus.9).

Increasing Poverty and Unemployment

Almost all of the participants agreed that the lockdown strategy to contain COVID-19 has increased poverty because many people lost their jobs – especially daily wage earners. Furthermore, poverty was also considered as the more important problem compared to the pandemic. This is illustrated by the following statement by a middle-aged man:

> "For us, the coronavirus is nothing. We are experiencing hunger every day. My family and I can usually afford two meals a day but because of this lockdown we cannot even afford one meal. So, for us, the coronavirus is no more frightening than the hunger we experience on a daily basis."

One elderly study participant said:

> "We have to fight on multiple platforms. We are fighting against COVID but, at the same time, we need to fight against hunger and poverty, which has increased alarmingly due to the last two months' lockdown."

Another participant who was working in a factory said:

> "Like me, many others are engaged in construction-, manufacturing- and maintenance-related jobs. Many of them are working on daily wages and all of these daily wage earners are jobless now due to this lockdown. The government needs to relax the lockdown so that people do not die from hunger."

One study participant in his late fifties opined:

> "People from the lower socioeconomic stratum are largely exposed to such an epidemic because of their lack of resources, such as money, knowledge, and social networking. They should be extra cautious."

Living Conditions and Living Environment

About 70% of the population in the Punjab lives in rural areas or urban slums. In the majority of these areas, there are small houses with two rooms with poor ventilation and basic facilities of water and sanitation. In the majority of houses in rural areas, an animal shed is also constructed within the premises of the house, leading to human-animal interaction. About two to three generations are

often living in one household. One of the study participants from an urban slum in Lahore said:

> "We are 15 people living in this small two-room house. I have three brothers and the families of all of my brothers are living in this small house. When some of the family members are outside, then it is good social isolation for us. Let me relate how 15 people can have social isolation in a small house with poor facilities."

Another participant while sharing his story narrated:

> "I live in the interior of the city where there are small houses with a high population density. Experts are talking about social distancing and handwashing. How can my family and I follow these measures when there is no proper sanitation facility available in our home to wash our hands frequently with soap and water?"

Gendered Dimension of Lockdown Strategy

Women have felt themselves more affected due to the COVID-19-related lockdown. Female study participants reported that there was more stress on women for household tasks as well as their work-related responsibilities. This creates more conflicts among family members. One of the female participants narrated:

> "We have lots of stress because of COVID. We [referring to women] need to do more cleaning at home, frequent cooking and more kitchen-related work compared to normal days when family members are not at home for the whole day because of school and office engagements."

One of the female respondents while narrating her story said:

> "My husband is a smoker, but he only used to smoke one or two cigarettes a day. Now, because of anxiety, he smokes a lot in a day. It creates conflict and quarrels between us."

Because of such domestic issues, the energies of families are tilted toward some non-issues and they are less interested in observing the protective and preventive measures to contain the virus.

Underdeveloped Healthcare System

In Pakistan, all travelers coming from other countries need to spend seven days in a quarantine center so they can be identified in case they have the coronavirus disease. A majority of the study participants from the community mentioned the poor condition of services provided at the quarantine and isolation centers as one of the reasons for not going for testing and screening even if symptoms were present. One of the participants narrated the story of his neighbor who spent some days at the quarantine center:

> "He [referring to the neighbor] told us that he was kept in very pathetic and unhygienic conditions. He felt as if he was a criminal. There was no doctor and food was thrown to him as if it was food given to dogs."

One public health expert, while sharing the grim situation of the healthcare system, reported:

> "The underdeveloped healthcare system is one of the major challenges for Pakistan to contain the coronavirus. In countries such as Pakistan, where healthcare facilities are not available according to the number of inhabitants, where there is one doctor for 10,000 population, one hospital bed for 1,000 population, one ventilator for 1,000,000 population [. . .] Then how can we fight against COVID if we are getting a huge number of cases every day? I am worried that the situation can get alarming."

Another doctor said:

> "The health indicators of our adult population are not good. Half of the adult population above 50 years of age has comorbidities, such as diabetics, cardiovascular problems, and chronic obstructive pulmonary diseases. This causes them to be more vulnerable to COVID complications. They are also coming to outpatient departments, which may result in contracting the virus from others."

One healthcare professional opined:

> "There is a lack of testing facilities in Pakistan. And because of this, it is very difficult to follow public health measures of randomly testing and isolating COVID-positive cases and tracking and tracing their contacts, although, it is necessary if we want to contain the coronavirus."

Infodemic and Fake News

False and misleading information about the coronavirus has significant consequences regarding containing the virus. It creates a challenge for the COVID-19 control program as well as a risk to the public. One of the study participants said:

> "Fake news is easy to spread and hard to stop. So, it spreads widely within a minute. For example, there are so many conspiracy theories regarding the origin of the coronavirus and many quick remedies are available as its treatment. Sometimes, such information leads to mental torture for the patients and sometimes it leads a further spread of the virus if it is presented as a less serious disease."

One female participant reported:

> "Fake news regarding quick remedies or household *totkas* [referring to remedy] got us confused. There is a bombardment of such kind of news on social media. I am confused now about what is true?"

One participant in his late twenties said:

> "One day we listen that vaccine is coming, so we get rid of the coronavirus soon. But the other day we hear that the vaccine will take another two years to come. So, I got confused what is true?"

One young participant opined:

> "The fake information was disseminated that the virus cannot infect young people. Many of my friends violated the preventive measures because they think that this disease can affect only the elderly population."

Some of the study participants were not happy with the media coverage related to COVID-19. One male study participant in his late forties said:

> "People are fearful of stigmatization. If they are positive, they have been shown on TV channels as if they have committed some crime."

Religious Rituals and Fatalistic Attitude

Many of the participants were fearful that the COVID-19 cases have increased due to congregational prayers during the month of Ramadan. They were of the view that it was very difficult for the COVID-19 control program to contain the virus spread during some religious activities where there was a gathering of many people at one place to follow the religious rituals. One of the healthcare professionals said:

> "Before the start of Ramadan, I was fearful that it would be very difficult for us to stop roadside arrangements for *Iftar* [the meal eaten by Muslim after sunset during Ramadan] and *Sehri* [referring to the meal eaten by Muslims before the sunrise during Ramadan] because it could spread the virus fast."

Almost all of the healthcare professionals were of the view that several approaches have been taken for infectious disease prevention, but these were not implemented in their true spirit. One male study participant in his late thirties narrated:

> "In our neighborhood, *jumma* [Friday] prayers were offered in the *jamat* [referring to congregation] on the rooftop of a house after the closure of mosques."

About half of the healthcare professionals reported that most of the preventive measures to control COVID-19 had not been recognized and accepted by the public. One public health expert opined:

> "The government advised people not to come out of their homes and to offer prayer at home five times instead of in the mosque. But people didn't listen to them."

About three-quarters of the participants thought that religious leaders could play a positive role in educating people about the use of protective measures.

> "Our religious leaders can guide the people in the light of religious teaching and according to the guidelines of healthcare professionals."

Almost all of the study participants shared the fact that despite healthcare professionals' instructions and governmental restrictions, social, and religious gatherings were observed during the time of religious festivities. The attitude that COVID-19 was the result of mankind's sins and punishment from heaven was prevalent among study participants. One elderly male study participant thought:

> "If it is written in my *kismet* [fate] that I will get infected with the virus, then nothing can stop it. So, we have to trust in Allah. Nothing will happen."

Another middle-age female participant said:

> "Allah is not happy with us. This is the wrath of Allah. We need to give more *sadaqa* [money given to the poor to make Allah happy]."

Culture of Denial

Many of the participants reported that the culture of denial regarding the existence of COVID-19 was prevalent among people in their neighborhoods. This was considered a big challenge to the implementation of public health strategies to contain COVID-19. A few of the study participants denied the existence of the COVID-19 pandemic. According to them "this is just a fiction." One of the study participants who was working as a general physician narrated:

> "Here, people totally deny that the COVID-19 pandemic exists. If people deny the existence of this disease, then how we can influence them to follow COVID-19 prevention public health measures?"

DISCUSSION

The paper is a qualitative and exploratory study of perceptions and attitudes of a small group of participants from the public and healthcare professionals. The study found that people's poor understanding of COVID-19 and the need for preventive measures, such as physical distancing, were the major challenges in implementing public health preventive strategies during the COVID-19 pandemic.

One of the most effective public health measures to counter the rapid growth of COVID-19 is social distancing. Several studies and epidemiological modeling have shown that the patterns of social networks or social contacts influence the spread of disease in a population strongly (17–19). The behavior of people influences the consequences of any public health intervention greatly. Link calls this a "social shaping of population health" (20). However, many of our study participants from general public did not agree with the concept of social distancing. Social distancing was extremely difficult to practice in densely populated countries such as Pakistan, where a significant number of people live under one roof along with extended families. Furthermore, they tended to believe that going to public places did not expose them to higher risks than confining themselves at home, where a large number of people was already living together (9). In such cases, even when someone was not feeling well, other family members shared the same room because they did not have any other option (21). Large gatherings at times of happiness and sorrow, handshaking and embracing

are part of everyday lives of people in Pakistan. Amid the outbreak of COVID-19, public health measures required people to change their routine behaviors to prevent the rapid spread of the coronavirus. Such a sudden change in everyday life was still a cultural shock for many people and they considered it as a threat to their culture. Despite the lockdown and restrictions on gatherings and going to public places, people were not taking the pandemic seriously and were still arranging gatherings for marriages, funerals, parties or other purposes (11).

Our study found that the underdeveloped healthcare system was a big challenge for the implementation of public health preventive measures as a majority of the study participants from the community shared the poor condition of services provided at quarantine and isolation centers. Financial and skilled human resources are very important to combat any health emergency. A developing country such as Pakistan, with strained political and economic structures, is already struggling to tackle poverty, extremism and other human insecurities. Therefore, a global pandemic such as COVID-19 could be much more devastating in developing countries than in developed ones (7, 22, 23). The health sector in Pakistan has not been a priority of successive governments. Only about 2% of its gross domestic product is spent on healthcare – compared to a global average of 10% (6). To date, the country has not been able to control diseases that have been eliminated elsewhere in the world, for example, polio (7). The Ministry of Health has already issued warnings to be mindful of the pandemic as the resource-limited country is not well-prepared to control any drastic situation caused by the pandemic. If coronavirus cases are not controlled, diagnosed, and treated in time, the situation may lead to a more devastating crisis (24). At the time when corona hit the country, there were 2,200 ventilators available in hospitals, out of which only about half were functional (6). The fragile public health infrastructure does not have the capacity to provide treatment to tens of thousands of patients of COVID-19, and the major threat for Pakistan is high fatalities due to the lack of healthcare services (10, 12).

Physicians, paramedics and nurses, as the backbone of the health infrastructure, are considered frontline fighters against COVID-19. However, they are also extremely vulnerable to being infected in the absence of personal safety measures (22). Cases have frequently been reported in different parts of the country where doctors and paramedics have refused to perform their duties and are protesting due to the lack of availability of personal protective equipment (10, 24, 25). Regarding the already limited healthcare services available in the country, the strike of healthcare personnel and their vulnerability to fall victim to the disease are leading to serious consequences in combatting the pandemic.

The review of opinions published in daily newspapers showed that many people in Pakistan believed that the government could not assess the severity of the issue and delayed framing its response strategy mainly due to the lack of political consensus (6, 26). Initially, coronavirus-positive cases were detected in Pakistan among those persons who had recently visited the neighboring country Iran, where COVID-19 had already spread (27, 28). However, at an early stage of the spread of the epidemic, due to a lack of proper coronavirus testing services, and quarantine facilities in the remote town of Taftan in Baluchistan province, bordering Iran, there was no proper screening of the visitors coming back into the country. Therefore, it became a source of spreading the virus (29). Based on these experiences, the government tried to take proactive public health measures for containing the spread of the pandemic.

In addition to the lack of healthcare services and knowledge about COVID-19, fear and stigmatization associated with the disease also restricted people from seeking early medical advice (30). The participants from the general public in our study perceived that – similar to other infectious diseases – COVID-19-positive cases were being stigmatized, because they might be responsible for transmitting the virus to other people. Moreover, some television channels breached individual privacy by revealing the personal identities of those people who had tested positive and showed clips of ambulances and police vans going to their homes as they were being "arrested." One study also indicated that a majority believed that coronavirus-related news on the media was exaggerated in Pakistan (15). Furthermore, many people had developed fears of getting exposed to the virus or testing positive and, therefore, stayed away from hospitals – even when they were not feeling well. Several alarming cases in different parts of the country have been reported in which confirmed and suspected patients of COVID-19 fled from the quarantine/isolation centers (31). Such irrational behavior was not only life-threatening for patients but also exposed others to the virus.

Another significant challenge reported by the study participants was related to religious gatherings and following ritual practices during the wake of the COVID-19 pandemic. A further study from Pakistan reported that 20.4% of the study participants believed that religious congregations were not the source of the spread of infection and 15% reported that they were not sure about it (32). It was a daunting task for the government to develop a consensus on the sensitive issue of religious gatherings due to diverse opinions among religious leaders (33). Some people in Pakistan believed that the coronavirus was a punishment from God for sins committed. Hence, instead of sitting at home, people gathered in mosques and collectively prayed for protection from the epidemic (7, 13, 34). Some people did not even follow the basic preventive measures, wearing masks, and maintaining social distance, considering that nothing could happen to them except what that which was already their fate (11). The government authorities held several meetings with the clerics to convince them to cooperate with the government in the implementation of the public health measures and restrict congregational prayers and rituals (33). Some of the public health experts were of the view that congregational prayers resulted in the "explosion" of coronavirus cases in the country (35). However, for many, spirituality could be a coping mechanism to relieve stress and anxiety during this pandemic time (36).

The views of healthcare professionals revealed that developing countries, such as Pakistan, were less likely to enforce appropriate preventive measures and would become more susceptible to a high penetration of any epidemic due to grave socioeconomic disparities and a lack of access to basic services, for example, water, sanitation, food, and shelter (6, 37, 38). Health risks are strongly associated with lifestyles shaped by socioeconomic structures because those segments of the population that are

already marginalized tend to be more vulnerable to infection (4, 6). The majority of the population in Pakistan live in small housing units and lack access to clean water even for drinking (7, 21). Large families are less likely to maintain physical distancing and frequent handwashing practices as preventive measures against COVID-19 (21). Moreover, millions of slum dwellers in the country are among the most vulnerable groups to get infected because maintaining personal hygiene and social distancing could not be practically possible for them (6, 7, 21). There is no option to work from home or stay at home for poor and daily wage earners in a lockdown situation. Furthermore, the country is amongst the malnourished countries in the world because a significant proportion of the population does not have access to basic healthy food, which makes them susceptible to acquiring the disease (6).

Pakistan's overall socio-economic situation created a challenge for the government to follow strict lockdown in the country. While many countries have ordered the lockdown to prevent the spread of COVID-19, reality is very different in countries such as Pakistan, because the lockdown could result in more severe fatal consequences than the pandemic itself. Almost a quarter of the total population of the country lives under conditions of poverty and earns <$2 a day (11, 27, 28, 39). For such underprivileged groups, the coronavirus is not only a health problem but an economic challenge (23). After the outbreak of COVID-19 in Pakistan, the government announced a partial lockdown, which further continued for 5 months with gradual relaxation as millions of people were daily wage earners who could not survive without work for a longer period. Despite limited economic resources, the government announced a support package which was directly distributed among 12 million low-income families (37). However, the gatherings of a large number of people to receive the financial assistance at designated places was a public health risk breaching social distancing measures (40). Moreover, keeping in view the large size of the population and density of poverty within Pakistan, it was not possible for the government to support every needy family and confine them to home for a longer period.

LIMITATIONS

The study findings may not be representative of Pakistan because the study was conducted in only one province. However, we recruited a large sample size for a qualitative study. The generalizability of results might be affected due to the purposive sampling. Nevertheless, one needs to keep in mind that it is a qualitative study. The heterogeneous sample let us include various perspectives in the analysis.

The interview guide was developed based on concepts that had emerged from the literature review and expert opinions. This allows for the inclusion of relevant aspects, although, one needs to keep in mind that the COVID-19 pandemic is also characterized by uncertainty and rapidly changing situations. Further, studies are needed which focus on cultural and regional-specific aspects promoting or hindering the implementation of public health measures in times of a pandemic.

CONCLUSIONS

Our study found that, in addition to other factors, contextual sociocultural factors play a significant role in shaping social behaviors, and determining the efficacy of COVID-19 preventive measures. However, their contribution is usually undermined while designing and implementing public health measures. Socio-culturally informed public health measures are needed to control COVID-19 effectively. Comprehensive and inclusive strategies are needed to improve people's understanding of COVID-19 itself, its mode of transmission, its impacts and the need for public health preventive measures. All stakeholders – including government, healthcare professionals, religious leaders, civil society, media, and communities – need to play their role in preventing and stopping stigmatization, correcting misconceptions and misinformation regarding COVID-19, and promoting the importance of prevention, such as social distancing, wearing protective equipment, early screening, and vaccination (41).

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Review Board, University of the Punjab (Reference No. 598/IRB/PU). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

RZ: conceptualization, methodology, and investigation. RZ, FY, and MZ: formal analysis. RZ and FY writing—original draft preparation. MZ and FF writing—review, editing, and supervision. All authors have read and agreed to the published version of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2021.703825/full#supplementary-material

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Physicians' Acceptance of Triage Guidelines in the Context of the COVID-19 Pandemic: A Qualitative Study

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Aims: One of the major ethical challenges posed by the Covid-19 pandemic comes in the form of fair triage decisions for critically ill patients in situations where life-saving resources are limited. In Spring 2020, the Swiss Academy of Medical Sciences (SAMS) issued specific guidelines on triage for intensive-care treatment in the context of the Covid-19 pandemic. While evidence has shown that the capacities of intensive care medicine throughout Switzerland were sufficient to take care of all critically ill patients during the first wave of the outbreak, no evidence is available regarding the acceptance of these guidelines by ICU staff. The aim of this qualitative study was to explore the acceptance and perceived implementation of the SAMS guidelines among a sample of senior physicians involved in the care of Covid-19 patients in the Canton of Ticino. Specific objectives included capturing and describing physicians' attitudes toward the guidelines, any challenges experienced in their application, and any perceived factors that facilitated or would facilitate their application.

Methods: We conducted face-to-face and telephone interviews with a purposive sample of nine senior physicians employed as either head of unity, deputy-head of unit, or medical director in either one of the two Covid-19 hospitals in the Canton of Ticino during the peak of the outbreak. Interviews were transcribed verbatim and thematically analyzed using an inductive approach.

Results: We found that participants held different views regarding the nature of the guidelines, saw decisions on admission as a matter of collective responsibility, argued that decisions should be based on a medical futility principle rather than an age criterion, and found that difficulties to address end-of-life issues led to a comeback of paternalism.

Conclusions: Results highlight the importance of clarifying the nature of the guidelines, establishing authority, and responsibility during triaging decisions, recognizing and addressing sources of interference with patients' autonomy, and the need of a cultural shift in timely and efficiently addressing end-of-life issues.

Keywords: COVID-19, triage, ethics, justice, autonomy, Switzerland, qualitative research

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INTRODUCTION

One of the major ethical challenges posed by the Covid-19 pandemic comes in the form of triage decisions for critically ill patients (1). These decisions relate to the fair prioritization of patients for specific treatments (e.g., mechanical ventilation) in a situation of limited life-saving resources (2). Based on current estimates, 80% of confirmed cases of Covid-19 can be treated as outpatients, up to 20% require hospitalization, and 5% become critically ill and need intensive care (3). The Swiss Society of Intensive Care Medicine (SSICM) assessed the occupancy of bed capacities of the 82 officially recognized or certified intensive care units (ICUs) in Switzerland between March 30 and June 16, 2020 (4). The SSICM reported that, despite the sharp temporary increase in the occupancy rates during April 2020, the capacities of intensive care medicine throughout Switzerland were sufficient to take care of all critically ill patients, but found substantial regional differences, with ICUs in the Ticino and Lake Geneva regions being the busiest (4).

Medical-ethical guidelines to support decision-making in individual cases arising in the day-to-day practice of intensive-care medicine have been developed by the Swiss Academy of Medical Sciences (SAMS) in 2013 (5). In view of the extraordinary challenges that the Covid-19 pandemic has posed to the health system, and particularly to ICUs, the SAMS – in collaboration with the SSICM – supplemented the 2013 guidelines on intensive care with an annex providing precise arrangements for triage of patients in the event of a shortage of resource (6). These guidelines, which were published at the end of March 2020, mostly overlap with other triage guidelines simultaneously developed in the rest of Europe (7). They consider prognosis an indispensable precondition for maximizing benefit; refer to short-term survival only as a key triaging criterion; reject an age limit as a criterion in itself (but mention age of 85+ as an exclusion criterion to ICU admission in case of shortage of beds); cite the will of the patient as guiding treatment choices; recognize futility as a justification to end treatment even against patient will; advocate for preferential treatment for healthcare professionals (HCPs); emphasize fair decision-making processes and good palliative care; call in for interprofessional teams to make and document triage decisions fairly and transparently; demand regular re-evaluation of the decisions taken; and call for psychosocial support for HCPs (6, 7). On December 17, 2020, the guidelines were updated to reflect the most recent scientific evidence and feedback collected from various stakeholders over the previous months (6). The main changes include clarification of the meaning of the principle of short-term survival prognosis, and that it is always about making decisions that limit the number of deaths as much as possible, the importance of respecting and re-evaluating the patient's wishes (6).

Some studies suggest that, although, recommendations for ICU triage are available, compliance with them is suboptimal (8–10). Decisions on whether to accord a critically ill patient ICU admission priority in a situation of limited bed capacity are complex, and entail balancing the potential risks and benefits for the individual patient with the admission and treatment implications for future ones (11). From 30 March to April 21, 2020, a survey was conducted in Switzerland with a sample of the French- and German-speaking population to investigate the extent to which the general public agrees with the SAMS guidelines introduced in late March 2020 (12). This survey provides an overview of how these guidelines have been received by the general population. However, while evidence from southern Switzerland, which was greatly impacted during the first wave of the epidemic, is lacking, it is also unknown how physicians working on the front line at the peak of the outbreak received the SAMS guidelines, and what implementation barriers and facilitators they perceived. Qualitative research can provide valuable insights into the nature of the physicians' perception, understanding, and acceptance of the SAMS guidelines, and on how these are used and applied accounting for patients' values and preferences. Moreover, through the consideration of context, and relevant details, and the application of a recursive approach, qualitative research favors the emergence of themes and topics that can inform the design and conduction of structured investigations, including surveys aimed at describing and quantifying practices, procedures, and behaviors as the pandemic unfolds, and its transformative impact on evidence-based clinical decisions evolves unpredictably.

The aim of this qualitative study was to explore the acceptance and perceived implementation of the SAMS guidelines among a sample of senior physicians involved in the care of Covid-19 patients in the Canton of Ticino during the peak of the outbreak. Specific objectives included capturing and describing physicians' attitudes toward the guidelines, any challenges experienced in their application, and any factors that facilitated or would facilitate their application.

MATERIALS AND METHODS

Study Design

We conducted a qualitative study employing face-to-face and telephone interviews to capture how the SAMS guidelines were received and applied by senior physicians employed in either one of the two Covid-19 hospitals in the Canton of Ticino during the peak of the pandemic. The use of the telephone as a medium for conducting the interviews was chosen to offer the greatest flexibility for the scheduling of interviews to fit in with the physicians' workload.

We recruited a sample of nine senior physicians through purposive sampling, corresponding to almost all senior physicians employed at the two hospitals ($N = 11$). To be eligible for the study, participants had to be employed as either head of unit, deputy head of unit or medical director at either the ICU, the intermediate care unit (IMCU), or emergency department (ED) of one of the two hospitals dedicated to Covid-19 patients in the Canton of Ticino during the peak of the outbreak. This allowed us to identify physicians who had gained substantial, direct experience with Covid-19 patients, and had taken a responsible role in the decision-making process regarding whether or not to accord priority to patients for intensive care. Participants were invited to the study by either e-mail or phone. All contacted participants agreed to participate.

Data Collection

We conducted semi-structured interviews at a time convenient for participants, between April 17 and July 15, 2020. After explicit consent from participants, all interviews were audio-recorded. Based on a semi-structured guideline (**Appendix 1**), we asked participants open-ended questions to elicit their (1) general attitude toward the guidelines, (2) perceived general implementation of the guidelines, (3) perceived implementation of specific aspects of the guidelines (e.g., protection of the HCPs involved), (4) the decision-making processes adopted, (5) any challenges experienced in the application of the guidelines, and (6) any factors that facilitated or would facilitate their application. Interviews lasted between 28 and 56 min. The interviewer (FM) was a female researcher and social worker who, at the moment of data collection, was undertaking her postgraduate training in philosophy, and had substantial experience in qualitative research.

Data Analysis

Audio-recordings were transcribed verbatim. One member of the research team (MF) independently conducted an inductive thematic analysis of the transcripts in the original language (Italian) following the six-stage comprehensive thematic analysis approach developed by Braun and Clarke (13). The analysis included reading the transcripts multiple times to familiarize with the text, identifying meaningful quotes regardless of their length, labeling them under broader concepts, organizing the generated labels around more general themes, and creating relationships between them. The last stage of the analysis process was devoted to identifying and highlighting thematic tensions experienced by participants. To validate the results, discussion between the interviewer and the coder took place at the end of the analysis. Disagreements in the interpretation of the findings were resolved through discussion and by making constant reference to the transcripts.

The Ethics Committee of the Canton of Ticino issued a favorable opinion on the study (Req-2020-01307). The objectives of the study and voluntary nature of participation were explained to participants both at first contact (either by phone or by e-mail) and before starting the interview (either in person or over the phone). Oral informed consent was obtained before each interview. Confidentiality was assured by replacing names with numbers and removing any identifying information from the transcripts. All audio recordings, transcripts and participants' personal data were saved on password-protected computers. In this article, we have followed the Standards for Reporting Qualitative Research guidelines (14).

RESULTS

Characteristics of the Sample

The sample was composed of nine physicians, of which seven were men (**Table 1**). The average age was 49.4 years (SD = 8.6; range = 38–64). Five participants were employed as head of unit, one as deputy head of unit, and three as medical directors. Six participants were employed at the ICU, two at the IMCU, and one at the ED. To preserve participants' privacy and confidentiality, only participants' gender and age will be provided after each quote. We extracted four main themes from the data: (1) between a shared source of direction and an individual decision, (2) a matter of collective responsibility, (3) beyond age: a matter of futility, and (4) paternalism's comeback.

TABLE 1 | Characteristics of study participants ($N = 9$).

Variable	N (%)
Gender	
Female	2 (22%)
Age	M = 49.4 (SD = 8.6; range: 38–64)
Specialty	
Intensive care unit	5 (55%)
Emergency	1 (11%)
Critical area	1 (11%)
Internal medicine	1 (11%)
Palliative care	1 (11%)
Role	
Head of unit	5 (55%)
Medical director	3 (33%)
Vice-head of unit	1 (11%)
Years of experience*	M = 23.5 (SD = 8.4; range: 11–39)

Years of experience are counted since obtaining medical degree.

Between a Shared Source of Direction and an Individual Decision

While almost all participants explicitly stated that they welcomed the SAMS guidelines in March 2020, they differed in the way they viewed them. On the one side, three participants viewed the guidelines as a source of direction, legitimization, and protection. As the following participant stated, the guidelines helped the team understand that they were making the right decision for the patient:

> "They [the guidelines] helped us understand that we were choosing correctly." (Participant 5, age range 51–60)

The following participant reported that the guidelines helped him because he felt that the criteria guiding his decision were broadly shared:

> "Criteria help because you don't feel that the limit you set is just your decision, but rather a broadly shared directive." (Participant 3, age range 41–50)

One participant explained that, because decisions on invasive procedures had to be made rapidly, the guidelines legitimized their decisions and ensured physicians' protection:

> "We also felt entitled to make uncomfortable decisions, and especially for us in the emergency room, they were acute decisions and you had to instantly decide whether to intubate or not to intubate. We felt protected when these directives came out." (Participant 4, age range 31–40)

On the other side, four participants stated that the guidelines should only serve as a general framework that is subject to interpretation and changes according to each physician's evaluation. According to the following participant, the attending physician should not only have the ultimate decision based on each patient's unique characteristics but also bear ultimate responsibility for any decisions:

> "I think that the problem is precisely to lean on the single case and that each patient is unique and unrepeatable. Having guidelines helps and takes some of the weight off, but obviously, you have to focus on the individual case and the weight of ethical responsibility cannot be completely removed from the physician." (Participant 6, age range 61–70)

In addition, the following participant felt legitimized in deviating from the guidelines once he understood that they were developed by a group of experts, as if this made the guidelines a "weaker" expert opinion document:

> "It was of help to us to have a scheme even if, at the beginning, it was important to understand where things came from, and this was missing. I can accept anything that is written, but it must be justified. It is a group of experts, then it is an expert opinion, and this was very important to understand how far one could go from these instructions. [. . .] When they talk about emodynamic instability with doses of Noradrenaline. . . because for us any dose of Noradrenaline is for intensive care as we don't have intermediate care, so this was changed immediately, it was very easy." (Participant 9, age range 31–40)

One participant felt a contradiction between the intended goal of the guidelines to provide a direction and the fact that he, as a physician, has the best understanding of the patient's condition:

> "On the one hand they are relieving because there is a frame of reference, on the other hand they were written for the urgency and for a disease that was not known and therefore, they are not like a cooking recipe. However, it gave us the peace of mind of having a framework to refer to. [. . .] The guidelines give us a framework, but WE decide where to be and then apply the directives in that area, and that was the hardest thing. [...] Then they are not as precise as other directives of the Swiss Academy of Medical Sciences are, and it was clear to me that they could not be. At a certain point there is a paradox, because the one who is treating the patient is me and I am the one who knows best how things are going, but they have to give me guidelines, and therefore, it is a bit contradictory. It is not a disease that you know and know what happens if you don't treat it, or what happens if you treat it. There were so many unknowns. . . Around me I heard people criticizing the fact that the guidelines had to be more precise, the age criterion had to be more precise. . . But, in the end, it was clear to me that these guidelines can only be a lighthouse that is most appropriate from an ethical and technical point of view." (Participant 1, age range 41–50)

A Matter of Collective Responsibility

Participants explained that the decision-making process regarding admission to ICUs in both hospitals included asking a second opinion from a senior physician operating in the other Covid-19 hospital. As the following participant reported, this process was justified because it was considered a matter of collective responsibility:

> "It is a matter of collective responsibility: we organize ourselves differently if a patient needs intensive care or not and avoid unpleasant situations." (Participant 9, age range 31–40)

In addition, as the following participant reported, asking for an external, second opinion would ensure that the responsibility would not fall on one individual only, but would be shared and documented:

> "These were the admission criteria and then there are many decisions during the stay in intensive care, but even there we tried to untie the individual physician from the decision making." (Participant 8, age range 41–50)

As the following participants explained, the decision to always include a second opinion was necessary to ensure fairness of the decision-making process:

> "We set up a system whereby if you didn't want to admit a patient to the ICU, you would talk to a physician from the other institution to try to be balanced." (Participant 1, age range 41–50)
> "Such a thing would have been against the principle of justice, because by doing so we would have done something unfair to the patients who would come later." (Participant 6, age range 61–70)

Finally, as the following participant stated, this process was also informed by a shared understanding of the short- and long-term implications of these decisions not only for patients and their families but also for the team:

> "These are very difficult situations, and this is why, in our group of intensivists, we said to ourselves that we risk carrying on our shoulders these very strong decisions for a week, a month, a year. . . And therefore, it must not be the individual who responds. We decided internally that, if I were confronted with such a situation, I would share it with an intensivist from the other hospital. [...] Therefore, with someone not directly involved with the patient's care, in order to have a shared decision and on the other hand with a certain traceability of our decision. . . not that one single individual decides." (Participant 2, age range 51–60)

The same participant added that it is necessary to discuss decisions with an external physician because accepting to rely on criteria that are mandated from above can be dangerous and may threaten individual responsibility:

> "We must be careful to refer to a group of decision makers because there are very dangerous psychological mechanisms, otherwise those things that happened in the Second World War will happen again. . . Everyone feels not responsible because they said that we must kill twenty-five Jews, so I only execute an order. In that case, I am not responsible, and I decide this way because, from above, they have decided that I will take that patient, while the other does not. We have chosen to have another intensivist referent on the

same hierarchical level who does not work here." (Participant 2, age range 51–60)

Beyond Age: A Matter of Futility

When asked about the perceived role of patients' age as an ICU admission exclusion criterion in the decision-making process, all participants reported that age was never considered a factor *per se* and they always relied on a futility rather than a distributive justice principle. The two main reasons they cited are that age is not an absolute but a negative prognostic factor, and that they were never in stage B (Stage A: ICU beds available, but national capacity is limited, and there is reason to believe that, within a few days, ICU beds may become unavailable in Switzerland and transfers to ICUs abroad may not be possible to a sufficient extent; Stage B: No ICU beds available). As the following two participants pointed out:

> "Basically, age does count because it is a negative prognostic factor, but it is not an absolute value. If possible, I would not use age as a killer factor." (Participant 1, age range 41–50)
> "Age as a single criterion has never been considered a killer criterion, luckily, since we have never been in a situation like Lombardy. We have never been in a real state of need. We went as far as to consider the criterion of futility." (Participant 8, age range 41–50)

The core question participants asked themselves was whether admission to the ICU would meet any criteria of medical futility. One participant explained that, following a futility principle, they would ensure that decisions would not change even if resources were available:

> "Even from a medical point of view, if we remove the variable concerning the availability of resources, but only look at the evolution, our suggestion would not probably change. [. . .] Along the way, the perception changed, and we told ourselves that we had to be careful about the resources we had. . . But we also told ourselves that we should do neither useless things nor heroic ones, knowing that we are facing something serious." (Participant 3, age range 41–50)

Participants cited frailty, diagnosis, and prognosis as better criteria compared to age to inform ICU admission decisions:

> "If we remain bound to the numerical aspect of age, we do not get out of it. I have found that a good method is the functional reserve, that is the reserves we have. [...] As the clinicians used to say in the past: such things should not be done now at this age, because they don't have the reserves, not because of age! So, we added more and more the frailty score, which is a score that geriatricians use a lot that shows you that a person who is vulnerable and dependent will never make it. It would be like asking this patient to walk to Mount Bre. This is the mechanism behind: access to intensive care is like asking the patient for something that he or she will never be able to do, so age is relativized because we look at the functional aspect." (Participant 2, age range 51–60)
> "I cannot say that, over the age of eighty, I no longer intubate anyone, but we have differentiated the two, saying that we must put the pathology and prognosis in the perspective of triage. So, these criteria are specific for Coronavirus patients because the prognosis is bad, and the intubation is long. For the others, who are usually here [in the hospital], the criteria are looser." (Participant 3, age range 41–50)
> "Age was one of the elements considered in the evaluation, but frailty and prognosis were much more important because there was a principle of non-maleficence behind it. A very frail patient would not have survived such a long stay in intensive care." (Participant 6, age range 61–70)

Few participants mentioned that they would not feel comfortable in employing an age criterion to refuse ICU admission, but would nevertheless respect the age threshold if they entered phase B, because mortality for patients who are 80+ has been shown to be close to 100%.

> "In the SAMS guidelines age was not so clear a factor, but in those of the Canton age was written and respected, because despite in some countries this limit has not been applied, mortality was practically 100%." (Participant 5, age range 51–60)
> "As a group, we agreed to limit access to intensive care above age 80 because it is known that mortality in or out of intensive care is exactly the same, so there is no gain on expectation of life and this is from an extra-Covid study that has been known for some time." (Participant 9, age range 31–40)

In addition, one of the participants reported that the general population considers age as the main criterion to establish ICU admission priority. As the following participant reported, physicians may not use age as a criterion, but when they confront the patients' families, these will make requests based solely on such a criterion:

> "Personally, I did not use age as a factor, but the family often reported age as a factor. Sometimes they said: "My mom is 90 years old, she lived her life." There was no knowledge about the pathologies she had, but the population considers age as the real point. Others said: "He is only 70 years old." But he had a heart disease, was cirrhotic, etc. So, there is a discrepancy there. Insiders never really considered age, but the population did." (Participant 4, age range 31–40)

Paternalism's Comeback

Participants reported that one of the main challenges they encountered was the difficulty to address the topic of end-of-life and of advance directives with the patients and their families. Some explained that this difficulty is due to cultural reasons:

> "I cannot deny that there have been some difficulties: a cultural difficulty from Ticino, Lombardy, etc., Compared to German-speaking Switzerland, where I worked, we are much more reluctant to discuss these things here. [...] Here, there is always a tendency to discuss these things at the last minute, in a very unprepared fashion, with the desire to make all family members agree. . . And that is something that always causes a big delay, especially in families with many children. We don't have a good culture on that. The population understands some words, like "therapeutic obstinacy," and in fact the idea is to use these words,

but not everyone is really able to understand them." (Participant 4, age range 31–40)

One participant added that the difficulty to address end-of-life issues is also common among HCPs and not only family members:

"Colleagues lack sensitivity on this… They are unable to discuss issues of end of life, how to deal with it… And this is a constant thing." (Participant 5, age range 51–60)

According to half of the participants, the reluctance to discuss end-of-life issues frequently led to situations in which physicians would propose a treatment pathway and families would simply accept it without questioning it. Participants referred to this phenomenon as a form of paternalism:

"Very often, patients told us to decide what we thought, so we assumed a bit of paternalism, that is, a bit of paternalism came back through the window, but in my opinion, it was not wrong. Patients were very different, and relatives too… It's a very strange thing." (Participant 6, age range 61–70)

Most participants reported that paternalism's comeback was due to the emotional burden investing patients and family members, characterized by fear and uncertainty:

"Try to identify yourself with a son or a daughter… Doctor [X] calls home and you don't know who she is, you don't not know what role she has, you don't know if her voice really matches what she is talking about, and she says that your mother or father is very serious… Think about how difficult this is to accept." (Participant 4, age range 31–40)

Participants also reported that the absence of the family members, who could not be close to the patients in the hospital and frequently interact with the care team, accentuated this form of paternalism and prevented a shared decision making approach.

"Who treats the patient? Physicians, nurses, and families, who are also part of the therapy. This is something that we lacked. We lacked the support of the families, the fact of having family members with the patient, who share a journey with the patient, and understand where the patient is going. They themselves told us: "We understand, we must stop, because he cannot make it." And we missed this great help in difficult decisions. We missed one therapeutic element, which is the family." (Participant 5, age range 51–60)

"The absence of family members, which we always asked to come when we saw that the situation was serious… They came, they stayed half an hour and left, not like the usual, when they can come and stay here. Also, the absence of patients' relatives, this loneliness, this fear, in my opinion, influenced the decisions, and I don't know how free these people were and if they were like ten days before getting sick." (Participant 6, age range 61–70)

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DISCUSSION

Allocation of scarce life-saving interventions in accordance with generally accepted ethical principles is a major challenge of the current pandemic and guidelines are available in many countries to provide support for rationing decisions. We aimed to explore how senior physicians involved in the care of Covid-19 patients during the first wave of the pandemic accepted and implemented locally issued guidelines on triage for ICU admission. We found that participants held different views regarding the nature of the guidelines, saw decisions on admission as a matter of collective responsibility, argued that decisions should be based on a medical futility principle rather than an age criterion, and found that difficulties to address end-of-life decisions led to a comeback of paternalism. In the next paragraphs, we contextualize our findings, and interpret their implications accounting for the limitations of the study.

Our finding that some participants viewed the guidelines as a source of protection resonate with the need for hospital leadership to ensure legal safeguard prior to establishing a triage system in order to ensure consistent application of triage protocols (15). In line with other studies conducted in Europe (10), half of our participants were aware of the guidelines but stated that they would adapt them according to their personal expertise and preferences. This is consistent with the argument that triage algorithms and protocols can be useful but can never replace the role of trained intensivists building their decisions on the involvement of multidisciplinary teams (16), and should therefore provide a general framework to be adapted to local health systems (17). However, such a variation in the application of national triage protocols is problematic and might represent a potential source of discrimination, as criteria for exclusion are selectively applied to only some types of patients, rather than to all patients being considered for critical care (18). Indeed, studies showed that reasons for poor compliance with ICU triage guidelines were unfamiliarity with the guidelines and disagreement with the fundamental approach underlying the guidelines (19).

In line with previous evidence, we found that collaborative decision-making facilitated choices on ICU admission (20). Our participants reported having involved external, senior physicians in the decision-making process on whether to accord priority to patients for intensive care. This can be due to awareness of the psychological implications of making ICU admission decisions. Such decisions have been previously described as being extremely difficult and emotionally burdensome, as physicians feel they are making life-death decisions (20–22). Several guidelines have recommended implementing specific programs to enhance HCPs' resilience to cope with the psychological burden triggered by this pandemic (15), and the SAMS state that HCPs are to be protected as far as possible against excessive psychological stress (6). The strategy to discuss ICU triage decisions with external physicians may also be due to participants' awareness that personal attitude may be a key driver of the decision and could jeopardize the fair allocation of limited resources. Variation in intensive care unit admission decision-making due to personal attitudes has been previously found by previous studies (23, 24). Extending responsibility for triage decisions to external decision-makers may also be due to a current controversy on who should have the authority to make such choices, and how physicians should best be supported (25). This is in line with recommendations from a task force of the World Federation of Societies of Intensive and Critical Care Medicine that triage should be led by intensivists considering input from nurses, emergency medicine professionals, hospitalists, surgeons, and allied professionals (16). Previous qualitative studies conducted in lower-middle income countries found that communication between staff constituted an obstacle to good quality care and identification of the critically ill patients (9). In contrast, our participants cited discussion with external physicians as a key facilitator of the decision-making process.

Participants also shared the view that age should not be a criterion for limiting intensive care. This reflects the principle that scarce resources should be fairly allocated regardless of age, sex or gender identity, race or ethnicity, religion, socioeconomic status, and similar individual factors (17, 26, 27), and that priority decisions should be primarily based on medical criteria (19, 28). However, frameworks have been proposed that give individuals who perform tasks vital to the public health response enhanced priority (29). Moreover, ethical dilemmas regarding rationing, allocation, and prioritization are not only a consequence of the severity of the Covid-19 disease and scarcity of life-saving resources, but also of how the concept of justice and other values are interpreted by care teams (30). Our study participants reported to be committed to the rule of rescue over the good of the many (31). This is consistent with the findings of a recent review of the literature which found that age 85+ is one of the least ranked criterion for exclusion (32), but not in line with previous evidence that patient's age had the largest impact at ICU admission (33). Beyond evidence, age represents an area of disagreement also among international triage recommendations (34). Next, criteria to withdrawing life support from one patient to provide it to another were not cited by our participants as reasons of contention, but the literature suggests that more evidence and guidance are needed (18). A recent review of more than one hundred research articles, guidelines and reviews on the topic of ICU resource allocation found that patient preference was the most common reason cited to exclude patients from ICU admission (32).

Interestingly, our participants referred to a revival of the paternalistic model, because they argued that physicians could not always carefully ascertain the patients' and their families' will, due to logistic and emotional barriers, many of which

were unprecedented and conceivably exceptional during the first wave of the epidemic in Southern Switzerland. And yet, previous evidence has shown that end-of-life decisions were perceived as more complex in the absence of family or of information about patients' end-of-life preferences, and when there was time pressure and a lack of training in end-of-life decision-making (21, 35, 36). Studies also found that patients with active advance directives were less likely to be admitted to the ICU (11, 37, 38). To give precedence to respect of a distributive justice principle, our participants reported to have downgraded principles of autonomy and beneficence (39, 40). This is in line with larger quantitative studies which found that patient-related factors were rated higher on their potential to affect decisions than scarcity-related or administrative-related factors (41). Our participants' difficulty in addressing end-of-life issues with patients and their families stresses the importance of providing just-in-time training and simulation sessions for non-ICU clinicians reassigned to work in ICU, to better prepare them for their roles and for addressing sensitive matters (15). Previous studies have identified specific cultural beliefs, values, and communication patterns that can be used to promote cultural competency among practitioners who provide care at end of life (42).

Our results have several potential implications. Since our participants reported to view the guidelines as either an inalterable set of instructions or a general framework apt to changes, national triage guidelines should clarify to what extent protocols can be adapted, which is key for acceptance, adherence, and integration in clinical practice. Furthermore, our results suggest that participants implemented a shared strategy to manage the individual responsibility of making ICU admission decisions (i.e., involving an external, senior physician in the decision-making process). This finding stresses the importance of clarifying issues of authority and responsibility during triaging decisions. A possible solution could be to establish functional roles and responsibilities of the internal personnel and interface agencies or sectors at national, regional, local, facility, and hospital levels, while providing appropriate training of triage staff (43). In addition, we found a shared belief that the age criterion should not be used as a criterion *per se* but as a prognostic factor. Guidelines should better explain the role of such criterion in guiding ICU admission and stay decisions, and provide supporting evidence from the literature. Finally, as a number of barriers make it difficult to ascertain the patient's wishes with regard to emergency treatment and intensive care at an early stage, training should be offered to healthcare staff to address end-of-life issues while campaigns and other activities should be promoted to raise public awareness of the importance of discussing and drafting one's advance directives.

LIMITATIONS AND CONCLUSIONS

Some limitations of our study are worth noting. First, this is a qualitative study conducted in the Italian-speaking Canton of Switzerland with a small sample of participants. While a substantial portion of the senior staff involved in the care of Covid-19 patients during the first wave of the pandemic was included in the study, our results should be generalized to other geographical and cultural contexts with caution. Second, we cannot exclude that participants answered our questions in a way that would be seen socially accepted. To mitigate such possible social desirability bias, we reassured participants that all the information they would share would be kept confidential. Third, the format of the interviews was semi-structured to limit its duration and fit in with the physicians' workload. While this allowed us to maximize our sample and answer our research question in a targeted way, opting for an in-depth format might have led to different results. Fourth, our interviews focused on the first wave of the pandemic, when participants did not have to face decisions on withdrawing intensive care treatment (the "bad" period) (44). Conducting the study during a period of more intense patient influx and higher demand of ICU beds (the "ugly" period) may have led to different results (44), but health services were, nonetheless, functioning close to their maximum capacity.

As cases increase exponentially, the need to optimize rationing decisions and triage of patients with Covid-19 at all health facility levels will intensify. Evidence-based guidelines should seek to address all the questions related to ICU admission, discharge, and triage, including questions regarding the healthcare team's perceived acceptance of the guidelines, and any barriers and facilitators to their implementation (45). Our results stress the importance of sensitizing both healthcare professionals and the general population regarding the intended nature of the guidelines, the benefits of discussing and compiling one's advance directives, and including family members as much as possible in the decision-making process regarding patients' ICU admission and stay. We call for policy makers to intensively engage with diverse groups (citizens, HCPs, ethicists, and disaster medicine experts) in the refinement of the guidelines and for future research to investigate the acceptance of the SAMS guidelines in other Swiss Cantons.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because there are ethical restrictions on sharing a de-identified data set as (1) data contain potentially sensitive information and (2) participants did not provide explicit consent to share indirectly identifiable data. For these reasons, we can only share portions of the de-identified data set. Requests to access the datasets should be directed to Ethics Committee of the Canton of Ticino, tel.: +41 91 814 30 57, e-mail: dss-ce@ti.ch.

ETHICS STATEMENT

The study was reviewed and authorized by the Ethics Committee of the Canton of Ticino. The participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

RM and ML made all the contacts with the participants. FM conducted the interviews. MF and FM led the analytic process

and analyzed the results. MF, FM, and RM contributed to the study design. MF verified the findings of the analysis and wrote the paper. All authors contributed to reviewing the paper.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2021.695231/full#supplementary-material

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Compliance With Protective Behavioral Recommendations in the Outbreak of COVID-19 Among People Working in the Urban-Based Informal Economy in Southern Ethiopia

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Regardless of the advocacies made by the media and numerous organizations about the need for preventing the spread of COVID-19, there still exists a gap as far as compliance to regular implementation of the preventive mechanisms within communities is concerned. The purpose of the present study was, therefore, to examine compliance to personal protective behavioral recommendations to contain the spread of COVID-19 among urban residents engaged in the informal economic activities in Wolaita Sodo town, Southern Ethiopia. A cross-sectional study design was used where quantitative data were collected through the survey research method. Three hundred and eighty-four participants of the urban-based informal economy were randomly selected and contacted in their own natural settings with an interviewer-administered questionnaire. Data were inserted into SPSS software for analysis that involved both descriptive and inferential statistics, including frequency and percentage distributions, binomial and multinomial logistic regressions. The results of the research indicated that only 35.4% of the respondents regularly wore a mask. In addition, 54.9% of the survey participants disclosed that they do not clean their hands with disinfectants after touching objects under circumstances where they cannot get access to water and soap. Moreover, the most commonly reported reason of respondents for non-compliance to regular wearing of a mask has been its inconvenience or discomfort (62.8%), followed by the need to appear indifferent because most people around them do not wear a mask (25.2%). Furthermore, experiences of the respondents of regularly wearing a mask are significantly associated with regular attendance of the media regarding the preventive mechanisms of COVID-19 (OR = 0.224; $P < 0.001$; 95%C.I: 0.109–0.460), knowledge of someone ever infected by COVID-19 (OR = 0.402; $P < 0.05$; 95%C.I: 0.190–0.851), the belief that COVID-19 causes a severe illness (OR = 0.444; $P < 0.05$; 95%C.I: 0.201–0.980), and perception of the likelihood of dying as a result of infection by COVID-19 (OR = 0.374; $P < 0.01$; 95% C.I: 0.197–0.711). The authors have found a low level of compliance to the

recommended safety measures, especially wearing of masks. It is, therefore, important that continued efforts of raising awareness should be done by all the concerned bodies. Above all, urban safety net programs that aim at keeping such social groups at home, at least during the critical wave of the pandemic, should also be strengthened.

Keywords: compliance, COVID-19, informal economy, washing hands, wearing mask

INTRODUCTION

It is widely reported that the COVID-19 pandemic has entered a new stage with rapid spread in almost all the countries of the world claiming the lives of more than 3 million people (1). It is expected, and of course, practically observed in some parts of the world that the healthcare systems face shortages of personnel and medical equipment supplies to treat the critically ill during the pandemic (2). Therefore, countries worldwide are encouraged to assess the existing community engagement structures and to use community engagement approaches to support contextually specific, acceptable, and appropriate COVID-19 prevention and control measures (3, 4). In addition, all members of the society must understand and practice measures for self-protection and for the prevention of transmission of infection to others (5, 6).

In developing countries such as Ethiopia where access to COVID-19 vaccine to every citizen is difficult to achieve, the most important way to control the disease among the populations is regular hand washing, regular wearing of face masks, the use of disinfectants, and the prevention of contact with the face and mouth after interacting with the infected environment (7). In response to the outbreak and spread of COVID-19, many countries have been using a combination of containment and mitigation activities with the intention of delaying major flow of patients and decreasing the demand for hospital beds, including different levels of contact tracing and isolation; avoiding touching of eyes, nose, and mouth; routine cleaning and disinfection of the environment; wearing face mask; social distancing; preparation of health systems for an outpour of severely ill patients who require isolation, oxygen, and mechanical ventilation; strengthening health facility infection prevention and control, with special attention to nursing home facilities; and postponement or cancelation of large-scale public gatherings (5, 6).

Nevertheless, regardless of the advocacies made by the media and numerous organizations about the need for preventing the spread of the pandemic, including the various ways of transmission, there still exists a gap as far as compliance to regular implementation of the preventive mechanisms within communities is concerned (8). Although many countries have been taking different preventive measures, some of these interventions became ineffective in stopping or at least reducing the fast spread of the pandemic which continued claiming millions of lives (9). According to Reference (6), the indications for personal protective equipment should be based on many circumstances, including the setting, target audience, risk of exposure, and the transmission dynamics of the pathogen. In addition, the overuse or misuse of personal protective equipment will have a further impact not only on its effectiveness of preventing the pandemic, but also in inducing shortages on the supply, and hence on its accessibility to the rest of the population.

Findings of previous researches (10–13) undertaken in Ethiopia reveal a mix of both high and low knowledge of people toward COVID-19. A study by (8) found that more than half (54.11%) of the research participants have inadequate knowledge about the prevention of COVID-19 in which sex, age, residence, educational status, experiences of seeking information from healthcare workers, social media, and mass media are the factors affecting such knowledge among the study population. On the other hand, another study undertaken in Addis Ababa, Ethiopia, by Desalegn et al. (14) found a positive attitude held among most (60.7%) of the respondents.

The presence of a strong relationship between the perceived credibility of information sources about COVID-19 and the engagement of people in self-protective behaviors has been found by Lep et al. (15). According to the study, research participants tend to exhibit relatively lower trust on the information from mass media, social media, politicians, and political institutions whereas they tend to trust information from medical professionals and scientists. It was suggested that information about COVID-19 from credible sources would lead to better protective behaviors among the public, which will help to contain the spread of the pandemic. Tomczyk et al. (16) found high compliance (25%) with all recommendations; public compliance (51%), with high compliance regarding public but not personal behaviors; and low compliance (24%) with most behavioral recommendations that help to contain the infection of COVID-19 where low compliance is associated with male sex, younger age, and lower public stigma.

In addition to its impact on the health of workers and their families, COVID-19 adversely affects specific societal groups who are more vulnerable to labor market conditions, especially unprotected workers, including the self-employed, casual, and gig workers, who are likely to be disproportionately hit by the virus as they do not have access to paid or sick leave mechanisms, and are less protected by conventional social protection mechanisms and other forms of income smoothing (17). According to Reference (18), the populations most at risk are those that depend heavily on the informal economy, occupy areas prone to shocks, have inadequate access to social services or political influence, have limited capacities and opportunities to cope and adapt, and

Abbreviations: SPSS, Statistical Package for Social Sciences; BA, Bachelor of Arts; BSc, Bachelor of Science; CSA, Central Statistical Agency; C.I, Confidence Interval; ERC, European Research Council; ILO, International Labor Organization; OR, Odds Ratio.

people who have no or limited access to technologies. In this regard, self-employed people working in areas having no regular income in Ethiopia, including youth and women involved in the informal economic activities, motorbike or taxi service providers, shoe-cleaners, lottery ticket sellers, and people engaged in all forms of daily labor can be considered as social groups most affected by the pandemic. Members of such social groups are double burdened not only because of their susceptibility to the disease but also that their livelihood is more likely to be severely affected by the pandemic during periods of economic and social lockdowns. The objective of the present research was, therefore, to explore the patterns of compliance to the use of protective devices (non-pharmaceutical interventions) to contain the spread of COVID-19 among the urbanites working in the informal economies in Southern Ethiopia.

METHODS AND MATERIALS

Research Design

A cross-sectional study was carried using quantitative research approach. Through the survey method, quantitative data were collected from a sample of people working in the urban-based informal economy.

Selection of Research Participants

The target group of the present research is the "urban poor" who are not able to earn a regular income as a result of working in the informal urban economy. Members of such social groups must always go to work to secure their daily bread. In doing so, these individuals should either stand amid or frequently move around relatively large gatherings of people, which puts them at a higher risk of infection by COVID-19. Moreover, living in the highly unpredictable tomorrow due to the irregular income does not allow members of this group to stay at home to protect themselves even during the critical periods of the pandemic. Therefore, it is important that they adhere to at least some of the personal protective behavioral recommendations such as wearing a mask and cleaning hands. Consequently, we have considered the inclusion of people commonly known to work in the urban informal economies including motorbike or taxi service providers, shoe-shine boys and girls, daily laborers, street vendors, lottery ticket sellers, and women working in the daily small markets (locally known as *gullit*). In order to determine the sample size, the researchers applied Cochran's (1977) formula for calculating the sample size of an unknown population as:

$$n = \frac{z^2 \times p(1-p)}{e^2} = 1.96^2 \times 0.5(1-0.5)/0.05^2 = 384$$

where n is the sample size, z is the selected critical value of desired confidence level, p is the estimated proportion of an attribute that is present in the population. Then, the final sample units were chosen on the basis of probability proportionate to the size sampling technique. The major inclusion criteria for sample selection were as follows: being the permanent resident of Wolaita Sodo town (having an urban residential background), employment or self-employment in the informal urban economy as a source of livelihood, and willingness to participate in the survey. From the 384 questionnaires used to collect data, 379 items were found to be correctly completed, making the response rate 98.7%.

Research Method and Source of Data

Primary data were gathered mainly through the use of the survey research method. A self-administered questionnaire was prepared in English and then translated in to the local (*Amharic*) language. Then, data collectors, all of whom were instructors of sociology and civics and ethical education departments, were trained about the items in the questionnaire and all the things to be done in the process of data collection. Following this, a permission letter was secured from the concerned body of Wolaita Sodo University. Next, a pilot test was undertaken to prove the compatibility of the questionnaire on 5% of respondents having similar characteristics with the actual survey population. On the basis of feedback and comments obtained from the pilot survey, slight improvements were made to the instrument of data collection. The same questionnaire, having similar items, was duplicated according to the already determined sample size. Finally, the actual data collection activity was held in April and May 2021 under the supervision of the principal investigator. Respondents were told to freely raise any question that is unclear to them. The reliability of the instrument was checked through internal consistency of the response items using Cronbach's α, whereas both content and face validity measures were used to maintain their validity.

Instrument Design

The questionnaire that served as an instrument of data collection in our research was partly taken from the studies of Lep et al. (15), Tomczyk et al. (16), and Zewude and Habtegiorgis (19) and adapted to the purpose at hand, whereas most other questions were developed by the researchers. The questionnaire mainly consists of two sections, namely, questions seeking the socio-demographic background of respondents and questions aimed at assessing the attitude of the research participants and experiences of implementing the personal protective behavioral recommendations. The first (background) section of the tool comprises variables such as sex, age, education, marital status, and the presence of children. In addition, this part also includes questions that aim at measuring perceptions of the respondent of COVID-19 and their previous contact or experience with the disease. For instance, respondents were asked if they believe that COVID-19 really exists in Ethiopia in general and the study area in particular, if they knew someone ever infected by or died of COVID-19, whether they believe that they can be infected by COVID-19, and their belief about whether they are likely to die from COVID-19, all with response categories of (1) Yes and (2) No.

The second section of the questionnaire aimed at measuring the experiences of the respondents in practicing the common personal protective behavioral recommendations. It involves questions such as "Do you regularly wear a mask?," "Do you frequently wash your hands after touching objects?," and "Where you cannot get access to water and soap, do you

TABLE 1 | Socio-demographic background of respondents.

Variables	Categories	Frequency (%)
Sex	Male	218 (57.5%)
	Female	161 (42.5%)
Educational status	Never attended school	49 (12.9%)
	Primary (1–8) level	96 (25.3%)
	Secondary (9-12) level	112 (29.6%)
	College diploma	58 (15.3%)
	BA/BSc degree	64 (16.9%)
Marital status	Never married	224 (59.1%)
	Married	136 (35.9%)
	Divorced	12 (3.2%)
	Widowed	7 (1.8%)
Do you have children?	Yes	127 (33.5%)
	No	252 (66.5%)
Do you regularly attend media regarding the preventive mechanisms of COVID-19?	Yes	258 (68.1%)
	No	121 (31.9%)
Do you believe that COVID-19 really exists in Ethiopia?	Yes	274 (72.3%)
	No	105 (27.7%)
Do you believe that COVID-19 really exists in Wolaita Sodo town (study area)?	Yes	214 (56.5%)
	No	165 (43.5%)
Do you know someone ever infected by COVID-19?	Yes	76 (20.1%)
	No	303 (79.9%)
Do you know someone died of COVID-19?	Yes	60 (15.8%)
	No	319 (84.2%)
Do you think that you can be infected by COVID-19?	Yes	169 (44.6%)
	No	210 (55.4%)
Do you think that COVID-19 causes severe illness?	Yes	262 (69.1%)
	No	117 (30.9%)
Do you think that you are likely to die if infected by COVID-19?	Yes	165 (43.5%)
	No	214 (56.5%)
	Total	379 (100%)

clean your hands with disinfectants after touching objects?" all with response categories of "yes" and "no". Moreover, the section also includes questions that intend to assess the extent to which respondents believe in the effectiveness of the protective behavioral recommendations. For instance, we have asked respondents "Do you believe that a mask can prevent the transmission of COVID-19?" and "Do you believe that cleaning hands immediately after touching any object can prevent COVID-19?" with response categories of "yes" and "no". Furthermore, with the expectation of non-compliance to the behavioral recommendations, potential reasons for such non-compliance were also included in the section.

Method of Data Analysis

The questionnaires returned from the field were first checked against completeness. The correctly completed ones were then inserted into a statistical package for social sciences software. Data generated from the software were presented using both descriptive and inferential statistical tools. Data analysis was conducted using statistical techniques, including percentages, frequency distributions, and logistic regression analysis. The descriptive statistical techniques were mainly used to present data regarding the frequency and percentage distribution of responses pertaining to the socio-demographic characteristics of the respondents, level of compliance to the protective behavioral recommendations, reasons for non-compliance, and beliefs about the protective behavioral recommendations. The logistic regression test was used to examine the association between the socio-demographic characteristics of respondents and their compliance to the protective behavioral recommendations. In this case, independent variables having a significance level ≤ 0.05 were considered to be significantly associated with the dependent variable, and those having a significance level >0.05 were considered as not significantly associated.

RESULTS

The mean age of respondents has been found to be 24.6 ($SD = 6.87$). According to the data presented in **Table 1**,

TABLE 2 | Distribution of compliance to personal protective behavioral recommendations.

Variables	Categories	Frequency (%)
Do you believe that a mask can prevent the transmission of COVID-19?	Yes	267 (70.4%)
	No	112 (29.6%)
Do you regularly wear a mask?	Yes	134 (35.4%)
	No	245 (64.6%)
Do you believe that cleaning hands immediately after touching any object can prevent COVID-19?	Yes	277 (73.3%)
	No	102 (26.9%)
Do you frequently wash your hand after touching objects?	Yes	216 (57%)
	No	163 (43%)
Where you can't get access to water and soap, do you clean your hand with disinfectants after touching objects?	Yes	171 (45.1%)
	No	208 (54.9%)
	Total	379 (100%)

57.5% of research participants are men and 42.5% are women. Furthermore, the educational background of the respondents reveals that most (29.6%) have attended secondary level education, followed by primary level education (25.3%), BA/BSc degree (16.9%), and college diploma (15.3%). It is also found that 59.1% of respondents have never been married and 35.9% are married. In addition, 66.5% of the survey participants did not have children during the time of data collection. Moreover, the majority (68.1%) of respondents disclosed that they regularly attend any media regarding the preventive mechanisms of COVID-19. It is also found that 72.3% of research participants believe that COVID-19 really exists in Ethiopia, whereas 56.5% of them believe that COVID-19 exists in the study area. Above all, most (79.9%) of the respondents disclosed that there is no one they know who was ever infected by COVID-19 and 84.2% replied that they do not know anyone who died of COVID-19. Data have also shown that 55.4% of respondents do not think they will be infected by COVID-19, whereas 56.5% of them perceive that they are not likely to die if infected by COVID-19. Importantly, 69.1% of respondents think that COVID-19 causes a severe illness.

Compliance With Preventive Behavioral Recommendations

Table 2 presents the frequency and percentage distributions of responses regarding the compliance of the respondents to the personal protective behavioral recommendations to contain the spread of COVID-19. Accordingly, though 70.4% of the research participants believe that a mask is effective in terms of preventing the transmission of COVID-19, only 35.4% of respondents reported to regularly wearing the mask. Furthermore, 73.3% of respondents believe that cleaning hands immediately after touching any object can prevent COVID-19 and 57% of them disclosed that they frequently wash their hands after touching objects. Moreover, 54.9% of respondents reported that they do not clean their hands with disinfectants after touching objects under circumstances where they cannot get access to water and soap.

According to the data presented in **Table 3**, the most commonly reported reason of respondents for non-compliance to regular mask wearing has been its inconvenience or discomfort (62.8%), followed by the need to appear indifferent because most people around them do not wear a mask (25.2%), the belief that COVID-19 does not really exist (22.5%), the belief that COVID-19 is not that serious concern in the work or residential area of the respondents (19.8%), and perceptions of lower risk of infection by COVID-19 (19.8%). In addition, lack of access to water and soap (58.3%), the belief that COVID-19 does not really exist (35.4%), the belief that COVID-19 is not that serious concern in the work or residential area of the respondents (25.1%), and reasons related to religion (14.3%) have constituted the main reasons that respondents do not frequently wash their hands after touching objects. Above all, lack of access to hand sanitizer/alcohol (58.5%), the belief that COVID-19 does not really exist (28.5%), the belief that COVID-19 is not that serious concern in the work or residential area of the respondents (25.1%), perceptions of lower risk of infection by COVID-19 (20.8%), the absence of belief that cleaning hands with disinfectants prevents infection (19.8%), and lack of adequate information (12.1%) have been found to be the main reasons for not cleaning hands with disinfectants after touching objects among the respondents.

Table 4 presents data pertaining to the extent (frequency) to which respondents comply with the major protective behavioral recommendations to contain the spread of COVID-19. It is found that 64.9% of respondents reported to occasionally wearing a mask and 9.2% said they never wore a mask. Moreover, 51.7% of respondents occasionally engage in frequent hand hygiene practices whereas 37.7% reported to regularly keep hand hygiene. Furthermore, 42.5% of the survey participants replied that they never keep adequate physical distance during public gatherings. Around 54.4% of the respondents disclosed habits of covering mouth and nose with flexed elbow or tissue when coughing or sneezing. In addition, 57.8% of the research participants never stay at home when they are feeling sick or symptomatic of COVID-19. It is also shown that 36.1% always participate in mass events (attending religious/cultural rituals, business/work meetings, social gatherings, etc.) while 58.6% of

TABLE 3 | Reasons of the respondents for non-compliance to personal protective behavioral recommendations.

Reasons	N (%)	% of Cases
Reasons for not regularly wearing a mask		
Due to its inconvenience/discomfort	162 (30.9%)	62.8%
I just want to appear indifferent because most people around me do not wear mask	65 (12.4%)	25.2%
I can't afford to buy one because of its cost	19 (3.6%)	7.4%
I don't believe that a mask can prevent infection	39 (7.4%)	15.1%
I don't believe that COVID-19 really exists	58 (11.0%)	22.5%
I believe that I have adequate natural immunity	6 (1.1%)	2.3%
I believe that I am not at risk of being infected by COVID-19	51 (9.7%)	19.8%
I believe that I can easily withstand the illness if infected by the disease	6 (1.1%)	2.3%
Lack of adequate information about it	14 (2.7%)	5.4%
Reasons related to belief/religion	33 (6.3%)	12.8%
COVID-19 is not that serious concern in my work or residential area	51 (9.7%)	19.8%
Other reasons	17 (3.2%)	6.6%
No reason	4 (0.8%)	1.6%
Total	525 (100.0%)	203.5%
Reasons for not frequently washing hands after touching objects		
Lack of access to water/soap	102 (29.3%)	58.3%
I avoid touching of objects from the outset	7 (2.0%)	4.0%
I don't believe that COVID-19 really exists	62 (17.8%)	35.4%
I don't believe that washing hands can prevent infection	23 (6.6%)	13.1%
Because I use chemical disinfectants instead of washing my hands	20 (5.7%)	11.4%
I believe that I have adequate natural immunity	6 (1.7%)	3.4%
I believe that I am not at risk of being infected by COVID-19	34 (9.8%)	19.4%
I believe that I can easily withstand the illness if infected by the disease	1 (0.3%)	0.6%
Lack of adequate information	11 (3.2%)	6.3%
Reasons related to belief/religion	25 (7.2%)	14.3%
COVID-19 is not that serious concern in my work or residential area	44 (12.6%)	25.1%
Other reasons	7 (2.0%)	4.0%
No reason	6 (1.7%)	3.4%
Total	348 (100.0%)	198.9%
Reasons for not cleaning hands with disinfectants after touching objects		
Lack of access to hand sanitizer/alcohol	121 (30.3%)	58.5%
I avoid touching of objects from the outset	13 (3.3%)	6.3%
I don't believe that COVID-19 really exists	59 (14.8%)	28.5%
I don't believe that cleaning hands with disinfectants prevents infection	41 (10.3%)	19.8%
I believe that I have adequate natural immunity	5 (1.3%)	2.4%
I believe that I am not at risk of being infected by COVID-19	43 (10.8%)	20.8%
I believe that I can easily withstand the illness if infected by the disease	5 (1.3%)	2.4%
Lack of adequate information	25 (6.3%)	12.1%
Reasons related to belief/religion	21 (5.3%)	10.1%
COVID-19 is not that serious concern in my work or residential area	52 (13.0%)	25.1%
Other reasons	10 (2.5%)	4.8%
No reason	4 (1.0%)	1.9%
Total	399 (100.0%)	192.8%

them do it occasionally. Above all, 34.3% reported to always shake hands, 32.2% of respondents disclosed that they would always touch their face, and 62.2% of them do the same occasionally. Occasional eating of raw/fresh foods (raw meat, vegetables, etc.) before cooking or washing has also been reported among 57% of the research participants.

Factors Affecting Compliance to Preventive Behavioral Recommendations

The data presented in **Table 5** show that the experiences of the respondents of regular mask wearing are significantly associated with regular attendance of the media regarding the preventive mechanisms of COVID-19 (OR = 0.224; $P < 0.001$; 95% C.I:

TABLE 4 | Extent of practices and compliances with the major protective behavioral recommendations.

Variables/questions	Categories of responses	Frequency (%)
Wearing a (medical) mask	Always	98 (25.9%)
	Occasionally	246 (64.9%)
	Never	35 (9.2%)
Frequent hand hygiene (use hand sanitizers, recurrent washing of hands with soaps, etc.)	Always	143 (37.7%)
	Occasionally	196 (51.7%)
	Never	40 (10.6%)
Keeping adequate (up to 2 meters) physical distance during gatherings	Always	34 (9%)
	Occasionally	184 (48.5%)
	Never	161 (42.5%)
Keeping your mask clean (by washing or replacing it with a new one)	Always	176 (46.4%)
	Occasionally	162 (42.7%)
	Never	41 (10.8%)
Covering mouth and nose with flexed elbow or tissue when coughing or sneezing	Always	136 (35.9%)
	Occasionally	206 (54.4%)
	Never	37 (9.8%)
Staying at home when feel sick/symptomatic	Always	42 (11.1%)
	Occasionally	118 (31.1%)
	Never	219 (57.8%)
Shaking hands with any person	Always	130 (34.3%)
	Occasionally	184 (48.5%)
	Never	65 (17.2%)
Touching one's face (i.e., eyes, nose, and mouth)	Always	122 (32.2%)
	Occasionally	232 (61.2%)
	Never	25 (6.6%)
Eating raw/fresh foods (raw meat, vegetables, etc.) before cooking or washing	Always	23 (6.1%)
	Occasionally	216 (57%)
	Never	140 (36.9%)
Participating in mass events (attending religious/cultural rituals, business/work meetings, social gatherings, etc.)	Always	137 (36.1%)
	Occasionally	222 (58.6%)
	Never	20 (5.3%)
Total		379 (100%)

0.109–0.460), knowledge of someone ever infected by COVID-19 (OR = 0.402; $P < 0.05$; 95% C.I: 0.190–0.851), the belief that COVID-19 causes severe illness (OR = 0.444; $P < 0.05$; 95% C.I: 0.201–0.980), and perception of the probability of dying as a result of infection by COVID-19 (OR = 0.374; $P < 0.01$; 95% C.I: 0.197–0.711).

Results of binary logistic regression coefficients presented in **Table 6** reveal that the experiences of the research participants of regularly washing hands after touching objects are significantly associated with regular attendance of the media regarding the preventive mechanisms of COVID-19 (OR = 0.467; $P < 0.05$; 95% C.I: 0.256–0.852), having children (OR = 0.347; $P < 0.05$; 95% C.I: 0.137–0.878), the belief that frequently washing hands helps to prevent the transmission of COVID-19 (OR = 9.871; $P < 0.001$; 95% C.I: 4.245–22.954), and age (OR = 1.050; $P < 0.05$; 95% C.I: 1.003–1.100).

The data presented in **Table 7** show coefficients of multinomial logistic regression pertaining to the association between the socio-demographic characteristics of the respondents and the frequency by which they practice protective behavioral recommendations. Accordingly, it is found that respondents with a better educational status (OR = 0.035; $P < 0.05$; 95% C.I: 0.002–0.595), those who think that they can be infected by COVID-19 (OR = 58.942; $P < 0.001$; 95% C.I: 7.703–451.023), and those who believe that wearing mask prevents the transmission of COVID-19 (OR = 7.732; $P < 0.005$; 95% C.I: 1.332–44.893) tend to regularly wear a mask.

Moreover, respondents with a better educational status (OR = 0.133; $P < 0.05$; 95% C.I: 0.021–0.839), who believe that wearing a mask prevents the transmission of COVID-19 (OR = 5.550; $P < 0.001$; 95% C.I: 1.549–19.882), and those who think that they are likely to be infected by COVID-19 (OR = 4.113; $P < 0.05$; 95% C.I: 1.253–13.503) are found to regularly engage in frequent hand hygiene (use hand sanitizers, recurrent washing of hands with soaps, etc.) practices. Above all, experiences of regularly shaking hands with someone have been found to be significantly associated with thinking that one is likely to be infected by COVID-19 (OR = 0.278; $P < 0.05$;

TABLE 5 | Binary logistic regression showing association between socio-demographic characteristics and practices of regular mask wear.

Variables	Categories	Do you regularly wear a mask?			Logistic Regression statistics		
		Yes	No	Total	*P*-value	OR	95% C.I.
Regular attendance of media	Yes	121	137	258	0.000***	0.224	0.109–0.460
	No	13	108	121			
Sex	Male	87	131	131	0.118	0.647	0.375–1.116
	Female	47	114	161			
Marital status	Never married	84	140	224	0.195	0.167	0.011–2.505
	Married	47	89	136			
	Divorced	2	10	12			
	Widowed	1	6	7			
Have children	Yes	46	81	127	0.257	0.571	0.217–1.504
	No	88	164	252			
Education	Never attended school	15	34	49	0.765	1.167	0.424–3.207
	Primary level	25	71	96			
	Secondary level	41	71	112			
	College diploma	24	34	58			
	BA/BSc degree	29	35	64			
Believe that COVID-19 exists in Ethiopia	Yes	118	156	274	0.890	0.939	0.385–2.288
	No	16	89	105			
Believe that COVID-19 exists in the study area	Yes	97	117	214	0.684	1.167	0.554–2.457
	No	37	128	165			
Knowledge of someone ever infected by COVID-19	Yes	44	32	76	0.017*	0.402	0.190–0.851
	No	90	213	303			
Know someone died of COVID-19	Yes	30	30	60	0.446	1.373	0.607–3.103
	No	104	215	319			
Think can be infected by COVID-19	Yes	95	74	169	0.082	0.565	0.297–1.074
	No	39	171	210			
Believe that COVID-19 causes severe illness	Yes	119	143	262	0.044*	0.444	0.201–0.980
	No	15	102	117			
Think die if infected by COVID-19	Yes	93	72	165	0.003**	0.374	0.197–0.711
	No	41	173	214			
Believe mask prevents COVID-19	Yes	120	147	267	0.276	0.641	0.288–1.427
	No	14	98	112			
Age					0.127	0.959	0.909–1.012

****P<0.001, **P<0.01, *P<0.05.*
OR, odds ratio; C.I, confidence interval.

95% C.I: 0.102–0.759) and the belief that a mask can prevent the transmission of COVID-19 (OR = 0.146; $P < 0.01$; 95% C.I: 0.036–0.590).

