

# JMIR Public Health and Surveillance

Impact Factor (2022): 8.5  
 Volume 7 (2021), Issue 5 ISSN 2369-2960 Editor in Chief: Travis Sanchez, PhD, MPH

## Contents

### Original Papers

Estimation of Asthma Symptom Onset Using Internet Search Queries: Lag-Time Series Analysis ( <a href="#">e18593</a> ) Yulin Hswen, Amanda Zhang, Bruno Ventelou. ....	4
Social Media Content of Idiopathic Pulmonary Fibrosis Groups and Pages on Facebook: Cross-sectional Analysis ( <a href="#">e24199</a> ) Andrew Kochan, Shaun Ong, Sabina Guler, Kerri Johansson, Christopher Ryerson, Gillian Goobie. ....	11
The Influence of the COVID-19 Epidemic on Prevention and Vaccination Behaviors Among Chinese Children and Adolescents: Cross-sectional Online Survey Study ( <a href="#">e26372</a> ) Zhiyuan Hou, Suhang Song, Fanxing Du, Lu Shi, Donglan Zhang, Leesa Lin, Hongjie Yu. ....	22
Dietary Structure and Nutritional Status of Chinese Beekeepers: Demographic Health Survey ( <a href="#">e28726</a> ) Boshi Wang, Zhangkai Cheng, Qian Xu, Tiangang Zhu, Lin Su, Mingshan Xue, Lin Pei, Li Zhu, Peng Liu. ....	35
Development of an Index for the Inspection of Aedes aegypti Breeding Sites in Brazil: Multi-criteria Analysis ( <a href="#">e19502</a> ) Yuri Lima, Wallace Pinheiro, Carlos Barbosa, Matheus Magalhães, Miriam Chaves, Jano de Souza, Sérgio Rodrigues, Geraldo Xexéo. ....	47
Geographical Disparities in HIV Seroprevalence Among Men Who Have Sex with Men and People Who Inject Drugs in Nigeria: Exploratory Spatial Data Analysis ( <a href="#">e19587</a> ) Amobi Onovo, Abiye Kalaiwo, Moses Katbi, Otse Ogorry, Antoine Jaquet, Olivia Keiser. ....	59
Burden of Cervical Cancer in the Eastern Mediterranean Region During the Years 2000 and 2017: Retrospective Data Analysis of the Global Burden of Disease Study ( <a href="#">e22160</a> ) Fereshteh Safaeian, Shidrokh Ghaemimood, Ziad El-Khatib, Sahba Enayati, Roksana Mirkazemi, Bruce Reeder. ....	75
Evaluating the Consistency Between Conceptual Frameworks and Factors Influencing the Safe Behavior of Iranian Workers in the Petrochemical Industry: Mixed Methods Study ( <a href="#">e22851</a> ) Azita Zahiri Harsini, Philip Bohle, Lynda Matthews, Fazlollah Ghofranipour, Hormoz Sanaeinasab, Farkhondeh Amin Shokravi, Krishan Prasad. 9	4
Increases in Naloxone Administrations by Emergency Medical Services Providers During the COVID-19 Pandemic: Retrospective Time Series Study ( <a href="#">e29298</a> ) Dalia Khoury, Alexander Preiss, Paul Geiger, Mohd Anwar, Kevin Conway. ....	110
SARS-CoV-2 Surveillance System in Canada: Longitudinal Trend Analysis ( <a href="#">e25753</a> ) Lori Post, Michael Doctor, Tariq Issa, Charles Moss, Robert Murphy, Chad Achenbach, Michael Ison, Danielle Resnick, Lauren Singh, Janine White, Sarah Welch, James Oehmke. ....	122

Protective Behaviors and Secondary Harms Resulting From Nonpharmaceutical Interventions During the COVID-19 Epidemic in South Africa: Multisite, Prospective Longitudinal Study ( <a href="#">e26073</a> ) Guy Harling, Francesc Gómez-Olivé, Joseph Tlouyamma, Tinofa Mutevedzi, Chodziwadziwa Kabudula, Ruth Mahlako, Urisha Singh, Daniel Ohene-Kwofie, Rose Buckland, Pedzisai Ndagurwa, Dickman Gareta, Resign Gunda, Thobeka Mngomezulu, Siyabonga Nxumalo, Emily Wong, Kathleen Kahn, Mark Siedner, Eric Maimela, Stephen Tollman, Mark Collinson, Kobus Herbst. . . . .	133
The Differential Effects of Social Media on Depressive Symptoms and Suicidal Ideation Among the Younger and Older Adult Population in Hong Kong During the COVID-19 Pandemic: Population-Based Cross-sectional Survey Study ( <a href="#">e24623</a> ) Xue Yang, Benjamin Yip, Arthur Mak, Dexing Zhang, Eric Lee, Samuel Wong. . . . .	150
The Association of Unfairness with Mental and Physical Health in a Multiethnic Sample of Adults: Cross-sectional Study ( <a href="#">e26622</a> ) Ken Resnicow, Minal Patel, Molly Green, Alyssa Smith, Elizabeth Bacon, Stefanie Goodell, Dylan Kilby, Madiha Tariq, Asraa Alhawli, Nadia Syed, Jennifer Griggs, Matthew Stiffler. . . . .	165
Performance of the Neonatal Tetanus Surveillance System (NTSS) in Sana'a, Yemen: Evaluation Study ( <a href="#">e27606</a> ) Khaled Al-Jamrah, Basheer Al Nabehi, Khaled Almoayed, Labiba Anam, Yousef Khader. . . . .	176
Risk Factors of Extensively Drug Resistant Typhoid Fever Among Children in Karachi: Case-Control Study ( <a href="#">e27276</a> ) Anum Vighio, Muhammad Syed, Ishfaq Hussain, Syed Zia, Munaza Fatima, Naveed Masood, Ambreen Chaudry, Zakir Hussain, Mirza Iqbal Baig, Mirza Baig, Aamer Ikram, Yousef S Khader. . . . .	193
Cutaneous Leishmaniasis Outbreak Investigation in Hajjah Governorate, Yemen, in 2018: Case-Control Study ( <a href="#">e27442</a> ) Abdulkareem Nassar, Mahmood Abdelrazzaq, Ali Almahaqri, Mohammed Al-Amad, Abulwahed Al Serouri, Yousef Khader. . . . .	199
Impact of the Protracted War in Yemen on the Acute Flaccid Paralysis Surveillance System: Retrospective Descriptive Analysis ( <a href="#">e27638</a> ) Riham Al-Dubaiee, Mutaher AL Qassimi, Ahmed Al-Dar, Abulwahed Al Serouri, Yousef Khader. . . . .	223
An Overview of the Treatment Options Used for the Management of COVID-19 in Pakistan: Retrospective Observational Study ( <a href="#">e28594</a> ) Hashaam Akhtar, Samar Akhtar, Fazal-UI Rahman, Maham Afridi, Sundas Khalid, Sabahat Ali, Nasim Akhtar, Yousef Khader, Hamaad Ahmad, Muhammad Khan. . . . .	234
YouTube Videos and Informed Decision-Making About COVID-19 Vaccination: Successive Sampling Study ( <a href="#">e28352</a> ) Charles Basch, Corey Basch, Grace Hillyer, Zoe Meleo-Erwin, Emily Zagnit. . . . .	243

## Corrigenda and Addenda

Correction: The Impact of COVID-19 Management Policies Tailored to Airborne SARS-CoV-2 Transmission: Policy Analysis ( <a href="#">e30007</a> ) Charles Telles, Archisman Roy, Mohammad Ajmal, Syed Mustafa, Mohammad Ahmad, Juan de la Serna, Elisandro Frigo, Manuel Rosales. . . . .	9
	2

## Viewpoints

The Impact of Implementing the Egypt Pandemic Preparedness Plan for Acute Respiratory Infections in Combating the Early Stage of the COVID-19 Pandemic, February-July 2020: Viewpoint ([e27412](#))  
Hanaa Abu El Sood, Shima Abu Kamer, Reham Kamel, Hesham Magdy, Fatma Osman, Manal Fahim, Amira Mohsen, Mohamad Abdelfatah, Mohamed Hassany, Salma Afifi, Alaa Eid. . . . . 183

Pakistan’s Response to COVID-19: Overcoming National and International Hypes to Fight the Pandemic ([e28517](#))  
Hashaam Akhtar, Maham Afridi, Samar Akhtar, Hamaad Ahmad, Sabahat Ali, Sundas Khalid, Sajid Awan, Shahzaib Jahangiri, Yousef Khader. . . . . 2 1 4

## Short Paper

Morbidity and Mortality Associated with Typhoid Fever Among Hospitalized Patients in Hyderabad District, Pakistan, 2017-2018: Retrospective Record Review ([e27268](#))  
Munaza Fatima, Santosh Kumar, Mudassar Hussain, Naveed Memon, Anum Vighio, Muhammad Syed, Ambreen Chaudhry, Zakir Hussain, Zeeshan Baig, Mirza Baig, Rana Asghar, Aamer Ikram, Yousef Khader. . . . . 208

## Notes from the Field

Notes From the Field: The Combined Effects of Tocilizumab and Remdesivir in a Patient With Severe COVID-19 and Cytokine Release Syndrome ([e27609](#))  
Sabahat Ali, Sundas Khalid, Maham Afridi, Samar Akhtar, Yousef Khader, Hashaam Akhtar. . . . . 228

Original Paper

# Estimation of Asthma Symptom Onset Using Internet Search Queries: Lag-Time Series Analysis

Yulin Hswen<sup>1,2</sup>, ScD, MPH; Amanda Zhang<sup>3</sup>, AB; Bruno Ventelou<sup>2</sup>, PhD

<sup>1</sup>Department of Epidemiology and Biostatistics, Bakar Computational Health Sciences Institute, University of California San Francisco, San Francisco, CA, United States

<sup>2</sup>Aix Marseille University, CNRS, AMSE, Marseille, France

<sup>3</sup>Mathematics Department, Harvard University, Cambridge, MA, United States

**Corresponding Author:**

Yulin Hswen, ScD, MPH

Department of Epidemiology and Biostatistics

Bakar Computational Health Sciences Institute

University of California San Francisco

490 Illinois St

San Francisco, CA, 94158

United States

Phone: 1 415 476 1000

Email: [yulin.hswen@ucsf.edu](mailto:yulin.hswen@ucsf.edu)

## Abstract

**Background:** Asthma affects over 330 million people worldwide. Timing of an asthma event is extremely important and lack of identification of asthma increases the risk of death. A major challenge for health systems is the length of time between symptom onset and care seeking, which could result in delayed treatment initiation and worsening of symptoms.

**Objective:** This study evaluates the utility of the internet search query data for the identification of the onset of asthma symptoms.

**Methods:** Pearson correlation coefficients between the time series of hospital admissions and Google searches were computed at lag times from 4 weeks before hospital admission to 4 weeks after hospital admission. An autoregressive integrated moving average (ARIMAX) model with an autoregressive process at lags of 1 and 2 and Google searches at weeks -1 and -2 as exogenous variables were conducted to validate our correlation results.

**Results:** Google search volume for asthma had the highest correlation at 2 weeks before hospital admission. The ARIMAX model using an autoregressive process showed that the relative searches from Google about asthma were significant at lags 1 ( $P<.001$ ) and 2 ( $P=.04$ ).

**Conclusions:** Our findings demonstrate that internet search queries may provide a real-time signal for asthma events and may be useful to measure the timing of symptom onset.

(*JMIR Public Health Surveill* 2021;7(5):e18593) doi:[10.2196/18593](https://doi.org/10.2196/18593)

**KEYWORDS**

digital epidemiology; Google queries; asthma; symptoms; health information seeking

## Introduction

Asthma is a significant contributor to disease burden globally [1]. It kills around 1000 people every day and affects over 330 million people worldwide, a number that continues to rise [2]. A major challenge for health systems is the length of time between symptom onset and care seeking, which could result in delayed treatment initiation and worsening of symptoms [3,4]. Consequently, the World Health Organization has prioritized reducing asthma burden, as over 330 million people

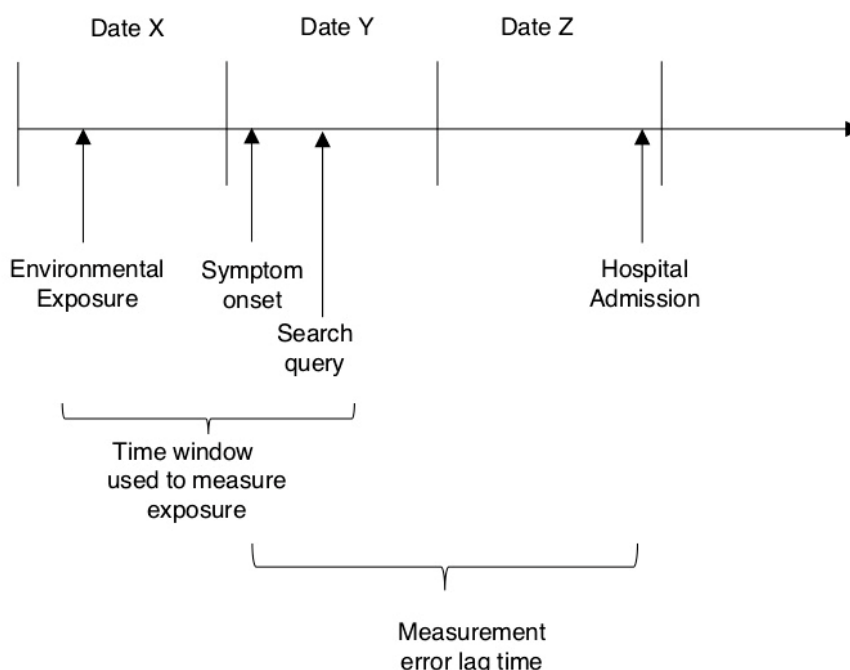
have asthma, and it is also the most common chronic disease of childhood. Avoidable asthma deaths still occur due to lack of early identification and inappropriate management [5]. Date of hospitalization has been used in the majority of time-series studies because it is the only available administrative data on the timing of the asthma event. However, evidence has emerged that assessment exposure based on hospitalization data may generate measurement bias and lead to misclassification of time of event onset [4]. The true onset of the symptomatic event may have occurred days prior to hospital admission, leading to underestimation of the strength of association between

environmental exposures such as ambient air pollution and acute clinical asthma events [3,6,7]. This is of particular concern for asthma because of its acute event onset and because it is sensitive to short-term ambient air pollution fluctuations.

Web searching has become integral for finding health-related information. Existing evidence shows that individuals use search engines to understand their health symptoms, especially at earlier stages of their illness, before making a medical visit or use the web to decide whether to admit themselves to a health care center [8,9]. Some individuals even use information gathered from the internet to make decisions on how to treat their illness

as opposed to visiting a provider [10]. Based on these information-searching behaviors, researchers have utilized internet search queries for early identification of disease onset, which has shown to be effective for the detection of infectious disease epidemics including influenza and Ebola [11-13]. However, research has yet to evaluate the potential utility of search queries to identify the onset of asthma symptoms and minimize measurement bias (Figure 1). This study examines whether internet search queries could reveal the lag time between onset of asthma symptoms and hospital admissions due to asthma events.

**Figure 1.** Potential difference in lag time between true time of onset and hospital admission. Diagrammatic representation of exposure measurement error. Date of hospital admission is not necessarily the date of symptom onset and may lead to misclassification, as exposure measurement does not fall within the period of hospital admission. Internet search queries may identify onset of symptoms in real time and earlier than administrative data and reduce measurement error.



## Methods

### Overview

To investigate the ability of internet search queries to detect the time of onset, we analyzed the lag time between internet search activity and asthma-related hospital visits in the Provence-Alpes-Côte d'Azur (PACA) region in France. France's health care system gives the rare opportunity to make a complete account of all admissions in a given territory (in both public and private hospitals) [14]. PACA, France, was chosen to be the focus for this study because of its high national emissions of air pollution [15,16]. The number of asthma-related hospitalizations (International Classification of Diseases [ICD]-10 codes J45 and J46) was collected from diagnosis-related group (DRG)-based Program for Medicalization of Information Systems (PMSI) from all the hospitals in the PACA region and aggregated at the weekly level [17].

### Google Relative Search Volumes

Time series of weekly Google relative search volumes (RSVs) for the term topic "asthme" (asthma) restricted to the PACA region were collected from January 1, 2017, to December 31, 2017, from Google Trends [18]. Google computes RSVs by dividing the total search volume for a query in a given geographical location by the total number of queries in that region at a given point in time [19]. Therefore, these data are normalized by the population density and search volume in a given geographical area and account for temporal fluctuations. This means that when we look at the search interest for the topic of asthma, it will be proportional to all searches on all topics on Google at that time and location. This function allowed us to measure the overall interest in the topic related to asthma in this study.

Because we were specifically interested in asthma hospital admissions in the PACA region in France, other related terms, such as "difficulty breathing," were not used, as they are not specific to asthma and overlap with other respiratory conditions. Search queries related to the topic term "saignement" (bleeding)

were collected as a control, as bleeding has no direct medical connection to asthma. Pearson correlation coefficients between the time series of hospital admissions and Google searches were computed at lag times from 4 weeks before hospital admission to 4 weeks after hospital admission. We further tested the Pearson correlation results with an autoregressive analysis using explanatory variables: autoregressive integrated moving average (ARIMAX) with an autoregressive process at lags of 1 and 2 and Google searches at weeks -1 and -2 weeks as exogenous variables (Table 1). This allowed us to assess how Google

searches were associated with hospital admissions while accounting for autocorrelation of the hospital admissions time series. The data that support the findings of this study were obtained from Google Trends that are available from [18] and from the DRG-based PMSI under a license for this study and are not publicly available; however, these can be obtained from the authors upon reasonable request and with permission of the DRG-based PMSI. All analyses were conducted using the statsmodels package in Python.

**Table 1.** ARIMAX<sup>a</sup> regression.

Variable	Coefficient	Standard error	P value	95% CI
AR <sup>b</sup> -1 (hospital admissions 1 week ago)	0.83	1.15	<.001	0.41 to 1.26
AR-2 (hospital admissions 2 weeks ago)	-0.31	1.05	.04	-0.59 to -0.02
“asthme” Google searches 1 week ago	3.67	0.22	.001	1.42 to 5.92
“asthme” Google searches 2 weeks ago	3.59	0.15	.001	1.52 to 5.65
Variance on error term	461.84	81.83	<.001	301.46 to 622.22

<sup>a</sup>ARIMAX: autoregressive integrated moving average.

<sup>b</sup>AR: autoregression.