DISCUSSION

During the period where COVID-19 pandemic has entered into a new stage of very fast spread across the world, the healthcare systems of most countries face shortages of personnel and medical equipment supplies to treat the critically ill (2). Therefore, all members of the society must understand and practice measures for self-protection and for prevention of transmission of infection to others (5, 6). Especially, in developing countries, such as Ethiopia, where access to COVID-19 vaccine to every citizen is difficult to achieve, the most important way to control the disease among the populations is the regular wearing of mask, regular hand washing, the use of disinfectants, and the prevention of contact with the face and mouth after interacting with the infected environment (7). Regardless of the advocacies made by the media and numerous organizations about the need for preventing the spread of the pandemic, including the various ways of transmission, there still exists a gap as far as compliance to regular implementation of the preventive mechanisms within communities is concerned (8). The purpose of the present study was to examine the experiences of compliance to personal protective behavioral recommendations (non-pharmaceutical interventions) to contain the spread of COVID-19 among urban residents

TABLE 6 | Binary logistic regression showing association between the socio-demographic characteristics of the respondents and practices of frequent hand wash.

Variables	Categories	Do you regularly wear a mask?			Logistic Regression statistics		
		Yes	No	Total	*P*-value	OR	95% C.I.
Regular attendance of media	Yes	168	90	258	0.013*	0.467	0.256–0.852
	No	48	73	121			
Sex	Male	119	99	218	0.097	1.575	0.921–2.694
	Female	97	64	161			
Have children	Yes	66	61	127	0.025*	0.347	0.137–0.878
	No	150	102	252			
Education	Never attended school	25	24	49	0.549	0.733	0.266–2.023
	Primary level	53	43	96			
	Secondary level	66	46	112			
	College diploma	29	29	58			
	BA/BSc degree	43	21	64			
Believe that COVID-19 exists in Ethiopia	Yes	174	100	274	0.289	1.604	0.669–3.844
	No	42	63	105			
Believe that COVID-19 exists in the study area	Yes	139	75	214	0.724	1.145	0.540–2.429
	No	77	88	165			
Know someone ever infected by COVID-19	Yes	52	24	76	0.361	0.693	0.316–1.522
	No	164	139	303			
Know someone died of COVID-19	Yes	40	20	60	0.993	1.004	0.435–2.314
	No	176	143	319			
Think can be infected by COVID-19	Yes	128	41	169	0.258	0.682	0.351–1.324
	No	88	122	210			
Believe that COVID-19 Causes serious illness	Yes	175	87	262	0.331	0.708	0.352–1.422
	No	41	76	117			
Think die if infected by COVID-19	Yes	122	43	165	0.360	0.738	0.386–1.413
	No	94	120	214			
Believe mask prevents COVID-19	Yes	184	83	267	0.464	0.739	0.329–1.661
	No	32	80	112			
Believe that frequently cleaning hands protects COVID-19	Yes	199	78	277	0.000***	9.871	4.245–22.954
	No	17	85	102			
Age					0.036*	1.050	1.003–1.100

****P<0.001, **P<0.01, *P<0.05.*
OR, Odds Ratio; C.I, Confidence Interval.

working in the informal economic activities in Wolaita Sodo town, southern Ethiopia.

The results of the research indicated that only 35.4% of the respondents regularly wore a mask. In addition, 54.9% of survey participants disclosed that they do not clean their hands with disinfectants after touching objects under circumstances where they cannot get access to water and soap. Furthermore, 64.9% of respondents reported to occasionally wearing a mask and 9.2% said they never wore a mask. Moreover, 51.7% of respondents occasionally engage in frequent hand hygiene practices, whereas 37.7% reported to regularly keep hand hygiene. Furthermore, 42.5% of survey participants replied to never keep adequate physical distance during public gatherings. The finding of the present study that there is a low practice of wearing mask contradicts the findings of previous studies undertaken in other parts of the world. For instance, Zhong et al. (20) found that nearly all of the participants (98.0%) wore masks. In addition, Azlan et al. (21) revealed that most participants were taking precautions such as avoiding crowds (83.4%) and practicing proper hand hygiene (87.8%) in the week before the movement-control order started. He also found 51.2% practices of wearing face masks, which the authors regarded as a "less common" practice. Furthermore, Czeisler et al. (22) found widespread adherence to recommended COVID-19 mitigation strategies in the United States of America, in which 79.5% reported the behavior of always or often keeping ≥6 feet apart from others. Tomczyk et al. (16) found high compliance (25%) with all recommendations; public compliance (51%), with high compliance regarding public but not personal behaviors; and low compliance (24%) with most behavioral recommendations that help to contain infection of COVID-19, where low compliance is associated with male gender, younger age, and lower public stigma.

TABLE 7 | Multinomial logistic regression coefficients.

Wearing a (medical) mask		*P*-value	OR	95% CI
Regularly	Education	0.020*	0.035	0.002–0.595
	Think can be infected by COVID-19	0.000***	58.942	7.703–451.023
	Believe mask prevents COVID-19	0.023*	7.732	1.332–44.893
Occasionally	Education	0.047*	0.066	0.004–0.966
	Think can be infected by COVID-19	0.000***	41.572	5.817–297.105
	Believe that COVID-19 Causes serious illness	0.019*	0.188	0.046–0.758
	Think die if infected by COVID-19	0.080*	0.279	0.067–1.167
	Believe mask prevents COVID-19	0.001**	15.989	3.318–77.061
Regularly	Frequent hand hygiene (use hand sanitizers, recurrent washing of hands with soaps, etc.)			
	Education	0.032*	0.133	0.021–0.839
	Think can be infected by COVID-19	0.020*	4.113	1.253–13.503
	Believe mask prevents COVID-19	0.008**	5.550	1.549–19.882
Occasionally	Marital status	0.000***	1.965	4.688–8.235
	Education	0.007**	0.080	0.013–0.498
	Believe mask prevents COVID-19	0.013*	4.216	1.359–13.080
Shaking hands with any person				
Regularly	Think can be infected by COVID-19	0.012*	0.278	0.102–0.759
	Believe mask prevents COVID-19	0.007**	0.146	0.036–0.590

*The reference category is: never; ***P<0.001, **P<0.01, *P<0.05.*
OR, Odds Ratio; C.I, Confidence Interval.

The findings of the study reveal a clear gap between the widely held belief about self-protection against COVID-19 and practices of implementing the recommended safety measures. For instance, 70.4% of respondents believe that a mask is effective in terms of preventing the transmission of COVID-19, and 73.3% of respondents believe that cleaning hands immediately after touching any object can prevent COVID-19. The findings of the present study that most research participants have a positive attitude toward the recommended protective measures are consistent with the findings of previous studies. A study undertaken in Addis Ababa, Ethiopia by Desalegn et al. (14) found a positive attitude held among most (60.7%) of the respondents. Another study Yonas Akalu et al. (13) stated that more than half (54.11%) of the research participants have inadequate knowledge about the prevention of COVID-19 in Ethiopia. Moreover, Alrubaiee et al. (23) concluded that the majority of health care providers in Yemen had adequate knowledge, optimistic attitude, moderate level of anxiety, and high-performance in preventive behaviors, 69.8, 85.10, 51.0, and 87.70%, respectively, toward COVID-19. Al-Hanawi et al. (24) also found that Saudi residents, especially women, have good knowledge, positive attitudes, and good practices toward COVID-19.

The results of our study have also revealed that the experiences of regular mask wearing of the respondents are significantly associated with regular attendance of the media regarding the preventive mechanisms of COVID-19, knowledge of someone ever infected by COVID-19, the belief that COVID-19 causes severe illness, and perception of the probability of dying as a result of infection by COVID-19. Moreover, it is also found that the experiences of research participants of regularly washing hands after touching objects is significantly associated with regular attendance of the media regarding the preventive mechanisms of COVID-19, having children, the belief that frequently washing hands helps to prevent the transmission of COVID-19, and age. Bashirian et al. (25) stated that threat and coping appraisal were predictors of protection motivation to conduct COVID-19 preventive behaviors. A study conducted by Shahnazi et al. (26) indicated that female sex, perceived barriers, perceived self-efficacy, fatalistic beliefs, perceived interests, and living in the city had the greatest preventive behaviors from COVID-19, respectively. Moreover, the presence of a strong relationship between perceived credibility of information sources about COVID-19 and engagement of peoples in self-protective behaviors has been found by Lep et al. (15). Tomczyk et al. (16) argued that low compliance to protective behavioral recommendations is associated with male gender, younger age, and lower public stigma. According to the health belief model, the key variables that determine the health behavior of an individual include perceived severity of an illness, whether the person thinks he is susceptible to certain ill-health conditions, perceived benefits that the person is likely to obtain as a result of engaging in a prohealth behavior, perceived barriers, the extent to which the individual is exposed to external events that prompt a desire to make a health change, and the self-efficacy of a person of bringing a health-related change (27–29).

CONCLUSIONS

The main objective of the present research was to assess the level of compliance to the personal protective behavioral

recommendations (non-pharmaceutical interventions) among the urban dwellers in Wolaita Sodo town working in the informal economic activities. The results of the study indicated that people engaged in the urban informal economy have a positive attitude toward the necessity of practicing protective behaviors that help to contain the spread of COVID-19. Nevertheless, we have found a low level of compliance to the recommended safety measures, especially wearing masks. The commonly identified reasons for the low compliance have been feelings of discomfort when wearing a mask, believing that COVID-19 does not exist at all or that it is not a serious concern in the residential or workplaces of the respondents, and perceptions of being at a lower risk of infection. Moreover, the study has also revealed that regular mask wearing among the research participants is significantly influenced by the experiences of regularly attending the media, knowledge of someone infected by COVID-19, the belief that COVID-19 causes a severe illness, and perception of the probability of dying as a result of infection by COVID-19. The findings of the study have great implications, especially when it comes to vulnerability and public health concerns. As in the case of the participants of the present study, urban dwellers whose livelihood predominantly relies on the informal economy characterized by irregular and unpredictable income should always remain outside of their homes in order to secure daily bread. These societal groups do not have the means to stay at home, even on witnessing the symptoms of COVID-19. This and many other characteristics of the group put them relatively at a higher risk of infection. It is therefore important that continued efforts of raising awareness should be done by all the concerned bodies. In addition, the government and other agencies in the area should devise mechanisms by which members of such group can get free access to the basic protective devices. Above all, urban safety net programs that aim at keeping such social groups at home at least during the critical wave of the pandemic should also be strengthened.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Wolaita Sodo University Ethics approval committee. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

BZ reviewed literatures and wrote the research proposal. TH, MT, WS, and BM carried out fieldwork and drafted the manuscript. All contributed to the conception, analysis and writing of the manuscript. All authors read and approved the final manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2021.716814/full#supplementary-material

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Screening High-Risk Groups and the General Population for SARS-CoV-2 Nucleic Acids in a Mobile Biosafety Laboratory

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The Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) pandemic has challenged public health systems worldwide. Therefore, large-scale testing capacity is extremely important diagnosis and exclusion diagnosis. However, fixed laboratories are limited or far away from remote areas. Fortunately, MBS-Lab is characterized by high mobility and rapid on-site detection of SARS-CoV-2 nucleic acid. MBS-Lab was first used in northern Australia during a melioidosis outbreak in 1997. The MBS-Lab and a well-trained diagnostic team were dispatched to Dongchang District, Tonghua City, Jilin Province, China to assist the SARS-CoV-2 virus screening and diagnosis on January 17, 2021. Altogether, 93,952 oropharyngeal swabs samples were collected and tested among the high-risk groups and the general population in Dongchang District. Two single samples were identified as positive in the second turn screening. In the second turn screening, 3 mixed samples (10 in 1) were identified as positive; 10 mixed samples were identified as positive in the third turn screening. By resampling again, one and four cases were identified as positive, respectively. The positive cases were properly isolated and treated in hospital and avoided to visit family members, friends, colleagues and any other persons. Through this way of large-scale screening, human-human spread of SARS-CoV-2 can be effectively avoided. In addition, all staff members strictly executed multiple safety precautions and reduce exposure risks. In the end, none of the staffs was infected with SARS-CoV-2 virus or other pathogens. As an emergency facility for infectious disease control, the MBS-Lab satisfies the requirements of ports and other remote areas far from fixed laboratories and supplements the capabilities of fixed laboratories.

Keywords: SARS-CoV-2, nucleic acid, real-time PCR, bio-protection, mobile biosafety laboratory

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INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has challenged public health systems worldwide. As of 21 June 2021, the total number of cases worldwide is over 178 million and the total number of deaths is 3.8 million (1). Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) has been widely used to qualitatively and quantitatively determine SARS-CoV-2 gene targets (2). However, the construction of new fixed molecular diagnostic laboratories takes time. This delay affects the prevention and control of SARS-CoV-2. Thus, a mobile biosafety laboratory (MBS-Lab) is urgently needed to cope with emergent epidemics.

MBS-Lab was first used in northern Australia during a melioidosis outbreak in 1997 (3). At that time, only a simple sample collection kit and light microscope were inside the lab. With the development of MBS-Lab, the fully self-reliant vehicles are equipped with the latest molecular diagnostic and biocontainment equipment (4, 5). Mobility is the main characteristic of MBS-Labs as it enables quick on-site screening. Many research and development centers have created MBS-Labs of various biosafety levels, including P2, P3, and P4. Recently, many MBS-Labs have been used for epidemiological research, infectious disease control and other health emergencies. From March 2014 to March 2015, a unit of the European consortium used the European Mobile Laboratory to diagnose Ebola virus disease and malaria in Guéckédou, Guinea (6). Starting in October 2017, the Praesens Foundation developed an all-terrain MBS-Lab and tested it in Senegal for 6 months under various ecological conditions, demonstrating the capability for effective field diagnostics. The MBS-Lab and staff were deployed to manage a dengue outbreak in Louga city from 25 October to 23 November 2017 (7). Therefore, the MBS-Lab can be a novel solution assisting in rapid disease outbreak response and monitoring.

In this study we aimed to evaluate the detection capability and safety of MBS-Lab in dealing with SARS-CoV-2 pandemic response. A total of 236,717 samples from high-risk groups and the general population were tested. All staff strictly followed safety precautions to reduce exposure risks. In the end, no staff were infected with SARS-CoV-2 virus or other pathogens. Thus, the MBS-Lab may play a significant role in SARS-CoV-2 outbreak response through offering accurate and timely diagnostics.

MATERIALS AND METHODS

Ethical Considerations

Ethical approval to conduct the study was provided by the First Hospital of Jilin University Ethics Committee (2021-296) and all participants had signed an informed consent form.

Laboratory Biosecurity

The MBS-Lab included a biosafety cabinet with a high-efficiency particulate air filter. The classification of the biosafety cabinet including class II was listed in **Table 1**. The Class II type B biosafety cabinets have hard-ducted and vent outdoors, Class II type A2 biosafety cabinets vent outdoors, and Class II type A1 biosafety cabinets vent indoors. The Class II type A (A1 and A2) biosafety cabinets have 70% airflow recirculating, Class II type B1 biosafety cabinets have 30% airflow recirculating, while Class II type B2 biosafety cabinets have 0% airflow recirculating (8). In MBS-Lab, Class II type A2 biosafety cabinet was used. The above conditions provided a safe environment for handling pathogens. Moreover, there was an ultraviolet germicidal lamp inside the biosafety cabinet, an ultraviolet disinfection lamp on the ceiling and mobile sterilization car in every area and corresponding buffer room. There was an autoclave ($>121^{\circ}$C and >205 kPa) in the corresponding buffer room of area II. The samples and personal protective equipment were autoclaved to avoid contamination of personnel and the environment. In addition, fumigation with hydrogen peroxide (H_2O_2) was regularly conducted within the truck and the workspace of the MBS-Lab. Moreover, all staff who worked in the MBS-Lab wore level 3 personal protective equipment (PPE), including work clothes, N95 protective masks, disposable hats, goggles, gloves, disposable shoe covers, face shields, medical protective clothing and disposable operation gowns. Other biosecurity measures include strengthening laboratory management, carrying out biosafety training, strengthening the protection awareness of staffs, developing specific standard operating procedures, establishing risk assessment and contingency procedures, monitoring fever or symptoms of staffs daily. Staffs were trained to have an appropriate sequence for safely donning and doffing PPE and practiced hand hygiene procedures. The disposal of laboratory waste was autoclaving and soaking with appropriate disinfectants. ultraviolet or air sterilizers were implemented in biosafety cabinets, every area and corresponding buffer rooms.

Study Setting

This study was carried out in eight mobile biosafety laboratories in Dongchang District. Before the official start, all staff received appropriate training, including (1) the standard operation procedure for entering and leaving the laboratory, (2) biosafety practices and procedures, (3) preventive measures for occupational exposure, (4) risk evaluation and precautions, and (5) data analysis and material management. The maintenance technicians and drivers also received job-specific training. Each team had five staff members. Area I accommodated one staff member, area II accommodated two staff members and area III accommodated one staff member. The last member worked as a liaison and was responsible for communication between the laboratory and external staff.

Study Population and Sampling

The study population included both high-risk groups and the general population. High-risk groups refer to exposure and proximity to the confirmed COVID-19 cases. This study included male and female of all ages who provided written informed consent to participate. However, for children under 18 years of age, parents or legal guardians signed the consent forms. After collecting on-site samples, we combined the samples from 10 individuals or one family in a single test tube for the general population. For high-risk groups, single samples rather than mixed samples were used.

Mobile Biosafety Laboratory Workflow

Reagent Preparation Area

The reagent preparation area is also called area I. It contained a biosafety cabinet, a pressure meter, a thermometer, a hygrometer, a telecommunication system and a biohazard waste container. A 4°C refrigerator was used for reagent storage. In addition, a -20°C freezer was used to store frozen reagents (**Figure 1**).

The Nucleic Acid Extraction Kit (Lot 510160, Zybio, Chongqing, China) was used to extract the SARS-CoV-2 RNA *in vitro* using a magnetic bead method. The Nucleic Acid Extraction Kit includes extraction reagent I, extraction reagent II, the elution buffer, proteinase K and the magnetic beads solution. If any

TABLE 1 | Classification of the biosafety cabinet.

Class	Type	Protection	Open mode	Inflow velocity	Airflow	Exhausted air
I	N/A	Personnel environment	Open front	Negative pressure	0% recirculating	Exhausts through HEPA filter to room or outdoors
II	A1	Personnel environment sample	Open front	75 ft/min	70% recirculating	Vent indoors
	A2			100 ft/min	70% recirculating	Vent outdoors
	B1			100 ft/min	30% recirculating	Hard-ducted vent outdoors
	B2			100 ft/min	0% recirculating	Hard-ducted vent outdoors
III	N/A	Personnel environment sample	Enclosed	100 ft/min	0% recirculating	Hard-ducted vent outdoors

crystals were present in extraction reagent I, the reagent was not used until they were fully dissolved. The aluminum wrapping film was removed from extraction reagent I, extraction reagent II and the elution buffer. The magnetic rod sleeves in the 96-well reagent kit were filled with magnetic beads. Proteinase K was mixed well to prepare it for use, and 15 μL was added to each well in the extraction reagent I plate. After thawing at room temperature, the components were mixed by oscillation and centrifuged at 8,000 rpm for several seconds before use. All reagents were unpacked, dissolved at room temperature and transferred to area II through the delivery window.

Specimen Preparation Area

The specimen preparation area is also called area II. It contained a biosafety cabinet, pressure meter, thermometer, hygrometer, telecommunication system, constant-temperature incubator, nucleic acid-isolation system and a biohazard waste container. Area II was equipped with a 4°C refrigerator for reagent storage and a −20°C freezer for frozen reagents (**Figure 1**).

In this area, the main operations were receiving samples, extracting nucleic acids and adding them to PCR tubes. The Detection Kit (Lot 2021007, Da'an, Guangzhou, China) was used to qualitatively detect the SARS-CoV-2 ORF1ab and N genes using a RT-qPCR assay. The Detection Kit includes the SARS-CoV-2 PCR reaction solution A, reaction solution B and positive and negative controls. After thawing at room temperature, the components were mixed by oscillation and centrifuged at 8,000 rpm for several seconds before use. PCR reaction solution A (17 μL) and PCR reaction solution B (3 μL) were added to each PCR tube. We used the nucleic acid-isolation system EXM6000 (Zybio Inc., Chongqing, China) to automatically isolate and purify the SARS-CoV-2 RNA.

Amplification Detection Area

The amplification detection area is also called area III. It included a pressure meter, thermometer, hygrometer, telecommunication system, amplification instrument, computer and biohazard waste container (**Figure 1**).

In this area, the main operations were nucleic acid amplification and analysis of the products. We used the amplification instrument Gentier 96E/96R (Xi'an Tianlong Science and Technology Development Co., Ltd., Xi'an, China) for amplification.

Testing Report and Analysis

The positive control is pseudovirus containing 2019-nCoV target fragments and 2019-nCoV internal control gene fragments (RNase P gene). The negative control is 2019-nCoV internal control gene fragments (RNase P gene). Negative controls required no Cq (quantification cycle) values or obvious amplification curve for *N* gene and *ORF1ab* gene and a Cq ≤ 25 for internal control gene. Positive controls required Cq-values ≤ 22 for *N* gene and *ORF1ab* gene. The above requirements were applied at the same time for each experiment.

Results were considered negative when there was a Cq-value > 30 or no Cq-value for *N* gene, a Cq-value > 30 or no Cq-value for *ORF1ab* gene and a Cq-value ≤ 30 for internal control gene. Results were considered positive when there was a Cq-value ≤ 30 for *N* gene and a Cq-value ≤ 30 for *ORF1ab* gene with no amplification curve for internal control gene. A retest was required for a Cq-value ≤ 30 for *N* gene and a Cq-value > 30 or no Cq-value for *ORF1ab* gene with or without an amplification curve for internal control gene. A retest was also required for a Cq-value > 30 or no Cq-value for *N* gene and a Cq-value ≤ 30 for *ORF1ab* gene with or without an amplification curve for internal control gene. In addition, a retest was required for a Cq-value > 30 or no Cq-value for *N* gene and a Cq-value > 30 or no Cq-value for *ORF1ab* gene with or without an amplification curve for internal control gene. If the retest result of *N* gene or *ORF1ab* gene was positive (Cq-value ≤ 30) and internal control gene was positive (Cq-value ≤ 30), the specimen was considered positive for SARS-CoV-2. If the retest results of *N* gene and *ORF1ab* gene were both negative (Cq-value > 30 or no Cq-value) and internal control gene was positive (Cq-value ≤ 30), the specimen was considered negative for SARS-CoV-2. If the retest results of *N* gene, *ORF1ab* gene and internal control gene were all negative (Cq-value > 30 or no Cq-value), the sampling and testing processes were repeated.

Staff Members and Worksite Layout

The team contained seven staff: one external contact, one infection control practitioner, one dedicated driver and four scientists, each engaged in specialized tasks (**Table 2**). One member worked as an external contact and was in charge of communications between staff in the laboratory and external staff. He or she coordinated between the local community and the laboratory, with roles including sample reception, data analysis and release of results.

FIGURE 1 | Layout of main devices in the mobile biosafety laboratory. (1) External view; (2) area I; (3) area II; (4) area III; (5) laboratory refrigerator; (6) constant-temperature incubator; (7) nucleic acid-isolation system; (8) biohazard safety equipment; (9) telecommunication system, pressure meter, thermometer and hygrometer.

TABLE 2 | Overview of the mobile biosafety laboratory diagnostic team and tasks.

Team role	Number of staff	Tasks
External contact	1	Communication between laboratory and external staff, sample reception, data analysis and release of results
Scientists	1	Area I (reagent preparation, recordkeeping, checking reagents, and consumable supplies)
	2	Area II (sample reception, serial numbering of samples, sample dosing, RNA extraction, storage of positive and negative controls, recordkeeping)
	1	Area III (nucleic acid amplification and analysis)
Infection control practitioner	1	Supervision and guidance to ensure that safety standards were strictly followed, monitoring the health condition of each staff member and assessing the risk of infection
Driver	1	Stabilizing the vehicle, setting up the laboratory, sterilization of lab trash, solving minor technical issues related to the vehicle and equipment, ensuring water and electricity supply and security of the environment around the laboratory

The staff member in area I filled in records including the humidity and temperature of area I, the refrigerator temperature and the usage of the biosafety cabinet and checked reagents and the supply of consumables. The staff members in area II kept records of daily experimental processes.

After completing each round of testing, cleaning of the laboratory was performed. Each day, MBS-Lab, PPE and the equipment inside were sterilized for three times. Instrument surface, floor and table was wiped and disinfected with preparing fresh 2,000 mg/L chlorine for 30 min each time. Then, chlorine was subsequently removed as it is caustic and may damage equipment. Seventy percentage Alcohol was used to wipe down the metal surfaces (9). In addition, the ultraviolet lamps in the biosafety cabinet, area II and the corresponding buffer room were turned on for 1 h in order to disinfect the air. The infection control practitioner monitored, observed and guided the implementation of the core infection control system. In the end, a 6 h sufficient formaldehyde stifling had diffused to sterilize the lab thoroughly.

Quality Control

The detection of SARS-CoV-2 nucleic acid requires extreme detection accuracy. Quality control is of great importance. Thus, it is necessary to establish a system of documentation to ensure SARS-CoV-2 nucleic acid testing results accurate. In China, we followed the principle of ISO 15,189 standard, including quality manuals, procedure files, operation instructions, and record forms. In addition, two kinds of external quality assessment (EQA) program were participated, China's Ministry of Health and Jilin province. Two positive controls and two negative controls were done every batch. Inter-laboratory comparison is with the nucleic acid testing base of the Central Hospital of Tonghua City and the First Hospital of Jilin University.

RESULTS

Epidemiology

The infection began to spread from an asymptomatic carrier for products sale in Dongchang District, Tonghua City, Jilin Province, China. The asymptomatic carrier called together many old people. According to the Notification of Tonghua Municipal Health Committee, the number of confirmed cases in Tonghua City grew to 123, including 30 cases with light type, 83 cases with common type, 7 cases with severe type, 3 cases with critical type until 20 January 2021. On Jan 18 the small city is in lockdown. At that time, the first round was completed by the nucleic acid testing base of the Central Hospital of Tonghua City. Then, the number of daily new cases started to increase. As of March 3, 2021, 320 laboratory confirmed COVID-19 cases with only 1 death.

Performance of the Mobile Biosafety Laboratory

The lab was powered by lithium-ion batteries. The batteries could be charged by a diesel generator and the local electrical grid, with automatic switching to ensure reliable and real-time power supply. In the event of a sudden power outage, a dedicated uninterruptible power supply was able to support experimental instruments, automatic control systems, illumination and ventilation for at least 45 min. The overall power supply system guaranteed the proper functioning of the laboratory. In addition, the MBS-Lab was equipped with an internal communications network and achieved safe communication channels between staff. There was also a video surveillance system. The status and data such as temperature, humidity, pressure, power system monitoring, local time, test reports and error logs were displayed on computer screens. The doors were interlocking. The setup allowed screening of suspected SARS-CoV-2 cases within 4 h after sample reception, while providing protection for humans, specimens and the environment.

The laboratory was equipped with an advanced ventilation system. The ventilation system used 100% fresh air purified by filters and the air renewal rate was up to 25 times per h. In addition, the pressure was reduced step-by-step, for instance, 15 Pa in area I, 10 Pa in the area I buffer room, −5 Pa in the area II buffer room, −10 Pa in area II, −10 Pa in the area III buffer room and −15 Pa in area III. This cascade of low pressure ensured that the air flow was unidirectional from the outside to the inside. The air cleanliness class was seven inside the lab.

Biosafety Risk Management

The MBS-Lab was specifically designed to handle SARS-CoV-2. It was able to protect humans and the environment from

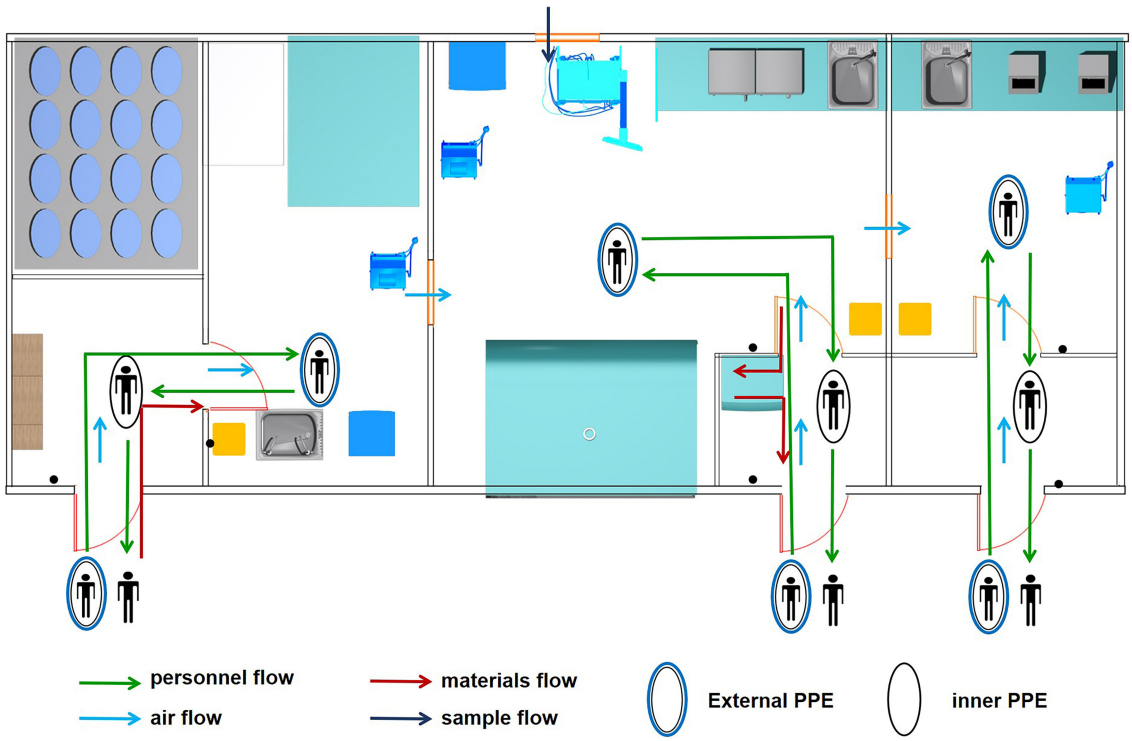

FIGURE 2 | Four flows involved in biosafety risk. Personnel, air, sample and material flows were the main components of biosafety risk in the mobile biosafety laboratory.

TABLE 3 | Samples and test results from 28 September to 11 November 2014.

Round	Date	Single samples tested/positive(‰)	Mixed samples (10 in 1 or one family in one) tested/positive (‰)	Resamples tested/positive (%)	Total samples tested	Total persons tested
Second	20 January 2021 to 22 January 2021	1,923/2 (1.04‰)	3,647/3 (0.82‰)	30/1 (3.33%)	5,600	38,393
Third	25 January 2021 to 27 January 2021	18/0 (0)	47,473/10 (0.21‰)	30/4 (13.33%)	47,521	102,676
Fourth	29 January 2021 to 31 January 2021	0/0	40,831/0(0)	0/0	40,831	95,648

exposure to the virus due to the safety equipment, facility design and laboratory practices. There were four flows (personnel, air, samples and materials) involved in the biosafety risk (**Figure 2**).

Under normal conditions, at most two staff worked in each room of the MBS-Lab to avoid affecting air flow. Before entering the MBS-Lab, all staff wore level 3 protection PPE. After finishing their tasks, staff took off their PPE layer by layer to reduce contamination. Furthermore, a seven-step hand-washing method was strictly followed. Staff then showered off-premises.

Samples were brought into area II through the external sample hatch with a pressure of −10 Pa. Other sterile materials were brought in through the personnel flow. Lab waste was transmitted to the area II buffer room and autoclaved using indicator tape.

Laboratory Testing Results

There were in all four rounds related to SARS-CoV-2 nucleic acid screening. The first round was completed by the nucleic acid testing base of the Central Hospital of Tonghua City. Because of the excessive amount of work, the MBS-Lab and a trained diagnostic team were dispatched to assist with screening and diagnosis on 17 January 2021 and joined in starting at the second round. The SARS-CoV-2 nucleic acid screening results are presented in **Table 3**.

In the second round, 5,600 samples from the high-risk groups and the general population were tested from 20 to 22 January 2021. Two single samples and three mixed samples (10 in 1) were identified as positive. By resampling from indicated patients again, 3 mixed samples (10 in 1) yielded 30 single samples. Thirty single samples were tested and only one was identified as positive.

TABLE 4 | The Cq-value of positive samples.

Positive samples	Cq-value		
	ORF1ab gene	*N* gene	Internal control gene
102422116721117	28.715	27.383	20.168
1018787901211F	27.473	25.246	20.074
10646744755809	26.184	28.418	20.231
104682244736074	27.452	23.510	20.027
10211801279300	28.745	27.301	20.340
12866101835273	24.523	26.401	20.052
10789430218546	26.770	28.553	20.131

In the third round, 47,521 samples were tested from 25 to 27 January 2021. All 18 single samples were identified as negative while 10 mixed samples (one family in one) were identified as positive. By resampling again, the 10 mixed samples (one family in one) yielded 30 single samples. These 30 single samples were tested, and four cases were identified as positive. In the fourth round, 40,831 samples were tested from 29 to 31 January 2021. All mixed samples (one family in one) were identified as negative. At the end of every round, the focus was turned to immediately isolating positive cases (**Table 4**). The positive cases were isolated and treated in hospital, avoiding visits family members, friends, colleagues and others.

DISCUSSION

In this study, a total of 93,952 samples were tested from 20 to 31 January 2021. The average sample turnaround for each round is 3 days. Three samples were positive in the second round, while four samples in the third round. There is no positive sample in the fourth round. The detectability and safety of MBS-Lab were evaluated in screening SARS-CoV-2 nucleic acids among high-risk groups and the general population. As an emergency facility for infectious disease control, the MBS-Lab satisfies the requirements of ports and other remote areas far from fixed laboratories and supplements the capabilities of fixed laboratories.

One limitation of our study is that we only tested one type of clinical sample. Testing of samples from multiple sites, including bronchoalveolar lavage fluid, nasal swabs, pharyngeal swabs, sputum, fiber bronchoscope brush biopsies, feces or blood, can improve the sensitivity of RT-qPCR for the diagnosis of SARS-CoV-2 infection (10). This can reduce false-negative test results. To screen more individuals, we mixed 10 individual oropharyngeal swabs into one tube as one sample to test the general population. For high-risk groups, individual samples were tested.

Another limitation of the lab is lack of a −80°C freezer inside the lab. For short-term storage (within 1 day), samples were stored in a 4°C freezer in area II. However, for long-term storage, samples should be stored in a −80°C freezer. The samples were packaged carefully, and after surfaces were disinfected with 0.25% chlorine-containing disinfectant they were transported to the Central Hospital of Tonghua City nearby.

Screening test results are important for the management of both infected asymptomatic and symptomatic individuals. The isolation of positive cases can prevent human-to-human transmission of SARS-CoV-2. Two negative results for oropharyngeal swabs can be regarded as an indicator that isolation is not necessary. Thus, the sensitivity and specificity of the test results are crucial. Currently, RT-qPCR is the gold standard method for the diagnosis of SARS-CoV-2 (11). The primary analytical methods focus on quantitative responses and cycle number determination. The Cq-value is the point when the fluorescence intensity grows above the background level and crosses a predetermined threshold value. Our diagnostic algorithm has a suggested Cq-value of 30. However, false-positive or false-negative results might exist, where the true number of infected individuals is smaller or larger than the number of positive tests, respectively. False-positive results are mainly from contamination with other pathogens and exogenous or endogenous interfering substances. At that time, time was limited and the task is heavy. It was uncertainty when control materials from the College of American Pathologists (CAP) could get through China Customs. So, two kinds of external quality assessment (EQA) program were participated, China's Ministry of Health and Jilin province. In EQA of Jilin province, there were 5 controls (2021101, 2021102, 2021103, 2021104, 2021105) to detect *ORF1ab* and *N* genes. The results we examined were consistent with the expected results, 2021101, 2021103, 2021105 were positive and 2021102, 2021104 were negative. In EQA of China's Ministry of Health, there were 5 controls (202111, 202112, 202113, 202114, 202115). The results we examined were consistent with the expected results, 202111, 20212, 202113, 202114 were positive, and 202115 were negative. Thus, reagent preparation and sample dosing were conducted in the biosafety cabinet. In addition, areas I, II and III and the biosafety cabinet were exposed to ultraviolet radiation periodically to eliminate nucleic acid contamination. At this point, SARS-CoV-2 has spread extensively for nearly 1 year, and the virus is prone to mutations. Scientists have identified 198 filtered recurrent mutations in the SARS-CoV-2 genome. Moreover, three sites in the *ORF1ab* gene were characterized as having a particularly large number of recurrent mutations (>15 events) (12). Therefore, genetic mutation of SARS-CoV-2, especially in the *ORF1ab* or *N* genes, may lead to false-negative results. In order to investigate the mutation of *N* genes, 31,421 SARS-CoV-2 genome samples were collected on July 23, 2020. Through computing the mutation rate and mutation h-index, the authors have found that *N gene* is one of the most non-conservative genes in the SARS-CoV-2 genome. This study assume that *N gene* is particularly prone to mutations (13). In addition, RT-PCR is apt to show false-negative results during the incubation period and recovery phase. A retrospective study described 1,014 infected patients and found an estimated 41% false-negative rate with RT-PCR diagnostic tests (14).

There are four biosafety levels defined by the CDC (15). CDC has permitted to handle suspected or confirmed COVID-19 patient clinical specimens in BSL-2 facilities with enhanced work

practices (16, 17). Thus, in specimen preparation area (area II), we used BSL-2 facilities with enhanced work practices, while in the reagent preparation area (area I) and amplification detection area (area III), we used BSL-2 facilities. Because all samples have been inactivated (18).

We collected oropharyngeal swabs rather than nasopharyngeal swabs to screen for SARS-CoV-2 in this study. The oropharyngeal swabs are less likely than the nasopharyngeal swabs to yield positive results (19). Luo et al. demonstrated that the sensitivity of oropharyngeal swabs was only 71% with one test, yet the sensitivity of oropharyngeal swabs reached 92.19% with a second round (20). Thus, to increase the sensitivity of oropharyngeal swabs for the rRT-PCR test, we conducted three rounds of screening within 10 days.

We mixed 10 oropharyngeal swabs in one tube for testing. In the second round of screening, three mixed samples were identified as positive; 10 mixed samples were identified as positive in the third round of screening. However, after resampling again, only one and four cases were identified as positive in the second and third rounds, respectively. Theoretically, if one mixed sample (10 in 1) is identified as positive, after resampling again, 10 single samples are tested, of which at least one should be positive. In other words, three mixed samples were identified as positive in the second round of screening; at least three of the 30 resampled single samples would be expected to be positive. Nevertheless, only one such sample was identified as positive, and the exact reasons for this are not known. Although relevant research is not available, we can speculate on possible causes. Due to the stage of infection, the viral load after resampling may be so low that the virus cannot be detected. Thus, further study is needed on the causes.

MBS-Labs have been successfully used to control Ebola virus disease and malaria in Guéckédou, Guinea (6), Ebola virus disease near Freetown, Sierra Leone, South Africa (4), a dengue outbreak in Louga city from 25 October to 23 November 2017 (7), whereas challenges still remain. The first challenge of MBS-Lab is lack high-level biosafety laboratories. No more than 70 BSL-4 laboratories have been established all over the world (21). Thus, the capacity of handle highly pathogenic microbes is limit. Secondly, due to the workplace is always in remote locations, there is no enough significant infrastructure to use, such as the refrigeration equipment, analysis equipment, sophisticated operational equipment. Thirdly, it is short of well-trained and experienced specialists. Although professional teams have been established in some countries, a relatively complete, independent management and professional group is in short supply in SARS-CoV-2 outbreak. In addition, the affairs of logistical requirements are another challenge, including accommodations, transportation into staffs, medication, food and clean water, access to electricity and security personnels (22).

As an emergency facility for infectious disease control, the MBS-Lab is characterized by high mobility and rapid on-site detection. It can detect the nucleic acids of SARS-CoV-2 and other pathogenic microorganisms. The MBS-Lab satisfies the requirements of ports and other remote far away from fixed laboratories for on-site inspection. Thus, the MBS-Lab acts as a key supplement to fixed laboratories. It is believed that the development prospects of the MBS-Lab will continue to improve, playing a greater role in disease control and prevention.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethical approval to conduct the study was provided by the First Hospital of Jilin University Ethics Committee (2021). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

ZG, JH, and JX drafted the main manuscript, performed the data analysis, were responsible for guiding and supporting the experiments, and manuscript revisions. ZG, JH, JX, LL, and YS planned and performed experiments. ZG, JH, LL, and JX were responsible for experimental design. All authors contributed to the article and approved the submitted version.

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Acceptability of COVID-19 Certificates: A Qualitative Study in Geneva, Switzerland, in 2020

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Immunity certificates related to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) have been under discussion since the beginning of the pandemic with conflicting opinions. In order to identify arguments in favor of and against the possible implementation of documents certifying immunity of an individual based on serological testing, we developed a qualitative study in Geneva, Switzerland. The study took place between two lockdowns with a sense of semi-normalcy during summer 2020 in Switzerland but at a time when no vaccine was available and seroprevalence was below 21%. Eleven focus groups with members of the public and 14 semi-structured interviews with stakeholders were conducted between July and November 2020, with a total of 68 participants with an age range between 24 and 77 years. Interviews and focus groups transcripts were coded with the ATLAS.ti CAQDAS. Few participants considered immunity certificates based on serological testing as an acceptable public health measure. Major concerns included the reliability of scientific data related to COVID-19 immunity and serological testing potential re-infection as well as the possibility that the use of certificates could result in deleterious outcomes. Discrimination, counterfeiting, incitement for self-infection, invasion of the private sphere, violation of personal integrity, and violation of medical secrecy were perceived as the major risks. Benefits of immunity certificates were more perceived when in relation to vaccination, and included gains in medical knowledge and protection in certain contexts involving leisure or work-related activities. The consequences of implementing immunity certificates are numerous, and the acceptability by the general population has to be considered when engaging in such policy. Even if the results provide a snapshot of arguments discussed around immunity certificates based on serological testing before the implementation of the COVID-19 vaccine, most of the issues discussed are central in the current debates about vaccination certificates.

Keywords: immunity certificates, COVID-19, anti-SARS-CoV-2 serology, social acceptability, qualitative study, public health policy

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INTRODUCTION

"Immunity passport," "risk-free certificate," "release certificate," "immunity certificate," "antibody(ies) certificate," "COVID-19 immunity-based licenses," many terms are employed to name a document aimed to certify immunity of an individual against severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the virus causing COVID-19 (1–3). In theory, such

a document—often compared with the yellow fever certification—would guarantee that "an individual has been infected and is purportedly immune to SARS-CoV-2" [(3) p. 1595]. Although antibodies and immunity against SARS-CoV-2 are starting to be better understood, they remain uncertain to date (3, 4). In 2020, when no vaccine was available, some countries were considering using a certification status based on anti-SARSCoV-2 as an alternative measure to prevent lockdowns and/or to relax restrictive measures (1, 3–6). Currently, with the COVID-19 vaccine rollout, conversation has intensified over this subject with immunity certificates seen as a solution to free individuals from social restrictive distancing regulations (5). Some governments see in this strategy a way to alleviate public health measures and to pave the way to normalcy, similar to a pre-pandemic state. Therefore, immunity certificates are perceived as useful to avoid additional lockdowns, to further individual freedom and end physical restrictions, to resume activities and restore economic markets by opening workplaces and facilitating travel, to enable close social interactions while mitigating complications from infection especially for some individuals whose work involves close interactions with "vulnerable" people and/or patients, to have access to facilities such as nursing homes, to socialize or even to offer psychological support to individuals, while protecting public health and healthcare services (3, 5).

For both types of certificates (natural or vaccine-acquired immunity), discussions about their implementation are dominated by ethical arguments (7). Indeed, if in 2020 the considerations to implement them were based on seroprevalence testing, in 2021 the debate is centered on vaccine certificates with vaccination programs initiated in many countries. At the time of the study, debates focused only on immunity certificates based on serological testing. Arguments in favor of immunity certificates were to pursue the "least infringement" public health principle or the "least restrictive alternative" for individuals (1, 8). Concerns against their implementation were related to the small number of people with a positive serological test, as evidenced in a Geneva-based study in June and December 2020 (6, 9), the reliability of scientific data to date (the presence of antibodies is to this day not seen as an accurate indicator of sterilizing immunity); equitable and legal challenges such as the risk of discrimination; violation of liberties; falsification; negative impact on behaviors and nonstandard applications (1, 3–5, 8). Additionally, risk-taking by individuals with a positive antibody test may increase the probability of transmission (1, 3, 4, 10). Even the term "immunity" seemed controversial when discussing natural immunity and could generate a "false sense of security" (5). At the time of publication, several of these issues remain unsolved, and discussions shifting toward vaccination certificates present similar arguments.

The objective of this qualitative study is to identify arguments in favor of and against the possible implementation of immunity certificates related to SARS-CoV-2 in Switzerland, and to pave the way to a policy-based discussion. We conducted interviews with stakeholders working in Switzerland and focus groups with members of the Geneva population to collect diverse opinions at a time when the public debate was limited. The study took place in Summer and Autumn 2020, between two lockdowns with a sense of semi-normalcy during summer 2020 in Switzerland, with less emphasis or perception of COVID-19-related pandemic pressure. At that time, the seroprevalence was below 21% (6). When the study was conducted, most governments were not considering immunity certificates yet. No immunity certificates were implemented in any country, and vaccine certificates were not publicly discussed.

METHODS

In June 2020, the ECI study (study on immunity certificates) was started to evaluate the acceptability, feasibility, and utility of immunity certificates in Switzerland. The study was comprised of three consecutive parts with an initial quantitative questionnaire sent to 1,520 participants of a Geneva-based seroprevalence study (SEROCoV-POP study[1]), a qualitative component described herein, followed by a quantitative questionnaire based on the results of the qualitative study.

The qualitative component was conducted between July and November 2020 and explored the acceptability, feasibility, and utility of implementing immunity certificates in-depth and provided insights for the elaboration of a second survey, sent in February 2021 to the same population. In this article, only the findings of the qualitative study are reported[2].

Fieldwork combined focus groups with members of the population and individual interviews with stakeholders.

Eleven focus groups (4–6 participants each) were conducted with people living in Geneva ($n = 54$). Participants were recruited from the SEROCoV-POP study *via* an online invitation, with over 1,000 email invitations sent. The two inclusion criteria were age (adults of 18 years and older) and language (ability to speak French or English). Individuals who lacked a capacity to consent and those whose physical participation was deemed unsafe to themselves or others (participants who were in self-isolation or quarantine) were excluded. Age was used to construct homogeneous groups as much as possible (one group aged between 24 and 26 years, three groups aged between 30 and 55 years, four groups aged between 41 and 72 years, one group aged between 66 and 77 years, and two mixed groups aged between 25 and 70 years old). This was in order to avoid a too strong polarization of views, which could negatively impact the focus group discussion. All groups were mixed in terms of gender, except one composed of women only.

Fourteen semi-structured interviews were conducted with stakeholders working in Switzerland and engaged in decisions related to the COVID-19 epidemic, including politicians, medical experts, public health experts, economists, entrepreneurs, information technology experts, experts in ethics, and representatives of civil society. They were recruited through a purposive sampling with a list of stakeholders we elaborated on

[1]Held by the University Hospitals of Geneva (HUG), the SEROCoV-POP study is a population-based serosurvey that took place in the population of Geneva, Switzerland.

[2]The results of the initial quantitative component of study are presented in the article by Nehme et al. (7).

the basis of their expertise in the above fields and connections with the COVID-19 pandemic management. Out of the 22 persons who were contacted, 14 accepted the interview.

Despite time pressure and limited access to the field in the pandemic context, over time, focus groups and stakeholders interviewed provided redundant opinions. We therefore considered having reached data saturation and terminated our fieldwork in November 2020.

For practical and public health reasons, interviews of stakeholders were conducted remotely by videoconference. Focus groups participants could choose between face-to-face and virtual meetings. Four out of the 11 focus groups were held in person and seven by videoconference.

All focus groups and interviews were conducted in French except for one interview in English. Interviews lasted 40 min on average and focus groups 90 min. With permission from participants, all interviews and focus groups were audio-recorded. The interview and focus group guides covered five main topics: (1) acceptability and utility to know the immunity status of an individual; (2) acceptability and utility to know the immunity status of others; (3) divulgation of immunity status of an individual; (4) expected information on the certificate; (5) implementation of an immunity certificate. To initiate the discussion, two scenarios were proposed one where a granddaughter could only visit her grandmother in a nursing home after providing an immunity certificate and the other where an employer imposed an antibody test on his employee in order to conduct business with customers (see the interview guides, **Annex 1**).

This study was approved by the Cantonal Research Ethics Committee of Geneva University Hospital, Switzerland (CCER-16-363). An information letter and written consent were signed by all participants prior to conducting the interviews and focus groups. Focus groups participants filled a questionnaire detailing sociodemographic characteristics.

Interviews and focus groups transcripts were coded with the ATLAS.ti CAQDAS (see the codes list, **Annex 2**). The coding process was conducted in two steps: (1) The interview guide topics provided the initial codes and (2) some inductive codes such as medical secrecy and immunity uncertainty were created from the collected data. A thematic analysis classifying arguments as in favor or against immunity certificates was adopted (11).

RESULTS

The age of the stakeholders varied between 41 and 74 years, and two-thirds were men. Out of the 54 focus groups participants, 30 were women and 24 men. Their age varied between 24 and 77 years, and the majority had a university diploma ($n = 34$; **Table 1**). Twenty-nine participants were Swiss, 22 European (outside of Switzerland) and three non-European. Twenty-five participants were employed full-time and 15 part-time, of which 11 were women and 4 men. Most of the participants were married or living with a partner ($n = 32$). The majority of them were living in the city of Geneva ($n = 44$).

TABLE 1 | Characteristics of the participants.

	Interviews of Stakeholders	Focus Groups	Total
Gender			
Men	10	24	34
Women	4	30	34
Education			
Lower to middle education*	0	20	20
Higher education**	0	34	34
Not available	14	0	14
Age range (years)			
24–30	0	7	7
31–50	4	18	22
>50	9	29	38
Not available	1	0	1
Total	**14**	**54**	**68**

Lower to middle education includes compulsory schooling, apprenticeship, maturity, and specialized schools.

**Higher education includes university diplomas.*

Arguments against and those in favor of immunity certificates are sequentially presented below, according to the data collected both during focus groups and during individual interviews. We consider these data jointly since there was no major divergence across the two study populations. Their respective extent reflects opinions of interviewees expressed spontaneously, with the interviewer keeping an independent stance. To preserve the anonymity of the participants, only the gender (man or woman) and the age of the participants of the focus groups are specified.

Immunity Certificate Disadvantages

Arguments against the implementation of immunity certificates were discussed around six main questions, recurrent across the focus groups, and interviews of stakeholders.

Is Scientific Knowledge on Immunity Certificate Reliable?

The limited reliability of scientific data related to COVID-19 immunity—including meaning, strength, and duration of the immunity; serological test, mutation of the virus; and potential re-infection—was the main reason brought up to reject immunity certificates. Most of the participants acknowledged that political decisions should not be made on the basis of weak evidence around antibody testing. Immunity certificates were seen as "*irrelevant*," "*useless*," and even "*dangerous*" as quoted by some interviewees:

> "*For the moment we don't know what it means to be immune, neither for how long, nor against what, [we don't know about] the mutation of the virus, so today it doesn't mean anything and it can't be relevant to have a certificate!" (stakeholder).*
>
> "*In the current state of knowledge, it doesn't mean you have the antibodies because you've had the disease. And, there's not really a link between having the antibodies and not being contagious either!" (36 year old man).*

For Which Purpose(s) Would the Immunity Certificate Be Used?

The majority of participants pointed out the importance to specify the purpose(s) for which immunity certificates could be used, as well as their period of validity prior to implementing them.

Most participants perceived immunity certificates as a tool for discrimination and restriction. The risk of creating a differentiated regime among those who are "positive" and those who are "negative," those who could travel, work and those who could not was often mentioned. Potential discrimination of those not holding a certificate proving their immunity, who could represent a burden for society, was discussed:

> "*The problem is not those who will have it, it is all those who will not have it. The immunity certificate could stigmatize those who are not yet immune, who are a burden to society because we have to protect them*" *(stakeholder).*

The separation between those who are immune, being the advantaged ones— "the immune-privileged" —and those who are not— "the immune-deprived" —was strongly denounced and perceived as deleterious to social cohesion:

> "*This immunity certificate will create a divided society with privileged people and unprivileged ones. We really need more social cohesion instead of a society that consists of two groups of people*" *(56-year-old woman).*

Immunity certificates were considered mostly as an open door to potential drifts and would set a "*dangerous*" precedent:

> "*It's the Pandora's box. Today we open a door for a particular case and tomorrow it becomes a generality and we extend it to any field of health*" *(68-year-old woman).*
> "*For sure it would set a precedent. And it is a really dangerous precedent*" *(47-year-old woman).*

The fear of the creation of "*ghettos*," with reference to "*yellow stars*" as well as unequal treatment related to child bearing or the AIDS epidemic, was mentioned:

> "*I'm afraid that it could lead to abuses and that history repeats itself. I really don't want to suddenly have a yellow star somewhere on my cloth*" *(54-year-old woman).*
> "*There was also the whole period of AIDS that was largely present in the late eighties. There were very strong questions about people's serological status and their place in society*" *(70-year-old man).*

Cost and access issues were also seen as possible sources of inequalities:

> "*Who pays for it? Is it the State? Is it the individual? Not everyone can necessarily afford such a certificate, even if it is 10 or 15 or 20-Swiss francs. We are not all equal. At the end, it could again create inequalities*" *(55-year-old man).*

Arguments about potential discrimination and inequalities also led to discussions about the value of an immunity certificate.

What Is the Value of an Immunity Certificate?

Its economic value such as professional advantages was often quoted, along additional risks of discrimination and professional difficulties:

> "*We're going to say this word of segregation between those who will have financial access to prove to their boss that they can come to work and meet clients and those who won't be able to*" *(58-year-old woman).*
> "*What do we do with all the people who finally didn't have 'the chance' to be exposed to the virus and develop antibodies? Are they being penalized in their work? Or in their search for work? Because we can imagine that the next step would be to say: we have a pool of employees but now we are going to recruit new people, do we ask these new people to have a test that confirms their immunity before recruiting them?*" *(50-year-old woman).*

This risk refers especially to professions involving close face-to-face interactions such as health professionals or teachers:

> "*I can already see the excesses where parents will require the teacher to go under... for fear of letting their children go to school. A teacher who is not immunized could be banned from public education! It scares me. Or maybe even in the medical field, would it be a requirement for nurses?*" *(61-year-old woman).*

Many participants feared that private companies would have access to these data, quoting particularly health insurances using immunity status to increase their premiums.

The potential economic value of the certificate implied risks of falsification and implementation of "*black markets of certificates*" as highlighted in all focus groups and interviews with stakeholders.

> "*It would open the door to fake certificates. When there's the job in the balance, that is to say that if the employer can tell you: 'Well listen, sorry but your test is negative, so goodbye,' or I don't know what, they'll put you at 50%, or in partial unemployment or whatever, there's going to be of course false certificates … or into trafficking dates because you were positive × time ago and negative afterwards. Well, I mean, the issue of work and employment is important enough so that people find biases and ways to face it*" *(57-year-old woman).*

The economic value of the immunity certificate was also perceived as an incentive to expose oneself to catch the disease, often expressed as an encouragement to take part in "*coronaparties*." As one stakeholder said: "*To become immune you have to catch the coronavirus!*" which could lead to intentional contaminations.

This collateral damage was considered as unacceptable both from a societal and from an ethical point of view potentiating the risk of people being voluntarily inoculated with the disease. This risk was seen as an individual and collective danger:

"*The immunity certificate, which would be based on serology, would send a signal that would be the opposite of individual protection. If you want to enter our country, you can only do so if you have exposed yourself to the risk and have had the disease. Somehow this is an incentive to catch it [the virus] in order to benefit from the certificate. So, the certificate is not something that is a solidarity and collective incentive to protect the health of the individual, but it is an individualistic incentive that aims to expose more people*" *(stakeholder).*

Furthermore, most interviewees insisted that immunity certificates should not be used to clear oneself or "*reward*" those who have caught the disease:

"*People who have a certificate or have had the Covid will have more freedom, will be able to do more things than people who haven't had it and I think that socially it would not be correct and not accepted by a large part of the population*" *(25-year-old woman).*
"*People who followed the rules, who really paid attention, if they're penalized for not having Covid, it wouldn't be fair either*" *(35-year-old man).*

Is the Certificate Compatible With Already-Implemented Public Health Measures?

The majority of interviewees argued that an immunity certificate could represent a threat to the current health measures that include wearing masks, physical distancing, contact tracing, quarantine of contacts, isolation of cases, and PCR tests. These measures were perceived as "*enough*," "*better*," and "*safer*" than serological testing:

"*With all the barrier gestures that we already have, we are obliged to disinfect our hands, to wear a mask, to be not closer than 1.5 m, so there is little risk of infecting anyone. I don't think the immunity certificate will bring a plus. Honestly, No!*" *(55-year-old woman).*

Several experts emphasized the importance "*to detect quickly infected people and isolate them*" rather than to know the immune status of an individual. For the majority of interviewees, current measures would still remain in place regardless of immunity certificates, emphasizing the futility of this document.
For some stakeholders and members of the population, this document was even seen as a disproportionate measure in relation to other risks related to health such as tobacco and alcohol, reinforced by the low-lethal nature of the COVID-19:

"*It's not acceptable to issue this certificate. It seems to me completely abusive because the average age of death of this disease is about 84 years and the life expectancy is similar. This disease is not a danger that justifies this kind of measures. It seems completely excessive. Yes, it has killed people but it was mostly people who were at the end of their lives and with conditions of connected diseases. For me it's completely disproportionate*" *(54-year-old man).*
"*Typhus 100 years ago or these kinds of diseases were extremely contagious, there was no treatment during pandemics, I can imagine that coercive measure could be justified. But here, it's a disease that is serious for certain groups of the population, but there are many people who, with or without treatment, are doing very well. This measure is too coercive and is absolutely not justified at this stage. It's not 'lethal enough' both in terms of the number of people infected and the risk… well, I'm a little embarrassed to say… the number… the proportion of the population affected… does not seem to justify coercive measures*" *(50-year-old man).*

Some participants feared that the COVID-19 vaccine would be the next "*forced step*" imposed by the government to obtain an immunity certificate:

"*Isn't there the drift that we're going to have to be vaccinated in order to have this immunity certificate? And we know very well that there are people who don't want to hear about vaccination and that it's a drift where we would be obligated to be vaccinated!*" *(54-year-old woman).*

For most participants, the immunity certificate did not bring any added value in the current management of the epidemic.

How Could (Health) Individual Privacy Be Guaranteed?

Finally, immunity certificates were perceived by the majority of interviewees as an invasion of the private sphere and a violation of personal integrity. Participants worried about the privacy of their health data. These concerns were stronger among focus groups participants and often quoted as the first argument against their implementation:

"*It is still an intrusion into people's state of health. Are we testing women to find out if they are pregnant? Well, I don't know, it's still shocking*" *(64-year-old woman).*

The risk of the violation of medical secrecy was also often highlighted:

"*It [the certificate] is going to attack the medical secrecy and that's a very big problem because medical secrecy is the basis of medicine. Medical secrecy is extremely important because it allows patients to talk about things that are important to him/her where he/she needs help and to know that his/her doctor is going to listen to him/her and he/she is not going to start making it public everywhere. So, there's already a breach of medical confidentiality and that's a big issue*" *(48-year-old man).*

For participants, the immunity status could not be kept confidential if it had to be presented in order to gain advantages. It was therefore a sensitive issue as individuals could easily "*lose control*" over the circulation of information. Additionally, long-term effects of the disease, as of yet unknown, could lead to potential further health complications, thus transforming immune status into a sensitive issue in the future:

"*The consequences of this information, in the absolute, may not be dramatic, but even though we don't know very well what it is, let's imagine that we find out something about the virus, for example, that some time later it reappears and all the people who were carriers of the virus develop this or that pathology, there the situation would be very delicate*" *(stakeholder).*

Immunity Certificate Benefits

Arguments in favor of the immunity certificate were related to some individual and collective benefits they could provide, but in a regulated context.

The Immune Status Is Not or Should Not Be Considered as Sensitive Data

If for the majority of the interviewees, the immune status was considered as sensitive data since it is a medical data, one stakeholder argued the opposite. Indeed, in comparison with the HIV+ status, highly sensitive due to the stigmatization attached to HIV/AIDS, the COVID-19 immunity does not represent any risk of discrimination for this expert who saw "immune-privileged" as a "*natural thing*:"

> "*I don't see much danger. There are always people who will cry out for discrimination but personally I don't think it's a real fear. The natural evolution of the epidemic is going to make that there are people who are immune, so they are privileged in a certain sense… there's nothing we can do about it! It's just the way it is!*" *(stakeholder).*

He added that knowing immunity of an individual could be useful both for immune and for nonimmune individuals. One participant of a focus group highlighted that since the purpose of the certificate was to gain some freedom, it could not be considered as a sensitive data.

> "*It's an information that if it's going to be useful, it's not possible to hide it, these two things don't go together*" *(55-year-old woman).*

If the immune status is not considered by these interviewees as a sensitive data, it is also the case regarding the disease. Indeed, some participants noticed that "*having had the covid*" today is "*something cool*." Some even mentioned that they had heard colleagues or friends "*being proud of having had the covid*." This illustrates how COVID-19 individual status is actually easily divulgated in the population and not perceived as stigmatizing.

To Know One's Immune Status Is Useful …

…for Medical Knowledge

Some stakeholders and participants perceived a medical interest in collecting the serological status of the population. It could serve scientific knowledge for medical research and public health prevention and actions, which suggested that, in that case, the use of immunity certificates was acceptable:

> " *It's interesting if it's used on a large scale and it allows you to implement strategies in terms of risk management for the population. I think scientists would probably need that kind of information*" *(64-year-old woman).*

… for Some Categories of People

Some interviewees considered the implementation of immunity certificates acceptable for some categories of people such as healthcare workers to treat patients:

> "*I believe that an immunity certificate might not be so bad in the medical field. For example, nurses who have a certificate, it is better that they take care of patients who have Covid*" *(56-year-old woman).*

A few participants stressed the importance to protect "*vulnerable people*," referring mostly to the elderly and often in line with a personal situation.

…for Some Transactions or Activities

For some participants, immunity certificates should serve as a "*facilitator*" or a "*transactional tool*" to resume some activities such as traveling, being the most systematically quoted example. In that case, certificates were seen as a document that could alleviate quarantine, masks, or PCR testing. However, the same interviewees specified that certificates should not be asked for all activities:

> "*You have to travel for your business, you'll travel with more ease than the others who don't have it. Some countries ask to have a Covid test done 72 h in advance and if you have the immunity certificate you could pass easily*" *(55-year-old woman).*

Acceptable Only in Relation to Vaccination

Some interviewees were in favor of immunity certificates only if related to vaccination, as quoted by this stakeholder:

> "*For me as long as it's not associated with a widely available vaccine, it's useless. It has to be in the context of wide availability of the vaccine, for me that's the way to start. So, the question you're asking is the right one but, in a vaccine-based temporality*" *(stakeholder).*

Because vaccination relies on a personal choice, i.e., a voluntary medical act and not the "*chance*" of having caught the disease, immunity certificates related to vaccination appeared more ethically acceptable:

> "*I'm not 100% against it, but if it's based on antibody tests, then people don't have the choice to have the certificate or not. You don't choose to have Covid and to be immunized, whereas if it was with a vaccine then in that case you have the choice*" *(25-year-old woman).*

However, interviewees stressed out that when the vaccination would be available, it should remain optional and affordable to everyone.

Implementation Framework

Finally, all participants agreed that if immunity certificates were to be implemented, a strong legal framework was needed in order to ensure that certificates could not be imposed by anyone in an unregulated manner. Criteria should be defined especially regarding the purpose(s) and duration of the certificates. Indeed, certificates should be limited in time, and data should be destroyed after a set duration. These documents should be issued by legitimate and recognized authorities. Appropriate authorities according to participants were at the national level, the Federal Office of Public Health (FOPH), and at the international level, the World Health Organization (WHO). Finally, an expert

stressed out that the data should be decentralized to guarantee data security.

DISCUSSION

This exploratory study is the first qualitative research incorporating opinions of the general population and of stakeholders on immunity certificates. The purpose of this article was to discuss the acceptability to issue a document certifying immunity of an individual against SARS-CoV-2 based on serological testing and its implementation. Qualitative studies do not aim at providing generalizable results. Nevertheless, our study allows us to identify different arguments proposed by stakeholders and members of the population, at the time of the study.

Consistent with other studies and according to the current state of scientific knowledge, disadvantages outweighed the perceived benefits (1, 2). At the time of the study, few participants considered immunity certificates as an acceptable public health measure due to the limited reliability of scientific data. The majority of stakeholders agreed that political decisions should not be made on the basis of serological testing.

Opinions in our study ranged from a light acceptance to total rejection, including ambivalent positions, favoring the use of immunity certificates only in specific cases to protect "vulnerable" populations or contexts such as traveling. We did not notice differences among women and men or among different age groups. Opinions were consensual between stakeholders and members of the public. Nevertheless, medical experts discussed vaccination certificates as a future option more than other participants.

Arguments in favor of immunity certificates were based on the nonsensitive nature of this particular health data. It was perceived as useful for medical knowledge, some categories of people, or personal interest (psychological reassurance). Some saw it as a facilitator to resume specific activities. Immunity certificates appeared more acceptable if based on vaccination status, considered a voluntary act.

Conversely, arguments against immunity certificates stressed the limited reliability of the data, serological tests, immunity (interpretation, duration), and potential mutations of the virus. Major concerns raised were creating discrimination and inequalities between those who are immune—the "immune-privileged" —and those who are not—the "immune-deprived." It could provoke negative behaviors such as encouraging individuals to catch the disease (intentional or self-infection) or counterfeiting documents. Certificates were seen as counterproductive to fight the spread of the disease; and as violating individual privacy and liberties when these were fundamental to preserve for the majority of the interviewees.

The main paradox quoted was that immunity certificates "incentivise infection" (3) rather than prevent them. Current measures were perceived as sufficient to fight the epidemic in Switzerland, and immunity certificates could undermine prevention efforts according to interviewees. Certificates could contribute to increase inequalities in relation to the costs and access to tests and certificates (4, 8). For interviewees, sanitary measures need to respect and ensure treatment equality and tests and antibody certificates should not "become a luxury of the rich" (5). Access to immune status information by private organizations was also questioned, especially the impact it could have on the premium of health insurances. Decentralized digital identity was perceived for one stakeholder as the best privacy preserving system. This statement is in line with Gruener (4) and Hicks et al. (5).

For some participants, especially in reference to HIV/AIDS, COVID-19 might not be stigmatizing yet because anyone could catch it, but immunity certificates could create stigmatization especially due to the fact that it would be accessible to a minority of individuals. In line with other studies (1, 3), this paradox of dividing the society based on the immunity status appeared unacceptable to all participants.

Employment, which has been greatly impacted by the pandemic, should not be linked to immunity certificates. Indeed, as mentioned by interviewees and in line with some studies, "employment decisions, such as hiring and firing, cannot be made on the basis of health status" [(4) p. 22]. An employer should not be able to impose antibody testing and immunity certificates to his/her employees in order to be able to resume work (10).

Persad and Emanuel (8) concluded that "immunity-based licenses have the potential to help realize important values, including enhancing the liberty of individuals who have been infected with COVID-19 without worsening the situation of those have not been infected, maximizing benefits to individual and society by allowing immune people to engage in economic activity, and protecting the least advantaged by allowing safer care for vulnerable populations" (p.2242). However, all these arguments were perceived discriminatory by the majority of the participants and stakeholders of our study. Finally, interviewees feared that people might be more willing to make compromises and be tempted to "*accept this measure and others*" if they ensured a return to a "*normal life*." Indeed, overtime, the COVID-19 "fatigue" (12), especially when confronted to recurrent lockdowns and relaxation measures, is strong and negatively affecting the majority of individuals according to participants.

These results provide a snapshot of arguments discussed around immunity certificates based on serological testing before the implementation of COVID-19 vaccination, when evidence on immunity was still provisional and public information limited. Today, digital COVID certificates are being implemented across European countries (13), taking into account, immunity,vaccination and testing for the presence of the virus during acute infection. These certificates are likely to change the population expectations and attitudes as reported elsewhere (14). Despite this new context, the majority of the arguments raised in this study are still relevant in Switzerland and in other countries. Most of the issues discussed above are indeed at the heart of current debates about vaccination certificates. They include scientific evidence about the strength and duration of immunity (natural and vaccine induced immunity); the different purposes that immunity certificates can fulfill; ethical issues such as discrimination and privileges; the competition

with implemented measures such as physical distancing and masks and security of personal health data.

Limitations

This study has some limitations. The interviews took place between two lockdowns with a sense of semi-normalcy during summer 2020 in Switzerland. They provide information specific to that time period, and we can expect that opinions will be different at later stages of the pandemic. The implementation and expansion of COVID-19 certificates are also likely to impact the attitudes of the population (15). This context might have influenced the participation of certain individuals encouraged to share their opinions that could have been influenced by pandemic "fatigue" or "anxiety" stemming from the overall conditions. Some potential participants might have been discouraged by the technology not managing virtual applications (a pre-focus group videoconference testing session was proposed to all participants if requested, in order to eliminate technology resistance or barriers). A selection bias is possible with participants having higher levels of education than the general population. We faced some difficulties to recruit "young" participants, with only six participants in-between 24 and 26 years. The majority of the focus groups interviewees are in-between 50 and 69 years ($n = 29$). Some interviewees made some inquiries on the topic prior to participating, showing their interest and commitment.

In conclusion, the COVID-19 pandemic has severe negative effects both at the collective (economic, political, and societal) and at the individual levels. However, there are several potentially adverse consequences of immunity certificates related to serological testing and the acceptability by the population has to be considered before any potential implementation. With vaccine rollout, vaccination certificates are now at the forefront of academic, political, economic, and medical discussions. Vaccines could answer some of the questions raised in this study, including the interpretability of immunity, its duration, and effectiveness; however, some questions remain around mandatory implementation of certificates, access and rights, freedom of choice as well as feasibility. Therefore, the empirical findings of this unique qualitative study conducted in 2020 bringing together opinions of stakeholders and members of the general public can clearly inform the current discussion about the implementation of vaccination certificates. They offer pioneer results before the development of large public and political discussion on this topic.

Engaging civil society in answering these questions is paramount, especially when such measures will affect the populations in general. Several participants thanked us for being called upon to express their opinions, wishing to be more involved and consulted about these subject matters, revealing that the management of this epidemic could benefit from conducting a public transparent and open dialog with the population.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

VF conducted all interviews with the stakeholders and nine focus groups, assisted in the qualitative protocol development, developed the qualitative tools (interview guidelines and documents), analyzed and interpreted the qualitative data, and wrote and finalized the manuscript. MN and IG were the main investigators of ECI study (CCER-16-363) and provided essential comments and correction to the final manuscript. CBJ conducted two focus groups, developed the qualitative protocol, and provided essential correction to the final manuscript. All authors participated in the recruitment of the participants and read and approved the final manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2021.682365/full#supplementary-material

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Qatar Healthcare Workers' COVID-19 Vaccine Hesitancy and Attitudes: A National Cross-Sectional Survey

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Introduction: Healthcare workers are the critical frontline workforce of the COVD-19 pandemic and are considered a target group for vaccination. Hesitancy to vaccinate is a major concern that can jeopardize the vaccination programme. The hesitancy rates in the general population and healthcare workers (HCWs) vary globally, and more importantly, hesitancy in HCWs is of particular concern, as it can influence the wider population.

Materials and Methods: The present study evaluated the vaccine hesitancy rate and its sociodemographic and attitudinal factors among the HCWs in the state of Qatar. We conducted a national cross-sectional survey using a validated hesitancy measurement tool between October 15 and November 15, 2020. A total of 7,821 adults above the age of 18 years out of the 2.3 million adult Qatari residents completed the survey. While majority of the participants were from the general public, 1,546 participants were HCWs. Sociodemographic data, along with attitudes and beliefs around COVID-19 vaccination, were collected from the respondents.

Results: We found that 12.9% of the study participants showed vaccine hesitancy, defined as definitely or probably will not take the vaccine if offered, and 25.31% reported that they were unsure about the uptake of the COVID-19 vaccine. Female respondents were more hesitant toward the vaccine. Safety and efficacy concerns of vaccine were the significant predictors of vaccine hesitancy. The primary predictor for vaccine acceptance was a better understanding of the disease and vaccine.

Discussion: Overall, 1 in 8 HCWs were reluctant to get vaccinated against COVID-19, mainly due to concerns about the vaccine's efficacy and safety. Education about the vaccine's safety and efficacy can potentially improve acceptance among healthcare workers.

Keywords: COVID-19 vaccine, hesitancy, healthcare workers, safety, efficacy, VAX scale

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HIGHLIGHTS

- This was the first study to report vaccine hesitancy in healthcare workers in Qatar, a country with the majority of the population being migrants.
- Vaccine hesitancy in HCWs was 12.9%, and it was much less compared to some other studies globally.
- The main predictors for vaccine hesitancy were female gender and concerns about the vaccine's safety and efficacy.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a highly contagious infectious disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) that has transformed the world into a state never witnessed in our lifetime. In the absence of any valid treatment, globally, many countries have imposed strict preventive control measures to restrict the COVID-19 outbreak by implementing social distancing and compulsory use of face mask (1). Further, the development and distribution of vaccines have been one of the cardinal preventive strategies to lessen the spread of COVID-19 (2).

After one of the fastest vaccine development processes by countries and pharmaceutical companies worldwide, currently, the vaccines are available globally, including in Qatar. The Qatar Ministry of Public Health approved Pfizer BioNTech and Moderna COVID-19 vaccines, and the early recipients of vaccines were healthcare professionals, elderly patients and individuals affected with chronic and autoimmune disorders. However, the successful outcome of any vaccination strategy mainly relies on a high vaccine acceptance rate (3). Therefore, vaccine hesitancy is challenging for healthcare professionals and the Ministry of health to build confidence in an emergency-released vaccine rollout to the public.

Vaccine hesitancy is defined as "the delay in acceptance or refusal of vaccination despite the availability of vaccination services." Further, it is not an all or none phenomenon, which means, some will definitely not take a Covid-19 vaccine if offered, whereas others are unsure of their intention to get vaccinated. Vaccine hesitancy is a global concern, and it is one of the crucial factors of under-vaccination (4). WHO in 2019 stated that vaccine hesitancy is one of the top ten global health threats and it acts as a significant barrier to the success of the immunization programs (5). Interestingly, negative information about the vaccine propagated in some social media platforms might also have been contributing to vaccine hesitancy (6).

Earlier studies reported that vaccine hesitancy was a major concern worldwide with a wide range of reasons for vaccine refusal (7, 8). The most common reasons for vaccine hesitancy, in general, have been perceived risks vs. benefits of vaccine, religious considerations, and most importantly, lack of awareness and knowledge (9–11). To a great extent, these factors are also applicable for COVID-19 vaccine hesitancy in general public and HCWs. In this regard, recent studies demonstrated a significant correlation between willingness to receive COVID-19 and its safety outcome (12), negative attitude and unwillingness to receive COVID-19 vaccines (13), and, importantly, the effect of religious belief and decreased intention to receive COVID-19 vaccines (14). Further, willingness to accept vaccines is governed by various other factors such as cognitive, psychological, sociodemographic and cultural that can also influence individual response to vaccine hesitancy (15).

Healthcare workers (HCWs) orchestrate a vital role in the success of immunization programs. Studies indicated that their knowledge and attitude toward vaccines play an important role in the success of any immunization programs. It has been shown that their knowledge and attitudes about vaccines govern their own vaccine uptake intentions and recommendations to the wider general populations (16, 17). Emerging reports indicate that vaccine hesitancy in HCWs can negatively impact on vaccine acceptance in the general population (18, 19). HCWs who elicit negative attitudes are hesitant toward own vaccinations, and more importantly, they can amplify these undesirable perceptions resulting in even poorer uptake of vaccinations in their patients (20).

A recent wider population-based study of the adult Qatar general population displayed an overall vaccine hesitancy of 20% toward the COVID-19 vaccine (21). The present report

TABLE 1 | Demographic data and characteristics of participants ($n = 1546$).