### Ethics and Consent

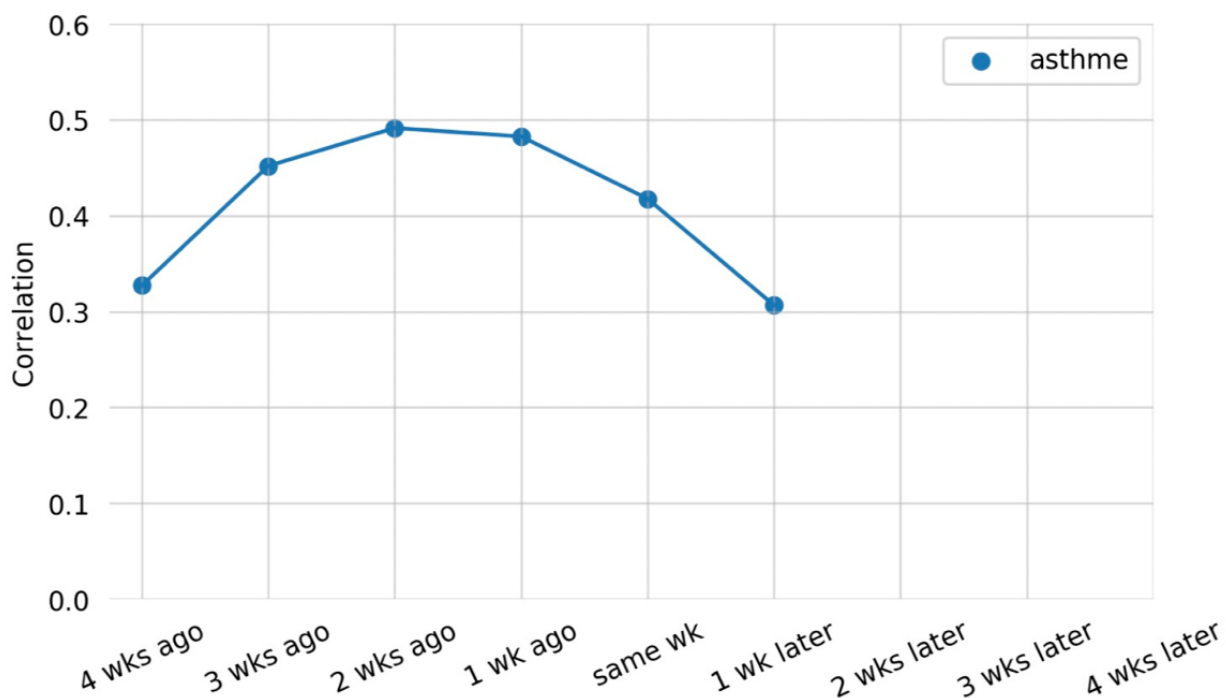
Public use data sets used in this study are in aggregate format and not individually identifiable such that their analysis is deemed nonhuman subject research.

### Results

Google RSVs for asthma had the highest correlation at 2 weeks before admission with a correlation of 0.491 ( $P < .001$ ; Figure

2, Table 2). Searches for “saignement” (bleeding) did not exhibit significant positive correlations with asthma-related hospital admissions at any lag time (Table 2). Our results of the Pearson correlation were further validated with our ARIMAX model, whereby the relative Google searches about asthma were significant at 1 ( $P < .001$ ) and 2 ( $P = .004$ ) weeks’ lags before hospital admissions, which were consistent with our correlation results.

**Figure 2.** Lag correlation between searches and admissions for “asthme,” 2017.



**Table 2.** Pearson correlations between Google search term and hospital admissions for asthma.

Lag time	“Asthme” (asthma) searches × asthma admissions		“Saignement” (bleeding) searches × asthma admissions	
	Correlation	<i>P</i> value	Correlation	<i>P</i> value
4 weeks before	0.327	.02	0.139	.34
3 weeks before	0.452	.001	0.123	.39
2 weeks before	0.491	<.001	0.046	.74
1 week before	0.483	<.001	−0.046	.74
Same week	0.418	.002	−0.034	.80
1 week after	0.307	.02	−0.082	.56
2 weeks after	0.013	.93	−0.220	.12
3 weeks after	−0.261	.07	−0.248	.08
4 weeks after	−0.426	.003	−0.268	.06

## Discussion

### Principal Findings

Results from our study suggest that internet search queries detect asthma symptom onset earlier than hospital admissions. Delay between time of symptom onset and time of hospital presentation for acute clinical events has been shown to result in considerable underestimation of the effects of ambient air pollution [4]. Our results show the greatest correlation at a lag of 2 weeks between Google RSVs for asthma and asthma hospital visits. In comparison to a recent study that tested the lag time between Google RSVs for terms related to COVID-19 and COVID-19 cases in Taiwan, significant time-lag correlations ranged from 0.33 to 0.72 [20]. Results from our time-series correlation were in between the range of these correlations at 0.49 ( $P < .001$ ) at 2 weeks. This effect size of 0.49 indicates a moderate relationship as correlations over 0.3 are considered to indicate an underlying relationship between 2 variables of interest [21,22]. The 1- and 2-week lag we found between asthma searches and asthma hospitalizations is consistent with previous studies that have on average a 2-week time lag between internet-based and traditional surveillance systems for disease surveillance [23]. In a study that looked at internet searches on dengue fever and local dengue occurrences, a lag time of 1 week was reported [24]. In a more recent study, the relationship between chest pain search volume on Google and new COVID-19 cases saw a lag time of 18 days (2-3 weeks) [25]. This consistent time lag of around 2 weeks may indicate the amount of time that elapsed between users developing symptoms and seeking in-person medical care.

Our results highlight that online internet search queries about symptoms may offer a novel approach to (1) identify the timing and the magnitude of future admissions, to prepare and manage resources efficiently at the hospitals (as suggested for opioids [10]) and (2) correct for measurement bias and misclassification of time of asthma onset. This finding is important, as short-term fluctuations in ambient air pollution can have significant effects on acute symptoms; therefore, hour-by-hour estimates are important to understand the impact of these environmental exposures on symptomatic changes in order to identify the onset of larger more severe health events. Epidemiological studies

measuring exposure and response should investigate the lag time between search queries and hospitalization to uncover insights about the actual timing of onset. Recent evidence has also indicated that the COVID-19 pandemic has led patients to use internet search on Google to seek out medical information and treatment in replacement of professional medical attention [25]. For instance, compared with previous years, there have been significant reductions in hospital presentations for acute myocardial infarctions and concurrent increases in out-of-hospital cardiac arrests during the COVID-19 pandemic and a marked spike in search volume for chest pain [26,27]. Therefore, internet search queries related to respiratory symptoms may offer insight into the true incidence of respiratory illnesses during COVID-19, as fear of contracting COVID-19 may prevent patients from seeking hospital care. Future studies should use internet search queries to estimate the incidence of disease, as hospital admissions may not be able to provide accurate measurements in the time of COVID-19.

### Limitations

We recognize that the population on the search engine Google may not be entirely representative of the French population. However, statistics show that Google holds the largest market share of all search engines in France (92% as of September 2020) [28]. The population of internet users in France is 82.0% and skewed toward younger age and higher education level [29]. In this study, we validated that search strategies were effective at identifying the onset of future emergency hospital use. Despite the limitation that searches on Google might not be generalizable to the entire French population, our results still suggest that this methodology may be applicable to other chronic diseases as well. However, we acknowledge that this method may not be applicable to all types of symptoms or hospital uses, especially when the disease to be treated is very specific to a subpopulation.

We also recognize that recent developments in time series such as time-series forecasting were not used for our analysis. However, in this study we sought to model trends in searches as they related to external factors such as emergency visits, whereas time-series forecasting seeks to forecast future values of that series such as using historical hospital visits to predict future hospital visits. We also chose to use the most standard

and frequently used time-series model for consistency in the research area related to environmental respiratory disease in order to identify the time lag between symptom onset and hospital admission [30-33].

### Future Directions

Based on our study findings, we believe that earlier identification of potential cases of asthma exacerbation through internet searches could help improve the efficiency of resource allocation within hospitals such as staff, beds, and respiratory assistance. Future studies should test the ability of Google searches in the hospital setting to predict cases and reduce the burden on hospitals. In addition, since the COVID-19 pandemic, it has been postulated that many patients are not seeking care for their arising symptoms because of fears of COVID-19 transmission [27]. Therefore, the use of internet search could help identify real-time and accurate onset of asthma during the

time of the COVID-19 pandemic. This information can be used to provide timely and correct patient education including informing the public about the appropriate course of action. Public health efforts should consider the utility of internet searches for respiratory conditions such as asthma to measure care-seeking behaviors and prevent severe long-term consequences.

### Conclusions

Asthma is one of the most significant noncommunicable diseases globally [34]. Improving surveillance is crucial for the control of asthma and the prevention of avoidable deaths due to this disease. The use of online digital surveillance offers the ability to capture the onset of asthma more accurately and rapidly and has the potential to reduce the burden and deaths caused by asthma.

### Acknowledgments

We thank Lisa Fressard, ORS PACA, for her assistance in retrieving the PMSI data for this study. This work was supported by the French National Research Agency Grant (No. ANR-17-EURE-0020). YH was funded by the Chateaubriand Fellowship Program, Make Our Planet Great Again, The Embassy of France.

### Conflicts of Interest

None declared.

### References

1. Guarnieri M, Balmes JR. Outdoor air pollution and asthma. *The Lancet* 2014 May;383(9928):1581-1592. [doi: [10.1016/s0140-6736\(14\)60617-6](https://doi.org/10.1016/s0140-6736(14)60617-6)]
2. Loftus PA, Wise SK. Epidemiology and economic burden of asthma. *Int Forum Allergy Rhinol* 2015 Sep 23;5 Suppl 1(S1):S7-10. [doi: [10.1002/alr.21547](https://doi.org/10.1002/alr.21547)] [Medline: [26010063](https://pubmed.ncbi.nlm.nih.gov/26010063/)]
3. Charlton I, Jones K, Bain J. Delay in diagnosis of childhood asthma and its influence on respiratory consultation rates. *Arch Dis Child* 1991 May 01;66(5):633-635 [FREE Full text] [doi: [10.1136/adc.66.5.633](https://doi.org/10.1136/adc.66.5.633)] [Medline: [2039256](https://pubmed.ncbi.nlm.nih.gov/2039256/)]
4. Lokken R, Wellenius G, Coull B, Burger MR, Schlaug G, Suh HH, et al. Air pollution and risk of stroke: underestimation of effect due to misclassification of time of event onset. *Epidemiology* 2009 Jan;20(1):137-142. [doi: [10.1097/ede.0b013e31818ef34a](https://doi.org/10.1097/ede.0b013e31818ef34a)] [Medline: [19244659](https://pubmed.ncbi.nlm.nih.gov/19244659/)]
5. Landrigan PJ, Fuller R, Acosta NJR, Adeyi O, Arnold R, Basu NN, et al. The Lancet Commission on pollution and health. *Lancet* 2018 Feb 03;391(10119):462-512. [doi: [10.1016/S0140-6736\(17\)32345-0](https://doi.org/10.1016/S0140-6736(17)32345-0)] [Medline: [29056410](https://pubmed.ncbi.nlm.nih.gov/29056410/)]
6. Lynch BA, Van Norman CA, Jacobson RM, Weaver AL, Juhn YJ. Impact of delay in asthma diagnosis on health care service use. *Allergy Asthma Proc* 2010 Jul 01;31(4):e48-e52 [FREE Full text] [doi: [10.2500/aap.2010.31.3358](https://doi.org/10.2500/aap.2010.31.3358)] [Medline: [20819315](https://pubmed.ncbi.nlm.nih.gov/20819315/)]
7. Delfino RJ, Becklake MR, Hanley JA. Reliability of hospital data for population-based studies of air pollution. *Arch Environ Health* 1993 Jun;48(3):140-146. [doi: [10.1080/00039896.1993.9940812](https://doi.org/10.1080/00039896.1993.9940812)] [Medline: [8333783](https://pubmed.ncbi.nlm.nih.gov/8333783/)]
8. The online health care revolution: How the Web helps Americans take better care of themselves. *Pew Internet & American Life: Online life report*. URL: [https://www.pewinternet.org/wp-content/uploads/sites/9/media/Files/Reports/2000/PIP\\_Health\\_Report.pdf.pdf](https://www.pewinternet.org/wp-content/uploads/sites/9/media/Files/Reports/2000/PIP_Health_Report.pdf.pdf) [accessed 2021-04-16]
9. Fox S, Rainie L, Horrigan J, Lenhart A, Spooner T, Burke M. The online health care revolution: How the Web helps Americans take better care of themselves. In: *Online*; 2000. URL: [https://www.pewinternet.org/wp-content/uploads/sites/9/media/Files/Reports/2000/PIP\\_Health\\_Report.pdf.pdf](https://www.pewinternet.org/wp-content/uploads/sites/9/media/Files/Reports/2000/PIP_Health_Report.pdf.pdf) [accessed 2021-04-15]
10. Forkner-Dunn J. Internet-based patient self-care: the next generation of health care delivery. *J Med Internet Res* 2003 May 15;5(2):e8 [FREE Full text] [doi: [10.2196/jmir.5.2.e8](https://doi.org/10.2196/jmir.5.2.e8)] [Medline: [12857664](https://pubmed.ncbi.nlm.nih.gov/12857664/)]
11. Alicino C, Bragazzi NL, Faccio V, Amicizia D, Panatto D, Gasparini R, et al. Assessing Ebola-related web search behaviour: insights and implications from an analytical study of Google Trends-based query volumes. *Infect Dis Poverty* 2015 Dec 10;4(1):54 [FREE Full text] [doi: [10.1186/s40249-015-0090-9](https://doi.org/10.1186/s40249-015-0090-9)] [Medline: [26654247](https://pubmed.ncbi.nlm.nih.gov/26654247/)]
12. Althouse BM, Ng YY, Cummings DAT. Prediction of dengue incidence using search query surveillance. *PLoS Negl Trop Dis* 2011 Aug 2;5(8):e1258 [FREE Full text] [doi: [10.1371/journal.pntd.0001258](https://doi.org/10.1371/journal.pntd.0001258)] [Medline: [21829744](https://pubmed.ncbi.nlm.nih.gov/21829744/)]



13. Yang S, Santillana M, Kou SC. Accurate estimation of influenza epidemics using Google search data via ARGO. *Proc Natl Acad Sci U S A* 2015 Nov 24;112(47):14473-14478 [FREE Full text] [doi: [10.1073/pnas.1515373112](https://doi.org/10.1073/pnas.1515373112)] [Medline: [26553980](https://pubmed.ncbi.nlm.nih.gov/26553980/)]
14. Weeks WB, Jardin M, Dufour J, Paraponaris A, Ventelou B. Geographic variation in admissions for knee replacement, hip replacement, and hip fracture in France: evidence of supplier-induced demand in for-profit and not-for-profit hospitals. *Med Care* 2014 Oct;52(10):909-917. [doi: [10.1097/MLR.0000000000000211](https://doi.org/10.1097/MLR.0000000000000211)] [Medline: [25215648](https://pubmed.ncbi.nlm.nih.gov/25215648/)]
15. Mazenq J, Dubus J, Gaudart J, Charpin D, Viudes G, Noel G. City housing atmospheric pollutant impact on emergency visit for asthma: A classification and regression tree approach. *Respir Med* 2017 Nov;132:1-8 [FREE Full text] [doi: [10.1016/j.rmed.2017.09.004](https://doi.org/10.1016/j.rmed.2017.09.004)] [Medline: [29229079](https://pubmed.ncbi.nlm.nih.gov/29229079/)]
16. Air PACA. Quelles mesures pour améliorer la qualité de l'air en Région Provence-Alpes-Côte-D'azur. Paris, France: Air PACA; 2020.
17. Moulis G, Lapeyre-Mestre M, Palmaro A, Pugnet G, Montastruc J, Sailler L. French health insurance databases: What interest for medical research? *Rev Med Interne* 2015 Jun;36(6):411-417. [doi: [10.1016/j.revmed.2014.11.009](https://doi.org/10.1016/j.revmed.2014.11.009)] [Medline: [25547954](https://pubmed.ncbi.nlm.nih.gov/25547954/)]
18. Google Trends. URL: <https://trends.google.com> [accessed 2021-04-15]
19. Wu L, Brynjolfsson E. The Future of Prediction: How Google Searches Foreshadow Housing Prices and Sales. In: Goldfarb A, Greenstein SM, Tucker CE, editors. *Economic Analysis of the Digital Economy*. Chicago, IL: University of Chicago Press; Apr 2015.
20. Husnayain A, Fuad A, Su EC. Applications of Google Search Trends for risk communication in infectious disease management: A case study of the COVID-19 outbreak in Taiwan. *Int J Infect Dis* 2020 Jun;95:221-223 [FREE Full text] [doi: [10.1016/j.ijid.2020.03.021](https://doi.org/10.1016/j.ijid.2020.03.021)] [Medline: [32173572](https://pubmed.ncbi.nlm.nih.gov/32173572/)]
21. Ratner B. The correlation coefficient: Definition. URL: <http://dmstat1.com/res/TheCorrelationCoefficientDefined.html> [accessed 2021-04-14]
22. Mukaka MM. Statistics corner: A guide to appropriate use of correlation coefficient in medical research. *Malawi Med J* 2012 Sep;24(3):69-71 [FREE Full text] [Medline: [23638278](https://pubmed.ncbi.nlm.nih.gov/23638278/)]
23. Chen Y, Zhang Y, Xu Z, Wang X, Lu J, Hu W. Avian Influenza A (H7N9) and related Internet search query data in China. *Sci Rep* 2019 Jul 18;9(1):10434 [FREE Full text] [doi: [10.1038/s41598-019-46898-y](https://doi.org/10.1038/s41598-019-46898-y)] [Medline: [31320681](https://pubmed.ncbi.nlm.nih.gov/31320681/)]
24. Li Z, Liu T, Zhu G, Lin H, Zhang Y, He J, et al. Dengue Baidu Search Index data can improve the prediction of local dengue epidemic: A case study in Guangzhou, China. *PLoS Negl Trop Dis* 2017 Mar 6;11(3):e0005354 [FREE Full text] [doi: [10.1371/journal.pntd.0005354](https://doi.org/10.1371/journal.pntd.0005354)] [Medline: [28263988](https://pubmed.ncbi.nlm.nih.gov/28263988/)]
25. Ciofani JL, Han D, Allahwala UK, Asrress KN, Bhindi R. Internet search volume for chest pain during the COVID-19 pandemic. *Am Heart J* 2021 Jan;231:157-159 [FREE Full text] [doi: [10.1016/j.ahj.2020.09.005](https://doi.org/10.1016/j.ahj.2020.09.005)] [Medline: [33010246](https://pubmed.ncbi.nlm.nih.gov/33010246/)]
26. Yom-Tov E. *Crowdsourced health: How what you do on the Internet will improve medicine*. Cambridge, MA: MIT Press; 2016.
27. Mavraganis G, Aivalioti E, Chatzidou S, Patras R, Paraskevaidis I, Kanakakis I, et al. Cardiac arrest and drug-related cardiac toxicity in the Covid-19 era. *Epidemiology, pathophysiology and management. Food Chem Toxicol* 2020 Nov;145:111742 [FREE Full text] [doi: [10.1016/j.fct.2020.111742](https://doi.org/10.1016/j.fct.2020.111742)] [Medline: [32916218](https://pubmed.ncbi.nlm.nih.gov/32916218/)]
28. Search Engine Market Share. URL: <https://gs.statcounter.com/search-engine-market-share/all/france> [accessed 2021-04-14]
29. Internet usage penetration in France from 2010 to 2019, by education level. URL: <https://www.statista.com/statistics/426201/internet-usage-penetration-study-level-france/> [accessed 2021-04-14]
30. Shokouhi M. Detecting seasonal queries by time-series analysis. New York, NY: Association for Computing Machinery; 2011 Presented at: SIGIR '11: Proceedings of the 34th international ACM SIGIR conference on Research and development in Information Retrieval; July 2011; Beijing, China.
31. Zhang Y, Milinovich G, Xu Z, Bambrick H, Mengersen K, Tong S, et al. Monitoring Pertussis Infections Using Internet Search Queries. *Sci Rep* 2017 Sep 05;7(1):10437 [FREE Full text] [doi: [10.1038/s41598-017-11195-z](https://doi.org/10.1038/s41598-017-11195-z)] [Medline: [28874880](https://pubmed.ncbi.nlm.nih.gov/28874880/)]
32. Nhung NTT, Amini H, Schindler C, Kutlar Joss M, Dien TM, Probst-Hensch N, et al. Short-term association between ambient air pollution and pneumonia in children: A systematic review and meta-analysis of time-series and case-crossover studies. *Environ Pollut* 2017 Nov;230:1000-1008. [doi: [10.1016/j.envpol.2017.07.063](https://doi.org/10.1016/j.envpol.2017.07.063)] [Medline: [28763933](https://pubmed.ncbi.nlm.nih.gov/28763933/)]
33. Ren M, Li N, Wang Z, Liu Y, Chen X, Chu Y, et al. The short-term effects of air pollutants on respiratory disease mortality in Wuhan, China: comparison of time-series and case-crossover analyses. *Sci Rep* 2017 Jan 13;7(1):40482 [FREE Full text] [doi: [10.1038/srep40482](https://doi.org/10.1038/srep40482)] [Medline: [28084399](https://pubmed.ncbi.nlm.nih.gov/28084399/)]
34. World Health Organization. Asthma (Fact Sheet). Geneva, Switzerland: World Health Organization URL: <https://www.who.int/news-room/fact-sheets/detail/asthma> [accessed 2021-05-05]

## Abbreviations

- ARIMAX:** autoregressive integrated moving average
- DRG:** diagnosis-related group
- ICD:** International Classification of Diseases
- PACA:** Provence-Alpes-Côte d'Azur

**PMSI:** Program for Medicalization of Information Systems

**RSV:** relative search volumes

*Edited by G Eysenbach; submitted 06.03.20; peer-reviewed by YH Liu, Y Cheng; comments to author 29.06.20; revised version received 26.11.20; accepted 11.03.21; published 10.05.21.*

*Please cite as:*

*Hswen Y, Zhang A, Ventelou B*

*Estimation of Asthma Symptom Onset Using Internet Search Queries: Lag-Time Series Analysis*

*JMIR Public Health Surveill 2021;7(5):e18593*

*URL: <https://publichealth.jmir.org/2021/5/e18593>*

*doi: [10.2196/18593](https://doi.org/10.2196/18593)*

*PMID: [33970108](https://pubmed.ncbi.nlm.nih.gov/33970108/)*

©Yulin Hswen, Amanda Zhang, Bruno Ventelou. Originally published in JMIR Public Health and Surveillance (<https://publichealth.jmir.org>), 10.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# Social Media Content of Idiopathic Pulmonary Fibrosis Groups and Pages on Facebook: Cross-sectional Analysis

Andrew Kochan<sup>1</sup>, MD; Shaun Ong<sup>2</sup>, MD; Sabina Guler<sup>3</sup>, MD, MSc; Kerri A Johannson<sup>4</sup>, MD, MPH; Christopher J Ryerson<sup>5,6</sup>, MD, MAS; Gillian C Goobie<sup>7,8</sup>, MD

<sup>1</sup>Division of Cardiology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

<sup>2</sup>Division of Respiriology, Department of Medicine, University of Toronto, Toronto, ON, Canada

<sup>3</sup>Department of Pulmonary Medicine, Bern University Hospital, University of Bern, Bern, Switzerland

<sup>4</sup>Division of Respiratory Medicine, Department of Medicine, University of Calgary, Calgary, AB, Canada

<sup>5</sup>Division of Respiratory Medicine, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

<sup>6</sup>Centre for Heart Lung Innovation, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

<sup>7</sup>Clinician Investigator Program, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

<sup>8</sup>Department of Human Genetics, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, United States

**Corresponding Author:**

Andrew Kochan, MD

Division of Cardiology

Department of Medicine

University of British Columbia

9th Floor Gordon and Leslie and Diamond Health Care Centre

2775 Laurel Street

Vancouver, BC, V5Z 1M9

Canada

Phone: 1 (604) 875 4111 ext 69821

Fax: 1 (604) 875 5504

Email: [andrew.kochan@alumni.ubc.ca](mailto:andrew.kochan@alumni.ubc.ca)

## Abstract

**Background:** Patients use Facebook as a resource for medical information. We analyzed posts on idiopathic pulmonary fibrosis (IPF)-related Facebook groups and pages for the presence of guideline content, user engagement, and usefulness.

**Objective:** The objective of this study was to describe and analyze posts from Facebook groups and pages that primarily focus on IPF-related content.

**Methods:** Cross-sectional analysis was performed on a single date, identifying Facebook groups and pages resulting from separately searching “IPF” and “idiopathic pulmonary fibrosis.” For inclusion, groups and pages needed to meet either search term and be in English, publicly available, and relevant to IPF. Every 10th post was assessed for general characteristics, source, focus, and user engagement metrics. Posts were analyzed for presence of IPF guideline content, useful scientific information (eg, scientific publications), useful support information (eg, information about support groups), and potentially harmful information.

**Results:** Eligibility criteria were met by 12 groups and 27 pages, leading to analysis of 523 posts. Of these, 42% contained guideline content, 24% provided useful support, 20% provided useful scientific information, and 5% contained potentially harmful information. The most common post source was nonmedical users (85%). Posts most frequently focused on IPF-related news (29%). Posts containing any guideline content had fewer likes or comments and a higher likelihood of containing potentially harmful content. Posts containing useful supportive information had more likes, shares, and comments.

**Conclusions:** Facebook contains useful information about IPF, but posts with misinformation and less guideline content have higher user engagement, making them more visible. Identifying ways to help patients with IPF discriminate between useful and harmful information on Facebook and other social media platforms is an important task for health care professionals.

(*JMIR Public Health Surveill* 2021;7(5):e24199) doi:[10.2196/24199](https://doi.org/10.2196/24199)

**KEYWORDS**

interstitial lung disease; idiopathic pulmonary fibrosis; patient education; social media; internet

**Introduction**

Idiopathic pulmonary fibrosis (IPF) is a progressive fibrotic interstitial lung disease (ILD) of unknown etiology characterized by declining lung function, worsening dyspnea, and a poor prognosis [1]. Prior surveys indicate that patients and caregivers perceive a lack of accessible resources and information regarding IPF despite the availability of consensus guidelines [2]. Many online resources provide information about IPF, but these are frequently biased and inaccurate [3]. For example, YouTube videos focused on IPF often contain incomplete, inaccurate, and potentially harmful information, with high levels of user engagement in videos containing inaccurate information [4]. Given recent controversy surrounding Facebook's policies on censorship of inaccurate or potentially harmful information, it is an especially prescient time to investigate the accuracy of information disseminated via Facebook as it relates to chronic diseases such as IPF [5].

Social media usage in US adults increased from 5% to 72% of the population between 2005 and 2018 [6]. Social media was initially limited to a younger demographic; however, over 40% of people above the age of 65 now use social media [6]. The most widely used forms of social media are YouTube and Facebook, with 72% and 69% of US adults using these platforms, respectively [6]. People frequently use social media for health advice and support, emphasizing the importance of evaluating content and quality of health-related information on these platforms [7-9]. On Facebook, users can post text, pictures, videos, or links, which can be commented on, reacted to, or shared by other users. Facebook pages enable any individual or organization to create public forums where people can interact. Facebook groups are designed for small-group communication where people can discuss topics of common interest, including discussion of medical conditions [10]. Facebook pages are often created by public figures, organizations, industry, and occasionally independent nonmedical users, but may have a more product- or message-based focus than groups [10]. To date, no study has evaluated the types of information available about IPF on Facebook, and whether this represents a useful or potentially harmful resource for patients with IPF and their families.

The objective of this study was to describe and analyze posts from Facebook groups and pages that primarily focus on IPF-related content. We assessed a variety of post characteristics, user engagement metrics, IPF-related content, and the presence of inaccurate information shared in Facebook posts on these groups and pages. We hypothesized that these

posts would often be biased, and would frequently contain inaccurate and potentially harmful information, similar to YouTube and other internet resources (see Table S1 in [Multimedia Appendix 1](#) for a complete list of prespecified hypotheses) [3,4].

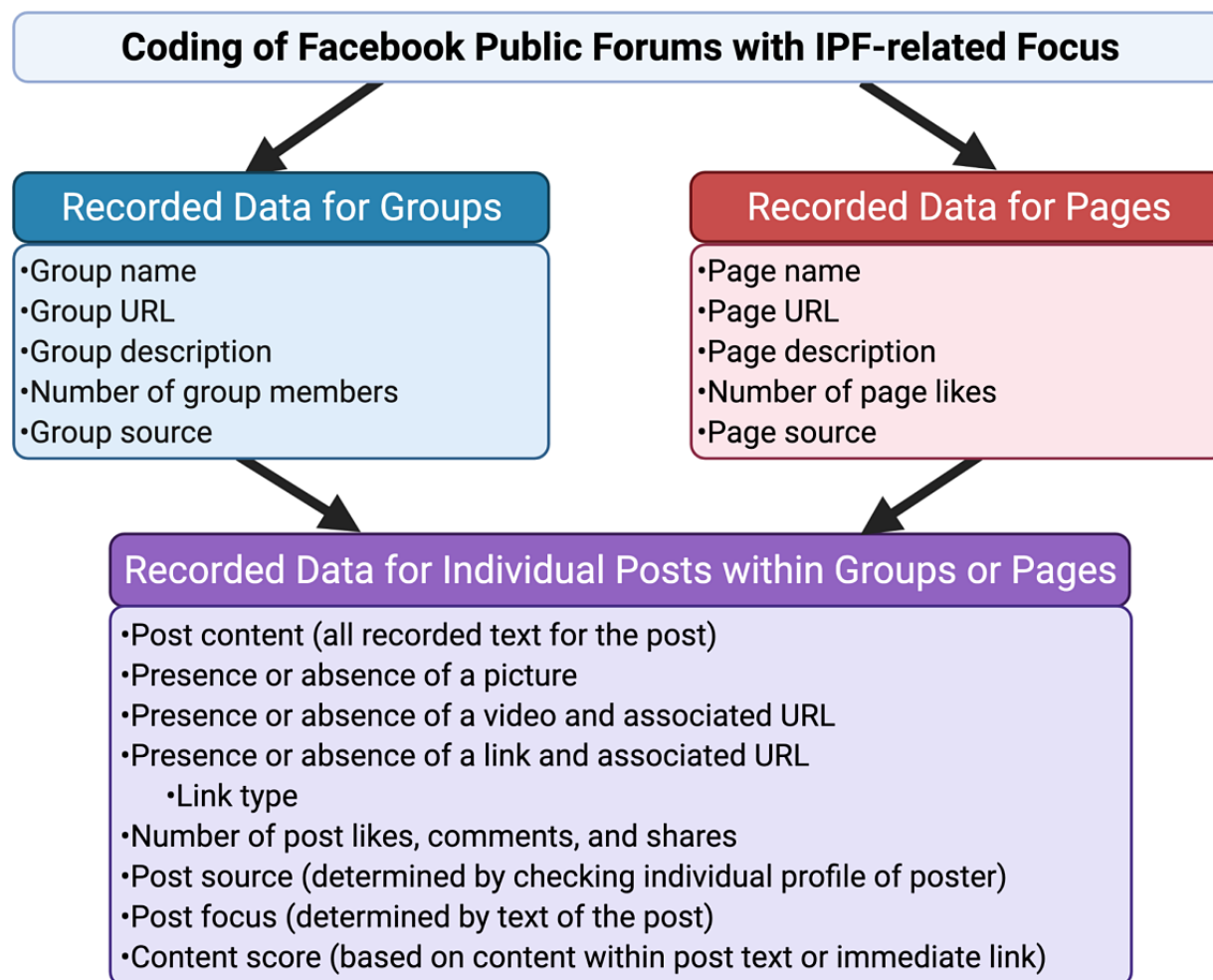
**Methods****Search Strategy and Page or Group Selection**

A new Facebook account was created after removing all history and cookies from the web browser (Google Chrome). The terms "IPF" and "idiopathic pulmonary fibrosis" were separately entered in Facebook's search function on January 4, 2019 to identify IPF-related groups and pages. Exclusion criteria included primary language not English, being a "closed" or "private" group, being a group or page with a focus other than IPF, or being a duplicate result.

For all groups or pages that met eligibility criteria, a single researcher recorded basic features, including group or page name, URL, description of group or page, and number of group members or page likes. Given the high number of individual posts, the same basic features were recorded from every 10th post in the group or page, including presence of an external link and its URL, the posting of any image or video, date of posting, and viewer engagement metrics. Three viewer engagement metrics were recorded for each post: the number of likes, shares, and comments.

**Data Extraction**

IPF-related data were captured in duplicate by two authors who independently reviewed each group or page and post for specific data as detailed in [Figure 1](#). The primary source of the group or page was categorized as scientific resources, medical foundations or organizations, news programs or other media sources, industry or for-profit organizations, private medical professional-generated content, nonmedical user-generated content, or other, as previously described [3]. Individual posts were also separately assigned to one of these sources since the source of a post is not necessarily the same as the source of the group or page. Each post was coded according to the primary focus, including guideline, advice (giving or requesting advice), news (posts about new scientific studies and advances), advertisement or fundraising, opinion (a personal opinion), insurance or health care cost, other IPF content (posts about IPF not falling into a prior category), or non-IPF content (no relation to IPF). If a link was present, the link type was coded as being related to a scientific source, foundation or advocacy, news or media, industry or for profit, or personal blog.

**Figure 1.** Data extracted from groups, pages, and from individual posts within groups or pages.

Two authors independently assigned posts a content score based on 30 prespecified guideline-supported IPF-related content items within the categories of definition, symptoms, risk factors, diagnosis, management, and prognosis (Figure 1, Table S2 in Multimedia Appendix 1) [1,11,12]. To assign content scores, authors also evaluated content on the immediate page accessed via any post links. Posts were considered to contain useful scientific information if the post or direct link quoted scientific studies regarding the natural history, diagnosis, or treatment of IPF. Posts were considered to contain useful support information for IPF patients or caregivers if they provided recommendations regarding IPF support networks, peer support, or other practical advice to caregivers or patients with IPF (eg, traveling with IPF, navigating the health care system, strategies for mitigating symptoms). Posts were considered harmful if they recommended pharmacologic or nonpharmacologic therapies (eg, stem cell transplant, specific dietary modifications) not recommended by current IPF guidelines (see Table S3 in Multimedia Appendix 1 for examples of nonrecommended therapies) [1,12].

### Statistical Analysis

Unweighted  $\kappa$  values were used to determine the level of agreement between reviewers for coding of the variables stated above. A  $\kappa$  cut-off value of 0.70 was deemed acceptable. In situations where  $\kappa$  was less than 0.70, a third independent author served as an arbitrator. Descriptive statistics were calculated

for overall group and page data, and general post information. Further statistical analysis was performed on individual group and page data as well as combined group and page data. Wilcoxon rank-sum, Spearman correlation, Kruskal-Wallis, and  $\chi^2$  tests were performed as appropriate to analyze potential associations of variables with content score. Wilcoxon rank-sum testing and Fisher exact test were used to identify variables associated with the presence of harmful content, useful scientific information, and useful supportive content.

Zero-inflated negative binomial regression was used to test the association of a higher content score with viewer engagement metrics, post source of foundation or medical professional, and guideline focus. This analysis was adjusted for clustering within groups and pages using a clustered sandwich estimator approach, as posts within individual pages or groups were considered to be dependent on each other [13]. The initial model included all variables considered to have a potential impact on content score followed by elimination of variables with  $P > .05$  to achieve a model that met convergence [14]. Multivariable logistic regression was used to identify variables associated with the presence of potentially harmful information within a post. This analysis was also adjusted for clustering within groups or pages using a clustered sandwich estimator approach.

Data are shown as mean (SD), median (IQR), or n (%). Statistical significance was defined by a two-tailed  $P < .05$  for all analyses. Analyses were performed using STATA/SE version 14 (StataCorp).

## Results

### Post Characteristics

The initial search yielded 126 groups and 191 pages, with 12 groups and 27 pages meeting the eligibility criteria (Figure 2). From the 39 included groups and pages, 523 posts were analyzed. Post source was most frequently from nonmedical users (445/523, 85.1%), followed by foundations or medical organizations (53/523, 10.1%), industry or for-profit organizations (24/523, 4.6%), and private medical professionals (1/523 0.2%). Of the 523 posts analyzed, 307 (58.7%) contained

URL links, 118 (22.6%) contained pictures, and 32 (6.1%) contained videos. Median post age was 630 days (IQR 259-1381), with a range from 0 to 4271 days. Viewer engagement, as indicated by the number of likes, comments, or shares, was generally low (Table 1). Post focus was on IPF-related news in 152 posts (29.1%), other IPF-related information in 131 (25.0%) posts, non-IPF commentary in 81 (15.5%) posts, advice to IPF patients or caregivers in 80 (15.3%) posts, advertisement in 65 (12.4%) posts, IPF guidelines in 5 (1.0%) posts, opinion in 7 (1.3%) posts, and insurance in 2 (0.4%) posts. The most common type of external link was to websites presenting IPF-related news (112/523 posts, 21.4%), followed by websites with a foundation or advocacy focus (96/523, 18.4%). Guideline-recommended content was present in 221 (42.3%), useful support in 127 (24.3%), and useful scientific information in 103 (19.7%) of the 523 posts (Figure S1 in Multimedia Appendix 1).

Figure 2. Search results, and selection of groups and pages.