Variables	Frequency (n)	Percentage (%)
Age group		
18–25	27	1.7
26–35	661	42.8
36–45	504	32.6
46–55	228	14.7
56–65	100	6.5
>65	26	1.7
Gender		
Male	672	43.5
Female	874	56.5
Nationality		
Qatari	83	5.4
Arab-non-Qatari	377	24.4
Asian	807	52.2
African	194	12.5
European	61	3.9
North-America	18	1.2
Central America	4	0.3
South America	2	0.1
Education		
High school degree	87	5.6
Trade/vocational training	29	1.9
University	1,226	79.3
Others	204	13.2
Occupation		
Salaried	1,456	94.2
Self employed	39	2.5
Unemployed	24	1.6
Retired	27	1.7
Marital status		
Single	285	18.4
Married	1,261	81.6
Are you pregnant or breast feeding? Pregnant	22	2.5
Breast feeding	75	8.7
N/A	769	88.8
How many members/individuals living with you?		
Median (IQR)	4.00 (3.00)	

TABLE 2 | Intention to accept vaccine, health conditions, worries about COVID-19, and general attitude toward vaccination.

Questions	Frequency (n)	Percentage (%)
Will you take the COVID-19 vaccine when it becomes available?		
Definitely	619	43.9
Probably	255	18.0
Not sure	358	25.3
Probably not	92	6.5
Definitely not	90	6.4
Total	1,414	100.0
Have you completed your childhood vaccination?		
Yes	1,395	94.9
No	75	5.1
Total	1,470	100.0
How often you receive the influenza vaccine		
Annually	893	60.7
Twice	176	12.0
Once	190	12.9
Never	211	14.4
Total	1,470	100.0
Do you have any medical illness?		
Yes	324	22.0
No	1,146	78.0
Total	1,470	100.0
Chronic illnesses		
DM	120	32.97
HTN	147	40.38
Dyslipidaemia	43	11.81
Asthma	44	12.09
IHD	10	2.75
Total	364	100.0
Do you have mental health illness?		
Yes	27	1.9
No	1,431	98.1
Total	1,458	1.9
Do you have any psychiatric disorders		
Depression	13	40.63
Anxiety	17	53.12
Bipolar	2	6.25
Total	32	100
Do you have chronic medications?		
Yes	427	30.2
No	987	69.8
Total	1,414	100
Have you or family member had COVID-19?		
I have had COVID-19	71	5.0
A family member has had COVID-19	84	5.9
I and at least one family member has had covid-19	61	4.3
Neither me nor them	1,198	84.7
Total	1,414	100.0
What are you most worried about during COVID-19?		
Fear of becoming infected	700	45.27%
Fear of a family member to be infected	962	62.2%
Financial worries	325	21.0
Job related worries	444	28.7
No available vaccine	539	34.9
Somewhat worried	265	17.1
No worries	159	10.3
Total	1,546	100.0
Why you are willing to take the vaccine?		
My understanding of the disease and the vaccination	714	82.5
Information from my doctor/hospital	81	9.4
Information from social media	30	3.5
Information from news	37	4.3
Information from family friend	3	0.3
Total	865	100.0
Will you recommend the vaccine?		
Definitely	613	44.0
probably	289	20.8
not sure	331	23.8
probably not	82	5.9
Definitely not	77	5.5
Total	1,392	100.0
Will you get your children vaccinated?		
Definitely	550	39.5
probably	278	20.0
not sure	326	23.4
probably not	131	9.4
definitely not	107	7.7
Total	1,392	100.0
Do you prefer to go Quarantine during traveling or take the vaccine?		
I would definitely take the vaccine	627	49.3
I would probably take the vaccine	372	29.2
Not sure	274	21.5
Total	1,273	100.0

specifically explores the hesitancy rates and attitudes among Qatar's HCWs toward COVID-19 vaccination.

MATERIALS AND METHODS

Study Design

We conducted a national cross-sectional survey in Qatar between October 15 and November 15, 2020, using an online survey among the HCWs. The survey link was posted online and advertised through local newspapers and various social media platforms of the Hamad Medical Corporation, the state-funded primary healthcare provider. The advertisements were accompanied by short videos in English and Arabic explaining the survey's rationale and nature. The survey was available in both English and Arabic languages.

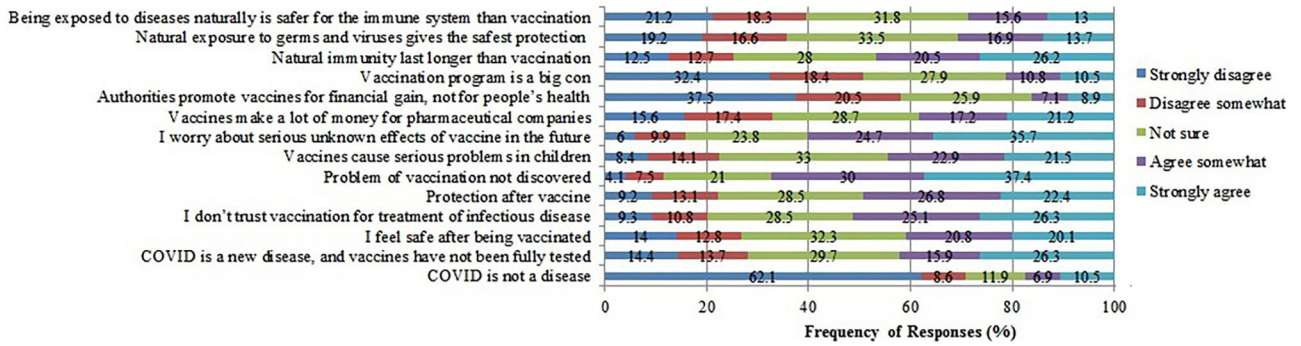

FIGURE 1 | Beliefs toward COVID-19 vaccine and immunity.

Participants

In the primary survey, all 2.3 million adult residents of Qatar were eligible. A total of 7,821 adults completed the survey. Among those, there were 1,546 HCWs, and the rest were general public. This report included 1,546 HCWs, 18 years of age and above, who consented to participate.

Study Materials

A validated vaccine hesitancy measurement tool, The Vaccine Attitudes Examination Scale (VAX) (22) was used as part of a composite questionnaire to assess the vaccine attitudes, awareness, and hesitancy among the study participants. This tool was translated into Arabic, and validation of the translated version was carried out using the guideline published by Sousa et al. (23). The survey also collected relevant demographic and contextual information of the participants.

Outcome Measures

The selection of study tools (VAX) and the composite questionnaire design were guided by the SAGE group recommendations to assess vaccine hesitancy. These included contextual factors such as ethnic origin, gender, socioeconomic status, educational level, media impact, and individual perception of the pharmaceutical industry; individual and group influences such as previous vaccination experience, beliefs and attitudes to vaccination in general, knowledge and awareness of the COVID-19 pandemic and vaccines, trust in health systems, and perception of risk and benefits of vaccines; and vaccine specific issues such as risks of a new vaccine, risk to children and older adults, and healthcare professionals' role.

Data Analysis

Descriptive statistics and multivariable logistic regression analysis were done using SPSS version 25.

RESULTS

Demographics

The total numbers of respondents of the study were 1,546. Forty two percent of the respondents were in the age group between 26–35 years, followed by 32.6% in the age group between 36–45 years. Further, 56.5% of respondents were males, and 81.6% were married. The majority of the respondents were Asians (52.5%), followed by Arab non-Qatari (24.4%) and Qatari (5.4%). Seventy nine percent were university graduates, and the majority of them were salaried employees (79.3%). The data are shown in **Table 1**. We did not ask participants to identify their professions to improve the response rate and respecting their privacy.

Intention to Accept the Vaccine, Health Conditions, Worries About COVID-19, and General Attitude Toward Vaccination

In response to the question, "Will you take the COVID-19 vaccine when it becomes available?", 61.81% responded that they would "probably or definitely" accept the vaccine. Twenty five percent were unsure, and 12.9% responded that they would "probably or definitely" not take the vaccine.

Almost 95% received childhood vaccination, 60.7% received influenza vaccine annually, 78% revealed no history of any illness, 40.38% had hypertension, and 1.9% had mental health illness. The major worries were family members getting infected (62.0 %) or individuals getting infected (45.3%). In response to the question, "why you are willing to take the vaccine?", 82.5% responded that they have a good understanding of the disease and the vaccination. Forty four percent of respondents reported that they would recommend the vaccine to others, 23.8% were unsure, and 20.8% reported probably they would take the vaccine. For the question, "Will you get your children vaccinated?", 39.5% responded definitely, 23.4% were unsure, and 20% reported as probably. For the question, "Do you prefer to go quarantine during traveling or take the vaccine?, 49.3% responded that they would definitely take the vaccine during traveling, 29.2% reported probably, and 21.5% were unsure. For the question, "Do you have any chronic medical conditions or are you taking any long-term medications", 61.6% reported that they had chronic condition. Only 11.7% had any chronic medical condition/s in the vaccine hesitancy group. The data are shown in **Table 2**.

TABLE 3 | Univariate analysis of demographics, variables related to attitude and perception of vaccination, comparing vaccine hesitators and non-hesitators.

Variables	Will you have the vaccine when it becomes available?		Total *n* (%)	*p*-value
	YES	NO		
	Vaccine non-hesitators *(definitely + probably) n* (%)	Vaccine hesitators *(definitely not + probably not) n* (%)		
Age				
from 18–25	20 (87.0)	3 (13.0)	23 (100.0)	0.027
from 26–35	550 (90.0)	61 (10.0)	611 (100.0)	
from 36–45	390 (83.7)	76 (16.3)	466 (100.0)	
from46–55	185 (88.5)	24 (11.5)	209 (100.0)	
from 56–65	69 (81.2)	16 (18.8)	85 (100.0)	
>65	2 (10.0)	18 (90.0)	20 (100.0)	
Total	1,232 (87.1)	182 (12.9)	1,414 (100.0)	
Nationality				
Qatari	49 (71.0)	20 (29.0)	69 (100.0)	0.001
Arab-non- Qatari	279 (78.6)	76 (21.4)	355 (100.0)	
Asian	682(92.8)	53 (7.2)	735 (100.0)	
African	159 (91.4)	15 (8.6)	174 (100.0)	
European	46 (79.3)	12(20.7)	58 (100.0)	
N. America	11 (64.7)	6 (35.3)	17 (100.0)	
C. America	4 (100.0)	0 (0.0)	4 (100.0)	
S. America	2 (100.0)	0 (0.0)	2 (100.0)	
Total	1,232 (87.1)	182 (12.9)	1,414 (100.0)	
Marital status				0.014
Single	212 (82.5)	45 (17.5)	257 (100.0)	
Married	1,020 (88.2)	137 (11.8)	1,157 (100.0)	
Total	1,232 (87.1)	182 (12.9)	1,414 (100.0)	
Gender				0.026
Male	541 (89.4)	64 (10.6)	605 (100.0)	
Female	691 (85.4)	118 (14.6)	809 (100.0)	
Total	1,232 (87.1)	182 (12.9)	1,414 (100.0)	
Influenza vaccination				
Annually	792 (92.3)	66 (7.7)	858 (100.0)	0.001
Twice	146 (84.4)	27 (15.6)	173 (100.0)	
Once	147 (81.2)	34 (18.8)	181 (100.0)	
Never	147(72.8)	55(27.2)	202 (100.0)	
Total	1,232 (87.1)	182 (12.9)	1,414 (100.0)	
Will you recommend the vaccine to your children?	546 (99.3)	4 (0.7)	550 (100.0)	0.001
Definitely	277 (99.6)	1 (0.4)	278 (100.0)	
Probably	305 (93.6)	21 (6.4)	326 (100.0)	
Not sure	64 (48.9)	67 (51.1)	131 (100.0)	
Probably not	18 (16.8)	89 (83.2)	107 (100.0)	
Definitely not	1,210 (86.9)	182 (13.1)	1,392 (100.0)	
Prefer quarantine over vaccine				0.001
Definitely will take the vaccine	621 (99.0)	6 (1.0)	627 (100.0)	
Probably will take the vaccine	354 (95.2)	18 (4.8)	372 (100.0)	
Not sure	129 (47.1)	145 (52.9)	274 (100.0)	
Total	1,104 (86.7)	169 (13.3)	1,273 (100.0)	
COVID-19 is not a disease	718 (90.9)	72 (9.1)	790 (100.0)	0.001
Strongly disagree	90 (81.8)	20 (18.2)	110 (100.0)	
Somewhat disagree	121 (80.1)	30 (19.9)	151 (100.0)	

(Continued)

TABLE 3 | Continued

Variables	Will you have the vaccine when it becomes available? YES	Will you have the vaccine when it becomes available? NO	Total *n* (%)	*p*-value
	Vaccine non-hesitators *(definitely + probably) n* (%)	**Vaccine hesitators *(definitely not + probably not)* *n* (%)**		
Not sure	72 (81.8)	16 (18.2)	88 (100.0)	
Somewhat agree	103 (76.9)	31 (23.1)	134 (100.0)	
Strongly agree	1,104 (86.7)	169 (13.3)	1,273 (100.0)	
COVID-19 vaccine will not be safe				
Strongly disagree	176 (96.2)	7 (3.8)	183 (100.0)	0.001
Somewhat disagree	169 (96.6)	6 (3.4)	175 (100.0)	
Not sure	363 (96.0)	15 (4.0)	378 (100.0)	
Somewhat agree	179 (88.6)	23 (11.4)	202 (100.0)	
Strongly agree	217(64.8)	118 (35.2)	335 (100.0)	
Total	1,104 (86.7)	169 (13.3)	1,273 (100.0)	
I feel safe after vaccination				
Strongly disagree	88 (49.4)	90 (50.6)	178 (100.0)	0.001
Somewhat disagree	126 (77.3)	37 (22.7)	163 (100.0)	
Not sure	383 (93.2%	28 (6.8)	411 (100.0)	
Somewhat agree	258 (97.4)	7 (2.6)	265 (100.0)	
Strongly agree	249 (97.3)	7 (2.7)	256 (100.0)	
Total	1,104 (86.7)	169 (13.3)	1,273 (100.0)	
I don't trust vaccine to manage pandemics				
Strongly disagree	76 (64.4)	42 (35.6)	118 (100.0)	0.001
Somewhat disagree	103 (74.6)	35 (25.4)	138 (100.0)	
Not sure	317 (87.3)	46 (12.7)	363 (100.0)	
Somewhat agree	295 (92.5)	24 (7.5)	319 (100.0)	
Strongly agree	313 (93.4)	22 (6.6)	335 (100.0)	
Total	1,104 (86.7)	169 (13.3)	1,273 (100.0)	
I will feel protected after vaccination				
Strongly disagree	61 (52.1)	56 (47.9)	117 (100.0)	0.001
Somewhat disagree	126 (75.4)	41 (24.6)	167 (100.0)	
Not sure	322(88.7)	41 (11.3)	363 (100.0)	
Somewhat agree	325 (95.3)	16 (4.7)	341 (100.0)	
Strongly agree	270 (94.7)	15 (5.3)	285 (100.0)	
Total	1,104 (86.7)	169 (13.3)	1,273 (100.0)	
Vaccination is for financial gain				
Strongly disagree	449 (93.9)	29 (6.1)	478 (100.0)	0.001
Somewhat disagree	223 (85.4)	38 (14.6)	261(100.0)	
Not sure	288 (87.3)	42 (12.7)	330 (100.0)	
Somewhat agree	71(78.0)	20 (22.0)	91 (100.0%	
Strongly agree	73 (64.6)	40 (35.4)	113 (100.0)	
Total	1,104(86.7)	169 (13.3)	1,273 (100.0)	
Vaccination programs are big Con				
Strongly disagree	375 (91.0)	37 (9.0)	412(100.0)	0.004
Somewhat disagree	198 (84.6)	36 (15.4)	234 (100.0)	
Not sure	309 (87.0)	46 (13.0)	355 (100.0)	
Somewhat agree	116 (84.1)	22(15.9)	138 (100.0)	
Strongly agree	106 (79.1)	28 (20.9)	134 (100.0)	
Total	1,104 (86.7)	169 (13.3)	1,273 (100.0)	

(Continued)

TABLE 3 | Continued

Variables	Will you have the vaccine when it becomes available? YES	Will you have the vaccine when it becomes available? NO	Total *n* (%)	*p*-value
	Vaccine non-hesitators *(definitely + probably) n* (%)	Vaccine hesitators *(definitely not + probably not) n* (%)		
Natural immunity last longer than vaccinations				
Strongly disagree	147 (92.5)	12 (7.5)	159 (100.0)	0.001
Somewhat disagree	153 (94.4)	9 (5.6)	162 (100.0)	
Not sure	316 (88.5)	41(11.5)	357 (100.0)	
Somewhat agree	227 (87.0)	34 (13.0)	261(100.0)	
Strongly agree	261 (78.1)	73 (21.9)	334 (100.0)	
Total	1,104 (86.7)	169 (13.3)	1,273 (100.0)	

VAX Scale of Hesitancy

There were 14 questions in the VAX scale of hesitancy. The questions included "COVID is not a disease, COVID is a new disease and vaccines have not been fully tested, I feel safe after being vaccinated, I don't trust vaccination for treatment of infectious disease, I feel protected after vaccination, Problems of vaccination not yet discovered, Vaccines cause serious problems in children, I worry about serious unknown effects of vaccines in the future, Vaccines make a lot of money for pharmaceutical companies, Authorities promote vaccines for financial gain and not for peoples' health, Vaccination program is a big con, Natural immunity lasts longer than vaccination, Natural exposure to germs and viruses gives the safest protection, and Being exposed to diseases naturally is safer for the immune system than vaccination". The questions were rated as strongly agree, agree somewhat, not sure, disagree somewhat, and strongly disagree. The data are shown in **Figure 1**.

Association Between Demographics, Variables Related to Attitude and Perception of Vaccination With Vaccine Hesitators vs. Non-hesitators

We divided the responders into vaccine hesitators and vaccine non-hesitators, and their associations with sociodemographic variables and variables related to attitude and perception regarding vaccination were analyzed. Several sociodemographic factors were significantly associated with vaccine hesitancy, including age, nationality, marital status, and gender.

The other significant factors related to attitude and perception were influenza vaccination history, recommendation of vaccine to children, preference of quarantine over the vaccine, the perception that COVID-19 is not a disease, COVID-19 vaccine is not safe, no protection from the vaccine, lack of trust in the vaccine's efficacy, lack of trust of pharmaceutical companies and their intentions, and a belief that natural immunity is better than vaccination. The univariate analysis results are shown in **Table 3**.

Multivariate logistic regression for the response to the question "Will you take the COVID-19 vaccine when it becomes available" (vaccine hesitancy) as the dependent (outcome) variable and items of VAX scale, sociodemographic variables and a few other items related to influenza vaccine as the independent (predictor) variables was done, after controlling for age, education, nationality, marital, and employment status. Female gender, "I feel safe after being vaccinated (strongly disagree, somewhat disagree, not sure)", "Covid-19 is a new disease and vaccines against it have not been fully tested and will not be safe (strongly disagree, somewhat disagree, not sure)", "I feel protected after being vaccinated (not sure)", and "I worry about the unknown effects of vaccines in the future (somewhat disagree, not sure)", were significantly associated with vaccine hesitancy. The results were shown in **Table 4**.

DISCUSSION

Our study is one of the largest surveys that addressed the attitudes toward vaccination in HCWs in the Middle East during the COVID-19 pandemic. The main finding of this study is that among the surveyed HCWs, 12.9% displayed hesitancy toward getting vaccinated with a COVID-19 vaccine, and a further 25.31% were unsure whether they would accept the vaccination or not. In a recent survey conducted among the Saudi HCWs ($n = 736$) in December 2020, using a non-standardized survey questionnaire, the vaccine hesitancy rate was reported to be 49.48% (24). Similarly, in an online survey conducted among the French HCWs between March and July 2020, the vaccine hesitancy rate reported was 25.9% (25). Another study done by Di Gennaro et al. (26) among the Italian HCWs, reported a vaccine hesitancy of 7%. The vaccine hesitancy rate of 12.9% in our study is much lower than the Saudi and French studies and slightly higher than the Italian study. This variation might be a reflection of the study methodology, the representative population, and the different healthcare systems.

In our study, age (older than 65 years) was significantly associated with vaccine hesitancy, which is in corroboration with the survey done by Schwarzinger et al. (27) where age displayed an inverted U-shaped relationship. In the same study, vaccine hesitancy was significantly higher in females than males, which is

TABLE 4 | Multivariate logistic regression showing predictors of vaccine hesitancy.

Predictors	OR (95% CI)	*p*-value
Female gender	0.69 (0.49–0.93)	0.016
Strongly disagree that I feel safe after being vaccinated	8.78 (3.67–20.99)	0.001
Somewhat disagree that I feel safe after being vaccinated	8.69 (3.89–19.40)	0.001
Not sure that I feel safe after being vaccinated	3.83 (1.89–7.77)	0.001
Strongly disagree that Covid-19 is a new disease and vaccines against it have not been fully tested and will not be safe	8.78 (3.67–20.99)	0.001
Somewhat disagree that Covid-19 is a new disease and vaccines against it have not been fully tested and will not be safe	0.40 (0.22–0.74)	0.003
Not sure I will feel protected after being vaccinated	3.00 (1.52–5.92)	0.002
Somewhat disagree that I worry about the unknown effects of vaccines in the future	0.39 (0.21–0.72)	0.003
Not sure that I worry about the unknown effects of vaccines in the future	0.32 (0.21–0.50)	0.001
Somewhat agree that I worry about the unknown effects of vaccines in the future	0.61 (0.41–0.92)	0.019
Strongly disagree that COVID-19 is not a disease	0.72 (0.41–1.26)	0.252
Salaried job	0.23 (0.05–1.06)	0.060
Unemployed	0.14 (0.01–1.13)	0.066

in line with our finding. A possible reason may be that females often consider the impact on their children and fertility (25). However, in contrast, in a study conducted in Saudi Arabia, the vaccine hesitancy was higher in males than females, although we don't have an explanation for this discrepancy (24). In our study, marital status has a strong influence on vaccine hesitancy, particularly among the married respondents. Previous studies also showed that marital status might affect vaccine hesitancy, with single parents or those divorced demonstrating increased vaccine hesitancy (28).

The main reason for vaccine acceptance in our survey was a better understanding of the disease and vaccines, which possibly enables the respondents to make an informed and confident decision on vaccine acceptance. Interestingly, a previous study showed that perceived susceptibility to and seriousness of a vaccine-preventable disease as an indicator of a better understanding of the disease that might lead to vaccine acceptance (25).

Recent studies showed that HCWs willing to accept the vaccine were more likely to recommend vaccines to friends, family, and patients (27–29). Similar findings were observed in our study.

In the VAX hesitancy scale, 26.3% of respondents reported negative attitudes about safety and trust about the vaccines. Furthermore, the hesitancy was also attributed to the concerns regarding safety among the children in their family, the chance of getting any unknown illness in the future, and a preference for natural over vaccine-induced immunity. Similar findings were also observed in our main survey on the general population (21) suggesting that these findings are not specifically applied to only HCWs.

Of note, on multivariate analysis, we found female gender, the perception that vaccines are not safe at the time of vaccination, a perceived lack of safety after vaccination, and doubts over vaccine protection were the significant predictors of vaccine hesitancy. Interestingly, having a chronic medical condition was not a significant predictor. To date, there are no large cohort studies available to authenticate the efficacy of COVID-19 vaccines. Therefore, the first generation may have limited efficacy, which leads to a loss of trust in the current COVID-19 vaccines (30). A previous study indicated that the safety, efficacy, and effectiveness of COVID-19 were the hallmark predictors of COVID-19 vaccine hesitancy (31).

The present study was conducted in a distinct part of the globe with diverse demographics, and the majority were migrant populations, including the HCWs. We also surveyed when COVID-19 vaccine producers reported their efficacy data and initiated mass immunization programs worldwide. Besides, we used a validated vaccine hesitancy tool, and the outcome measures were based on internationally established vaccine hesitancy parameters.

CONCLUSION

Vaccine hesitancy has a significantly negative impact on a planned immunization program's successful outcome, and it has been considered a global threat to universal immunization programs. In our study, the majority of the HCWs accepted to take the COVID-19 vaccine. However, 1 in 8 HCWs was vaccine hesitant. The significant predictors of vaccine hesitancy were female gender, concerns about vaccine safety, safety after the vaccination, and doubts about the vaccine's protection. Education about the vaccine's safety and efficacy can potentially improve acceptance among healthcare workers.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Medical Research Council of the Hamad Medical Corporation. MRC approval-01-20-930. The

patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

RK: conceptualization, data analysis, and interpretation and writing—original draft and editing. MA: conceptualization, methodology, supervision, validation, and writing—review and editing. NE: data analysis, interpretation, and writing—editing. SR: conceptualization, methodology, supervision, validation, and writing—review and editing. All authors contributed to the interpretation of the results, critically revised the paper, and agreed on the final version for submission.

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OPINION
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HIV/AIDS Epidemic and COVID-19 Pandemic in Africa

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INTRODUCTION

COVID-19 pandemic has transmitted significantly and become ubiquitous globally, instantly as the disease's information spread from a city in China named Wuhan since December 2019, it become a global public health threat. COVID-19 was declared a pandemic on March 12, 2020, by the World Health Organization (Huang et al., 2020). Research has shown that about 37.9 million people who are HIV carriers (Joint United Nations Programme on HIV/AIDS, 2020) are vulnerable to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which results in Coronavirus Disease 2019 (Joint United Nations Programme on HIV/AIDS, 2020).

Various African countries have been responding to different health problems such as HIV/AIDS and Tuberculosis, which indicates that millions of people are immune-compromised and many are vulnerable to high health problems due to the respiratory disorder obtained from the virus. In the same vein, the increased number of people having malaria in African countries has made more people susceptible to it (Aborode et al., 2021a). This may deceive diagnostic testing because high fever is part of the symptoms of both malaria and COVID-19 (Aborode et al., 2021a).

The inception of a new disease can have a catastrophic and long-lasting effect on already fragile health systems. For instance, about 10,600 people lost their lives to HIV/AIDS, Malaria, and Tuberculosis in some countries in West Africa due to the weakened healthcare system caused by the Ebola epidemic (Aborode et al., 2021b). Painfully, parents' and children's health was highly reduced, and no iota of recovery was recorded after the epidemic. Another example is the Republic of Congo, where the health sector lost its focus on reducing measles transmission due to the outbreak of Ebola in some parts of the country (Yoo, 2020). Although various international organizations are in partnership with the governments and local collaborators in improving services to HIV carriers, the COVID-19 pandemic outbreak has led to different challenges in implementing these services (McCloskey et al., 2014).

However, the introduction of quarantine, social distancing, and self-isolation strategies has led to people's inability to access continued HIV testing. As a result, this might affect the completion of UNAIDS's first 90-90-90 global target (Levi et al., 2016). Secondly, the time plan organized for HIV/AIDS care service could be affected during the COVID-19 pandemic. HIV carriers might be delayed in getting antiretroviral therapy (ART) in hospitals because hospitals' focus is to treat patients with COVID-19 pandemic and Healthcare visitation has been restricted due to the country's implementation lockdowns (Jiang et al., 2020; World Health Organization, 2020b). Also, to control COVID-19 pandemic transmission and vaccine production, most public health funds are

targeted at organizations focused on achieving these goals, thereby reducing the resources allocated for HIV/AIDS care services (Von Bogdandy and Villarreal, 2020).

PANDEMICS SHOULD REFORM AFRICA'S PUBLIC HEALTH SYSTEM

Some recent scientific studies have looked into the connections between HIV/AIDS and COVID-19 pandemic, and few similarities were reported. For instance, research carried out by He et al. provided evidence that COVID-19 pandemic reduces T-Lymphocytes which is similar to the mechanism of HIV (He et al., 2020). Another research by Guillen et al. reported that different individuals with COVID-19 pandemic severe cases might have lymphopenia or an atypically low number of lymphocytes in the blood (Guillen et al., 2020).

Another significant similarity between HIV/AIDS and the novel coronavirus disease 2019 (COVID-19) is that there are no licensed pharmaceuticals for COVID-19 vaccine or drug research, just as during the early days of the HIV/AIDS pandemic. As a result, people's behavior toward the pandemics will determine the pandemic trajectory of COVID-19 (Anderson et al., 2020), just as it is for HIV/AIDS.

However, COVID-19 and HIV/AIDS exhibit some differences too. Firstly, untreated and unattended HIV/AIDS infection usually leads to the patient's death, while COVID-19 pandemic most times kills people with underlying health conditions and old age. Secondly, behavioral changes expected to reduce the rate of transmission are different. For HIV/AIDS, reducing sexual behavior and needle sharing is very important for COVID-19, physical proximity, and handwashing (May and Anderson, 1988).

Besides, the time interval for the infections is different. For HIV/AIDS, early cases increased over 6–12 months, while for COVID-19 pandemic, the interval of infection is a matter of days. In light of these difficulties in managing COVID-19 with HIV/AIDS, WHO, UNAIDS, and the Global Network of People Living with HIV are cooperating to improve with the arrangement of HIV anticipation, testing, and treatment administrations (UNAIDS, 2020a,b; World Health Organization, 2020c). On March 20, 2020, The US Department of Health and Human Services discharged effective methods for COVID-19 and HIV/AIDS carriers (UNAIDS, 2020b), which guaranteed that HIV/AIDS patients ought to keep up at least a 30-day supply and preferably a 90-day supply of ART and all other medications if possible.

In the same vein, the Chinese National Center for AIDS/STD Control and Prevention certified information guaranteeing free antiviral drugs for special treatment management agencies in China and released a list of ART clinics (UNAIDS, 2020a). HIV/AIDS carriers can retake antiviral drugs either at the nearest local center for Disease Control and Prevention or by post to maintain enrolment in treatment programs and continue ART (UNAIDS, 2020a). Furthermore, healthcare suppliers in Thailand are to administer antiviral medications in 3–6-month dosages to meet HIV/AIDS bearers' therapeutic requirements and decrease office visits. Besides, community-based organizations are playing significant roles in keeping up HIV administrations. For example, UNAIDS is associated with the BaiHuaLin coalition of HIV/AIDS carriers and other organizations to reach and help the individuals who will come up short on antiviral medications soon (UNAIDS, 2020a).

Since Wuhan's lockdown on January 23, 2020, a network-based association (Wuhan Tong Zhi Center) has committed assets to guarantee the supply of antiviral medications and opened a hotline to provide consultations. As of March 31, 2020, this association has provided 5,500 counsels with individuals living with HIV and has helped about 2,664 people get antiviral medications. The Thai Red Cross AIDS Research Center set up visible platforms outside their facility with a screening framework for people, giving HIV testing and avoidance supplies (e.g., condoms, post-exposure prophylaxis, and pre-introduction prophylaxis) (UNAIDS, 2020b). As COVID-19 keeps on spreading worldwide, many developing countries face the danger of SARS-CoV-2 disease with hindrances and difficulties in keeping up the HIV care continuum. The circumstance could be more terrible in places with frail healthcare services frameworks. For example, in Nigeria, as revealed in a Feature by Paul Adepoju, the danger of SARS-CoV-2 affects HIV and tuberculosis reactions as patients decide to socially separate by not going to their health providers for treatment and drugs collection (Adepoju, 2020). The reactions to COVID-19 in low-resources, high HIV burden settings will fundamentally be different from the high-asset settings to a great extent.

Some countries have moved to strict movement controls, recognizing that the informal sector provides jobs for the vast majority of citizens. In sub-Saharan Africa, frameworks set up to manage HIV and the cleverness that portrays the healthcare services reaction may be an incredible resource in the battle against the new pandemic (De Cock et al., 2003).

Furthermore, the involvement with battling for reasonable access to new medicines might be more significant than any other time in the coming weeks. For the time being, SARS-CoV-2 will distract the attention given to HIV, disrupt treatment and prevention programs, and may lead to a rise in disease burden and even HIV incidence as a result. Several pieces of research suggest that severe interruption of antiretroviral therapy services during COVID-19 could lead to a 1.5- to 3-fold increase in mortality (Adepoju, 2020; UNAIDS, 2020b; World Health Organization, 2020c). Like HIV, the spread of the COVID-19, which as of June 4, 2020, had infected more than 6,151,298 individuals globally and caused 388,459 deaths, which is joined by stigma (World Health Organization, 2020a).

Around the globe, stigmatizing conduct is accounted for against those diagnosed with COVID-19 and individuals are seen as conceivably contaminated with the coronavirus regularly because of their national starting point (Al Jazeera, 2020). For instance, In the Central African Republic, the declaration of the first COVID-19 constructive individual, a Catholic minister who had lived in the nation for a long time and had quite recently come back from an outing to Italy, prompted verbal and composed assaults against the patient and Catholics and outsiders by and large viewed as vectors of the illness (Radio Ndeke Luka, 2020). As COVID-19 keeps on spreading far and

wide, so too have bits of rumors, misinformation, and fake news about the pandemic. Recordings, voice messages, writings, and stories have swirled around clashing data, from problematic fixes to strange cases that Africans are in one way or another safe from COVID-19, regardless of an abundance of opposite proof.

Tending to the damages of falsehood should, therefore, be a priority with COVID-19, and indeed compelling reactions to the pandemic would incredibly benefit from all the exercises of the multi-sectoral and rights-based ways to deal with the HIV epidemic. The impact of COVID-19 on HIV state in Africa particularly in weak healthcare systems will become double burden considering the insufficient medical resources and weak diseases surveillance will disrupt the attention of HIV patients to have easy access to healthcare centers, seek medical attention and increase drug shortage such as ART drugs for HIV patients (Nachega et al., 2021). The disproportionate proportion of COVID-19 pandemic on HIV and other vulnerable people like children, old aged, sickle cell diseases, and undernutrition is a significant burden for the underequipped healthcare systems in Africa to fight and contain and this, therefore, increase the mortality and morbidity rates of infections in Africa and affect child health (Coker et al., 2021).

EFFORTS AND RECOMMENDATIONS

Viable public health responses must be grounded in sound logical proof on the methods of transmission of the epidemic, its prevention, and (potential) treatment. Logical proof must guide the activities of political pioneers and chiefs. Health experts and health institutions upheld by the World Health Organization (WHO) assume a fundamental job in the turn of events and dispersal of logical information on the epidemic and reaction. Proof on the prevention and management of COVID-19 must be very much conveyed to the media and networks, with unique endeavors to address "counterfeit news" and expose myths.

There is need for Africa healthcare systems should increase and improving their diseases testing among priority and undertested and underprivileged populations during the pandemic. There should be a strategic plan organized by national and international technical organizations that will create an avenue where populations can test for HIV by distributing the HIV kits and create awareness and education on how to test, while COVID-19 testing should be made available everywhere where anyone can have access anytime.

Positive encounters from nations confronting the epidemic should manage reactions elsewhere. In the battle against HIV, encounters from Senegal, Thailand, Switzerland, and Uganda were methodically portrayed and utilized as outstanding practice. Regarding COVID-19, encounters from China and South Korea are being utilized, and bits of knowledge from early triumphs should be made promptly accessible (Al Jazeera, 2020). Advancements have likewise been executed to help those families generally vulnerable to mobility restrictions and the economic hardships this creates. Helping them meet fundamental work needs, for example, access to food, can lessen the danger of spread in Africa's many rambling urban informal settlements where COVID-19 could spread like wildfire because of a big clog, poor cleanliness, and previous well-being conditions.

Given Africa's significant destitution levels, lockdowns without social security plans could prompt serious outcomes, including starvation and consumption of ways of dealing with stress, especially among the most powerless. Conflicts between residents and security forces resulting from movement restrictions have prompted deaths and wounds in Nigeria, Rwanda, South Africa, and Uganda (Crisis Group, 2020). Helping them meet basic livelihood needs, for example, access to food, can diminish the danger in Kenya's casual settlements. Indigenous associations, for example, Mutual Aid Kenya and various associations are strengthening the administration's reaction system by identifying at-risk families and providing targeted assistance through direct cash transfers, food bundles, and elective supply chains to give essential items spread in Africa's many rambling urban casual repayments where COVID-19 could fan out quickly because of gigantic blockage, poor cleanliness, and previous well-being conditions (Radio Ndeke Luka, 2020).

In Kibera, the biggest of these settlements, a network-run association called Shofco has set up handwashing stations, network toilets, and clean-water booths in all passageways, staffed by volunteers and a system of health workers. Three thousand of the territory's most helpless families accept an immediate money move of $24 every month for 3 months to meet their fundamental needs, with financing originating from the private neighborhood segment and the Kenya Diaspora in North America (Duerksen, 2020). In Botswana, a paid sponsorship totaling 1 billion pula ($84 million) has been given to independent companies as a motivation to hold their employees during the shutdown. The administration will also contribute 50 percent of the basic pay of each furloughed resident or perpetual occupant for 3 months, alongside the sponsorship of 1,000–2,000 pula ($80–168) every month to address fundamental issues (Africa Center for Strategic Studies, 2020; Duerksen, 2020; Smith, 2020).

Africans are responding to the challenge in various manners. In South Africa, a private firm, Praekelt.org, made a WhatsApp-based helpline that gives continuous information and robotized reactions in various dialects to teach and sharpen. The application enlisted 3.5 million endorsers inside the initial 10 days of launching. Praekelt.org has now cooperated with the World Health Organization to do a similar service to reach a global audience.

Africa Check, Africa's pioneer fact-checking association, gives devoted COVID-19 assistance in an organization with Facebook. Facebook is additionally working with Nigerian media organizations to battle falsehood via web-based networking media. The Nigerian Presidential COVID-19 Task Force has likewise established a 24-h hotline giving forward-thinking data to educate and shield the general population from deception and bits of gossip. Numerous presidents and senior well-being pioneers utilize their day-by-day briefings to dispel bits of gossip and deception about COVID-19 (Africa Center for Strategic Studies, 2020; Duerksen, 2020; Smith, 2020).

We must think to rebuild and reshape the HIV response once the initial wave of COVID-19 is passed and nations learn to live with the dual pandemic. Like HIV, the COVID-19 pandemic isn't just a well-being concern, but it is a social, economic, and human security issue. However, as part of COVID-19 pandemic preparedness, maintaining a sufficient supply of ART is critical. A public health response is a need in establishing and maintaining a consistent drug supply chain. The United Nations Security Council perceived HIV as a harmony and security issue on January 10, 2000, when it met to examine the scourge's effect in Africa. This was the first run through the Security Council, which had tended to a medical problem as a danger to harmony and security, making ready for the appropriation of Resolution 1,308 on HIV/AIDS and worldwide peacekeeping tasks (UN Security Council, 2000).

Reacting to pandemics, for example, HIV and COVID-19, require a multi-sectoral approach that activates initiative at the most significant level. From Malaysia to Uruguay, to Italy and the Central African Republic, Heads of State and governments are occupied with the reaction to COVID-19 and are administering measures to control its spread. The inclusion of Heads of State is expected to bring all offices and organizations into the reaction, initiate emergency instruments and assets, and pass on the circumstance's direness.HIV pandemic is a significant cause of multilateralism and worldwide cooperation. Thanks to network activism, global solidarity, and collaboration in the fields of science and medication, 24.5 million individuals are on antiretroviral treatment today, generally in poor and middle-income nations (UNAIDS, 2019).

The United Nations Secretary-General and the Director-General of WHO at the G20 Leaders' Extraordinary Summit on COVID-19 on March 26, 2020, focused on the critical need to quicken worldwide organization solidarity in response to the pandemic (United Nations, 2020b). This solidarity must be tied down in a multilateral system to help and finance the worldwide reaction and recuperation with explicit regard for nations generally influenced and those generally delicate. These standards are additionally explained in the Secretary General's report, Shared duty, worldwide solidarity: Responding to the economic effects of COVID-19 (United Nations, 2020a).

With a health system severely debilitated by many years of political precariousness and strife, perhaps the most negligible proportion of qualified well-being laborers per capita on the planet, and the more significant part of its populace needing helpful help, the Central African Republic is one of the most delicate nations confronting COVID-19 (Coordination of Humanitarian Affairs, 2020). With the help of WHO, MINUSCA, the World Bank, UNICEF, and other UN offices and accomplices, early measures adopted by the legislature seem to have been compelling with just six essentially imported instances of COVID-19 recorded toward the end of March and constrained proof of nearby transmission.

As nations adopt various strategies to control the pandemic, we should portray what measures are working by and assess how individuals react, and be aware of unintended impacts. Similarly, modelers must shield their forecasts, so policymakers should clarify their behavioral interventions' proof and hypothesis. Straightforwardness encourages assessment and empowers examining suspicions, prompts better practice, and tackles thoughts from a scope of logical orders.

CONCLUSION

As COVID-19 keeps on spreading the world over, numerous areas are confronting the danger of SARS-CoV-2 disease and obstructions and difficulties for keeping up the HIV care on high standards. The situation, unfortunately, is worse in countries with weak healthcare systems. We suggest that legislatures, network-based associations, and international accomplices should cooperate to keep up the HIV care continuum during the COVID-19 pandemic, with specific endeavors to guarantee convenient access to and maintain a strategic distance from disturbance routine HIV administrations.

AUTHOR CONTRIBUTIONS

ATA conceptualized the research idea. AA and GB review and make substantial revision on the first draft. ATA and GB write the second draft and AA revised the second draft. All authors draft out the first manuscript. All authors read and revise and approve the final draft of the manuscript.

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Social Factors Associated With Adherence to Preventive Behaviors Related to COVID-19 Among Rural and Semi-urban Communities in Western Maharashtra, India

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Background: To control the transmission of the coronavirus disease 2019 (COVID-19) infection, the Government of India (GoI) had taken stringent precautionary measures during the lockdown period. This study aimed to explore determinants affecting adherence to protective measures against COVID-19 infection among rural and semi-urban settings of Maharashtra, India.

Methods: A cross-sectional telephonic survey among 1,016 adults from randomly selected households was conducted between June 5 and July 16, 2020. The data were explored for knowledge, awareness, practices related to protective measures, and self-risk perception. Socio-demographic and attitudinal correlates of failure to use protective measures against COVID-19 were measured.

Results: In the survey, 72% of the participants were men. The mean age was 46 years (SD: 13.8). The main source of information was television (91%); however, information from healthcare providers (65%) and mass media announcements (49%) was trustworthy. Washing hands immediately with soap after returning from outdoors was reported by 95% of the respondents, always using a mask while outdoors by 94%, never attended social gatherings by 91%, always using hand sanitizer while outside by 77%, and 68% of the respondents followed all protective measures. The knowledge score [mean score 20.3 (SD: 2.4) out of 24] was independently associated with the risk of not using protective measures, with each unit increase in knowledge score, the risk of not using protective measures reduced by 16%. No source of income was independently associated with not using protective measures [AOR 1.5 95% *CI* (1.01–2.3)].

Conclusions: The COVID-19 public health interventions and behavior change communication strategies should be specifically directed towards the low socio-economic populations through trusted sources. The association between knowledge and practices demonstrates the importance of accurate public health communication to optimally follow preventive measures, such as structural interventions to address poverty and employment policies to address the unemployment crisis are required. Surveillance activity is needed to understand the actual behavior change among the population.

Keywords: COVID-19, lockdown, handwashing, face-mask, adherence, personal protective measures, rural, India

INTRODUCTION

The coronavirus disease 2019 (COVID-19) has had a devastating effect globally since it was first identified in China in December 2019 (1). The acceleration of the transmission is confirmed by the fact that while it took 1 month since December 31, 2019 for the number to reach 10,000, and by March 6, 2020, over 100,000 cases were reported (2, 3). Toward the end of March 2020, there were 528,025 cases and 23, 669 deaths due to COVID-19 reported in over 190 countries (4).

Governments across the globe applied a series of behavioral interventions in the countries to minimize the transmission and burden of COVID-19 on the healthcare system and contain the transmission. These included infection prevention and control measures, that is, promotion of the use of masks along with following regular and thorough hand hygiene practices through handwashing with soap and water or alcohol-based hand rub, international and internal travel-related restrictions, and following social distancing (5, 6). Although randomized controlled trials (RCTs) demonstrate that personal protective measures such as hand hygiene and face masks have a small effect on respiratory infection transmission, higher compliance in a severe pandemic might improve the effectiveness (5, 7–9). However, adoption of such protective behaviors for curbing the spread of influenza and social distancing policies were reported of being of uncertain effectiveness, expensive, unpopular, difficult to implement (10–12), and highly disruptive to society (5, 13). However, in the absence of a vaccine, behavioral strategies for reducing the transmission of COVID-19 are vital to the global pandemic response (14). The efficacy and impact of these strategies depend on the compliance of the community and their cooperation. Historically, the adoption of such behaviors has depended on many factors related to personal perceptions and beliefs about the effectiveness of the preventive measures, the perceived risk of contracting the disease by self or family, and the perceived severity of health and economic consequences (15–18).

According to the Government of India (GoI) and the World Bank, 22% of population in India is poor which means 1 in 5 Indians is poor, with 80% of the poor population residing in rural areas (19, 20). COVID-19 has directed renewed attention to the informal employment sector of India, the migrant poor who move, often seasonally, from the villages to cities in search of work, and who in troubled times like these seek to return to villages where they feel more secure and have greater access to food and shelter (21–23). However, in rural and semi-urban communities, owing to family structures, close-knit communities, adherence to social isolation, preventing social gatherings, following social distancing behaviors may pose practical, motivational, and social barriers.

Therefore, this study aimed to explore determinants affecting adherence to protective measures against COVID-19 infection among communities in rural settings in India. A better understanding of behaviors, beliefs, concerns, knowledge, and associated predictive factors of people, during an emerging pandemic, is of crucial importance for public health officials and decision-makers, to enhance communication efforts for the promotion of individual and community health.

METHODS

Study Design

A telephonic cross-sectional survey was conducted between June 5 and July 16, 2020.

Study Setting and Participants

Satara and Sangli districts in the western region of Maharashtra were selected for the study purposively to have access to the rural population. Satara district is divided into 11 subdivisions and has a population of 3,003,741, whereas Sangli district is divided into 10 subdivisions and has a population of 2,822,143 persons. The rural population is 74.51 and 81.01% for Sangli and Satara districts, respectively (24, 25). The four purposively selected villages (clusters) in the Karad block were Khubi, Gondi, Shere, and Dushere which are rural, and the Karad Panchayat is considered semi-urban. The fifth village Lavanmachi was selected from the Walwa block of Sangli district.

Sample Size

To assess the level of awareness about COVID-19, using a confidence level of 95%, the margin of error of 3.5%, and 50% awareness for COVID prevention measures, the sample size was estimated to be 800, adding 30% non-responsive to reach at a sample size of 1,000. Further, the sample size was adjusted by 30% to account for the households that had wrong contact numbers or for the contact numbers that were not reachable on the phone. The final sample size was 1,300.

Sampling

Community support was sought from the village heads, local health officials, officials at the municipal corporation office, and police department before the study was initiated to gain access to household data and contact people on the telephone. The local police were informed of the commencement of the telephonic survey to keep them in the loop in case any of the respondents filed complaints about receiving a request for a telephonic survey. The local health authorities were informed not for any kind of penalty to the participant but only for keeping authorities in the loop for conducting a telephonic survey in the community.

A line list of all households in the six clusters was procured with support from the village head and the local government offices. The list included the name of one adult person in the household, their address, and contact number. A list of 1,300 households to be contacted was selected from these six clusters using a random number list. After contacting the household, they were asked to provide information on the number of adult members in the household, further, the Kish grid method (26) was used to select one adult respondent from each of these households randomly, and then, they were interviewed on the contact number provided in the household list or if they preferred to be called on a different number, this was noted and they were contacted on a number that they provided. Individuals, 18 years of age and above, currently residing in the study clusters, and who could understand and respond in Marathi, were eligible for participation.

Survey Instruments

A semi-structured questionnaire was used for data collection. It explored demography (age, sex, education, source of income, and family size), knowledge and level of awareness of the community about COVID-19 infection, such as transmission routes, symptoms, prevention, and treatment measures, practices related to handwashing, wearing a face mask, using hand sanitizers, following social distancing, reducing physical contact, perceived risk of acquiring infection, the susceptibility of acquiring infection when at crowded places, sources of information about COVID-19 infection, and trust of participants in these information systems and sources.

Data Collection

In the survey, 12 interviewers were trained over 4 weeks for data collection. Pilot testing of the telephonic survey was completed between May 15 and May 31, 2020 by the trained 12 interviewers. Each household was approached using the contact number from the household list. Adults answering the call were given information about the study. One participant from each contacted household was selected randomly using the Kish method. In case the participant selected did not understand or respond in Marathi or not able to provide the informed consent (not able to hear or speak), resampling of the participant from the same household was conducted. At least six attempts were made to contact the household or the participant at different times (**Table 1**). The participants were interviewed as per their availability between 8:00 a.m. and 10:00 p.m. and the survey lasted for approximately 30 minutes. If the adult in the household was selected or if the participant refused to participate, they were considered as household or participant refusal, respectively. If participants decided to withdraw their participation from the study after consenting then they were counted as "discontinued." In case, the male members or the head of household refused to give an appointment for the female members to be interviewed from the family, they were offered an option for a female surveyor to call them at a time convenient to them. An SMS was sent out to a household contact or participants to request their participation in the study, to participants who never answered calls or continued asking the surveyor to call them back later each time they called, and to those who disconnected calls or refused to participate before hearing about the study and ignored subsequent calls from the study team. **Figure 1** illustrates steps involved in contacting a household and selecting a participant, and completing the interview.

Ethics Approval

The study was approved by the Institutional Ethics Committee of ICMR-National AIDS Research Institute, Pune, Krishna Institute of Medical Science Deemed-to-be University, Karad, and KEM Hospital Research Center, Pune. The data were collected after verbal informed consent by the participant, and the survey was audio-recorded if the participant consented.

Measurement of Variables

1) Demographic information, such as questions about age in completed years, sex, current place of residence, level of education completed, and the main source of income in the last 12 months.
2) Knowledge and level of awareness of the community about COVID-19 infection, such as questions on transmission routes, symptoms, availability of prevention, and treatment measures, perception on complete recovery, duration of transmission of infection to others, knowledge about the high-risk populations, measures to prevent COVID-19 infection, and if they had heard about social distancing.
3) Practices related to the protective measures adopted for COVID-19, such as using soap for handwashing and sanitizer while being outdoors, wearing masks, following social distancing, and reducing physical contact (staying indoors).
4) Perceived risk of acquiring infection and susceptibility.

Data Analysis

Independent Variables

A standard descriptive summary for age, family size was expressed in percentages or as the mean and SD. Education was categorized as—never attended school, primary, upper primary, secondary, senior secondary, undergraduate, post-graduate and above, and vocational training. The variable of self-risk perception was categorized as—yes, no, and do not know. The frequency for looking for COVID-19 updates on media was categorized as—once a day, many times a day, and not every day/never. Feeling worried about having COVID-19 symptoms as—worried/very worried, somewhat worried, and rarely/not worried. Knowledge scores ranged from 0 to 24; this was included as a continuous variable based on 13 questions related to knowledge of prevention measures for COVID-19.

TABLE 1 | No. of phone call attempts made and the interview status.

Interview status	No. of phone call attempts made					
	1	2	3	4	4 and above	Median (Range)
Complete (956)	134	190	165	96	371	3 (1–54)
Discontinued (60)	4	3	5	3	45	9 (1–32)
Refusal by participants (73)	7	16	8	10	32	4 (1–24)
Household refusal (147)	12	21	16	14	84	5 (1–32)
Never reachable (99)					99	10 (1–50)
Wrong number (132)	13	14	9	11	85	6 (1–20)
Excluded (12)	5	0	0	1	6	3 (1–13)

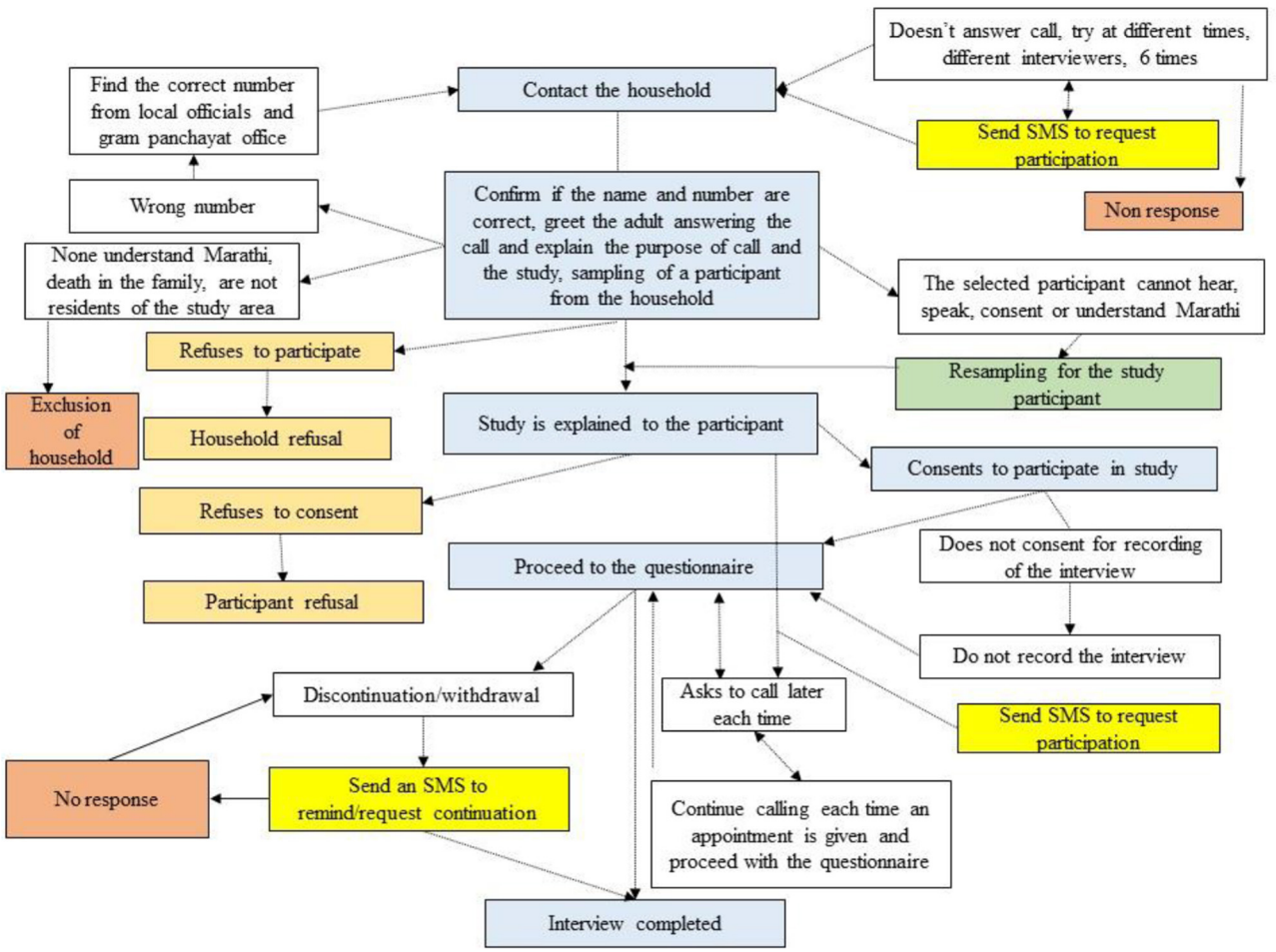

FIGURE 1 | The steps involved in contacting a household, selecting a participant, and completing the interview.

Dependent or Response Variable

The responses indicating proper use of protective measures were coded as 1 and otherwise 0. This included an "**Always**" response to questions on wearing a mask while going outside the house, washing hands with soap and water when coming from outside, using hand sanitizer while outside or after coming home, while a "NO" response to attending social gatherings in past 15 days. Combining the responses to these variables, a variable was generated to capture the data about failing to use/follow any of these protective measures. Correlates of failing to use protective measures were identified using univariate and multivariate logistic regression models. A multivariable logistic regression analysis was performed to identify factors related to knowledge, attitudes, and practice. A multivariable

regression model was used to understand socio-demographic and attitudinal correlates of not following protective measures related to COVID-19. All analyses were done using STATA software; version 16.0 (Stata Corp. 2019. Stata Statistical Software: Release 16. College Station, TX, USA: Stata Corp LLC.).

RESULTS

A total of 1,479 households/individuals were contacted for the study, of which 220 households and participants refused to participate in the study, 132 contact numbers were incorrect, 100 potential participants were never reachable, and 11 households were excluded from the study. The final sample consists of 1,016 respondents. Of these, 956 participants had completed all the items in the interview and 60 participants completed the interview partially. The response rate was 69%. In order to complete the survey, 8,532 calls were made. **Table 1** describes the number of phone call attempts made and the outcome of the interviews.

Of the enrolled participants 72% (734) were men. The higher representation of male participants in the study may be a coincidence. Nearly half of the participants were in the age group between 30 and 50 years, 39% of the participants had completed secondary education, 28% were self-employed or owned a business followed by 24% salaried, and 14% of the participants reported farming to be the main source of income (**Table 2**). The missing information is not presented in the data.

Knowledge of Transmission of COVID-19 Infection

The findings showed that 94% (955) of the respondents had correct knowledge of COVID-19 transmission, and 97% (988) knew that it could be transmitted through coughing, sneezing, and close physical contact. The knowledge regarding the symptoms of COVID-19 showed that 65% (664) of the population knew that the dry cough, fever, and shortness of breath (all) could be symptoms of COVID-19. The major source of COVID-19 related information was reported to be television (91%), local announcements (84%), and local healthcare providers (82%); however, a great deal of trust was more of local healthcare providers (65%) and local announcements 49%. **Tables 3A–5** show responses to items related to knowledge, attitude, and practices toward COVID-19.

Attitudes of Respondents Toward COVID-19

The attitudes of the respondents toward COVID-19 were assessed, and the results (**Table 4**) showed that 88% (890) of the respondents believed that persons having COVID-19 infection can recover completely and, 77% (738) had felt that COVID-19 infection is completely preventable at present; however, 30% believed that there is the availability of specific treatment of COVID-19 at present. Most respondents reported that the persons who have traveled to an area affected by COVID-19 (90%) have come in contact with a person having the infection (93%), and elderly persons above 60 years of age (94%) are the "high risk" population for COVID-19 infection. In addition, 46% (470) did not consider themselves as susceptible to the infection and approximately half 49% (499) felt that a person having COVID-19 infection would transmit the infection to others up to 13–15 days. Nearly, one-fifth of the participants (21%) did not know for how long a person who has an infection could transmit it to others. Additionally, only 56% (569) of the respondents felt

TABLE 2 | Socio demographic characteristics of the study participants.

Characteristics	*N* = 1016 No. of participant (%)	Characteristics	*N* = 1016 No. of participant (%)
Gender		**Age (years)**	
Male	734 (72)	Mean (SD)	46.2(13.8)
Female	282 (28)	<30	148 (15)
Education		31 to 40	241 (24)
Never attended school	53 (5)	41 to 50	254 (25)
Primary	71 (7)	51 to 60	200 (20)
Upper primary	104 (10)	>60	169 (17)
Secondary	251 (25)	**Occupation**	
Senior secondary	147 (14)	Business/ Self employed	282 (28)
Undergraduate	276 (27)	Salaried (Private/Govt.)	252 (25)
Post graduate and above	73 (7)	Agriculture	144 (14)
Vocational training	36 (4)	Laborer*	104 (10)
Family size		Retired	97 (10)
One or Two	82 (8)	Unemployed	58 (6)
3 to 6	692 (68)	Student	47 (5)
More than 6	174 (17)	Refused/ missing	19 (2)
Median (IQR)	4 (4, 6)	Home Maker	13 (1)

**Laborer included agriculture labor, casual, maid and other. The total number of participant will differ in each category due to non-response.*

TABLE 3A | Participants knowledge and their level of awareness related to COVID- 19 infection.

Response category (correct response)	No. of correct responses (%)
Transmission of coronavirus infection	
Through coughing, sneezing, close contact (Yes)	988 (97)
Transmissible from person to person (Yes)	955 (94)
Mosquito bite (No)	921 (91)
Through food or water (No)	780 (77)
Not transmissible (No)	663 (65)
Transmitted by animals to human only (No)	602 (59)
Symptoms of coronavirus infections correctly mentioned	
Fever	898 (88)
Shortness of breath	803 (79)
Dry cough	798 (79)
All (dry cough, fever, shortness of breath)	664 (65)
Knowledge about measures to prevent coronavirus infection	
Maintain personal hygiene and frequent hand washing with soap and water	983 (97)
Obey the advisories issued by government and health administrations	980 (96)
Wearing mask when sick or having some symptoms	969 (95)
Maintain social distancing	968 (95)
Avoid traveling to known affected area	939 (92)
Avoid touching your eyes, nose and mouth with unwashed hands	911 (90)
All the above	832 (82)

TABLE 3B | Participants reporting sources of information for Covid and level of trust.

Source of information	Individuals reporting source *n* (%)	Very little trust *n* (%)	Great deal of trust *n* (%)
Television	929 (91)	52 (6)	378 (41)
Local announcement	850 (84)	52 (6)	406 (48)
Local healthcare providers	837 (82)	22 (3)	542 (65)
WhatsApp/Facebook/Twitter	723 (71)	165 (23)	102 (14)
Newspaper	691 (68)	38 (6)	184 (27)
Local groups	602 (59)	46 (8)	239 (40)
Web based information	508 (50)	53 (10)	143 (28)
Other (family, friends, relatives, known contacts)	173 (17)	–	–
Other (Social workers in village)	36 (3.5)	–	–

TABLE 4 | Responses of participants to attitudinal statements regarding COVID 19.

Statement	No. of responses (%)
A person with coronavirus infection disease recover completely	890 (88)
Coronavirus infection is completely preventable at present	783 (77)
Availability of specific treatment at present	308 (30)
Risk perception	
High-risk population for coronavirus infection	
Elderly people (above 60 years of age)	956 (94)
Contact with confirmed COVID positive case	945 (93)
Recent travel history to the affected area	918 (90)
Persons with preexisting morbidity	891 (88)
Pregnant women and children	860 (85)
All of the above	725 (71)
How susceptible do you consider yourself to an infection	
Very highly/ somewhat susceptible	390 (38)
Not at all susceptible	470 (46)
Chances of getting infected in crowded places	
Very high chance	479 (47)
Somewhat high chance	337 (33)
Very less chance	101 (10)
No chance	78 (8)
Social distancing can break the spread of coronavirus infection	
Yes, definitely	569 (56)
Yes, somewhat	301 (30)
Yes, but very little chance	60 (6)
No, not at all	36 (4)
Do not know	29 (3)
How long a person infected can spread coronavirus	
<= 4 days	49 (5)
<= 8 days	72 (7)
10 to 12 days	45 (4)
13 to 15 days	499 (49)
16 to 21 days	25 (2)
Chances of getting infected in crowded places	
Very high chance	479 (47)
Somewhat high chance	337 (33)
Very less chance	101 (10)
No chance	78 (8)
Heard about social distancing	
Yes	863 (85)
Opinions about the meaning of the word "social distancing"	
Avoiding rush at workplaces	934 (92)
Avoiding shaking hands	915 (90)
Keeping 2 meter distance from people	915 (90)
Avoiding social gatherings	894 (88)
Avoiding public places	866 (85)
Avoiding going out of the house	776 (76)
All of the above	643 (63)

that following social distancing can break the spread of COVID-19 infection. Approximately 81% of respondents believed that the lockdown was an important strategy to prevent the spread of COVID-19.

Practices Related to Social Distancing

The survey results showed that a total of 95 participants (9.4%) have attended a social gathering and visited a friend for tea/discussion in the last 15 days. Of the total 95% (967) reported

TABLE 5 | Reported practices and behavior related to COVID 19.

Practice	No. of responses (%)
Wash hands with soap and water after coming home from outside	967 (95)
Wearing a mask ALWAYS while going outside the house	953 (94)
Feels necessary to ALWAYS cover your face/mouth while coughing or sneezing	923 (91)
Always using hand sanitizer while outside	779 (77)
In past 15 days, attended social gatherings visited friends for tea, socializing	95 (9)
Looking for updates on social media	
Once in a day	223 (22)
Many times a day	650 (64)
Not every day/never	67 (7)
Feel worried by COVID symptoms	
Worried/very worried	375 (37)
Somewhat worried	240 (24)
Rarely/not worried	328 (32)

immediate washing of hands after returning home, followed by 94% (953) stating wearing a mask while going outside, and always using a hand sanitizer while being outside was reported by 77% (779) of the participants.

Stress

The current situation was stressful for families, and feeling lonely due to the pandemic situation was reported by 55 and 49% of the respondents, respectively. Additionally, 24% (241) reported feeling angry and more anxious than in the past. Furthermore, 16% reported having faced difficulty in availing healthcare due to lockdown.

Association Between Socio-Demographic Variables and Not Following Protective Measures

Association between socio-demographic variables and not following protective measures is described in **Table 6**. The socio-demographic variables, such as age, sex, and education, were not independently associated with risk-taking behavior (not following protective measures). Association between socio-demographic variables and not following protective measures showed no difference in peri-urban and rural settings. Not having any source of income was independently associated with not following protective measures for COVID-19 prevention AOR 1.5 (95% *CI* 1.01–2.3). Among men, "having no source of income" was associated with not following protective measures as compared with men who had a source of income [*OR* 1.8, 95% *CI*: 1.1–2.9, $p = 0.015$]. The knowledge score was independently associated with the risk of not using protective measures for COVID-19 prevention. With each unit increase in knowledge score, the risk of not using protective measures reduced by 16%.

DISCUSSION

This study was conducted to explore the determinants affecting compliance to protective measures against COVID-19 infection among rural and semi-urban communities in the western region of Maharashtra, India. The study highlighted high knowledge about COVID-19 among rural and semi-urban communities. The findings in this survey suggest socio-demographic factors that influence the adherence to the protective measures for COVID-19 prevention and government advisories that would prove useful in planning behavioral change communication programs for containment of the current COVID-19 pandemic and also new emerging infectious diseases in these regions.

The seroprevalence of COVID-19 showed an increase between May and August 2020 in India (27). The third round of the serosurvey conducted in India in August–September 2020 and December 2020–January 2021 showed an increase in seroprevalence in the urban areas, while the rural population is still at risk and surveillance has been recommended (27, 28). We conducted an epidemiological survey aimed at assessing knowledge, attitudes, and practices and identifying opportunities to target interventions to contain the spread of COVID-19 infection in rural and semi-urban regions of India. When compared with a study conducted in Nigeria (29), most of the study participants reported accurate knowledge and compliance with following the protective measures. The majority of the current study participants reported maintaining social distancing, frequent handwashing with soap and water, wearing a mask while leaving the house, and obeying government advisories. The study conducted by Dkhar et al. in April, 2020 among social media users in Jammu and Kashmir, showed similar results that respondents exhibited good knowledge, positive attitudes regarding COVID-19 during the pandemic with most of them reporting regularly wearing masks, washing hands with soap and water regularly, following lockdown guidelines, and maintaining social distancing (30). Similarly, cross-sectional online survey conducted in India also showed the correct rate of knowledge (74.7%), perception (57.6%), and practices (88.1%) toward COVID-19 (31). While closer to the outbreak, reports showed poor attitudes toward disease prevention and control in Thailand (32).

The current study was conducted between the fourth and fifth phase of lockdown in the month of May and June 2020 with unlock being initiated in the state of Maharashtra at this time. The accurate knowledge of COVID-19 reported by the participants and compliance with following personal protective measures in this study could be attributed to the months-long campaigning efforts targeted toward making messaging more effective through pre-recorded public local announcements and using locally available resources, such as rickshaw/tempo in the rural areas of Maharashtra, India (33). In addition, local news resources have reported that community social workers are utilizing innovative and simplified ways of using umbrellas to explain social distancing (34). Several regions during this data

TABLE 6 | Association between socio-demographic variables and not following protective measures.

Characteristic	No. of individuals (% out of 1016)	No. of individuals not following protective measures (%)	OR (95% CI)	AOR (95% CI)	*P* value
Age group					
30 & Below	148 (15)	42/143 (29)	1	1	
31–40	241 (24)	53/240 (22)	0.7 (0.4–1.1)	0.92 (0.5–1.6)	0.756
41–50	254 (25)	72/247 (29)	0.99 (0.63–1.6)	1.02 (0.6–1.7)	0.927
51–60	200 (20)	70/195 (36)	1.3 (0.85–2.1)	1.7 (0.99–2.9)	0.055
Above 60	169 (17)	64/162 (40)	1.6 (0.97–2.5)	1.4 (0.8–2.6)	0.221
Gender					
Male	734 (72)	222/715 (31)	1	1	
Female	282 (28)	79/273 (29)	0.9 (0.7–1.2)	1.01 (0.7–1.5)	0.948
Education					
Illiterate	53 (5)	16/49 (33)		1	
Primary	175 (17)	47/171 (27)	0.78 (0.4–1.6)	1.3 (0.5–3.2)	0.610
Secondary and senior secondary	398 (39)	121/388 (31)	0.93 (0.5–1.8)	1.9 (0.8–4.6)	0.142
Above senior secondary	385 (38)	117/379 (31)	0.92 (0.5–1.7)	2.3 (0.9–5.5)	0.075
Having source of income					
Yes	782 (77)	217/763 (28)	1	1	
No	215 (21)	79/211 (37)	1.5 (1.1–2.1)	1.5 (1.01–2.3)	0.048
Family size (No. of members)					
Small (1 to 4)	501 (49)	145/501 (29)	1	1	
Large (more than 4)	447 (44)	140/447 (31)	1.1 (0.8–1.5)	1.3 (0.9–1.7)	0.157
Self-risk perception (consider susceptible to infection)					
No	470 (46)	145/461 (31)	1	1	
Yes	390 (38)	116/389 (30)	0.93 (0.7–1.2)	1.1 (0.8–1.6)	0.496
Do not know	136 (13)	37/132 (28)	0.85 (0.6–1.3)	0.86 (0.5–1.4)	0.545
Look for COVID update on media					
Once in a day	223 (22)	65/223 (29)	1	1	
Many times a day	650 (64)	192/650 (30)	1.02 (0.7–1.4)	1.03 (0.7–1.5)	0.879
Not every day/never	67 (7)	24/67 (36)	1.4 (0.8–2.4)	1.03 (0.6–1.9)	0.924
Feel worried by COVID 19 symptoms					
Worried/Very worried	375 (37)	105/375 (28)	1	1	
Somewhat worried	240 (24)	61/240 (25)	0.87 (0.6–1.3)	0.7 (0.5–1.1)	0.082
Rarely/Not worried	328 (32)	117/328 (36)	1.4 (1.03–1.96)	1.2 (0.8–1.7)	0.410
Knowledge					
COVID 19 knowledge score (ranging from 1 to 24)	Mean (SD) 20.3 (2.4) Median(IQR) 21 (19, 22)	Mean (SD) 19.7 (3.1) Median(IQR) 20 (18, 22)	0.86 (0.81–0.91)	0.84 (0.78–0.90)	< 0.01
Outbreak is stressful					
No	390 (38)	115/390 (29)	1	1	
Yes	556 (55)	167/556 (30)	1.03 (0.77–1.36)	1.01 (0.74–1.4)	0.931
Locality					
Peri-urban	864 (85)	260/841 (31)	1	1	
Rural	150 (15)	40/145 (28)	0.85 (0.57–1.26)	0.9 (0.6–1.4)	0.641

collection period were considered as containment and micro-containment zones where the village borders and also smaller localities were sealed. The local news resources reported that this led to fear and panic among the communities (35, 36). This may imply active observation and discussions within groups in these study areas, facilitated through the local healthcare providers, social workers, and local announcements, which have the trust of the community. GoI launched a "*jan andolan*" (public campaign) for COVID-19 appropriate behaviors (37). The participants in the current study scored 90% (median score) for the efforts of the state government to contain the pandemic.

Although participants reported having good knowledge about preventive measures, 46% perceived no risk of acquiring COVID-19 infection. Low self-risk perception is contrary to the findings reported during the early stage of the pandemic in China, where studies showed more than 70% of the respondents were worried about them or a family member acquiring the infection (38–40). Similar to the current study findings, low-risk perception (median score of 5 out of 10) was reported in a study conducted in the United States (41). This low self-risk perception in the present study is an indication of complacency that might set in once prevention fatigue rises in the community. It could also result in vaccine hesitancy. Therefore, local communication strategies should emphasize creating public awareness and bringing about a behavior change through population tailored interventions to help communities sustain following protective measures, since, it is likely that adherence to protective measures may not be sustained when the penalties are revoked. Further, novel approaches to estimate compliance with lockdown measures in the COVID-19 pandemic may be adopted (42). In addition, face masks are proposed to be the most obvious measure to prevent transmission and they can generate peer pressure kind of response in the communities (43). It would be important to continue with efforts for personal protective measures to avoid a false sense of security among those who receive vaccine which is currently being rolled out (43).

This study highlighted the evidence about the source of COVID-19 related information for the community and their level of trust in them. For 91% of the participants, television was the source of COVID-19 related information, local announcements 84%, local healthcare providers 82%, and social media 71%; however, participants had a great deal of trust in the healthcare providers and local announcement systems. Similarly, Zhong et al. also reported that social media was a primary source for COVID-19 information, whereas the most trusted sources were healthcare professionals (40). Therefore, these sources must be involved while delivering health information and interventions tailored to the needs of the community.

Mental health concerns and treatment are left out when the limited resources are mobilized for pandemic containment (44). History suggests that any infectious disease outbreak or pandemic brings with it a major setback in the mental health front. In 2014, during the Ebola outbreak, anxiety-depression and symptoms of post-traumatic stress disorder (PTSD) were more prevalent even after 1 year of Ebola response (45). Mental health concerns, such as stress, anxiety, depression, insomnia, denial, anger, and fear were reported by Roy et al. through a scientific review (44). In the context of India, mental health concerns of the COVID-19 pandemic may be more complex due to a large proportion of the socially and economically vulnerable population, migrant workers, and laborers who have been reported to be affected the most. In India, within hours of the lockdown announcement on March 25, 2020, millions of migrant laborers began reverse migration (46, 47). The phenomenon produced loneliness, panic, fear, feelings of isolation, and economic anxiety. The migrant workers having a serious nervous breakdown and depressive psychotic disorders were reported in the media (48). In the current study, more than half of the participants (55%) reported that this period was stressful for the family as they experienced loneliness and suffered "more stress and anxiety" than in the past.

In the current study, it was reported that persons with no source of income were not following the protective measures. The spike of COVID-19 infections in rural areas in Maharashtra was attributed to the reverse migration of workers returning from the urban areas (49) and until September 2020, rural areas contributed to 49.7% of all cases in the country, and Maharashtra being the major destination state for reverse migration for migrant laborers (50, 51). In Australia, during a pandemic influenza outbreak, it was reported that individuals who are employed but not able to work from home are less likely to report intended compliance with quarantine restrictions (52). On the contrary to the current study findings for a swine flu outbreak in the United Kingdom in 2009, where participants who were not employed, were poor, had an annual household income of less than GBP £30,000, or had no educational qualifications were significantly more likely to adopt avoidant behaviors (e.g., avoiding large crowds or public transport) (53).

In the present study, 28% of the participants were self-employed, 14% were engaged in agricultural activities as their main source of income, and 10% worked as laborers. The government restricted commercial and industrial activity and imposed a ban on the movement of people and goods deemed "non-essential" from March 25, 2020 that affected the income-generating activities. During the months of April and May, 2020, these exemptions were maintained and further supported by opening up agricultural input stores, machinery repair shops, and agribusinesses. Inter-district travel was prohibited other than for emergency purposes, and public transport facilities remained shut down until mid-May, 2020, and the movement of people, such as agricultural laborers, remained severely constrained (54). This necessitates the need for attention to the underserved and marginalized populations, and people from low socio-economic status to prevent long-lasting adverse health outcomes.