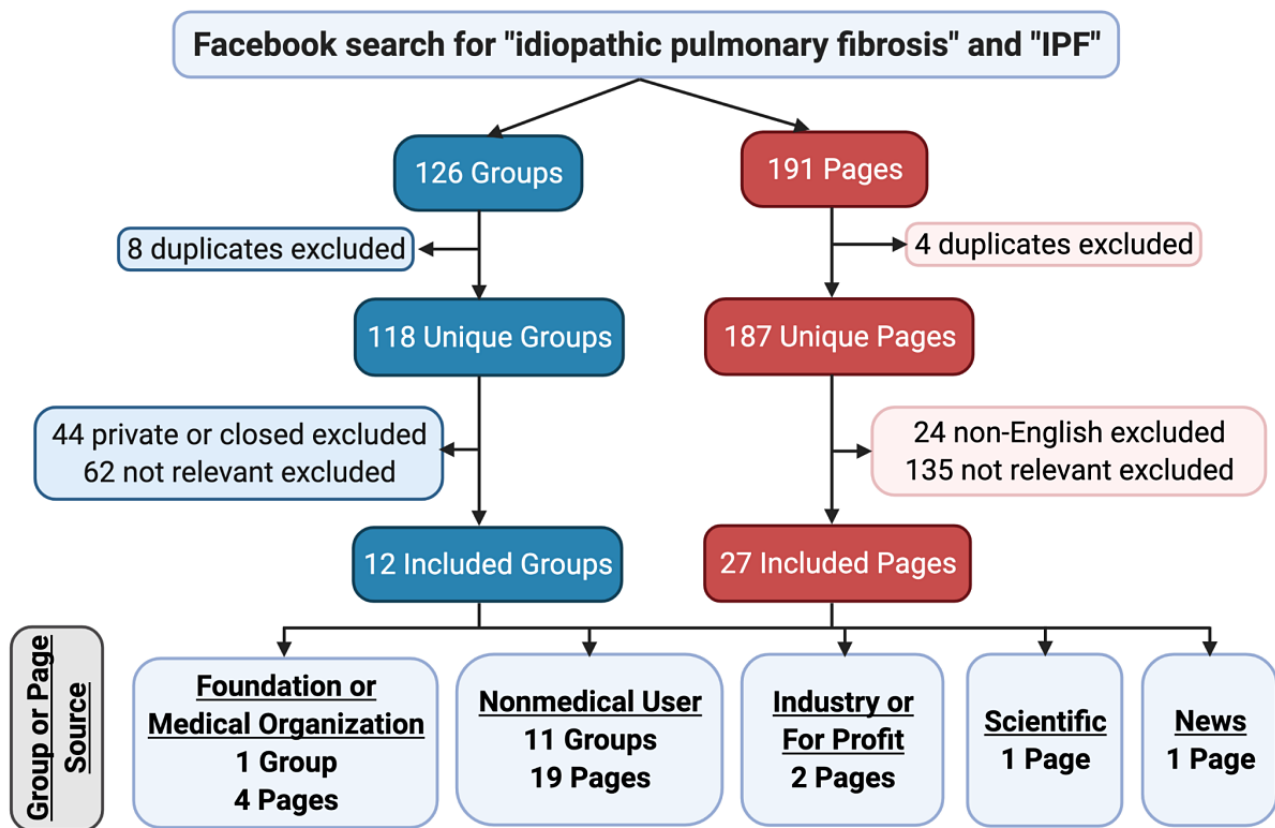


Table 1. Baseline characteristics of posts included in study.

Post characteristics	Groups	Pages	Combined
Total posts, N	220	303	523
Picture present, n (%)	32 (14.5)	86 (28.4)	118 (22.6)
Video present (n, %)	5 (2.3)	27 (8.9)	32 (6.1)
Likes per post, mean (SD)	2 (7)	7 (13)	5 (11)
Shares per post, mean (SD)	0 (1)	3 (7)	2 (5)
Comments per post, mean (SD)	1 (3)	1 (3)	1 (3)
Post age (days), median (IQR)	1117 (192-1930)	888 (347-1337)	630 (259-1381)
Link present, n (%)	124 (56.4)	183 (60.4)	307 (58.7)

## Post Content

We hypothesized that post source of a foundation/medical organization or medical professional, post with a guideline focus, and a post with greater viewer engagement would be associated with higher content scores. On unadjusted analysis, posts from a foundation or medical organization had a numerically higher content score, although this was not statistically significant (Table 2). Posts from an industry source were associated with lower content scores on adjusted analysis (Table 3). Posts with a guideline-related focus had a significantly higher content score (Table 2, Figure 3). On adjusted analysis, post focus on IPF guidelines was associated with lower odds

of having a content score of zero, whereas a non-IPF post focus was associated with higher odds of having a content score of zero (Table 3).

With regard to viewer engagement, on unadjusted analyses, there was a negative correlation between number of likes or comments and content score, and posts with a higher number of likes and comments were significantly less likely to contain any guideline-recommended content (Figure 4). There was no correlation between content score and number of shares. Conversely, on adjusted analysis, the number of comments was positively associated with a higher content score (Table 3).

**Table 2.** Mean post content scores broken down by post source and content category from groups and pages combined.

Post variable	Content score <sup>a</sup> , mean (SD)	P value <sup>b</sup>
<b>Source</b>		.78
Foundation or medical organization (n=53)	2.8 (6.1)	
Industry or for profit (n=24)	0.2 (0.5)	
Medical professional (n=1)	0.0 (0.0)	
Nonmedical user (n=445)	1.4 (2.9)	
<b>Focus</b>		<.001
Guideline (n=5)	11.2 (10.0)	
Advice (n=80)	1.3 (2.1)	
News (n=152)	2.3 (3.1)	
Advertisement (n=65)	0.7 (1.4)	
Opinion (n=7)	0.9 (0.9)	
Insurance or health care cost (n=2)	1.5 (2.1)	
Other IPF <sup>c</sup> -related focus (n=131)	1.7 (4.6)	
Non-IPF-related focus (n=81)	0.1 (0.3)	

<sup>a</sup>Maximum total score of 30.

<sup>b</sup>Calculated using the  $\chi^2$  test.

<sup>c</sup>IPF: idiopathic pulmonary fibrosis.

**Table 3.** Variables associated with content score in individual posts on adjusted analysis.<sup>a</sup>

Variables	Coefficient (95% CI)	OR <sup>b</sup> or IRR <sup>c</sup> (95% CI)	P value
<b>Zero-inflation model variables<sup>d</sup></b>			
<b>Post focus</b>			
Guideline	-6.58 (-10.21 to -2.95)	0.00139 (0.0000368-0.0523)	<.001
Non-IPF-related	25.68 (19.60, 31.77)	1.42×10 <sup>11</sup> (3.25×10 <sup>8</sup> - 6.27×10 <sup>13</sup> )	<.001
Age of post (days)	0.00189 (0.000493 to 0.00329)	1.002 (1.0005-1.003)	.008
<b>Count model variables<sup>e</sup></b>			
Number of comments	0.0496 (0.00738 to 0.0918)	1.05 (1.01-1.10)	.02
Industry post source	-2.55 (-2.84 to -2.26)	0.0783 (0.0586-0.104)	<.001
<b>Post focus</b>			
Guideline	Comparator	Comparator	N/A <sup>f</sup>
Other IPF-related	-1.41 (-1.92 to -0.89)	0.245 (0.146-0.411)	<.001
Non-IPF-related	-3.18 (-4.44 to -1.93)	0.0415 (0.0118-0.146)	<.001
Age of post (days)	0.000213 (0.0000392 to 0.000387)	1.0002 (1.00004-1.0004)	.02
Presence of link	1.64 (1.09 to 2.20)	5.18 (2.96-9.04)	<.001

<sup>a</sup>Clustered according to Facebook page or group that the post was made in.

<sup>b</sup>OR: odds ratio (for zero-inflated model variables).

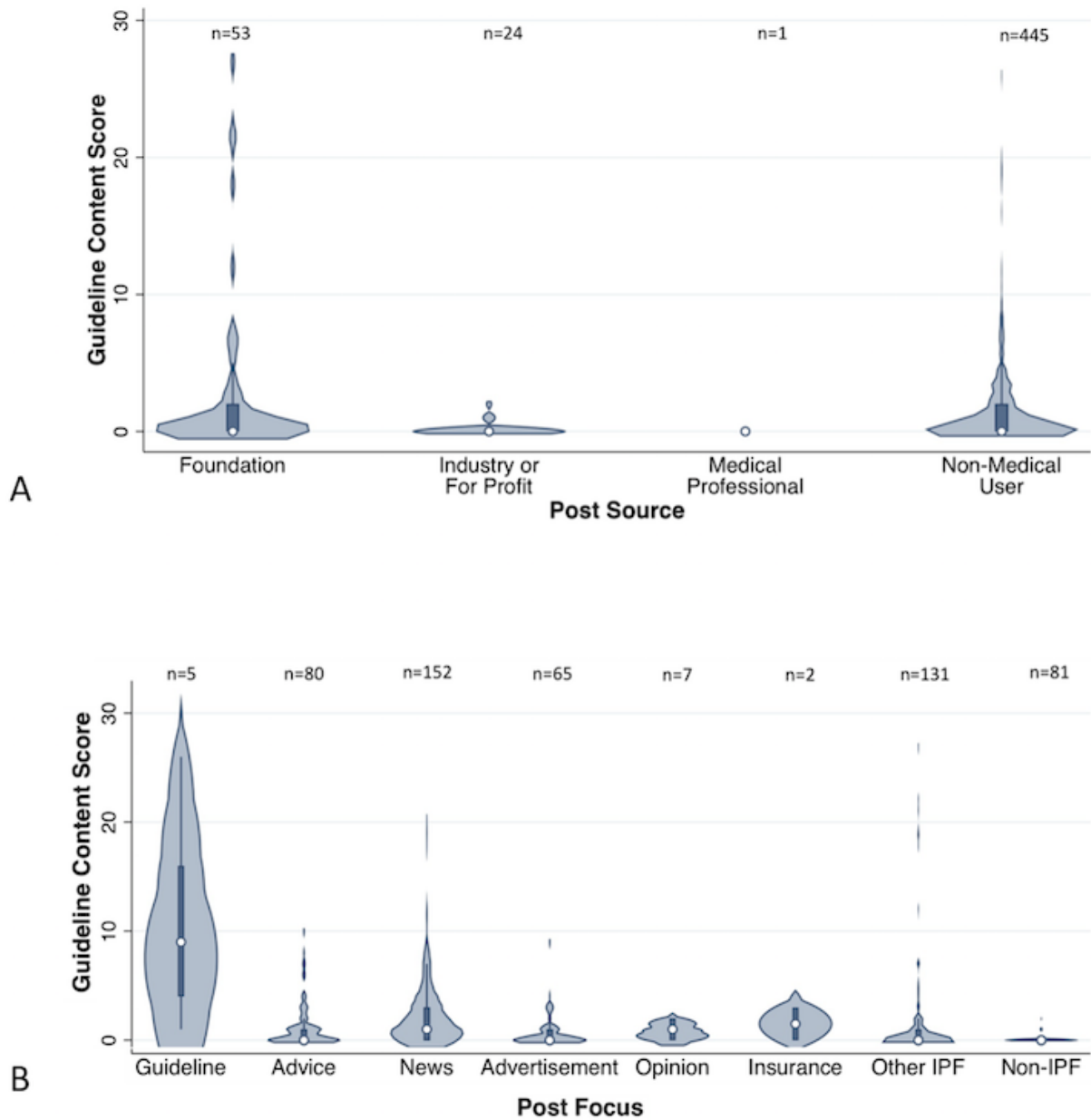
<sup>c</sup>IRR: incident rate ratio (for count variables).

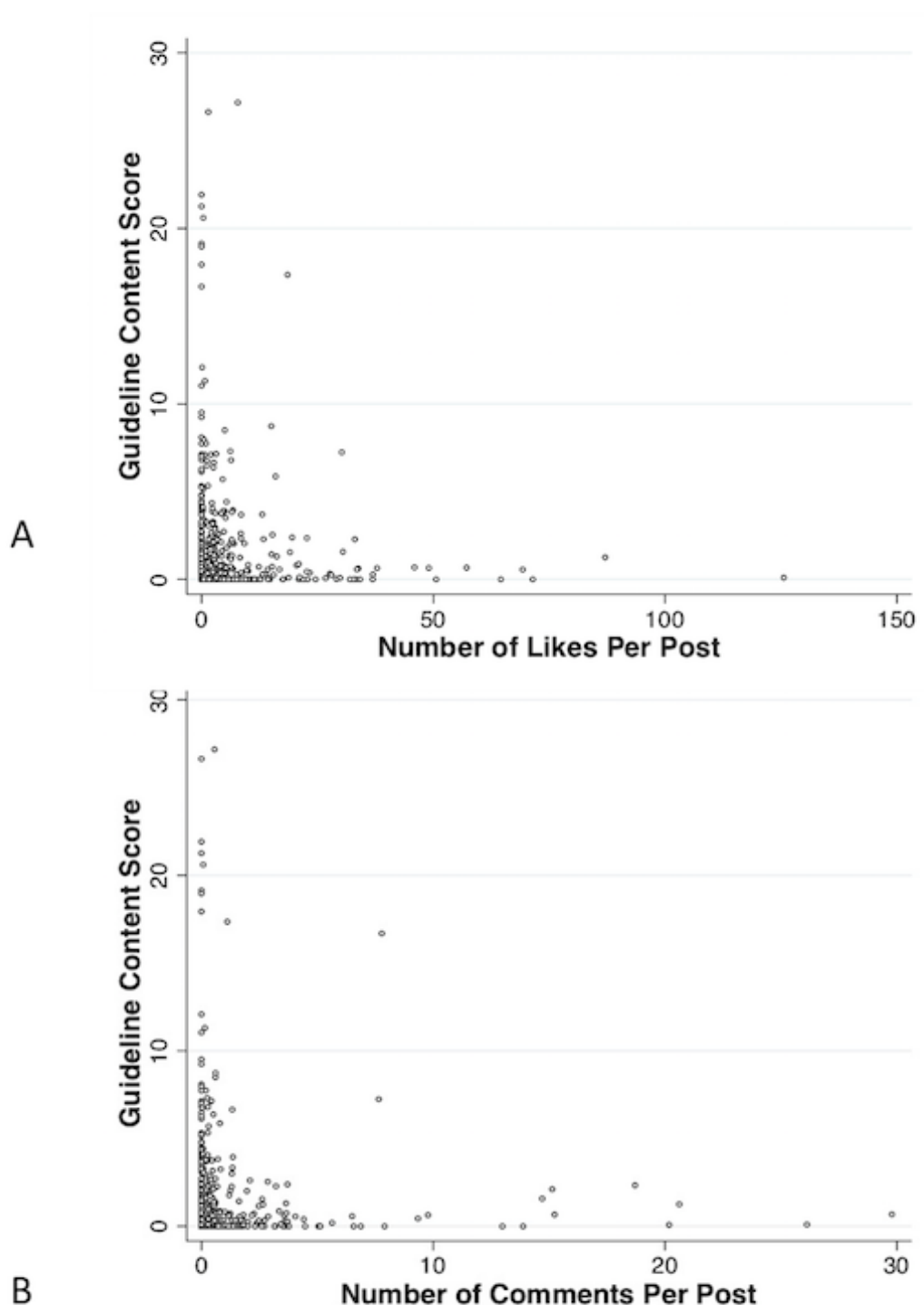
<sup>d</sup>Original zero-inflated model included a trinomial variable for post source and a trinomial variable for post focus.

<sup>e</sup>Original count model included number of likes, number of shares, trinomial post source variable, and presence of video or picture in a post.



**Figure 3.** Content score reflecting the number of guideline-recommended content contained in each post or immediate link from groups and pages combined (maximum score=30). The width of the plot at each level corresponds to the number of posts within that group that had that score. Medians with IQRs are presented as a box plot within the violin plot. Posts are delineated by source (A) and focus (B).



**Figure 4.** Correlation between number of post likes (A) or number of post comments (B) and content score from groups and pages combined.

Although not identified as a prespecified hypothesis, posts containing an external link had a higher content score on both unadjusted and adjusted analyses (Table 3). Posts containing useful scientific information generally had lower viewer engagement. By contrast, posts that contained useful supportive content had higher viewer engagement.

### Harmful Post Content

Only 5% of the posts contained potentially harmful information, but 35% of all groups or pages contained such posts. Although we hypothesized that posts with higher content scores would be less likely to contain potentially harmful content, we found that posts with higher content scores were actually more likely to contain potentially harmful information on both unadjusted and adjusted analyses (Table S4 in Multimedia Appendix 1).

We also hypothesized that post source other than a foundation/medical organization or medical professional, post with a focus other than IPF guidelines, and posts with greater viewer engagement would be associated with higher odds of a post containing potentially harmful content. On unadjusted analysis, groups or pages with a nonmedical user source were more likely to contain potentially harmful content compared to other sources. On adjusted analysis, posts with an industry source were less likely to contain potentially harmful content, and no other sources had an association with posts containing potentially harmful content. On adjusted analysis, posts with a guideline focus were less likely to contain potentially harmful content (Table S4 in [Multimedia Appendix 1](#)).

With respect to viewer engagement, posts containing potentially harmful content had significantly fewer likes on unadjusted analysis. On adjusted analysis, posts with greater than 5 likes or greater than 5 comments had a lower likelihood of containing potentially harmful content. Number of post shares was not associated with potentially harmful content.

## Discussion

### Principal Findings

To our knowledge, this is the first study to assess the content and quality of information about IPF on Facebook. Facebook is the second most widely used social media platform in the United States [6], emphasizing the importance of evaluating the content of health-related information disseminated through this platform. Prior studies have assessed content of Facebook posts from groups or pages in other diseases [15-20], but few have assessed post quality, instead focusing on descriptive analyses. Assigning content scores to posts based on guideline recommendations is a novel method for analyzing health-related posts on Facebook.

Previous surveys have shown that patients with pulmonary fibrosis perceive a lack of available resources and information about their disease [2]. Other studies demonstrate that social media is perceived by patients as an important resource for medical information and dialogue with health professionals [15,21]. We found that most of the identified posts in our study were made by nonmedical users, with very few posts coming from foundations, industry, or medical professionals. The relatively few posts from medical professionals highlights an area for future initiatives aimed at improving access to reliable health-related information on social media for patients with IPF and their caregivers.

The most frequent foci of posts pertaining to IPF included comments on IPF-related news (29%), asking for or receiving advice (15%), and advertising (12%). The frequency of posts with an advertisement focus was lower in our study than reported in previous studies of other chronic diseases [16,18,19], which may represent the small number of commercially available treatments for IPF. We found that 20% of posts presented useful scientific information and 24% provided other useful forms of support (eg, providing information regarding IPF support group meetings). The percentage of useful posts in our study was higher than that reported in similar studies

evaluating Facebook content for other chronic diseases [16,22]. This may be related to a tight-knit network of patients with IPF that engage on social media or could reflect our strict inclusion criteria that excluded evaluation of pages or groups more peripherally associated with IPF, although this requires further study.

We found a negative correlation between number of likes or comments and content score. This suggests that Facebook posts containing more useful content may generate less attention, similar to findings seen in IPF-related YouTube videos [4]. Finding ways to make posts with useful content more visible represents an important area for future research. Although relatively few posts (5%) contained potentially harmful information, one third of pages or groups contained posts with potentially harmful content. This is a lower rate of harmful IPF content than observed on YouTube and other internet resources [3,4].

We found an association between higher content score and posts containing potentially harmful information. This indicates that harmful information about IPF on Facebook is surrounded by useful guideline information, which likely makes it more challenging for patients to distinguish accurate from harmful information. A possible explanation for this association is the presence of old posts discussing historical management approaches that have more recently been disproven (eg, inhaled N-acetylcysteine) [23]. Our findings suggested less frequent harmful content from groups or pages with a nonmedical user source and in posts from an industry source or with a guideline focus. These findings could be used to help direct patients to posts that are less likely to contain harmful information, although more research in this area is required.

### Strengths and Limitations

A strength of our study was not restricting our analysis to the most recent posts; however, this required evaluating every 10th post for content to ensure feasibility. This reduced our sampling of less common post sources such as medical professional-generated content, and we may have missed encountering specific harmful interventions that are only rarely discussed. We also only included open or public groups in the English language, as we were unable to access closed groups or reliably translate posts made in other languages. It is unclear if inclusion of these closed or non-English groups or pages would have led to significantly different findings. Additionally, we only included pages or groups focused on IPF. If we examined pages or groups about any form of ILD, our sample size would have been greater, although less specific for IPF and guideline-related content.

### Conclusions

This study shows that there is useful information about IPF that is available to patients and their caregivers on Facebook. Despite these findings, patients lack clear instruction on how to distinguish between posts containing useful versus harmful information. This is further complicated by the fact that potentially harmful information is often paired alongside useful guideline content. Moving forward, health care professionals need to identify ways to help patients discriminate between

useful and potentially harmful information presented on social media. Post focus or source may provide clues in this regard. Health care professionals should also strive to increase medical professional-generated content aimed at patient education about

IPF on Facebook. Additionally, encouraging posts that contain useful information to generate increased viewer engagement (likes, shares, and comments) will be critical to enhancing the dissemination of accurate medical information on Facebook.

### Authors' Contributions

Study conceptualization and design: AK, SO, GCG, and CJR. Data collection: AK, SO. Statistical analysis: GCG. Interpretation of results: AK, GCG, CJR. Manuscript preparation: AK, GCG, CJR. Approval of final version of the manuscript: AK, SO, SG, KAJ, GCG, CJR.

### Conflicts of Interest

KAJ reports personal fees and other from Boehringer-Ingelheim, Hoffman La Roche Ltd, Theravance, and Blade Therapeutics; grants from Chest Foundation, University of Calgary School of Medicine, and Pulmonary Fibrosis Society of Calgary; and personal fees from Three Lakes Foundation, outside the submitted work. The other authors have no conflicts of interest to declare.

Multimedia Appendix 1

Supplementary data: Tables S1-S4, Figure S1.

[DOCX File , 151 KB - [publichealth\\_v7i5e24199\\_app1.docx](#) ]

### References

1. Raghu G, Remy-Jardin M, Myers JL, Richeldi L, Ryerson CJ, Lederer DJ, American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, Latin American Thoracic Society. Diagnosis of idiopathic pulmonary fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med* 2018 Sep 01;198(5):e44-e68. [doi: [10.1164/rccm.201807-1255ST](#)] [Medline: [30168753](#)]
2. Collard HR, Tino G, Noble PW, Shreve MA, Michaels M, Carlson B, et al. Patient experiences with pulmonary fibrosis. *Respir Med* 2007 Jun;101(6):1350-1354 [FREE Full text] [doi: [10.1016/j.rmed.2006.10.002](#)] [Medline: [17107778](#)]
3. Fisher JH, O'Connor D, Flexman AM, Shapera S, Ryerson CJ. Accuracy and reliability of internet resources for information on idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2016 Jul 15;194(2):218-225. [doi: [10.1164/rccm.201512-2393OC](#)] [Medline: [26849779](#)]
4. Goobie GC, Guler SA, Johannson KA, Fisher JH, Ryerson CJ. YouTube videos as a source of misinformation on idiopathic pulmonary fibrosis. *Ann Am Thorac Soc* 2019 May;16(5):572-579. [doi: [10.1513/AnnalsATS.201809-644OC](#)] [Medline: [30608877](#)]
5. Garrett L. COVID-19: the medium is the message. *Lancet* 2020 Mar 21;395(10228):942-943 [FREE Full text] [doi: [10.1016/S0140-6736\(20\)30600-0](#)] [Medline: [32171075](#)]
6. Social media fact sheet. Pew Research Center Internet & Technology. 2019. URL: <https://www.pewresearch.org/internet/fact-sheet/social-media/> [accessed 2020-09-08]
7. Fox S, Purcell K. Social media and health. Pew Research Center Internet & Technology. 2010. URL: <https://www.pewresearch.org/internet/2010/03/24/social-media-and-health/> [accessed 2020-09-08]
8. Antheunis ML, Tates K, Nieboer TE. Patients' and health professionals' use of social media in health care: motives, barriers and expectations. *Patient Educ Couns* 2013 Sep;92(3):426-431. [doi: [10.1016/j.pec.2013.06.020](#)] [Medline: [23899831](#)]
9. Moorhead SA, Hazlett DE, Harrison L, Carroll JK, Irwin A, Hoving C. A new dimension of health care: systematic review of the uses, benefits, and limitations of social media for health communication. *J Med Internet Res* 2013 Apr 23;15(4):e85 [FREE Full text] [doi: [10.2196/jmir.1933](#)] [Medline: [23615206](#)]
10. What's the difference between a profile, page and group on facebook? Facebook Help Center. 2020. URL: <https://www.facebook.com/help/337881706729661> [accessed 2020-09-08]
11. Raghu G, Collard HR, Egan JJ, Martinez FJ, Behr J, Brown KK, ATS/ERS/JRS/ALAT Committee on Idiopathic Pulmonary Fibrosis. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011 Mar 15;183(6):788-824 [FREE Full text] [doi: [10.1164/rccm.2009-040GL](#)] [Medline: [21471066](#)]
12. Raghu G, Rochwerg B, Zhang Y, Garcia CAC, Azuma A, Behr J, American Thoracic Society, European Respiratory society, Japanese Respiratory Society, Latin American Thoracic Association. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis. An Update of the 2011 Clinical Practice Guideline. *Am J Respir Crit Care Med* 2015 Jul 15;192(2):e3-e19. [doi: [10.1164/rccm.201506-1063ST](#)] [Medline: [26177183](#)]
13. McCullagh P, Nelder J. Generalized linear models. 2nd edition. London: Chapman & Hall/CRC; Aug 01, 1989.
14. Wang Z, Ma S, Wang C. Variable selection for zero-inflated and overdispersed data with application to health care demand in Germany. *Biom J* 2015 Sep;57(5):867-884 [FREE Full text] [doi: [10.1002/bimj.201400143](#)] [Medline: [26059498](#)]

15. Jacobs R, Boyd L, Brennan K, Sinha CK, Giuliani S. The importance of social media for patients and families affected by congenital anomalies: A Facebook cross-sectional analysis and user survey. *J Pediatr Surg* 2016 Nov;51(11):1766-1771. [doi: [10.1016/j.jpedsurg.2016.07.008](https://doi.org/10.1016/j.jpedsurg.2016.07.008)] [Medline: [27522307](https://pubmed.ncbi.nlm.nih.gov/27522307/)]
16. Abedin T, Al Mamun M, Lasker MAA, Ahmed SW, Shommu N, Rumana N, et al. Social media as a platform for information about diabetes foot care: a study of Facebook Groups. *Can J Diabetes* 2017 Feb;41(1):97-101. [doi: [10.1016/j.cjcd.2016.08.217](https://doi.org/10.1016/j.cjcd.2016.08.217)] [Medline: [28126155](https://pubmed.ncbi.nlm.nih.gov/28126155/)]
17. Al Mamun M, Ibrahim HM, Turin TC. Social media in communicating health information: an analysis of Facebook groups related to hypertension. *Prev Chronic Dis* 2015 Jan 29;12:E11 [FREE Full text] [doi: [10.5888/pcd12.140265](https://doi.org/10.5888/pcd12.140265)] [Medline: [25633486](https://pubmed.ncbi.nlm.nih.gov/25633486/)]
18. Hassona Y, Abu Ghosh M, Abu Ghlassi T, Scully C. Public engagement with oral cancer on Facebook. *Oral Oncol* 2016 Jun;57:e6-e7. [doi: [10.1016/j.oraloncology.2016.04.014](https://doi.org/10.1016/j.oraloncology.2016.04.014)] [Medline: [27160026](https://pubmed.ncbi.nlm.nih.gov/27160026/)]
19. Bender JL, Jimenez-Marroquin M, Jadad AR. Seeking support on facebook: a content analysis of breast cancer groups. *J Med Internet Res* 2011 Feb 04;13(1):e16 [FREE Full text] [doi: [10.2196/jmir.1560](https://doi.org/10.2196/jmir.1560)] [Medline: [21371990](https://pubmed.ncbi.nlm.nih.gov/21371990/)]
20. Apperson A, Stelfson M, Paige SR, Chaney BH, Chaney JD, Wang MQ, et al. Facebook Groups on chronic obstructive pulmonary disease: social media content analysis. *Int J Environ Res Public Health* 2019 Oct 09;16(20):3789 [FREE Full text] [doi: [10.3390/ijerph16203789](https://doi.org/10.3390/ijerph16203789)] [Medline: [31600907](https://pubmed.ncbi.nlm.nih.gov/31600907/)]
21. Klee D, Covey C, Zhong L. Social media beliefs and usage among family medicine residents and practicing family physicians. *Fam Med* 2015 Mar;47(3):222-226 [FREE Full text] [Medline: [25853534](https://pubmed.ncbi.nlm.nih.gov/25853534/)]
22. Koball AM, Jester DJ, Pruitt MA, Cripe RV, Henschied JJ, Domoff S. Content and accuracy of nutrition-related posts in bariatric surgery Facebook support groups. *Surg Obes Relat Dis* 2018 Dec;14(12):1897-1902. [doi: [10.1016/j.soard.2018.08.017](https://doi.org/10.1016/j.soard.2018.08.017)] [Medline: [30274739](https://pubmed.ncbi.nlm.nih.gov/30274739/)]
23. Idiopathic Pulmonary Fibrosis Clinical Research Network, Raghu G, Anstrom KJ, King TE, Lasky JA, Martinez FJ. Prednisone, azathioprine, and N-acetylcysteine for pulmonary fibrosis. *N Engl J Med* 2012 May 24;366(21):1968-1977 [FREE Full text] [doi: [10.1056/NEJMoa1113354](https://doi.org/10.1056/NEJMoa1113354)] [Medline: [22607134](https://pubmed.ncbi.nlm.nih.gov/22607134/)]

## Abbreviations

**ILD:** interstitial lung disease

**IPF:** idiopathic pulmonary fibrosis

*Edited by G Eysenbach; submitted 08.09.20; peer-reviewed by K Moor, D Schatell, J Edwards; comments to author 17.11.20; revised version received 25.11.20; accepted 17.04.21; published 31.05.21.*

*Please cite as:*

*Kochan A, Ong S, Guler S, Johannson KA, Ryerson CJ, Goobie GC*

*Social Media Content of Idiopathic Pulmonary Fibrosis Groups and Pages on Facebook: Cross-sectional Analysis*

*JMIR Public Health Surveill* 2021;7(5):e24199

URL: <https://publichealth.jmir.org/2021/5/e24199>

doi: [10.2196/24199](https://doi.org/10.2196/24199)

PMID: [34057425](https://pubmed.ncbi.nlm.nih.gov/34057425/)

©Andrew Kochan, Shaun Ong, Sabina Guler, Kerri A Johannson, Christopher J Ryerson, Gillian C Goobie. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 31.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# The Influence of the COVID-19 Epidemic on Prevention and Vaccination Behaviors Among Chinese Children and Adolescents: Cross-sectional Online Survey Study

Zhiyuan Hou<sup>1,2\*</sup>, PhD; Suhang Song<sup>3\*</sup>, PhD; Fanxing Du<sup>1</sup>, MPH; Lu Shi<sup>4</sup>, PhD; Donglan Zhang<sup>5</sup>, PhD; Leesa Lin<sup>6</sup>, PhD; Hongjie Yu<sup>1,7</sup>, PhD

<sup>1</sup>School of Public Health, Fudan University, Shanghai, China

<sup>2</sup>Key Laboratory of Health Technology Assessment (National Health Commission), Fudan University, Shanghai, China

<sup>3</sup>Taub Institute for Research in Alzheimer's Disease and the Aging Brain, Columbia University, New York, NY, United States

<sup>4</sup>Department of Public Health Sciences, College of Behavioral, Social and Health Sciences, Clemson University, Clemson, SC, United States

<sup>5</sup>Department of Health Policy and Management, College of Public Health, University of Georgia, Athens, GA, United States

<sup>6</sup>Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, United Kingdom

<sup>7</sup>Key Laboratory of Public Health Safety (Ministry of Education), Fudan University, Shanghai, China

\*these authors contributed equally

**Corresponding Author:**

Zhiyuan Hou, PhD

School of Public Health

Fudan University

Mailbox 250, 138# Yixueyuan Road, Xuhui District

Shanghai, 200030

China

Phone: 86 2133563935

Email: [zyhou@fudan.edu.cn](mailto:zyhou@fudan.edu.cn)

## Abstract

**Background:** The COVID-19 epidemic and the related containment strategies may affect parental and pediatric health behaviors.

**Objective:** The goal of this study was to assess the change in children's and adolescents' prevention and vaccination behaviors amid China's COVID-19 epidemic.

**Methods:** We conducted a cross-sectional online survey in mid-March 2020 using proportional quota sampling in Wuhan (the epidemic epicenter) and Shanghai (a non-epicenter). Data were collected from 1655 parents with children aged 3 to 17 years. Children's and adolescents' prevention behaviors and regular vaccination behaviors before and during the epidemic were assessed. Descriptive analyses were used to investigate respondents' characteristics, public health prevention behaviors, unproven protection behaviors, and vaccination behaviors before and during the COVID-19 epidemic. Univariate analyses were performed to compare differences in outcome measures between cities and family characteristics, using chi-square tests or Fisher exact tests (if expected frequency was <5) and analyses of variance. Multivariate logistic regressions were used to identify the factors and disparities associated with prevention and vaccination behaviors.

**Results:** Parent-reported prevention behaviors increased among children and adolescents during the COVID-19 epidemic compared with those before the epidemic. During the epidemic, 82.2% (638/776) of children or adolescents always wore masks when going out compared with 31.5% (521/1655) before the epidemic; in addition, 25.0% (414/1655) and 79.8% (1321/1655) had increased their frequency and duration of handwashing, respectively, although only 46.9% (776/1655) went out during the epidemic. Meanwhile, 56.1% (928/1655) of the families took unproven remedies against COVID-19. Parent-reported vaccination behaviors showed mixed results, with 74.8% (468/626) delaying scheduled vaccinations and 80.9% (1339/1655) planning to have their children get the influenza vaccination after the epidemic. Regarding socioeconomic status, children and adolescents from larger families and whose parents had lower education levels were less likely to improve prevention behaviors but more likely to take unproven remedies. Girls were less likely than boys to always wear a mask when going out and wash their hands.

**Conclusions:** Prevention behaviors and attitudes toward influenza vaccination have improved during the COVID-19 epidemic. Public health prevention measures should be continuously promoted, particularly among girls, parents with lower education

levels, and larger families. Meanwhile, misinformation about COVID-19 remains a serious challenge and needs to be addressed by public health stakeholders.

(*JMIR Public Health Surveill* 2021;7(5):e26372) doi:[10.2196/26372](https://doi.org/10.2196/26372)

## KEYWORDS

COVID-19; prevention; vaccination; behavior; children; China

## Introduction

On December 31, 2019, the government in Wuhan, China, announced an outbreak of a new infectious disease, formally named COVID-19. The COVID-19 outbreak spread quickly across China and the world [1]. In order to control the severe epidemic, the Chinese government launched a variety of containment strategies between January and April 2020, including lockdown policies, stay-at-home orders, school closures, and suspension of mass gatherings. The city of Wuhan, the epicenter of the COVID-19 outbreak, went through a complete lockdown from January 23 [2] to April 8, 2020 [3], whereas the Shanghai municipality, a city significantly affected by imported COVID-19 cases from Wuhan, activated the highest-level public health emergency response on January 24, 2020 [4], and later loosened it on March 24, 2020 [5]. Vaccination clinics were closed and then reopened in both Wuhan and Shanghai [6,7]. After the human-to-human transmission was confirmed on January 20, 2020, the National Health Commission of China issued the personal protection guidelines that included respiratory protection and hand hygiene [1], as well as health monitoring and social distancing [8]. Simultaneously, misinformation or rumors about COVID-19 started to spread on mass media and social media. The People's Daily, the largest newspaper group in China, reported that Shuanghuanglian, an unproven herbal remedy, could inhibit COVID-19; 2 days later, it clarified that Shuanghuanglian cannot prevent COVID-19 [1]. The rumor that *garlic can prevent COVID-19* appeared on social media, and the People's Daily refuted it again [1].

It is likely that the COVID-19 epidemic and subsequent containment strategies could have influenced the prevention and vaccination behaviors for adults and children [9]. Previous studies assessed the effectiveness of personal protective behaviors, indicating that behaviors such as mask-wearing, social distancing, and handwashing can help prevent COVID-19 transmission [10-12]. Some studies reported the positive impact of social distancing strategies, like the stay-at-home order, on the spread of the COVID-19 epidemic and health outcomes [13,14]. The public's perception and compliance played an important role in the practice of personal protective behaviors, especially for children and adolescents who usually had a lower adherence to the recommended hygiene behaviors [15,16]. However, most studies focused on compliance with personal protective behaviors among adults during the COVID-19 epidemic [10,11,16-19], and few investigated children and adolescents. For Chinese adults, previous online surveys found that from February to March 2020, nearly 80% of adult residents complied with personal protection strategies, such as stay-at-home orders, mask-wearing, temperature self-monitoring,

and hand sanitization, whereas adult migrant workers reported a higher compliance with mask-wearing in public places (95.7%) but a lower compliance with hand sanitization (70.9%) [20-22]. In addition, misinformation may bias the public's perception and mislead the behavioral response to the epidemic [23]. It is plausible that these cognitive and behavioral challenges among the adult population could also occur among minors; therefore, assessing behavioral changes among children and adolescents may help identify the challenges associated with their adherence to containment strategies.

Public resources and services have long been unequally distributed among population subgroups in China and worldwide [24-28], which explained why the public responded to the COVID-19 epidemic differently in different places [29]. This epidemic may have led to various effects across population subgroups, and the public's behavioral responses may differ by their demographic and socioeconomic status [30]. Previous studies have investigated the factors influencing adults' behavioral responses to the COVID-19 epidemic and reported differential behaviors by socioeconomic status and gender [17,31-33]. Therefore, investigating the disparities in children's behavioral responses and influencing factors would assist in identifying the subgroups with the highest needs, and could help in developing tailored interventions for children and adolescents to cope with the impacts of COVID-19. In addition, the COVID-19 epidemic and containment strategies were somehow different in the epicenter and nonepicenters, and comparison of prevention behaviors between the epicenter and nonepicenters could help us understand the influence of containment strategies with different degrees of severity.

Our study aimed to assess children's and adolescents' prevention behaviors and factors influencing their behavioral change amid the COVID-19 epidemic in China, and to further explore the disparities of behavioral changes among children and adolescents based on parent-reported records.