This study was conducted at a time when there was a complete lockdown and no one was venturing out. We had success in conducting large-scale telephonic surveys in rural and peri-urban settings. The data collection for this study was conducted using telephone calls, therefore, the households that did not have a telephone were not included in the study. Furthermore, homeless populations might not have been enumerated in the gram panchayat and Nagar panchayat list and therefore may have been missed from the study. Another limitation with the telephonic method of data collection would have been that participants may be reluctant to speak with an unknown caller, leading to household and participant refusals. It is natural to have a shorter attention span over telephonic interviews than in face-to-face interviews. Therefore, there were few missing data and discontinued interviews in this study. Since this was a telephonic survey, we had to rely on self-reported instead of observed practices, thus were unable to verify whether the responses were affected by social desirability bias.

A positivist approach was used and, therefore, we included all socio-demographic and behavioral factors that could influence corona appropriate behaviors in the community. However, cultural and religious factors were not explored which was a limitation. These factors would have been difficult to explore on the telephone. Qualitative exploration was not possible considering the situation. Therefore, these factors were not explored in order to prevent any adverse comprehension by the interviewee. A face-to-face in-person interviewing was not possible due to the travel restrictions and social distancing guidelines. Owing to the lockdowns and inaccessibility to the study participants except through telephone, the Kish method was the most feasible method of data collection. However, the anticipated high intra-cluster similarity may have weakened the generalizability of the results.

CONCLUSION

The study shows that the lower knowledge score and having no source of income were independently associated with the risk of not following COVID-19 preventive behaviors. The COVID-19 public health interventions and behavior change communication strategies should be specifically directed towards the low socio-economic populations through the trusted sources, such as structural interventions to address the poverty and employment policies to address the unemployment crisis. The association between knowledge and practices demonstrates the importance of prompt and accurate public health communication to follow preventive measures optimally.

Although protective measures during the study duration were high, surveillance activity is needed to understand the actual behavior change among populations. Local interventions to mitigate the effect of mental health concerns in this population are necessary. Perception of risk should be encouraged, and risk communication should be tailored to this rural population considering mental health while developing these strategies.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The study was approved by the Institutional Ethics Committees of ICMR-National AIDS Research Institute, Pune, Krishna Institute of Medical Science Deemed-to-be University, Karad, and KEM Hospital Research Centre, Pune. The data was collected after verbal informed consent by the participant, the survey was audio-recorded if the participant consented.

AUTHOR CONTRIBUTIONS

SS, SJ, and SR were involved in the conceptualization of the study. The study methodology was developed by SS, SJ, SR, RK, SB, and SPS. SPS, SR, RK, and SS trained the team for data collection. SPS, RP, and AJ implemented the study. The data were curated by SPS and RP. The data analysis plan was developed and the data were analyzed by SSS, SPS, DU, and SS. SPS and SS wrote the first draft of the article. All authors contributed to reviewing, editing the drafts, and approving the manuscript.

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Supportive or Confining? The Impact of War Metaphors From the COVID-19 Pandemic on Persons With Disabilities in Mainland China

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Ensuring the well-being of persons with disabilities (PWDs) is a priority in the public sector during the coronavirus disease 2019 (COVID-19) pandemic. To contain this unprecedented public crisis in China, a set of nationwide anti-epidemic discourse systems centered on war metaphors has guided the epidemic's prevention and control. While the public is immersed in the joy brought by the stage victory, most ignore the situation of the disadvantaged PWDs. Accordingly, this study adopts and presents a qualitative research method to explore the impact of war metaphors on PWDs. The results showed that while there was some formal and informal support for PWDs during this period, they were increasingly marginalized. Owing to the lack of a disability lens and institutional exclusion, PWDs were placed on the margins of the epidemic prevention and control system like outsiders. Affected by pragmatism under war metaphors, PWDs are regarded as non-contributory or inefficient persons; therefore, they are not prioritized and are thus placed into a state of being voiceless and invisible. This research can provide inspiration for improving public services for PWDs in the context of COVID-19.

Keywords: COVID-19, war metaphors, persons with disabilities, pragmatism, identity segment

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INTRODUCTION

Coronavirus disease 2019 (COVID-19), which emerged at the end of 2019, spread rapidly worldwide because of its fast transmission speed, high infection rate, and difficulty to prevent and control. COVID-19 has become an urgent public health issue that threatens human life and health. Accordingly, the World Health Organization (WHO) designated COVID-19 as a global health emergency of international concern on January 30, 2020. With the recent large-scale spread of COVID-19 infections in India, there is a trend of resurgence. At the time of this writing, more than 180 countries have reported confirmed cases. The cumulative number of confirmed COVID-19 cases worldwide is 170,178,953, with 3,538,858 deaths (1). Notably, studies have shown that persons with disabilities (PWDs) are more likely to have underlying health problems and live in collective care settings, which increases the risk of infections and other secondary problems (2). It is estimated that there are more than 1 billion people—equivalent to about 15% of the world's population—who have some form of disability, and this number is increasing due to the aging of the population and the growth of chronic diseases (3). The WHO calls for disabilities to be regarded

as an important public health issue and included in the work of the health sector. Therefore, in the context of a major public health event such as COVID-19, more priority should be given to PWDs, which are perceived as vulnerable and susceptible populations.

Compared with the general public, PWDs are at a relative disadvantage in terms of physical functioning, economic status, education, and information access, which leads them into the double jeopardy of marginalization regarding their preventive health care and nursing during the COVID-19 period (4). Since the outbreak of COVID-19, hospitals, clinics, and rehabilitation institutions have been considered as potential sites for virus transmission, and many of these facilities have reduced their activity or have been completely closed (5). Consequently, appropriate treatment and rehabilitation services are not available for PWDs during the COVID-19 outbreak. In addition, the experience of a lack of freedom caused by behavioral restrictions during home quarantine makes people with physical, intellectual, and mental disabilities more likely to develop serious mental health problems such as cabin fever (6). In these particular situations, PWDs are vulnerable to isolation and psychological distress, mainly because of social distancing and quarantine measures. Therefore, COVID-19 poses a greater threat to PWDs in terms of public health, society, and politics. As a key event in the life course of PWDs, COVID-19 will have an immeasurable impact on them. If necessary measures that truly meet the actual needs of PWDs are not taken, it will be detrimental in protecting them from COVID-19.

At the end of 2019, the Chinese people were preparing for the country's largest traditional festival, the Lunar New Year. Those who work in other cities would go home to spend the Spring Festival with their families, and this is also regarded as the world's largest population migration (7). This undoubtedly accelerated the speed and breadth of the spread of COVID-19 in China. Subsequently, China immediately closed off Wuhan, starting from January 23, 2020, and put the country into a state of emergency; moreover, it also activated the highest-level emergency response mechanism to control the spread of COVID-19. China then adopted a series of prevention and control measures, such as blocked cities and villages, and strictly restricted population movements and collective activities that may spread the virus. COVID-19 attracted the attention of domestic and foreign media and became a priority agenda in the process of the epidemic. Given this, studies have shown that war metaphors are pervasive in the media coverage, with epidemic control as a war that must be won and COVID-19 as the enemy (8). Although the use of the rhetorical method of war metaphors is more common in the world, this feature is particularly obvious in Chinese media.

Previous studies have explored the war metaphor during the COVID-19 outbreak and its impact on epidemic prevention and control. There are also numerous studies discussing the reasons for the success of China's epidemic prevention and control and the key influencing factors and main mechanisms. However, most existing studies have overlooked the marginalized groups of PWDs. What do the war metaphor and epidemic prevention and control measures dominated by this discourse mean to PWDs? What impact does it have on them? Few researchers have focused on this issue. Therefore, based on the qualitative research method, this study is an exploration of the impact of war metaphors—whether it is positive or negative—on PWDs.

LITERATURE REVIEW

War Metaphors and COVID-19

As a linguistic device, a metaphor is deeply rooted in language, thought, and action, pervading everywhere in everyday life. Accordingly, the "covert" and "possibly unconscious" intentions of language users can be revealed through critically analyzing metaphors (9). Lakoff and Johnson (10) point out that the essence of a metaphor is a common and unavoidable way of thinking. We often unconsciously adopt metaphorical systems to understand abstract things—to understand and experience another kind of thing with one kind of thing—claiming that metaphors exist not only in language but also in daily life, thoughts, and actions (10). Studies have found that war metaphors or military metaphors are important frameworks for the media to construct a disease. Such metaphors can create a sense of urgency, provide a common basis for thinking and action, and are an important means of motivating society and mobilizing people (11). Diseases are often presented in the form of war metaphors such as strikes, attacks, invasions, and spreads, which are common metaphors used to describe illness. The coping methods used by humans to fight diseases include defense, struggle, and resistance (12).

The use of war metaphors can be traced back to Pasteur and Koch's early research on infectious diseases. The most classic study comes from Sontag's (13) research of the metaphor of disease and acquired immunodeficiency syndrome (AIDS). She revealed the process of the metaphorical construction of the disease. This research shows that what people see is not the real appearance of disease but is rooted in the special cultural context and social background of each period. As Sontag clarified, the metaphor of "disease is war" is dominant in people's conceptualization of disease. In the public health discourse system guided by the war metaphor, disease is often described as an enemy invading society, and efforts to control the spread of a pandemic and reduce infection and mortality are referred to as "a fight, a struggle or a war" (13).

The image system of war metaphors helps to provide us with a view of COVID-19 in some aspects. Through the use of war metaphors, the disease itself is endowed with social significance in addition to its biological meaning (11). To provide the audience with an idealized vision of society, the selection or presentation of metaphors by news media is conscious and often carries the purpose of persuasion. The "unverifiable" nature of metaphor and its selective "reinforcement" and "concealment" toward reality contribute to the expression of the news media's political stance (9). Notably, the power of war metaphors is that they can make people in a fearful situation take defensive actions and also mobilize people to cope with emergencies (12).

The war metaphor is consistent with the current context of the prevention and control of COVID-19. As the most authoritative form of media in China, the war metaphor is the dominant framework for the *People's Daily* to report on COVID-19. It

is described as the enemy of the whole nation, emphasizing the ruthless and barbaric characteristics of the virus such as the ferocious virus, cunning human natural enemies, etc., thus classifying the virus as an evil other, highlighting its antagonistic relationship with humankind (14). The metaphor, envisaging dreaded diseases "as an alien 'other,' as enemies" in modern war (13), attempts to create a sense of urgency and mobilize the public to fight against a common threat.

COVID-19 and Persons With Disabilities

The COVID-19 outbreak has created continuous challenges for PWDs. As they face many disadvantages in health care services and community life, coupled with physical defects and a series of social barriers, the cumulative effect of disadvantage puts them at greater risk during the COVID-19 pandemic (15). They had to interrupt their routine activities, were forced to suspend their work, and could not participate in community life and enjoy some services. In particular, PWDs living in collective care settings, such as group homes, centralized nursing institutions, and long-term residential care facilities, are at greater risk of infection and death—which are several times higher than the general population (16). In addition, the impact of COVID-19 on PWDs shows certain differences among the different types of PWDs. Among them, those with intellectual and developmental disabilities (IDD) are more susceptible to the impact of COVID-19, which occurs in the areas of their physical and mental health, the social sphere, and setbacks to human rights (17). Related data analysis results show that the death rate of those with IDD is two to six times higher than that of people without IDD when at risk of COVID-19 infection, and they are more likely to die from pulmonary complications (2).

To achieve normal social participation and social integration, PWDs often have higher needs than non-disabled people in terms of education, employment, healthcare services, and media support (15). However, services related to PWDs were forced to cease owing to the impact of COVID-19 and the implementation of a strict lockdown policy during the pandemic. The allocation of medical products and related services poses a significant threat to the human rights of PWDs, and certain states in the United States have even formulated disability-based exclusion from lifesaving treatments (4). Specifically, telemedicine is seen as a way to partially compensate for the health care needs of PWDs during home quarantine and reduce the risk of COVID-19 infection and save costs. However, when using telemedicine, PWDs still face many barriers, primarily including infrastructure and access barriers, operational challenges, regulatory barriers, communication barriers, and legislative barriers (18).

Even more serious is that COVID-19 poses significant challenges to the rehabilitation services, care, and mental health of children with disabilities. Owing to the lack of an inclusive humanitarian response, neglect, abuse, and separation from family members may put disabled children in desperate circumstances and cause lifelong trauma (19). Therefore, to support PWDs in responding to the public health crisis, relevant suggestions should be proposed. For example, this could be data collection about disease, recovery, and mortality rates from COVID-19 among PWDs. Moreover, short-term and long-term compensation measures and related plans, such as medical treatment, rehabilitation, and vaccination, could be developed (4).

In summary, existing studies have focused not only on the discourse system of war metaphors related to COVID-19 but also on the difficulties and challenges faced by PWDs in this major crisis. Accordingly, scholars have put forward corresponding countermeasures and suggestions from the perspectives of the government, social organizations, and public health. However, the critical impact of war metaphors on PWDs during the COVID-19 outbreak has not been systematically examined in the existing literature. Therefore, based on the qualitative method, we attempt to explore this important topic from the subjective perspective of PWDs to bridge the gap in current research.

THEORETICAL PERSPECTIVE AND METHODS

Theoretical Perspective: War Metaphors During the COVID-19 Outbreak in China

Based on an analysis of existing literature and news reports, this paper summarizes the manifestations and specific features of war metaphors during the prevention and control of COVID-19 in China. This mainly includes two aspects: first, the conceptual set of war metaphors in China; second, the top-down command chain and organization-action system under the war metaphor.

The Conceptual Set of War Metaphors in China

The war metaphor in medical discourse is used to connect the two conceptual systems of medical treatment and war—the mapping relationship between the source and target domains or the tenor and vehicle (20). Thus, it constitutes the conceptual metaphor of "medical treatment is war", which is coherent with the metaphor. Whether it is an official's speech or a news report about COVID-19, war metaphors are used as the dominant narrative method during the anti-epidemic period, which has penetrated the entire society. This is related to the cultural heritage of the communist armed struggle during the Chinese Revolution (21). In addition, the war metaphor is the dominant framework for the *People's Daily*—which is regarded as the most authoritative medium in China—to report on COVID-19. Moreover, this "epidemic prevention and control war" is divided into "technical assault war", "scientific research war", and "material support war", and it is still a "general war" and a "people's war" (14). Frequently used terms include "war of containment" (*zujizhan*), "all-out war", etc. War metaphors convey a strong sense of urgency and can also be used as emotional mobilizations to call on citizens to act in compliance with mandatory measures for epidemic prevention and control (8).

To more clearly present the war metaphor during the COVID-19 period, we enumerated the mapping relationship between war (source domain) and anti-epidemic (target domain) (as shown in **Figure 1**). The elements presented in **Figure 1** include the following: (1) The war participants, including the

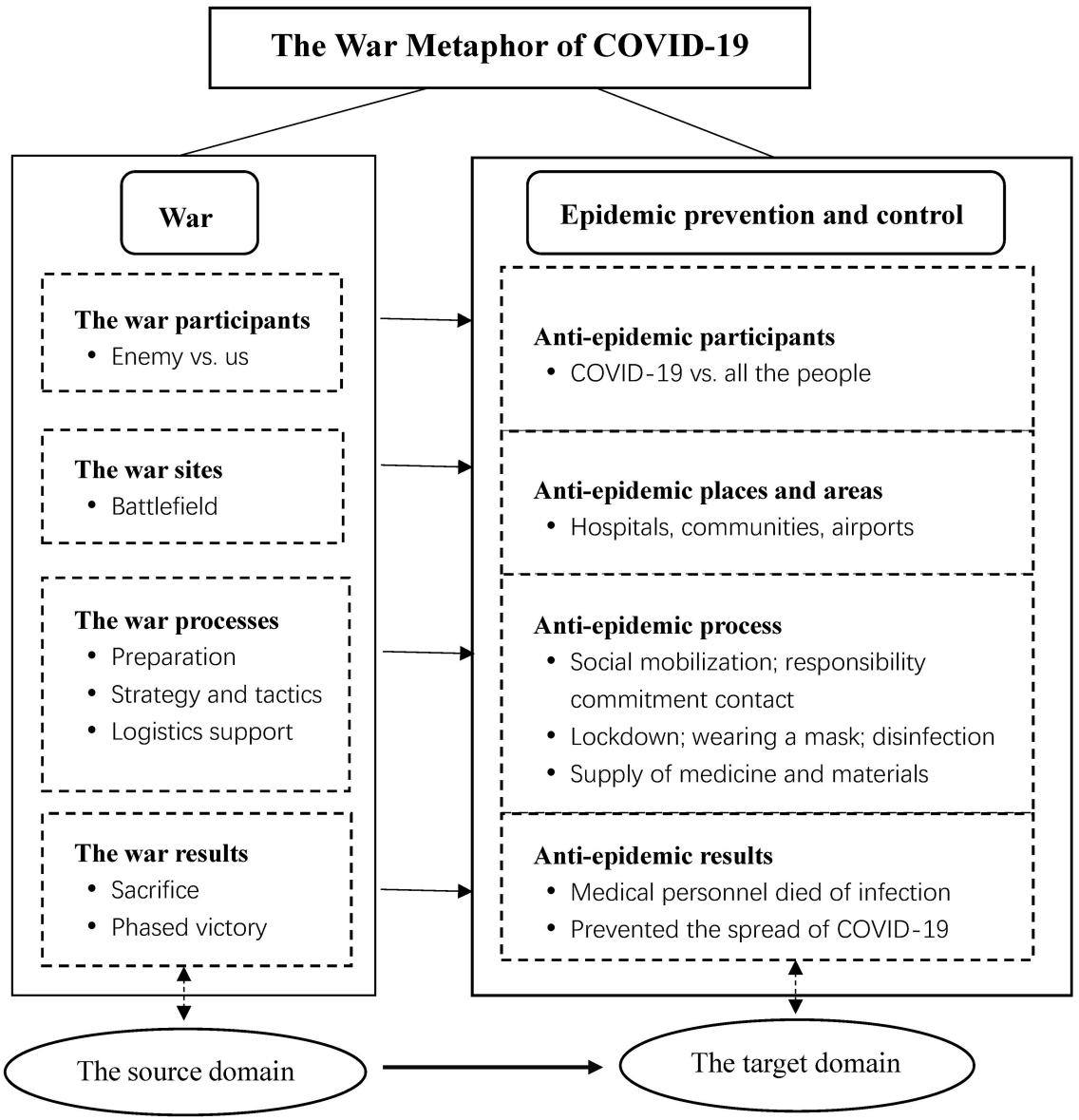

FIGURE 1 | The mapping relationship between the war metaphor and COVID-19.

enemy (COVID-19) and our side (medical staff represented by Zhong Nanshan; frontline epidemic prevention personnel in the community; all the people, etc.). (2) The war sites—the key places and areas for epidemic prevention and control, such as hospitals, communities, and airports. (3) The war process, including pre-war preparations (e.g., social mobilization, epidemic prevention training, and officials signing responsibility commitment contracts); formulating strategies and tactics (lockdowns of cities and villages; wearing masks, disinfection and sterilization, resource allocation, personnel transfer, etc.); logistics support (the supply of drugs and medical devices, and the support of living materials). (4) The war results, such as sacrifice (medical staff who died due to infection), phased victory (preventing the spread of the epidemic), and triumphant return (assisting medical staff in the hardest-hit areas to return home).

Based on the mapping relationship between the source and target domains, we can clearly see how the war metaphor is constructed in China. Affected by the war metaphor, China launched a nationwide campaign against COVID-19 and has managed to contain this unprecedented public health crisis. In particular, this is due to the relatively hardcore epidemic prevention and control measures under the war metaphor (22). Therefore, comparing COVID-19 to war will increase the public's sense of urgency and crisis and serve as a significant social mobilizing force for the whole country to unite in response to this unprecedented public crisis.

Top-Down Command Chain and Organization-Action System

The war metaphor is not only a mapping relationship between war and COVID-19 but also a mapping of war practices and experiences into the specific practices of epidemic prevention and control. Such a metaphor constructs a top-down national anti-epidemic strategy system and shapes the image of national unity to win the fight against COVID-19 (8). To address this unprecedented public health crisis involving COVID-19, an effective chain of command should be established to confront this situation, which is essential for effective communication and interdepartmental coordination.

On January 20, 2020, the Joint Prevention and Control Mechanism of the State Council was officially launched. On January 25, 2020, China established the Central Leading Group for COVID-19 Prevention and Control (CLG) as the highest decision-making institution and command center for China's response to COVID-19. The instruction of the CLG is considered an uncompromising political task that all participants must complete. Simultaneously, governments at all levels have also established epidemic prevention and control centers, thus forming a top-down command chain. Notably, war metaphors have certain advantages in mobilizing resources to respond to crises. The state will uniformly allocate resources and deploy human and material resources in a top-down manner so that rapid social mobilization can be conducted (23).

To win the war against COVID-19, China has formed a rigorous top-down organization-action system. First, strict anti-epidemic strategies and measures have been formulated, and a nationwide lockdown and home quarantine plan have been urgently implemented to restrict the movement of non-essential people. Second, China provides political incentives for local officials with outstanding contributions through "battlefield promotion", thereby prompting them to perform better in the anti-epidemic war (22). By allowing civil servants to sign a "responsibility contract", which is similar to a "military order", they are required to perform their duties. Various disciplinary actions, including suspension, demotion, and dismissal, have been taken against cadres for their poor performance in the fight against COVID-19. For example, to support Wuhan, the hardest-hit area, China has selected medical personnel from various provinces and cities. Moreover, in this regard, they have taken an oath before going to the front line of the epidemic, which is seen as an effective form of mobilization.

The war metaphor is the dominant framework for constructing COVID-19 in the Chinese media. It emphasizes national speed and power, enhances the collective identity and national identity of the audience, and realizes the authority and

TABLE 1 | Description of research participants.

1. Participant I: Persons with disabilities (PWDs)

No.	Gender	Age	Household registration	Education	Disability type	Degree of disability	Current status
C-1	Female	32	Urban, Beijing	University	Physical	Moderately disabled	Company's cashier
C-2	Male	28	Urban, Shenzhen	Senior in high school	Physical	Profoundly disabled	Phone customer support
C-3	Male	48	Rural, Changchun	Primary school	Visual	Profoundly disabled	Unemployed single man
C-4	Male	45	Rural, Jinan	Senior in high school	Visual	Profoundly disabled	Blind masseur
C-5	Female	26	Urban, Jinhua	Post-graduate	Cerebral palsy	Moderately disabled	Company staff
C-6	Female	36	Rural, Wuhan	Primary school	Mental	Mildly disabled	Unemployed
C-7	Male	16	Urban, Guizhou	Primary school	Autism	Moderately disabled	Stay at home
C-8	Female	33	Rural, Zhengzhou	Vocational	Intellectual	Mildly disabled	Pastry chef
C-9	Male	36	Urban, Chengdu	University	Hearing	Profoundly disabled	Illustrator
C-10	Male	37	Rural, Shanghai	University	Physical	Moderately disabled	Civil servant
C-11	Female	42	Rural, Jinan	Primary school	Intellectual	Mildly disabled	Cleaning crew

2. Participant II: Faculty of department of disabled persons' federation

No.	Gender	Age	Education	Job title
F-1	F	34	University	Deputy Chief of Rehabilitation Department
F-2	M	42	Senior in high school	Staff of Disabled Persons' Federation
F-3	F	25	University	Staff of Disabled Persons' Federation

3. Participant III: Staff in the community who provide services for PWDs

	Gender	Age	Education	Job title	Work experience
S-1	M	38	University	Staff in X district	12 years
S-2	F	36	Senior in high school	Staff in J district	8 years
S-3	F	28	Senior in high school	Staff in N district	4 years

legitimacy of anti-epidemic (14). The war metaphor regards COVID-19 as an "enemy" that invades the country, and every citizen's body may become an occupied "city". Each aspect of the cognition, response, and action involving COVID-19 is expressed in a war-like expression, aiming to create an atmosphere of urgency and crisis, and mobilizes the population to stand on their own posts to win the anti-epidemic war.

Methods

Research Design and Sampling

To explore the impact of the war metaphor under COVID-19 on PWDs, a qualitative research method was chosen as the design guide for this study, using the interpretivist approach to understand the interviewees' understanding of the world of social life. It allows researchers to be deeply involved in the observation and understanding of the participants with a natural attitude and develop a familiar relationship with them, and the resulting observations and interactions led to genuine revelations (24). Moreover, it can critically reflect on the participants' cultural interpretations of their social situations as well as the themes and assumptions they bring to the study (25).

We recruited the interviewees through online methods. We posted recruitment advertisements on WeChat, QQ, and Weibo, the three largest online platforms in China. The advertisements explained the research content, research objectives, and basic requirements of the interviewees. After the registration deadline, we received 25 letters from potential participants. In order to collect as much potential information as possible related to the research topic, this study adopts purposive sampling to select the interviewees who can provide the most information (26). Our main criterion for selecting interviewees is "the richest information" in order to achieve "saturation of the most diverse information" (26). After the researcher's preliminary trial interviews and screening, 11 interviewees were finally determined. The age of the interviewees ranged from 16 to 48; the group comprised six males and five females, covering different categories and degrees of PWDs. Geographically, they came from the southeast coastal areas (five), the central-western region (four), and the northeast region (two). When selecting the participants, we tried to consider factors such as age, gender, household registration, and education. Other important criteria were related to the type of disability and degree of disability, as they provide a different subjective experience. This study enhanced the reliability and validity of the research by improving the heterogeneity of the interviewees. In addition, to explore the research issues from a multidimensional perspective, through purposive sampling, we selected three staff members working in the Disabled Persons' Federation and three members of the community serving PWDs to achieve a more comprehensive and detailed understanding. The descriptions of the research participants and their general characteristics are presented in **Tables 1**, **2**.

TABLE 2 | General characteristics of the research participants ($N = 11$).

Variables		*N* (%)
Gender	Male	54.5
	Female	45.5
Age	≤30	27.3
	30–40	45.5
	40–50	27.3
Household registration	Rural	55.5
	Urban	45.5
Education	Primary school	36.4
	Senior in high school	27.3
	University and above	36.4
Disability type	Physical disability	27.3
	Visual disability	18.2
	Intellectual and developmental disability	9.1
	Hearing disability	36.3
	Mental disability	9.1
Degree of disability	Mildly disabled	27.3
	Moderately disabled	36.4
	Profoundly disabled	36.4

Data Collection and Data Analysis

Semi-structured in-depth interviews were conducted to collect raw data. Based on the research questions and content, we created an interview outline. Subsequently, we revised the interview outline based on the trial interviews. For PWDs, the content of the interview involved how they viewed the war metaphor under COVID-19 and what this metaphor meant to them. For the Disabled Persons' Federation and community workers, the questions focused on their experience of providing support, benefits, and services for PWDs. These included their methods, service descriptions, and their thoughts and opinions on PWDs during COVID-19. We used WeChat voice or telephone interviews, and each participant's interview consisted of two rounds. The first round followed the interview outline; subsequently, the interview contents were sorted promptly to find out the missing contents or the contents that needed another interview. The second round of interviews were then conducted, and each one was audio-recorded with the consent of the interviewees and lasted between 60 and 90 min. Finally, the recordings were transcribed by authors.

We adopted an inductive thematic analytic approach to categorize and analyze the raw data; accordingly, the NVivo 10 software package was used as an analysis tool. Following the guidelines laid out by Braun and Clark (27) in a recursive process, the data encoding and thematic analysis mainly included three steps. The first step was open coding based on thorough reading and a comprehensive understanding of the interview data to prepare the primary coding list and make important notes and memos. The second step involved the process of categorization, in which the primary coding with similar content and logic was classified under the same category to form a secondary coding system. Finally, the third step was the process of abstraction and conceptualization, extracting the dominant core categories. When there was no new coding, we believed that we reached theoretical saturation; therefore, we stopped the further recruitment of interviewees.

We conducted a dialog with the existing literature to examine the characteristics and manifestations of war metaphors during COVID-19. We analyzed government-promulgated policy documents and files related to PWDs during the COVID-19 epidemic and improved the validity of the research results by supplementing evidence from multiple sources. With reference to the framework proposed by Lincoln and Guba (28), this study mainly conducts reliability and validity analysis from four dimensions. (1) Credibility, that is the truthfulness of the qualitative data. Researchers use interview techniques effectively to seek the authenticity of the data by different questioning methods, and conduct multiple checks on the interview data, pursuing the authenticity of it. (2) Transferability. Researchers made a thick description of the interviewee's experience, and fully presented the feelings, experiences and actions expressed by the interviewee. (3) Dependability. Interviews and data transliteration were done by the researchers in cooperation to ensure the stability and consistency of the data. (4) Confirmability. When analyzing and interpreting data, the researcher eliminates personal prejudice and remains neutral to ensure that the experience and facts expressed by the participants are truly presented. The ethics committee of the researcher's University approved the ethical issues involved in this study. Before the interviews and recordings, the researchers obtained written consent from the interviewees. To protect the privacy of interviewees, each participant was anonymized in this paper.

FINDINGS

In the preceding article, this study focused on the manifestations and specific features of war metaphors during the prevention and control of COVID-19 in China. By introducing the measures and results of China's anti-epidemic efforts, we can gain insight into the construction logic of war metaphors and lay a foundation for understanding the situation of the PWDs in China. In the epidemic prevention and control system dominated by war metaphors, although the PWDs have received formal support from the government and informal support from civil society, on the whole, the PWDs are increasingly marginalized. Affected by the war metaphors, the PWDs are regarded as noncontributory person and therefore are not given priority. This has led to the allocation of public health resources to focus more on anti-epidemic work rather than the PWDs care, which made the PWDs suffer a loss of medical resources and a higher risk of life. We established the logical framework of this study based on the interview data (**Figure 2**).

Sounds Like Positive Protection: Minor Increase in the Well-Being of PWDs Under War Metaphors

PWDs are considered to be at greater risk in this public health crisis; therefore, healthcare and related services should be given priority. The Convention on the Rights of Persons with Disabilities (CRPD) states that all measures necessary to ensure the protection and safety of PWDs are provided to guarantee the right to life and health. Affected by the war metaphor, the government formulated relevant welfare policies to deal with this crisis and launched a wide range of social mobilizations to solve the difficult situation of PWDs. We divided these measures into formal support from the government and informal support from civil society.

Formal Support From the Government

First, necessary measures have been taken to guarantee the basic living standards of PWDs. A typical feature of war metaphors is the establishment of a top-down command chain and a rigorous organization-action system. Notably, to alleviate the impact of COVID-19 on the daily life of PWDs, the government has rapidly increased the living allowance for the poor PWDs and the nursing allowance for the profoundly disabled (two-subsidies), which is regarded as the core of social welfare for PWDs in China. Therefore, using Wuhan as an example, during the epidemic, the government increased the living allowance by 50 yuan from the original standard of 130 yuan per month (urban areas)/110 yuan per month (rural areas). Further, the nursing allowance was increased from 100 yuan to 150 yuan per month. The government has appropriately relaxed the scope of social assistance—including more PWDs with difficulties—into the minimum living security system and temporary assistance system, and correspondingly raised assistance standards. In addition, the government has provided rehabilitation services subsidies and temporary price subsidies for PWDs, subsidies for home-assisted services for the profoundly disabled without work, and subsidies for nursing care for elderly PWDs. Based on this, a comprehensive guarantee system with Chinese characteristics was established.

Second, employment subsidies and employment services were required, which stabilized the employment rate of PWDs. COVID-19 has had a greater impact on the employment of the PWDs. Affected by the war metaphors, the state prefers the allocation of resources to the employment and income growth for the PWDs to ensure social stability and epidemic prevention and control. The government adopts preferential policies such as reduction or exemption of social insurance premiums, deferred payment of taxes and fees, and reduction or exemption of rents to support businesses or shops (blind massage institutions, etc.) run by PWDs to maintain normal operations. The government also provides incentives for companies to hire PWDs or reduce the risk of being laid off by offering job stability and recruitment subsidies. The government has increased employment opportunities for PWDs through the establishment of public welfare positions, subsidies for job hunting and entrepreneurship, and subsidies for job training. Methods such as centralized and decentralized, online and offline, and home delivery of courses are used to conduct vocational skills training for PWDs to enhance their employability. Moreover, the government provides employment assistance services for registered unemployed PWDs and provides unemployment insurance and unemployment subsidies to ensure their basic livelihoods.

Third, services for PWDs have been restored and promoted in an orderly manner, which has improved their social well-being. China's Disabled Persons' Federation promulgated the "Notice on

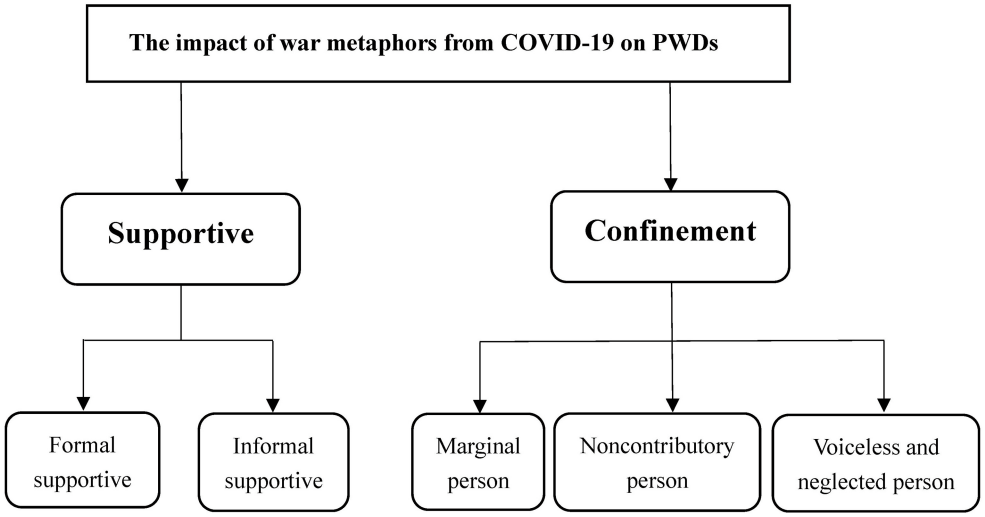

FIGURE 2 | The logical framework of this study.

Focusing on Special Operations for Visiting Families of Disabled with Special Difficulties under the Impact of the Epidemic", emphasizing the development of visits and condolences. Community workers should visit families of disabled people who have special difficulties in basic daily care, medical treatment, and schooling due to the epidemic and coordinate efforts to solve practical difficulties. Communities conduct a guarantee contact system that coordinates Party members, cadres, community workers, and volunteers in communities (villages) and implement the insured contacts one by one for PWDs who are lonely or unable to take care of themselves for various reasons. Specific services include regular visits, policy publicity, voluntary services, agency assistance, and spiritual comfort to ensure that PWDs can receive timely and effective assistance when they encounter emergencies. In addition, the government has adopted corresponding incentive measures to encourage family doctors to provide services such as family beds and outpatient visits for PWDs on the premise of self-protection to ensure continuous and uninterrupted home services.

Informal Support From Civil Society

During epidemics, certain types of PWDs are unable to access communication and information platforms to acquire valuable information, which puts them in a more vulnerable position where they are more susceptible to virus attacks and impacts. This can be attributed to social, financial, and technological reasons (29). Affected by social mobilization in the context of war metaphors, relevant social organizations were encouraged to provide accurate and accessible health information about COVID-19 and methods of continuous self-protection for PWDs to compensate for the absence of government in this field. For example, Shouyuzhe, a non-profit organization in Wuhan that specializes in serving hearing disabilities, continuously updates the latest information about the epidemic by making sign language videos, which are seen as key to protecting PWDs during the epidemic.

Under the war metaphor, caring and non-disabled people support PWDs through various channels, which is regarded as a virtue and a commendable charity. Consequently, during the COVID-19 pandemic, there was a scattered patchwork of social support for PWDs. For example, the Beijing Disabled Persons' Federation has set up a 12385 psychological counseling service hotline to provide timely psychological support, emotional counseling, crisis intervention, and other mental health services for PWDs and their relatives to prevent extreme events caused by psychological stress. Some medical institutions provide online rehabilitation consultation and telemedicine rehabilitation guidance for PWDs to perform well in home rehabilitation training and epidemic prevention. In addition, some commercial organizations participate in helping PWDs improve their social reputation. For example, the Huaxia Insurance Company specially designed a COVID-19 exclusive insurance of 200,000 yuan for PWDs, and eligible PWDs can participate in the insurance free of charge.

Actual Confinement: Further Marginalization of PWDs Under the War Metaphor

Reinforced Isolation: Further Social Distance From the Outside World

Outsiders: PWDs Were Placed on the Margins of the Anti-epidemic System

While COVID-19 is a fatal threat to all, the challenge is even more complex for PWDs, who have faced various forms of social exclusion—visible and invisible—during the pandemic. Strict home quarantine measures make it difficult for PWDs to interact with the outside world, which significantly increases their risk of being neglected or abused. Information accessibility is another

challenge for PWDs, as much of the information is not converted into an accessible format (7). Consequently, PWDs cannot obtain accessible and valuable information, and the chains of their interactions with others are severed. This deepens the isolation and distance between PWDs and the outside world, making it more difficult for them to achieve social integration. In addition, during the pandemic, China developed an app called *Jiankangbao* that requires the individual to input their temperature, travel declaration, and scan code registration, which is regarded as a "passport" for citizens. However, this is a significant challenge for PWDs, especially those with IDD. To avoid causing trouble for others, most PWDs choose to stay at home instead of going out.

> *In the early days of the outbreak, I had no idea what was going on and could only get bits and pieces of information from my family. That fear of the unknown has always affected me, making me feel like it's the end of the world. I tried to catch something, but it was a needless struggle. Suddenly, I feel that everything happening around me is so strange, I am like an invisible person, and the world seems to have nothing to do with me. (C-3)*

In addition, there are paradoxes and contradictions between strict epidemic prevention and control measures and the survival needs of PWDs under the war metaphor. To cut off the spread of COVID-19 through person-to-person transmission, social distancing is required to avoid direct contact with others. However, for certain categories of PWDs, social alienation and self-quarantine can be challenging (30). For example, for persons with hearing disabilities, oral language is critical to their communication, but the veil of a mask significantly limits their ability to communicate. Moreover, people with visual disabilities need to walk with the arms of others or get information by touching Braille characters along with the surfaces in public spaces. Some profoundly disabled people who cannot take care of themselves often rely on the care of others. Finally, it is difficult for those with IDD to understand the sudden home quarantine and related measures, which makes them extremely confused. Therefore, one sentence often mentioned by interviewees is "I seem to be an outsider".

> *I haven't been out for a long time, and it hasn't been communicated with my peers for a while (hearing disability) because wearing masks makes it difficult for us to read lip language. Further, seeing the entire face is very important for our communication. However, this was not possible. So, for me, I feel very lonely now. (C-9)*

Institutional Exclusion: Deepening Social Inequality

Institutional exclusion refers to the process of PWDs being excluded from the system and unable to obtain the support of necessary social resources because of the limitations or deficiencies of the system—thus becoming a more vulnerable group (31). This separation seems to be due to the lack of ways for PWDs to express their interests. However, essentially, the advantaged groups repel disadvantaged groups to protect their interests from losses in the process of resource allocation. It is perceived as a rationalized social deprivation caused by non-disabled people based on the negative perception of disability. This exclusion is reflected in the fact that experts in epidemic prevention and control, led by medical professionals, often associate disability with adverse health conditions. This bias has a decisive influence on medical futility decisions (32). This prejudice against disability prevents PWDs from obtaining the equipment or medical services they need; it may also lead to them not being prioritized in resource allocation. Therefore, it can be said that the outbreak of COVID-19 is questioning the commitment to equality.

The consequence of institutional exclusion is social inequality led by the concept of quality of life, which holds that PWDs have a poor quality of life and a lower life expectancy and even account for a waste of resources. Experts who controlled the discourse will evaluate them through wartime triage so that those with the greatest chance of survival and successful treatment will be given priority regarding medical and healthcare services (33). In this situation, priority will be given to young and healthy groups, rather than disadvantaged and marginalized groups such as PWDs. Therefore, PWDs are excluded from priority access to health services and related anti-epidemic medical resources, even if they are in greater need of these services than non-disabled individuals.

The larger coordinates of the threat became apparent that pre-established frameworks for ethical decision-making in health crises excluded PWDs because of preconceived notions about their quality of life (34). It can be concluded that judgments about their quality of life are typically made by someone with no experience of disability as well as from an ableist perspective (35).

> *I need to take medication (for mental disability) regularly; otherwise, it will get worse. However, I did not prepare enough pills. Strict lockdown was adopted during the epidemic, and I could not go to the pharmacy or hospital to buy medicine. I contacted the community director, and he told me, "At present, it's a wartime situation, all resources are concentrated on the front lines, and I really can't take care of you". In their opinion, the disabled seem to be unimportant, and mental health is far less important than physical pain. (C-6)*

Non-contributory Person: the "Product" of Pragmatism Under the War Metaphor

Perception Biases Under War Metaphors: PWDs Are Considered Non-contributory

As suggested in traditional Chinese culture, PWDs are perceived as individual tragedies, their impaired body implies a moral or social loss, and they cannot fulfill their responsibility to their family and society (36). In Chinese history, PWDs are called *canfei*, which means useless and incapable, and they were given negative labels such as "parasite", "crap", "dependency", "burden", and "troublesome" (24). However, the requirements for individuals under war metaphors are highly efficient. They must be "high-quality", "quality-guaranteed", "easy to use", "usable", and "capable of winning". Obviously, PWDs are regarded as unqualified and inefficient "parts" of the giant political-economic machine under the war metaphor (24) because they are considered to be unable to contribute

to the victory of this anti-epidemic war and thus become the "invisible person".

Under the war metaphor, to win this anti-epidemic war, those who were effective and non-disabled were mobilized, such as medical workers and scientific researchers. As they are regarded as warriors who can win the war, these people should rush to the front line for the greatest possible guarantee of victory in the war against COVID-19. The war metaphor also encourages "pioneers" and "warriors", such as medical staff and community volunteers who are on the front lines of the anti-epidemic war. They have been given the characteristics of "indomitable fighters", "daring to fight hard battles", and "brave and fearless". The title of "anti-epidemic hero" emphasizes their contribution to the prevention and control of the epidemic. However, affected by the war metaphor, we hardly see the participation of PWDs in the process of epidemic prevention and control. As PWDs are labeled as useless and noncontributory, they are regarded as a burden and a hindrance to epidemic control. In this context, non-disabled people expect PWDs to stay at home and not come out to cause trouble to others and society.

> *In the critical period of epidemic prevention and control, I applied for the community pioneer post to participate in the fight against COVID-19, helping to do some basic work such as distribution of supplies, epidemic publicity, and temperature measurement. However, the community director rejected my application and told me, "You can take care of yourself during the home quarantine period, you're not qualified for these works, please don't cause us trouble". (C-1)*

Pragmatism Under War Metaphors: Personal Sacrifice Seen as a Virtue

In response to this unprecedented public health crisis, China immediately established a top-down militarized epidemic prevention and control system, with resource allocation under the unified command of the state. The war metaphor reinforces the concept of "a community of common destiny", brings all people into the united front, and requires them to obey the requirements of epidemic prevention and control. Therefore, sacrificing part of one's personal interests is regarded as a virtue because it is conducive to forming an atmosphere of unity to fight COVID-19. Collectivist values strengthened by communist ideologies inherently require citizens to exercise self-restraint when individual interests clash with collective interests and also require individual interests to be subordinated to collective interests (22). Certain forms of personal sacrifice are still considered a virtue in contemporary China, despite the powerful promotion of individualist values in society through marketization (37).

> *At present, our country is in distress, and all people should unite to fight against COVID-19. Residents in the community must strictly abide by relevant rules. What does personal gain or loss matter in the face of national security? Although there is little that PWDs can do, they can at least do will in home quarantine. (S-1)*

Pragmatism, derived from war metaphors, has been the guiding principle in the entire epidemic prevention and control process. Pragmatism refers to the idea of preserving the basics and the overall situation—it is possible to give up the interests of the minority to protect the interests of the majority. Therefore, the resource allocation method dominated by pragmatism follows distributive rather than formal justice. Distributive justice refers to the fair allocation of resources and services in healthcare. This is rooted in the principle of maximizing benefits for the largest number of people (38). As mentioned above, PWDs are regarded as useless, inefficient, and unable to make contributions. Consequently, the interests of PWDs as a minority are shielded during the anti-epidemic war. In this context, the actions of PWDs seeking personal interests are seen as selfish and disregarding in the context of the overall situation.

> *In fact, we have also noticed the difficulties and challenges faced by the disabled. But we can't help it. We only have three staff members in our community and a few volunteers, and there is a shortage of workforce. The current focus is on the frontline of the fight against the epidemic, with no regard for the disabled. In addition, most of them stay at home with their families to take care of them. We mainly focus on those who are in and out of the community. (S-3)*

Lack of a Disability Lens: PWDs Are Voiceless and Neglected

One-Size-Fits-All: The Product of the Dominating Ableist Perspective

Affected by the war metaphor, PWDs are regarded as marginalized groups that will not be prioritized. This kind of discourse often immerses us in a society dominated by the ableist perspective and neglects the needs of PWDs (7). Moreover, almost all decisions and plans are made by experts in a superior position, with no participation of the disabled. This has led to the formulation and implementation of one-size-fits-all epidemic prevention and control measures without considering the special difficulties and challenges faced by PWDs. This means that PWDs will receive the same treatment as non-disabled people in the event of a pandemic. This one-size-fits-all standard and lack of disability lenses have led to greater inequity. In some cases, ignoring the rights of PWDs can be fatal (7).

> *During the epidemic, I did not receive any special care or support. I have expressed my difficulties and needs to the Disabled Persons' Federation, but they did not respond. I made suggestions to them more than once, hoping they would consider PWDs when formulating relevant policies, but none of these suggestions worked. (C-11)*

This neglect of PWDs and the one-size-fits-all approach is reflected in relevant legal documents and policy texts. For example, the Law on Prevention and Treatment of Infectious Diseases (LPTID) does not mention the need for PWDs in an emergency public health crisis (COVID-19). The notice on social assistance during COVID-19 prevention and control did not mention PWDs or list them as the target of special assistance. In addition, the Ministry of Civil Affairs has successively issued

more than 10 documents on social assistance for the extremely poor groups, which stipulates that the recipients of assistance are minimum living-hood guarantee (MLG) recipients, special hardship people, etc. However, there is no mention of the disabled. Further, the neglect of PWDs is also reflected in the lack of statistics related to them during the COVID-19 pandemic, which makes it difficult to accurately grasp the impact of the epidemic on them as a whole and the related trends.

> *Although the law clearly requires equal treatment of PWDs, in fact, no one except family members cares about us sincerely. PWDs often remain an afterthought, living as invisible citizens without any sense of existence. (C-8)*

Emphasis on Unity Over Individuality: The Individualized Differences of PWDs Are Ignored

The epidemic prevention and control measures under the war metaphor emphasize coordinating all the activities of the nation as a whole—focusing on the unity of the majority rather than the individual differences of the minority. To win this anti-epidemic war, most measures tend to adopt standardized and unified methods because this is cost-saving and efficient. Owing to the lack of personalized prevention policies for the differences in PWDs, they are left behind. For people with hearing and speech disabilities, most news coverage of COVID-19 is without sign language, which increases the barriers for them to obtain valuable information. The lack of publication of Braille information on COVID-19 also made it difficult for the visually disabled to access relevant information on time. During the home quarantine period, rehabilitation services for children with disabilities were suspended. Therefore, interviewees often refer to themselves as "the invisible person who has been forgotten in the corner".

> *During the epidemic, almost all institutions and services were suspended, and I was isolated from the outside world. At that time, the responsibility of taking care of me was entirely borne by my family, and there was almost no support from others. I felt very depressed and could not do anything, like a burden on my family and society. I was in a state of depression, anxiety, and hopelessness at that time. (C-7)*

Identity Segment: Eligibility for Benefits Based on Poverty Rather Than Disability

We reviewed policy documents on social welfare and social assistance issued during the COVID-19 pandemic. Based on an analysis of the policy text, we found that eligibility for such assistance was based on whether the applicant was in poverty, which was measured by economic income, and whether they were supported by family members rather than disability identity. For example, we extracted the definition of welfare recipients in the "Notice on Protecting People in Difficulties During the Period of Epidemic Prevention and Control": "During the COVID-19 pandemic, temporary assistance will be given monthly to those in need, such as those living with the minimum living standard allowance and lived in extreme poverty, vulnerable children, at twice the minimum living allowance standard". It can be inferred that welfare eligibility is poverty-based or income-based rather than a disability identity. As there is a strong correlation between poverty and disability, which has been confirmed by numerous studies, the beneficiaries of these policies are mostly PWDs. Some interviewees stated that they hardly received any benefits during the epidemic, mainly because they were not poor.

> *I was fired during that time, and suddenly, there was no income, making my livelihood very difficult. I applied for social assistance from the community, hoping to obtain temporary assistance. However, my application was rejected because I am not poor, and my income level does not meet the conditions for being rescued. So, I hardly received any help or support. (C-5)*

CONCLUSION AND DISCUSSION

We adopted qualitative research methods to explore the impact of war metaphors during the COVID-19 outbreak on PWDs in mainland China. Based on the analysis of interview data and policy documents, we found that the war metaphor dominated the principles and measures of epidemic prevention and control, which, in turn, affected the situation of PWDs. Although PWDs received formal or informal support during COVID-19, their situation worsened as they were further marginalized in the face of increasing social inequalities. Affected by the war metaphor, institutional segregation excludes PWDs from the epidemic prevention and control system. They are like outsiders, facing many visible and invisible social exclusions. Pragmatism derived from the war metaphor constructs the disabled as useless or non-contributory; therefore, PWDs are perceived as the minority who can be personally sacrificed. In a dominant "ableist" society, because of the lack of a disability lens and one-size-fits-all prevention and control measures, PWDs have not been given priority but neglected intentionally or unintentionally. In view of this, we need to reexamine the war metaphors during the COVID-19 pandemic and pay more attention to the voiceless and marginalized PWDs.

The war metaphor, as a rhetoric type that describes epidemic prevention and control with war discourse, aims to arouse the public's cognition of COVID-19 and create a sense of urgency and crisis, thus being regarded as an effective way of social mobilization. Undeniably, the war metaphor has played a key role in curbing the spread of this unprecedented public health crisis in China. However, it also has some negative and obscured effects. Although the war metaphor in medical discourse highlights the urgency and confrontational characteristics of war, it conceals its violent, compulsive, and destructive nature and ignores the irrationality and blind obedience it may cause (39). In addition, the one-sidedness of this overly exaggerated war metaphor has led to the concealment of social problems, such as the shutdown of economic production, local intensified social conflicts, and the suffering of vulnerable groups such as PWDs (40).

COVID-19 presents complex and multifaceted challenges for PWDs that require an inclusive and equitable response in the areas of public health and social responsibility. CRPD prohibits all discrimination, exclusion, or restriction based on disability and ensures that PWDs can enjoy free or affordable healthcare and services of the same quality and standard on an equal

basis with others. Therefore, necessary laws and related policies need to be formulated to meet the basic life, social, emotional, and mental health needs of PWDs to ensure that they are not left behind in this crisis and are included (15). In addition, information and communication remain important weapons in the fight against COVID-19. Accordingly, CRPD requires appropriate facilities for PWDs to obtain information and meet their communication and information needs by providing them with specific technologies, languages, and accessible formats (29).

To improve the overall conditions of PWDs during COVID-19, rights-based strategies and community-based inclusive measures are key to ensuring that PWDs participate in and assume social responsibility in the process of policy design and implementation. It is necessary to give full play to the role of social organizations and support centers for PWDs to provide them with accessible and valuable information about COVID-19. Support needs to be provided for PWDs to use electronic information equipment so that they can strengthen their social interaction and connection with the outside world through online means as much as possible to reduce the sense of isolation. Further, for those profoundly disabled individuals who rely on family care, more attention should be paid not only to them but also to the family burden and the emotional health and quality of life of their family members. Correspondingly, a comprehensive social support system centered on families living with disabilities should be established.

This is a pioneering study on the impact of war metaphors on PWDs in the context of COVID-19. However, this study had two main limitations. First, it covered different types of PWDs and focused on exploring more general experiences that cannot go deep into individualized experiences about specific categories of PWDs. Subsequently, future studies can explore the unique experiences of this theme with a specific category of PWDs. Second, affected by COVID-19, face-to-face interviews cannot be conducted, and we have to recruit interviewees through online. However, in China, especially in the vast rural areas, affected by economic conditions and technical levels, many children and elderly persons with disabilities have limited ability to use related communication devices, which limits their use of WeChat, QQ, and Weibo. This makes it difficult for us to reach a wider range of people with disabilities through online recruitment. We adopted a qualitative method with a small-scale sample and whether the conclusions of this study are universally generalizable remains to be discussed. Therefore, we may not be able to overcome some of the limitations of qualitative research methods. Perhaps a hybrid research method combining qualitative and quantitative research can be applied to explore this important topic. Furthermore, when the COVID-19 is effectively prevented and controlled, the "legacy" and long-term effects of the war metaphor may still exist. Future study can carry out more in-depth exploration on this topic.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Academic Committee of Renmin University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

R-XC: conceptualization, methodology, data collection and data analysis, writing-original draft, and writing-review and editing. Z-MG: conceptualization, methodology, data collection and data analysis, writing-original draft, writing-review and editing, and administration. S-LH: methodology, data collection and curation, and writing-original draft. W-ZT: methodology, data collection and curation, and funding acquisition. All authors contributed to the article and approved the submitted version.

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Comparing Fear of COVID-19 and Preventive COVID-19 Infection Behaviors Between Iranian and Taiwanese Older People: Early Reaction May Be a Key

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This study assessed fear of the novel coronavirus-2019 (COVID-19), preventive COVID-19 infection behaviors, and the association between fear of COVID-19 and preventive COVID-19 infection behaviors among older people in Iran and Taiwan. Older people aged over 60 years ($n = 144$ for Iranians and 139 for Taiwanese) completed the Fear of COVID-19 Scale (FCV-19S) and two items on preventive COVID-19 infection behaviors (i.e., hand washing and mouth covering when sneezing). Iranian older people had a significantly higher level of fear of COVID-19 than did Taiwanese older people. Moreover, Iranian older people had significantly lower frequencies of preventive COVID-19 infection behaviors than did Taiwanese older people. Different timings in implementing COVID-19 infection control policies in Iran and Taiwan may explain why Iranian older people had greater fear of COVID-19 and lower preventive COVID-19 infection behaviors than did Taiwanese older people.

Keywords: COVID-19, elder, infection preventive behavior, Iran, Taiwan

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INTRODUCTION

Depression, anxiety, and stress are relatively common among older adults (1, 2). Indeed, nearly 10% of older adults suffer from depressive and anxiety symptoms (3). Beyond their direct impact, mood disorders make a significant contribution to a range of poor health outcomes (4, 5). Therefore, understanding the factors related to mood problems among older adults is an important area of research. To date, several factors have been reported, including sleeping quality and underling disorders such as cerebellar degenerative disease (6, 7). Beyond the common factors reported in the

literature, the novel coronavirus-2019 (COVID-19) has the potential to significantly impact both the mental and physical health of older adults. Moreover, the impacts of COVID-19 on individuals' stress and mental health have been frequently reported worldwide (8–12).

COVID-19 has a rapid transmission rate and has quickly spread worldwide, with nearly 5.6 million confirmed cases and more than 350,000 deaths at the time of writing (29 May 2020). Therefore, the World Health Organization (WHO) has announced that the COVID-19 infection is a global pandemic (13). The impact of COVID-19 may be especially severe for older adults, with recent evidence demonstrating that older people are especially vulnerable to COVID-19 infection (14). More specifically, the mortality rates of COVID-19 infection for people aged over 70 are 12.8% in Italy and 8.0% in China (14). Further, the mortality of COVID-19 infection is highly associated with chronic diseases, especially those that tend to be more common among older adults, such as cardiovascular disease, dementia, Parkinson's disease, and cancer (14–17). Given their increased risk, older adults may be more fearful of COVID-19 which could, in turn, contribute to the increased incidence of stress and anxiety associated with the COVID-19 pandemic (18, 19).

Recently, Ahorsu et al. developed the Fear of COVID-19 Scale (FCV-19S) (20). The FCV-19S was completed by an Iranian sample and revealed that there was a very high level of fear in the peak of COVID-19 outbreak; that is, March 2020 (21). An appropriate amount of fear motivates an individual to perform appropriate preventive behaviors (22). Indeed, several behavioral theories (e.g., the Protection Motivation Theory, the Health Believe Model, and the Fear Drive Model) have proposed that fear may lead people to adhere to healthy behaviors and decrease unhealthy behaviors, such as increasing exercise while also quitting smoking (23, 24). At the same time, high levels of fear may negatively impact health (25, 26). Therefore, finding the right balance with respect to the fear of COVID-19 may be critical to encouraging adherence to behaviors that aim to prevent the spread of COVID-19.

The present study investigated fear of COVID-19 and preventive COVID-19 infection behaviors among older people from two different countries (Iran and Taiwan). By comparing these two countries, the present study aims to shed some light on the effectiveness of the different public health approaches applied in these two countries in response to the COVID-19 outbreak. More specifically, both Iranian and Taiwanese governments used universal policies (e.g., boarder control, encouragement of preventive COVID-19 infection behaviors, and instant reporting of COVID-19 information through different social media platforms) to control the spread of COVID-19. The Taiwanese government, however, had a much quicker response to the COVID-19 pandemic than the Iranian government. For example, the Taiwanese government implemented infection control policies in late January, while the Iranian government only implemented similar policies in late February. Moreover, during the initial COVID-19 outbreak period, the Iranian government canceled sporting events and closed public places, with a lockdown conducted between 28 March and 9 April 2020. In contrast, the Taiwanese government did not cancel large events and did not close public places, instead using strict regulations during events and in public places (e.g., requiring face masks, enforcing physical distancing).

Regarding the COVID-19 infection development in Iran, Qom had the earliest confirmed cases of COVID-19 (on 19 February 2020). Following this, an additional 18 cases, four of whom died, were reported 2 days later (on 21 February). The increase of COVID-19 infection cases grew dramatically between February and March, with 16,169 confirmed cases and 988 deaths by 17 March. In order to control the COVID-19 outbreak, the Iranian government disseminated guidelines and related information via TV, SMS, and the internet. Moreover, the government set up COVID-19 hotlines to answer COVID-19 queries from the general population (27). By 29 May, 2020, there were 143,849 confirmed cases and 7,627 deaths.

Regarding the COVID-19 situation in Taiwan, the earliest confirmed case of COVID-19 occurred on 21 January 2020 and the first death was reported nearly 1 month later (on 16 February). The increase of COVID-19 infection cases was generally well-controlled from January to May, with 441 confirmed cases and 7 deaths by 28 May. Moreover, only 91 cases were infected in the community, with the remaining 350 infected abroad. Similar to the Iranian government, the Taiwanese government disseminated guidelines and related information though standard channels (i.e., TV, SMS, and the internet) and set up COVID-19 hotlines to answer COVID-19 queries from the general population. Furthermore, the Taiwanese government paid special attention to the COVID-19 infection development in the early stages, with border control, quarantine, and isolation all being implemented since the first infection was confirmed. The government also responded to all the potential risks of COVID-19 transmission, such as cruise ships coming to Taiwan (28, 29). For example, the Diamond Princess cruise ship, which reported COVID-19 outbreak at the Yokohama on 5 February 2020, had been docked at Keelung harbor in Taiwan on 31 January 2020. With the aforementioned information reported by the media, a temporary public panic concerning the risk of community spread was triggered (28, 30). Thus, the government implemented additional precautionary measures, including comprehensive contact tracing and a mitigation plan to minimize COVID-19 infection spread (28).

Table 1 further summarized the COVID-19 situations between Iran and Taiwan. In brief, the Taiwan government seemed to respond more quickly to the COVID-19 outbreak when compared to the Iran government. Therefore, the infection status of COVID-19 was different between the two countries, and this may subsequently lead to differences in preventive behaviors and the degree of fear between the two countries' older people. In this regard, the present study hypothesized that (i) Iranian older people will report higher levels of fear of COVID-19 than Taiwanese older people; (ii) the association between fear of COVID-19 and preventive COVID-19 infection behaviors will be stronger in Iranian older people than in Taiwanese older people.

TABLE 1 | COVID-19 situations and present study's recruitment information between Iran and Taiwan.

Comparisons	Iran	Taiwan
Data collection period in the present study	Entire April 2020	Late April to early May 2020
Recruitment method in the present study	Online from community population	In-person from patient population
The earliest confirmed cases of COVID-19 infection	19 February 2020 (in Qom)	21 January 2020 (in Taoyuan airport)
The earliest death(s)	21 February 2020 (4 deaths)	16 February 2020 (1 death)
Growth of COVID-19 infection cases	Between February and March (16169 confirmed cases with 988 deaths) Between February and May (143849 confirmed cases with 7627 deaths)	Between January and May (441 confirmed cases with 7 deaths)
Government action	1. Disseminating guidelines and related information via TV, SMS, and online resources 2. Setting up COVID-19 hotlines to answer COVID-19 queries	1. Disseminating guidelines and related information via TV, SMS, and online resources 2. Setting up COVID-19 hotlines to answer COVID-19 queries 3. Paying special attention to the COVID-19 infection development in the early stages. Border control, quarantine, and isolation all being implemented since the first infection was confirmed.

METHODS

Taipei Medical University's ethical committee approved the study with registered numbers of TMU-JIRB N202005044. Also, ethics committee of Qazvin University of Medical Sciences approved the study with registered number of IR.QUMS.REC.1398.375.

Participants and Recruitment Procedure

For recruitment of Iranian older adults, online social media platforms, including telegram, Instagram, and WhatsApp, were used. The three online platforms are the most popular social media platforms in Iran, and the link that described study aims and descriptions together with questionnaires was posted on these platforms. The Iranian data were collected throughout April 2020. For recruitment of Taiwanese older people, the target population were older adult patients who visited and consulted a physician from one medical center in Taipei, Taiwan. During their visits, several research assistants explained the study aims and descriptions to them. Then, the research assistants let the participants who agreed to participate in the study sign a written informed consent form before interviewing them using the survey questionnaires. All the interviews were done face-to-face and were administered in a private room. Similar to the timeline in Iran, the Taiwanese data were collected from late April to early May 2020. Different methods in data collection were applied because during the survey period, Iran had severe COVID-19 outbreak and it was unable to approach the participants in person. However, Taiwan was in mild severity of COVID-19 outbreak and we believed that completing the survey using face-to-face method can better control the data quality.

The inclusion criteria of the present study's participants were (i) aged 60 years and above; (ii) voluntarily agreeing to participate in the study; and (iii) the ability to understand the survey questions. There were no other exclusion criteria for the participants.

Measures

Fear of COVID-19

Fear of COVID-19 was measured using a well-established instrument [i.e., Fear of COVID-19 Scale; FCV-19S; (20)]. The FCV-19S includes seven items that assess an individual's fear toward COVID-19 with a five-point Likert scale (1 = strongly disagree; 5 = strongly agree). A higher score in the FCV-19S indicates greater fear of COVID-19. Moreover, the FCV-19S has promising psychometric properties in different language versions, including Persian (20), Bangla (31), Russian (32), Turkish (33), Italian (34), Arabic (35), and Hebrew (36). For example, the unidimensional structure of the FCV-19S has been verified using both confirmatory factor analysis and exploratory factor analysis (20, 31). The internal consistency of the FCV-19S in the present sample was satisfactory: $\alpha = 0.79$ for Taiwanese older people and 0.91 for Iranian older people.

Preventive COVID-19 Infection Behaviors

Two preventive COVID-19 infection behaviors were designed according to the suggestions made by the World Health Organization (WHO) to fight COVID-19 (37). The two behaviors are hand washing and mouth covering when sneezing, and they were measured using a five-point Likert scale (1 = almost never; 5 = almost always). Thus, a higher score indicates higher frequencies in performing these preventive behaviors. Although the WHO proposed other three behaviors of wearing a mask, physical distancing, and avoid touching eyes nose mouths, the present study did not assess the three behaviors because of the following reason. The use of mask for prevention was still under debate (38) during our data collection period. Therefore, we did not assess this behavior. Regarding physical distancing and avoid touching eyes nose mouth, we considered that the two behaviors are very likely to be misreported. Specifically, one usually moves close to another person and was not aware of this action when they are talking. Similarly, one usually touches his/her eyes,

nose, or mouth unawareness. Therefore, the present study mainly focused on the behaviors of hand washing and mouth covering when sneezing.

Background Information

A background information sheet was used to measure the participants' demographic and clinical characteristics. More specifically, the demographic information included the participants' age, gender, living area (urban or not), and educational level. The clinical characteristics included the following chronic diseases: diabetes mellitus, hypertension, heart disease, renal disease, and cancer.

Data Analysis

Descriptive statistics, including mean with standard deviation (SD) and frequency with percentage, were firstly carried out to understand the demographics and clinical characteristics of the participants. Moreover, the participants' fear of COVID-19 and preventive COVID-19 infection behaviors were presented using descriptive statistics. Then, independent *t*-tests and χ^2-tests were applied to examine whether there were significant differences between Iranian and Taiwanese older people. Lastly, four regression models were constructed to examine the factors that explain fear of COVID-19 and abiding by preventive COVID-19 infection behaviors. More specifically, the first regression model used fear of COVID-19 as the dependent variable; demographics (age, gender, education, and living area), clinical characteristics (having a diabetes mellitus, hypertension, heart disease, renal disease, and cancer), and group (Iranian or Taiwanese older people) as independent variables. The second to the fourth regression models used hand washing, mouth covering when sneezing, and total behavior (i.e., adding both hand washing and mouth covering behaviors) as the dependent variables, respectively. Moreover, the independent variables were the same as those used in the first regression model, with the addition of the FCV-19S. All the statistical analyses were performed using the IBM SPSS 24.0 (IBM Corp., Armonk, NY).

RESULTS

Participants' demographic and clinical characteristics are presented in **Table 2**, which shows that the Iranian sample ($n = 144$; mean = 65.59; $SD = 6.65$) was significantly younger than the Taiwanese sample ($n = 139$; mean = 71.73; $SD = 7.90$; $p < 0.001$). Moreover, the Taiwanese sample had significantly more females (69.8 vs. 29.2%; $p < 0.001$), were better education (2.9% illiterate vs. 24.3% illiterate; $p < 0.001$), and had more participants living in urban areas (91.4 vs. 50.7%; $p < 0.001$). Regarding chronic diseases, no significant differences were found in the percentages of having hypertension and cancer between the two groups. However, Taiwanese sample as compared with Iranian sample had a significantly lower prevalence of diabetes mellitus, heart disease, and rental disease ($ps < 0.001$). A significantly higher level of fear of COVID-19 was observed in Iranian older people (mean = 3.36; $SD = 1.04$) when compared to Taiwanese older people (mean = 1.80; $SD = 0.80$; $p < 0.001$). Interestingly, a significantly lower frequencies of preventive COVID-19 infection behaviors were observed in Iranian older people (mean = 4.06–4.15; $SD = 0.89$–1.03) when compared to Taiwanese older people (mean = 4.78–4.86; $SD = 0.54$–0.68; $ps < 0.001$).

The regression models supported this finding that Iranian older adults had greater fear of COVID-19 than Taiwanese older adults (standardized coefficient [β] = 0.60; adjusted odds ratio [AOR] = 1.82; $p < 0.001$) but performed fewer preventive COVID-19 infection behaviors (β = −0.42 to −0.58; AOR = 0.66–0.56; $ps < 0.001$) when demographics and clinical characteristics were controlled (**Table 3**). Fear of COVID-19 was another significant predictor in explaining older people's preventive COVID-19 infection behaviors: greater fear was associated with more preventative COVID-19 infection behaviors (β = 0.27, AOR = 1.31, and $p < 0.001$ for hand washing; β = 0.14, AOR = 1.15, and $p = 0.01$ for mouth covering when sneezing; β = 0.26, AOR = 1.30, and $p < 0.001$ for total behavior).

DISCUSSION

To the best of the present authors' knowledge, no studies have compared the fear of COVID-19 and preventive COVID-19 infection behaviors between two countries, especially for their older populations. The present study presents important information for healthcare providers and health policy makers, helping them to understand the importance of timing in implementing infection control policies. The fear of COVID-19 was moderate among Iranian older people (scored 3.36 out of a 5-point scale) and low among Taiwanese older people (scored 1.80 of a 5-point scale). The preventive COVID-19 infection behaviors were high in both Iranian older people (scored 4.06–4.15 of a 5-point scale) and Taiwanese older people (scored 4.78–4.86 of a 5-point scale). Moreover, Taiwanese older people as compared with Iranian older people had lower levels of fear of COVID-19 and higher levels of preventive COVID-19 infection behaviors. A significantly positive association was also found between fear of COVID-19 and preventive COVID-19 infection behaviors. Moreover, the association between fear of COVID-19 and preventive COVID-19 infection behaviors was stronger in Iranian older people than in Taiwanese older people.

As compared with the fear found in a general Iranian population (20), the fear of COVID-19 in the present sample was lower. Ahorsu et al. reported a score of approximately 4 from a 5-point scale and the present study reported 3.36 for Iranians and 1.80 for Taiwanese (20). Potential reasons include (i) the communities and governments have better knowledge and information on COVID-19 during the data collection period for the present study; (ii) the governments have applied different methods to correctly disseminate the COVID-19 information for citizens. Indeed, Ahorsu et al. collected data at the peak of COVID-19 infection in Iran (March) and the present study collected the data during a flatter period of COVID-19 infection (April) (20). Some studies (31, 33–35) collected data after Ahorsu et al. also found a lower fear as compared with Ahorsu et al.'s fear findings (20). Therefore, with the governments' efforts in

TABLE 2 | Comparing participants' characteristics, fear of COVID-19, and behaviors between Iranian and Taiwanese older people.

	Mean (SD) or *n* (%)		*t* or χ^2 (*p*-value)
	Iranian (*N* = 144)	**Taiwanese (*N* = 139)**	
Age (year)	65.59 (6.65)	71.73 (7.90)	7.07 (<0.001)
Gender (female)	42 (29.2)	97 (69.8)	46.69 (<0.001)
Education			48.03 (<0.001)
Illiterate	35 (24.3)	4 (2.9)	
Primary school	15 (10.4)	31 (22.3)	
Secondary school	15 (10.4)	45 (32.4)	
Diploma or above	79 (54.9)	59 (42.4)	
Living area (urban)	73 (50.7)	127 (91.4)	56.45 (<0.001)
Chronic disease (no)			
Diabetes mellitus	81 (56.3)	115 (82.7)	23.30 (<0.001)
Hypertension	79 (54.9)	88 (63.3)	2.09 (0.15)
Heart disease	106 (73.6)	122 (87.8)	9.06 (0.003)
Renal disease	126 (87.5)	134 (96.4)	7.51 (0.01)
Cancer	124 (86.1)	125 (89.9)	0.39 (0.53)
Fear of COVID-19	3.36 (1.04)	1.80 (0.80)	14.22 (<0.001)
Hand washing	4.15 (0.96)	4.78 (0.68)	6.43 (<0.001)
Mouth covering	4.06 (1.03)	4.86 (0.57)	8.17 (<0.001)
Total behavior	4.11 (0.89)	4.82 (0.54)	8.24 (<0.001)

Mouth covering indicates covering mouth when sneezing.
Total behavior includes both hand washing and mouth covering when sneezing.

providing correct COVID-19 information, the fear of COVID-19 was not high, even in a higher risk population such as older adults (14, 39).

The effectiveness of disseminating COVID-19 information can be somewhat verified by the high preventive COVID-19 infection behaviors found in the present study. This finding echoes the Protection Motivation Theory (24), the Health Belief Model (22), and the Fear Drive Model (23) that disseminating the potential impact of COVID-19 may improve adherence to performing preventive COVID-19 infection behaviors. More specifically, both Iranian and Taiwanese governments have set up different platforms to disseminate COVID-19 information, including the preventive behaviors (27, 28, 30). Therefore, the extremely high preventive COVID-19 infection behaviors found in the present study may be due to the information dissemination. Another possible explanation for the high preventive COVID-19 infection behaviors is an adequate level of fear of COVID-19. If an individual can properly handle fear, the individual will be aware of the risks of COVID-19 and subsequently take appropriate action to reduce their chances of contractive the virus (21). Indeed, the regression models in the present study found that higher levels of fear were associated with greater preventive behaviors. Moreover, the regression findings justify that the present sample had adequate levels of fear instead of an overwhelming level of fear.

However, an interesting finding is that Taiwanese older people had lower level of fear of COVID-19 but higher levels of preventive COVID-19 behaviors, which contradicts the regression findings on greater fear associated with more preventive COVID-19 behaviors. The main reason may be due to the different levels of COVID-19 severity and government efficiency between the two countries. In Taiwan, the COVID-19 severity was mild and the dissemination of correct COVID-19 preventive behaviors was efficient, which led to low level of fear of COVID-19 and high level of adherence to preventive behaviors. In Iran, the COVID-19 severity was severe and unfortunately the government efficiency in disseminating COVID-19 preventive behaviors was less efficient than Taiwan government (27, 28, 30). Therefore, Iranians as compared with Taiwanese had higher levels of fear and lower levels of adherence to preventive behaviors. However, if we controlled the country effects in the regression models, the results showed that greater fear led to higher levels of adherence to preventive behaviors.

An important finding in the present study is the different levels of fear and preventive behaviors between Iranian and Taiwanese older people. Counter intuitively, Taiwanese older people had less fear but adhered more to preventive behaviors as compared with Iranian older people. A potential explanation is the implementation of infection control policies on Taiwan. With the early reaction in late January (28, 29), the Taiwanese government was able to control the spread of COVID-19 infection and minimize the confirmed cases and deaths. Subsequently, the population, including older people, may feel safe and have more confidence in the government's actions. Regarding the Iranian government, the action taken was slower than the Taiwanese government and the infection rate became hard to control in March (27). Moreover, the COVID-19 outbreak happened to overlap with New Year celebrations in

TABLE 3 | Regression models in explaining fear of COVID-19 and preventive COVID-19 behaviors.

	B (SE)/β (*p*-value)			
	Fear of COVID-19	**Hand washing**	**Mouth covering**	**Total behavior**
Age	0.02 (0.01)/0.12 (0.02)	0.01 (0.01)/0.05 (0.45)	−0.01 (0.01)/−0.09 (0.13)	−0.003 (0.01)/−0.03 (0.67)
Gender (ref: female)	0.10 (0.13)/0.04 (0.42)	−0.36 (0.11)/−0.20 (0.001)	−0.27 (0.11)/−0.15 (0.02)	−0.32 (0.10)/−0.19 (0.002)
Education[a]	0.03 (0.12)/0.01 (0.78)	−0.02 (0.11)/−0.01 (0.85)	0.04 (0.11)/0.02 (0.72)	0.01 (0.09)/0.01 (0.93)
Living area (Ref: urban)	0.25 (0.13)/0.10 (0.06)	−0.11 (0.12)/−0.06 (0.38)	0.13 (0.12)/0.07 (0.27)	0.01 (0.11)/0.01 (0.90)
Chronic disease (Ref: no)				
Diabetes mellitus	−0.03 (0.13)/−0.01 (0.81)	0.01 (0.11)/0.002 (0.97)	−0.12 (0.11)/−0.06 (0.29)	−0.06 (0.10)/−0.03 (0.56)
Hypertension	−0.01 (0.11)/−0.004 (0.92)	0.08 (0.10)/0.04 (0.46)	0.29 (0.10)/0.16 (0.005)	0.18 (0.09)/0.11 (0.04)
Heart disease	0.29 (0.14)/0.10 (0.04)	0.15 (0.13)/0.07 (0.24)	0.17 (0.13)/0.07 (0.19)	0.16 (0.11)/0.08 (0.16)
Renal disease	0.37 (0.20)/0.08 (0.07)	0.03 (0.18)/0.01 (0.88)	0.16 (0.19)/0.05 (0.39)	0.09 (0.16)/0.03 (0.57)
Cancer	0.48 (0.17)/0.13 (0.005)	−0.01 (0.15)/−0.004 (0.95)	0.001 (0.15)/<0.001 (0.99)	−0.004 (0.14)/−0.002 (0.98)
Fear of COVID-19	–	0.20 (0.06)/0.27 (<0.001)	0.14 (0.06)/0.19 (0.01)	0.17 (0.05)/0.26 (<0.001)
Group (Ref: Taiwanese)	1.45 (0.15)/0.60 (<0.001)	−0.75 (0.16)/−0.42 (<0.001)	−1.07 (0.16)/−0.58 (<0.001)	−0.91 (0.14)/−0.56 (<0.001)
Mode fit statistics				
F-value (*p*-value)	25.70 (<0.001)	6.62 (<0.001)	8.86 (<0.001)	9.38 (<0.001)
R^2 (Adjusted R^2)	0.49 (0.47)	0.21 (0.18)	0.27 (0.24)	0.28 (0.25)

[a] *Reference group of education is those who had completed secondary school or below.*
Mouth covering indicates covering mouth when sneezing.
Total behavior includes both hand washing and mouth covering when sneezing.