## Methods

### Study Design

From March 12 to 17, 2020, a cross-sectional online survey was conducted in Wuhan (the epicenter) and Shanghai (a nonepicenter) among parents with children aged 3 to 17 years. During our survey period, both Wuhan and Shanghai implemented the highest level of public health emergency response, including stay-at-home orders, closure of shops and schools, as well as suspension of mass gatherings [34]; as a result, the number of new COVID-19 cases reduced to 5 or lower in both cities. This study included children and adolescents at all stages of education, from kindergarten through high school, who were affected most by the school closure

policy during the epidemic. During our survey period, children and adolescents spent most of their time staying at home with their parents, and all the personal prevention behaviors that we measured—going out, wearing of face masks, or handwashing—happened during the city lockdown. Although some parents resumed work in mid-February 2020 in Shanghai and in mid-March 2020 in Wuhan, most parents worked from home. Therefore, parents were children's primary caregivers, and parents' recall bias may not have been a big issue that affected the reliability of the measurement.

Our survey was operationalized by the ePanel data company [35], which maintains a national online survey panel with individuals' phone numbers, email addresses, and basic information. This survey panel included millions of residents from major cities in China, including Shanghai and Wuhan. Residents in the two cities were randomly selected from this survey panel, and families with children aged 3 to 17 years were eligible to access the full survey. After accepting the survey invitation, one parent with children aged 3 to 17 years would provide informed consent and complete the questionnaire. In China, most households had a single child because of the one-child policy, especially in megacities such as Wuhan and Shanghai. Even if some households had multiple children, one parent was required to complete the questionnaire for only one of their children in our survey. The questionnaire (Multimedia Appendix 1) was pilot-tested with 30 participants who were excluded from this analysis. In addition, proportional quota sampling [36,37] was employed to ensure that respondents were demographically representative of the population according to local census data [38]. The final sample size—around 800 in each city—provided a sampling error of 3%. Once the numbers of survey respondents across children's gender and age groups were reached in the same proportions of the Wuhan census and the Shanghai census, the predefined quota was then met and no more sampling was conducted. The study was approved by the Institutional Review Board (IRB) of the School of Public Health, Fudan University (IRB No. 2020-01-0801-S).

Between March 12 and 17, 2020, the survey was emailed to 73,000 residents in Wuhan and Shanghai, and 2960 (4.1%) residents accepted the survey invitation (Multimedia Appendix 2). In total, 2065 residents had children aged 3 to 17 years and were eligible to participate in the study, of whom 410 residents either did not finish or had missing data in their responses, leaving data from 1655 respondents (816 in Wuhan [49.3%] and 839 in Shanghai [50.7%]) in the final analytic sample.

## Measures

This study classified the behaviors of interest among children or adolescents into three categories: (1) public health prevention behaviors (ie, mask-wearing, handwashing, self-monitoring of COVID-19 symptoms, and social distancing), (2) unproven protection behaviors (ie, use of unproven or potentially harmful treatments), and (3) vaccination behaviors (ie, influenza vaccination and regularly scheduled vaccinations, but not COVID-19 vaccination). These behaviors were measured twice: once during the COVID-19 epidemic and once before the epidemic. Prevention behaviors were measured by the frequency of children or adolescents wearing masks when going out before

and during the epidemic, the frequency and duration of washing hands after coming home before and during the epidemic, and the frequency of monitoring body temperature and going out during the epidemic. This study used the monitoring of body temperature to represent the behavior of self-monitoring of COVID-19 symptoms, since fever is one of the main symptoms of COVID-19. Unproven protection behaviors were measured by the instances of buying or taking unproven herbal remedies or garlic during the epidemic, which were believed to prevent COVID-19 through rumors. Vaccination behaviors included the delay of scheduled vaccinations, whether the parent was informed about alternative vaccination arrangements during the epidemic, and the receipt of the influenza vaccination in the past and their future intentions after the epidemic.

Data about the characteristics of parents and children or adolescents were also collected, including parents' education level, household size (ie, number of family members living together), children's or adolescents' gender and age, and whether there were confirmed or suspected COVID-19 cases in their neighborhood. The questionnaire is included in [Multimedia Appendix 1](#).

## Statistical Analysis

Descriptive analysis was used to investigate respondents' characteristics, public health prevention behaviors, unproven protection behaviors, and vaccination behaviors before and during the COVID-19 epidemic. Univariate analyses were performed to compare differences in outcome measures between cities and family characteristics, using chi-square tests or Fisher exact tests (if expected frequency was <5) for categorical measures and analyses of variance for continuous measures. Multivariate logistic regressions were used to identify the factors and disparities associated with prevention and vaccination behaviors during the epidemic. Each of the following eight behavioral indicators during the epidemic was modeled as a dependent variable separately: (1) frequency of mask-wearing (always vs not always), (2) frequency of handwashing (always vs not always), (3) duration of hand washing (<40 seconds vs ≥40 seconds), (4) frequency of monitoring body temperature (>3 times/week vs ≤3 times/week), (5) whether they went outside or not, (6) whether they took unproven remedies or not, (7) whether they delayed scheduled vaccinations or not, and (8) whether they planned to receive the influenza vaccination or not after the epidemic. Independent variables in each regression model included all available characteristics of the parents and children or adolescents. The proportions and odds ratios (ORs) with 95% CIs were reported. All statistical analyses were performed using Stata 14.0 (StataCorp LP).

## Results

### Characteristics of Respondents

The sample characteristics are presented in [Table 1](#). The gender and age distributions of sampled children and adolescents were similar to the two cities' censuses, indicating the representativeness of our sample. Of 1655 respondents, 1077 (65.1%) were mothers of children and 1225 (74.0%) reported obtaining bachelor's degrees or above; in addition, there were an average of 3.5 (SD 1.30) members in the sampled families.



There were no significant differences in respondents' characteristics between Wuhan and Shanghai. Due to the more severe epidemic in Wuhan, more respondents in Wuhan (277/816, 33.9%) reported that there were confirmed or suspected COVID-19 cases in their neighborhood, compared to those in Shanghai (88/839, 10.5%).

**Table 1.** Characteristics of respondents in Wuhan and Shanghai during the COVID-19 epidemic, March 2020.

Characteristic	Total (N=1655)	Wuhan (n=816)	Shanghai (n=839)	P value
<b>Gender of child or adolescent, n (%)</b>				.75 <sup>a</sup>
Male	830 (50.2)	406 (49.8)	424 (50.5)	
Female	825 (49.9)	410 (50.3)	415 (49.5)	
<b>Age of child or adolescent (years), n (%)</b>				.84 <sup>a</sup>
3-5	321 (19.4)	160 (19.6)	161 (19.2)	
6-9	432 (26.1)	217 (26.6)	215 (25.6)	
10-14	359 (21.7)	180 (22.1)	179 (21.3)	
15-17	543 (32.8)	259 (31.7)	284 (33.9)	
<b>Respondent, n (%)</b>				.10 <sup>a</sup>
Mother of child or adolescent	1077 (65.1)	547 (67.0)	530 (63.2)	
Father of child or adolescent	578 (34.9)	269 (33.0)	309 (36.8)	
<b>Education level of parent, n (%)</b>				.32 <sup>a</sup>
High school or below	103 (6.2)	45 (5.5)	58 (6.9)	
Some college	327 (19.8)	170 (20.8)	157 (18.7)	
Bachelor's degree or above	1225 (74.0)	601 (73.7)	624 (74.4)	
Household size, mean (SD)	3.5 (1.30)	3.5 (1.26)	3.5 (1.34)	.39 <sup>b</sup>
<b>COVID-19 cases in neighborhood, n (%)</b>				<.001 <sup>a</sup>
Yes	365 (22.1)	277 (33.9)	88 (10.5)	
No or unclear	1290 (78.0)	539 (66.1)	751 (89.5)	

<sup>a</sup>P value was calculated from a chi-square test.

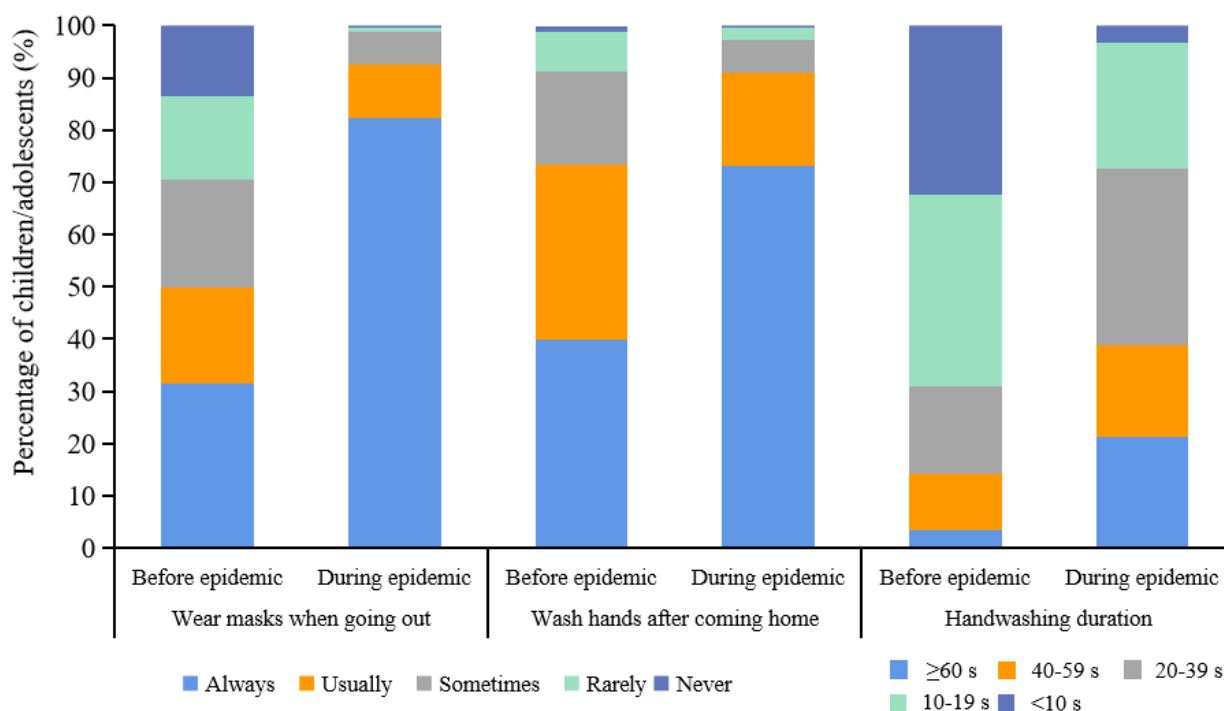
<sup>b</sup>P value was calculated from an analysis of variance.

## Prevention and Vaccination Behaviors Among Children and Adolescents During the Epidemic

Figure 1 and Table 2 describe prevention behaviors, unproven protection measures, and vaccination behaviors among children and adolescents before and during the COVID-19 epidemic. Only 46.9% (776/1655) of children or adolescents went out since the beginning of the epidemic (Table 2). There were 82.2% (638/776) of children or adolescents who always wore masks when going out during the epidemic compared with 31.5% (521/1655) before the epidemic (Figure 1). Primary reasons for not always wearing masks during the epidemic included having no masks (61/144, 42.4%), children and adolescents thinking

mask-wearing was unattractive or uncomfortable (41/144, 28.5%), and parents thinking mask-wearing had limited protective effect (37/144, 25.7%) (Table 2). During the epidemic, both the frequency and duration of handwashing after coming home increased significantly among children or adolescents (Figure 1), with 25.0% (414/1655) and 79.8% (1321/1655) having increased the frequency and duration of handwashing, respectively. During the epidemic, 57.5% (952/1655) of families monitored children's or adolescents' body temperature more than 3 times each week (Table 2). There were 56.1% (928/1655) of families who bought or took unproven herbal remedies, and 30.3% (501/1655) took garlic, as a result of a rumor that it was protective (Table 2).

**Figure 1.** Comparison of prevention behaviors among children and adolescents in Wuhan and Shanghai before and during the COVID-19 epidemic, March 2020.



Among 626 children or adolescents with scheduled vaccinations, 468 (74.8%) delayed vaccination, of whom 70.1% (328/468) delayed more than 2 weeks and 55.6% (260/468) were worried about vaccination delay (Table 2). A total of 90.9% (569/626) of parents reported being informed about alternative vaccination arrangements during the epidemic. During the 2019 flu season, 54.7% (905/1655) of families had taken their children or adolescents to receive the influenza vaccination, and 80.9% (1339/1655) of parents intended to vaccinate their children or adolescents against influenza in the future after the epidemic, a rate much higher than that before the epidemic (Table 2).

Findings of univariate analysis between Wuhan and Shanghai are shown in Table 2 and by respondents' characteristics in

Multimedia Appendix 3. In comparison with the Shanghai sample, parents in Wuhan were significantly more likely to monitor body temperature of their children or adolescents, and their children were less likely to go out during the epidemic. There was no significant difference in taking unproven remedies or garlic to prevent COVID-19 between the two cities. More children and adolescents in Wuhan had delayed their scheduled vaccinations and delayed for a longer time than those in Shanghai, but a similar proportion of parents in the two cities expressed concerns about the delay and were informed of alternative vaccination arrangements. In addition, there were no significant differences in parents' future intentions to vaccinate their children against influenza after the epidemic between the two cities.

**Table 2.** Prevention, unproven protection, and vaccination behaviors among children and adolescents in Wuhan and Shanghai during the COVID-19 epidemic, March 2020.

Prevention, unproven protection, and vaccination behavior	Total (N=1655), n (%)	Wuhan (n=816), n (%)	Shanghai (n=839), n (%)	P value
<b>Public health prevention behavior</b>				
<b>Frequency of child or adolescent going out during the epidemic</b>				<.001 <sup>a</sup>
Never	879 (53.1)	479 (58.7)	400 (47.7)	
<1 time/week	505 (30.5)	229 (28.1)	276 (32.9)	
1-2 times/week	220 (13.3)	93 (11.4)	127 (15.1)	
3-5 times/week	47 (2.8)	13 (1.6)	34 (4.1)	
Nearly everyday	4 (0.2)	2 (0.3)	2 (0.2)	
<b>Reasons for child or adolescent not always wearing a mask when going out during the epidemic (n=144)<sup>b</sup></b>				.64 <sup>a</sup>
They had no masks	61 (42.4)	21 (39.6)	40 (44.0)	
Child or adolescent thought mask-wearing was unattractive	26 (18.1)	10 (18.9)	16 (17.6)	
Child or adolescent thought mask-wearing was uncomfortable	15 (10.4)	4 (7.6)	11 (12.1)	
Parent thought masks had limited protective effects	37 (25.7)	17 (32.1)	20 (22.0)	
Parent thought the epidemic was not severe	5 (3.5)	1 (1.9)	4 (4.4)	
<b>Frequency of monitoring body temperature of child or adolescent during the epidemic</b>				<.001 <sup>c</sup>
Never	120 (7.3)	27 (3.3)	93 (11.1)	
≤1 time/week	264 (16.0)	106 (13.0)	158 (18.8)	
2-3 times/week	319 (19.3)	125 (15.3)	194 (23.1)	
4-5 times/week	366 (22.1)	209 (25.6)	157 (18.7)	
6-7 times/week	586 (35.4)	349 (42.8)	237 (28.3)	
<b>Unproven protection behavior</b>				
Family members bought or took unproven herbal remedies to prevent COVID-19	928 (56.1)	451 (55.3)	477 (56.9)	.52 <sup>c</sup>
Family members took unproven garlic remedy to prevent COVID-19	501 (30.3)	252 (30.9)	249 (29.7)	.59 <sup>c</sup>
<b>Vaccination behavior</b>				
Delayed the scheduled vaccinations for child or adolescent during the epidemic (n=626) <sup>b</sup>	468 (74.8)	239 (78.6)	229 (71.1)	.03 <sup>c</sup>
<b>How long child or adolescent vaccination was delayed during the epidemic (n=468)<sup>b</sup></b>				.03 <sup>c</sup>
<2 weeks	140 (30.0)	68 (28.5)	72 (31.4)	
2 weeks to 1 month	143 (30.6)	86 (36.0)	57 (24.9)	
>1 month	185 (39.5)	85 (35.6)	100 (43.7)	
Parent was worried about the delay of child or adolescent vaccination (n=468) <sup>b</sup>	260 (55.6)	140 (58.6)	120 (52.4)	.18 <sup>c</sup>
Parent was informed of alternative vaccination arrangements during the epidemic (n=626) <sup>b</sup>	569 (90.9)	282 (92.8)	287 (89.1)	.11 <sup>c</sup>
Child or adolescent had received influenza vaccination in 2019 flu season	905 (54.7)	467 (57.2)	438 (52.2)	.04 <sup>c</sup>
Planned to vaccinate child or adolescent against influenza after the epidemic	1339 (80.9)	655 (80.3)	684 (81.5)	.52 <sup>c</sup>

<sup>a</sup>P value was calculated from a Fisher exact test.

<sup>b</sup>These questions were only asked based on the response to a prior question, and the total number of respondents was marked separately.

<sup>c</sup>P value was calculated from a chi-square test.

### Factors Associated With Prevention and Vaccination Behaviors Among Children and Adolescents During the Epidemic

Table 3 presents the factors associated with children's prevention and vaccination behaviors during the epidemic using multivariate logistic regressions. This analysis showed that during the epidemic, children or adolescents in Shanghai, compared to Wuhan, were more likely to go outside (OR 1.56, 95% CI 1.26-1.92), less likely to monitor body temperature more than 3 times per week (OR 0.42, 95% CI 0.34-0.52), and less likely to delay scheduled vaccinations (OR 0.60, 95% CI 0.40-0.88). The education level of parents was significantly associated with prevention, unproven protection, and vaccination behaviors, with negative associations with the prevalence of going outside and taking unproven remedies and positive associations with other behaviors. Specifically, children and adolescents whose parents had lower education levels were more likely to go outside and take unproven remedies, and they

were less likely to wear masks, wash hands, and monitor body temperature during the epidemic. Their parents were also less likely to delay scheduled vaccinations during the epidemic and had lower intentions of having their children receive the influenza vaccination after the epidemic, compared to children and adolescents whose parents had higher levels of education. During the epidemic, children and adolescents from larger families were more likely to go outside and take unproven remedies as well, while they were less likely to wash their hands for 40 seconds or more or take their body temperature more than 3 times per week. Girls were less likely to wear masks (OR 0.61, 95% CI 0.41-0.91) or wash their hands (OR 0.64, 95% CI 0.45-0.90) than boys during the epidemic. Children's and adolescents' ages were significantly and negatively associated with the taking of unproven remedies and intentions to receive the influenza vaccination after the epidemic. Having a father or mother as their caregiver and COVID-19 prevalence in their neighborhood also influenced some preventive behaviors of children and adolescents.

**Table 3.** Factors associated with prevention, unproven protection, and vaccination behaviors among respondents in Wuhan and Shanghai during the COVID-19 epidemic by multivariate logistic regression, March 2020.