Iran (Persian New Year began on 3 March 2020), which may have made Iranians reluctant to perform preventive COVID-19 infection behaviors as they wanted to celebrate the big event with large family gatherings (27).

There are some limitations in the present study. First, given that different countries have different cultures and habits, the early policies on COVID-19 infection control used in Taiwan may not be applicable to people in Iran. Also, it is unclear whether the effectiveness of such policies is due to the specific populations or due to the early policies that were adopted. Of course, given the nature of this area of research, it is not possible to answer this question directly given experimental designs cannot be employed. A tentative conclusion is that implementing infection control policies in an early stage may be effective in preventing infection spread. Second, there were subtle differences between the two samples (e.g., Iranian older adults were younger than Taiwanese older adults). Thus, the significant differences found in the independent *t*-tests might be due to these subtle differences. The regression models, however, control for these differences. Third, the methods of data collection were different between the Iranian and Taiwanese samples; therefore, it is possible that the different methods used for data collection will cause any answering bias (40). These differences are unlikely to introduce serious bias, as measurement invariant properties between different methods of data collection have been found (41). Fourth, the Iranian participants were recruited using social media and the sample only represents those who were active on the social media and may have sampling bias (42). Fifth, all the measures are based on self-report and at risk of social desirability (e.g., willing to report a high preventive behaviors). Sixth, the representativeness of the present samples is limited because of the use of convenience sampling. Seventh, some important confounders, such as whether participants were contracted with COVID-19, were not assessed. The lack of controlling these confounders may result in biases of our findings. Lastly, given that the present study adopted a cross-sectional design, causality cannot be inferred.

CONCLUSION

In conclusion, the present study demonstrated that Iranian older people as compared with Taiwanese older people had higher levels of fear of COVID-19 but implemented a lower frequency of preventive COVID-19 infection behaviors. Such findings remained even when controlling for important confounders (i.e., age, gender, educational level, living area, and various chronic diseases). Moreover, higher levels of fear of COVID-19 were associated with more preventive COVID-19 infection behaviors. However, the level of fear of COVID-19 in the present study was not high (3.36 out of 5 from Iranians and 1.80 out of 5 from Taiwanese). The lower level of fear, but higher level of preventative behaviors in the Taiwanese sample, may reflect the benefits of their government's early and swift reaction to the COVID-19 infection.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Taipei Medical University's ethical committee

approved the study with registered numbers of TMU-JIRB N202005044. Also, ethics committee of Qazvin University of Medical Sciences approved the study with registered number of IR.QUMS.REC.1398.375. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AP, C-hL, W-LH, Y-PC, Y-JK, Y-PL, C-YL, and DS contributed conception and design of the study. C-hL, W-LH, Y-PC, and Y-JK organized the database. AP and C-YL performed the statistical analysis and wrote the first draft of the manuscript. AP, C-hL, W-LH, Y-PL, and C-YL interpreted the results. C-hL, Y-PC, and Y-JK wrote sections of the manuscript. C-hL, W-LH, Y-PL, C-YL, and DS critically review the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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OPINION
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Success in Vaccination Efforts of Vulnerable Populations in the WHO/European Region: Focus on Prisons

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Keywords: prisons, vulnerable populations, vaccination, COVID-19, Europe

COVID-19 has brought the world's attention to the fragility of mankind in general, highlighting particular risk for vulnerable populations from being hit and having more severe outcomes, including death. The concept of vulnerability generates considerable disagreement, ranging from considerations of social justice factors to the impact on health (1). There is, however, consensus that vulnerability is not a static characteristic but a situational descriptor that may change over time. For example, the restrictions measures imposed because of COVID-19 have led some people to situations of vulnerability, when for instance becoming unable to pay for their house due to job losses. The same concept applies to people who, at a certain moment in life, become deprived of liberty.

The increased susceptibility of people living in detention to contracting infectious diseases is well-established, and most measures implemented focus on preventing the virus to enter prison walls. There is no doubt that the potential impact of COVID-19 in the prison population is higher because access to healthcare is often suboptimal and because the burden of underlying health conditions is higher. In March 2021, Neufeld et al., called for the need for prisons to be included in global and national vaccination efforts against COVID-19 (2). This message was strengthened by an advocacy brief launched in June by the WHO Health in Prisons Programme (WHO-HIPP), developed in collaboration with the United Nations Office on Drugs and Crime and Penal Reform International (3). The announced intention of this brief was to advocate for the reduction of inequalities in healthcare provision for all vulnerable groups to ensure full attainment of universal health coverage by leaving no one behind, aligned with the bold intentions of the WHO European Programme of Work 2020–2025 (4). In this follow-up piece we further highlight the notable efforts of selected Member States to ensure COVID-19 vaccination coverage.

WHO-HIPP has developed a surveillance system for places of detention that relies on voluntary reports from Member States (5). In February 2021 this reporting system was adapted to include information on vaccines administered to people in prison, staff and health workers in the criminal justice system.

Since March, all healthcare workers in Spanish prisons have been vaccinated (100% coverage). Vaccination of detainees is also rapidly increasing, with only 3.6% refusal rate. Most recent data, obtained in early July, indicate that 84% are fully covered and another 13% have received their first dose, totalling 97% of vaccine coverage. Even though this data does not include Catalonia, as this region is managed under a different administration, it represents the vast majority of Spain, enabling a rough comparison against the vaccination roll-out in the general population. In fact, according to the WHO dashboard, in the same date, the proportion of Spanish citizens living in the community with full coverage represented 34.2% (as opposed to 84.0% in prison) (6).

The strategy adopted in the United Kingdom for prisons has been described as aligned with the general prioritization criteria, which led to some fears given the difficulties to identify people meeting the eligibility criteria because of poor information records (even

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if better than in most of Europe) (7). However, data obtained from Northern Ireland in June, as one of the five UK nations, indicated a vaccination coverage of 87.3% among the detainees. Also, in Poland, since early July, 74.0% vaccination coverage has been reached among people in prison, considerably higher than reported for population data in the WHO dashboard (44.1% with one dose and 33.5% with full coverage).

There are other countries also progressing, even though not as quickly, but worth highlighting as positive experiences in the region. Finland, Ireland and Sweden have reported, respectively, 34.4, 43.7, and 59.1% coverage amongst detainees in early July. However, whilst in Finland, population coverage is notably higher, with 57.9% having received one dose in early July (and 17.7% fully vaccinated), in Ireland, the roll-out in the general population is going at similar pace as in prison; currently with 49.6% having received one dose (and 32.5% fully vaccinated), and finally, in Sweden vaccination in the general population is considerably lower, currently with 45.8% having received one dose (and 28.9% fully vaccinated). Despite these variations, the general trend supports one of WHO's recommendations on adopting facility-wide vaccination as a more efficient strategy for protecting the vulnerable, with benefits also for surrounding communities (3). These good practice examples are encouraging and are expected to progressively expand in Europe and beyond, leaving no one behind in the pursuit of universal health coverage.

Differences in countries' ability to include people living and working in prison in national COVID-19 vaccination efforts may result from various factors, including political will and financial resource constraints to name a few. Regardless of reasons, the impact of exclusion in terms of social justice, respect for human rights and health outcomes is clear. COVID-19 vaccines are innovative health technologies and, in many ways, an opportunity for societies to advance their health equity commitments by ensuring universal healthcare access for people living in prisons. With this in mind, we highlight the notable efforts of selected Member States to ensure COVID19 vaccination coverage reaches people in prisons. These examples may serve as inspiration to other Member States to follow until equal, fair and universal care is offered to all people deprived of liberty.

AUTHOR CONTRIBUTIONS

CF-B conceived the platform through which information is collected and critically revised the dataset created. FA wrote the manuscript and supervised data collection. YA reviewed the literature and provided critical comments to improve the manuscript. All authors reviewed and approved the final version of the manuscript.

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No Sex Differences in Psychological Burden and Health Behaviors of Healthcare Workers During the COVID-19 Stay-at-Home Orders

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Background: Females with novel coronavirus disease 2019 (COVID-19) state-ordered home isolation were associated with higher anxiety and reduced sleep quality than males. Sex differences in psychobehavioral changes during the COVID-19 stay-at home orders among healthcare workers remained unclear. The purpose of this study was to explore the sex differences in psychological burden and health behaviors among these persons.

Methods: This was a cross-sectional study using online data available in the open Interuniversity Consortium for Political and Social Research (OPENICPSR). Healthcare workers including females and males who transitioned to working from home during the COVID-19 stay-at-home orders were included. Sex differences were compared using the chi-square test and Student's *t*-test. We performed logistic and linear regression analyses to determine the association of females with psychological burden and health behaviors.

Results: A total of 537 respondents (425 females and 112 males) were enrolled in our study. Sex differences in age (42.1 ± 12.3 years vs. 46.6 ± 15.7 years, $t = -2.821$, $p = 0.005$), occupation ($\chi^2 = 41.037$, $p < 0.001$), mood change ($n = 297$, 69.9% vs. $n = 61$, 54.5%, $\chi^2 = 9.482$, $p = 0.002$), bedtime schedule ($\chi^2 = 6.254$, $p = 0.044$) and news consumption ($n = 344$, 80.9% vs. $n = 76$, 67.9%, $\chi^2 = 8.905$, $p = 0.003$) were statistically significant. Logistic regression showed that females was negatively associated with better mood status (OR = 0.586, 95% CI 0.153–2.247, $p = 0.436$). In addition, linear regression showed that females were not correlated with total sleep time after adjusting for sio-demographics, mental health outcomes and health behaviors ($B = 0.038$, 95% CI −0.313–0.388, $p = 0.833$).

Conclusion: No sex differences in psychological burden and health behaviors of healthcare workers were found during the COVID-19 stay-at-home orders. The COVID-19 state-ordered home isolation may be a potential way to reduce disproportionate effects of COVID-19 pandemic on females and help to minimize sex differences in psychological burden and health behaviors among healthcare workers.

Keywords: sex difference, COVID-19, stay-at-home orders, healthcare worker, psychological, health behaviors

INTRODUCTION

COVID-19, caused by severe acute respiratory coronavirus 2 (SARS-CoV-2), has been a major public health emergency since the end of January 2020 (1). Rapid transmission of the virus tremendously threatened public health and dramatically challenged healthcare systems across the world (2–4), especially in the US (5). Social distancing policies were enacted from the beginning of March 2020, and many people, including some healthcare workers, were forced to stay at home to reduce the spread of the virus (6, 7). Interestingly, females affected by the COVID-19 state-ordered home isolation were proven to be associated with higher anxiety and reduced sleep quality in the general population (8).

Healthcare workers, a unique population who continued working during the COVID-19 state-ordered home isolation, with their frontline peers directly engaged in the clinical management of patients with COVID-19, are at high risk of mental morbidity (9–11) and negative health behaviors (12–14). A cross-sectional study consisting of 1,257 healthcare workers from China showed that females working in hospitals were predisposed to be psychologically stressed, with greater symptoms of anxiety, depression and distress than their male counterparts (15). Similarly, males in France reported lower occurrence rates of symptoms of anxiety and depression working in intensive care units (ICUs) with severe COVID-19 patients (16). Additionally, changes in health behaviors, including sleep problems, work overload, less exercise, increased smoking and drinking, and unhealthy diets, were commonly reported among healthcare workers during the COVID-19 outbreak (7, 14). The total sleep time was significantly shortened in those who continued working on frontlines (7). The rates of smoking and drinking were higher, and both were conversely proven to be protective against anxiety and depression, leading better mental health finally (14).

However, the sex differences in psychological burden and health behaviors due to COVID-19 state-ordered home isolation among healthcare workers who transitioned to working from home remain unclear. Herein, we sought to investigate the sex differences and hypothesized that the COVID-19 state-ordered home isolation could minimize sex differences and help to reduce psychological burden and improve health behaviors of females.

METHODS

Study Design

We conducted a cross-sectional, survey-based, region-stratified study using online data. The overall research workflow is depicted in **Figure 1**. Thereinto, patient selection, data extraction, and statistical analysis were employed. A brief description is as follow. First, we selected the healthcare workers who reported transition of work to home based on the inclusion and exclusion criteria. The records for sex and related items were then extracted from the respondents selected. Next, logistic and linear regression analyses were performed to determine the association of females with psychological burden and health behaviors. Finally, we concluded that there were no sex differences in psychological burden and health behaviors among healthcare workers.

Data Source

The data was collected by means of online research consisting of 29 items (Q1-Q29) in the questionnaire, and was available in the open Interuniversity Consortium for Political and Social Research (OPENICPSR, https://www.openicpsr.org/openicpsr). Totally, this survey contains nine main items, in which 5 questions are related to health behaviors (Q10, Q12-Q28) including sleep time and schedule, work time and schedule, COVID-19-related media exposure, physical activity and diet; while the others are mainly about the psychological burden (Q29) i.e., mental health outcomes (Q29a, Q29b, Q29c, and Q29d) in the questionnaire. Most questions are yes/no and multiple-choice, except for total sleep time before and after stay-at-home orders, screen time before bed and their occupations. The main question about their mood status was "Please tell us how your mood has changed." We converted this item as bivariate variables as better/worse, same as before. Detailed information about the study design of the online research have been previously reported (7). This research was approved by the University of Michigan Institutional Review Board (HUM00180147), and studies using the dataset are granted a waiver of informed consent.

Patient Selection

A total of 936 records about the anonymous responses were collected. And $n = 834$ completed the survey. Then the 834 individuals were included in preliminary analysis by *Conroy DA* et al. The effects of COVID-19 stay-at-home order on sleep, health, and working patterns were compared between healthcare workers who transitioned working from home and those who continued working in person. While in this study, all participants were selected based on the following inclusion criteria: (1) healthcare workers with completed questionnaires, including demographic and psychobehavioral records; (2) healthcare workers currently working from home; and (3) job conducted from home between March 28 and April 29, 2020. Ultimately, 399 individuals were excluded because of no completion of the questionnaire ($n = 102$), no transition to working from home ($n = 294$) and no disclosure of their sex information ($n = 3$), leaving 537 healthcare workers enrolled in this study. It is worth noting that the investigators were not involved in our present study. The mood status records and other variables, including sex, age, occupation, total sleep time and sleep schedule, work time and schedule, media exposure, substance consumption and exercise, were extracted and compared.

Statistical Analysis

Normally distributed continuous variables including age, total sleep time before and after stay-at-home orders, and screen time before bed are expressed as means ± standard deviations, while other parameters are presented as numbers (percentages). Baseline characteristics were summarized based on their sexes. Both baseline data and sex differences focused on the variables of

Abbreviations: COVID-19, novel coronavirus disease 2019; the US, the United States; ICU, intensive care unit; SARS, severe acute respiratory syndrome.

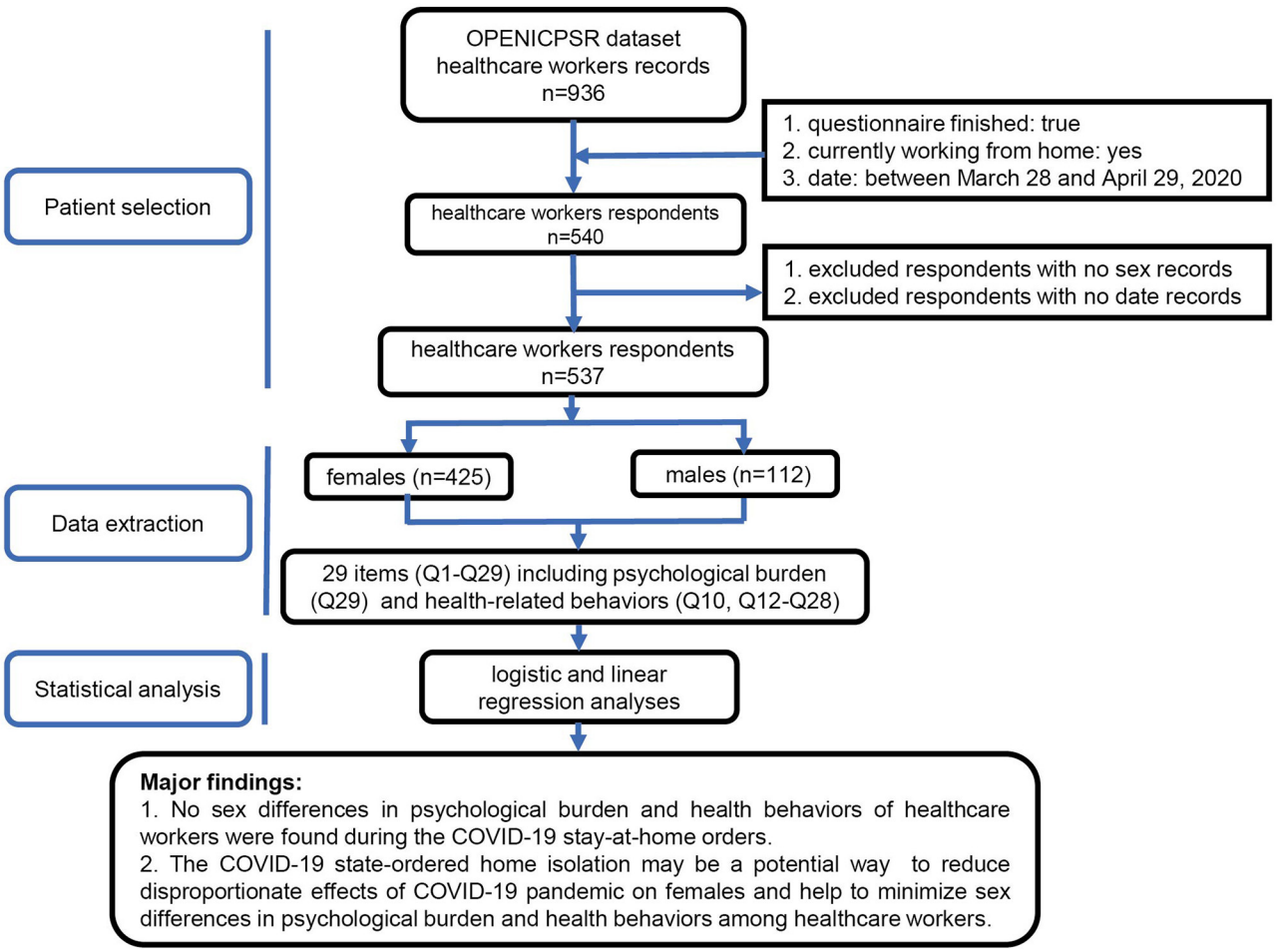

FIGURE 1 | Workflow and major findings of this study. OPENICPSR, open Interuniversity Consortium for Political and Social Research; COVID-19, novel coronavirus disease 2019.

psychological burden and health behaviors were compared using the chi-square test in this study. We performed logistic and linear regression to determine odds rations (ORs) for the association of females with psychological burden and total sleep time after, respectively. Adjusted variables included age, occupation, mood change, bedtime, news time, ethnicity, race, care for COVID-19 patients directly, total sleep time before, work hours, work schedule, work schedule change, and screen time before bed. Moreover, the mood status (better) was adjusted for total sleep time after and the total sleep time after was adjusted for mood status (better) in turn. All statistical analyses were performed by using SPSS Statistics version 26.0 (IBM) software. A two-sided P-value < 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics of the Included Healthcare Workers During the COVID-19 Stay-at-Home Orders by Sex

During the first 31 days after implementing the COVID-19 stay-at-home orders in the US, a total of 537 healthcare workers working from home, including 425 (79.1%) females and 112 (20.9%) males, completed the survey. Only 3.4% of the sample reported to care for COVID-19 patients directly. The average and standard deviation of the 537 respondents age was 43 ± 13.2 years, and the majority were non-Latino (n = 511, 95.2%). Of these 537 individuals, 149 (27.7%) were psychologists, 78 (14.5%) were physicians, and 74 (13.8%) were researchers.

Descriptive sio-demographic characteristics of the 537 participants based on sexes are shown in **Table 1**. Respectively, 2.6% ($n = 11$) of the females and 6.3% ($n = 7$) of the male counterparts were reported to be once engaged in the clinical managements of patients with COVID-19 ($\chi^2 = 3.162$, $p = 0.206$). The average and standard deviation of females age was 42.1 ± 12.3 years, younger than that of males with 46.6 ± 15.7 years ($t = -2.821$, $p = 0.005$). Among these female healthcare workers who continued working from home, 27.1% were psychologists, 9.9% were physicians and 14.6% were researchers; while 30.4% of the males were psychologists, 32.1% were physicians and 10.7% were researchers ($\chi^2 = 41.037$, $p < 0.001$). The total sleep time before staying at home was 7.22 ± 0.91 h in females, which was similar to 7.07 ± 0.71 h in males (t

TABLE 1 | Baseline characteristics of the included healthcare workers during the COVID-19 stay-at-home orders by sex.

Characteristics		Overall	Female	Male	*t* (*p*-value) or χ^2 test of independence
		Mean ± SD or *n* (%)	Mean ± SD or *n* (%)	Mean ± SD or *n* (%)	
Subjects		537 (100.0)	425 (79.1)	112 (20.9)	
Age, years		43.0 ± 13.2	42.1 ± 12.3	46.6 ± 15.7	$t = -2.821$, df = 149, $\mathbf{p = 0.005}$
Ethnicity					$\chi^2(1) = 0.609$, $p = 0.435$
	Non-Latino	511 (95.2)	406 (95.5)	105 (93.8)	
	Others	26 (4.8)	19 (4.5)	7 (6.3)	
Race					$\chi^2(2) = 3.200$, $p = 0.202$
	White	456 (84.9)	363 (85.4)	93 (83.0)	
	Asian	34 (6.3)	23 (5.4)	11 (9.8)	
	others	47 (8.8)	39 (9.2)	8 (7.1)	
Occupation					$\chi^2(3) = 41.037$, $\mathbf{p < 0.001}$
	Psychologist	149 (27.7)	115 (27.1)	34 (30.4)	
	Physician	78 (14.5)	42 (9.9)	36 (32.1)	
	Researcher	74 (13.8)	62 (14.6)	12 (10.7)	
	Others	236 (43.9)	206 (48.5)	30 (26.8)	
Care for COVID-19 patients					$\chi^2(2) = 3.162$, $p = 0.206$
	Yes	18 (3.4)	11 (2.6)	7 (6.3)	
	No	216 (40.2)	172 (40.5)	44 (39.3)	
	Not provided	303 (56.4)	242 (56.9)	61 (54.5)	
Children at home					$\chi^2(2) = 0.726$, $p = 0.696$
	Yes	220 (41.0)	175 (41.2)	45 (40.2)	
	No	128 (23.8)	98 (23.1)	30 (26.8)	
	Not applicable	189 (35.2)	152 (35.8)	37 (33.0)	
Alcohol consumption					$\chi^2(5) = 8.922$, $p = 0.112$
	Never	92 (17.1)	75 (17.6)	17 (15.2)	
	Once a month or less	119 (22.2)	100 (23.5)	19 (17.0)	
	2–4 times a month	163 (30.4)	128 (30.1)	35 (31.3)	
	2–3 times a week	121 (22.5)	93 (21.9)	28 (25.0)	
	4 or more times a week	37 (6.9)	24 (5.6)	13 (11.6)	
Total sleep time, hours					$t = 1.835$, df = 219, $p = 0.068$
	Before stay-at-home	7.19 ± 0.88	7.22 ± 0.91	7.07 ± 0.71	
Date of stay-at-home					$\chi^2(4) = 4.461$, $p = 0.347$
	March 1–7	29 (5.4)	20 (4.7)	9 (8.0)	
	March 8–14	101 (18.8)	78 (18.4)	23 (20.5)	
	March 15–21	245 (45.6)	201 (47.3)	44 (39.3)	
	March 22–28	106 (19.7)	80 (18.8)	26 (23.2)	
	March 29-April 4	56 (10.4)	46 (10.8)	10 (8.9)	

Normally distributed continuous variables including age, total sleep time are presented as the mean ± standard deviation and are compared using T-test. Remaining categorical variables were presented as numbers (percentages) and compared using chi-square test. COVID-19, novel coronavirus disease 2019. P < 0.05 was considered significant and presented in bold.

$= 1.835$, $p = 0.068$). No significant sex differences were found in ethnicity ($\chi^2 = 0.609$, $p = 0.435$), race ($\chi^2 = 3.200$, $p = 0.202$), children at home ($\chi^2 = 0.726$, $p = 0.696$), alcohol consumption ($\chi^2 = 8.922$, $p = 0.112$) and date of stay-at-home ($\chi^2 = 0.4.461$, $p = 0.347$).

Sex Differences in Psychological Burden of Healthcare Workers During the COVID-19 Stay-at-Home Orders

Most healthcare workers changed their mood status during the COVID-19 stay-at-home orders, with higher prevalence of 69.9% ($n = 297$) in females and relatively lower prevalence of 54.5% ($n = 61$) in males ($\chi^2 = 9.482$, $p = 0.002$). As presented in **Table 2**, most of them who reported that their mood changed were predisposed to experience worse moods regardless of their sexes (female: $n = 254$, 85.5% vs. male: $n = 51$, 83.6%), while only few of them (female: $n = 43$, 14.5% vs. male: $n = 10$, 16.4%) reported to be better ($\chi^2 = 0.147$, $p = 0.701$). Of those females whose mood worsened, 24.4% ($n = 62$) had varying degrees of anxiety, 6.7% ($n = 17$) had depression, 7.1% ($n = 18$) were irritable, 27.2% ($n = 69$) had two of them, and 34.6% ($n = 88$) had all of the above. As for the males whose mood worsened, 21.6% ($n = 11$) had varying degrees of anxiety, 5.9% ($n = 3$) had depression, 15.7% (n

TABLE 2 | Sex differences in psychological burden and health behaviors of healthcare workers during the COVID-19 stay-at-home orders.

Variables		Overall Mean ± SD or *n* (%)	Female Mean ± SD or *n* (%)	Male Mean ± SD or *n* (%)	*t or* χ^2 (*p*-value)
Psychological burden					
Mood change					$\chi^2(1) = 9.482$, ***p* = 0.002**
Same as before		179 (33.3)	128 (30.1)	51 (45.5)	
Better/worse		358 (66.7)	297 (69.9)	61 (54.5)	$\chi^2(1) = 0.147$, $p = 0.701$
Better		53 (14.8)	43 (14.5)	10 (16.4)	$\chi^2(1) = 0.135$, $p = 0.713$
	Mild-to moderate better	42 (79.2)	35 (81.4)	7 (70.0)	
	Much better	11 (20.8)	8 (18.6)	3 (30.0)	
Worse		305 (85.2)	254 (85.5)	51 (83.6)	$\chi^2(4) = 3.479$, $p = 0.481$
	Anxious	73 (23.9)	62 (24.4)	11 (21.6)	
	Depressed	20 (4.3)	17 (6.7)	3 (5.9)	
	Irritable	26 (8.5)	18 (7.1)	8 (15.7)	
	Two of them	82 (26.9)	69 (27.2)	13 (25.5)	
	All of the above	104 (34.1)	88 (34.6)	16 (31.4)	
Health behaviors					
1. Total sleep time, hours					$t = 0.240$, df = 535, $p = 0.810$
	During stay-at-home	7.22 ± 1.25	7.21 ± 1.33	7.18 ± 1.17	
2. Sleep schedule change					
Bedtime		385 (76.7)	341 (73.9)	71 (63.4)	$\chi^2(2) = 6.254$, $p = **0.044**$
	Bedtime later	246 (63.9)	199 (63.4)	47 (66.2)	
	Bedtime earlier	40 (10.4)	28 (8.9)	12 (16.9)	
	Bedtime same	99 (25.7)	87 (27.7)	12 (16.9)	
Waketime		386 (71.9)	315 (74.1)	71 (63.4)	$\chi^2(2) = 1.797$, $p = 0.407$
	Waketime later	285 (73.8)	229 (72.7)	56 (78.9)	
	Waketime earlier	51 (13.2)	45 (14.3)	6 (8.5)	
	Waketime same	50 (13.0)	41 (13.0)	9 (12.7)	
3. Work hours		266 (49.5)	205 (48.2)	61 (54.4)	$\chi^2(1) = 1.619$, $p = 0.203$
	More hours	69 (25.9)	57 (27.8)	12 (19.7)	
	Fewer hours	197 (74.1)	148 (72.2)	49 (80.3)	
4. Work schedule					$\chi^2(1) = 1.919$, $p = 0.166$
	Fixed	271 (50.5)	221 (52.0)	50 (44.6)	
	Not fixed	266 (49.5)	204 (48.0)	62 (55.4)	
5. Work schedule change		532 (99.1)	420 (98.8)	112 (100.0)	$\chi^2(1) = 1.860$, $p = 0.173$
	Yes	312 (58.6)	240 (57.1)	72 (64.3)	
	No	220 (41.4)	180 (42.9)	40 (35.7)	
6. Work-time		228 (42.4)	175 (41.2)	53 (47.3)	$\chi^2(1) = 3.211$, $p = 0.073$
	Starting work earlier	70 (30.7)	59 (33.7)	11 (20.8)	
	Starting work later	158 (69.3)	116 (66.3)	42 (79.2)	
7. End-time		216 (40.2)	176 (41.4)	40 (35.7)	$\chi^2(1) = 0.760$, $p = 0.383$

(Continued)

TABLE 2 | Continued

Variables		Overall Mean ± SD or *n* (%)	Female Mean ± SD or *n* (%)	Male Mean ± SD or *n* (%)	*t or* χ^2 (*p*-value)
	Ending work earlier	100 (46.3)	79 (44.9)	21 (52.5)	
	Ending work later	116 (53.7)	97 (55.1)	19 (47.5)	
8. News time					$\chi^2(1) = 8.905$, ***p* = 0.003**
	More	420 (78.2)	344 (80.9)	76 (67.9)	
	Less	117 (21.8)	81 (19.1)	36 (32.1)	
9. COVID-19 news time					χ^2 (4) = 0.613, p = 0.962
	0–0.5 h	87 (16.2)	70 (16.5)	17 (15.2)	
	0.5–1 h	167 (31.1)	131 (30.8)	36 (32.1)	
	1–2 h	172 (32.0)	135 (31.8)	37 (33.0)	
	2–3 h	80 (14.9)	63 (14.8)	17 (15.2)	
	3+ h	31 (5.8)	26 (6.1)	5 (4.5)	
10. Screen time before bed, hours					
	During stay-at-home	1.34 ± 0.88	1.31 ± 0.87	1.42 ± 0.90	$t = -0.793$, df = 314, $p = 0.428$
11. Substance consumption					
Food change		279 (52.0)	233 (54.8)	46 (41.1)	$\chi^2(1) = 0.308$, p = 0.579
	More food	76 (27.2)	65 (27.9)	11 (23.9)	
	Less food	203 (72.8)	168 (72.1)	35 (76.1)	
Food change after		304 (56.5)	252 (59.3)	52 (46.4)	$\chi^2(1) = 0.098$, p = 0.754
	More healthy	146 (48.0)	120 (47.6)	26 (50.0)	
	Less healthy	158 (52.0)	132 (52.4)	26 (50.0)	
Alcohol change					$\chi^2(1) = 0.321$, p = 0.571
	No	362 (67.4)	289 (68.0)	73 (65.2)	
	Yes	175 (32.6)	136 (32.0)	39 (34.8)	
Alcohol change after		175 (32.6)	136 (32.0)	39 (34.8)	$\chi^2(1) = 1.870$, p = 0.171
	More	147 (84.0)	117 (86.0)	30 (76.9)	
	Less	28 (16.0)	19 (14.0)	9 (23.1)	
12. Exercise/movement		435 (81.0)	345 (81.2)	90 (80.3)	$\chi^2(1) = 0.749$, p = 0.387
	Less	224 (41.7)	174 (50.4)	50 (55.6)	
	More	211 (39.3)	171 (49.6)	40 (44.4)	

Normally distributed continuous variables including total sleep time, and screen time before bed are presented as the mean ± standard deviation and are compared using T-test. Remaining categorical variables were presented as numbers (percentages) and compared using chi-square test. COVID-19, novel coronavirus disease 2019. P < 0.05 was considered significant and presented in bold.

= 8) were irritable, 25.5% ($n = 13$) had two of them, and 31.4% ($n = 16$) had all of the above ($\chi^2 = 3.479$, $p = 0.481$). Once more, we emphasized that although higher occurrence of mood change was identified among female healthcare workers, there were no particular differences in psychological burden with males.

Sex Differences in Health Behaviors of Healthcare Workers During the COVID-19 Stay-at-Home Orders

Sex Differences in Total Sleep Time and Schedule

Sex differences in health behaviors, including sleep time and schedule, work patterns, media exposure and screen time before bed, food and alcohol consumption, and exercise frequency, were assessed in **Table 2**. Differences in bedtime ($\chi^2 = 6.254$, $p = 0.044$) between sexes was significantly noted. The females and males estimated their bedtime to be later ($n = 199$, 63.4% vs. $n = 47$, 66.2%), earlier ($n = 28$, 8.9% vs. $n = 12$, 16.9%), or the same as before ($n = 87$, 27.7% vs. $n = 12$, 16.9%). However, the total sleep times for females and males was not significantly different (7.21 ± 1.33 h vs. 7.18 ± 1.17 h, $t = 0.240$, $p = 0.810$).

Sex Differences in Work Patterns

Table 2 shows that 221 (52.0%) females were required to follow a fixed work schedule when working from home, while over half

TABLE 3 | Logistic and linear analyses determining the association of females with mood status and total sleep time during the COVID-19 stay-at-home orders.

Variable	Mood status (better)		Total sleep time after	
	OR (95% CI)	*P*-value	B (95% CI)	*P*-value
Unadjusted	1.148 (0.558–2.363)	0.708	0.033 (−0.238–0.304)	0.810
Model 1#	1.002 (0.980–1.024)	0.857	0.048 (−0.225–0.321)	0.729
Model 2*	0.962 (0.413–2.239)	0.928	0.104 (−0.171–0.379)	0.459
Model 3@	0.760 (0.204–2.828)	0.682	0.033 (−0.323–0.389)	0.854
Model 4^	0.586 (0.153–2.247)	0.436	0.038 (−0.313–0.388)	0.833

#Adjusted for age, occupation.

**Adjusted for age, occupation, mood change, bedtime, news time.*

@Adjusted for age, occupation, mood change, bedtime, news time, ethnicity, race, care for COVID-19 patients, total sleep time before, work hours, work schedule, work schedule change, screen time before bed.

^Adjusted as model 3 with further adjustment for total sleep time after in logistic regression analysis and with further adjustment for mood status in linear regression analysis.

Logistic regression was performed to determine the association between females and mood status. Linear regression was used to illustrate the association between females and total sleep time after. OR, Odds ratio; COVID-19, novel coronavirus disease 2019. P < 0.05 was considered significant.

($n = 62$, 55.4%) of the males had a non-fixed schedule ($\chi^2 = 1.919$, $p = 0.166$). As a result, 64.3% of the males adjusted their working schedules ($\chi^2 = 1.860$, $p = 0.173$). A total of 79.2% of them started work later ($\chi^2 = 3.211$, $p = 0.073$), and 52.5% ended work earlier ($\chi^2 = 0.760$, $p = 0.383$), which was not different from females. Eliminating the missing data, 72.2% ($n = 148$) of the females and 80.3% ($n = 49$) of the males similarly worked for fewer hours ($\chi^2 = 1.619$, $p = 0.203$).

Sex Differences in Media Exposure and Screen Time Before Bed

Despite of the fact that females consumed more news time than males ($n = 344$, 80.9% vs. $n = 76$, 67.9%, $\chi^2 = 8.905$, $p = 0.003$), the average and standard deviation of media time regarding COVID-19 was not significantly different. Majorities of them in both groups ($n = 266$, 62.6%, and $n = 73$, 65.1%, respectively) tended to consume 0.5–2 h each day ($\chi^2 = 0.613$, $p = 0.962$). The average screen time before bed in females was 1.31 ± 0.87 h, which was similar to 1.42 ± 0.90 h in males ($t = -0.793$, $p = 0.428$).

Sex Differences in Substance Consumption and Exercise

Finally, there were no sex differences in food consumption ($\chi^2 = 0.308$, $p = 0.579$), food quality ($\chi^2 = 0.098$, $p = 0.754$), and alcohol consumption ($\chi^2 = 1.870$, $p = 0.171$) during the COVID-19 stay-at-home orders. Furthermore, over half of the healthcare workers ($n = 174$, 50.4% of females and $n = 50$, 55.6% of males) exercised less when staying at home, with no sex difference ($\chi^2 = 0.749$, $p = 0.387$).

Logistic and Linear Analyses Determining the Association of Females With Mood Status and Total Sleep Time During the COVID-19 Stay-at-Home Orders

Logistic and linear regression analyses were performed in **Table 3** to determine the association of females with mood status and total sleep time during the COVID-19 stay-at-home orders. Findings showed that in logistic regression analysis, females had no relationship with better mood status (OR = 1.148, 95% CI 0.558–2.363, $p = 0.708$), even after adjusting for age and occupation in model 1 (OR = 1.002, 95% CI 0.980–1.024, $p = 0.857$), with further adjustment for mood change, bedtime, and news time in model 2 (OR = 0.962, 95% CI 0.413–2.239, $p = 0.928$), with further adjustment for ethnicity, race, care for COVID-19 patients, total sleep time before, work hours, work schedule, work schedule change and screen time before bed in model 3 (OR = 0.760, 95% CI 0.204–2.828, $p = 0.682$), and finally with further adjustment for total sleep time after in model 4 (OR = 0.586, 95% CI 0.153–2.247, $p = 0.436$). In addition, in linear regression analysis, females were not correlated with total sleep time after adjustments for age, occupation, mood change, bedtime, news time, ethnicity, race, care for COVID-19 patients, total sleep time before, work hours, work schedule, work schedule change, screen time before bed and mood status ($B = 0.038$, 95% CI −0.313–0.388, $p = 0.833$).

DISCUSSION

This is the first study to illustrate sex differences in mental and physical impacts of the COVID-19 state-ordered home isolation on healthcare workers. The major findings are summarized as follows: (1) No sex differences in psychological burden and health behaviors of healthcare workers were found during the COVID-19 stay-at-home orders. (2) The COVID-19 state-ordered home isolation may be a potential way to reduce disproportionate effects of COVID-19 pandemic on females and help to minimize sex differences in psychological burden and health behaviors among healthcare workers.

The psychological and behavioral responses among healthcare workers in this study were consistent with previous studies (17, 18), but sex-stratified differences were not quite the same as those in the general population during the COVID-19 stay-at-home orders (8). Connor et al. has reviewed multi-factors including health, economic and social systems that could contribute to exacerbated sex differences in health risks and outcomes on females, and implicated that such differences could be expanded during the COVID-19 pandemic (19). Female

healthcare workers, serving as the mainstream of healthcare workforce who were at high risk of SARS-CoV-2 exposure has been proven to be disproportionately affected by the shortage of personal protective equipment, limited testing capacity and increased unemployment during the COVID-19 outbreak (2, 16, 20, 21). Thus, the COVID-19 stay-at-home orders was implemented aiming to reduce the risks posed by COVID-19 pandemic. And the online research initiated by Conroy et al. have demonstrated that both mood status and total sleep time were virtually improved in overall population regardless of their sexes during the COVID-19 stay-at-home orders, but were unfortunately identified to be associated with higher anxiety and reduced sleep quality in female population (8). However, recent studies focused on sex differences in the US and worldwide revealed controversial opinions. For example, some studies suggested a high prevalence of psychological symptoms in females (15, 16), some indicated a higher prevalence in males (22, 23), while others showed no difference, as in this study (24, 25). A parallel study consisting of 103 participants launched in the US identified a stronger association between females and stay-at-home anxiety (8). Among the participants, there were 61 (59.2%) females and 42 (40.8%) males, with a lower percentage of females compared with our study. The average age of the females was less than 40 years and they potentially possessed less working experience. Previous studies have suggested that age is a critical determinant of mental morbidity. In detail, young adults aged 18–49 years are more likely to develop anxiety than older adults aged >50 years (26). Although the females in our study were younger than the males, both were older than 40 years, indicating that more working experience matters when faced with such an unprecedented time like the COVID-19 pandemic. Besides, more females were reported to be unemployed (62.2 vs. 37.8%) and laid off (62.5 vs. 37.5%) than males in this parallel study, making themselves struggling with severe economic stress. While in our research, 85.4% of the females were white, and 95.5% were non-Latino. They represented middle-to-high levels of income and were less likely to experience inadequate health insurance, financial stress, and caregiving burden (19) and thus were less likely to experience psychological burden. Moreover, females serving as medical and domestic caregivers were proven to experience a higher prevalence of social isolation and spiritual distress during home isolation (27) and were predisposed to develop symptoms of anxiety in the early phase of the pandemic and depression in the repair phase (10, 28, 29). Xiao et al. have verified that social support was capable to influence anxiety during home isolation. And the anxiety could further act as a medicator between social isolation and sleep disturbance (30). It's noting that this cross-sectional study included 180 healthcare workers who treated patients with COVID-19 in January and February 2020 in Wuhan, China. While in our study, only 3.4% of the sample were engaged in caring for COVID-19 patients directly, which means reduced risks posed by COVID-19 outbreak and helps to elucidate negative results of disproportionate effects on females in our study.

Likewise, a web-based cross-sectional survey incorporating 7,236 respondents including 3,952 (54.6%) females and 3,284 (45.4%) males implied that there were no sex differences in depressive symptoms and sleep quality during the COVID-19 outbreak (25). Liu et al. also showed negative association of females with symptoms of depression and anxiety among young adult individuals aging 18–30 years in the US (24). More interestingly, another survey study engaging 1,210 respondents including 3,437 (60.3%) males reported higher prevalence of stress and anxiety in males (22). These included respondents were patients hospitalized with confirmed COVID-19. And this population were thought to have more risks posed by the COVID-19 outbreak to develop disproportionate effects on females. However, the results were dramatically opposite. More researches are needed to identify whether the females are susceptible to be disproportionately affected during the unprecedent time. In the present study, we found that more females reported mood change during the COVID-19 stay-at-home orders, which may be helpful to eliminate such disproportionate effects posed by the COVID-19 pandemic. Further studies are necessary to determine the association of females with psychological burden after implementing the COVID-19 state-ordered home isolation.

In addition, changes of total sleep time, sleep quality and sleep schedules were essential parts of health behaviors during the COVID-19 stay-at-home orders. Contrary to our hypothesis, we did not observe sex difference in total sleep time after enacting the COVID-19 state-ordered home isolation. While some studies showed positive findings (7, 31), some hold opposite views (8, 9), while others identified no sex differences as presented in our study (30). Compared with healthcare workers who continued working on the frontlines, Conroy et al. found that the total sleep time was longer in those who transitioned to working from home during the COVID-19 state-ordered home isolation (7). Similar findings were found in the population of university students that the total sleep time increased significantly in weekdays and weekends during the COVID-19 stay-at-home orders than before (31). However, the sleep quality was not different between sexes in healthcare workers and in general population (8, 31), which is consistent with our findings in this research. It's noting that we identified significant difference in bedtime schedule between females and males, but there are still no particular association of females with total sleep time after adjustment. Besides, alcohol consumption was reported to be associated with better mental health in healthcare workers because it helps to relieve mental stress (14). But it is quite disputed for smoking. Previous studies have illustrated that cigarettes may help to relieve negative emotions such as anxiety and stress (32). A cross-sectional study of 7,124 healthcare workers in 19 hospitals and health centers in Vietnam has confirmed that smoking was related to lower anxiety and depression likelihood during the COVID-19 pandemic (14). While other studies found that daily smoking contributed to extending influence on mental stress (33). Currently, smoking and its influence on females are still controversial (34). In the sex-stratified analysis, the association of perceived stress with smoking and alcohol consumption was similar between females and males (32, 35), which is concordant with our findings. Furthermore, we observed sex differences in occupation status and news time before bed. All findings indicated no specific association of females with mood status and total sleep time

after adjustments. Finally, we also present concerns about the workplace environment and its impact on healthcare workers during the COVID-19 stay-at-home orders (36). Medical staff in hospital workplace conditions are susceptible to develop fatigue, which is associated with increased anxiety and emotional stress (37). Previous studies have demonstrated that such impacts can be mitigated during the COVID-19 stay-at-home orders (7). However, the sex difference in indirect (mediating) effects of non-hospital workplace conditions were not the primary question in this study. Further investigation is needed to determine the association with workplace culture, a potential mediator in sex differences of psychological burden and health behaviors.

Limitations

There were some limitations in our study. First, it was confined in terms of ethnic scope. Healthcare workers were mostly non-Latino whites living in Michigan, and thus, it was limited to reflecting the interactive effects between sex and ethnicity (particularly Black, Latinx, low-income, and immigrant populations). Second, this research was simply focused on immediate changes of psychobehavioral responses from March 28 to April 29, 2020, ∼4 weeks after the implementation of the COVID-19 stay-at-home orders. Therefore, sex-stratified long-term differences in mental and physical implications among this population are worth further investigation.

Perspectives and Significance

Contrary to previous findings, there are insufficient evidence supporting sex differences in psychological burden and health behaviors during the COVID-19 stay-at-home orders. The disproportionate effects of COVID-19 pandemic on females no longer existed, indicating that the distancing intervention i.e., the COVID-19 state-ordered home isolation may be a potential way to minimize sex differences among healthcare workers. Eliminating sex differences is an important step to maintain healthcare workforce during such unprecedented times. More policies, like the COVID-19 state-ordered home isolation, are needed to promote the recovery of the mentally and physically documented posttraumatic effects on females.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. This data can be found here: https://www.openicpsr.org/openicpsr.

ETHICS STATEMENT

The dataset was approved for research use by the University of Michigan Institutional Review Board (HUM00180147) and studies using the dataset are granted a waiver of informed consent. All methods were performed in accordance with the relevant guidelines and regulations.

AUTHOR CONTRIBUTIONS

YZ and JW contributed to conception and design of the study. WG, XL, and RS had full access to all data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. XL and WG performed the statistical analysis. WG and RS wrote the first draft of the manuscript. YJ, ZCa, MW, JM, and ZCh wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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Uneven Use of Remote Work to Prevent the Spread of COVID-19 in South Korea's Stratified Labor Market

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Background: This research analyzed whether South Korean companies adopted remote work during the COVID-19 pandemic by focusing on the dual labor market structure comprising of primary sector (large corporations) and secondary sector [small and medium enterprises (SMEs)]. Companies in the dual labor market were classified based on firm size.

Methods: We used August supplementary data from the Economically Active Population Survey covering 2017–2020 provided by Statistics Korea. In this empirical study, a Linear Probability Model was used to analyze the probability that employees would work for companies that introduced remote work since COVID-19 depending on the size of the company.

Results: This study showed three main results. First, unlike other flexible work systems, the use of remote work has increased rapidly since COVID-19. Second, the larger the size of the company, the higher the probability that employees would work for companies that introduced remote work after COVID-19. Third, according to the analysis by industry, the difference in remote work utilization between large corporations and SMEs was relatively small because of a similar working method in manufacturing.

Conclusion: Results of this study suggested that polarization within the dual labor market structure also spilled over to adoption of remote work, which was initially introduced to prevent the spread of the pandemic. This study examined the system and factors of labor-management relations contributing to such polarization and presented policy directions for the current labor market structure.

Keywords: COVID-19, remote work, dual labor market, polarization, collective bargaining, revision of employment rules unfavorably to workers

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INTRODUCTION

A lockdown as one of the most stringent measures to combat the spread of a virus has resulted in the halt of production and services. Businesses worldwide have increased the use of remote work to continue corporate activities during this period. In Denmark, Netherlands, and Sweden, employees working from home have increased after the pandemic-induced lockdown (1).

In Republic of Korea (henceforth, simply South Korea), although remote work had already been adopted before the pandemic, only 3% of companies implemented it in 2016 (2). A Ministry of Employment and Labor survey in 2019 regarding the intention of firms to introduce remote work showed that only 4% of respondents intended to adopt remote work, indicating that the reluctance of South Korean businesses to implement this policy (3). However, remote work has emerged as a prominent temporary measure to maintain a certain level of production and services amidst setbacks and as a measure to prevent the spread of COVID-19 in South Korea (4).

Although the use of remote work is expected to continue even in the post-pandemic era, the extent of its adoption is likely to vary depending on the labor environment of each country and characteristics of its economic entities. This difference is likely to lead to variations in the effect of remote work on the labor market (5). Some scholars have argued that polarization, one of the major issues faced by the South Korean labor market, could be a likely cause affecting the adoption of remote work by firms during the COVID-19.

Therefore, the impact of a polarized labor market on remote work implemented during the pandemic needs to be analyzed so that measures could be devised to address this issue. To this end, aims of this study were: (1) to check whether the use of remote work had increased since the outbreak of COVID-19; (2) to determine whether there was a difference in the use of remote work after the outbreak of COVID-19, focusing on the size of the company; and (3) to determine whether there was a difference in the use of remote work after the outbreak of COVID-19, focusing on dividing the industry into manufacturing and service. A primary sector (large corporations) was defined when the number of employees was more than 300. A secondary sector (SMEs) was defined if the number of employees was <300. Based on research results, the use of remote work amidst the pandemic was confirmed, with a focus on the dual labor market structure. Also, manufacturing and service industries differ in their working methods. Therefore, results were analyzed by taking the type of industry into consideration.

Based on results of an empirical analysis showing that polarization within a dual labor market structure could also be spilled over into whether companies adopted remote work, which was initially introduced to prevent the spread of the pandemic, this study examined the system and factors of labor-management relations contributing to such polarization and presented policy directions for the current labor market structure. Previous literature, the dual labor market in South Korea, the trend of COVID-19 in South Korea and use of remote work, data and analysis methods, results, and the legal process for the establishment of remote work in primary and secondary sectors are described in order.

Abbreviations: EAPS, Economically Active Population Survey; ILO, International Labor Organization; IMF, International Monetary Fund; LPM, Linear Probability Model; MDIS, Micro Data Integrated Service; OECD, Organization for Economic Cooperation and Development; SMEs, small and medium enterprises; UK, United Kingdom; US, United States.

LITERATURE ON REMOTE WORK DURING COVID-19 AND THE LABOR MARKET POLARIZATION

COVID-19 Outbreak and Deepening of the Labor Market Polarization

COVID-19 has severely and adversely affected economies of each country, industries, and the daily lives of citizens. Although impact of the pandemic on the labor market varied from country to country, it accelerated the polarization that existed even before its outbreak. Numerous recent studies have predicted the possibility that the pandemic may further intensify polarization in the local labor market.

The OECD announced that COVID-19 would especially impact low-wage and unstable jobs, and workers from these types of jobs would be more seriously affected by the social distancing rule and lockdown measures in the service sectors such as restaurants and hotels (6). Furthermore, the OECD maintained that due to the coronavirus, self-employed, temporary workers, and part-time laborers were significantly exposed to risk of unemployment and income loss, and that the lockdown measures taken by the European members of the OECD could adversely affect nearly 40% of the jobs in such vulnerable sectors (7).

The World Bank has also stressed the importance of support in hiring and maintaining the productivity of vulnerable, informal economy workers and small firms to cope with the negative effect of COVID-19 (8). Additionally, the ILO also highlighted negative impact of the pandemic on SMEs, and small business owners, the self-employed, informal economy workers, temporary workers, and new types of workers working in the gig economy. COVID-19 is expected to further aggravate labor poverty and inequality because its negative effect is more damaging to small business owners and workers who were already vulnerable (9). An IMF Working Paper also warned that the COVID-19 outbreak could deepen inequity in Asia, especially related to gender-based income inequality and economic imbalance between cities and rural areas (10).

Empirical studies reporting about the pandemic-induced polarization in the local labor market also presented similar predictions. A US-based study on the effect of COVID-19 on job markets argued that the reduction in hiring due to the pandemic was the most prominent in low-income communities and areas with a wide income gap. The study also found that a fall in hiring was the most severe in industries with a high unionization rate and in local service sectors such as education, public health, retail, and construction (11).

Some studies reported that the coronavirus pandemic particularly adversely affected the female workers. They found that in the United States, married women were more likely to have experienced reduced work hours or job loss due to COVID-19, suggesting its long-term effect on female employment and the deepening of gender inequality (12). In addition, other studies found that whereas cyclical economic downturns had a more significant impact on male jobs, social distancing rules amidst COVID-19 had greater impact on the employment of female workers than males (13).

Working From Home Amidst COVID-19 Pandemic and Labor Market Polarization

Working from home is necessary for reducing economic loss while maintaining economic activity during the pandemic, and can also potentially improve other social and economic indicators such as productivity, employee welfare, and reduce local income inequality (14). In most countries, work from home has been largely induced by the coronavirus pandemic. Nevertheless, although the OECD has cited the advantages of working from home as a response to the pandemic, in reality, its use has been confined to only a limited number of workers. In fact, in the UK and Europe, prior to COVID-19, remote work was only allowed to high-paying employees such as managers, professionals, public administrators, and other senior business staff (15). In contrast, after the pandemic, low-income workers are more likely to lose their jobs because they are ill prepared for remote work and are pessimistic about continuing earning income through remote work, whereas people in high-income positions are 50% more likely to work remotely (16). Furthermore, the COVID-19 crisis is prompting employers to extend remote working opportunities where possible, leading to greater investment in remote work infrastructures, which could bring some long-term benefits. However, these measures would not help frontline workers who cannot work remotely and are more exposed to infection (17). An International Monetary Fund Working Paper reported that after the COVID-19 outbreak, hiring was most severely hit in sectors where remote work is not possible, such as service sector jobs in hospitality and tourism industries. In addition, workers from industries where remote work is not affordable are more likely to earn lesser average income than those in other industries. Thus, overall, the pandemic would exacerbate income inequality in sectors where remote work is not possible (18).

Empirical studies have found that the COVID-19 pandemic will further deteriorate the labor market inequality between workers who can work remotely and those who cannot. Studies that analyzed the practice of remote work in the UK, the US, and Germany after the pandemic found that in all three countries, workers who can work from home during the pandemic are far less likely to lose their jobs, whereas workers exposed to the risk of infection are more likely to become unemployed. Moreover, in the US and the UK, workers who work remotely for fewer hours are more likely to experience a decrease in income (19).

In Germany, a study that assessed employment inequality during the lockdown from the first wave of the pandemic found that while low-income workers seriously suffered from unemployment, employees with superior qualifications could afford to work remotely. Employees who continue to work from home are much less concerned about their job security than those who cannot their change work hours or workplaces. Additionally the infection risk only increased for individuals who began working on-site after being laid-off (20). In addition, some researchers analyzed the impact of increased remote work opportunities on the labor market in Italy during the pandemic, which has the lowest rate of remote work among the European countries. They found that the rise of remote work benefited males, the elderly, and workers with good education and high income, which could most likely reinforce wage inequality that had existed prior to the pandemic (21).

The probability of safe working environments through measures such as remote work stems from two factors. The first factor is technology intensity. The second factor is the work conditions before the pandemic. For instance, those who earned high income prior to the pandemic and could afford to work even during lockdowns are more likely to work safely at home. Hence, remote work indicates the possibility of an increase in income polarization (22).

Working from home during the pandemic is slated to help maintain economic activities, reduce economic loss, as well as potentially boost or improve social and economic indicators such as productivity and employee welfare, while reducing local inequality. Developing countries that have an inadequate digital infrastructure must focus on introducing or modifying policies, laws, and regulations in many sectors to reap the benefits of remote work, including digitalization and other related practices (14).

THE IMPACT OF DUAL LABOR MARKET STRUCTURE ON REMOTE WORK DURING COVID-19 IN SOUTH KOREA

Trend of COVID-19 Spread in South Korea and the Use of Remote Work

Figure 1 shows the spread of COVID-19 cases in Korea. Since the first confirmed case of COVID-19 in Korea, the government announces the status of confirmed cases every day (http://ncov.mohw.go.kr/). Daily confirmed cases were collected directly. **Figure 1** was prepared using such data. The X axis represents the timeline from January 20, 2020, when the first COVID-19 case occurred in the country, to February 2020. The Y axis on the left indicates daily cases, while the y axis on the right refers to cumulative cases. The solid line shows the number of cases per day and the dashed line indicates the cumulative number of cases. **Figure 1** confirmed that South Korea had three massive outbreaks during this period. The first wave happened in February and March 2020, with viral spread due to large-scale religious gatherings in Daegu and Gyeongbuk areas attended by coronavirus-infected individuals who had previously visited China. During the first wave, people were afraid of being infected with Covid-19. Therefore, the South Korean government took strong measures such as a ban on movement between regions, social distancing, and remote work to nip the rapid spread of the contagion. At that time, companies began to introduce remote work. Owing to these efforts, by April 2020, cases dropped sharply. The world praised South Korea for its efforts to contain the pandemic. Nevertheless, the sudden adoption of the remote work system was ill-equipped to sustainably tackle the economic crisis at home and abroad. Therefore, many businesses eventually began to revert to an offline mode of work (23, 24).

The second wave occurred after a rally in downtown Seoul held around the National Liberation Day on August 15, 2020.

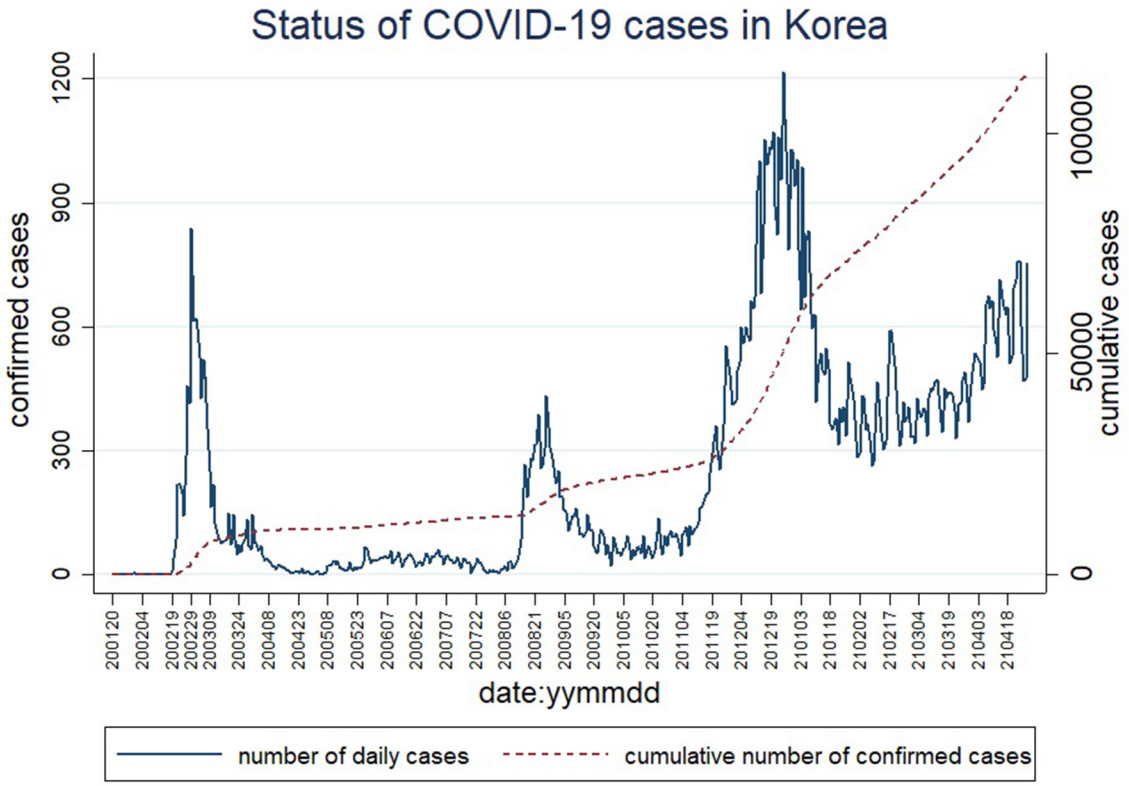

FIGURE 1 | Daily trend and cumulative trend of COVID-19 confirmed cases in South Korea. Both the daily trend and the cumulative trend of COVID-19 confirmed cases use the number of people as a unit. The first two digits of the six digits of the date indicate the year 2020 or 2021. The middle two digits represent January through December. The last two digits represent the date from the 1st to the 31st.

Seoul and metropolitan areas surrounding the capital city had the highest spike in cases. Consequently, the government took a stern measure by banning meetings involving five or more persons in the Seoul metropolitan area and reducing service hours of restaurants and supermarkets. The government decided to reinstate remote work to prevent the spread of the infection (25, 26).

The third wave of the pandemic began due to a sharp rise in cases in November 2020. Daily number of cases surpassed the record number of 1,200. This accelerating infection rate revived citizens fear infection again. By February 2021, cases had dropped to around 400, easing an upward trend. However, daily cases have failed to fall further. Realizing that the pandemic would not end in the near future, South Korean businesses have started building remote work infrastructure (27) for the future, while relying on offline work when the pandemic has slowed down and implementing remote work when cases have surged.

Impact of Dual Labor Market Structure on Labor Market Polarization in South Korea

Labor market polarization in South Korea was already present prior to the coronavirus pandemic. In general, labor market polarization in South Korea is synonymous with its dual labor market structure (28), which is comprised of the primary sector, including large corporations, and regular employees with labor unions, and the secondary sector representing SMEs and non-regular workers without the support of union.

TABLE 1 | Dual labor market structure of Korea.

Category	Primary labor market	Secondary labor market
(1) Share of workers (*N*, %)	859,237, 4.4	4,991,345, 27.9
(2) Wage (KRW)	4,128,000	1,603,900
(3) tenure (Years)	14.47	3.21

(1) Primary labor market refers to regular workers who joined a labor union while working for large corporations.
(2) Secondary labor market refers to non-regular workers who did not join the labor union while attending small and medium-sized enterprises (SMEs).
(3) In the table, row (1) refers to share of total number of salaried workers. Row (2) indicates average monthly wage of workers in each market. Row (3) represents average tenure of workers in each market.

Table 1 shows the number of workers, average monthly wages, and their work years in primary and secondary sectors of the labor market. **Table 1** used the same data used in the main analysis, the August 2019 supplementary survey of the

Economically Active Population Survey (EAPS) of South Korea Statistics (https://mdis.kostat.go.kr/). A detailed description of the data is provided in the data section. As of 2019, primary sector and secondary sector represented 4.4% (859,237 persons) and 27.9% (4,991,345 persons) of total wage earners in South Korea, respectively. Both sectors had a significant gap in their working conditions. The average monthly income of workers in the primary sector was 2.57 times that of the secondary sector workers. The primary sector workers worked about six times the number of years worked by secondary sector workers. The large wage gap between the two sectors can be attributed to difference in earnings to the pay-out between large corporations and SMEs as well as differences in their wage practices. That is, in Korea, large businesses will increase wages of employees in proportion to the number of years worked, following a seniority-based wage system.

In Korea, educated male workers are likely to occupy the primary sector (29). Regular positions mostly involve white-collar jobs employing disproportionate number of male workers with degree of Bachelor. Additionally, the primary sector offers a highly automated and digitalized working environment. Hence, the workers in the primary sector can easily adapt to remote work during the pandemic. Moreover, 62.9% of the large companies in the primary sector have labor unions; therefore, workers in the primary sector are free from the risk of losing jobs and hardly experience significant variation in wages and salaries (30, 31).

Meanwhile, the secondary sector comprises of non-regular workers in SMEs, of which only 10% are unionized. That is, companies in the secondary sector have fewer earnings to pay for wages and because their employees are not unionized, they are less likely to protect their jobs or build the infrastructure required to achieve digitalization.

Polarization in the Use of Remote Work Among South Korean Firms

In South Korea, remote work saw a sharp increase as a temporary measure in several companies to maintain business activities that were suspended due to COVID-19. However, the use of remote work in South Korea is highly limited by its dual labor market structure, which further intensified during the coronavirus pandemic, showing that dual labor market structure and remote work influence each other reciprocally. Remote work is mostly prevalent among large corporations (32), whereas nearly half the SME employees reported to work on-site amidst the polarization between the two types of companies (33). In addition, public institutions reported double the rate of remote work use compared to SMEs (34).

Most of the workers in the secondary labor market are least likely to have an option to work remotely. Additionally, companies in the secondary labor market have insufficient financial resources to pay out wages compared to those in the primary sector, and thus cannot afford to continue paying wages to employees working from home. Consequently, due to its inability to offer remote work opportunities, workers in the secondary sector have a higher chance of unemployment during the pandemic than the primary sector.

METHODS

Data

To analyze characteristics of South Korean workers who worked from home before and after the outbreak of the pandemic, we required pre- and post-outbreak remote work data. The August supplementary survey by the Economically Active Population Survey (EAPS) of South Korea Statistics (https://mdis.kostat.go.kr/) provided us with such data. South Korea Statistics provided the original data of the EAPS and the august supplementary survey by the EAPS. These data were approved by Statistics Korea to be used by all persons who had applied through MDIS, the website of Statistics Korea. This research analyzed raw EAPS data from MDIS.

The EAPS focuses on the labor supply data collected through household visits each month, which is used as a base data to investigate the monthly employment and unemployment rates. In addition to the monthly EAPS, the August supplementary survey divides workers into salaried and non-salaried workers depending on labor type of the respondents, and collects additional information about labor quality through data on labor contracts, labor hours, and employment insurance by labor type. Thus, since 2001, the EAPS August supplementary survey has been providing detailed information on approximately 35,000 households by economic activity and labor type, as of August. This survey also offers data on the use of flexible work arrangements by salaried workers, including remote work. Thus, it is useful to analyze the trends and characteristics of employees working remotely before and after the outbreak of the pandemic.

This study analyzed the characteristics of the workers who worked remotely before and after the outbreak of the coronavirus pandemic and measured the effect of the dual labor market structure on remote work. This study considered employees who reported receiving flexible work opportunities from their employers a week before the survey, and identified the use of remote work as respondents (samples) answering "work from home" or "remote work" in response to the question "Which type of flexible work system do you use?." The samples did not include salaried workers who are engaged in agriculture, forestry, and fishery; those engaged in domestic activities; and instances of self-consumption and production activities that are not classified into any specific category. In addition, to compare the pre- and post-outbreak data, the analysis period covered every August from 2017 to 2020, where August 2020 belongs to the period after the coronavirus outbreak. Among the samples satisfying these conditions, we eliminated those containing missing values in the explanatory variables and finally included 100,136 samples in our analysis.

Methodology

This study used the linear probability model (LPM) to analyze the use of remote work among salaried workers. The LPM can be used when the dependent variable is not continuous and discrete. The dependent variable, which is the focus of this study, is a binary variable indicating whether the company where employee works used remote work. During the analysis period, the use of remote work by salaried workers was indicated as 1 and non-use

of remote work was labeled as 0. When a dependent variable was a binary variable, it was analyzed mainly using a logit or probit model. When there was interaction term in non-linear model, Ai and Norton (2003) highlighted the issue of interaction effects in non-linear models (35). To resolve this, this paper used LPM to address this problem.

$$y_{it} = \begin{cases} 1, \ if \ z_{it} > 0 \\ 0, \ if \ z_{it} \leq 0 \end{cases}$$
$$where \ z_{it} = \beta_0 + \sum_{k=1}^{K} \beta_k x_{kit} + u_{it} \quad (1)$$

In formula (1), the subscript i is an individual, and t is time. x_{it} indicates the explanatory variables related to the personal characteristics and job characteristics of individuals i during t time. The explanatory variables included age, residence area, gender, education, marital status, position at workplace, occupation, the number of employees (firm size), and the year dummy variable.

In formula (1), z_{it} represents the sum of a linear combination of the constant and explanatory variables and the error term. Considering $E(u_{it}) = 0$ to provide an unbiased estimate, $E(y_{it}|X_{it})$, which is a conditional expectation of y_{it} *given* X_{it}, is a conditional probability of $y_{it} = 1$ and expressed below as formula (2) (36).

$$E[y_{it}|X_{it}] = \Pr(y_{it}|X_{it}) = \beta_0 + \sum_{k=1}^{K} \beta_k x_{kit} \quad (2)$$

Furthermore, to determine the impact of the firm size on the use of remote work after the outbreak of COVID-19, total number of employees and the year 2020 were added as interaction terms. In formula (3), the expected values were added to both sides of the regression equation to interpret interaction effect.

$$\begin{aligned} E[y_{it}|X_{it}] = \Pr(y_{it}|X_{it}) = \ & \beta_0 \\ & + \sum_j \beta_j \cdot 1\{total \ number \ of \ employees_{it} = j\} \\ & + \sum_{k=2018}^{2020} \beta_k \cdot 1\{t = k\} \\ & + \left(\sum_j \sum_{k=2018}^{2020} \delta_{jk} \cdot 1\{total \ number \ of \ employee_{it} = j\} \right. \\ & \times \left. 1\{t = k\} \right) + X_{it}'\alpha \end{aligned} \quad (3)$$

In formula (3), i is the number of employees of a firm where an individual i works. The number of employees is a categorical variable with four groups: 1–4 persons (base), 5–29 persons, 30–299 persons, and 300 persons or more. κ is a categorical variable that divides the analysis period into four: 2017 (base), 2018, 2019, and 2020. X_{it} is a variable that represents the personal and job characteristics of an individual (i), which also represent the explanatory variables used in formula (2).

FIGURE 2 | It shows share of salaried workers working in companies that introduced remote work.

EMPIRICAL ANALYSIS

Basic Statistical Analysis

Figure 2 shows the proportion of salaried workers who worked remotely out of the total number of salaried workers, based on the EAPS August supplementary survey. The share of remote workers steadily surged from 0.30% in 2017 to 0.40% in 2018, and 0.47% in 2019. In 2020, after the outbreak of COVID-19 pandemic, the share of workers attending companies that implemented remote work soared by five times to 2.49% from 2019.

Figure 3 presents the proportion of salaried workers who have worked in companies with flexible work arrangements except for remote work. The share of workers using flexible work systems steadily increased from 4.7% in 2017 to 12.0% in 2020. That is, unlike **Figures 2**, **3** shows a steady increase in the proportion of salaried workers using flexible work arrangements regardless of COVID-19. **Figure 3** shows that remote work among flexible work arrangements is heavily affected by COVID-19.

Table 2 presents the annual statistics of salaried workers working for companies that implemented remote work. Specifically, it shows that among the salaried workers employed in companies with the remote work option, the share workers residing in *dong* (urban areas) exceeded that of salaried workers living in *eup/myeon* (rural areas). In 2020, regardless of the region, the share of salaried workers attending companies with remote work rose sharply; however, the share of 2020 relative to 2019 surged by about six times in *dong* (urban) areas, far outranking the increase in *eup/myeon* areas. There was no significant difference between male and female workers working in companies with the remote work option. Additionally, the higher the education level, the higher the share of workers with companies allowing remote work. In particular, the share of workers with the degree of Masters in remote-based roles rose to 6.9% in 2020. Meanwhile, on an average, during the survey period, only 0.5% of the workers who graduated from

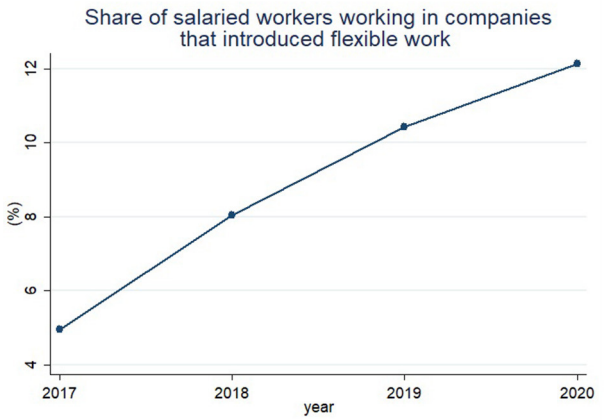

FIGURE 3 | It shows share of salaried workers working in companies that introduced flexible work arrangements except for remote work.

a technical college or lower were employed by companies that offered a remote work option. However, irrespective of the education levels, the share of workers with remote-based jobs rose by seven times during 2019 to 2020, showing the most prominent increase for all educational levels. In 2017, the share of employees working remotely did not vary significantly with marital status: unmarried persons 0.1%, married persons 0.3%, and the divorced/widowed 0.2%; however, in 2020, the share of both married and unmarried persons rose to 2.2% while that of divorced/widowed workers climbed to 0.5%, representing a substantial change.

Regarding job characteristics, managers constituted the most significant figure (1.7%), followed by clerical workers (1.3%) and sales workers (0.9%). The share of managers who attended companies offering remote work has steadily risen since 2017. The share of clerical workers in 2018 and 2019 showed a change from 0.4 and 0.6%, indicating less steady growth than the managers. However, the ratio showed a 6-fold increase from 2019

TABLE 2 | Annual statistics on workers employed in companies offering remote work.

Main category	Middle category	Variables	2017	2018	2019	2020	Mean
Personal characteristics	Region	Cities (%)	0.3	0.4	0.4	2.3	0.8
		Rural (%)	0.1	0.1	0.2	0.8	0.3
	Gender	Male (%)	0.2	0.3	0.4	2	0.7
		Female (%)	0.3	0.5	0.4	2	0.8
	Education	High school or lower (%)	0.1	0.1	0.1	0.4	0.2
		Technical college or lower (%)	0.2	0.3	0.2	1.4	0.5
		University or lower (%)	0.4	0.6	0.7	3.6	1.4
		Master's degree or higher (%)	0.6	1.2	1.2	6.9	2.5
	Marital	Unmarried (%)	0.1	0.2	0.4	2.2	0.7
	status	Married (%)	0.3	0.4	0.5	2.2	0.9
		Divorced /widowed (%)	0.2	0.2	0.1	0.5	0.2
Job characteristics	Occupation	Manager (%)	0.4	0.7	1	4.5	1.7
		Clerical workers (%)	0.4	0.6	0.6	3.8	1.3
		Service workers (%)	0	0.1	0.1	0.3	0.1
		Sales workers (%)	0.5	0.5	0.5	2	0.9
		Technicians (%)	0	0.1	0	0.3	0.1
		Workers of simple labor (%)	0	0	0	0.1	0
	Industry	Manufacturing (%)	0.1	0.2	0.4	1.2	0.4
		Construction, other manufacturing (%)	0.1	0.2	0.2	0.4	0.2
		Wholesale and retail, food, accommodation (%)	0.2	0.3	0.3	1.1	0.4
		Transport, communication (%)	0.4	0	0	1.4	0.5
		Finance, insurance, real estate (%)	0.5	0.4	0.4	3.5	1.2
		Public social and personal services (%)	0.1	0.4	0.4	3.3	1
		Education, healthcare, social service, art (%)s	0.2	0.4	0.3	2	0.8
		Others (%)	0.5	0.7	0.9	4.1	1.5
	Number of employees	1–4 (%)	0.1	0.1	0.2	0.3	0.2
		5–29 (%)	0.3	0.3	0.4	1	0.5
		30–299 (%)	0.2	0.5	0.5	2.9	1
		300 or more (%)	0.4	0.6	0.6	6	1.9
Total			0.2	0.3	0.4	2	0.7

Total in the last row represents employees' rate employed in companies offering remote work in each year.

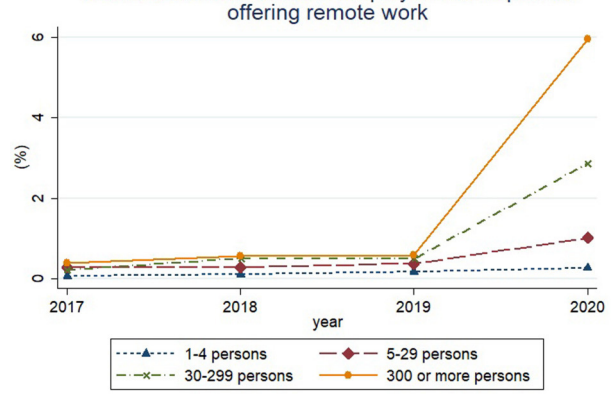

FIGURE 4 | It indicates share of salaried workers employed in companies offering remote work divided by company size. The company size was divided into four groups based on the number of employees. The four groups consist of small businesses with 1–4 employees, small enterprises with 5–29 employees, medium-sized enterprises with 30–299 employees, and large corporations with more than 300 employees.

to 2020. In terms of industry type, the share of remote workers was higher in finance, insurance, real estate, public social service, personal service, and others. Sectors such as finance, insurance, real estate, transportation/communication, public social service, personal service, and others showed a sharp increase in the share of workers working remotely from 2019 to 2020. The size of companies was found to be positively related to the share of workers engaged in remote work. The share for companies with 1–4 employees was 0.2%, 5–29 employees was 0.5%, 30–299 employees was 1.0%, and those with 300 plus employees was 1.9%. Large companies employing more than 300 workers saw the share of workers engaging in remote work soaring by ten times from 0.6% in 2019 to 6% in 2020.

Figure 4 shows the trends for the share of salaried workers working in companies implementing remote work by firm size and year, based on data from **Table 2**. The X axis indicates the year, and the Y axis indicates the share of salaried workers working in companies with remote work opportunity. The dotted line with a triangle marker indicates the share of salaried workers working in companies with 1–4 employees. The dashed line with a diamond marker represents firms with 5–29 employees, the dash-dotted line with an X marker indicates firms with 30–299 employees, and the solid line with a circle marker shows the share of workers attending large companies with over 300 employees. Regardless of the number of employees, we found that the share of workers working from home steadily rose from 2017 to 2020. Notably the share in 2020 climbed sharply in proportion to the firm size.

RESULTS

Table 3 presents the result of the analysis from considering "whether the company where employee works used remote work" as the dependent variable. The results were derived by using the Linear Probability Model, which included the variables likely to affect whether the companies introduced remote work. Results of **Table 3** are similar to the results of the basic statistics in **Table 2**. Specifically, regarding the personal characteristics variables, employees with a degree of Master are more likely to work for companies with remote work system by 1.09 percentage points.

Regarding job characteristics-related variables, the number of employees within a firm is particularly relevant. Employees in large companies with over 300 employees are 1.28 percentage points more likely to work remotely than employees working in small companies with 1–4 employees. For the year variable, salaried workers are increasingly more likely to work for companies offering remote work opportunities as the year approached 2020, compared with 2017. Additionally, the coefficient of the correlation was prominent in year 2019 and 2020 and the probability of workers engaged in remote work was higher by 1.78 percentage points in 2020 than in 2017.

Table 4 lists the results of the analysis of whether adoption of remote work by companies was influenced by firm size after the outbreak of the pandemic. That is, by checking the interaction term between the number of employees in a firm and the COVID-19 period variable, we measured the variation in the probability of introduction of remote work of the company after the COVID-19 depending on its number of employees. As in **Table 3**, our analysis considered the dependent variable as a dummy variable with value 1 if companies with salaried workers provide remote work opportunities, and value 0 if not. The explanatory variables for personal characteristics and job characteristics of the employee remained the same as in **Table 3**. We then measured the interaction effect of the number of employees in a firm and year variables using the year dummies.

Our analysis found that, considering firms with 1–4 employees for the year 2017 as the base, in 2020, employees from companies with 5–29 employees were 0.56 percentage points more likely to work from home, and employees from companies with 30–299 employees were 2.51 percentage points more likely to work remotely compared to the base case. For companies with 300 employees, the probability of employees working from home in 2020 rose by 5.40 percentage points from the base case. Similar to **Tables 3**, **4** shows that workers attending companies with a size larger than 1–4 employees after the outbreak of COVID-19 are proportionately more likely to work from home.

Tables 5, **6** show results of analysis by dividing the sample into manufacturing and service industries. The manufacturing industry consisted of manufacturing, construction, and other manufacturing sectors. The service industry consisted of including wholesale and retail, food and accommodation, etc. The reason for analyzing samples by industry was because the working method differed depending on the industry. There were also differences in the utilization of remote work. In addition, even within the same industry, there were differences in working methods depending on the size of the company, which might affect the utilization of remote work. **Table 5** shows whether there is a difference in the utilization of remote work after the outbreak of COVID-19 depending on the size of the company for workers

TABLE 3 | Results of analysis of the dependent variable.

Main category	Middle category	Variables	Status of introduction of remote work	
			Coef.	Robust Std. Err.
Personal characteristics	Age	Age	−0.0001**	0.000
	Residence area	Base: Cities		
		Rural	−0.0012**	0.001
	Gender	Base: Male		
		Female	0.0029***	0.001
	Education	Base: High school or lower		
		Technical college	−0.001	0.001
		University	0.0040***	0.001
		Master's degree or higher	0.0109***	0.002
	Marital status	Base: Unmarried		
		Married	0.0033***	0.001
		Divorced/widowed	0.0027***	0.001
Job characteristics	Employment status	Base: Regular positions		
		Temporary, day laborers	−0.0021***	0.001
	Occupation	Base: Service workers		
		Managers and professionals	0.0097***	0.001
		Clerical workers	0.0061***	0.001
		Sales workers	0.0054***	0.001
		Technicians	0	0.001
		Workers engaged in simple labor	−0.0012*	0.001
	Industry	Base: Manufacturing		
		Construction and other manufacturing	0.0012	0.001
		Wholesale and retail trade, food, accommodation	0.0034***	0.001
		Transportation/communication	0.0026**	0.001
		Finance, insurance, real estate	0.0042***	0.002
		Public social service, personal service	0.0040***	0.001
		Education, healthcare, social service, arts	−0.0021**	0.001
		Others	0.0091***	0.001
	Number of employees	**Base: 1–4 persons**		
		5–29 persons	0.0031***	0.001
		30–299 persons	0.0070***	0.001
		300 or more persons	0.0128***	0.001
		Log (average wage of recent three months)	0.0020***	0.001
		Working hours	−0.0001***	0
Year	Year dummy	**Base: 2017**		
		2018	0.0008	0
		2019	0.0013**	0.001
		2020	0.0178***	0.001
		Constant	−0.0145***	−0.003
		Sample Size	100,136	
		R-squared	0.019	

(1) Dependent variable in this result is whether the company where employee works used remote work.
*(2) Statistically significant at significance level of ***1%, **5%, *10%.*

engaged in the manufacturing industry. **Table 6** analyzes workers in the service industry.

Manufacturing is main industry in South Korea. It has a similar production method regardless of the size of the company. It is difficult to introduce remote work except for some jobs in large corporations. In addition, SMEs are unlikely to use remote work because of limitations of their working methods and the vulnerable digital environment. According to results shown in **Table 5**, only workers working for large corporations with more than 300 employees increased the probability of working

TABLE 4 | Interaction term analysis using the number of employees in a firm and year variables.

Main category	Middle category	Variables	Status of introduction of remote work	
			Coef.	Robust Std. Err.
Job characteristics	Status of employment	Base: Regulated employees		
		Temporary, day laborers	−0.0016**	0.001
	Number of employees	**Base: 1–4**		
		5–29	0.0017**	0.001
		30–299	−0.0004	0.001
		300 or more	−0.0016	0.001
Period	Year dummy	**Base: 2017**		
		2018	0.0001	0.001
		2019	0.0005	0.001
		2020	0.0015*	0.001
Interaction term	Number of employees X Year	**Base: 1–4 employees X 2017**		
		(1) X 2018	−0.0003	0.001
		(1) X 2019	0.0001	0.001
		(1) X 2020	0.0056***	0.001
		(2) X 2018	0.0021*	0.001
		(2) X 2019	0.0019	0.001
		(2) X 2020	0.0251***	0.002
		(3) X 2018	0.0013	0.002
		(3) X 2019	0.0008	0.002
		(3) X 2020	0.0540***	0.004
Control variables	Personal characteristics		O	
	Occupation		O	
	Industry		O	
	Log (average wage in the past three months)		−0.0016**	−0.001
	Actual hours of employment in a major job		−0.0002***	0
	Sample size		100,136	
	R-squared		0.026	

(1) Dependent variable in this result is whether the company where employee works used remote work.
(2) In the table, column 3 refers to interaction term for company size and year. (1) In column 3 represents there are 5–29 employees in the company. (2) Indicates there are 30–299 employees in the company. (3) Indicates the company has more than 300 employees.
*(3) Statistically significant at significance level of ***1%, **5%, *10%.*

in companies using remote work by 2.3 percentage point since the COVID-19 outbreak. The coefficient value was less than half that of **Table 4**. **Table 5** shows that the difference in remote work utilization between large corporations and SMEs is relatively small because of a similar working method.

Unlike manufacturing, the service industry differs greatly in terms of working method between large corporations and SMEs. Large corporations operate mainly on-site services through outsourcing except for internal main management. Therefore, it is difficult for SMEs to use remote work compared to large corporations. Results of **Table 6** showed that employees, regardless of the size of the company, increased the probability of working in companies using remote work. In addition, the larger the company, the more likely the remote work would be used by employees. However, due to differences in working methods, the probability of working for companies through remote work increased to 7.21 percentage point after the COVID-19 outbreak, widening the gap between employees of large corporations and employees of SMEs.

Robustness Check

Samples were reconstructed to test the robustness of the results analyzed in **Table 4**. If workers changed jobs after the COVID-19 outbreak or had a special employment, it might affect the probability of working for a company that introduced remote work. Therefore, when the survey year was August 2020, workers who worked for the company for <8 months were excluded from the sample.

Results are as follows. Employees for companies with 5–29 employees were 0.60 percentage points more likely to work from home and employees for companies with 30–299 employees were 2.54 percentage points more likely to work remotely compared to the base case. For companies with 300 employees, the probability of employees working from home in 2020 rose by 5.54 percentage points from the base case. In other words, **Table 7** shows results of analysis after excluding samples that might have transferred to companies that adopted telecommuting during COVID-19. This confirms that results in **Table 4** are robust.

TABLE 5 | Interaction term analysis for the manufacturing industry.

Main category	Middle category	Variables	Status of introduction of remote work	
			Coef.	Robust Std. Err.
Interaction term	Number of employees X Year	**Base: 1–4 employees X 2017**		
		(1) X 2018	0.0025	(0.002)
		(1) X 2019	0.0029	(0.002)
		(1) X 2020	0.0040	(0.003)
		(2) X 2018	0.0021	(0.002)
		(2) X 2019	0.0020	(0.002)
		(2) X 2020	0.0060**	(0.003)
		(3) X 2018	0.0005	(0.002)
		(3) X 2019	0.0044	(0.003)
		(3) X 2020	0.0232***	(0.005)
Control variables	Personal characteristics		O	
	Work characteristics		O	
	Year dummy		O	
	Sample size		28,870	
	R-squared		0.013	

1) Dependent variable in this result is whether the company where employee works used remote work.
2) It analyzed only workers in the manufacturing industry.
3) In the table, column 3 refers to interaction term for company size and year. (1) In column 3 represents there are 5-29 employees in the company. (2) Indicates there are 30–299 employees in the company. (3) Indicates the company has more than 300 employees.
*4) Statistically significant at significance level of ***1%, **5%, *10%.*

TABLE 6 | Interaction term analysis for the service industry.

Main category	Middle category	Variables	Status of introduction of remote work	
			Coef.	Robust Std. Err.
Interaction term	Number of employees X Year	**Base: 1-4 employees X 2017**		
		(1) X 2018	−0.0011	(0.001)
		(1) X 2019	−0.0005	(0.001)
		(1) X 2020	0.0066***	(0.002)
		(2) X 2018	0.0028*	(0.002)
		(2) X 2019	0.0027*	(0.002)
		(2) X 2020	0.0352***	(0.003)
		(3) X 2018	0.0027	(0.003)
		(3) X 2019	−0.0004	(0.003)
		(3) X 2020	0.0721***	(0.006)
Control variables	Personal characteristics		O	
	Work characteristics		O	
	Year dummy		O	
	Sample Size		71,266	
	R-squared		0.033	

1) Dependent variable in this result is whether the company where employee works used remote work.
2) It analyzed only workers in the service industry.
3) In the table, column 3 refers to interaction term for company size and year. (1) In column 3 represents there are 5-29 employees in the company. (2) Indicates there are 30–299 employees in the company. (3) Indicates the company has more than 300 employees.
*4) Statistically significant at significance level of ***1%, **5%, *10%.*

IMPLICATIONS OF INCREASED USE OF REMOTE WORK IN SOUTH KOREA IN THE POST-PANDEMIC ERA

Procedure of Labor Relation Laws Governing Remote Work in South Korea

As discussed earlier, the remote work system in South Korea was introduced mostly as a temporary measure after the outbreak of the pandemic to stem the spread of the COVID-19, and was adopted without any adjustment process. This conclusion stems from the variation in the level of remote work depending on the fluctuations of COVID-19 caseloads in South Korea. The decision to establish a remote work system is not expected to receive any opposition from the employees if it is implemented while keeping intact the current task assessment and remuneration schemes.

However, the first challenge of allowing remote work is to devise methods to measures the work attitude and task performance of remote workers. Because of the difficulties in controlling their work status on a real-time basis while they work from home, companies would need to modify their performance assessment and compensation system. This would hardly be supported by employees because unlike a temporary use of remote work during the pandemic, a long-term system would involve a strict assessment of employees working status and performance, as well as wage reduction.

Introducing a remote work system in South Korea involves two legal procedures. The first is to revise the collective agreement between companies and employees. Whether employees agree to the introduction of remote work proposed by employers would be determined by collective bargaining. Trade unions and employers may decide whether to introduce remote work after an adjustment of performance assessment and compensation system.

The second procedure for introducing remote work involves an amendment to the employment rules. Employment rules are rules about working conditions unilaterally prescribed by employers in order to systematically and consistently control the working conditions of employees. According to the current laws, the employment rules cannot breach the provisions of a collective (37); however, unless a collective agreement specifically bans the use of remote work, the employment rules can be revised to introduce remote work. Meanwhile, in case the amendment of the employment rules is favorable to the employees, obtaining the consent of the trade unions or the majority of the employees is not necessary. However, if the employment rules are amended in a way that disadvantages the interests of the workers, the amendment must obtain the consent of the trade union or the majority of workers (38).

TABLE 7 | Robustness check of **Table 4**'s results.

Main category	Middle category	Variables	Status of introduction of remote work	
			Coef.	Robust Std. Err.
Interaction term	Number of employees X Year	**Base: 1–4 employees X 2017**		
		(1) X 2018	0.0004	(0.001)
		(1) X 2019	0.0006	(0.001)
		(1) X 2020	0.0060***	(0.002)
		(2) X 2018	0.0016	(0.001)
		(2) X 2019	0.0017	(0.001)
		(2) X 2020	0.0254***	(0.002)
		(3) X 2018	0.0013	(0.002)
		(3) X 2019	0.0013	(0.002)
		(3) X 2020	0.0554***	(0.005)
Control variables	Personal characteristics		O	
	Work characteristics		O	
	Year dummy		O	
	Sample Size		95,189	
	R-squared		0.027	

*(1) In the table, column 3 refers to interaction term for company size and year. (1) In column 3 represents there are 5–29 employees in the company. (2) Indicates there are 30–299 employees in the company. (3) Indicates the company has more than 300 employees. (2) Statistically significant at significance level of ***1%, **5%, *10%.*

For instance, if while establishing a remote work system the employers wish to impose a strict performance evaluation or wage adjustments that might deteriorate the current working conditions of the workers, the amendment would require the consent of the majority of workers.

Furthermore, recently the Supreme Court of South Korea established a precedent that even after obtaining a majority consent, an amendment to the employment rule that puts workers at a disadvantage would have no effect for a certain worker unless a labor contract with the said individual worker is revised accordingly (Supreme Court, November 14, 2019, Sentence 2018 da 200709) (39). This implies that even if the introduction of remote work was decided through the difficult process of amending the employment rules, the use of remote work cannot be finalized in case the amendment requires an additional procedure of revising the labor contract with individual workers. This suggests that the current legal environment makes it difficult to introduce remote work at workplaces.

Rigidity in Collective Bargaining in the Primary Sector

In South Korea, the primary sector labor market saw an increase in the adoption of remote work after the outbreak of the COVID-19; however, depending on the fluctuation of caseloads, the use of remote work and the return to office-based work occurred without an adjustment in the working conditions. That is, due to the unique circumstances during the pandemic, companies implemented remote work without applying special procedures such as obtaining a majority consent of the workers. However, going forward, in the post-pandemic era, the continued use of remote work in the primary sector may not be easily accommodated by labor organizations if the existing performance assessment and remuneration schemes are modified.

In South Korea, a trade union representing two-thirds or more workers of a particular workplace, can sign a union shop clause that would allow the trade union to force an organization to meet its demands (Trade Union Act §94-1) (38). For example, trade unions of large companies who have signed the union shop provision can make all eligible employees to become members of the trade unions. Hence, the high prevalence of trade unions within large primary sector companies in South Korea implies that companies cannot implement a remote work policy without a collective agreement that such a policy. Even when a collective agreement does not have a provision that prohibits the introduction of remote work, an amendment to the employment rules for the insertion of a remote work system requires the consent of the trade union or a majority votes of the workers. Therefore, with good cooperation between labor organizations and the management regarding corporate competitiveness and productivity is essential for the insertion of provisions on the use of remote work into collective agreement or employment rules. However, the negotiation culture between labor organizations and the management in South Korea has not been cooperative, so much so that the national competitiveness in terms of the labor-management relations is a major source of concern. In fact, among 140 countries, South Korea ranked 135th in 2016 and 2017, 124th in 2018, and 130th in 2019 in the labor-management relations assessment confirmed by the World Economic Forum (40).

Nevertheless, remote work is likely to continue in the post-pandemic era in a way that benefits both employer and employees. Accordingly, companies that anticipate the use of remote work need to establish improved systems and conditions allowing employees to choose a remote work. This is because remote work requires companies to modify their existing business performance and compensation framework, which is currently suitable only for the existing mode of work.

Rigidity in Revising Unfavorable Employment Rules for Secondary Sector Workers

The secondary sector faced considerable obstacles for implementing remote work during the pandemic. SMEs with non-regular workers in the secondary sector reduced workforce instead of offering remote work opportunities due to a lack of financial resources to pay wages to the workers. While the primary sector driven by large corporations, responded to the pandemic by suspending hiring and reducing costs, the secondary sector mostly comprised of SMEs, had to lay off even their skilled workers (41). However, after the pandemic even the SMEs would need to consider introducing remote work.

In case the secondary sector intends introduce remote work, similar to the primary sector, the workers are unlikely to accept the policy easily if it involves modifications to the existing task performance evaluation and compensation methods. As the secondary sector pays workers a smaller compensation amount, it cannot afford to adjust performance assessment and remuneration schemes implementing remote work. Nevertheless, the use of remote work in the primary sector is likely to influence its adoption in the secondary sector.

In the secondary labor market, only 12.3% of middle market enterprises with 122–299 employees and 2.7% of medium-sized companies with 30–99 employees have trade unions (30). Moreover, most of the trade unions in the secondary sector are so small that they are poorly equipped to use their collective bargaining power to have their demand accepted through labor strikes and other means. Therefore, the secondary sector companies are more likely to consider introducing remote work through revision of the employment rules instead of collective bargaining. Even so, the introduction of remote work by amending the employment rules requires the consent of the majority of employees, which could pose a challenge. As mentioned earlier, even with the consent of the majority of the employees, if a concerned employee requires a revision of a labor contract, companies must make such a revision. Therefore, overall, the introduction of remote work in the secondary labor market in South Korea is not easy under the current legal system.

CONCLUSION

This study empirically analyzed whether companies use remote work after the outbreak of COVID-19, focusing firm size, using the August supplementary survey of the EAPS released by Statistics Korea. Focusing on determining whether the gap in the use of remote work by firm size narrowed in an effort to combat the coronavirus, we found that the probability of large corporations implementing remote work after the outbreak of COVID-19 in 2020 surged more rapidly than small companies, thus widening the gap in the labor market.

Although this research analyzed the use of remote work in connection with the dual labor market, this research had several limitations. The first limitation was that the recent situation could not be included in the analysis due to data limitations. Although the EAPS provides monthly data published by Statistics Korea, the main variable used in this study, whether remote work was used or not, was included in the August Supplementary Survey of the EAPS, which was surveyed every August. The most recent data were the August 2020 data. The recent introduction of vaccines and the spread of mutated viruses were not considered in this analysis.

The second limitation was that we did not fully control the endogeneity problem. Companies that introduced remote work were large, had the ability to pay, and prepared to measure workload and performance online. Employees who worked for these companies might mainly have outstanding competencies in addition to their academic background. In this research, there was a limitation in controlling the competency of workers because panel analysis such as fixed effect could not be applied. Follow-up studies are needed to address these limitations.

Given dual labor market structure in South Korea, companies require customized support to establish a remote work system after the pandemic. The government of South Korea has recently been supporting SMEs to establish remote work infrastructure (42). These efforts may be considered as a policy reflecting the dual labor market structure. Additionally, during the pandemic, the South Korean government designated workers engaging coronavirus prevention efforts, with services employees working on-site, including parcel delivery, frontline workers protecting the safety of ordinary citizens and the socially vulnerable sections, and care-based workers acting as "essential workers." The South Korean government also implemented policies ensuring the safety and social protection for these people (43). Such policy is similar to protective measures for essential workers in the UK (44) and protection of essential workers and the HEROES Act in the United States (45, 46).

The secondary sector, which faces greater difficulties in implementing remote work, requires rapid, targeted, and intensive support. Without an appropriate support, SMEs in the secondary sector cannot overcome the obstacle of insufficient financial resources, which can hinder their survival and lead to massive unemployment, resulting in a sharp increase in the cost of unemployment benefits. In a country like South Korea, where there is a clear distinction of labor market between primary and secondary sectors, a timely support needs to be provided to eligible targets, without which the disparity in the dual labor market structure will further intensify.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. The raw data can be found here: https://mdis.kostat.go.kr/.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

SP: collected data, analyzed the result, wrote and edited initial draft, and revised the draft. SL: provided conceptualization direction and wrote initial draft. JC: provided conceptualization direction, design of collection tools, policy dimensions, and supervision. All authors read and approved the final manuscript.

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Racial Disparities in 30-Day Outcomes Following Index Admission for COVID-19

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We investigated racial disparities in a 30-day composite outcome of readmission and death among patients admitted across a 5-hospital health system following an index COVID-19 admission. A dataset of 1,174 patients admitted between March 1, 2020 and August 21, 2020 for COVID-19 was retrospectively analyzed for odds of readmission among Black patients compared to all other patients, with sequential adjustment for demographics, index admission characteristics, type of post-acute care, and comorbidities. Tabulated results demonstrated a significantly greater odds of 30-day readmission or death among Black patients (18.0% of Black patients vs. 11.3% of all other patients; Univariate Odds Ratio: 1.71, $p = 0.002$). Sequential adjustment via logistic regression revealed that the odds of 30-day readmission or death were significantly greater among Black patients after adjustment for demographics, index admission characteristics, and type of post-acute care, but not comorbidities. Stratification by type of post-acute care received on discharge revealed that the same disparity in odds of 30-day readmission or death existed among patients discharged home without home services, but not those discharged to home with home services or to a skilled nursing facility or acute rehab facility. Collectively, the findings suggest that weighing comorbidity burdens in post-acute care decisions may be relevant in addressing racial disparities in 30-day outcomes following discharge from an index COVID-19 admission.

Keywords: readmission, COVID-19, racial disparity, comorbidity, post-acute care

INTRODUCTION

Racial disparities in infection, hospitalization, and mortality from coronavirus disease 2019 (COVID-19) have been documented, particularly for Black Americans (1). Recent studies have investigated readmission rates following hospitalization for COVID-19 (2, 3), showing that most readmissions occur within 10 days of discharge (4). There is limited data on the effect of post-acute care on racial disparities in 30-day readmissions. Evaluating determinants of racial disparities in COVID-19 readmissions could enable targeted interventions to address inequities. Thus, we analyzed 30-day outcomes of COVID-19 patients surviving to discharge across a 5-hospital health system.

MATERIALS AND METHODS

This retrospective study of 30-day readmission or death among patients hospitalized between 3/1/2020 and 8/21/2020 for COVID-19 was conducted within the University of Pennsylvania Health System and approved by the University's Institutional Review Board. Patients were identified using a dataset of all patients with an order for any COVID-19 test and chest imaging completed within the health system. Only patients admitted within 14 days of placement on the health system's COVID-19 positive registry and with primary diagnosis ICD-10 codes consistent with COVID-19 were included. Patient characteristics from the medical record were compared by race using the chi-squared and Mann-Whitney tests. Logistic regression of 30-day outcome was sequentially adjusted for demographics, index admission characteristics, type of post-acute care, and comorbidities (5). We tested the interaction of race with post-acute care using the likelihood-ratio test and performed stratified regression analyses. All analyses were completed on Stata MP Version 15.1 (StataCorp).

RESULTS

Of 1,461 admitted COVID-19 patients, 1,174 survived to discharge. 625 patients were Black (53.0%); a majority of the remaining patients were White (n = 427, 37.1%), and 10% reported Hispanic ethnicity. Black patients were younger, more likely female, had different forms of insurance, and a greater burden of comorbidities. Index admission length and frequency of mechanical ventilation were similar between Black patients and patients of other races, but the distribution of post-acute care on discharge differed (**Table 1**).

Amongst all discharged patients, 176 patients (15.0%) were readmitted or died within 30 days: 116 Black patients (18.0%) vs. 60 patients of other races (11.3%) (**Table 1**). A univariate odds ratio of 30-day readmission or death among Black patients was 1.71 (CI: 1.23–2.40, p = 0.002) without meaningful change on sequential adjustment for demographics, index admission, and post-acute care (**Table 2**, Models 1–4). Addition of comorbidities, however, attenuated the odds ratio for race with 30-day readmission or death, and it was no longer statistically significant (**Table 2**, Model 5).

When stratified by post-acute care, univariate odds of readmission or death were significantly greater for Black patients discharged to home without services (OR = 2.12, 95% CI: 1.19–3.78, p = 0.010) but not to home health care (OR = 1.18, CI: 0.64–2.17, p = 0.594) or skilled nursing or acute rehab facilities (OR = 1.70, CI: 0.87–3.32, p = 0.119). However, the interaction between Black race and post-acute care was not statistically significant (p-interaction = 0.309).

Multiple sensitivity analyses were performed. With 30-day readmission as the sole endpoint and patients who died in the timeframe excluded, the same trend in greater odds of readmission among Black patients was observed on serial adjustment for contributory variables, where odds of readmission were no longer significant after adjustment for comorbidities. Identical trends were observed on sensitivity analyses using eight individual comorbidities instead of the Charlson Comorbidity Index, excluding readmissions to other health systems, and including COVID-19 registry patients with any ICD-10 code.

DISCUSSION

Black patients were more likely to be readmitted or die at 30 days following admission for COVID-19 across an urban health system after adjusting for demographics, post-acute care, and index admission characteristics. To our knowledge, this is the first study to note a racial disparity in 30-day outcomes following COVID-19 hospitalization. This is consistent with disparities in readmissions seen for conditions that frequently cause hospitalizations, such as myocardial infarctions, decompensated heart failure, and pneumonia (6). For these conditions, disparities in readmissions were also related to the sites of care such that hospitals serving larger minority populations similar to the population in our study had larger disparities in readmission rates. Analysis in 2018 following the institution of Medicare's Hospital Readmission Reduction Program, which penalizes hospitals for higher than expected 30-day readmissions for acute myocardial infarction, heart failure, and pneumonia, suggest that racial disparities have persisted and may have widened for non-targeted conditions at safety net hospitals that care for larger populations of Black patients (7). While the site of care has been associated with racial disparities in readmissions, there are other structural inequities that could contribute to greater readmissions among Black patients. In a national study of readmissions in diabetic patients, other demographic factors, most notably household income, also contributed to the disparity in readmissions along with the site of care (8). We lacked data on household income or other measures of socioeconomic status beyond insurance status.

It should be noted that a greater proportion of the Black patients admitted in our study were females, though sex was not found to be statistically significant in our regressions on 30-day outcomes. The larger proportion of females admitted for COVID-19 among the Black population in our study could reflect a differential impact of the pandemic on the sexes across racial groups. It has been observed that COVID-19 outcomes among males and females can differ between Black and White patients, though previously presented data have described worse outcomes among Black males rather than females (9). Alternatively, the higher proportion of Black females admitted for COVID-19 in our study may be attributable in part to regional population level differences in the ratio of females to males by race above the age of 50 (10), which are due to shorter life expectancy among Black men (11).

Differences in the burden of comorbidities largely explained the racial difference in 30-day outcomes. Greater comorbidities among Black patients have previously been attributed to the effects of structural racism on health and limited access to care (12). Though analyses of racial disparities in readmissions during epidemics and pandemics are limited, there is a robust literature documenting the disproportionate impacts of disease outbreaks on racial minorities, and thorough analysis of the 1918

TABLE 1 | Characteristics of Black and Non-Black patients by site of discharge following index admission for COVID-19.

	Total	Black patients	All other patients	*P*-value*
n	1,174	645	529	
Racial sub-groups				
Black (%)	645 (54.9)			
White (%)	427 (36.4)			
Other (%)	102 (8.7)			
Ethnicity				
Hispanic	124 (10.6)	22 (3.4)	102 (19.3)	
Additional demographics				
Age, median (yrs, IQR)	62 (49, 74)	61 (48, 71)	63 (50, 77)	**0.022**
Female, *n* (%)	566 (48.2)	340 (52.7)	226 (42.7)	**0.001**
Insurance				
Private (%)	282 (24.0)	159 (24.7)	123 (23.3)	**<0.001**
Medicare (%)	555 (47.3)	290 (45.0)	265 (50.1)	
Medicaid (%)	223 (19.0)	154 (23.9)	69 (13.0)	
Uninsured (%)	38 (3.2)	8 (1.2)	30 (5.7)	
Unknown (%)	76 (6.5)	34 (5.3)	42 (7.9)	
Comorbidities				
Charlson comorbidity index, mean (SD)	3.2 (3.3)	3.9 (3.6)	2.3 (2.7)	**<0.001**
Type 2 diabetes mellitus (%)	437 (37.2)	289 (44.8)	148 (28.0)	**<0.001**
Chronic obstructive pulmonary disease (%)	124 (10.6)	80 (12.4)	44 (8.3)	**0.023**
Congestive heart failure (%)	243 (20.7)	156 (24.2)	87 (16.4)	**0.001**
Chronic kidney disease (%)	197 (16.8)	147 (22.8)	50 (9.5)	**<0.001**
Hypertension (%)	786 (67.0)	483 (74.9)	303 (57.3)	**<0.001**
Cancer (%)	219 (18.7)	124 (19.2)	95 (18.0)	0.579
History of cerebrovascular infarction (%)	189 (16.1)	128 (19.8)	61 (11.5)	**<0.001**
Sickle cell disease (%)	21 (1.8)	21 (3.3)	0 (0.0)	**<0.001**
Index admission				
Length of stay (days, IQR)	6 (3, 12)	5 (3, 12)	6 (3, 11)	0.164
Mech. ventilated (%)	152 (12.9)	87 (13.5)	65 (12.3)	0.542
Post-acute care on discharge				
Home (without services) (%)	523 (44.5)	271 (42.0)	252 (47.6)	**<0.001**
Home health care (%)	352 (30.0)	230 (35.7)	122 (23.1)	
SNF/acute rehab (%)	241 (20.5)	114 (17.7)	127 (24.0)	
Other (%)	58 (4.9)	30 (4.7)	28 (5.3)	
30-day outcomes				
Readmission (%)	161 (13.7)	105 (16.3)	56 (10.6)	**0.005**
Time to readmission (median days, IQR)	7 (3,14)	6 (3, 15)	7 (3, 13.5)	0.9674
Death at 30 days (%)	20 (1.7)	14 (2.2)	6 (1.1)	0.175
Readmission or death 30 Days (%)	176 (15.0%)	116 (18.0)	60 (11.3)	**0.002**

**All p-values are for chi-squared or Mann-Whitney tests; chi-squared tests were used for categorical variables and Mann-Whitney tests were used for continuous variables. Bold values denote p-values that were statistically significant at the $p < 0.05$ level.*

Influenza Pandemic suggests that structural inequities in access to care contributed to racial disparities in outcomes such as mortality (13). In fact prior to the COVID-19 pandemic, some had predicted that a future pandemic influenza was likely to result in worse outcomes in Black populations due to greater barriers to care and burdens of comorbidities among Black patients (14).

The racial disparity appeared most pronounced among patients discharged home without services. It has previously been noted that readmissions are driven not just by the inpatient care received, but also by the outpatient care and socioeconomic resources available after discharge (15). Post-acute care can range from home services, such as visiting nurses, to care in a facility. Without post-acute care, the effects of structural racism on access to care may be exacerbated. Our study suggests that racial disparities in 30-day outcomes may be most evident in the absence of post-acute care. Paired with the finding that comorbidities explained much of the disparity in 30-day outcomes, these results suggest that weighing comorbidity burdens in post-acute care decisions may help address racial disparities in outcomes of discharged COVID-19 patients.

TABLE 2 | Odds ratios of 30-day readmission or death among Black patients vs. all other patients with different post-acute care on discharge after sequential adjustment for other demographics, index admission characteristics, and comorbidities.

	Model 1: univariate*		**Model 2: adjusted for age, sex, insurance†**		**Model 3: additionally adjusted for index length of stay and ventilation‡**		**Model 4: additionally adjusted for discharge site§**		**Model 5: additionally adjusted for Charlson comorbidity index‖**	
	Odds ratio (95% CI)	***P*-value**	**Odds ratio (CI)**	***P*-value**	**Odds ratio (CI)**	***P*-value**	**Odds ratio (CI)**	***P*-value**	**Odds ratio (CI)**	***P*-value**
All patients ($n = 1,174$)	1.71 (1.23, 2.40)	**0.002**	1.81 (1.28, 2.56)	**0.001**	1.80 (1.27, 2.55)	**0.001**	1.79 (1.26, 2.55)	**0.001**	1.39 (0.96, 2.01)	0.085
Patients discharged home without services ($n = 523$)	2.12 (1.19, 3.78)	**0.010**	2.09 (1.15, 3.80)	**0.015**	2.06 (1.13, 3.76)	**0.018**			1.74 (0.93, 3.24)	0.082
Patients discharged to home health care ($n = 352$)	1.18 (0.64, 2.17)	0.594	1.31 (0.69, 2.49)	0.417	1.28 (0.67, 2.45)	0.457			0.93 (0.47, 1.86)	0.844
Patients discharged to SNF/acute rehab ($n = 241$)	1.70 (0.87, 3.32)	0.119	2.00 (0.99, 4.06)	0.054	1.91 (0.93, 3.90)	0.076			1.39 (0.64, 3.00)	0.405

Model Definitions (all regressed on 30 readmission or death, bolded independent variables were significant at the $p < 0.05$ level in the all patient regression).
Model 1: **Black race alone (univariate).*
*†Model 2: **Black race**, sex, **patient age**, and **insurance**.*
*‡Model 3: **Black race**, sex, patient age, **insurance**, index admission length of stay (days), index admission mechanical ventilation.*
*§Model 4: **Black race**, sex, patient age, **insurance**, index admission length of stay (days), index admission mechanical ventilation, post-acute care on discharge.*
*‖Model 5: Black race, sex, patient age, **insurance**, index admission length of stay (days), index admission mechanical ventilation, post-acute care on discharge, **Charlson Comorbidity Index**.*

There are several limitations of this study. First, without information on the reasons for 30-day readmission or death, it is difficult to understand the degree to which 30-day outcomes were driven primarily by COVID-19 versus other conditions. Additionally, this study captured only deaths occurring in the 30-day period after discharge that were recorded in the electronic medical record. Consequently, it is possible that some deaths may have been missed with unclear impacts on the composite 30-day outcome of readmission and death.

Nevertheless, this study has illustrated that Black patients across an urban health system were more likely to be readmitted or die within 30 days after an index admission for COVID-19 in the initial surge of the pandemic. Existing comorbidities appeared to play an important role in explaining racial disparities, particularly among patients without post-acute care. Future studies should explore whether these findings are present in other cohorts, including at different time points in the pandemic. Validation across other cohorts would motivate interventional studies that interrogate the formal incorporation of burdens of comorbidities into the assignment of post-acute care at discharge following hospitalization for COVID-19 as a means of reducing racial disparities in readmissions.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available due to the need to maintain patient confidentiality. Requests to access the de-identified datasets should be directed to annemcc@pennmedicine.upenn.edu.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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Another New Year, Will the Chinese Residents Wear Face Masks Again? A Cross-Sectional Survey

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Background: As more and more countries enter the low-transmission phase, maintaining prevention awareness among the population is critical to prevent a secondary outbreak. With large-scale interpersonal communication, whether Chinese residents can maintain a high awareness of prevention and control and adhere to the use of masks during the Chinese New Year of 2021 is worth studying.

Methods: A cross-sectional survey was conducted in China from February 4 to 26, 2021. A convenient sampling strategy was adopted to recruit participators. Participants were asked to fill out the questions that assessed the questionnaire on face mask use. Descriptive statistics were used to assess the mask-wearing behaviors of the public. A binary logistic regression analysis was performed to identify the risk factors affecting mask-wearing behaviors.

Results: A total of 2,361 residents filled out the questionnaire. In the mixed-effect logistic regression analysis, Chinese residents who were older (OR = 7.899, 95%CI = 4.183–14.916), employed (OR = 1.887, 95%CI = 1.373–2.594), had a chronic disease (OR = 1.777, 95%CI = 1.307–2.418), reused face masks (OR = 22.155, 95%CI = 15.331–32.016) and have read the face mask instructions (OR = 3.552, 95%CI = 1.989–6.341) were more likely to use face masks in interpersonal communication during the Spring Festival; while people who have breathing discomfort caused by face masks (OR = 0.556, 95%CI = 0.312–0.991) and considered that using masks repeatedly is wasteful (OR = 0.657, 95%CI = 0.482–0.895) were more unlikely to use face masks.

Conclusions: Our results revealed that 83.86% of people wore face masks during the Chinese New Year; however, some aspects require further promotion. By investigating

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the use of masks by Chinese residents during the Spring Festival and its influencing factors, we can reflect the prevention awareness of the residents during the low transmission period of COVID-19, which can provide a reference for Chinese and global public health policymakers.

Keywords: face masks, low transmission period, interpersonal communication, COVID-19, public health

BACKGROUND

The origin of the outbreak of COVID-19 was initially detected in Wuhan, China in December 2019 (1). The virus is mainly transmitted from person to person through the mouth, nose, or eyes through respiratory droplets, aerosols, or contaminants (2, 3).

It can live on surfaces for up to 72 h (4) and contact with contaminated surfaces and then touching the face is another possible source of transmission (5). Wearing a face mask is a reasonable way to reduce the spread of respiratory viruses and minimizes the risk of respiratory droplets reaching the nasal or oral mucosa of the wearer (5).

A growing number of places recommend wearing masks in community settings. The WHO and the U.S. Centers for Disease Control and Prevention (6) strongly recommend that people with symptoms or known infections wear masks to prevent the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to others (7). There is some evidence supporting the effectiveness of using masks in health care settings (8, 9) and as source control for patients infected with SARS-CoV-2 or other coronaviruses (10). Wearing a mask in a community setting is recommended to reduce the transmission of SARS-CoV-2 (7, 9) as it protects the uninfected wearers (protective effect) and reduces the transmission from the infected wearers (source control).

The Chinese New Year holiday, which coincides with the COVID-19 outbreak, is one of the most festive times of the year in China, with a lot of human interaction (11). The Chinese government quickly proclaimed prevention and control measures for interpersonal communication during the Spring Festival, especially the use of face masks, to impede transmission in health care and community settings (12). In the year 2020, the Chinese government strongly advocated the universal use of face masks in public places as a means of source control during the COVID-19 pandemic (13). Chinese residents generally supported the use of masks in public places (14) as a supplement to social distancing and hand hygiene to contain or slow the exponential growth of the epidemic (15). Universal masking prevents the inevitable cross-spread of person-to-person contact during the lockdown and reduces the risk of a resurgence during the relaxation of social distancing measures.

Currently, the COVID-19 epidemic has been controlled and China has entered a period of low transmission (16). At this stage, the Chinese government is still asking the public to increase their vigilance against COVID-19, keeping the use of face masks in communities and reducing concentration. February 4–26, 2021, is considered the Chinese New Year. With the large-scale interpersonal communication, whether or not Chinese residents can maintain a high awareness of prevention and control and adhere to the use of masks is worth studying. As more and more countries enter the low-transmission phase, maintaining prevention awareness among the population is critical in preventing a secondary outbreak. By investigating the use of masks by Chinese residents during the Spring Festival and its influencing factors, we can reflect on the prevention awareness of the residents during the low transmission period of COVID-19, which can provide a reference for the Chinese and global public health policymakers.

METHODS

Ethics Statement

This study scheme was approved by the Institutional Review Committee of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China. All the methods are performed in accordance with relevant guidelines and regulations. The respondents were informed that their participation was voluntary and implied consent on the completion of the questionnaire.

Study Participants and Survey Design

A cross-sectional survey was conducted in China from February 4 to 26, 2021. We stratified the respondents mainly according to the eastern, central, and western regions of China. We selected residents from eastern (Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Hainan), central (Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, and Hunan), and western (Chongqing, Sichuan, Guizhou, Yunnan, Tibet, Shaanxi, Gansu, Qinghai, Ningxia, Xinjiang, Inner Mongolia, and Guangxi) China to complete the survey. A convenient sampling strategy was adopted to recruit the participants; the research team used WeChat, the most popular social media platform in China, to publicize and distribute the survey links to their network members. The network members were asked to distribute the survey invitations to all of their contacts. The participants were informed that their participation was voluntary and their consent was implied by their completion of the questionnaire. The applicants should be Chinese citizens aged 18 or above and are able to understand and read Chinese.

Instruments

The questionnaire was compiled according to the guidelines issued by the National Health Commission of China (17, 18). The final version of the questionnaire was entitled "Questionnaire

TABLE 1 | The statistical description of the study samples: univariate analysis of the differences of the willingness of residents to use face masks in their interpersonal communication during the Spring Festival.

Variables	*N* (%)	χ^2	*P*
Total	2,361 (100)	NA	NA
Using face masks in interpersonal communication during the Spring Festival			
Yes	1,980 (83.86)	NA	NA
No	381 (16.64)		
Gender			
Male	942 (39.90)	4.140	0.042
Female	1,419 (61.10)		
Age group, y			
18–44	1,845 (78.14)	36.610	<0.001
45–59	369 (15.63)		
>60	111 (4.70)		
Highest educational level			
Primary school or below	68 (2.88)	1.738	0.419
Middle school	186 (7.88)		
College degree or above	2,107 (89.24)		
Place of residence			
Urban	1,372 (58.11)	14.202	<0.001
Rural	989 (41.89)		
Region			
Eastern China	421 (17.83)	17.906	<0.001
Central China	1,470 (62.26)		
Western China	470 (19.91)		
Employment status			
Employed	1,014 (42.95)	21.262	<0.001
Unemployed	1,347 (57.05)		
Have a chronic disease (diagnosed by a doctor)			
Yes	1,621 (68.66)	226.324	<0.001
No	740 (31.34)		
Main types of face masks			
Respirators (N95 and FFP)	614 (26.01)	3.343	0.188
Surgical mask	1,059 (44.85)		
Cloth masks	688 (29.14)		
Main sources of face masks			
Purchased	2,023 (85.68)	86.693	<0.001
Free (community, work unit, etc provide)	338 (14.32)		
Reuse face masks			
Yes	1,435 (60.78)	1,279.010	<0.001
No	926 (39.22)		
Have read the face mask instructions			
Yes	1,136 (48.12)	831.344	<0.001
No	1,225 (51.88)		
Face masks cause breathing discomfort			
Yes	1,224 (52.69)	781.840	<0.001
No	1,117 (47.31)		
Consider that using masks repeatedly is wasteful			
Yes	726 (30.75)	181.024	<0.001
No	1,635 (69.25)		
Consider that using masks repeatedly is too troublesome			
Yes	622 (26.34)	0.905	0.341
No	1,739 (73.66)		
Clean the used masks before discarding			
Yes	239 (10.12)	0.023	0.880
No	2,122 (89.88)		

(Continued)

on Face Masks Use for the Public during the 2021 New Year (Except Healthcare Workers)" and consisted of two parts: (1) socio-demographic characteristics, with seven items, including gender, age, highest educational level, place of residence, religion, employment status, and "have a chronic disease (diagnosed by a doctor)," and (2) mask-wearing behaviors and attitudes, with 16 items, including "main types of face masks," "main sources of face masks," "reuse face masks," "have read the face mask instructions," "face masks cause breathing discomfort," "consider that using masks repeatedly is wasteful," "consider that using masks repeatedly is too troublesome," and "clean the used masks before discarding."

The electronic (e)-questionnaires were compiled using Wenjuanxing (www.wjx.cn), a survey platform widely used in China. Online posters with access codes or links to the questionnaires were distributed in one of these two ways:(1) posted on our WeChat; (2) distribution was made through the WeChat group, and each person was to be compensated 1–2 ¥ on average. To avoid duplicate submissions, each person can only participate one time for each WeChat account.

Statistical Methods

The data were analyzed using *SPSS*™ for Windows, Version 22.0 (SPSS, Inc., Chicago, Illinois, United States). We dichotomized the answers of the residents regarding their willingness to use face masks as "Yes" and "No." The descriptive statistics were presented as the percentage (%) of the number of observations, and we analyzed the differences in the demographic statistics using a Chi-square (χ^2) test. Due to the disparities in the socioeconomic status in the different regions, the data has a typical hierarchical structure. We performed a mixed-effect logistic regression model with a random cluster effect (geographic regions) to investigate the adjusted odds ratio (OR) (95% CI) of the influencing factors of the willingness of residents to use face masks. Further, we explored the factors influencing the willingness of the participants to use face masks in Eastern, Central, and Western China, respectively, through multivariable logistic regression analysis. The significance level was accepted as $P < 0.05$ (two-sided).

RESULTS

Descriptive Statistics

A total of 2,453 residents received the questionnaire, of which 21 did not reply and 71 did not accomplish the questionnaire. The response rate was 96.24%. The results were analyzed using

TABLE 2 | Univariate analysis of the differences in the willingness to use face masks in interpersonal communication during the Spring Festival among the included residents stratified by geographic characteristics.

Variables	Eastern China			Central China			Western China		
	N (%)	χ^2	*P*	N (%)	χ^2	*P*	N (%)	χ^2	*P*
Total	421 (100)	NA	NA	1,470 (100)	NA	NA	470 (100)	NA	NA
Using face masks in interpersonal communication during the Spring Festival									
Yes	367 (87.17)	NA	NA	1,185 (80.61)	NA	NA	428 (91.06)	NA	NA
No	54 (12.83)			285 (19.39)			42 (8.94)		
Gender									
Male	181 (42.99)	0.162	0.687	558 (37.96)	1.675	0.196	203 (43.19)	2.353	0.125
Female	240 (57.10)			912 (62.04)			267 (56.81)		
Age group, y									
18–44	323 (76.72)	7.089	0.029	1,175 (79.93)	19.178	<0.001	347 (73.83)	7.648	0.022
45–59	61 (14.49)			232 (15.78)			76 (16.17)		
>60	37 (8.79)			63 (4.29)			47 (10.00)		
Highest educational level									
Primary school or below	17 (4.04)	2.454	0.293	27 (1.84)	2.519	0.284	24 (5.11)	2.092	0.351
Middle school	24 (5.70)			123 (8.37)			39 (8.30)		
College degree or above	38 (90.26)			1,320 (89.80)			407 (86.60)		
Place of residence									
Urban	288 (68.41)	0.442	0.506	754 (51.29)	8.185	<0.001	330 (70.21)	1.624	0.203
Rural	133 (31.59)			716 (48.71)			140 (29.79)		
Employment status									
Employed	270 (64.13)	0.091	0.763	508 (34.56)	35.699	<0.001	236 (50.21)	3.508	0.061
Unemployed	151 (35.87)			962 (65.44)			234 (49.79)		
Have a chronic disease (diagnosed by a doctor)									
Yes	286 (67.93)	40.954	<0.001	985 (67.01)	140.892	<0.001	350 (74.47)	38.785	<0.001
No	135 (32.07)			485 (32.99)			120 (25.53)		
Main types of face masks									
Respirators (N95 and FFP)	97 (23.04)	5.342	0.069	405 (27.55)	2.364	0.307	112 (23.83)	1.388	0.500
Surgical mask	200 (40.51)			637 (43.33)			222 (47.23)		
Cloth masks	124 (29.45)			428 (29.12)			136 (28.94)		
Main sources of face masks									
Purchased	357 (84.80)	10.902	<0.001	1,259 (85.65)	58.561	<0.001	407 (86.60)	17.841	<0.001
Free (community, work unit, etc provide)	64 (15.20)			211 (14.35)			63 (13.40)		
Reuse face masks									
Yes	259 (61.52)	169.104	<0.001	854 (58.10)	863.413	<0.001	322 (68.51)	241.527	<0.001
No	162 (38.48)			616 (41.90)			148 (31.49)		
Have read the face mask instructions									
Yes	199 (47.27)	132.368	<0.001	672 (45.71)	543.494	<0.001	265 (56.38)	148.066	<0.001
No	222 (52.73)			798 (54.29)			205 (43.62)		
Face masks cause breathing discomfort									
Yes	212 (20.36)	122.873	<0.001	815 (55.44)	520.793	<0.001	217 (46.17)	131.530	<0.001
No	209 (49.64)			655 (44.56)			253 (53.83)		
Consider that using masks repeatedly is wasteful									
Yes	139 (33.02)	34.222	<0.001	462 (31.43)	112.694	<0.001	125 (26.60)	31.417	<0.001
No	282 (66.98)			1,008 (68.57)			345 (73.40)		
Consider that using masks repeatedly is too troublesome									
Yes	109 (25.89)	0.159	0.690	393 (26.73)	1.055	0.304	120 (25.53)	0.342	0.559
No	312 (74.11)			1077 (73.27)			350 (74.47)		
Clean the used masks before discarding									
Yes	37 (8.79)	0.920	0.337	151 (10.27)	1.129	0.288	51 (10.85)	0.689	0.407
No	384 (91.21)			1,319 (89.73)			419 (89.15)		

the 2,361 complete questionnaires. **Table 1** reports the social-demographic characteristics of the 2,361 respondents. The mean age was 29.72 years (SD = 6.94) and the majority of respondents were female (60.10%). Among the respondents, 421 (17.83%), 1,470 (62.26%), a1nd 470 (19.91%) were from Eastern, Central, and Western China, respectively. Most respondents (89.24%) have a bachelor's degree or higher. More than half of the participants (57.05%) were unemployed.

Out of all the participants, 1,980 (83.86%) have used face masks in their interpersonal communication during the Spring Festival. The results of the univariate analysis suggested that the gender, age, place of residence, region, employment status, "have a chronic disease," "main sources of face masks," "reuse face masks," "have read the face mask instructions," "face masks cause breathing discomfort," and "consider that using masks repeatedly is wasteful" were statistically significant influencing factors for "using face masks in interpersonal communication during the Spring Festival"($P < 0.05$) (**Table 1**).

Univariate analysis of the participants from Eastern, Central, and Western China was conducted, taking the sampling differences across the geographical regions into account (**Table 2**). In the mixed-effect logistic regression analysis, the Chinese residents who were older (OR = 7.899, 95%CI = 4.183–14.916), employed (OR = 1.887, 95%CI = 1.373–2.594), had a chronic disease (OR = 1.777, 95%CI = 1.307–2.418), reused face masks (OR = 22.155, 95%CI = 15.331–32.016), and have read the face mask instructions (OR = 3.552, 95%CI = 1.989–6.341) were more likely to use face masks in their interpersonal communication during the Spring Festival, while the people who experienced breathing discomfort from face masks (OR = 0.556, 95%CI = 0.312–0.991) and considered that using masks repeatedly is wasteful (OR = 0.657, 95%CI = 0.482–0.895) were not inclined to use face masks (**Table 3**).

TABLE 3 | Mixed-effect logistic regression analysis on the influencing factors of the willingness of residents to use face masks in interpersonal communication during the Spring Festival.

Variables	Coefficient	*S.E.*	*P*	*OR*	95% *CI*
Age group, y (Ref: 18–44)					
45–59	0.597	0.191	0.002	1.817	1.250–2.641
>60	2.067	0.324	<0.001	7.899	4.183–14.916
Employment status (Ref: Unemployed)					
Employed	0.635	0.162	<0.001	1.887	1.373–2.594
Have a chronic disease (Ref: No)					
Yes	0.575	0.157	<0.001	1.777	1.307–2.418
Reuse face masks (Ref: No)					
Yes	3.098	0.188	<0.001	22.155	15.331–32.016
Have read the face mask instructions (Ref: No)					
Yes	1.267	0.296	<0.001	3.552	1.989–6.341
Face masks cause breathing discomfort (Ref: No)					
Yes	−0.587	0.295	0.046	0.556	0.312–0.991
Consider that using masks repeatedly is wasteful (Ref: No)					
Yes	−0.420	0.158	0.008	0.657	0.482–0.895

In addition, we stratified the study samples by region and performed multivariate logistic regression analysis. The results showed that the "main source of purchase of face masks" (OR = 32.587, 95%CI = 19.439–54.629) was also a related factor for the increase in the willingness to use face masks among residents in Central China (**Table 4**).

DISCUSSION

Our study, based on a cross-sectional survey, determined the willingness to use face masks in interpersonal communication and its influencing factors during the Spring Festival among Chinese residents. We found that 83.86% of the citizens have used the face masks, and this rate is lower than that in another study about the rate of face masks usage among Chinese citizens (99%)

TABLE 4 | Stepwise multivariate logistic regression analysis on the influencing factors of the willingness of residents to use face masks in interpersonal communication during the Spring Festival.

Variables	Coefficient	*S.E.*	*P*	*OR*	95% *CI*
Eastern China					
Age group, y (Ref: 18–44)					
>60	1.945	0.602	0.001	6.993	2.149–22.757
Have a chronic disease (Ref: No)					
Yes	0.698	0.354	0.049	2.010	1.004–4.024
Reuse face masks (Ref: No)					
Yes	2.257	0.391	<0.001	22.155	15.331–32.016
Have read the face mask instructions (Ref: No)					
Yes	2.290	0.638	<0.001	9.878	2.826–34.528
Consider that using masks repeatedly is wasteful (Ref: No)					
Yes	−0.420	0.158	0.008	0.657	0.482–0.895
Central China					
Age group, y (Ref: 18–44)					
>60	1.776	0.520	0.001	5.908	2.131–16.377
Employment status (Ref: Unemployed)					
Employed	1.155	0.219	<0.001	3.175	2.067–4.876
Have a chronic disease (Ref: No)					
Yes	0.691	0.206	0.001	1.997	1.334–2.988
Main sources of face masks (Ref: Free)					
Purchased	0.524	0.245	0.032	1.689	1.045–2.730
Reuse face masks (Ref: No)					
Yes	3.484	0.264	<0.001	32.587	19.439–54.629
Have read the face mask instructions (Ref: No)					
Yes	1.035	0.395	0.009	2.816	1.298–6.109
Consider that using masks repeatedly is wasteful (Ref: No)					
Yes	−0.458	0.207	0.027	0.633	0.421–0.949
Western China					
Age group, y (Ref: 18–44)					
45–59	1.345	0.458	0.003	3.838	1.565–9.412
>60	1.790	0.656	0.006	5.992	1.658–21.660
Reuse face masks (Ref: No)					
Yes	3.777	0.508	<0.001	43.699	16.134–118.355

by Tan et al. (14) during the rapid spread of COVID-19. Nearly one-fifth of the participants demonstrated bad compliance in terms of mask-wearing behaviors in the period of low transmission without realizing the risk of intense interpersonal communication. Moreover, this study found some factors associated with good compliance, including age, employment status, "have a chronic disease," "reuse face masks," "have read the face mask instructions," "face masks cause breathing discomfort," "consider that using masks repeatedly is wasteful," and "main sources of face masks."

Age can be a factor in mask-wearing behavior. Consistent with previous studies that examined the changes in public behavior during influenza outbreaks (19, 20), the older participants in our survey showed a trend toward better compliance with age. In addition, the people who were unemployed exhibited better compliance with face mask use than the employed participants. This phenomenon may be related to the lower risk resistance and psychological resilience of the elderly and the non-employed (21). In addition, as a survey method of convenience sampling was adopted in this study, many students were included as participants. Therefore, the proportion of unemployed respondents is relatively large. The results of this analysis should be treated with more caution.

We also observed that different situations affect the behavior of people. Compliance is much better in patients with chronic diseases. This may be due to their concerns about the high risk of COVID-19 transmission in these settings and the association between the perception of high risk and good compliance with mask use (19, 22). Similarly, compliance was worse among residents who agreed that wearing masks caused discomfort in breathing. In real life, when people have symptoms of breathing disorders, they may feel uncomfortable, and the frequent use of masks can lead to worse compliance (14).

Among the factors influencing mask-wearing behaviors, we found that people exposed to the instructions on how to use masks showed better compliance than people who are not. Interestingly, there was no significant relationship between educational background and compliance. Thus, good mask-wearing habits seem to depend on how much education is received about mask use, rather than on the level of education. This finding also supported the hypothesis proposed by Greenhalgh et al. (23) that, in the case of COVID-19, people can be taught to use masks properly and to stick with them without abandoning other important anti-infection measures. This evidence, combined with our findings on the methods by which the participants obtained relevant information, suggests that institutions and the academe should put effort into dissemination guidance through a variety of means, of which social media is the most beneficial to the public.

Economic factors are crucial. The participants who considered that using masks repeatedly is wasteful are more likely to refuse using face masks. Similarly, reusing face masks also increases compliance. Whether or not people will reduce their health protection to save money has not been reported, but it is still an important Research Topic during periods of low transmission. Notably, the residents who bought masks out of their own pocket also demonstrated low compliance, but this phenomenon was only seen in central China, thus the effect of this factor needs further investigation.

Strengths and Limitations

Wearing masks in large-scale interpersonal interactions can reflect the awareness of residents regarding the prevention of COVID-19. This is the first study to investigate the mask-wearing behaviors of the general public in the period of low COVID-19 transmission. We used a nationwide sample of the Chinese population. The findings provide evidence about the way the public uses masks and the factors that influence their behavior, which is of great significance to China and other countries. First of all, this research takes social media as the main communication survey method. Participants who do not have Internet access may not be included. Therefore, the strategy of simultaneous online and offline development should be adopted in future research. Online surveys rely on social software, while offline surveys rely on community or rural health service institutions, medical personnel, and primary management personnel. This method of the survey will include a wider range of residents and reduce the bias caused by online surveys. Second, the study participants were unevenly distributed in different regions (421:1,470:470). Therefore, the subgroups of the variables may not be representative of the population. Third, the study was unable to determine how many participants have seen the online posters or surveys but decided not to complete them, therefore, the existence of the non-response bias cannot be evaluated. Finally, since these behaviors are self-reported, reporting bias is possible. In general, the generalization of the results should be viewed with caution.

CONCLUSIONS

Because of the highly infectious nature of COVID-19 and the ongoing severity of the global epidemic, wearing masks has become a part of daily life. Although more and more countries are entering the low-infection period, face masks can still play an important role in preventing a second outbreak. Therefore, understanding how the public uses masks and what factors are associated with good compliance will help determine ways to promote proper mask-wearing behaviors.

Our results show that 83.86% of the Chinese residents wore masks during the Spring Festival. However, there are still some areas that need further promotion. In future evidence dissemination or behavior change interventions, particular emphasis should be placed on wearing masks among young people, employed persons, and healthy residents. In addition, the reusing of masks and the instructions for the use of masks should not be ignored. In the period of low transmission, it is important to take as many publicity measures as possible to promote the wearing of masks by the public. Therefore, different influencing factors should be considered in the dissemination of evidence to reach different populations. Methods should be adopted for the clear and ubiquitous dissemination of government warnings and alerts. Social media is the most powerful way to reach an audience and facilitate data collection. However, further research on how social media can promote public behavior change is needed.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

This study protocol was approved by the Institutional Review Board of the Tongji Medical College of Huazhong University of Science and Technology, Wuhan, China.

AUTHOR CONTRIBUTIONS

XS, SY, and YG conceived and designed the study. JF and ZL participated in the acquisition of data. XS and SY analyzed the data and drafted the manuscript. HC, YZ, and ZN provided advice for the methodology. YG, CL, and XH revised the manuscript. YG is the guarantor of this work and had full access to all the data in the study and takes responsibility for its integrity and the accuracy of the data analysis. All authors contributed to the article and approved the submitted version.

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COVID-19 Vaccine Uptake, Acceptance, and Hesitancy Among Persons With Mental Disorders During the Second Stage of China's Nationwide Vaccine Rollout

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Persons with mental disorders (PwMDs) are a priority group for COVID-19 vaccination, but empirical data on PwMDs' vaccine uptake and attitudes toward COVID-19 vaccines are lacking. This study examined the uptake, acceptance, and hesitancy associated with COVID-19 vaccines among Chinese PwMDs during China's nationwide vaccine rollout. In total, 906 adult PwMDs were consecutively recruited from a large psychiatric hospital in Wuhan, China, and administered a self-report questionnaire, which comprised standardized questions regarding sociodemographics, COVID-19 vaccination status, attitudes toward COVID-19 vaccines, and psychopathology. Vaccine-recipients were additionally asked to report adverse events that occurred following vaccination. PwMDs had a much lower rate of vaccination than Wuhan residents (10.8 vs. 40.0%). The rates of vaccine acceptance and hesitancy were 58.1 and 31.1%, respectively. Factors associated with vaccine uptake included having other mental disorders [odds ratio (OR) = 3.63], believing that ≥50% of vaccine-recipients would be immune to COVID-19 (OR = 3.27), being not worried about the side effects (OR = 2.59), and being an outpatient (OR = 2.24). Factors associated with vaccine acceptance included perceiving a good preventive effect of vaccines (OR = 12.92), believing that vaccines are safe (OR = 4.08), believing that ≥50% of vaccine-recipients would be immune to COVID-19 (OR = 2.20), and good insight into the mental illness (OR = 1.71). Adverse events occurred in 21.4% of vaccine-recipients and exacerbated pre-existing psychiatric symptoms in 2.0% of vaccine-recipients. Nevertheless, 95.2% of vaccine-recipients rated adverse events as acceptable. Compared to the 58.1% vaccine acceptance rate and the 40.0% vaccination rate in the general population, the 10.8% vaccine coverage rate suggested a large unmet need for COVID-19 vaccination in Chinese PwMDs. Strategies to increase vaccination

coverage among PwMDs may include provision of reliable sources of information on vaccines, health education to foster positive attitudes toward vaccines, a practical guideline to facilitate clinical decision-making for vaccination, and the involvement of psychiatrists in vaccine consultation and post-vaccination follow-up services.

Keywords: COVID-19, vaccine, uptake, acceptance, hesitancy, mental disorders, China

INTRODUCTION

During the ongoing COVID-19 pandemic, accumulating evidence has shown significant associations of pre-existing mental disorders with an increased risk of COVID-19 infection and COVID-19-related physical complications and mortality (1–3). Accordingly, there have been increasing calls for prioritizing persons with mental disorders (PwMDs) for COVID-19 vaccination, and a few countries have prioritized PwMDs in their updated vaccination strategies (4–6). Findings from acceptability studies of COVID-19 vaccines have revealed that the intention to get vaccinated against COVID-19 is associated with an individual's psychological characteristics (7, 8). Due to the impaired insight and decision-making capacity of PwMDs, caution is needed when seeking informed consent from these individuals for COVID-19 vaccination (9). To maximize the uptake of COVID-19 vaccines among PwMDs, more targeted interventions are warranted. Importantly, empirical data on PwMDs' attitudes toward COVID-19 vaccination are a prerequisite for developing an effective vaccination strategy.

To date, the acceptance of and hesitancy toward COVID-19 vaccines have been extensively examined in general populations of various countries (7, 8, 10–16). In these studies, 37.3–83.6% of the adults were willing to receive the vaccine, while 17.1–62.6% of them were hesitant (11, 16). Commonly reported factors associated with acceptance included male sex, old age, fear of COVID-19 infection, and trust in the efficacy and safety of COVID-19 vaccines; while factors associated with hesitancy included concerns about the efficacy and side effects of COVID-19 vaccines, not having received the influenza vaccine, and no trustworthy information sources related to COVID-19 vaccines (11, 12, 14, 17, 18). However, available data regarding PwMDs' intention to get vaccinated and uptake of the COVID-19 vaccine have been very limited. To our knowledge, only one empirical study from Denmark has investigated the acceptability of COVID-19 vaccines among PwMDs (19). This study found an 84.8% acceptance rate of COVID-19 vaccines among PwMDs, which was slightly lower than that in the Danish general population (89.5%). Nevertheless, because considerable variations in COVID-19 vaccine acceptance rates in general populations have been observed across countries (10), it remains unknown whether PwMDs have similarly high acceptance rates in other countries. In addition, the relationships between vaccine acceptance and vaccination and psychiatric symptoms among PwMDs may inform the development of a focused vaccination strategy. Unfortunately, the aforementioned study did not focus on this topic.

A notable limitation of prior studies on COVID-19 vaccine acceptance is that almost all of them were conducted before COVID-19 vaccines were available to the public (20). Because determinants of vaccine acceptance are context-dependent and attitudes and beliefs toward vaccines are different between persons with and without mental disorders (20, 21), it is difficult to generalize the findings from prior studies to PwMDs during the recent mass rollout of COVID-19 vaccines. Furthermore, given the large gap between the intention and actual behavior to receive a vaccine against COVID-19 (20, 21), it is important to additionally examine the uptake of COVID-19 vaccines, but few studies have examined this topic. As suggested by an influenza vaccination study in the United States, the uptake rate of influenza vaccine is much lower in PwMDs than in the general population (28.4 vs. 40.9%) (22).

China's current nationwide COVID-19 vaccination program was implemented in a two-stage manner. The first stage, from December 2020 to January 2021, focused on nine subpopulations with a high risk for COVID-19 infection, including medical staff, inspection and quarantine personnel, international migrant workers, and cold-chain food workers (15). The second stage focused on adult residents and was launched since February 2021, a period when COVID-19 vaccines had been widely available for Chinese residents (23). To increase the accessibility of vaccine administration services, vaccines are freely provided to all residents by the Chinese government, and all community-dwelling residents could conveniently take vaccines at primary care facilities nearest to their residence places. Nevertheless, in China, PwMDs are not listed in the priority subpopulations for COVID-19 vaccines (9). Moreover, there are also no clinical guidelines for the vaccination in PwMDs (23, 24), which may result in difficulties in clinical decision-making regarding COVID-19 vaccination in this population. For example, since the nationwide COVID-19 vaccination program, in our hospital, an increasing number of psychiatric patients have sought clarifications on their eligibility to receive the vaccine, but no clear answers were provided.

In China, some debates exist as to whether PwMDs should be prioritized to take COVID-19 vaccines (9). Given the importance of patient involvement in clinical decision-making process (25), understanding PwMDs' attitudes toward COVID-19 vaccines would facilitate the decision making for vaccination in this vulnerable population. In addition, first-hand data on vaccination status among PwMDs and vaccinated PwMDs' post-vaccination experiences are helpful for developing an effective vaccination strategy in this population. Research questions to be answered in this study are (i) How many psychiatric patients have got vaccinated and how many PwMDs are willing

to take the vaccines? (ii) What factors are associated with uptake and acceptance of the vaccines? and (iii) What are the subjective experiences of PwMDs after getting vaccinated? This study examined acceptance, hesitancy, and uptake of COVID-19 vaccines in Chinese PwMDs during the second stage of China's nationwide vaccine rollout, as well as the subjective experiences of vaccine-recipients among PwMDs.

METHODS

Subjects and Settings

Between March 24 and April 27, 2021, a cross-sectional survey was conducted at Wuhan Mental Health Center, which is the largest psychiatric specialty hospital in Wuhan, China. The center has 950 inpatient beds and mainly provides mental health services to local residents, with catchment areas of ∼ 10 million people. The average annual total number of outpatient visits and hospital admissions were 330,000 and 11,000, respectively, in the past 5 years. We consecutively enrolled both outpatients and inpatients who were 18 years old or older, had confirmed diagnoses of mental disorders, sought psychiatric treatment at the center during the survey period, and were deemed "able to complete the survey" by their treating psychiatrists, and voluntarily participated in the study. We excluded patients who had been infected with COVID-19 and those who were considered "unable to complete the survey" due to severe physical illnesses or cognitive disorders by their treating psychiatrists. According to an official report, the total number of COVID-19 vaccination doses administered in Wuhan had reached ∼4 million by April 7, 2021 (26), translating to a vaccine uptake rate of roughly 40.0% in Wuhan residents during the period of our survey.

Vaccine acceptance was the primary outcome of interest of this study. In our pilot study, the prevalence of vaccine acceptance was 52.9%. Therefore, parameters needed for estimating the sample size of this cross-sectional study were set as below (27): (1) a prevalence of 0.53, (2) a confidence interval of 95%, (3) a confidence interval width of 0.07, and (4) a response rate of 0.90. By using PASS 11 (LLC, Kaysville, UT, USA), the minimum sample size of PwMDs was estimated to be 898.

The authors assert that all procedures contributing to this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study protocol was approved by the Institutional Review Board of Wuhan Mental Health Center. Informed consent was obtained from the participating patients or their guardians when necessary.

Procedures and Measures

All participants completed a self-administered anonymous questionnaire, which was provided in an online or paper-pencil manner, depending on participants' preference. Six trained psychiatrists and master students in clinical psychology were assigned to recruit participants, facilitate the completion of the questionnaire, and check the quality of the questionnaire before submission. These investigators also read out questions for participants who had difficulties in completing the questionnaire. Before the main study, a pilot study ($n = 17$) was conducted to test the feasibility of study procedures and questionnaire, and the survey questionnaire was finalized thereafter.

Sociodemographic variables in the questionnaire included sex, age, education, marital status, and self-rated family financial status (good, fair, poor).

We used a checklist to assess the presence of chronic medical conditions (28), including heart disease, hypertension, stroke and other cerebrovascular diseases, diabetes, chronic obstructive pulmonary disease, cancer, chronic nephritis, and chronic hepatitis.

Risk perception of COVID-19 (**Table 1**). Five questions were used to assess participants' perceived likelihood of COVID-19 infection, risk of death due to COVID-19 if a person were infected, infectivity of COVID-19, and level of agreement on large-scale secondary outbreaks of COVID-19 in China.

Two questions were used to assess the negative impact of the COVID-19 pandemic on the economic income and current daily life of PwMDs (**Table 1**).

COVID-19 vaccination and attitudes toward COVID-19 vaccines (**Table 1**). Participants were asked whether they agreed that PwMDs should take COVID-19 vaccines, whether they had taken the COVID-19 vaccine, and whether they were willing to take a COVID-19 vaccine. In accordance with previous studies, persons who were willing to take the vaccine were vaccine-accepting individuals, while persons who were unwilling or unsure about taking the vaccine were vaccine-hesitant individuals (18, 29). Other attitude questions included the perceived preventive effect of COVID-19 vaccines, perceived percentage of vaccine-recipients who would be immunized to COVID-19, perceived safety of COVID-19 vaccines, and worry about side effects of COVID-19 vaccines.

Clinical Characteristics

Clinical variables included clinical setting (outpatient vs. inpatient), primary diagnosis of mental disorder, family history of mental disorders, insight into mental disorders, and psychiatric symptoms. Two items adapted from the Chinese Insight and Treatment Attitudes Questionnaire (30), were used to assess patients' insight into mental disorders: "Do you agree that you have a mental health problem?" and "Do you agree that you are in need of psychiatric treatment to manage your mental health problem or maintain your mental health?" Each question was rated on a three-point scale: 1 = completely agree, 2 = partly agree, and 3 = disagree. Total scores of the two insight items of two, three to five, and six were operationally defined as good, partial, and poor insight, respectively. Depressive symptoms were assessed with the Chinese two-item version of Patient Health Questionnaire (PHQ-2) (31). In China, a cutoff score of two or more is used to denote the presence of clinically significant depressive symptoms (32). Insomnia symptoms were assessed by asking the following question: "In the past month, how often do you have difficulties falling asleep, maintaining sleep, or waking too early and getting back to sleep?" (33). Responses were coded as no, occasionally, sometimes, often, and always. Respondents

TABLE 1 | Questions used for assessing risk perception of COVID-19, negative impact of the COVID-19 pandemic, COVID-19 vaccination, and attitudes toward COVID-19 vaccines in the survey questionnaire.

Variables	Questions	Response option
Risk perception of COVID-19		
Likelihood of COVID-19 infection	Would you please give me an estimate of the likelihood that you would be infected with COVID-19?	Very high, high, low, very low
Risk of death due to COVID-19 infection	To the best of your knowledge, what is the possibility of dying due to COVID-19 if a person were infected with COVID-19?	Very high, high, low, very low, unknown
Infectivity of COVID-19	To the best of your knowledge, what is the infectivity of COVID-19?	Very high, high, low, very low
Re-outbreak of COVID-19	Do you agree that there would be another large-scale COVID-19 outbreak in the future in China?	Very agree, agree, disagree, very disagree
Negative impact of the COVID-19 pandemic		
Economic income	What is the impact of the COVID-19 pandemic on your income?	No impact, decrease, substantial decrease
Daily life	What is the impact of the COVID-19 pandemic on your current daily life?	No impact, inconvenience, substantial inconvenience
COVID-19 vaccination		
General attitude toward COVID-19 vaccination	Do you agree that persons with mental disorders should take COVID-19 vaccines?"	Agree, disagree, unknown
Vaccine acceptance and hesitancy	Are you willing to take a COVID-19 vaccine?	Yes, no, unsure
Vaccine uptake	Have you taken the COVID-19 vaccine?	Yes, no
Attitudes toward COVID-19 vaccines		
Preventative effect of COVID-19 vaccines	To what extent do you agree that COVID-19 vaccines are effective in preventing COVID-19?"	Very agree, agree, disagree, very disagree
% of immunized persons among vaccine-recipients	To the best of your knowledge, how many people would be immunized to COVID-19 after getting vaccines against COVID-19?	All, most, a half, some, none
Safety of COVID-19 vaccines	To the best of your knowledge, how safe is the COVID-19 vaccine?	Very safe, safe, unsafe, very unsafe
Worry about side effects of COVID-19 vaccines	Are you worried about side effects of the COVID-19 vaccine?	Very worried, worried, not worried
Subjective experiences of vaccine-recipients		
Side effects	Do you have any of the following side effects after taking the COVID-19 vaccine?	None, deterioration of pre-existing psychiatric symptoms, local adverse reactions (i.e., injection site pain, itching, induration, redness, swelling), fatigue, fever, muscle pain, headache, cough, diarrhea, nausea, anorexia, allergy, others (please indicate_____)
Acceptability of side effect	Do you think that the above reported side effects are acceptable?	Acceptable, unacceptable

answering "often" and "always" to the question were classified as having insomnia symptoms.

Subjective experiences of COVID-19 vaccine-recipients. Vaccine-recipients were additionally asked to report side effects that occurred after receiving the COVID-19 vaccine, in particular the exacerbation of pre-existing psychiatric symptoms and acceptability of side effects (**Table 1**).