Characteristic	Public health prevention behavior, OR <sup>a</sup> (95% CI)					Unproven protection behavior, OR (95% CI)	Vaccination behavior, OR (95% CI)	
	Always wear a mask (n=776)	Always wash hands (n=774)	Wash hands ≥40 seconds (N=1655)	Monitor body temperature >3 times/week (N=1655)	Go outside (N=1655)		Take unproven remedies (N=1655)	Delay scheduled vaccination (n=626)
Shanghai (ref <sup>b</sup> : Wuhan)	0.69 (0.46-1.04)	1.09 (0.77-1.55)	0.84 (0.68-1.04)	0.42** (0.34-0.52)	1.56** (1.26-1.92)	1.16 (0.94-1.43)	0.60** (0.40-0.88)	1.22 (0.93-1.59)
<b>Education of parent (ref: bachelor's degree or above)</b>								
Some college	0.42** (0.27-0.64)	0.37** (0.26-0.55)	0.75* (0.58-0.98)	0.55** (0.42-0.71)	1.46** (1.13-1.88)	1.30* (1.01-1.69)	0.75 (0.46-1.21)	0.51** (0.37-0.69)
High school or below	0.30** (0.17-0.55)	0.19** (0.11-0.33)	0.93 (0.60-1.42)	0.47** (0.30-0.71)	1.66* (1.08-2.53)	1.12 (0.73-1.70)	0.30** (0.15-0.59)	0.63 (0.38-1.05)
Household size	0.96 (0.87-1.06)	1.01 (0.91-1.11)	0.89* (0.80-0.99)	0.83** (0.75-0.93)	1.27** (1.13-1.43)	1.19** (1.06-1.34)	1.10 (0.96-1.26)	1.02 (0.92-1.13)
Female child or adolescent (ref: male)	0.61* (0.41-0.91)	0.64* (0.45-0.90)	1.23 (0.99-1.51)	1.22 (0.99-1.51)	1.01 (0.82-1.24)	0.96 (0.78-1.18)	1.10 (0.75-1.63)	0.79 (0.61-1.04)
<b>Age of child or adolescent (years) (ref: 3-5 years)</b>								
6-9	1.02 (0.60-1.74)	1.61 (0.98-2.67)	0.56** (0.41-0.76)	0.89 (0.65-1.21)	1.12 (0.83-1.51)	0.71* (0.52-0.97)	1.90** (1.19-3.05)	0.87 (0.55-1.37)
10-14	1.21 (0.65-2.24)	1.37 (0.79-2.37)	1.00 (0.74-1.37)	0.72* (0.52-0.99)	0.81 (0.59-1.12)	0.63** (0.46-0.87)	1.92* (1.04-3.55)	0.56* (0.36-0.87)
15-17	1.65 (0.96-2.82)	1.15 (0.72-1.82)	1.10 (0.83-1.46)	1.03 (0.77-1.38)	1.28 (0.96-1.70)	0.49** (0.37-0.66)	1.32 (0.80-2.19)	0.33** (0.22-0.50)
Father respondent (ref: mother)	0.92 (0.61-1.37)	0.78 (0.55-1.12)	1.40** (1.12-1.74)	0.75* (0.60-0.94)	1.92** (1.55-2.39)	1.19 (0.96-1.48)	1.15 (0.76-1.75)	0.56** (0.43-0.73)
COVID-19 cases in neighborhood	1.27 (0.77-2.10)	2.16** (1.35-3.44)	1.22 (0.95-1.57)	1.19 (0.92-1.55)	1.09 (0.84-1.40)	1.46** (1.13-1.89)	0.74 (0.48-1.15)	1.31 (0.94-1.83)
Received influenza vaccination in 2019 season	N/A <sup>c</sup>	N/A	N/A	N/A	N/A	N/A	N/A	2.05** (1.57-2.67)

<sup>a</sup>OR: odds ratio.<sup>b</sup>ref: reference.<sup>c</sup>N/A: not applicable; this item was only applicable to the vaccination behavior *plan influenza vaccination after epidemic*.

\*P&lt;.05.

\*\*P&lt;.01.

## Discussion

### Principal Findings

This study provides evidence regarding the change of public health prevention behaviors, unproven protection behaviors, and vaccination behaviors among children and adolescents amid the COVID-19 epidemic in China. In this online survey of 1655 parents with children aged 3 to 17 years in Wuhan and Shanghai, there was an increase in the frequency of prevention behaviors and unproven protection behaviors, as compared with the pre-epidemic time. We documented the parent-reported delay of scheduled vaccinations and their intention to receive the

influenza vaccination after the epidemic. This study also observed disparities in prevention behaviors, unproven remedies taken, and vaccination behaviors by child gender, parental education attainment, and family size.

This study found prevention behavior changes among children and adolescents (ie, increasing frequencies of mask-wearing and self-monitoring of COVID-19 symptoms, an increasing frequency and duration of handwashing, and a decrease in the frequency of going outside during the COVID-19 epidemic). The increasing frequency of washing hands and mask use was consistent with previous studies in Europe and North America [17,39]. On the other hand, few previous studies compared the prevalence of mask use, symptom self-monitoring, and going

outside during and before the epidemic. The mask-wearing mandate has been proven to be associated with mitigating the spread of COVID-19 [10,11]. Previous studies also provided evidence that the shutdown policy was associated with delaying the COVID-19 epidemic in other cities and with reductions in total incidence [34,40]. Thus, it is of great importance to maintain the recommendation of prevention behaviors, which will warrant maintenance of the existing strategies to protect children and adolescents from the transmission of COVID-19. It is worth noting that this study was conducted in mid-March 2020, when China was going through a period of critical shortages of personal protective equipment; thus, the observed insufficient protection for children and adolescents may be closely related to the limited supply of personal protective equipment. Additionally, for the implementation of the mandate, we need to be aware that children's adherence is usually lower than that of adults, and their willingness should be taken into consideration, specifically [15]. As reported in this study, besides the primary reason of lack of access to masks, the other reason for children and adolescents' lack of compliance with the mask mandate could be their reluctance. Thus, it is necessary to obtain children's cooperation with the help of their parents and to adopt other measures simultaneously, such as staying at home and keeping social distance, if children's compliance with the mask mandate is too difficult to achieve [15].

Our findings about unproven protection behaviors showed that over half of the families bought or took unproven herbal remedies. Since disease incidence and mortality are increasing globally during the COVID-19 epidemic, using unproven remedies is an understandable temptation [41]. Yet, misinformation related to these therapies has spread online at a surprising rate during the epidemic, which has a negative impact on controlling the transmission of COVID-19 [20] and could ultimately result in poor health outcomes among individuals [42]. Thus, to detect and debunk misinformation or anecdotal information, multisectoral efforts are needed from public health stakeholders, such as social media, health care professionals, or experts. Decision makers should also help regulate relevant law enforcement to ensure that accurate information on COVID-19 is provided.

This study also found a delay in the use of vaccines during the epidemic but an increase in the demand for influenza vaccination, which might be an indirect consequence of the shutdown policy. All vaccinations were expected to be delayed due to the closure of vaccination clinics and risk of COVID-19 infection, regardless of whether they were covered by the National Immunization Program in China, a program that aims to provide free immunization services for Chinese children. A notable decline in childhood vaccination was also observed in the United Kingdom, Ireland, the United States, and globally [43-45]. Delaying vaccination appears to signal that there may be a spike in demand for vaccines immediately after the COVID-19 epidemic [12]. Parents may still worry about the risk of getting COVID-19 when going out or in a crowded vaccination clinic, and are hesitant to get their children vaccinated. In addition, COVID-19 also increased people's attention toward influenza vaccination, and, as reported in the Results section, 80.9% of parents planned to have their child

receive the influenza vaccination after the epidemic. In China, where the influenza vaccination rate has been low—9.4% among the general population—compared with other countries [46], this increase in demand for influenza vaccinations could be one of the unexpected beneficial consequences of the COVID-19 epidemic. This means that, at least in Shanghai and Wuhan, there will be a dramatic increase in the utilization of influenza vaccination, which reminds the vaccination providers to prepare for and store more vaccine doses. Since September 2020, China has seen a great demand for, and a shortage of, influenza vaccination. In the long run, since the increase in demand for vaccinations may be sustained beyond the COVID-19 epidemic, the government should develop a sustainable and effective plan for pediatric vaccine schedules.

The disparities in prevention and vaccination behaviors existed among children and adolescents by child gender, parental education attainment, and family size. Girls wore masks and washed hands at significantly lower frequencies than boys during the epidemic, but no significant differences by gender were found for other prevention behaviors. The children and adolescents who had parents with lower education levels and who came from larger families were more likely to have used unproven remedies and less likely to have exhibited the recommended prevention behaviors. First, it is worth noting that the findings of less frequent mask-wearing and handwashing among girls were opposite to the findings among adults, wherein female adults wore masks and washed hands at higher frequencies [16,18,19]. Girls at those ages might have concerns about how they are looked at by others and their body size, shape, or weight [47,48]. Hence, the low frequency of mask-wearing among girls may be due to their concerns about appearance. Second, the findings regarding behavior disparities as a function of parental education attainment were consistent with previous studies, which explained this result as an increased awareness of perceived susceptibility and severity of disease [33]. Parents with higher educational attainment may have a better understanding of the effectiveness, perception, and guidance of public health prevention behaviors [49]. Third, the behavior disparity regarding unproven remedy use as a function of household size may have resulted from a higher risk of exposure to misinformation, as people living in larger households could experience a higher probability of exposure to misinformation and spread it to other family members. In addition, given that the average number of family members in the recruited families in this study was 3.5, our study sample may include children who live with grandparents. Since the elderly have been more inclined to share misinformation compared to younger adults [50], larger families with grandparents have been more likely to take unproven remedies. Thus, more attention is needed regarding health education for girls under the context of an epidemic, and public health stakeholders should tailor expanded multisectoral efforts to children and adolescents living in larger families whose parents have lower educational levels.

### Limitations

This study is subject to several limitations. First, the results may be affected by selection bias from an online survey. While almost all families have access to the internet or a telephone in

Wuhan and Shanghai [51], and quota sampling enhanced the representativeness of our sample to minimize selection bias, we are aware that our sample is not a probabilistic random sample of residents from the two cities. Similar to other online surveys [52], the response rate was below 10% in our study. Second, there may be recall bias due to the self-reported data. Since we conducted the survey while most children and adolescents were still staying at home with their parents, recall bias might be limited as we were measuring ongoing behavioral patterns. Meanwhile, while the anonymous survey addressed the concern of reporting bias regarding sensitive information, social desirability bias could still exist to affect the reporting of behaviors that have been mandated by the government. Finally, since our survey took place in mid-March 2020, the results of this study may be applicable to the early phase of the COVID-19 outbreak. As the COVID-19 pandemic was initially under control in China at that time, this study may have limited significance for current prevention. In addition, the behaviors performed and measures taken by parents were not reflected in

this paper. As the epidemic evolves, we plan to conduct follow-up surveys to study the long-term behavioral changes among children and their parents. A better understanding of how the epidemic affects the behaviors of children and their parents can help guide future prevention strategies.

### Conclusions

During the COVID-19 epidemic, children and adolescents improved in their prevention behaviors and attitudes toward influenza vaccination. Public health prevention measures should be continuously promoted, particularly among girls, parents with lower educational attainment, and larger families. Misinformation about COVID-19 remains a serious challenge and needs to be addressed by public health stakeholders. In addition, the epidemic led to a serious delay of regular vaccination services yet increased the willingness to get the influenza vaccination; thus, it is vital to ensure a sufficient supply of different kinds of vaccines to meet the surging vaccination need after the pandemic [53].

---

### Acknowledgments

This study was supported by the National Natural Science Foundation of China (grant 71874034), the National Science Fund for Distinguished Young Scholars (grant 81525023), and the National Science and Technology Major Project of China (grants 2017ZX10103009-005, 2018ZX10713001-007, and 2018ZX10201001-010). The funders had no role in the design and conduct of the study. We are thankful to Qian Lv, Qian Wang, and Hao Jiang from the School of Public Health, Fudan University, for helping with data collection. We thank the families and the children that participated in this study.

---

### Authors' Contributions

ZH conceptualized and designed the study, drafted the initial manuscript, and revised the manuscript. SS codrafted the initial manuscript. FD carried out the data analysis. LS, DZ, and LL critically revised the manuscript for important intellectual content. HY conceptualized and designed the study. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

---

### Conflicts of Interest

None declared.

---

#### Multimedia Appendix 1

Study questionnaire.

[DOCX File, 21 KB - [publichealth\\_v7i5e26372\\_app1.docx](#) ]

---

#### Multimedia Appendix 2

Flowchart of participant recruitment.

[PNG File, 37 KB - [publichealth\\_v7i5e26372\\_app2.png](#) ]

---

#### Multimedia Appendix 3

Prevention and vaccination behaviors among children and adolescents by respondents' characteristics during the COVID-19 epidemic, March 2020.

[DOCX File, 27 KB - [publichealth\\_v7i5e26372\\_app3.docx](#) ]

---

### References

1. Hou Z, Du F, Zhou X, Jiang H, Martin S, Larson H, et al. Cross-country comparison of public awareness, rumors, and behavioral responses to the COVID-19 epidemic: Infodemiology study. *J Med Internet Res* 2020 Aug 03;22(8):e21143 [FREE Full text] [doi: [10.2196/21143](#)] [Medline: [32701460](#)]
2. Announcement of Wuhan COVID-19 epidemic prevention and control headquarters. The State Council of the People's Republic of China. URL: [http://www.gov.cn/xinwen/2020-01/23/content\\_5471751.htm](http://www.gov.cn/xinwen/2020-01/23/content_5471751.htm) [accessed 2020-01-23]

3. Wuhan, Restart!. The State Council of the People's Republic of China. URL: [http://www.gov.cn/xinwen/2020-04/08/content\\_5500277.htm#1](http://www.gov.cn/xinwen/2020-04/08/content_5500277.htm#1) [accessed 2020-04-08]
4. Shanghai, Tianjin, Chongqing, and Anhui launch a primary response mechanism for major public health emergencies. The State Council of the People's Republic of China. URL: [http://www.gov.cn/xinwen/2020-01/24/content\\_5472050.htm](http://www.gov.cn/xinwen/2020-01/24/content_5472050.htm) [accessed 2020-01-24]
5. Shanghai decided to adjust the primary response of major public health emergencies to the secondary response. Shanghai Municipal Government. URL: [http://www.shanghai.gov.cn/nw48635/20200826/0001-48635\\_64496.html](http://www.shanghai.gov.cn/nw48635/20200826/0001-48635_64496.html) [accessed 2020-03-24]
6. Wuhan resumes vaccination clinics from today. Wuhan Municipal Health Commission. URL: [http://wjw.wuhan.gov.cn/ztl\\_28/fk/tzgg/202004/t20200430\\_1196743.shtml](http://wjw.wuhan.gov.cn/ztl_28/fk/tzgg/202004/t20200430_1196743.shtml) [accessed 2020-03-14]
7. Some vaccination clinics in Shanghai adjusted their working hours and the community adopts appointment for vaccination. The Paper News. URL: [https://www.thepaper.cn/newsDetail\\_forward\\_5732405](https://www.thepaper.cn/newsDetail_forward_5732405) [accessed 2020-01-31]
8. What to do for the public to prevent COVID-19? Chinese Center for Disease Control and Prevention. URL: [http://www.chinacdc.cn/jkzt/crb/zl/szkb\\_11803/jszl\\_2275/202001/t20200125\\_211447.html](http://www.chinacdc.cn/jkzt/crb/zl/szkb_11803/jszl_2275/202001/t20200125_211447.html) [accessed 2020-01-25]
9. Van Bavel JJ, Baicker K, Boggio PS, Capraro V, Cichocka A, Cikara M, et al. Using social and behavioural science to support COVID-19 pandemic response. *Nat Hum Behav* 2020 May;4(5):460-471. [doi: [10.1038/s41562-020-0884-z](https://doi.org/10.1038/s41562-020-0884-z)] [Medline: [32355299](https://pubmed.ncbi.nlm.nih.gov/32355299/)]
10. Lyu W, Wehby GL. Community use of face masks and COVID-19: Evidence from a natural experiment of state mandates in the US. *Health Aff (Millwood)* 2020 Aug;39(8):1419-1425. [doi: [10.1377/hlthaff.2020.00818](https://doi.org/10.1377/hlthaff.2020.00818)] [Medline: [32543923](https://pubmed.ncbi.nlm.nih.gov/32543923/)]
11. Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schünemann HJ, COVID-19 Systematic Urgent Review Group Effort (SURGE) study authors. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: A systematic review and meta-analysis. *Lancet* 2020 Jun 27;395(10242):1973-1987 [FREE Full text] [doi: [10.1016/S0140-6736\(20\)31142-9](https://doi.org/10.1016/S0140-6736(20)31142-9)] [Medline: [32497510](https://pubmed.ncbi.nlm.nih.gov/32497510/)]
12. Jaklevic MC. Flu vaccination urged during COVID-19 pandemic. *JAMA* 2020 Sep 08;324(10):926-927. [doi: [10.1001/jama.2020.15444](https://doi.org/10.1001/jama.2020.15444)] [Medline: [32818238](https://pubmed.ncbi.nlm.nih.gov/32818238/)]
13. Djulbegovic B, Weiss DJ, Hozo I. Evaluation of the US governors' decision when to issue stay-at-home orders. *J Eval Clin Pract* 2020 Oct;26(5):1347-1351 [FREE Full text] [doi: [10.1111/jep.13458](https://doi.org/10.1111/jep.13458)] [Medline: [32794332](https://pubmed.ncbi.nlm.nih.gov/32794332/)]
14. Tull MT, Edmonds KA, Scamaldo KM, Richmond JR, Rose JP, Gratz KL. Psychological outcomes associated with stay-at-home orders and the perceived impact of COVID-19 on daily life. *Psychiatry Res* 2020 Jul;289:113098 [FREE Full text] [doi: [10.1016/j.psychres.2020.113098](https://doi.org/10.1016/j.psychres.2020.113098)] [Medline: [32434092](https://pubmed.ncbi.nlm.nih.gov/32434092/)]
15. Esposito S, Principi N. To mask or not to mask children to overcome COVID-19. *Eur J Pediatr* 2020 Aug;179(8):1267-1270 [FREE Full text] [doi: [10.1007/s00431-020-03674-9](https://doi.org/10.1007/s00431-020-03674-9)] [Medline: [32388722](https://pubmed.ncbi.nlm.nih.gov/32388722/)]
16. Guzek D, Skolmowska D, Głabska D. Analysis of gender-dependent personal protective behaviors in a national sample: Polish Adolescents' COVID-19 Experience (PLACE-19) Study. *Int J Environ Res Public Health* 2020 Aug 10;17(16):5770 [FREE Full text] [doi: [10.3390/ijerph17165770](https://doi.org/10.3390/ijerph17165770)] [Medline: [32785004](https://pubmed.ncbi.nlm.nih.gov/32785004/)]
17. Haischer MH, Beilfuss R, Hart MR, Opielinski L, Wrucke D, Zirgaitis G, et al. Who is wearing a mask? Gender-, age-, and location-related differences during the COVID-19 pandemic. *PLoS One* 2020;15(10):e0240785 [FREE Full text] [doi: [10.1371/journal.pone.0240785](https://doi.org/10.1371/journal.pone.0240785)] [Medline: [33057375](https://pubmed.ncbi.nlm.nih.gov/33057375/)]
18. Zhong B, Luo W, Li H, Zhang Q, Liu X, Li W, et al. Knowledge, attitudes, and practices towards COVID-19 among Chinese residents during the rapid rise period of the COVID-19 outbreak: A quick online cross-sectional survey. *Int J Biol Sci* 2020;16(10):1745-1752 [FREE Full text] [doi: [10.7150/ijbs.45221](https://doi.org/10.7150/ijbs.45221)] [Medline: [32226294](https://pubmed.ncbi.nlm.nih.gov/32226294/)]
19. Sadiq A, Saleem SM, Malik M, Malik MI, Akhtar FK, Waheed K. How COVID-19 is changing behaviors of population: A study from Punjab? *Biomedica* 2020;36(3 (COVID19-S2)):253-259 [FREE Full text]
20. Xu X, Chew KA, Xu X, Wu Z, Xiao X, Yang Q. Demographic and social correlates and indicators for behavioural compliance with personal protection among Chinese community-dwellers during COVID-19: A cross-sectional study. *BMJ Open* 2021 Jan 06;11(1):e041453 [FREE Full text] [doi: [10.1136/bmjopen-2020-041453](https://doi.org/10.1136/bmjopen-2020-041453)] [Medline: [33408203](https://pubmed.ncbi.nlm.nih.gov/33408203/)]
21. Pan Y, Fang Y, Xin M, Dong W, Zhou L, Hou Q, et al. Self-reported compliance with personal preventive measures among Chinese factory workers at the beginning of work resumption following the COVID-19 outbreak: Cross-sectional survey study. *J Med Internet Res* 2020 Sep 29;22(9):e22457 [FREE Full text] [doi: [10.2196/22457](https://doi.org/10.2196/22457)] [Medline: [32924947](https://pubmed.ncbi.nlm.nih.gov/32924947/)]
22. Pan Y, Xin M, Zhang C, Dong W, Fang Y, Wu W, et al. Associations of mental health and personal preventive measure compliance with exposure to COVID-19 information during work resumption following the COVID-19 outbreak in China: Cross-sectional survey study. *J Med Internet Res* 2020 Oct 08;22(10):e22596 [FREE Full text] [doi: [10.2196/22596](https://doi.org/10.2196/22596)] [Medline: [32936776](https://pubmed.ncbi.nlm.nih.gov/32936776/)]
23. Leng Y, Zhai Y, Sun S, Wu Y, Selzer J, Strover S, et al. Misinformation during the COVID-19 outbreak in China: Cultural, social and political entanglements. *IEEE Trans Big Data* 2021 Mar 1;7(1):69-80. [doi: [10.1109/tbdata.2021.3055758](https://doi.org/10.1109/tbdata.2021.3055758)]
24. Marmot M. The health gap: The challenge of an unequal world. *Lancet* 2015 Dec 12;386(10011):2442-2444. [doi: [10.1016/S0140-6736\(15\)00150-6](https://doi.org/10.1016/S0140-6736(15)00150-6)] [Medline: [26364261](https://pubmed.ncbi.nlm.nih.gov/26364261/)]
25. Wang T, Zeng R. Addressing inequalities in China's health service. *Lancet* 2015 Oct 10;386(10002):1441. [doi: [10.1016/S0140-6736\(15\)00402-X](https://doi.org/10.1016/S0140-6736(15)00402-X)] [Medline: [26466037](https://pubmed.ncbi.nlm.nih.gov/26466037/)]