Statistical Analysis

Prevalence rates of vaccination and vaccine acceptance and hesitancy were calculated. Chi-square test was used to compare sociodemographic characteristics, risk perception of COVID-19, perceived negative impact of the COVID-19 pandemic, attitudes toward COVID-19 vaccines, and clinical characteristics between vaccine-recipients and vaccine-hesitant individuals. The Multiple logistic regression model with a backward stepwise entry of all significant variables in the Chi-square test was used to identify factors associated with the vaccine uptake. Specifically, the backward stepwise model started with all significant variables from the univariate analysis, and then removed the variable with the largest P value. Next, the model was refitted and the variable with the largest *P*-value in the new model was removed. This process was repeated to eliminate variables one-by-one until no further variables can be deleted without a statistically insignificant loss of fit (34). Factors associated with vaccine acceptance were identified in the same manner. The subjective experiences of vaccine-recipients were presented as frequencies and percentages. Odds ratios (ORs) and their 95% confidence intervals (95% CIs) were used to quantify associations between factors and outcomes. The statistical significance level was set at

TABLE 2 | Characteristics of COVID-19 vaccine-recipients and vaccine-accepting individuals in comparison to vaccine-hesitant individuals among Chinese persons with mental disorders (PwMDs), *n* (%).

Variables		Total sample (*n* = 906)	Vaccine-recipients (*n* = 98)	Vaccine-accepting individuals (*n* = 526)	Vaccine-hesitant individuals (*n* = 282)	Take vs. hesitancy		Acceptance vs. hesitancy	
						χ2	*P*	χ2	*P*
Sociodemographic									
Sex	Male	355 (39.2)	31 (31.6)	217 (41.3)	107 (37.9)	1.252	0.263	0.838	0.360
	Female	551 (60.8)	67 (68.4)	309 (58.7)	175 (62.1)				
Age group (years)	18-34	477 (52.6)	49 (50.0)	291 (55.3)	137 (48.6)	3.827	0.148	6.642	0.036
	35-44	286 (31.6)	37 (37.8)	162 (30.8)	87 (30.9)				
	45+	143 (15.8)	12 (12.2)	73 (13.9)	58 (20.6)				
Education	Middle school and below	498 (55.0)	39 (39.8)	288 (54.8)	171 (60.6)	12.779	<0.001	2.592	0.107
	College or above	408 (45.0)	59 (60.2)	238 (45.2)	111 (39.4)				
Marital status	Never-married	464 (51.2)	40 (40.8)	281 (53.4)	143 (50.7)	8.713	0.013	1.195	0.550
	Married, remarried, or cohabiting	330 (36.4)	50 (51.0)	182 (34.6)	98 (34.8)				
	Divorced, separated, or widowed	112 (12.4)	8 (8.2)	63 (12.0)	41 (14.5)				
Family financial status	Good	152 (16.8)	27 (27.6)	79 (15.0)	46 (16.3)	7.935	0.019	1.575	0.455
	Fair	598 (66.0)	60 (61.2)	358 (68.1)	180 (63.8)				
	Poor	156 (17.2)	11 (11.2)	89 (16.9)	56 (19.9)				
Chronic medical condition	No	695 (76.7)	81 (82.7)	403 (76.6)	211 (74.8)	2.506	0.113	0.324	0.569
	Yes	211 (23.3)	17 (17.3)	123 (23.4)	71 (25.2)				
Risk perception of COVID-19									
Likelihood of COVID-19 infection	Low	816 (90.1)	88 (89.8)	468 (89.0)	260 (92.2)	0.544	0.461	2.141	0.143
	High	90 (9.9)	10 (10.2)	58 (11.0)	22 (7.8)				
Risk of death due to COVID-19 infection	Low	282 (31.1)	37 (37.8)	145 (27.6)	100 (35.5)	3.971	0.137	16.387	<0.001
	High	476 (52.5)	49 (50.0)	305 (58.0)	122 (43.3)				
	Unknown	148 (16.3)	12 (12.2)	76 (14.4)	60 (21.3)				
Infectivity of COVID-19	Low	107 (11.8)	12 (12.2)	50 (9.5)	45 (16.0)	0.786	0.375	7.365	0.007
	High	799 (88.2)	86 (87.8)	476 (90.5)	237 (84.0)				
Large-scale re-outbreak of COVID-19	Disagree	728 (80.4)	75 (76.5)	422 (80.2)	231 (81.9)	1.345	0.246	0.337	0.562
	Agree	178 (19.6)	23 (23.5)	104 (19.8)	51 (18.1)				
Negative impact of the COVID-19 pandemic									
Economic income	No impact	445 (49.1)	52 (53.1)	234 (44.5)	159 (56.4)	0.325	0.569	10.400	0.001
	Reduction	461 (50.9)	46 (46.9)	292 (55.5)	123 (43.6)				
Daily life	No impact	324 (35.8)	39 (39.8)	174 (33.1)	111 (39.4)	0.006	0.940	3.173	0.075
	Inconvenience	582 (64.2)	59 (60.2)	352 (66.9)	171 (60.6)				
Attitudes toward COVID-19 vaccines									
COVID-19 vaccination in PwMDs	Agree	561 (61.9)	79 (80.6)	411 (78.1)	71 (25.2)	93.617	<0.001	218.224	<0.001
	Disagree	76 (8.4)	4 (4.1)	18 (3.4)	54 (19.1)				
	Unknown	269 (29.7)	15 (15.3)	97 (18.4)	157 (55.7)				

(Continued)

TABLE 2 | Continued

Variables		Total sample (n = 906)	Vaccine-recipients (n = 98)	Vaccine-accepting individuals (n = 526)	Vaccine-hesitant individuals (n = 282)	Take vs. hesitancy		Acceptance vs. hesitancy	
						χ^2	P	χ^2	P
Preventive effect of vaccines	Good	852 (94.0)	94 (95.9)	522 (99.2)	236 (83.7)	9.520	0.002	76.482	<0.001
	Bad	54 (6.0)	4 (4.1)	4 (0.8)	46 (16.3)				
% of immunized persons among vaccine-recipients	≥50%	842 (92.9)	94 (95.9)	509 (96.8)	239 (84.8)	8.367	0.004	38.560	<0.001
	<50%	64 (7.1)	4 (4.1)	17 (3.2)	43 (15.2)				
Safety of vaccines	Safe	854 (94.3)	94 (95.9)	518 (98.5)	242 (85.8)	7.250	0.007	52.686	<0.001
	Unsafe	52 (5.7)	4 (4.1)	8 (1.5)	40 (14.2)				
Worry about the side effects of vaccines	Worried	568 (62.7)	48 (49.0)	315 (59.9)	205 (72.7)	18.382	<0.001	13.131	<0.001
	Not worried	338 (33.3)	50 (51.0)	211 (40.1)	77 (27.3)				
Clinical									
Setting	Outpatient	317 (35.0)	54 (55.1)	164 (31.2)	99 (35.1)	12.090	0.001	1.290	0.256
	Inpatient	589 (65.0)	44 (44.9)	362 (68.8)	183 (64.9)				
Family history of mental disorder	Yes	198 (21.9)	19 (19.4)	121 (23.0)	58 (20.6)	0.063	0.802	0.632	0.427
	No	708 (78.1)	79 (80.6)	405 (77.0)	224 (79.4)				
Diagnosis	Psychotic disorders	231 (25.5)	10 (10.2)	149 (28.3)	72 (25.5)	20.995	<0.001	5.628	0.131
	Mood disorders	316 (34.9)	23 (23.5)	198 (37.6)	95 (33.7)				
	Anxiety disorders	117 (12.9)	16 (16.3)	67 (12.7)	34 (12.1)				
	Other disorders	242 (26.7)	49 (50.0)	112 (21.3)	81 (28.7)				
Insight into mental disorders	Poor	186 (20.5)	33 (33.7)	86 (16.3)	67 (23.8)	3.930	0.140	8.024	0.018
	Partial	455 (50.2)	41 (41.8)	271 (51.5)	143 (50.7)				
	Good	265 (29.2)	24 (24.5)	169 (32.1)	72 (25.5)				
Depressive symptoms	No	360 (39.7)	54 (55.1)	196 (37.3)	110 (39.0)	7.680	0.006	0.238	0.626
	Yes	546 (60.3)	44 (44.9)	330 (62.7)	172 (61.0)				
Insomnia symptoms	No	682 (75.3)	78 (79.6)	401 (76.2)	203 (72.0)	2.184	0.139	1.757	0.185
	Yes	224 (24.7)	20 (20.4)	125 (23.8)	79 (28.0)				

$P < 0.05$ (two-sided). SPSS software version 18.0 package (SPSS Inc., Chicago, IL, USA) was used for all analyses.

RESULTS

Our analysis included a final sample of 906 psychiatric patients: 317 outpatients (35.0%) and 589 inpatients (65.0%). The average age of this sample was 36.2 years (standard deviation [SD]: 13.2, range: 18-78) and 355 (39.2%) were men. Detailed sociodemographic, COVID-19-related, and clinical characteristics of the total sample are displayed in the third column of **Table 2**.

In total, 561 patients (61.9%) agreed that PwMDs should take COVID-19 vaccines, 98 (10.8%) had taken the vaccine at the time of this survey, 526 (58.1%) reported that they were willing to take the vaccine, and 282 (31.1%) were hesitant to take the vaccine (17.1% unwilling and 14.0% unsure).

Compared to vaccine-hesitant persons, vaccine-recipients were more likely to have a college-level education or above (60.2 vs. 39.4%, $P < 0.001$), be married, remarried, or cohabiting (51.0 vs. 34.8%, $P = 0.013$), rate their family financial status as "good" (27.6 vs. 16.3%, $P = 0.019$), agree that the preventive effect of vaccines is good (95.9 vs. 83.7%, $P = 0.002$), believe that at least half of vaccine-recipients would be immune to COVID-19 (95.9 vs. 84.8%, $P = 0.004$), believe that vaccines are safe (95.9 vs. 85.8%, $P = 0.007$), be not worried about the side effects of vaccines (51.0 vs. 27.3%, $P < 0.001$), be outpatients (55.1 vs. 35.1%, $P = 0.001$), have mental disorders other than psychotic, mood, and anxiety disorders (50.0 vs. 28.7%, $P < 0.001$), and be not depressed (55.1 vs. 39.0%, $P = 0.006$) (**Table 2**). In the multiple logistic regression, factors significantly associated with vaccine uptake were an educational attainment of college or above (OR = 1.99, $P = 0.010$), a good family financial status (OR = 2.76, $P = 0.027$), believing that ≥50% of vaccine-recipients would be immune to COVID-19 (OR = 3.27, $P = 0.034$), being not worried about the side effects of vaccines (OR = 2.59, $P < 0.001$), being outpatients (OR = 2.24, $P = 0.003$), and having other mental disorders (OR = 3.63, $P = 0.001$) (**Table 3**).

Compared to vaccine-hesitant persons, vaccine-accepting individuals were more likely to be aged 18-34 years (55.3 vs. 48.6%, $P = 0.036$), perceive a high risk of death due to COVID-19 infection (58.0 vs. 43.3%, $P < 0.001$), rate the infectivity of COVID-19 as high (90.5 vs. 84.0%, $P = 0.007$), have reduced income due to the COVID-19 pandemic (55.5 vs. 43.6%, $P = 0.001$), agree that the preventive effect of vaccines is good (99.2 vs. 83.7%, $P < 0.001$), believe that ≥50% of the vaccine-recipients would be immune to COVID-19 (96.8 vs. 84.8%, $P < 0.001$), believe that vaccines are safe (98.5 vs. 85.8%, $P < 0.001$), be not worried about the side effects of vaccines (40.1 vs. 27.3%, $P < 0.001$), and have good insight into mental disorders (32.1 vs. 25.5%, $P = 0.018$) (**Table 2**). In the multiple logistic regression, factors significantly associated with vaccine acceptance were perceiving a high risk of death due to COVID-19 infection (OR = 1.64, $P = 0.007$), having reduced income due to the COVID-19 pandemic (OR = 1.68, $P = 0.002$), perceiving a good preventive effect of vaccines (OR = 12.92, $P < 0.001$), believing that ≥50% of vaccine-recipients would be immune to COVID-19 (OR = 2.20, $P = 0.029$), believing that vaccines are safe (OR = 4.08, $P = 0.001$), and having good insight into mental disorders (OR = 1.71, $P = 0.024$)

TABLE 3 | Factors associated with COVID-19 vaccine uptake and acceptance among Chinese persons with mental disorders (reference category: vaccine hesitancy).

Variables		OR (95%CI)	*P*
Vaccine uptake			
Education	Middle school or below	1	
	College or above	1.99 (1.18, 3.35)	0.010
Family financial status	Poor	1	
	Good	2.76 (1.13, 6.79)	0.027
% of immunized persons among vaccine-recipients	<50% ≥50%	1 3.27 (1.10, 9.73)	0.034
Worry about the side effects of vaccines	Worried	1	
	Not worried	2.59 (1.53, 4.39)	<0.001
Setting	Inpatient	1	
	Outpatient	2.24 (1.33, 3.79)	0.003
Diagnosis	Psychotic disorders	1	
	Other disorders	3.63 (1.65, 8.01)	0.001
Vaccine acceptance			
Risk of death due to COVID-19 infection	Low	1	
	High	1.64 (1.14, 2.36)	0.007
Negative impact of the COVID-19 pandemic on economic income	No impact Reduced	1 1.68 (1.22, 2.31)	0.002
Preventive effect of domestic vaccines	Bad	1	
	Good	12.92 (4.41, 37.85)	<0.001
% of immunized persons among vaccine-recipients	<50% ≥50%	1 2.20 (1.08, 4.45)	0.029
Safety of domestic vaccines	Unsafe	1	
	Safe	4.08 (1.72, 9.65)	0.001
Insight into mental disorder	Poor	1	
	Good	1.71 (1.07, 2.73)	0.024

Among the 98 vaccine-recipients, 21 (21.4%) reported at least one adverse event (**Table 4**); of whom 20 (95.2%) believed these side effects were acceptable while only one (4.8%) felt unacceptable because of muscle pain. The most common adverse event was local adverse reactions ($n = 9$, 9.2%), followed by muscle pain ($n = 7$, 7.1%). Two patients (2.0%) endorsed exacerbated psychiatric symptoms after the vaccine uptake (**Table 4**).

DISCUSSION

To the best of our knowledge, this is the first study in China that examined the uptake and acceptance of COVID-19 vaccines among PwMDs during the second stage of China's nationwide vaccine rollout. The main findings of this study are: first, the vaccination rate among PwMDs was 10.8%, which was

TABLE 4 | Adverse events after getting the COVID-19 vaccine among the 98 COVID-19 vaccine-recipients.

Adverse event	*n* (%)
None	77 (78.6)
Any adverse event	21 (21.4)
Deterioration of pre-existing psychiatric symptoms	2 (2.0)
Local adverse reactions	9 (9.2)
Fatigue	2 (2.0)
Fever	1 (1.0)
Muscle pain	7 (7.1)
Headache	2 (2.0)
Cough	0 (0.0)
Diarrhea	1 (1.0)
Nausea	2 (2.0)
Anorexia	0 (0.0)
Allergy	0 (0.0)
Others	1 (0.0)

much lower than the 40.0% concurrent vaccination rate among Wuhan residents; second, the rates of vaccine acceptance and hesitancy among PwMDs were 58.1 and 31.1%, respectively; third, in addition to sociodemographic variables, COVID-19-related and clinical factors were associated with vaccine uptake and acceptance; and, fourth, although adverse events occurred in 21.4% of the vaccine-recipients, the vast majority (95.2%) of PwMDs reported that the adverse events they experienced were acceptable. Notably, 2.0% of the vaccine-recipients reported exacerbated pre-existing psychiatric symptoms.

In the Chinese general population, rates of vaccine acceptance and hesitancy were 67.1-88.6 and 11.4-32.9%, respectively (10, 15). Compared to the general population, PwMDs have a slightly lower level of acceptance and a relatively higher level of hesitancy, suggesting that PwMDs are less willing to get vaccinated. Nevertheless, the relatively low acceptance rate should not be the primary reason for the very low vaccine coverage rate among PwMDs. Jefsen and colleagues have argued that vaccine hesitancy is not a major barrier for vaccine uptake among PwMDs in Denmark (19). Accordingly, the present study revealed a very large gap between vaccine acceptance and uptake rates (58.0 vs. 10.8%) in Chinese PwMDs. We speculate that other barriers to vaccination that are specific to mental disorders in China may complicate vaccine uptake such as controversy regarding the priority of PwMDs for COVID-19 vaccination, stigma surrounding mental disorders, impaired decision-making ability of PwMDs, and lack of clinical guidelines for vaccination for PwMDs.

In prior studies, a high level of education, major medical conditions, and trust in the efficacy, safety, and benefits of the COVID-19 vaccine were significant factors associated with vaccine uptake in the general population (15, 20). Similarly, in the present study, having a college-level education or above, believing that ≥50% of vaccine-recipients would be immune to COVID-19, and being not worried about the side effects of the vaccine were significant factors associated with vaccine uptake in PwMDs. Since vaccines are provided free of charge in China, the significant association between good family economic status and vaccine uptake should not be ascribed to the higher vaccine affordability for economically advantageous PwMDs. We speculate that PwMDs with a good economic status might have less burden of childcare and be more likely to use smartphones to successfully make appointments for COVID-19 vaccination.

Among PwMDs, we did not replicate significant relationships of vaccine acceptance with sociodemographic factors that have been reported in the general population (11, 12, 14, 17, 18). Instead, only COVID-19-related factors were associated with vaccine acceptance such as risk perception of COVID-19 and perceived efficacy and safety of the COVID-19 vaccine, which are partly consistent with findings from general population-based studies (11, 12, 14, 15, 17, 18, 20). These findings are interesting given that knowledge and attitudes toward COVID-19 and vaccines are modifiable and can be improved via health education (35).

The unique findings of this study are associations between some clinical factors and vaccine acceptance and uptake among PwMDs. Because the rollout of COVID-19 vaccines is community-based in China, a significantly higher uptake rate in outpatients than in inpatients is expected. In the current study, persons with psychotic disorders were least likely to take the vaccine, which may be attributed to the severe impairment in decisional capacity of these people (36). For example, evidence from theory of mind studies shows that patients with schizophrenia significantly accept more disadvantageous offers and reject more advantageous offers (37). Overall, COVID-19 vaccination is beneficial for the health of patients with schizophrenia but with some uncertainties about the efficacy and safety; thus, these patients are more likely to delay or reject vaccination. PwMDs with good insight are more aware of the need for treatments to maintain their health, including vaccination; therefore, a significant positive association between good insight and vaccine acceptance is expected.

The results from the official surveillance report of adverse events of COVID-19 vaccines in China indicate that adverse reactions to COVID-19 vaccines are rare in Chinese residents and that most adverse reactions are normal reactions, such as fever and swelling (38). In this study, we investigated a broad range of adverse events by self-report. Although over one-fifth of the vaccine-recipients reported adverse events, these events were generally acceptable, suggesting the good safety of COVID-19 vaccines for PwMDs. Nevertheless, the 2.0% rate of exacerbated pre-existing psychiatric symptoms indicates that psychiatric follow-up is needed for PwMDs following the vaccination.

This study has several limitations. First, the study was conducted only during the early to middle period of the nationwide massive inoculation of vaccines; therefore, the current situations of vaccination in PwMDs during the late period of the massive inoculation of vaccines remain unclear. Second, our data on the safety of vaccines for PwMDs are preliminary given the small number of PwMDs who were vaccinated ($n = 98$). Third, this is a cross-sectional study; thus, the causal relationships between factors and vaccine

uptake and acceptance need to be further examined in longitudinal studies. Fourth, a qualitative in-depth interview is useful for understanding the barriers to vaccination among PwMDs but we did not perform it. Finally, our assessment of psychiatric symptoms, based on self-report measures without verification from treating psychiatrists, might be subject to subjective bias. In addition, there might be social desirability bias in the results of assessment of PwMDs' attitudes toward COVID-19 vaccines.

In China, 17.5% of the adults suffer from a mental disorder during the prior month (39); therefore, to achieve the 80% COVID-19 herd immunity threshold, COVID-19 vaccination of PwMDs should not be neglected. In this study, ∼60% of the PwMDs were willing to take the vaccine but only 10.8% of them were vaccinated. Our study revealed large discrepancies in the rates of vaccine acceptance and uptake among PwMDs and in the rates of COVID-19 vaccination coverage between PwMDs and the general population, which indicates that removing barriers to vaccination to increase PwMDs' vaccination coverage is an urgent task for both public health and mental health workers. Although our preliminary data show that vaccines are generally safe for PwMDs, the significant relationships between some clinical factors and vaccine uptake and acceptance suggest that the clinical characteristics of PwMDs should be considered in the development of targeted intervention strategies. PwMDs-specific strategies may include provision of reliable sources of information on vaccines, health education to improve their awareness of the efficacy and safety of vaccines, the development of a specialized guideline to facilitate primary care physicians' clinical decision-making for vaccination, joint vaccine consultation services that involve immunologists and psychiatrists, and psychosocial support and post-vaccination psychiatric follow-up services to prevent the relapse of mental disorders. In addition, more studies are warranted to recognize barriers to vaccination in PwMDs.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Institutional Review Board of Wuhan Mental Health Center. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

B-LZ and HH designed the study, conducted the analyses, and wrote the initial version of this manuscript. HH, X-MZ, P-WL, Z-MF, WL, and Y-MM collected the sample and performed the literature review. X-MZ and HF-KC revised the manuscript. All authors edited, read, and approved the last version of this manuscript.

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OPINION
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Discussing the Drawbacks of the Implementation of Access and Benefit Sharing of the Nagoya Protocol Following the COVID-19 Pandemic

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Keywords: COVID-19 pandemic, Nagoya protocol, ABS, genetic resources, DSI

INTRODUCTION

"When we think of the major threats to our national security, the first to come to mind are nuclear proliferation, rogue states, and global terrorism. But another kind of threat lurks beyond our shores, one from nature, not humans - an avian flu pandemic" (1). In 2005, Barack Obama and Richard Lugar identified and vocalized the need for a permanent framework that would be used in reducing the spread of infectious diseases. In the realm of infectious diseases, a pandemic is always the worst-case scenario. With over 200,000,000 globally confirmed cases and over 4 million deaths, COVID-19 is the reason behind the turbulent start of a new decade; COVID-19 also marks the beginning of a new era where nothing in the world will ever be the same (2). The pandemic has induced several vast changes that have resulted in the adaptation of a new way of life. We have experienced unprecedented social and economic disruptions that have pointed out the significance of rapid pandemic response and recovery mechanisms.

Both the samples and the digital sequence information (DSI) of the SARS-CoV-2 that causes COVID-19 were collected and called to be part of the operationalization of fair and equitable benefit sharing, as recognized by the Convention for Biological Diversity and Nagoya Protocol (3). The rapid sharing of these samples and their DSI have been pivotal to the discovery of research work in diagnostic, therapeutics, and COVID-19 vaccine development. Forty global and regional civil society organizations, 228 national organizations, and 124 individuals from 77 countries expressed the need to the UN Secretary-General and the WHO Director-General to facilitate a "coordinated global research roadmap" to rapidly find a solution to COVID-19. Countries, organizations, institutes, conglomerates, and scientists have all come together to fight the battle against this modern-day pandemic.

The first genetic sequence data for SARS-CoV-2 was generated by the Chinese Center for Disease Control and Prevention in a record time of 16 days after the Wuhan outbreak in January 2020 and a week after Beijing's outbreak in June 2020 (4). The same authors revealed that data was freely and rapidly shared with the Global Initiative of Sharing All Influenza Data. Similar to influenza, SARS-CoV-2 has mutated and already spread around the world. Keeping in mind the provisions and legally binding obligations arising from the Nagoya Protocol, an issue of concern is whether China would have been able to rapidly share the SARS-CoV-2 genetic sequences had it followed the requisite procedures. COVID-19 serves as a reminder that frameworks governing the use of genetic resources should avoid impeding the research community, especially in emergencies. However, these laws should be structured in a way that does not undermine the sovereignty of countries over their genetic resources, be they pathogens of other forms of biological material.

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In 2020, the pandemic resulted in various travel bans and restrictions. It also wreaked havoc on economic activity, resulting in what seems to be the present-day "stock-market crash" (5). Multiple businesses have been forced to close their doors, turning their backs on their employees. Furthermore, because of nationwide lockdowns, the non-essential workers are left confined to their homes. Some countries have taken different approaches varying from total confinement (early days in China), partial lockdown (Kenya), and to more flexible methods (Sweden).

BRIEF LEGISLATIVE FRAMEWORK BACKGROUND

As sequentially illustrated by **Figure 1**, the tenth meeting of the Conference of the Parties (COP10) to the Convention on Biological Diversity (CBD) was held in Nagoya, Aichi Prefecture on the October 18, 2010 (6). The 10-day conference had over 13,000 participants from different parties to the convention, relevant international, and nongovernmental organizations (6). A key priority for this meeting was the initiative to support the compilation of national strategies on biological diversity aimed at assisting countries in the development of capacity building regarding access and benefit-sharing (ABS) related to genetic resources. COP10 adopted the Nagoya Protocol on ABS and the New Strategic Plan of the CBD (the "Aichi Target") from 2011 onward (6). The protocol officially came into force in 2014 (7).

FIGURE 1 | Legislative framework background.

The Nagoya Protocol is an internationally binding treaty, and the third component of the protocol highlights the "fair and equitable sharing of the benefits arising out of the utilization of genetic resources" (7). Focusing primarily on the third objective of the CBD, the Nagoya Protocol defined the "rules of the game" outlining the requisite sharing of genetic resources between countries (8). It determines that the genetic resources in principle are owned by the country where they have been found or by whoever the government decides to grant ownership to.

The Nagoya Protocol enforces the concept of state sovereignty by giving countries the ability to determine, control, and monitor the use of biological material accessed within their territory (7). This is guaranteed by way of Material Transfer Agreements (MTAs), Prior Informed Consent (PIC), and Mutually Agreed Terms (MAT) between the Provider and the User. The aforementioned is catered for in Article 6 of the Protocol. Before any transfer of genetic material occurs, a consortium must be in place. The users of the genetic material must comply with the requisite procedures and domestic laws of the providing country. All parties must agree on the terms before the transfer of the material. These negotiations, procedures, and technicalities often consume a lot of time as every party is trying to ensure the transaction protects their rights and interests unequivocally.

Despite the strengths and flaws in its implementation framework as illustrated in **Figure 2**, Article 4 (2) of the Nagoya Protocol provides that "Nothing in this Protocol shall prevent the Parties from developing and implementing other relevant international agreements, including other specialized access and benefit-sharing agreements, provided that they are supportive of and do not run counter to the objectives of the Convention and this Protocol." As a result of the pandemic, the COVID-19 samples and genetic sequence information were called to be part of the operationalization of fair and equitable benefits sharing, as recognized by the Convention for Biological Diversity (CBD) and Nagoya Protocol. The WHO has specific frameworks in place that regulate and pandemics related to human health. Even though access and benefit sharing (ABS) is primarily catered for in the Nagoya Protocol, it leaves many gray areas on the standard mode of operation during a pandemic. There is a need to unpack the Nagoya Protocol in its entirety to understand the appropriate implementation during a pandemic.

Keeping in mind the working mechanism of the Nagoya Protocol, there is a need to understand the scope of genetic resources as this highlights the importance of this discussion during a worldwide pandemic. The term "Genetic Resources" refers to anything that contains genetic material (DNA, RNA) like plants, animals, microbes, and human beings (8). The Convention for Biological Diversity (CBD) - Nagoya Protocol (NP) regulates all of these except the human genome. However, in its definition of genetic resources, the terms used in the Nagoya Protocol have collectively been construed to include microbes (bacteria, parasites, viruses, and fungi) that may infect humans, animals, and plants. As a result, the use of pathogens for public health purposes is subject to the ABS requirements and procedures of individual countries (8). This automatically means that the country from which a virus sample was isolated has the sovereign authority to determine how and by whom that sample is utilized. This potentially affects all international sharing of any and such materials, even though they are to be used for public health purposes.

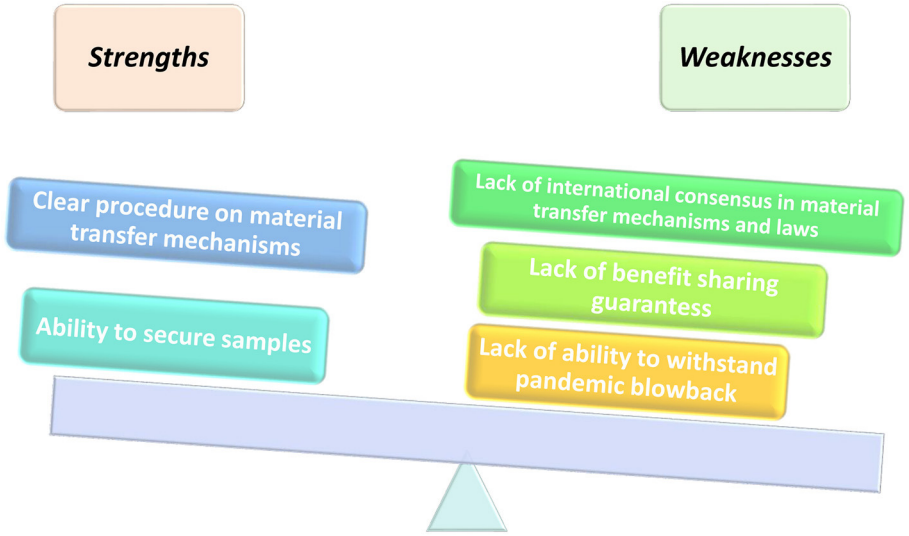

FIGURE 2 | Strengths and flaws of the current PIP framework.

THE NAGOYA PROTOCOL IMPLEMENTATION AND PUBLIC HEALTH IMPLICATIONS

The Director-General of the International Federation of Pharmaceutical Manufacturers (IFPMA) is of the view that the Nagoya Protocol potentially hinders research collaboration specifically in instances where the development of a new vaccine or treatment for a new virus or other pathogen is of utmost urgency (9). He further argues that had China followed the requirements of the Nagoya Protocol following the discovery of SARS-CoV-2, it could have embarked on discussions with each country, one by one, on how to share the sequence of this pathogen. This would have initiated the process of bilateral negotiations with the governments of all the interested countries. Subsequently, this would mean that the parties willing to access and use these genetic resources for outbreak-related research and response would have had to negotiate conditions bilaterally with governments for each material needed (8). Hypothetically speaking, in the event of an international scientific consortium that would require diagnostic testing for a new pathogen, the collation of samples from all affected countries would be imperative to this exercise and would require approval from all the member states to access and use the various samples. This is a very daunting scenario, especially during a public health crisis where time is very important. There are enormous demands for rapid access to information about this new virus, the patients and communities affected, and the response, but equally crucial is the need to ensure that this data is reliable, accurate, and independently scrutinized (9). As fate would have it, we are currently living in a time where we need not hypothesize these issues anymore. COVID-19 is a public health crisis, therefore it is a concern for all of humanity. Subsequently, this raises the need for an assessment on how pandemic preparedness and response as a global community has previously, currently, and potentially been affected by the current implementation of the Nagoya protocol.

It took slightly over a week for WHO to confirm the existence of the new coronavirus and for the Chinese scientists to publish its genetic sequence after the outbreak's first report. This efficiency and swiftness are the first of their kind. The rapidity of this information dispensation still remains unprecedented. This is only possible because the WHO's policy on ethical issues and outbreak management mandates the rapid sharing of data during an unfolding health emergency, as this aids in the identification of etiological factors, prediction of disease spread, evaluation of existing and novel treatments, symptomatic care and prevention measures, and lastly the guidance on the deployment of limited resources (9). Although this policy advances the efforts of the public health sector during an unfolding health emergency, it constitutes a breach of the Nagoya Protocol. There is a need to evaluate the magnitude of the effects occasioned on the public health sector as a result of the current implementation of the Nagoya Protocol, especially about existing and emerging infectious pathogens that require global research consortia to save lives.

As mentioned in the preceding sections of this study, the Nagoya Protocol enforces the concept of state sovereignty, giving countries the ability to set out conditions that determine the way their genetic material will be transferred and used. Viral sovereignty, as defined by Inkstone (10), continues to be an issue that has inadvertent effects on public health. In addition, political dissent always seems to push this agenda further. In 2007, Indonesia refused to give WHO their samples of an H5N1 influenza strain from an outbreak in the country until it was guaranteed fair access to any vaccines created from that material (10). Similarly, in 2018 and without any explanation, China withheld laboratory samples of the H7N9

bird flu despite repeated requests from the United States and the United Kingdom to share the material (11). In 2020, the United States Intelligence has accused Beijing of concealing information about the COVID-19 outbreak, claims that the Chinese authorities have rejected (12). Several other elements challenge the sovereignty claims that a country may lay on a virus. The transmissibility nature of the virus and its effect on the human population are some of the elements to consider.

The crux of the issue in this study is that time and time again, the global community has failed to reach a consensus on the scope of the exact obligations that States have to share genetic sequence information relating to pathogens, more so amid a worldwide pandemic. The ownership of pathogens and related information emerging in different states is part of a long-standing debate. A discussion that touches an exploitative colonial nerve suggests that wealthy countries still plunder the natural resources and biodiversity of poorer nations and are actively profiting from it (10). Furthermore, there are dissenting opinions about whether Digital Sequencing Information (DSI) is covered in the Nagoya protocol.

The US, European Union, and Japan have consistently argued that the NP applies only to tangible biological materials; however, many other countries including Brazil, Ethiopia, India, and Malaysia assert that the protocol also applies to information from genetic resources, including DSI (13). In implementing their legislation for the protocol, these countries and others are applying ABS requirements to DSI from pathogens. Scientists are concerned that the soured political atmosphere combined with loopholes in existing international frameworks could impede the sharing of genetic data and virus samples in the future.

One thing that is clear is the fact that the Nagoya Protocol serves as one of the existing international frameworks for access and benefit-sharing of genetic resources. The different interpretation of the protocol and approaches for the implementation of different domestic legislation on the same has often been the genesis for the claims of sovereignty for isolated pathogens. The Nagoya Protocol provides that some of its measures may be implemented through policy, legislative, and administrative instruments which bring about non-uniformity. None of the provisions of the Nagoya Protocol so far has been the subject of a judicial interpretation. It is important to take note of the dissenting views and how they affect the intended interpretation of the Nagoya protocol.

Consequently, the WHO has tried to resolve the issue with the pandemic influenza preparedness (PIP) framework that was adopted in 2011 (10). These rules affirmed state sovereignty as a legal norm and imposed no direct legal ramifications for not sharing influenza viruses with the WHO. Further, WHO's International Health Regulations mandate the member states to notify the organization with all relevant information that would result in a public health emergency of international concern (13). At the same time, the rules having been formulated in an international law context are a form of international cooperation. This debate has reemerged in the context of COVID-19, particularly on state obligations to inform the world when a pandemic outbreak occurs, and the WHO's responsibility to declare a pandemic. Unfortunately, these rules do not classify genetic sequence data or physical pathogen samples as health information, and it is unclear whether these regulations and the PIP framework apply to COVID-19.

The COVID-19 death toll has displayed different patterns in various parts of the globe, and this has raised the question of whether countries can claim ownership of pathogens that have emerged within their borders and if so, how do we guarantee sharing of benefits? As well as the costs of losses occasioned by the pathogen? This is a question which was asked in the past, not only in the context of H5N1 but also in biocontrol of plant pests with countries that host the natural predator to a pest asking whether they will share in the benefits arising from the eradication of the pest in the receiving country (14). The normal response is whether they would be willing in the first place, to share in the losses occasioned by the pest. These gaps and flaws in the implementation of the Nagoya Protocol have very far-reaching impacts on global public health. Impacts include impediment and unnecessary delay in international research collaborations, pathogen sample sharing, infectious disease research, pandemic and epidemic preparedness and response, medical countermeasure development efforts, and investor interest in vaccine development.

These effects on public health are visible, extreme, and very real. Even though the World Health Assembly Report on the Public Health implications of implementation of the Nagoya Protocol posited that the protocol actively provides an opportunity to advance public health, it failed to consider the other significant risks occasioned by the treaty (15). The current implementation of the protocol has been at the origin of significant delays in sharing influenza viruses' information, including from national influenza centers in Southeast Asia and South America with a long-standing record of timely sharing as required under the terms of reference in the Global Influenza Surveillance and Response System (GISRS) (15). Those national influenza centers found themselves having to delay the sharing of influenza viruses due to conflict with national legislation on ABS arising from the recent implementation of the Nagoya Protocol and consequently missed the timing for the seasonal vaccine composition meeting (16).

A similar situation occurred in Europe as well where the WHO Collaborating Centers of GISRS experienced a delay of 3 months before a candidate vaccine virus, falling under France's Nagoya Protocol legislation, could be shipped to manufacturers. In another case, in Switzerland, there was a delay of 3 weeks in the ability to use a WHO-recommended candidate vaccine virus for manufacturing due to a lack of clarity of the consent process to be followed and who the "user" of the strain was; furthermore, it was not clear whether seasonal influenza fell under the scope of the Swiss ABS legislation or not (16).

Delays in virus sharing often harm the vaccine development procedure as the quality of the vaccine and its supply are actively compromised. These delays further affect the timeliness and comprehensiveness of the entire procedure. The ABS principles should attempt to find a balance between protecting the interests of providers and users whilst aiding and enhancing public health and pandemic preparedness and response. It is imperative to public health that the present ABS mechanisms be amended

to encompass and ensure global systems that guarantee global benefit sharing. The global community must begin to ask itself as to what can be done to effectively protect public health equities in the context of the Nagoya Protocol and national-level ABS implementation?

The principle that countries should equitably share benefits arising from the utilization of genetic resources in their jurisdictions is no new feat as it is catered for in the UN Convention on the Law of the Sea (adopted in 1982) and the CBD (adopted in 1992). The Nagoya Protocol and the WHO, PIP framework (WHO–PIP) are just the latest additions to the expression of this principle. National ABS legislations therefore can be viewed as a basic expression of the "general principles of law recognized by civilized nations" (art. 38 of the statutes of the ICJ).

In 1948, the WHO was founded and trusted to establish the canons that are currently in place for global health. Enshrined in the WHO constitution as one of the main functions of the organization is the stimulation and advancement of the work to eradicate epidemic, endemic, and other diseases. In addition, the UN body's mandate is further strengthened by its capacity to promote and establish guidelines on public health, preventive care, clinical medicine, ethical research, and ensuring that emerging technologies improve worldwide safety and well-being (17). WHO has successfully developed a wide array of guidelines and principles that have previously and are still being used to promote global health.

Beneficence, reciprocity, and solidarity are often terms that should be considered when taking a glance at the principles used to manage ethical issues during infectious disease outbreaks. From the onset, different obligations arise for both governments and the international community in the event of infectious disease outbreaks. Governments play a critical role in preventing and responding to infectious disease outbreaks by improving the social and environmental conditions, facilitating the provision of well-functioning and accessible health systems, as well as engaging in public health surveillance and prevention activities (18).

States have an ethical obligation to ensure that they are equipped with the long-term capacity of the necessary systems required to carry out effective epidemic prevention and response. However, these are not the only obligations that countries have, they extend beyond their borders. All countries must carry out their responsibilities under the International Health Regulations (IHR) to participate in the global surveillance efforts truthfully and transparently. This includes providing prompt notification of events that may constitute a public health emergency of international concern, regardless of any negative consequences that may be associated with the notification. Negative consequences would include issues such as a potential reduction in trade or tourism (18).

Referring to the preceding sections of this study, it was mentioned briefly that global pandemic response has continually faced challenges, more so at the pathogen sample sharing stage. This is an issue that was brought to the worldview in 2007. Spearheaded by Indonesia, matters regarding ABS were for the first time placed in the limelight. A further look at the state of affairs in this Southeast Asian Republic unearthed some rather appalling discoveries as Siti Fadilah Supari, the Minister of Health at the time came forward and announced that they would immediately suspend the sharing of virus samples with the WHO Collaborating Centers. This was attributed to the fact that Indonesia at that time was severely affected by the highly pathogenic H5N1 virus. Furthermore, it was brought to their attention that the virus samples they had shared with the collaborating centers had been used for vaccine development without their consent and were subsequently being offered to Indonesia by an Australian drug company at $20 a dose (19). This was a rather unfortunate and unfair twist of events. The Indonesian population at the time stood at over 200 million, the amount of money required to purchase the drug from the Australian company was unfathomable if not absurd. It was clear that the "provider" countries were being exploited although they shared their samples in good faith.

At the time, the situation dictated that the affected countries would send potentially pandemic avian flu virus samples to certain national laboratories designated as the collaboration centers. These laboratories were in developed countries and would sequence the virus thereafter developing candidate vaccine strains (20). Unfortunately, in violation of the WHO guidelines, they sent the viruses to the commercial sector for vaccine development, without the consent of the providing countries. Worse still, the vaccines developed by the private sector, using the samples accessed from the Global Influenza Surveillance Network (GISN) were unavailable and/or not affordable to developing countries. It also soon became apparent that the GISN's operations were inconsistent with the principles and provisions of the CBD that required PIC and MAT to kick off the material transfer process. Based on these controversies, these issues were discussed at the 60th World Health Assembly, kicking off tense negotiations that lasted 4 years and eventually led to the adoption of the PIP framework.

The year 2011 saw the members of the WHO adopt a ground-breaking agreement: the PIP framework. The WHO–PIP framework for the first time provided a link between access to pathogens and the fair and equitable sharing of benefits arising from their use (20). The PIP framework aimed at building on the legal principles encompassed in the CBD, recognizing the sovereign right of states over their biological resources. Furthermore, the PIP framework recognized that the members of the WHO have a commitment to virus-sharing and benefit-sharing on an "equal footing," as they are "equally important parts of the collective action for global public health."

The main objective of the PIP framework is to improve pandemic influenza preparedness and response. It also aims at strengthening the protection against pandemic influenza by improving the Global Influenza Surveillance and Response System (GISRS), thus resulting in a fair, transparent, equitable, efficient, and effective system. Over the years, the PIP framework has largely been considered to be a success story. Sharing of seasonal influenza viruses and influenza viruses with human pandemic potential (IVPP) is governed by two different but mutually reinforcing and supportive regimes (21). These are the GISRS and the PIP framework.

Under these regimes, National Influenza Centers (NIC) are designated by the health ministry of the country concerned and are recognized by WHO. The designation requires formally agreeing to comply with the GISRS seasonal influenza terms of reference (TORs) and the PIP framework, under which NICs agree, inter alia, to share influenza virus samples with other GISRS and non-GISRS laboratories. It is important to take note of the fact that the IVPP framework does not extend to seasonal influenza viruses or any other pathogens (20).

The framework subjects all transfers of the IVPP among the WHO–GISRS laboratories and with entities outside the GISRS system to the standard MTAs (SMTAs) and commits all recipients of PIP biological material to benefit-sharing. In addition, the framework also puts in place a transparent traceability mechanism, the influenza virus tracking mechanism, which tracks real-time the movement of PIP biological material into, within, and out of the WHO–GISRS.

Five years after the implementation of the PIP framework, an expert review commended the framework, referring to it as an "essential instrument" for pandemic influenza preparedness. The report further posited that the implementation has led to greater confidence and predictability in the global capacity to respond to an influenza pandemic (20). True as this may be, the PIP framework has still left a lot of stones unturned. The PIP framework presents a different set of both continuing and developing challenges, specifically those relating to other pathogens shared within the network of the WHO.

In the wake of continuous technological developments, the issue of DSI still presents itself as a challenge for the PIP framework. It is no secret that thanks to the combined efforts of scientists across the globe pathogens can be developed, modified, and generated from DSI. Matters relating to DSI in both the NP and the PIP framework continue to be an area that lacks global consensus. These issues ought to be handled with utmost importance and urgency mainly because most of the research conducted as a result of pathogen isolation yields benefits that the initial providers are most times unable to access. Genetic material and the DSI resulting from the same material ought to be viewed in equal light by all the frameworks involved.

There is a need to actively enforce a balanced data-sharing ABS model for other pathogens. The SARS and MERS outbreaks were full of controversies as the scientists tasked with fighting the outbreak applied for virus genome patents (20). Furthermore, pathogen samples were actively being shared without the consent of the provider. These controversies are symptomatic of the inequities and bias prevailing in global health governance. The WHO is uniquely positioned with the capabilities and the resources to facilitate pandemic preparedness at the national and international levels. In addition, they are more than capable of developing benefit-sharing structures for other pathogens shared in situations of emergencies. There is a need to develop international rules governing the use of pathogens and DSI, especially those establishing fair and equitable benefit-sharing consistent with the objectives and provisions of the CBD and the Nagoya Protocol (20). It is also imperative to the global community that this process involves all stakeholders.

The lack of international rules governing access to pathogens, fair and equitable benefit-sharing is a major deficiency. This brings to life the potential risk of the reoccurrence of controversies seen during the SARS, MERS, and avian flu. Unfortunately, this would result in the erosion of trust and the weakening of pandemic preparedness and response. Despite the current outbreak of COVID-19, these controversies are still with us.

Amidst the quest for COVID-19 treatment, Dr. Tedros Adhanom Ghebreyesus, the WHO Director-General, has come forward to support the idea of creating a voluntary pool to collect patent rights, regulatory test data, and other information that could be shared for developing drugs, vaccines, and diagnostics (22). An idea that has not received the warmest welcome as pharmaceutical companies across the world have openly expressed their resistance to this idea (23). This idea is premised on the fact that COVID-19 medical products may not be accessible for poorer populations. By establishing a voluntary mechanism under the auspices of the WHO, the goal is to establish a pathway that will attract numerous governments, as well as industry, universities, and nonprofit organizations.

The proposal for a patent pool is modeled around the medicines patent pool and was initially proposed by Costa Rica. It has other proponents (Netherlands) and opponents (US, UK, and others) with each side having its arguments. This pool could potentially provide a system of enabling deployment (access) of pharmaceutical products to large masses rapidly, as opposed to if the patents were under the control of one or fewer entities. Speaking at a forum organized by IFPMA, Pascal Soriot, the Chief Executive at AstraZeneca argued that intellectual property (IP) is a fundamental part of the pharmaceutical industry, and the potential lack of IP protection extracts all innovation incentives (22). He further added that the present issue of importance is the voluntary provision of products, at no profit, in the time of pandemic crisis.

The lack of a foundational balanced model of reciprocity for global public health that could be applied to other pathogens will always create a reoccurrence of the aforementioned controversies. Consequently, this frustrates all efforts to move forward with global health. There is a need to objectively look at the inconsistencies at hand and deal with them once and for all to avoid inequities in global health and overall inefficiency in pandemic preparedness and response.

AN ACCESS AND BENEFIT-SHARING MODEL FOR OTHER PATHOGENS

It is evident that there is a need for the global community to kick off the discussion on the regulation and management of other pathogens. COVID-19 has been able to illuminate the flaws of the existing pathogen-specific ABS instrument. It has also been able to identify the fact that the documents in development should attempt to address those flaws sufficiently. However, to identify the specific problems that the proposed ABS sharing model should address, we must discuss the flaws

of the existing pathogen-specific ABS instrument, which is the PIP framework.

The Milbank Quarterly Journal in 2019 revealed that during an influenza pandemic, the PIP framework is likely to secure access to necessary virus samples but highly unlikely to secure the promised benefits for countries in need (24). This established that in practice the PIP framework only upholds one side of the access and benefit-sharing bargain. This often leaves countries unsettled because if the framework is unable to secure promised benefits like vaccines and antivirals, then they may feel they are better positioned to protect their populations from an influenza pandemic by conducting the access and benefit-sharing transaction outside the remit of the multilateral PIP framework. Unfortunately, this results in the direct transaction between the provider and the potential users of the resources, and the position assumed by the WHO as an intermediary is rendered redundant. This kind of scenario has ripple effects that would potentially result in interference of the entire global surveillance system that has been vital to monitoring and responding to the threat posed by influenza.

In addition, a further look at the PIP framework suggests that during a pandemic, the framework would not be able to withstand the blowback, yet this is the very basis of the document's creation. One of the main inconsistencies with the PIP framework is the fact that the SMTA does not create any directly binding agreements between the member states and third-party recipients of influenza viruses. In the lead-up to and during a pandemic, the SMTA1 secures access to influenza viruses for the WHO and the SMTA2 secures access for commercial users of virus samples. However, the SMTA2 may be ineffective in securing tangible benefits for the sovereign providers of those materials. An issue for consideration is whether the PIP framework through the SMTA1 and SMTA2 creates a multilateral system of access and sharing of benefits, and if so, what is the scope of this system? In addition, how do we ensure that this system's operational outlook delivers sufficient and tangible results?

In a bid to enhance engagement among stakeholders, Manheim (13) stated the need to actively identify and provide examples of monetary or non-monetary benefits to the global public health system. Specifically, the examples are facilitated by international sharing of pathogens, biospecimens, pathogen genetic sequence data, and/or relevant metadata. Manheim (13) further expressed the need to identify other pathogen-specific issues and examples that could affect global pandemic preparedness and response or efforts to combat seasonal outbreaks. It is also important for us to identify the non-ABS challenges and barriers to sharing pathogens internationally or those that might merit additional attention or analysis due to the significant implications they would have on global pandemic or epidemic preparedness and response efforts. More research is necessary to examine the possible course of action for a working ABS model that can deliver for other pathogens, especially under the pressure of a pandemic.

RECOMMENDATIONS AND CONCLUSIONS

The One Health approach has often been mentioned when considering the alternative avenues for other pathogen-specific ABS models. Comprehensive research attempting to address the present-day challenges has never been greater. Sharing of information, data, and interdisciplinary collaboration are at an all-time high. The One Health approach to research ensures that human, animal, and environmental health questions are evaluated in an integrated and holistic manner. This aims to provide an exhaustive understanding of the problem and the potential solutions that would be impossible as a result of siloed approaches (25). Nonetheless, the OH approach is complex, and there is limited guidance available for investigators regarding the practical design and implementation of OH research.

On the face of it, the prospective gains of the OH approach are largely enshrined in the increasing public health efficiency and cost-effectiveness through a better understanding of disease risk. This can be achieved through shared control and detection efforts. As a result, this will benefit human, animal, and ecosystem health (26). The efforts to identify, systematize, and assess the perceived OH efficiency metrics reveal that standardized evaluations of the One Health approaches are generally lacking (26). The benefits that are widely cited have mainly been premised on modeled projections, rather than outcomes of implemented interventions.

A literature review on this approach further revealed that, out of a pool of over 1,800 unique papers, only seven reported quantitative outcomes. These assessments did not follow the shared methodology and several reviewed only intermediate outcomes. The findings on the One Health approach are largely subjective and the absence of a standardized framework to capture metrics across disciplines could potentially hinder the widespread adoption of One Health among stakeholders (26).

The OH initiative promotes integrated research, surveillance, control programs, and policy frameworks. Considering the transboundary nature of people, pathogens, and ecosystems, ensuring that these international partnerships are built based on these strong foundations is highly important. The vast majority of emerging infectious diseases in humans are zoonotic (27). Often, they escape their natural wildlife reservoirs and infect captive or domestic animals and humans upon cross-species transmission. More often than not, these pathogens spread limitedly among humans; however, once they evolve and transmission has become viable, the effects result in disastrous epidemics, if not pandemics.

The SARS-CoV-2 is an example of novel human pathogens transmitted across borders. This pathogen has had very far-reaching effects on human welfare resulting in a threat to the global community. In light of the above, we must consider the unforeseeable burden that emerging infectious diseases place on global health and the economy. Infectious disease surveillance and pandemic preparedness are essential to mitigate the impact of future threats. Unified global surveillance networks provide unprecedented monitoring data on plant, animal, and human infectious diseases. Using such sources, we can report on current major One Health threats.

The COVID-19 pandemic has established the need for an integrated framework that will grow a strong evidence base to inform decision-making and solution creation. The combined multidisciplinary responses advocated for by the OH approach could potentially do more harm than good; however, it requires that conglomerates and state investment before such a crisis. Surveillance is the key to preparedness. By identifying and monitoring new threats to plant, animal, and human health, early-warning flags can be raised regarding changing epidemiology. This will fast-track pandemic preparedness and response against emerging diseases.

The One Health agenda could potentially be extended to increased international collaborations for drugs and vaccine research and the development of an efficient coronavirus sharing system that includes the DSI of the pathogen. In addition, the OH Agenda can further be promoted by benefit-sharing enforcement across the globe and a review of the technological hindrances between countries that affect and limit fair and equitable sharing.

Based on the preceding discussions in this study, an issue that comes out is the existing gaps in the current ABS mechanism. In addition, this study has briefly highlighted the current and the potential consequences of turning both a deaf ear and a blind eye to the issues at hand. As we continue to tackle COVID-19, perhaps there is a need to take a step back and establish how the ABS/pathogen-sharing process can be streamlined while also taking into account unforeseen circumstances. There is a need to review the overall implementation of this document. Furthermore, there is a need to ask compelling questions that would force the international community to admit that it did not take things into consideration.

There is a need to ponder on the efficiency of the Nagoya Protocol, its implementation, and how this impacts the response to epidemics and pandemics. In addition, the international community must debunk the efficiency of the current pathogen-specific ABS Instruments. Do the pathogen-specific ABS Instruments that are currently in place override or undermine the interests of public health? Finally, is there a way that we can actively ensure compliance to ABS mechanisms as we pursue the journey to COVID-19 treatment and other pathogens?

As we deliberate on the aforementioned, one of the potential solutions to these concerns is the recognition and rapid enforcement of a specialized international instrument for pandemic pathogens under the Nagoya Protocol. The picture that history paints show us the urgency of such an instrument. Moreover, there is a need to develop and implement legislation to support world public health emergencies.

In conclusion, we should consider and explore further fair and equitable worldwide solutions. This could be achieved through transparent open fora, participatory approach, well-defined scope, and governance in consideration of world traditional knowledge and heritage. As Cueni (9) succinctly stated, "Pathogens know no borders, so any obstacle to sharing them and/or their associated information will hinder essential global collaborations with the private and public sectors needed to develop effective countermeasures to disease outbreaks. It is time to question the sense of retaining pathogens within the scope of the Nagoya Protocol and associated national legislation." It is time for a framework that accommodates and withstands pandemic pressure.

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Strategies to Estimate Prevalence of SARS-CoV-2 Antibodies in a Texas Vulnerable Population: Results From Phase I of the Texas Coronavirus Antibody Response Survey

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and immunity remains uncertain in populations. The state of Texas ranks 2nd in infection with over 2.71 million cases and has seen a disproportionate rate of death across the state. The Texas CARES project was funded by the state of Texas to estimate the prevalence of SARS-CoV-2 antibody status in children and adults. Identifying strategies to understand natural as well as vaccine induced antibody response to COVID-19 is critical.

Materials and Methods: The Texas CARES (Texas Coronavirus Antibody Response Survey) is an ongoing prospective population-based convenience sample from the Texas general population that commenced in October 2020. Volunteer participants are recruited across the state to participate in a 3-time point data collection Texas CARES to assess antibody response over time. We use the Roche Elecsys® Anti-SARS-CoV-2 Immunoassay to determine SARS-CoV-2 antibody status.

Results: The crude antibody positivity prevalence in Phase I was 26.1% (80/307). The fully adjusted seroprevalence of the sample was 31.5%. Specifically, 41.1% of males and 21.9% of females were seropositive. For age categories, 33.5% of those 18–34; 24.4% of those 35–44; 33.2% of those 45–54; and 32.8% of those 55+ were seropositive. In this sample, 42.2% (89/211) of those negative for the antibody test reported having had a COVID-19 test.

Conclusions: In this survey we enrolled and analyzed data for 307 participants, demonstrating a high survey and antibody test completion rate, and ability to implement a questionnaire and SARS-CoV-2 antibody testing within clinical settings. We were also able to determine our capability to estimate the cross-sectional seroprevalence within Texas's federally qualified community centers (FQHCs). The crude positivity prevalence

for SARS-CoV-2 antibodies in this sample was 26.1% indicating potentially high exposure to COVID-19 for clinic employees and patients. Data will also allow us to understand sex, age and chronic illness variation in seroprevalence by natural and vaccine induced. These methods are being used to guide the completion of a large longitudinal survey in the state of Texas with implications for practice and population health.

Keywords: antibodies, COVID-19, health disparities, population methods, Federally Qualified Health Center (FQHC)

INTRODUCTION

Since January 2020, the Centers for Disease Control (CDC) has recommended county and state level reporting of all laboratory-confirmed cases of SARS-CoV-2 infection (1). However, reported cases likely represent only a fraction of SARS-CoV-2 infections across the United States, as a still unknown proportion of cases are mild or asymptomatic (2–5), especially in young adults or children (5–10). Other challenges for SARS-CoV-2 surveillance include under-reported cases due to local health department capacity, delays in recording of testing and various methods of test reporting (2–4, 11). Also missing is our understanding of the human response to natural and vaccine induced antibodies over time. Understanding of who is To obtain a more accurate representation of infection, many states and countries have turned to estimating SARS-CoV-2 seroprevalence from blood antibody assays allowing for an estimate of the prevalence of the human antibody response (11–14).

Published data from the COVID-19 first and second wave indicate infections rates vary widely among different populations and geographic regions within a state (11). Highly exposed populations include front line essential workers such as health care workers, teachers and educational staff, and those working in service, business, and retail, including grocery stores (4). Furthermore, ethnic minorities are at higher risk of contracting COVID-19 (7, 8) as are vulnerable populations such as those without health insurance, people experiencing homelessness, or those with pre-existing conditions such as type 2 diabetes, hypertension and asthma (15–17). Black and Latino communities have been especially hard hit by COVID-19 (18–20); for example, in a New York State Department of Health (NYSDOH) convenience sample of 15,000 New Yorkers *employed* at 99 grocery stores across 26 counties representing 87.3% of the state's population found an adjusted seroprevalence ranging from 8.1% in non-Hispanic whites to 29.2% in Latinos, with an overall seroprevalence in New York City of 22.7%, vs. a state-wide prevalence of only 8.9%. Other large seroprevalence studies are being conducted in California, Colorado, Georgia and Ohio (11, 18, 20).

Texas is the second largest state in the country and has a diverse population over 28,250,000 and a majority minority, with ∼40% of residents identifying as Hispanic ethnicity, 12% as Black non-Hispanic and 7% other ethnicity. More than 34% of Texans live below 200% of federal poverty level (FPL). Texas is geographically diverse with ∼85% of residents living in urban centers with vast rural areas requiring over 1 h of travel to regional hospital systems (21). Several areas of Texas have seen a high incidence of confirmed coronavirus disease (COVID-19) cases across two surges (July and December), including Dallas, Harris, Nueces, Cameron and Hidalgo counties. Furthermore, the prevalence of confirmed COVID-19 varies significantly across the state and by employment industry. For example, higher proportions of confirmed tests have been observed in underserved urban areas such as Dallas and Houston (22, 23) and in areas with a high prevalence of vulnerable or Latino populations, such as San Antonio and McAllen, and in areas with multi-generational households, where viral transmission may be increased due to higher household density and with varied age groups within one household. Additionally, disparate burden of infection in rural areas with immigration detention centers (Willacy Co.) and meatpacking plants in the Texas Panhandle region (23).

To ascertain estimate exposure to SARS-CoV-2 in the state of Texas, and to obtain an understanding of exposure across Texas, the Texas Coronavirus Antibody Research survey (Texas CARES) was designed as a longitudinal antibody surveillance study using a convenience sample approach from among highly exposed populations. This is a unique project as it purposely uses a voluntary approach to reach communities across Texas to explore both natural and vaccine induced antibody response and its duration. Phase I of Texas CARES was designed to identify the feasibility of partnering and reaching vulnerable patients at Federally Qualified Health Centers (FQHCs) and to estimate seroprevalence of the 319 participants in this phase. There are currently 73 FQHCs serving patients in Texas, operating more than 500 sites and two FQHC lookalikes which offer FQHC-like services. The FQHCs are located across 126 counties and serve over 400,000 Medicaid patients, 28% of all FQHC patients, with 1,426,019 million patients served annually and over 5,300,000 patient visits annually (24). We report here our Phase I sub-study of seroprevalence in a sample of 319 adults enrolling at three FQHC sites in Texas. Allowing us to better identify and understand natural and vaccine responses in vulnerable and underserved populations for which mitigation efforts may not be afforded, understanding their response over time will allow us to better prepare future public health responses.

METHODS

All study protocols were reviewed and approved by the University of Texas Health Science Center Houston Institutional Review Board prior to any data collection. The Texas CARES program is a partnership with Texas Department of State Health

Services and the University of Texas System with a statewide laboratory partner, Clinical Pathology Laboratories (CPL). The Texas Association of Community Health Centers (TACHC) partnered with us to introduce the program to FQHC sites. In total 40 or more FQHCs will be enrolled in the program over time.

Study Population

The Phase I sub study of 307 participants presenting at or working at three FQHCs was performed as part of the larger Texas CARES study. The larger study aims to enroll participants from four populations across the state of Texas; pediatric school children 5–17 years of age, FQHC or community clinic patients, kindergarten to −12th grade educators and allied staff and Texas workforce employees who will be tested for SARS-CoV-2 antibodies at three points over a 6–12 month period. The Texas CARES uses a convenience sample of Texans representing the four populations across the state. The next phases of Texas CARES have expanded to recruitment of all Texans across industries with an emphasis on teachers, education setting employees, universities and community residents. We have also begun collecting natural and vaccine induced antibody response in the total Texas CARES program population.

For Phase I, on the day patients presented for their healthcare appointments, an FQHC healthcare team member offered adults 18–80 years of age literature on the Texas CARES and the Roche Elecsys® Anti-SARS-CoV-2 test (2021 Roche Diagnostics, North America), and invited them or their children (5–17 years of age) to enroll in the study. Participation was limited to two representatives from the same household between 5 and 80 years of age. Enrollment required contact information, demographic characteristics and informed consent for three blood draws over 6–12 months. Patients who consented to enroll in Texas CARES were provided a questionnaire collecting demographic information, employment, baseline medical conditions and comorbidities, prior COVID-19 tests and diagnoses, physician diagnosis of COVID-19 and other high-risk chronic illnesses such as type 2 diabetes, asthma and hypertension, COVID-19 symptoms and severity, and COVID-19 behavioral health (25).

SARS Cov-2 Antibody Assay Roche Diagnostics

The primary outcome was a positive antibody assay qualitatively assessed using the Roche Elecsys® Anti-SARS-CoV-2 Immunoassay developed to detect antibodies to SARS-Cov-2. The Anti-SARS-CoV-2 Immunoassay has received Emergency Use Authorization (EUA) by the U.S. Food and Drug Administration. The Elecsys® Anti-SARS-CoV-2 Immunoassay detects high-affinity antibodies to SARS-CoV-2 using a modified recombinant protein representing the nucleocapsid (N) antigen for the determination of SARS-CoV-2 antibodies. The test has a published sensitivity of 99.82% sensitivity (95% CI: 99.69–99.91) and 99.91% specificity in diagnostic specimens ($n = 2{,}861$) (26). The qualitative test results are provided to participants by text to ensure receipt, follow up by phone or email is made as needed to reach the vulnerable population.

Questionnaire

A programmed questionnaire was designed to be completed in 10–15 min to capture demographic and clinical characteristics including BMI, comorbidities, prior COVID-19 virus testing, positivity, COVID-19 symptoms, previous antibody testing and mental health during the pandemic (27). To help ensure validity, wherever possible, all questionnaire headers, questions, and response formats were harmonized to the PhenX Toolkit for COVID-19 and the BRFSS questionnaires. PhenX Toolkit items were reviewed for appropriateness, BRFSS and U.S. Census race/ethnicity questions were used. All study materials, including the questionnaire, were available in both English and Spanish.

It was decided *a priori* that a survey weblink would be emailed and texted to those completing fewer than 50% of questions at their medical visit (28, 29). Those who did not respond by completing the survey received a phone call from a team member to collect the survey data. The survey completion percentage in our phase I study of 307 participants prior to the phone call was 96%, which is an indicator both of good validity and construction of our protocols.

Primary Outcomes and Statistical Analyses

The primary outcomes of Phase I included: (1) feasibility of implementation of the questionnaire and SARS-CoV-2 testing in a highly vulnerable population including children, and (2) estimation of Texas demographic and assay-adjusted cross-sectional seroprevalence based on antibody test results in these participants. The descriptive statistics are reported.

Prevalence Estimation Methods

The SARS-CoV-2 cumulative prevalence was estimated from observed antibody reactivity using two sequential steps: (1) post-stratification weighting to standardize to the Texas population and (2) adjustment by antibody test sensitivity and specificity. First, crude observed seroprevalence was adjusted by age- and sex using weights derived from the U.S. census population projections for the state of Texas. Age in years was categorized into four categories: 18–34 years, 35–44 years, 45–54 years, and 55 years or greater. Post-stratification weights were computed to standardize our sample to the greater Texas population according to the 2019 projected census; the weight was computed as a ratio of the proportion of a given level of a stratum in the census, divided by the equivalent proportion in the sample. An adjustment for the assay sensitivity (99.82%) and specificity (99.91%) was applied as per Royal and colleagues. The full adjustment analysis was completed using IBM® Statistical Package for the Social Science (SPSS®) Statistics Version 27 (United States) and by hand. The weights are then applied to the individuals in our data set using standard survey weighting methods. Finally, to adjust for assay characteristics, the cumulative adjusted prevalence is computed as per Rosenberg et al. (4):

$$cumulative\ prevalence = \frac{proportion\ positive + specificity - 1}{sensitivity + specificity - 1}.$$

Estimates that are age and sex-standardized and adjusted for test characteristics are henceforth called "fully adjusted estimates." "Crude estimates" refer to the observed seroprevalence estimates.

RESULTS

SARS-CoV-2 Antibodies Among Total Sample

Crude and adjusted SARS-CoV-2 antibody seropositivity are shown in **Table 1**. The crude antibody positivity prevalence in Phase I was 26.1% (80/307). The fully adjusted seroprevalence of the sample was 31.5%. Specifically, 41.1% of males and 21.9% of females were seropositive. For age categories, 33.5% of those 18–34; 24.4% of those 35–44; 33.2% of those 45–54; and 32.8% of those 55+ were seropositive.

Demographic and Clinical Correlates of Seropositivity

Demographic and clinical characteristics, by SARS-CoV-2 antibody seropositivity are presented for the total Phase I sample, FQHC clinical staff, and FQHC patient population in **Table 2**. As shown in **Table 2**, 17.7% (14/79) FQHC employees tested were positive and 27.9% (57/204) of FQHC patients were positive. The mean age of the entire sample ($N = 307$) was 43.7 (SD = 13.5). The group was primarily female (79%, $n = 252$), white (95.3%, $n = 286$), and of Hispanic ethnicity (81.7%, $n = 255$), with 8.7% ($n = 25$) having some high school or less and 19.8% ($n = 57$) having an advanced professional or academic degree. A total of 78% ($n = 221$)] was employed full-time and 79% ($n = 228$) reported having some type of health insurance. The clinical characteristics of the sample indicate that 27.7% ($n = 78$) were overweight and 59.9% ($n = 169$) were obese with the mean BMI = 32.6 (SD = 7.6). The majority of participants reported not using tobacco products in the past 2 weeks (88.7%, $n = 260$) and did not report use of vaping products in the past 2 weeks (96.8%, $n = 272$).

SARS-CoV-2 Symptoms and Previous Diagnoses

In **Table 3**, of those 80 people with a positive SARS-CoV-2 antibody test 78.9% (56/71) reported having had at least one symptom of COVID-19. Of those 227 who were negative, 38% (71/186) reported presence of COVID-19 symptoms. More than half (53.1%, 154/290) of the participants reported having had a previous COVID-19 test. Of the 154, 152 responded whether that test was positive or negative: 61/152 indicated it was positive (40.1%). In this sample, 42.2% (89/211) of those negative for the antibody test reported having had a COVID-19 test.

Of the 61 respondents with a prior positive COVID-19 test, 55 (90.2%) had antibodies and 6 (9.8%) did not have antibodies. Of those diagnosed with COVID-19 by a health professional without a test, 7 (70.0%) had a positive antibody test and 3 (30%) had a negative antibody test result. The most commonly reported symptoms in the sample positive for SARS-CoV-2 antibodies were new loss of taste or smell, fatigue, muscle or body aches, and headaches.

TABLE 1 | Seroprevalence rates by age and gender, standardized to Texas Census data and adjusted for assay characteristics.

		Crude (observed) antibody N and %				TX census weighted N and %					Adjusted for assay (Spec = 99.81%)		
		Antibody N		Antibody %			Weighted Antibody N		Weighted Antibody %		Adjusted antibody proportion		
	Phase I	Positive	Negative	Positive	Negative	Weighted	Positive	Negative	Positive	Negative	Positive	Estimated infection experienced	Proportion of estimated infection experienced
Overall	307	80	227	26.1%	73.9%	307	97	210	31.6%	68.4%	31.5%	6795393	100%
Sex													
Male	63	26	37	41.3%	58.7%	155	62	89	41.1%	58.9%	41.0%	4352534	64.1%
Female	243	54	189	22.2%	77.8%	152	35	121	22.4%	77.6%	22.3%	2444240	36.0%
Age group													
18–34	90	24	66	26.7%	73.3%	98	33	65	33.7%	66.3%	33.5%	2378518	35.0%
35–44	69	14	55	20.3%	79.7%	58	14	43	24.6%	75.4%	24.4%	962657	14.2%
45–54	74	23	51	31.1%	68.9%	76	25	50	33.3%	66.7%	33.2%	1180189	17.4%
55+	74	19	55	25.7%	74.3%	76	24	51	32.0%	68.0%	31.9%	2233957	32.9%

TABLE 2 | Demographics and clinical characteristics, TX CARES, all phase 1 participants, 2020.

Demographics	Overall ($n = 319$)*	SARS-CoV2 antibody status	
		Positive ($n = 80$)	Negative ($n = 227$)
	N (%)	N (%)	N (%)
Cohort ($n = 291$)			
FQHC Employee	82 (25.7)	14 (17.5)	65 (28.6)
FQHC Patient	209 (65.5)	57 (71.3)	147 (64.8)
Missing	28 (8.8)	9 (11.3)	15 (6.6)
Gender ($n = 319$)			
Male	67 (21.0)	26 (32.5)	38 (16.7)
Female	252 (79.0)	54 (67.5)	189 (83.3)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
Race ($n = 300$)			
White	286 (89.7)	73 (91.2)	202 (89.0)
Black/African American	5 (1.6)	0 (0.0)	5 (2.2)
Asian	3 (0.9)	1 (1.2)	2 (0.9)
[-0.4pt] Hawaiian or Other Pacific Islander	1 (0.3)	0 (0.0)	1 (0.4)
American Indian or Alaska Native	2 (0.6)	0 (0.0)	1 (0.4)
Multi-racial	3 (0.9)	1 (1.2)	2 (0.9)
Missing	19 (6.0)	5 (6.2)	14 (6.2)
Hispanic Ethnicity ($n = 312$)			
Yes	255 (79.9)	75 (93.8)	171 (75.3)
No	57 (17.9)	3 (3.8)	51 (22.5)
Missing	7 (2.2)	2 (2.5)	5 (2.2)
Education ($n = 288$)			
Less than high school	12 (3.8)	6 (7.5)	6 (2.6)
Some high school	13 (4.1)	4 (5.0)	9 (4.0)
High school graduate/GED	78 (24.5)	27 (33.8)	48 (21.1)
Some college, no degree	68 (21.3)	20 (25.0)	48 (21.1)
Two- or four-year college degree	60 (18.8)	12 (15.0)	46 (20.3)
Advanced professional or academic degree	57 (17.9)	4 (5.0)	50 (22.0)
Missing	31 (9.7)	7 (8.8)	20 (8.8)
Employment ($n = 283$)			
Full-time	221 (69.3)	39 (48.8)	175 (77.1)
Part-time	12 (3.8)	6 (7.5)	6 (2.6)
Unemployed	38 (11.9)	19 (23.8)	18 (7.9)
Other	12 (3.8)	5 (6.2)	7 (3.1)
Missing	36 (11.3)	11 (13.8)	21 (9.3)
Has Insurance ($n = 289$)			
Yes	228 (71.5)	40 (50.0)	181 (79.7)
No	61 (19.1)	30 (47.5)	30 (13.2)
Missing	30 (9.4)	10 (12.5)	16 (7.0)
BMI, categorical ($n = 282$)			
Underweight	3 (0.9)	2 (2.5)	1 (0.4)
Normal	32 (10.0)	6 (7.5)	23 (10.1)
Overweight	78 (24.5)	21 (26.2)	56 (24.7)
Obese	169 (53.0)	41 (51.2)	124 (54.6)
Missing	37 (11.6)	10 (12.5)	23 (10.1)
Frequency of smoking or use of other tobacco products in past 2 weeks ($n = 293$)			
Not at all	260 (81.5)	67 (83.8)	186 (81.9)
Rarely	8 (2.5)	2 (2.5)	6 (2.6)
Once a day	9 (2.8)	3 (3.8)	5 (2.2)
More than once a day	16 (5.0)	1 (1.2)	15 (6.6)
Missing	26 (8.2)	7 (8.8)	15 (6.6)
Frequency of using vaping products in past 2 weeks ($n = 281$)			
Not at all	272 (85.3)	69 (86.2)	195 (85.9)
Rarely	6 (1.9)	0 (0.0)	6 (2.6)
Once a day	0 (0.0)	0 (0.0)	0 (0.0)
More than once a day	3 (0.9)	1 (1.2)	2 (0.9)
Missing	38 (11.9)	10 (12.5)	24 (10.6)
	Mean (±SD)	Mean (±SD)	Mean (±SD)
Age, years ($n = 317$; missing = 2)	43.7 (13.5)	43.3 (13.8)	43.6 (13.4)
Height, inches ($n = 287$; missing = 32)	64.2 (3.8)	64.6 (4.5)	64.0 (3.6)
Weight, pounds ($n = 288$; missing = 31)	191.4 (46.9)	188.1 (43.5)	192.0 (47.3)
BMI, continuous ($n = 281$; missing = 38)	32.6 (7.6)	31.6 (6.8)	33.0 (7.8)

Twelve individuals completed a survey, but did not complete an antibody test.

Presence of Chronic Diseases in the Texas CARES Phase I Sample

From **Table 4**, those with a positive SARS-CoV-2 antibody test were most likely to report having the following chronic diseases: hypertension (21/68, 30.9%), diabetes (18/68, 26.5%), asthma (18/68, 26.5%), and obesity (14/68, 20.6%).

DISCUSSION

In this study we enrolled and analyzed 307 participants, demonstrating a high survey and antibody test completion rate, and ability to implement a questionnaire and SARS-CoV-2 antibody testing within FQHC clinical settings. We were also able to determine our capability to estimate the cross-sectional seroprevalence within Texas's FQHC clinical settings. The crude positivity prevalence for SARS-CoV-2 antibodies in this sample was 26.1% indicating potentially high exposure to COVID-19 for FQHC clinic employees and patients. We also demonstrated feasibility and capability to determine the presence of IgG antibodies to SARS-CoV-2 in populations with and without previous COVID-19 positive diagnosis. The inclusion of COVID-19 positive and negative participants is important as it has been a limitation of other studies and

TABLE 3 | SARS-CoV2 symptoms and previous diagnosis, TX CARES, all phase 1 participants, 2020.

Previous COVID-19 diagnosis/symptoms	Overall ($n = 319$)*	SARS-CoV2 antibody status	
		Positive ($n = 80$)	Negative ($n = 227$)
	N (%)	N (%)	N (%)
Any COVID-19 Symptoms ($n = 265$)			
Yes	130 (40.8)	56 (70.0)	71 (31.3)
No	135 (42.3)	15 (18.8)	115 (50.7)
Missing	54 (16.9)	9 (11.3)	41 (18.1)
Previous COVID-19 test ($n = 290$)			
Yes	154 (48.3)	62 (77.5)	89 (39.2)
No	136 (42.6)	10 (12.5)	122 (53.7)
Missing	29 (9.1)	8 (10.0)	16 (7.0)
Previous positive COVID-19 test result ($n = 152$)			
Yes	61 (19.1)	55 (68.8)	6 (2.6)
No	91 (28.5)	6 (7.5)	82 (36.1)
Missing	167 (52.4)	19 (23.8)	139 (61.2)
Diagnosed with COVID-19 by health professional without test ($n = 290$)			
Yes	11 (3.4)	7 (8.8)	3 (1.3)
No	279 (87.5)	65 (81.2)	207 (91.2)
Missing	29 (9.1)	4 (33.3)	17 (7.5)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**
Symptoms**			
Fever or Chills ($n = 68$)	3.00 (2.00–4.00)	3.00 (2.00–4.00)	3.00 (2.50–4.00)
Missing n (%)	253 (79.3)	51 (63.8)	192 (84.6)
Cough ($n = 71$)	3.00 (2.00–4.00)	3.00 (2.00–4.00)	3.00 (2.00–4.00)
Missing n (%)	249 (78.1)	48 (60.0)	190 (83.7)
Shortness of breath/difficulty breathing ($n = 53$)	3.00 (2.00–4.00)	3.50 (3.00–4.75)	3.00 (2.00–4.00)
Missing *n* (%)	266 (83.4)	50 (62.5)	206 (90.7)
Fatigue ($n = 79$)	4.00 (3.00–4.00)	4.00 (3.00–5.00)	3.00 (3.00–4.00)
Missing n (%)	242 (75.9)	47 (58.8)	185 (81.5)
Muscle or body aches ($n = 72$)	3.00 (3.00–4.00)	4.00 (3.00–4.75)	3.00 (3.00–4.00)
Missing n (%)	248 (77.7)	46 (57.5)	192 (84.6)
Headaches ($n = 83$)	4.00 (3.00–5.00)	4.00 (3.00–5.00)	3.00 (3.00–4.00)
Missing n (%)	237 (74.3)	46 (57.5)	181 (79.7)
Congestion or runny nose (n = 63)	3.00 (2.00–4.00)	3.00 (2.00–4.00)	3.00 (2.00–4.00)
Missing n (%)	257 (80.6)	55 (68.8)	190 (83.7)
Diarrhea ($n = 44$)	3.00 (2.00–3.00)	3.00 (2.00–4.00)	3.00 (2.00–3.00)
Missing n (%)	276 (86.5)	60 (75.0)	204 (89.9)
Nausea or vomiting (n = 37)	3.00 (2.00–4.00)	3.00 (2.00–5.00)	3.00 (2.00–4.00)
Missing n (%)	282 (88.4)	63 (78.8)	207 (91.2)
New loss of taste or smell ($n = 44$)	5.00 (4.00–5.00)	5.00 (4.00–5.00)	4.00 (3.50–5.00)
Missing n (%)	276 (86.5)	45 (56.3)	220 (96.9)
Sore throat ($n = 68$)	3.00 (2.00–4.00)	3.00 (2.00–4.00)	3.00 (2.00–3.25)
Missing n (%)	253 (79.3)	55 (68.8)	187 (82.4)

**Twelve individuals completed a survey, but did not complete an antibody test.*

***Symptom severity based on a scale from 1 to 5 with 1 being minimal and 5 being severe.*

allows us to more accurately determine the seroprevalence and human response over time in a diverse representative population. Therefore, ability to determine antibodies in individuals with no previous history of COVID-19 over time is a unique aspect of our program approach that may inform understanding of the timing of neutralizing antibodies across a 6-month period; current estimate indicate antibodies may be stable for 5–7 months after SARS-CoV-2 infection (13). Ongoing analysis is focused on determining the time of contracting COVID-19 infection, antibody test and response over time with preliminary findings noting natural antibody levels may peak at 120 days with natural antibody test response lasting

TABLE 4 | Chronic diseases, TX CARES, all phase 1 participants, 2020.

Chronic disease	Overall ($n = 270$)	SARS-CoV2 antibody status	
		Positive ($n = 68$)	Negative ($n = 193$)
	N (%)	N (%)	N (%)
Asthma	56 (20.7)	18 (26.5)	33 (17.1)
COPD	4 (1.5)	1 (1.5)	2 (1.0)
Cancer	7 (2.6)	0 (0.0)	7 (3.6)
Cardiovascular	8 (3.0)	2 (2.9)	5 (2.6)
Diabetes	56 (20.7)	18 (26.5)	35 (18.1)
Hypertension	83 (30.7)	21 (30.9)	58 (30.1)
Obesity	60 (22.2)	14 (20.6)	43 (22.3)
Sickle cell	0 (0.0)	0 (0.0)	0 (0.0)
Immunocompromised	8 (3.0)	1 (1.5)	6 (3.1)
Kidney disease	2 (0.7)	0 (0.0)	2 (1.0)
Other	17 (6.3)	2 (2.9)	13 (6.7)

200–500 days. Analysis to be reported elsewhere with oral presentation to the American Public Health Association, October 25, 2021.

Although self-reported the COVID-19 test positivity and self-report of symptoms allows us to better determine the cycle and decline of antibody levels in a large sample of Texans over a 6-month period. It is estimated that over one-third of patients that have recovered from COVID-19 have antibodies given mild or asymptomatic disease (11), it is important to note that in our sample, 68.7% of those with a previous positive COVID-19 test had a positive SARS-CoV-2 antibody test. As with other research we found that the links with BMI, previous history of chronic illness and age (2–9) were correlated to human response in this sample. It is also important that as public health practitioners we understand the impact of co-morbidities and different needs of populations and how demographics, behavioral and social variables impacted antibody response over time.

The timing of the data collection from the start of the first reported cases in Texas was ∼6-months from the start of our data collection. The positive cases will be monitored for decline of antibody levels and collection of additional COVID-19 testing, positive results and symptoms over a further 6-month enrollment period. Although the highest neutralizing antibody titers are found in severe disease (19), the expected waning of antibody presence is yet unknown. We posit that the presence of antibodies will vary by populations, previous exposures and symptoms. The design of our program allows us to collect survey data to best identify the demographic and clinical characteristics associated with seroprevalence response across a large state. It is estimated that there may be 10 times more SARS-CoV-2 infections than the number of reported cases (14). Understanding the presence of antibodies in a large sample of diverse populations with and without COVID-19 diagnosis may also be used to inform state-wide initiatives, vaccination distribution and restrictions across large populations.

The Phase I setting is important to consider as we enrolled FQHCs to participate in the program to determine the presence of antibodies in both employees and patient populations. Given the predicted long-term health consequences of COVID-19 (19) the Texas CARES program focuses on reach of populations that are underinsured and likely to have co-morbid chronic conditions. The inclusion of this population will allow for the identification of percentage of high-risk patients with antibodies, informing their long-term care for cardiovascular, pulmonary, neurologic and emotional well-being. These data will allow for informed planning by FQHCs and state leaders to determine and address vulnerable patient population needs and for the development of interventions and strategies to best care to mitigate poor health effects of COVID-19 over time.

Among this sample, we found that our adjustments indicate that male patients may have a higher proportion of positivity for antibodies, likely due to greater exposure to COVID-19 by industry and continuation of work during restriction periods. Although the male and female sample sizes are unequal we adjusted to the Texas Census population allowing us to estimate the adjusted human response. This finding aligns with positive proportions of COVID-19 found in males as well as lower antibody levels found in women (30). Additionally, it is important to note the successful reach and high survey completion rate as a result of our engagement and communication strategies designed using a participatory approach to support community-academic partnerships. The engagement of FQHCs who primarily serve vulnerable populations disproportionately impacted by COVID-19 was purposeful as it allowed for reach and determination of antibody response in highly vulnerable patients.

This report has several limitations. First, the participants are voluntary and are not a representative sample of Texas residents. However, the sample represents patients and populations in three counties and areas with varied COVID-19 infection rates. Second, the data collection for COVID-19 test positivity are self-reported, however, we believe the pandemic and impact on communities increases reliability of self-reported testing and positive diagnosis. We have considered false-positive and false-negative results in analysis and are working on analysis to ensure that responses are better understood. As the TX CARES sample increases we hypothesize the prevalence of antibody positive will decrease as the Phase I population represented three specific FQHC clinic settings and communities. Third, this sample was primarily women, representing the employee demographic of FQHCs and patient populations within the clinics. Nevertheless, these findings suggest the feasibility to recruit participants from high-risk populations seeking care at FQHCs and employees serving the population. We also found that the high proportions of survey completion point to interest in the population to engage in research to identify antibody status.

CONCLUSIONS

This program was designed to identify the humoral immune response to SARS-CoV-2 infection in a large sample over time and may assist in determining potential vulnerability to a surge in COVID-19 cases across a large state population.

We found a high estimation of seroprevalence in this first phase of our program using a high specificity and sensitivity assay in a primarily White Hispanic population. Estimating seroprevalence is important given the potential for reinfection and severity of COVID-19 in vulnerable populations with co-morbidities while vaccination uptake and reach across a state continues.

As part of this first phase we have worked to enroll, reach and include vulnerable populations in antibody surveys to identify antibody response. Our additional analysis is now focused on identifying natural human response as well as vaccine induced response over time (6-months). This is important as public health must better understand the response over time and how long immunity may last. The Texas CARES program is collecting follow-up antibody testing data and behavioral, social and illness questionnaires to further identify not only natural human response but vaccine induced response and long term COVID-19 impact on chronic disease management in vulnerable populations, to date we have enrolled over 2,800 participants from FQHCs across Texas.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

Infection rates of SARS CoV-2 are documented across the world, however, estimates of true infection and "natural" immunity are still unclear. It is also important to understand the human response in vulnerable populations and those that serve them at community clinics.

WHAT IS ADDED BY THIS REPORT?

This survey allows us to better understand "natural" immunity and exposure in a underserved population receiving care at Federally Qualified Health Centers (FQHCs) across the state of Texas. TX CARES also contributes to our understanding of engagement of underserved communities using strategies such as champions at the FQHC sites.

WHAT ARE THE IMPLICATIONS FOR PUBLIC HEALTH PRACTICE?

Implications of this work include greater understanding of seroprevalence response as well as exposure across ages 5–80 years at FQHCs. Estimating seroprevalence is important for public health practices given the potential for reinfection and severity of COVID-19 in vulnerable populations with co-morbidities while vaccination of a larger portion of the population continues.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Texas Health Science Center in Houston Institutional Review Board. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

EB, DL, MS, JS, SP, and MV-S were responsible for the conception and design of the survey. MV-S led the relationship with regional FQHCs. MS, SD, AY, and LW lead the data coordination components including survey operation, including the coordination of data acquisition and logistics. MV-S and SM developed the operational protocols for field work and were responsible for training the involved administrative and health personnel. MV-S, AY, LW, MG, MS, and SD were in charge of statistical analyses and table and figure design. All remaining authors in the TX CARES group contributed to participant recruitment, data acquisition, laboratory analyses, and quality control for their respective populations. The first draft was written by MV-S and SD. All authors had full access to all study data, contributed to data interpretation, critically reviewed the first draft, approved the final version, and agreed to be accountable for the work.

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COVID-19 Burden on HIV Patients Attending Antiretroviral Therapy in Addis Ababa, Ethiopia: A Multicenter Cross-Sectional Study

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Background: There has been promising progress toward screening, testing, and retaining patients with HIV in care in Ethiopia. Concern exists that possible disruptions in HIV programs due to coronavirus disease 2019 (COVID-19) could result in a more HIV-related mortality and new HIV infections. This study aimed to investigate the real-time burden of COVID-19 on patients with HIV attending antiretroviral therapy.

Methods: We conducted a facility-based, multicenter, and cross-sectional study among patients with HIV attending antiretroviral therapy in 10 healthcare facilities in Addis Ababa, Ethiopia, in the COVID-19 pandemic period. Data were collected using adapted, interviewer-based questionnaires, and entered into EpiInfo version 7 and exported to SPSS version 26 for analysis.

Result: A total of 212 patients with HIV were included. The participants who missed visits for refill were 58 (27.4%). When the effects of other independent variables on appointments/visits for refill were controlled, the following characteristics were found to be the most important predictors of missed appointments ($p < 0.05$): age ≥ 55 [adjusted odds ratio (AOR) = 6.73, 95% CI (1.495–30.310)], fear of COVID-19 [AOR = 24.93, 95% CI (2.798–222.279)], transport disruption [AOR = 4.90, 95% CI (1.031–23.174)], reduced income for traveling to a health facility [AOR = 5.64, 95% CI (1.234-25.812)], limited access to masks [AOR = 7.67, 95% CI (1.303–45.174)], sanitizer [AOR = 0.07, 95% CI (0.007–0.729)], and non-medical support [AOR = 2.32, 95% CI (1.547–12.596)]. The participants were well aware of the COVID-19 preventive measures. The most costly COVID-19 preventive measures that cause financial burden to the patients were the costs for buying face masks (63.7%), disinfectants (55.2%), and soap for handwashing (22.2%). The participants who missed follow-up diagnostic tests were 56 (26.4%). Variables, which were found to be statistically significant, include the following: age ≥ 55 [AOR = 0.22, 95% CI (0.076–0.621)], partial lockdown [AOR = 0.10, 95% CI (0.011–0.833)], limited access to health services [AOR = 0.15, 95% CI (0.045–0.475)], reduced income for traveling to health facility [AOR = 0.18, 95% CI (0.039–0.784)], and unable to get masks [AOR = 0.12, 95% CI (0.026–0.543)]. The participants who missed counseling services were 55 (25.9%). In multivariate logistic regression, the following were statistically significant: age ≥ 55 [AOR = 0.21, 95% CI (0.078–0.570)], fear of

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COVID-19 [AOR = 0.11, 95% CI (0.013–0.912)], reduced income [AOR = 0.17, 95% CI (0.041–0.699)], unable to get face masks [AOR = 0.19, 95% CI (0.039–0.959)], and partial lockdown [AOR = 0.08, 95% CI (0.008–0.790)].

Conclusions: The COVID-19 had a significant burden on patients with HIV to attend their routine clinical care and treatment, which may lead to treatment failure and drug resistance. The impact was on their appointments for medication refills and clinical and laboratory follow-ups. Targeted initiatives are needed to sustain HIV clinical care and treatment services and improve the well-being of people living with HIV.

Keywords: coronavirus disease 2019 (COVID-19), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), HIV, clinical care, treatment, antiretroviral therapy, Ethiopia

BACKGROUND

Coronavirus disease 2019 (COVID-19) could be the most catastrophic pandemic in modern history. It has infected over 173,674,509 people globally and resulted in more than 3,744,408 deaths as of June 9, 2021 (1). Countries have been taking strong preventive measures to reduce and curve the transmission (2–4). Many health care professionals shifted and health facilities were repurposed into targeted COVID-19 centers to manage patients (5–7). Evidence showed these measures have led to restrictions of health facilities to the management of emergency medical conditions and chronic diseases care and treatment services (8, 9). Ethiopia, a country in sub-Saharan Africa (SSA), is categorized under COVID-19 epidemic phase III (advancing outbreak) according to the Africa Centers for Disease Control and Prevention (Africa CDC) classification (10). On March 13, 2020, the first known case of COVID-19 in Ethiopia was reported in the capital city (11). As of December 17, 2021, people that have been diagnosed with the coronavirus were 374,402, of whom 6,855 (1.83%) died, 16,850 (4.50%) are still sick, and 350,697 (93.67%) have recovered (12). Addis Ababa became the first major city in Ethiopia to report cases and deaths from COVID-19. In Ethiopia, COVID-19 imposed a burden on physical infrastructure and exacerbated the preexisting weaknesses of health systems. As the country has limited numbers of hospitals and health centers, it presented a significant challenge to manage the pandemic and other diseases simultaneously (11–13).

By the end of 2020, it was estimated that 37.6 million people have HIV infection globally, and 1.5 million are newly infected. Only 27.4 million of them are on treatment with antiretroviral therapy (ART), which means 10.2 million (27%) people are still remains untreated with ART (14). The HIV remains highly prevalent in Africa, accounting for more than 67% of the people living with HIV/AIDS (PLWH) worldwide (15). The sub-Saharan region is the most affected place in the world with 25.6 million PLWH (16). Ethiopia is one of the majorly affected countries in sub-Saharan Africa with a national prevalence rate 0.9% (17). Concern exists that possible disruptions in HIV programs due to COVID-19 could result in more HIV-related mortality and new HIV infections.

The double burden of COVID-19 and HIV is one of the major health challenges, especially in developing countries with high HIV prevalence (18). The PLWH might be particularly at high risk for infection with poor clinical outcomes (19–22). Containment measures, disruptions to supply chains, and loss of income have the potential to exacerbate the impacts of the pandemic on patients with HIV (23). While these impacts will vary significantly across countries, some recommended providing ART for 3–6 months, and others began to offer home delivery services through volunteers to reduce the adverse health outcomes (24, 25). The extensive demand for physicians has led to the rescheduling of routine reviews and hospital visits of patients with HIV (26–28). Fear of COVID-19 exacerbated food insecurity, and COVID-19 protective behaviors hindered voluntary HIV testing and healthcare services.

Many countries warned that they are at risk of stock-outs of antiretroviral (ARV) medicines, and some have critically low stocks as a result of the pandemic (29). In addition, PLWH were doubtful about the availability of ART services and about which HIV clinic to attend in the pandemic period (30).

There are limited real-time patient-level pieces of research on how effective and useful country-level COVID-19 interventions were for patients with HIV. As well, the impact of the COVID-19 pandemic on HIV at a population level is not well-known. With the limited level of evidence in the world and as to our knowledge, no research was done on the impact of the pandemic on patients attending HIV care and treatment services in Ethiopia. There is an urgent need for adequately powered studies that investigate the impact of COVID-19 on HIV clinical care and treatment to augment the health of people living with HIV.

Thus, this study aimed to investigate the real-time burden of COVID-19 on people living with HIV who were attending antiretroviral therapy facilities in Addis Ababa, Ethiopia.

Abbreviations: AAU, Addis Ababa University; COVID-19, Coronavirus Disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; HIV, human immunodeficiency virus; PLWH, people living with HIV; HC, health center; ICU, intensive care unit; PPE, personal protective equipment; WHO, World Health Organization; AOR, adjusted odds ratio; CI, confidence interval.

METHODS

Design and Setting

A cross-sectional multi-center study was carried out at 10 primary health care centers in Addis Ababa, from March 15

TABLE 1 | Sampling procedure.

Name of the health facility	Sub-city	No. of. HIV cases on ART
Addis raey HC	Addis ketema	20
Akaki HC	Akakikality	50
Kebena HC	Arada	18
Goro HC	Bole	11
Addisugebya HC	Gulele	16
Kazanchis HC	Kirkos	30
Alem bank	Kolfe	10
T/haymanot HC	Lideta	36
Woreda 02 HC	Nifas-silk lafto	10
Woreda 13 HC	Yeka	11

to April 25, 2021. The city has 10 sub-cities and 116 woredas, and has different government health facilities, including six hospitals and 106 public health centers. In Ethiopia, the COVID-19 pandemic is higher in the capital Addis Ababa (31). Addis Ababa is the highest in HIV prevalence next to Gambella regional state (32). The study was conducted in 10 health facilities, one in each sub-city, which has high flow of patients with HIV.

Participants

In this study, the source population was all patients with HIV of age > 18 years attending care and treatment in the selected health centers. The study population were those who were attending care and treatment services during the data collection period. The participants were included if they were (I) the patients with HIV, as confirmed within the study facilities or result referred from another health facility; (II) a man or a woman aged ≥ 18 years; (III) volunteered to participate in the study. As this study was conducted during the high COVID-19 time in Ethiopia, we approached only 212 participants to minimize the exposure for the pandemic during the interview. All eligible participants who have been attending clinical care and treatment in those study sites during the data collection period were considered with strict precautions to prevent the transmission of the corona virus. The health facilities were selected purposively, one in each subcity, where routine HIV care and treatment services are given and provide services for large number of patients with HIV in comparison with other health centers in the subcities. Patients with HIV who attend clinical care and treatment services during the data collection period were taken from each health facility (**Table 1**).

Data Collection

The questionnaire was developed by reviewing relevant literature to ensure reliability. The questionnaire was adapted, pre-tested, and structured to collect primary data for the assessment of the overall impact of COVID-19. During data collection procedures, all the collected data were reviewed and checked daily for their completeness. The data collection instrument was developed in English and was translated to Amharic, and later back-translated to English to check for any inconsistencies or distortion in the meaning and concepts of the words by another person.

TABLE 2 | Sociodemographic characteristics of respondents, Addis Ababa, Ethiopia, May 2021.

Variables	Category	Frequency	Percentage
Sex	Male	79	37.3%
	Female	133	62.7%
Age	18–34	55	25.9%
	35–54	103	48.6%
	≥55	54	25.5%
Marital status	Single	50	23.6%
	Married	88	41.5%
	Widowed	40	18.9%
	Divorced	26	12.3%
	Separated	8	3.8%
Level of education	No education	46	21.7%
	Can read and write	30	14.2%
	Primary education	59	27.8%
	Secondary education	44	20.8%
	Diploma and above	33	15.6%
Religion	Orthodox	146	68.9%
	Muslim	36	17.0%
	Protestant	21	9.9%
	Catholic	3	1.4%
	Others	6	2.8%
Occupation	Student	3	1.4%
	Daily laborer	41	19.3%
	Merchant	22	10.4%
	Governmental employee	51	24.1%
	Private/NGO employee	43	20.3%
	Farmer	5	2.4%
	Housewife/unemployed	47	22.2%

Eligible participants who were attending the selected health centers were invited to participate. The participants were given information about the study through an information sheet and signed a consent form if they agreed to be part of the study. The data collectors and supervisors were trained before the actual data collection period regarding the approach, objective of the study, and ethical issues. The data collection was interviewer administered, and the questionnaire includes sections, such as sociodemographic characteristics, awareness about preventive measures, care, and treatment services.

Data Analysis and Interpretation

All questionnaires were checked for completeness every day by the principal investigator and supervisors. Data cleaning was conducted at the end of the data entry. The analysis was done using bivariate and multivariate logistic regression to observe the effects of independent variables on the outcome variable while simultaneously controlling for other potential confounding factors. The raw data entered into Epi Info version 7 to control entry errors and exported to SPSS 26 for analysis.

TABLE 3 | Awareness of respondents on COVID-19 preventive measure, Addis Ababa, Ethiopia, May 2021.

Variables	Category	Frequency	Percentage
Stay at home	No	48	22.6%
	Yes	164	77.4%
Maintain physical distancing	No	87	41.0%
	Yes	125	59.0%
Avoid close contact	No	85	40.1%
	Yes	127	59.9%
Cover mouth nose with facemask	No	28	13.2%
	Yes	184	86.8%
Frequent handwashing with soap	No	43	20.3%
	Yes	169	79.7%
Avoid touching of eyes nose and mouth with unwashed hands	No	68	32.1%
	Yes	144	67.9%
Avoid mass gathering	No	92	43.4%
	Yes	120	56.6%
Restrict movement	No	98	46.2%
	Yes	114	53.8%
Use disinfectant	No	50	23.6%
	Yes	162	76.4%

TABLE 4 | Financial burden of the respondents on the COVID-19 preventive measures, Addis Ababa, Ethiopia, May 2021.

Variables	Category	Frequency	Percentage
Facemask	No	77	36.3%
	Yes	135	63.7%
Soap for frequent hand washing	No	165	77.8%
	Yes	47	22.2%
Disinfectant	No	95	44.8%
	Yes	117	55.2%

RESULTS

Sociodemographic Characteristics

A total of 212 patients with HIV were enrolled in the study, with a response rate of 100%, and 133 (62.7%) were female. Of the total, 103 (48.6%) were in the age group 35–54 years. Most of them (41.5%) were married, and 59 (27.8%) had attended primary education. One hundred and forty-six (68.9%) were Orthodox Christian, and 24.1% were governmental employees (**Table 2**).

TABLE 5 | Response of study participants on health care facilities and service delivery, Addis Ababa, Ethiopia, May 2021.

Variables	Category	Frequency	Percentage
Obliged to change the health center because of this pandemic?	Yes	3	1.4%
	No	209	98.6%
Denied health services?	Yes	27	12.7%
	No	185	87.3%
Politeness and respect of health professionals?	Yes	211	99.5%
	No	1	0.5%
Willingness of professionals to listen and answer your questions?	Yes	211	99.5%
	No	1	0.5%
Attention of professionals to your individual needs?	Yes	210	99.1%
	No	2	0.9%
Staff seemed uncomfortable with you?	Yes	23	10.8%
	No	189	89.2%
Contact care provider when there is a health problem or comorbidities quickly?	Yes	101	47.6%
	No	111	52.4%

Most Effective Preventive Measure of COVID-19

Most participants (86.8%) responded "Cover mouth nose with a face mask" is the most effective preventive measure of COVID-19. Responses of the study participants on preventive measures such as "stay at home" and "use disinfectant" were 77.4%, 76.4%, respectively (**Table 3**).

The Financial Burden of COVID-19

The most costly COVID-19 preventive measures that cause financial burden to the patients were costs for buying face masks [135 (63.7%)], disinfectants [117 (55.2%)], and soap for handwashing [47 (22.2%)] (**Table 4**).

HIV Care and Treatment Services During COVID-19

The participants who obliged to change a health center were three (1.4%), and 27 (12.7%) denied health services. Almost all the participants said health care providers were polite and respectful

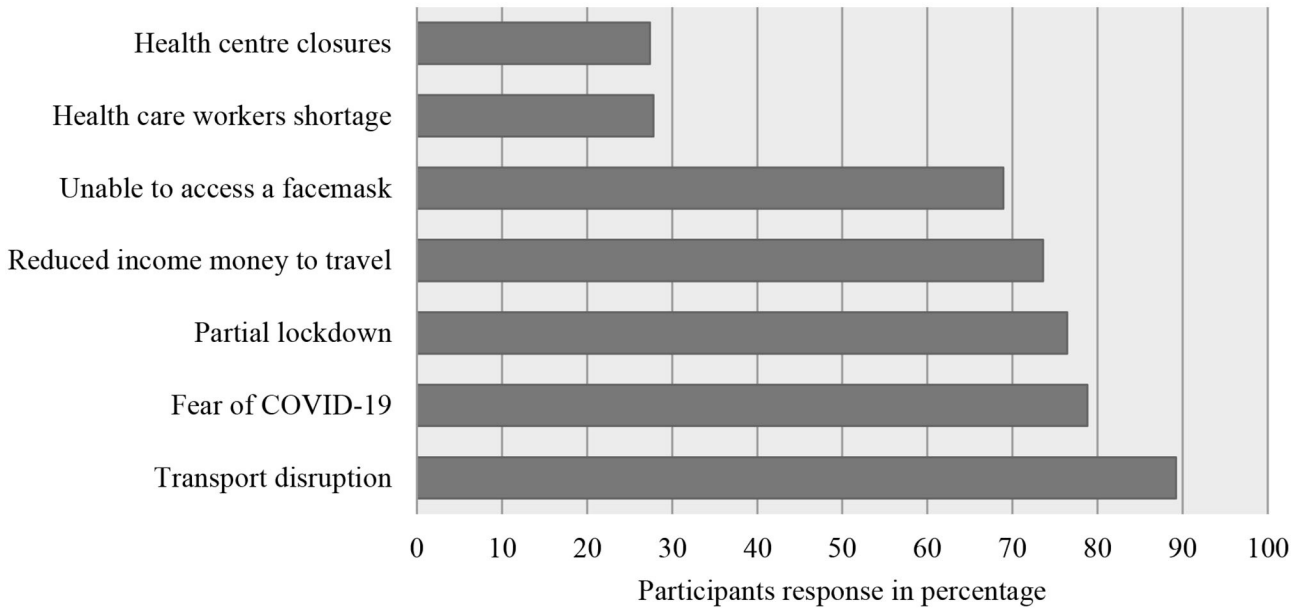

FIGURE 1 | Response of the study participants regarding barriers in accessing health care and treatment during the pandemic, Addis Ababa, Ethiopia, May 2021.

(99.5%), willing to listen and answer their questions (99.5%), give attention to their individual needs (99.1%) (**Table 5**).

Main Barriers to Access Health Care During the Pandemic

Among the study subjects, 189 (89.2%) said transport disruption was the main barrier to access health care. Fear of getting infected with COVID-19 (78.8%) was the second main barrier for the participants (**Figure 1**).

COVID-19 Precaution Measures in Healthcare Facilities

Among the participants, 143 (67.5%) responded that health centers provide screening services for COVID-19, and all health professionals wear masks. The participants responded that there were water (97.2%) and soap (95.8%) at the gate of the healthcare facilities, but not sanitizer (74.1%) (**Table 6**).

Medications and Follow-Ups During COVID-19

Among the total participants, 125 (59.%) said that the ordered drugs were available. Two hundred (94.3%) were able to collect their multi-month drug supply. The participants who missed appointments, follow-up tests, and counseling services were 58 (27.4%), 56 (26.4%), and 55 (25.9%), respectively (**Table 7**).

Logistic Regression Analysis of Missing Appointments/Visits for Medication Refill Variable

Bivariate and Multivariate Logistic Regression analysis showed that the following variables are significantly associated with the likelihood of missing appointments and medication refill. Independent variables, such as older age, less education, fear of COVID-19, transport disruption, reduced income, inability to access mask, no sanitizer availability, and high cost of disinfectant, were related to more missed appointments (**Table 8**).

Logistic Regression Analysis of the Follow-Up Tests Variable

In Bivariate and Multivariate Logistic Regression analysis of the follow-up tests variable, the following variables found to be significant: age, denied health services, reduced income/money to travel, partial lockdown, and inability to access face masks (**Table 9**).

Logistic Regression Analysis of the Counseling Variable

Bivariate and Multivariate Logistic Regression analysis of the counseling variable, factors such as age, education, fear of COVID-19, reduced income money to travel, inability to access face masks, and partial lockdown were significant (**Table 10**).

TABLE 6 | Response of the study participants to the precautions of health facilities for COVID-19 protection, Addis Ababa, Ethiopia, May 2021.

Variables	Category	Frequency	Percentage
Health center provide screening service for COVID-19?	Yes	143	67.5%
	No	69	32.5%
Health professionals wear the gloves during caregiving?	Yes	211	99.5%
	No	1	0.5%
Health professionals wear the mask during caregiving?	Yes	212	100%
	No	0	0.0%
Water available at the entrance of the health center for hand washing?	Yes	206	97.2%
	No	6	2.8%
Soap available at the entrance of the health center for hand washing?	Yes	203	95.8%
	No	9	4.2%
Sanitizer available at the entrance of the healthcentre for cleaning of hands?	Yes	55	25.9%
	No	157	74.1%

TABLE 7 | Response of the study participants to medications and follow-up, Addis Ababa, Ethiopia May, 2021.

Variables	Category	Frequency	Percentage
Availability of ordered drugs?	Yes	125	59.0%
	Some	80	37.7%
	Not at all	7	3.3%
Non-medical support since COVID 19?	Same as before	163	76.9%
	Slightly harder	15	7.1%
	Much harder	23	10.8%
	Impossible	11	5.2%
Have you had multi-month drug supply	Yes	200	94.3%
	No	12	5.7%
For how many months	3 months	90	42.5%
	6 months	110	51.9%
Have you missed appointments (visits)	Yes	58	27.4%
	No	154	72.6%
Follow-up tests done	Yes	156	73.6%
	No	56	26.4%
Counseling done on your medication or healthstatus?	Yes	157	74.1%
	No	55	25.9%

DISCUSSIONS

To the best of our knowledge, this study was the first of its kind to assess the impact of COVID-19 on HIV care and treatment services in Ethiopia. We studied the overlap between the two ongoing pandemics (HIV and COVID-19) in Ethiopia. The findings underscore several factors rendering HIV care and treatment services more difficult. A significant number of participants have missed appointments, follow-up tests, and counseling services due to COVID-19. The COVID-19 containment measures taken by the government, sociodemographic characteristics of the patients, and inconsistent access to personal protective equipment are the main factors that have hindered the retention and adherence of patients with HIV to their routine HIV care and treatment.

The patient living with HIV had great concerns about whether they are at high risk for the pandemic and the worse outcomes if they get infected with COVID-19. Research findings on these concerns have been in agreement with previous studies conducted elsewhere (12, 18, 19, 21, 22, 33, 34). Studies indicated that, although the pandemic affected the health care for all disease conditions, chronic patients such as people living with HIV are likely to be uniquely vulnerable (4, 17, 35). It has been reported that the elderly and the people with chronic conditions are more likely to be infected with COVID-19, and patients with HIV may miss appointments as a result. According to this study, older patients with HIV were more likely to miss the clinical care and treatment services given by the health centers. This finding is in agreement with the study done in Addis Ababa in Tikur Anbessa Specialized Hospital (TASH), Dessie town government, and private hospitals where older chronic patients were more likely to miss clinical appointments/visits (36, 37). The result of another study in Uganda was also consistent with this finding that older people were more likely to miss ART and related services (19, 38). In our findings, those who had formal education are more likely to have care and treatment services. This might be because the respondents who had formal education may have a deeper understanding of the negative consequence if they missed their follow-up visits and they could have more tendency to request and to access information about COVID-19 and its preventive measures.

Our results also indicated that patients with HIV, who had a fear of getting infected with COVID-19, were more likely to miss appointments for care and treatment. This is also consistent

TABLE 8 | Bivariate and multivariate logistic regression analysis of missing appointments/visits for the medication refill variable, Addis Ababa, Ethiopia, 2021.

		Missed appointments		Odds ratio		
Variables	**Category**	**No**	**Yes**	**COR (CI)**	**AOR (CI)**	***P*-value**
Age	18–34	43 (28.0%)	12 (20.7%) 11	1	1 0.41 (0.091–1.875) 6.73	0.252
	35–54	92 (59.7%)	(19.0%) 35	0.43 (0.175–1.048)	(1.495–30.310)	0.013*
	≥55	19 (12.3%)	(60.3%)	6.60 (2.823–15.434)		
Education	No education	14 (9.1%)	31 (53.5%) 11	1	1 0.01 (0.001–0.165) 0.02	0.001*
	Read + write	19 (12.3%)	(19.0%) 9 (15.5%)	0.25 (0.096–0.670)	(0.002–0.229) 0.05	0.002*
	Primary edu.	50 (32.5%)	6 (10.3%) 1 (1.7%)	0.08 (0.031–0.203)	(0.003–1.022) 0.01	0.052
	Secondary edu.	38 (24.7%)		0.07 (0.024–0.201)	(0.001–1.002)	0.997
	≥ Diploma	33 (21.4%)		0.01 (0.0012–1.021)		
Fear of COVID-19	No	44 (28.6%)	1 (1.7%) 57	1	1 24.93 (2.798–222.279)	0.004*
	Yes	110 (71.4%)	(98.3%)	22.80 (3.062–169.782)		
Transport disruption	No	22 (14.3%)	1 (1.7%) 57	1	1 4.90 (1.031–23.174)	0.038*
	Yes	132 (85.7%)	(98.3%)	9.50 (1.250–31.185)		
Reduced income	No	53 (34.4%)	3 (5.2%) 55	1	1 5.64 (1.234–25.812)	0.026*
	Yes	101 (65.6%)	(94.8%)	9.62 (2.873–32.219)		
Unable to access mask	No	64 (41.6%)	2 (3.4%) 56	1	1 7.67 (1.303–45.174)	0.024*
	Yes	90 (58.4%)	(96.6%)	19.91 (4.687–84.577)		
Sanitizer available	No	110 (71.4%)	47 (81.0%) 11	1	1 0.07 (0.007–0.729)	0.026*
	Yes	44 (28.6%)	(19.0%)	0.58 (0.278–1.231)		
For how many months	3 months	52 (35.9%)	38 (69.1%) 17	1	1 0.33 (0.132–0.825)	0.018*
	6 months	93 (64.1%)	(30.9%)	0.25 (0.129–0.486)		
Cost of disinfectant	No	85 (55.2%)	10 (17.2%) 48	1	1 16.64 (1.462–189.569)	0.023*
	Yes	69 (44.8%)	(82.8%)	5.91 (2.788–12.539)		
Non-medical support since COVID-19	Same as before	130 (84.4%)	33 (56.9%) 3	1	1 3.68 (0.434–31.204) 3.78	0.233
	Slightly harder	12 (7.8%)	(5.2%) 13 (22.4%)	0.98 (0.263–3.693)	0.774–18.421) 2.32	0.100
	Much harder	10 (6.5%)	9 (15.5%)	5.12 (2.064–12.705)	(1.547–12.596)	0.044*
	Impossible	2 (1.3%)		17.72 (3.655–85.987)		

**Statistically significant at p < 0.05, COR, crude odds ratio at 95% confidence interval; AOR, adjusted odds ratio at 95% confidence interval.*

TABLE 9 | Bivariate and multivariate logistic regression analysis of the follow-up tests variable, Addis Ababa, Ethiopia, 2021.

		Followup test		Odds ratio		
Variables	**Category**	**No**	**Yes**	**COR (CI)**	**AOR (CI)**	***P*-value**
Age	18–34	12 (21.4%)	43 (27.6%) 93	1	1 2.65 (0.913–7.670) 0.22	0.073
	35–54	10 (17.9%)	(59.6%) 20	2.59 (1.041–6.472)	(0.076–0.621)	0.004*
	≥55	34 (60.7%)	(12.8%)	0.16 (0.070–0.382)		
Partial lockdown	No	1 (1.8%)	49 (31.4%) 107	1	1 0.10 (0.011–0.833)	0.034*
	Yes	55 (98.2%)	(68.6%)	0.04 (0.005–0.295)		
Denied health services	No	35 (62.5%)	150 (96.2%) 6	1	1 0.15 (0.045–0.475)	0.001*
	Yes	21 (37.5%)	(3.8%)	0.07 (0.025–0.177)		
Reduced income	No	3 (5.4%)	53 (34.0%) 103	1	1 0.18 (0.039–0.784)	0.023*
	Yes	53 (94.6%)	(66.0%)	0.11 (0.033–0.369)		
Unable to get mask	No	2 (3.6%)	64 (41.0%) 92	1	1 0.12 (0.026–0.543)	0.006*
	Yes	54 (96.4%)	(59.0%)	0.05 (0.013–0.226)		

**Statistically significant at p < 0.05, COR, crude odds ratio at 95% confidence interval; AOR, adjusted odds ratio at 95% confidence interval.*

with other findings (39–41). Containment measures of COVID-19 taken in Ethiopia had a significant contribution to halting the spread of COVID-19 in Ethiopia; however, they had their own implications on HIV care and treatment services as the response from the patients with HIV as indicated. Transport disruption, partial lockdown that impaired mobility, and income reduction were significant factors in missing health care visits, which was in agreement with previous studies conducted in Ethiopia (13, 42), and elsewhere in the world (43–50) that the COVID-19 containment measure had a significant impact on patients' access to healthcare facilities.

Undue expenses related to protective equipment, including face masks and sanitizers, were a burden for the people living with HIV. This finding is in agreement with previous findings in Ethiopia (14) and elsewhere in Africa, wherein sufficient money to buy protective equipment was commonly reported effects of

TABLE 10 | Bivariate and multivariate logistic regression analysis of the counseling variable, Addis Ababa, Ethiopia, 2021.

		Counslingdone		Odds ratio		
Variable	**Category**	**No**	**Yes**	**COR (CI)**	**AOR (CI)**	***P*-value**
Age	18–34	12 (21.8%)	43 (27.4%) 93	1	1 2.28 (0.842–6.170) 0.21	0.105
	35–54	10 (18.2%)	(59.2%) 21	2.59 (1.041–6.472)	(0.078–0.570)	0.002*
	≥55	33 (60.0%)	(13.4%)	0.18 (0.077–0.412)		
Education	No education	29 (52.7%)	16 (10.2%) 19	1	1 3.68 (1.230–11.022) 11.46	0.020*
	Read + write	11 (20.0%)	(12.1%) 51	3.24 (1.241–8.449)	(3.906–33.615) 6.48	0.000*
	Primary edu.	8 (14.5%)	(32.5%) 38	11.95 (4.572–31.251)	(1.921–21.876) 1.23	0.003*
	Secondary edu.	6 (10.9%)	(24.2%) 33	11.87 (4.142–34.047)	(0.238–6.412)	0.801
	≥Diploma	1 (1.8%)	(21.0%)	4.60 (0.391–15.227)		
Fear of COVID-19	No	1 (1.8%)	44 (28.0%) 113	1	1 0.11 (0.013–0.912)	0.041*
	Yes	54 (98.2%)	(72.0%)	0.05 (0.006–0.354)		
Reduced income	No	3 (5.5%)	53 (33.8%) 104	1	1 0.17 (0.041–0.699)	0.014*
	Yes	52 (94.5%)	(66.2%)	0.11 (0.034–0.380)		
Unable get face mask	No	2 (3.6%)	64 (40.8%) 93	1	1 0.19 (0.039–0.959)	0.044*
	Yes	53 (96.4%)	(59.2%)	0.05 (0.013–0.233)		
Partial lockdown	No	1 (1.8%)	49 (31.2%) 108	1	1 0.08 (0.008–0.790)	0.031*
	Yes	54 (98.2%)	(68.8%)	0.04 (0.005–0.304)		

**Statistically significant at p < 0.05, COR, crude odds ratio at 95% confidence interval; AOR, adjusted odds ratio at 95% confidence interval.*

the COVID-19 on attending HIV clinical care and treatment services (51). The city of Addis Ababa introduced innovative measures providing ART medications for 3 to 6 months to mitigate these challenges. In our finding, those who collect medications for 6 months were less likely to miss appointments for medication refill compared to those who took for 3 months.

Indirect impacts arising from the pandemic, which reduced non-medical support, had economical burdens. The participants who said non-medical support was much harder and impossible were more likely to miss clinical visits. Similar observations were reported in other studies as well (52). Furthermore, WHO stated that the COVID-19 pandemic has affected the availability of medicines and non-medical supports in many countries as the world focused on the COVID-19 pandemic (53, 54). Indeed, health centers in Addis Ababa have had preeminent COVID-19 precaution procedures and measures to protect their clients from the pandemic. Availability of sanitizer, water, and soap at the health facilities' gates encouraged the patients with HIV to attend their routine care. These results are in line with a finding from North Shoa health care facilities, where patients who got sanitizer and other supports to protect themselves from the pandemic were more satisfied by health services and attended the clinical appointments/vests (14, 55).

Our study has some limitations. The study was limited to healthcare facilities in Addis Ababa, and, therefore, may not be representative of Ethiopia. As the study design was a cross-sectional study, it does not show a causal relationship and only provides a view of the impacts of COVID-19 in a specific period. Otherwise, the study was based on real-time, patient-level primary data, and it was conducted in a resource-constrained, high-HIV-burden country context.

CONCLUSION

The COVID-19 had a significant burden on patients with HIV to attend their routine clinical care and treatment, which may lead to treatment failure and drug resistance. The impact was on their appointments for medication refills and clinical and laboratory follow-ups. Targeted initiatives are needed to sustain HIV clinical care and treatment services and improve the well-being of people living with HIV. Stakeholders, such as the Addis Ababa health bureau, the ministry of health, and others, should work in partnership to reduce the impact of this pandemic on those patients to maintain their economic well-being.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Scientific and Ethics Review Committee of the Center for Innovative Drug Development and Therapeutic Trials for Africa (CDT-Africa), College of Health Sciences, Addis Ababa University. Ethical clearance and support letters were obtained from Addis Ababa public health research and emergency directorate, Addis Ababa City Government Health Bureau. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

DC collected the primary data, conducted the analyses, and drafted the manuscript. TM and YW contributed to the data collection and analysis and reviewed the manuscript. All the authors have read and approved the manuscript.

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Addressing Privacy Concerns in Sharing Viral Sequences and Minimum Contextual Data in a Public Repository During the COVID-19 Pandemic

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COVID-19 was declared to be a pandemic in March 2020 by the World Health Organization. Timely sharing of viral genomic sequencing data accompanied by a minimal set of contextual data is essential for informing regional, national, and international public health responses. Such contextual data is also necessary for developing, and improving clinical therapies and vaccines, and enhancing the scientific community's understanding of the SARS-CoV-2 virus. The Canadian COVID-19 Genomics Network (CanCOGeN) was launched in April 2020 to coordinate and upscale existing genomics-based COVID-19 research and surveillance efforts. CanCOGeN is performing large-scale sequencing of both the genomes of SARS-CoV-2 virus samples (VirusSeq) and affected Canadians (HostSeq). This paper addresses the privacy concerns associated with sharing the viral sequence data with a pre-defined set of contextual data describing the sample source and case attribute of the sequence data in the Canadian context. Currently, the viral genome sequences are shared by provincial public health laboratories and their healthcare and academic partners, with the Canadian National Microbiology Laboratory and with publicly accessible databases. However, data sharing delays and the provision of incomplete contextual data often occur because publicly releasing such data triggers privacy and data governance concerns. The CanCOGeN Ethics and Governance Expert Working Group thus has investigated several privacy issues cited by CanCOGeN data providers/stewards. This paper addresses these privacy concerns and offers insights primarily in the Canadian context, although similar privacy considerations also exist in other jurisdictions. We maintain that sharing viral sequencing data and its limited associated contextual data in the public domain generally does not pose insurmountable privacy challenges. However, privacy risks associated with reidentification should be actively monitored due to advancements in reidentification methods and the evolving pandemic landscape. We also argue that during a global health emergency such as COVID-19, privacy should not be used as a blanket measure to prevent such genomic data sharing due to the significant benefits it provides towards public health responses and ongoing research activities.

Keywords: privacy, data-sharing strategy, health information access, contextual data, COVID-19, viral sequence, metadata, genomic (or scientific) governance

CONTEXT AND INTRODUCTION

Accessible contextual data accompanying genomic sequence data are necessary for informed public health responses to emergencies such as COVID-19. As of May 2021, the COVID-19 pandemic has claimed the lives of over 22 thousand individuals in Canada alone (Public Health Agency of Canada, 2020). With global cases exceeding 140 million and an international death toll of over three million individuals, COVID-19 continues to be a public health emergency devastating the populations and economies of countries around the globe (John Hopkins Coronavirus Resource Center, 2020). While accelerated efforts in vaccine development and production hold significant promise (BBC News, 2020; CBC, 2020), it is evident that continued public health interventions will be needed to bring an "end" to the COVID-19 pandemic (Levin et al., 2020). Specifically, viral genomic data sharing by researchers and public health authorities will be crucial to informing ongoing local, provincial, national, and international public health responses (Walport and Brest, 2011; van Panhuis et al., 2014; Dye et al., 2016; Edelstein et al., 2018). For example, analyzing SARS-CoV-2 viral genomic sequences has been essential in elucidating transmission patterns, identifying variants with enhanced transmissibility or clinical severity, and the real-time analysis of outbreaks (Fang and Meng, 2020).

Beyond informing public health policy, rapidly depositing SARS-CoV-2 genomic sequences in open databases have been of fundamental importance for quickly developing COVID-19 vaccines, testing kits, and other research efforts. For example, the first SARS-CoV-2 genomic sequences deposited in the Global Initiative on Sharing Influenza (GISAID) database allowed for rapidly developing the Pfizer-BioNTech BNT162b2 vaccine candidate (Polack et al., 2020). Similarly, the SARS-CoV-2 sequences deposited in GISAID have also provided the basis for the accelerated development and deployment of numerous diagnostic testing kits (Bohn et al., 2020). Recently, the importance of COVID-based genomic data sharing has been increasingly underscored with the emergence of novel SARS-CoV-2 Variants of Concern (VOCs) (To et al., 2020; Mahase, 2021). The Canadian and international response to VOCs relies centrally on viral genomic sequencing to detect and track VOC transmission and to investigate key mutations that affect disease severity and the virus's ability to escape natural and post-vaccination immunity (Volz et al., 2020). For example, the B.1.1.7 (Alpha), B.1.351 (Beta), and P.1 (Gamma) VOCs were all detected largely through a combination of epidemiological, contextual, and genomic data sharing (Volz et al., 2020; Mahase, 2021). This detection is hugely significant. Although it is impossible to fully quantify, failing to detect more virulent and or deadly VOCs in a timely manner would likely cause substantial delays in enacting the appropriate response measures (Davies et al., 2021).

Recognizing the promise of genomic data sharing, the Canadian COVID-19 Genomics Network (CanCOGeN) was launched to coordinate and upscale existing genomics-based research and surveillance efforts, with the goals of tracking viral introductions, informing the public health response, and exploring the relationship of viral and human genomes in individual outcomes (Genome Canada, 2021a). CanCOGeN is mandated to sequence up to 10,000 individuals (host) genomes and up to 150,000 viral sample genomes (Genome Canada, 2021b). The sometimes innately differing nature of data sharing in human genomics versus pathogen genomics elicits varying legal, ethical, governance, technological, and other practical concerns. Accordingly, the CanCOGeN project comprises of two main subgroups- CanCOGeN-HostSeq and CanCOGeN-VirusSeq to address topics specific to the individual and viral data sharing respectively, while overarching committees, such as the CanCOGeN Ethics and Governance, Implementation, and Coordination Committees also exist to synchronize the efforts of these two groups. As a part of its mandate, the Ethics and Governance Committee has been tasked with exploring the privacy and ethical concerns of sharing SARS-CoV-2 genomic sequences along with the relevant associated contextual data. Sequencing data alone provides little to no utility (Schriml et al., 2020). Interpreting sequence data alongside high-quality contextual data provides exponentially more meaningful findings. Descriptive data fields such as the date of sample collection, geographic region of origin, and the age of the individual are critical for the proper contextual interpretation of the sequencing data and analytical results when conducting genomic surveillance and investigating a broad range of research questions. In an effort to increase the utility of archived pathogen genomic data, using existing pathogen contextual data standards (MIxS and MIGS) and considering Canadian legislation, VirusSeq developed a concise list of 16 minimal contextual data fields (see **Table 1**) to be associated with deposited SARS-CoV-2 sequences.

Despite the broadly accepted benefits of such data sharing towards both health policy and research, the CanCOGeN Ethics and Governance Committee has found that privacy and the protection of personal information are frequently stated as justifications to resist sharing minimal contextual data in direct association with the viral sequences they describe (Joly, 2020). Privacy as a challenge to data sharing is not exclusive to COVID-19 and has been well-documented (Butler, 2007; van Panhuis et al., 2014; Sorani et al., 2015; Bernier and Knoppers, 2020; Bonomi et al., 2020). In the current context, there are concerns that publicly archiving SARS-CoV-2 viral sequencing data in combination with the minimal set of contextual data will allow for the reidentification of individuals (Shean and Greninger, 2018; Joly, 2020). This paper reviews and addresses potential privacy risks of sharing pathogen sequencing data along with its accompanying minimum contextual data mainly under the Canadian legal context. However, many of the principles and reasoning used here can be similarly applied in an international context. The first section introduces the key concepts of identifiability and personal information. The second section discusses whether publicly sharing SARS-CoV-2 genomic sequences inherently threatens the privacy of individuals. The third section focuses on the privacy considerations of publicly

TABLE 1 | MIxS Compliance and Implementation Metadata Standards (Genomics Standards Consortium, 2021).

Field Name	Definition
sample collector sample ID	The user-defined name for the sample.
sample collected by	The name of the agency that collected the original sample.
sequence submitted by	The name of the agency that generated the sequence.
sample collection date	The date on which the sample was collected.
geo_loc_name (country)	The country where the sample was collected.
geo_) loc_name (state/province/territory)	The province/territory where the sample was collected.
organism	Taxonomic name of the organism.
Isolate	Identifier of the specific isolate.
isolation source	The material sampled (this information is encoded by 6 additional fields which need only be filled as applicable, depending on sample type; anatomical material, anatomical site, body product, environmental material, environmental site, collection device, collection method).
host (scientific name)	The taxonomic, or scientific name of the host.
host disease	The name of the disease experienced by the host.
host age	Age of host at the time of sampling.
host gender	The gender of the host at the time of sample collection.
sequencing instrument	The model of the sequencing instrument used.
consensus sequence software name	The name of software used to generate the consensus sequence.
consensus sequence software version	The version of the software used to generate the consensus sequence.

archiving four (age, gender, province/territory of collection, and sample collection date) minimal contextual data fields associated with the viral sequences. The fourth section then discusses situations where the privacy risks are elevated in sharing specific fields of contextual data in certain contexts and outlines precautions that can be used to mitigate such risks. Finally, as a part of the deliberations of the VirusSeq Ethics and Governance Working Group, some concerns were raised regarding the risk of individual self-identification in publicly available formats. The final section addresses this point specifically and focuses on the question of whether the definition of "identifiability" includes self-identification.

A Brief Review on the Definition of Personal Information and Its Relationship to Privacy

To assess the privacy risks of sharing viral sequencing data and its associated minimum contextual data, it is important to first address concerns as to whether such data constitutes "personal information," which, in general, requires the individual's consent or other justified reasons to share in the context of research (Office of the Privacy Commissioner of Canada, 2013). In Canada, with a federal-provincial division of powers, personal information is protected under numerous forms of federal and provincial privacy legislation (Bernier and Knoppers, 2020). At the national level, personal information collected by federal entities is subject to the *Privacy Act* (Privacy Act, 1985; Office of the Privacy Commissioner of Canada, 2019), while the *Personal Information Protection and Electronic Documents Act (PIPEDA)* applies to the personal information collected throughout the commercial sector (Office of the Privacy Commissioner of Canada, 2020; PIPEDA, 2000). Additionally, each province is entitled to enact its own privacy legislation, if such provincial legislation is considered "substantially similar" to PIPEDA (Office of the Privacy Commissioner of Canada, 2017). Indeed, there are numerous applicable laws in Canada. Despite this broad variety of laws governing the collection and disclosure of personal information in Canada, the definition of what constitutes "personal information" is relatively uniform, focusing on the feature of "identifiability." For example, PIPEDA defines personal information as "information about an identifiable individual" (that is recorded in any form . . .) (Office of the Privacy Commissioner of Canada, 2019; PIPEDA, 2000). Similarly, at the provincial level in Quebec, personal information is "information concerning a natural person that allows the person to be identified" (Act respecting Access to documents held by public bodies and the Protection of personal information, Québec, 1982). In British Columbia (BC), the BC *Personal Health Information Access and Protection of Privacy (E-Health) Act*, BC *Personal Information Protection Act*, and BC *Freedom of Information Protection of Privacy Act*, all hold similar definitions as those provided by the above laws (Freedom of Information and Protection of Privacy Act, British Columbia, 1996; Personal Information Protection Act, British Columbia, 2003; E-health (Personal Health Information Access And Protection of Privacy) Act British Columbia, 2008). Lastly, the Information and Privacy Commissioner of Ontario summarises that information is "personal" if "it is reasonable to identify an individual from the information (either alone or by combining it with other information)" (Information and Privacy Commissioner of Ontario, 2016b). Other countries around the globe have similarly emphasized the concept of "identifiability" in their privacy legislation. For example, the European Union's *General Data Protection Regulation* (GDPR) states that personal information is "relating to an identified or identifiable natural person" (General Data Protection Regulation, 2016). In the United States, "personal health information" is designated individually identifiable information relating to the "(...) health status of an individual (...)" by the *Health Insurance Portability and Accountability Act* (HIPAA) (HIPPA, 1996). Similarly in China, personal information is defined as "information that can identify specific natural persons either by itself or when combined with other information and in Australia, the Australian *Privacy Act* also

focuses on identifiability as a component of personal information (The Privacy Act, 1988; Civil Code of the People's Republic of China, 2020). These numerous legal definitions across a wide variety of jurisdictions emphasize that identifiability is a necessary and ubiquitous requirement concerning the definition of personal information. As such, in evaluating the privacy risks of publicly archiving viral genomic data and its associated contextual data, it will be key to assess whether such data can be considered personal information. Here, we will focus on this question by discussing the potential identification risks of sharing SARS-CoV-2 viral genomic sequences and their associated contextual data.

Does Publicly Archiving of SARS-CoV-2 Viral Sequences Inherently Create Privacy Risks?

While concerns regarding the privacy risks of certain contextual data fields have been raised, it seems intuitive to first consider whether SARS-CoV-2 viral genomic sequences alone generate any privacy risks. Is it possible for an individual to be identified through only publicly archived pathogen sequences? To consider this question, it is important to assess whether the SARS-CoV-2 viral genome can be used as an identifier. Viruses are frequently characterized by their "serial interval" and "mutation rate." The serial interval describes the time between the onset of symptoms in an infector (individual that transmits the virus) individual and the infectee (individual infected by the virus from the infector), and with the SARS-CoV-2 virus, the serial interval is estimated to be close to 4 days (Du et al., 2020). While the mutation rate has been predicted to be once every 10–15 days (Duchene et al., 2020). Since the serial interval is shorter than the mutation rate, multiple infector-infectee pairs will likely share the same viral sequence. If different individuals are likely to share the same pathogen sequence, the pathogen sequence alone cannot be used to effectively distinguish between various sequenced individuals. It is also extremely unlikely that each tested individual would have a unique viral sequence, therefore it is equally improbable for SARS-CoV-2 sequences to pose a significant reidentification risk to the host. Moreover, if at the time of sequencing, an individual is found to be infected with a unique form of the virus, the mutation rate of the SARS-CoV-2 virus are such that if the individual were to be tested again in the future, they would be unlikely to possess the same viral sequence (Du et al., 2020; Duchene et al., 2020). Overall, it is extremely unlikely for SARS-CoV-2 sequences derived from an individual to be used as an effective identifier. Some have noted that it is possible for pathogen samples to be "contaminated" with human DNA. In this scenario, sharing viral sequencing data can be argued as possibly also sharing human genomic information (Population Health and Genomics Foundation, 2020). While possible, such risks are also very unlikely given that technical safeguards are routinely implemented to systematically and robustly subtract any human-like or non-viral sequences of all public-level viral sequence datasets (this task is often termed "de-hosting") (Population Health and Genomics Foundation, 2020; Public Health Agency of Canada - National Microbiology Laboratory, 2021). De-hosting is a very common technique used to remove human-reads from pathogen sequence datasets. Tools used for de-hosting remove genomic reads that map onto to human reference genome and are well-validated. Applying such quality control and safety techniques ensure that the risk of reidentification from public-level viral sequencing data is extremely low. In summary, the innate characteristics of the SARS-CoV-2 virus are such that it is statistically unlikely for one-to-one unique host-to-pathogen matches to occur. Additionally, various computer-based techniques are employed to sufficiently remove human-like sequences from the viral sequences to further minimize reidentification risks before publicly archiving in any public database.

Does the Minimum Contextual Data (List 1) CanCOGeN Intends to Pubicly Deposit Constitute "Personal Information" According to Canadian Privacy Legislation?

As previously mentioned, the utility of sequencing data from a public health or research perspective is often highly dependent on the thoroughness and quality of its accompanying contextual data (Schriml et al., 2020). Some typical examples of contextual data include "laboratory of origin, date of collection, individual age and gender, method of sampling, etc." (Griffiths et al., 2020). Concerns have been raised that publicly releasing these data fields in association with the samples they describe could violate the privacy of individuals (Shean and Greninger, 2018; Joly, 2020). Here, the core question to assess is whether the minimal contextual data makes the associated pathogen data "identifiable" and is thus considered "personal information." While the law often writes of identifiability in binary terms (i.e., an individual is either identifiable or non-identifiable), statistically speaking, identifiability is better conceived as a spectrum of probabilities. These probabilities range from 0 to 100%, where the percentage describes the certainty with which information can be attributed to a person (Rocher et al., 2019). As noted, oftentimes, the term "identifier" is used in this context to describe information that contributes to the reidentification or identification of an individual (Sweeney, 2000; Golle, 2006; Rocher et al., 2019). Many specific denominations of the term, such as "unique" identifier, "quasi-identifier", or "direct" identifiers exist, all emphasizing their potential to increase the probability of personal identification. For example, a quasi-identifier refers to a combination of traits or attributes in a dataset that is not independently capable of identification, but when in combination with other accessible data, becomes highly identifying (Sweeney, 2000). Typical examples of quasi-identifiers include characteristics such as date of birth, gender, visible minority status, and profession (Sweeney, 2000).

While identifiability is not a simple binary nor a "yes" or "no" concept, few resources specifically address the question of when an individual statistically and quantitatively passes from the qualitative terms of "non-identified/non-

identifiable" to "identified/identifiable." Despite this, resources do exist. Echoing the stances of privacy researchers and data-release precedent, the Information and Privacy Commissioner of Ontario has published the *De-identification Guidelines for Structured Data*, a guide on the identifiability, privacy, and the release of data (Information and Privacy Commissioner of Ontario, 2016a). What is considered "identifiable" does not merely depend on the statistical probability of attribution, but rather it is also affected by the sensitivity (also sometimes referred to as the degree of the potential "invasion of privacy") (Dyke et al., 2015; Information and Privacy Commissioner of Ontario, 2016a). The sensitivity of data considers the consequences to an individual if the privacy of such data were to be invaded. Some data is more sensitive because the contents it reveals are usually of greater consequence. For example, in general, the repercussions of revealing an individual's psychiatric history are typically greater than revealing the same individual's rhesus blood type (Dyke et al., 2015). For more sensitive data deemed to present a higher invasion of privacy, the criteria for what is considered identifiable is stricter. What is considered non-identifiable for information with low sensitivity can conversely be considered identifiable if such information were to be considered highly sensitive (Information and Privacy Commissioner of Ontario, 2016a). Ontario's *De-identification Guidelines for Structured Data* defines a reidentification risk of below 5% to be considered acceptable for information with the potential for high sensitivity (a high invasion of privacy) (Information and Privacy Commissioner of Ontario, 2016a). In other words, if the combination of reasonably available information can "single out" 20 or fewer individuals from a pool of potential candidates, the individual who the information is about, should be considered "identifiable," if the information is considered sensitive (Information and Privacy Commissioner of Ontario, 2016a). The smaller the pool of potential candidates, the more identifiable an individual is. Here, COVID-19 related testing data are considered more sensitive due to their revealing implications on an individual's past or present health condition/status and past medical testing that they have undergone. In Canada, such health-based information is generally considered as sensitive if identifiable (Townsend v. Sun Life Financial, 2012). The de-identification guide thus recommends a threshold of 5% for high sensitivity data, 7.5% for medium, and 10% for low sensitivity data (Information and Privacy Commissioner of Ontario, 2016a).

In evaluating the potential privacy risks of openly depositing SARS-CoV-2 genomic sequences and their minimum contextual data, we are aware that the four data fields of 1) age (displayed in intervals of 10-years), 2) gender, 3) province/territory of collection, and 4) date of collection, are considered more problematic from a privacy and reidentification standpoint by various stakeholders (Sweeney, 2000; Golle, 2006; Rocher et al., 2019). The other 12 fields while useful for statistical analyses, do not appreciably impact the risk of reidentification (except in situations where these other fields indirectly act as an indirect proxy for one of these four fields, which will also be discussed). Therefore, we will primarily explore the privacy and reidentification risks of those four fields. As a reminder, the important primary consideration is whether these four data fields in combination with other "reasonably available" information can allow for the identification of an individual, and accordingly, whether the various privacy legislations of Canada and other jurisdictions are called into effect. Based on the most recently available census data available from each province and territory, and considering the three fields of age, gender, province/territory location, if the population were to be stratified by contextual data fields such as age and gender (note the data released by Stats Canada uses age intervals of 5 years instead of CanCOGeN Virus-Seq's proposed 10-years intervals. The 5-years interval is more identifying, since a more specific age range will be inherently more identifying), the number of individuals in the majority of categories greatly exceeds 20 individuals (Statistics Canada, 2020a). This is true for even the most sparsely populated provinces/territories such as Prince Edward Island or Nunavut (Statistics Canada, 2020b; Statistics Canada, 2020c). This means that by using the contextual data identifiers of age category, province/territory, and gender, the vast majority of individuals are not considered identified to the threshold of 5%. In short, for most individuals in Canada, the three traits of province/territory, gender, and age do not constitute personal information, as they cannot be used to sufficiently identify an individual. Potential exceptions for this will be discussed in the next section. Lastly, the data-field "collection date" may appear to be a strong quasi-identifier for stratifying the population. Yet, this is not an accurate conceptualization of reidentification, as a reasonably competent third-party will not be able to link such information to the other contextual data fields. This is because the date that an individual is tested for COVID-19 cannot be information that is considered "reasonably available" (Townsend v. Sun Life Financial, 2012). A third-party individual cannot be expected to have access to an individual's COVID-19 testing history (including date that the test was performed on) and to use this information in conjunction with the contextual field released in public databases to reidentify. In other words, the field of collection date cannot be used as an identifier (Sweeney, 2000; Golle, 2006; Rocher et al., 2019). Taken together, the four proposed contextual data fields should not be considered "personal information" and can be shared publicly. It is, however, important to note that identifiability is a contextual matter that sometimes exceeds factors such as identifiability and data sensitivity. There is a plethora of other factors such as the costs of identification, time available, the technology available, population pool, etc. that must also be considered (Beauvais, 2020). In some circumstances, certain data fields may disproportionately raise the risk of reidentification, for example, the field of "province" in low-population provinces such as Prince Edward Island (estimated pop. of 159,713 in 2020), and

these cases will be discussed in the following section (Statistics Canada, 2020b).

Situations Where Sharing the Sample's Province of Origin, Gender, and Date of Collection May Disproportionately Increase the Risk of Identification

Identifiability is contextual and contingent on factors such as the population pool and confirmed cases in that specific province, and more (Information and Privacy Commissioner of Ontario, 2016a). This section discusses the reidentification risk in these scenarios. For provinces with a larger population, the risk of reidentification is inherently lower. The *Gordon* v. *Canada (Health)* 2008 federal court case established that the data field of "province" or "territory" can create a disproportionate risk of reidentification in provinces and territories with a smaller population (such as Prince Edward Island) (Gordon V. Canada (Health), 2008). Recognizing this, the CanCOGeN project has proposed to begin the data sharing process by replacing the "province" and "territory" field as "other" in all provinces/territories outside of British Columbia, Alberta, Ontario, and Quebec. The population, among other factors, in these four last provinces allow for the safe inclusion of this data field without appreciably raising the possibility of reidentification of such individuals. As a final note, data providers should be cautious about the level of geographic specificity they reveal when providing the methodologically relevant fields such as "collection agency." For example, it is not uncommon for the collection agency to be the name of a local hospital, which then can reveal more detailed geographical location and increase the risk of reidentification. In short, measures should be taken so that information indicating an inappropriate level of geographic specificity is not provided.

Disclosing age and gender in conjunction with other fields can increase the risk of reidentification (Sweeney, 2000; Golle, 2006; Rocher et al., 2019). However, despite this increase, the ability to identify such individuals still falls below the previously mentioned threshold of 5% as already explained. However, it is important to note that the privacy risks of disclosing age are not uniform, as the number of very elderly or very young individuals make up a significantly smaller fraction of the population, and this should be considered (Statistics Canada, 2020a).

In some cases, provincial data report forms include non-traditional options for gender (e.g., non-binary and transgender) (CanCOGeN, 2021). Because individuals who do not conform to traditional binary terms make up a very small percentage of the population there is an increased risk of reidentification (Waite and Denier, 2019). Accordingly, VirusSeq has proposed to encompass all non-tradition gendered options into "non-disclosed" when publicly archived, consistent with what is done with the other initiatives (Statistics Canada, 2021). At the same time, such demographic information on non-binary individuals should still be collected as it contributes to equity, diversity, inclusion, and improves scientific representation of individuals and groups traditionally excluded from research (Bentley et al., 2017). These efforts will better ensure that the conducted research and their accompanying medical technical advances will represent marginalized individuals and groups as well as those who are traditionally well-represented. To reduce the potential privacy risks of this inclusion, this demographic data could be made available through controlled-access procedures.

The date of collection is another data field that originally had been thought to unacceptably increase privacy risks. Most of the current Health Canada diagnostic tests used for SARS-CoV-2 are based on Reverse Transcription polymerase Chain Reaction (RT-PCR), with results typically obtained 24–48 h after the date of sample collection (Health Canada, 2020). These delays considerably reduces the chances of associating the reported daily cases with the specific collection date. Furthermore, the typical range is not absolute, making it extremely unlikely to associate the testing date with the data release, as such, it will be equally unlikely for the collection date to be used as an identifier even if such information were to become public. In conjunction with what has already been written about the "reasonably available" standard, the date of collection does not appreciably increase the risk of reidentification. Notably, the introduction and mass dissemination of rapid COVID-19 testing kits, and potentially, other future advancements, may lead to the collection date and testing date being the same (Aguiar et al., 2020; Albert et al., 2021). If this were to unfold, and this date was disclosed with other identifying fields (e.g., province, when the province in question is "small", gender, age, and the number of daily cases by province/neighbourhood), the risk of reidentification may increase. Although whether any increase makes a meaningful difference in terms of privacy is questionable and would also be case-dependent and contingent on multiple factors. Therefore, we recommend periodically monitoring reidentification risk to account for the increased efficiency of diagnostic methods, and other relevant developments that could potentially increase privacy risks.

Does the Definition of "Identifiable" Include Self-Identification?

In the previous sections, we have emphasized that the concept of identifiability is an important component in the definition of "personal information." Concerns regarding the risk of individual self-identification in publicly available formats have been raised. To be specific, if an individual is capable of identifying themself based on a list of contextual data and their viral genomic sequence in a public data repository or reported information, would that then mean that their information should be considered "identifiable" and cannot be shared publicly? The right to privacy is historically defined as being able to protect one's personal life from intrusion by third parties (Warren and Louis, 1890). Similarly, in contemporary legislation, the concept of identifiability relates to identifiability from the perspective of an unauthorized third party and not that of an individual with access to high-level privy information. The emphasis on third parties is particularly important. The central notion

proposed is that identifiability should be evaluated from the perspective of a third party, and not the individual themselves. This is confirmed by various precedents set by Canadian and European case-laws, best-practice documents, and peer reviewed literature guidelines which assess identifiability from a third person's perspective. In the Canadian context, the 2008 *Gordon v. Canada (Health)* lawsuit, the federal courts considered the likelihood of individual reidentifiability specifically through the perspective of a third party attempting to reidentify an individual with access to information that is reasonably available (Gordon V. Canada (Health), 2008). More recently, in 2019, in the case *Canada (Information Commissioner) V. Canada (Public Safety and Emergency Preparedness) 2019*, the Federal courts once again assessed what constituted as "identifiable" and accordingly, the definition of what "personal information" is (Canada (Information Commissioner) v. Canada (Public Safety and Emergency Preparedness), 2019). Recall that the Canadian *Privacy Act* states that information is personal, "if there is a serious possibility that the information could be used to identify an individual either on its own or when combined with other available information." In this case, the meaning of what "other available information" should mean was explored. The court reasoned, "the goal of the Privacy Act (. . .) is to prevent the undue disclosure of one's personal information to others, not to oneself (. . .). That an individual might know that it is their name that is redacted from a document, for example, does not make the remainder of the document personal information." (Canada (Information Commissioner) v. Canada (Public Safety and Emergency Preparedness), 2019). Similarly, in the EU Court of Justice, the issue of what constituted as personal information was once again considered through the perspective of a third party attempting to reidentify an individual (Patrick Bryer v. Bundesrepublik Deutschland, 2016). Likewise, the *Deidentification Guidelines for Structured Data* released by the Information and Privacy Commissioner of Ontario also evaluates and discusses the risks of reidentification from the perspective of either a "prosecutor" or "journalistic" third party (Information and Privacy Commissioner of Ontario, 2016a). Finally, in all scientific publications reviewed, identifiability is also always written in terms of an unauthorized third party (Sweeney, 2000; Golle, 2006; Rocher et al., 2019; Beauvais, 2020). The legal and logical basis of identifiability is always referred to from the perspective of an unauthorized third party with access to reasonably available information. The focus on third parties with respect to identifiability is justified given an individual's knowledge of themselves and their personal information typically greatly exceeds that of any third party. A self-identification criterion would create a subjective, individually variable, and arbitrary standard to determine the exact definition and scope of personal information. In this sense, using a self-identification criterion would create an unnecessary, illogical, and inconsistent barrier to the free flow of information and ideas.

CONCLUSION

Our paper presents the first attempt to analyze the privacy risks of sharing viral genomic sequences and their accompanying contextual data in the public domain, and this is likely relevant for many countries. The open disclosure of a minimal set of contextual data fields associated with the viral samples is crucial towards the timely promotion of research, collaboration, and scientific advancement in a time when it is desperately needed. We demonstrated using the Canadian privacy and public health framework that it is not contradictory to privacy laws to share a small amount of such data in association with genomic viral sequences. However, in certain scenarios when privacy risks may be disproportionately elevated, we also recommend considering special mitigating measures to significantly reduce risks. Measures such as disclosing age in intervals rather than the exact age and revealing the province/territory of origin only for Canadian provinces and territories with sufficiently large populations can be essential in ensuring the privacy of individuals. Despite our findings that legal privacy barriers are surmountable, concerns outside privacy are also appreciable. For example, despite an inability to sufficiently single out an individual, broad contextual information can still negatively implicate and stigmatize certain social groups or communities (Quigley, 2012). Although beyond the scope of this paper, issues beyond privacy must also be considered.

The COVID-19 pandemic has quickly evolved into a devastating global public health and economic crisis. In these circumstances, the free flow of low-privacy risk viral sequences and their associated contextual data is key in better understanding key factors surrounding COVID-19, from patience variability, transmission, to the creation of better testing, effective treatments, reliable vaccines, and beyond. Global public health emergencies should be understood by policymakers and privacy bodies as creating an imperative to review whether existing privacy laws offer sufficient flexibility to permit public health authorities and the research community to carry out their work for the public good. The Canadian Office of Privacy Commissioner declared that "during a public health crisis, privacy laws still apply, but they are not a barrier to appropriate information sharing." Similar statements have also been made by other provincial privacy commissioners, including those of Alberta, Saskatchewan, and Ontario (Office of the Privacy Commissioner of Canada, 2020). Sharing SARS-CoV-2 genomic sequences alongside a minimal set of contextual data in the public domain with appropriate mitigating measures is, according to our findings, not contrary to the protection of personal information and privacy and is necessary for providing governments and researchers with the best available evidence to inform intervention. Our work mostly addresses concerns surrounding personal information and privacy. It does not explore the validity of arguments based on laws providing additional emergency powers to public health authorities in times of pandemics. It is our view that robust pathogen genomic surveillance should be facilitated in this day and age given the well-documented benefits in disease prevention and intervention responses (Grubaugh et al., 2019;

Naveca et al., 2020). Indeed, while such data sharing is perhaps "beneficial" in regular times, in a global pandemic, data sharing ought to be characterized as both urgent and "necessary."

AUTHOR CONTRIBUTIONS

LS: Performed research, authored sections of the manuscript, and coordinated between different experts. Authored the introduction, the abstract, and the conclusion-provided input on other sections. HL: Performed research, analysis, authored sections of the manuscript, and coordinated between different experts. Authored section on personal information and privacy, identifability of viral sequences, contextual data and personal information/identifability, data fields with disproportionate risks, and self-identification and personal information-provided input on other sections. FB, ErG, EmG, WH, SS-K, SM, GD, MZ and YJ Chair of Committee: provided input and suggestions on paper direction and content.

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The reviewer CHH declared a past co-authorship with the authors YJ, MHZ and LS to the handling editor.

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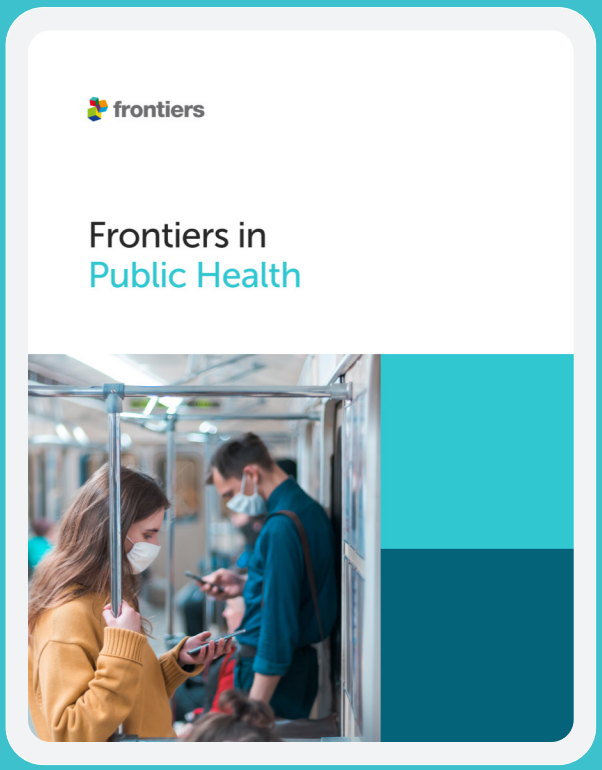

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