26. Song S, Yuan B, Zhang L, Cheng G, Zhu W, Hou Z, et al. Increased inequalities in health resource and access to health care in rural China. *Int J Environ Res Public Health* 2018 Dec 25;16(1):49 [FREE Full text] [doi: [10.3390/ijerph16010049](https://doi.org/10.3390/ijerph16010049)] [Medline: [30585243](https://pubmed.ncbi.nlm.nih.gov/30585243/)]
27. Wang S, Xu J, Jiang X, Li C, Li H, Song S, et al. Trends in health resource disparities in primary health care institutions in Liaoning Province in Northeast China. *Int J Equity Health* 2018 Dec 04;17(1):178 [FREE Full text] [doi: [10.1186/s12939-018-0896-8](https://doi.org/10.1186/s12939-018-0896-8)] [Medline: [30514300](https://pubmed.ncbi.nlm.nih.gov/30514300/)]
28. Song S, Ma X, Zhang L, Yuan B, Meng Q. Precision targeting for more equitable distribution of health professionals in rural China. *Health Policy Plan* 2018 Sep 01;33(7):821-827. [doi: [10.1093/heapol/czy061](https://doi.org/10.1093/heapol/czy061)] [Medline: [29992255](https://pubmed.ncbi.nlm.nih.gov/29992255/)]
29. Wang Z, Tang K. Combating COVID-19: Health equity matters. *Nat Med* 2020 Apr;26(4):458. [doi: [10.1038/s41591-020-0823-6](https://doi.org/10.1038/s41591-020-0823-6)] [Medline: [32284617](https://pubmed.ncbi.nlm.nih.gov/32284617/)]
30. Yao H, Chen J, Xu Y. Patients with mental health disorders in the COVID-19 epidemic. *Lancet Psychiatry* 2020 Apr;7(4):e21 [FREE Full text] [doi: [10.1016/S2215-0366\(20\)30090-0](https://doi.org/10.1016/S2215-0366(20)30090-0)] [Medline: [32199510](https://pubmed.ncbi.nlm.nih.gov/32199510/)]
31. Abedi V, Olulana O, Avula V, Chaudhary D, Khan A, Shahjouei S, et al. Racial, economic, and health inequality and COVID-19 infection in the United States. *J Racial Ethn Health Disparities* 2021 Jun;8(3):732-742 [FREE Full text] [doi: [10.1007/s40615-020-00833-4](https://doi.org/10.1007/s40615-020-00833-4)] [Medline: [32875535](https://pubmed.ncbi.nlm.nih.gov/32875535/)]
32. Chung RY, Dong D, Li MM. Socioeconomic gradient in health and the COVID-19 outbreak. *BMJ* 2020 Apr 01;369:m1329. [doi: [10.1136/bmj.m1329](https://doi.org/10.1136/bmj.m1329)] [Medline: [32238351](https://pubmed.ncbi.nlm.nih.gov/32238351/)]
33. Chen X, Ran L, Liu Q, Hu Q, Du X, Tan X. Hand hygiene, mask-wearing behaviors and its associated factors during the COVID-19 epidemic: A cross-sectional study among primary school students in Wuhan, China. *Int J Environ Res Public Health* 2020 Apr 22;17(8):2893 [FREE Full text] [doi: [10.3390/ijerph17082893](https://doi.org/10.3390/ijerph17082893)] [Medline: [32331344](https://pubmed.ncbi.nlm.nih.gov/32331344/)]
34. Pan A, Liu L, Wang C, Guo H, Hao X, Wang Q, et al. Association of public health interventions with the epidemiology of the COVID-19 outbreak in Wuhan, China. *JAMA* 2020 May 19;323(19):1915-1923 [FREE Full text] [doi: [10.1001/jama.2020.6130](https://doi.org/10.1001/jama.2020.6130)] [Medline: [32275295](https://pubmed.ncbi.nlm.nih.gov/32275295/)]
35. ePanel. URL: <https://www.epanel.cn/> [accessed 2021-05-04]
36. Sedgwick P. Proportional quota sampling. *BMJ* 2012 Sep 26;345(sep26 3):e6336-e6336. [doi: [10.1136/bmj.e6336](https://doi.org/10.1136/bmj.e6336)]
37. Rubin GJ, Amlôt R, Page L, Wessely S. Public perceptions, anxiety, and behaviour change in relation to the swine flu outbreak: Cross sectional telephone survey. *BMJ* 2009 Jul 02;339:b2651 [FREE Full text] [doi: [10.1136/bmj.b2651](https://doi.org/10.1136/bmj.b2651)] [Medline: [19574308](https://pubmed.ncbi.nlm.nih.gov/19574308/)]
38. Sixth Census of China. National Bureau of Statistics of the People's Republic of China. URL: [http://www.stats.gov.cn/zjtj/zdtjgz/zgrkpc/dlcrkpc/dcrkpcyw/201104/t20110428\\_69407.htm](http://www.stats.gov.cn/zjtj/zdtjgz/zgrkpc/dlcrkpc/dcrkpcyw/201104/t20110428_69407.htm) [accessed 2011-04-28]
39. Głowska D, Skolmowska D, Guzek D. Population-based study of the influence of the COVID-19 pandemic on hand hygiene behaviors—Polish Adolescents' COVID-19 Experience (PLACE-19) Study. *Sustainability* 2020 Jun 17;12(12):4930. [doi: [10.3390/su12124930](https://doi.org/10.3390/su12124930)]
40. Tian H, Liu Y, Li Y, Wu C, Chen B, Kraemer MUG, et al. An investigation of transmission control measures during the first 50 days of the COVID-19 epidemic in China. *Science* 2020 May 08;368(6491):638-642 [FREE Full text] [doi: [10.1126/science.abb6105](https://doi.org/10.1126/science.abb6105)] [Medline: [32234804](https://pubmed.ncbi.nlm.nih.gov/32234804/)]
41. Rome BN, Avorn J. Drug evaluation during the Covid-19 pandemic. *N Engl J Med* 2020 Jun 11;382(24):2282-2284. [doi: [10.1056/NEJMp2009457](https://doi.org/10.1056/NEJMp2009457)] [Medline: [32289216](https://pubmed.ncbi.nlm.nih.gov/32289216/)]
42. Tasnim S, Hossain MM, Mazumder H. Impact of rumors and misinformation on COVID-19 in social media. *J Prev Med Public Health* 2020 May;53(3):171-174 [FREE Full text] [doi: [10.3961/jpmph.20.094](https://doi.org/10.3961/jpmph.20.094)] [Medline: [32498140](https://pubmed.ncbi.nlm.nih.gov/32498140/)]
43. Santoli JM, Lindley MC, DeSilva MB, Kharbanda EO, Daley MF, Galloway L, et al. Effects of the COVID-19 pandemic on routine pediatric vaccine ordering and administration - United States, 2020. *MMWR Morb Mortal Wkly Rep* 2020 May 15;69(19):591-593 [FREE Full text] [doi: [10.15585/mmwr.mm6919e2](https://doi.org/10.15585/mmwr.mm6919e2)] [Medline: [32407298](https://pubmed.ncbi.nlm.nih.gov/32407298/)]
44. Olsen SJ, Azziz-Baumgartner E, Budd AP, Brammer L, Sullivan S, Pineda RF, et al. Decreased influenza activity during the COVID-19 pandemic - United States, Australia, Chile, and South Africa, 2020. *MMWR Morb Mortal Wkly Rep* 2020 Sep 18;69(37):1305-1309 [FREE Full text] [doi: [10.15585/mmwr.mm6937a6](https://doi.org/10.15585/mmwr.mm6937a6)] [Medline: [32941415](https://pubmed.ncbi.nlm.nih.gov/32941415/)]
45. Lynn RM, Avis JL, Lenton S, Amin-Chowdhury Z, Ladhani SN. Delayed access to care and late presentations in children during the COVID-19 pandemic: A snapshot survey of 4075 paediatricians in the UK and Ireland. *Arch Dis Child* 2021 Feb;106(2):e8 [FREE Full text] [doi: [10.1136/archdischild-2020-319848](https://doi.org/10.1136/archdischild-2020-319848)] [Medline: [32586927](https://pubmed.ncbi.nlm.nih.gov/32586927/)]
46. Wang Q, Yue N, Zheng M, Wang D, Duan C, Yu X, et al. Influenza vaccination coverage of population and the factors influencing influenza vaccination in mainland China: A meta-analysis. *Vaccine* 2018 Nov 19;36(48):7262-7269. [doi: [10.1016/j.vaccine.2018.10.045](https://doi.org/10.1016/j.vaccine.2018.10.045)] [Medline: [30340886](https://pubmed.ncbi.nlm.nih.gov/30340886/)]
47. Positive parenting tips for young teens (12-14 years of age). Centers for Disease Control and Prevention. URL: <https://www.cdc.gov/ncbddd/childdevelopment/positiveparenting/adolescence.html> [accessed 2021-02-22]
48. Positive parenting tips for teenagers (15-17 years of age). Centers for Disease Control and Prevention. URL: <https://www.cdc.gov/ncbddd/childdevelopment/positiveparenting/adolescence2.html> [accessed 2021-02-22]
49. Sim S, Moey K, Tan N. The use of facemasks to prevent respiratory infection: A literature review in the context of the Health Belief Model. *Singapore Med J* 2014 Mar;55(3):160-167 [FREE Full text] [doi: [10.11622/smedj.2014037](https://doi.org/10.11622/smedj.2014037)] [Medline: [24664384](https://pubmed.ncbi.nlm.nih.gov/24664384/)]

50. Swire-Thompson B, Lazer D. Public health and online misinformation: Challenges and recommendations. *Annu Rev Public Health* 2020 Apr 02;41:433-451. [doi: [10.1146/annurev-publhealth-040119-094127](https://doi.org/10.1146/annurev-publhealth-040119-094127)] [Medline: [31874069](https://pubmed.ncbi.nlm.nih.gov/31874069/)]
51. Annual Report of China Radio Management 2018. State Radio Regulation of China. URL: <http://www.srrc.org.cn/article22917.aspx> [accessed 2019-03-25]
52. Horrell LN, Hayes S, Herbert LB, MacTurk K, Lawhon L, Valle CG, et al. Telemedicine use and health-related concerns of patients with chronic conditions during COVID-19: Survey of members of online health communities. *J Med Internet Res* 2021 Feb 18;23(2):e23795 [FREE Full text] [doi: [10.2196/23795](https://doi.org/10.2196/23795)] [Medline: [33539307](https://pubmed.ncbi.nlm.nih.gov/33539307/)]
53. Lazzerini M, Barbi E, Apicella A, Marchetti F, Cardinale F, Trobia G. Delayed access or provision of care in Italy resulting from fear of COVID-19. *Lancet Child Adolesc Health* 2020 May;4(5):e10-e11 [FREE Full text] [doi: [10.1016/S2352-4642\(20\)30108-5](https://doi.org/10.1016/S2352-4642(20)30108-5)] [Medline: [32278365](https://pubmed.ncbi.nlm.nih.gov/32278365/)]

## Abbreviations

**IRB:** Institutional Review Board

**OR:** odds ratio

*Edited by T Sanchez; submitted 09.12.20; peer-reviewed by Z Wang, Q Guo, R Zeng, D Li; comments to author 29.12.20; revised version received 08.02.21; accepted 19.04.21; published 26.05.21.*

*Please cite as:*

*Hou Z, Song S, Du F, Shi L, Zhang D, Lin L, Yu H*

*The Influence of the COVID-19 Epidemic on Prevention and Vaccination Behaviors Among Chinese Children and Adolescents: Cross-sectional Online Survey Study*

*JMIR Public Health Surveill* 2021;7(5):e26372

URL: <https://publichealth.jmir.org/2021/5/e26372>

doi: [10.2196/26372](https://doi.org/10.2196/26372)

PMID: [33882450](https://pubmed.ncbi.nlm.nih.gov/33882450/)

©Zhiyuan Hou, Suhang Song, Fanxing Du, Lu Shi, Donglan Zhang, Leesa Lin, Hongjie Yu. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 26.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# Dietary Structure and Nutritional Status of Chinese Beekeepers: Demographic Health Survey

Boshi Wang<sup>1\*</sup>, MSc; Zhangkai Jason Cheng<sup>2\*</sup>, PhD; Qian Xu<sup>1</sup>, BSc; Tiangang Zhu<sup>1</sup>, PhD; Lin Su<sup>1</sup>, PhD; Mingshan Xue<sup>2</sup>, MSc; Lin Pei<sup>1</sup>, PhD; Li Zhu<sup>3</sup>, BSc; Peng Liu<sup>1</sup>, PhD

<sup>1</sup>Department of Clinical Nutrition, Peking University People's Hospital, Beijing, China

<sup>2</sup>State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

<sup>3</sup>Wuhan Bao Chun Royal Jelly Co, Ltd, Wuhan, China

\*these authors contributed equally

**Corresponding Author:**

Peng Liu, PhD

Department of Clinical Nutrition

Peking University People's Hospital

11 Xizhimen South Street

Xicheng District

Beijing, 100044

China

Phone: 86 13501273877

Email: [liupengpku@163.com](mailto:liupengpku@163.com)

## Abstract

**Background:** Beekeeping and honey gathering are traditional forms of agricultural farming in China. However, only few studies have focused on the nutritional status and health level of this special occupational group.

**Objective:** By comparing the health status of apiculturists (beekeepers) and vegetable farmers in plain areas of Hubei Province, and analyzing the influence of dietary structure and intake on their nutritional level, this paper provides a scientific theoretical basis for the further development of health education and disease prevention for beekeepers.

**Methods:** From February to April 2016, 191/236 beekeepers (80.9% of the total beekeepers) with large-scale breeding (300-500 colonies) and 182 vegetable farmers in the same area were sampled by the cluster sampling method. Their nutrient composition was analyzed using a human body composition analyzer, dietary structure information was collected using the dietary frequency query method, and cognitive function was investigated. In addition, blood samples of both groups were collected.

**Results:** A total of 362 valid questionnaires (beekeepers/vegetable farmers: 185/177) were collected, with an effective response rate of 97.1% (362/373). Both beekeepers and vegetable farmers were overweight, and the beekeepers' grip strength was much stronger than that of the vegetable farmers' regardless of gender. The dietary structure of beekeepers is very unique: 29.7% (55/185) of beekeepers indicated consuming royal jelly regularly for more than 10 years. Their main foods are grain, cereals, and fresh vegetables; 68.1% (126/185) of the beekeepers never drank milk and other dairy products, and their overall nutrient intake is unbalanced. The average intake of cellulose in this group was also significantly higher than that in the epidemiological survey in the same sex and age group. The intake of vitamin A and selenium in the beekeepers group was significantly higher than that in the vegetable-farmers group (all  $P < .001$ ). The blood indices of creatinine ( $P = .03$ ) and blood copper ( $P < .001$ ) in the beekeepers group were significantly higher than those in the vegetable-farmers group, and the total protein, albumin, calcium, sodium, potassium, phosphorus, folic acid, and vitamin B12 in the beekeepers group were significantly lower than those in the vegetable-farmers group ( $P < .03$  for potassium and  $P < .001$  for others). The total Mini-Mental State Examination (MMSE) score of the beekeepers group was 28.1, significantly higher ( $P = .006$ ) than that of the vegetable-farmers group (23.3).

**Conclusions:** The beekeepers in this area have their special dietary structure, body nutrient level, and disease characteristics. The cognitive level of the beekeepers who regularly consume royal jelly is significantly higher than that of their peers. The chronic diseases of this special occupational group are closely related to their lifestyle and nutritional status, so more attention and in-depth studies are needed to improve the quality of life of this population.

**KEYWORDS**

beekeeper; body composition; nutrition survey; MMSE

## **Introduction**

China is a traditional beekeeping country, and has a long history of beekeeping. According to the statistics of the World Food and Agriculture Organization, in 2011, China was ranked number 1 in the world in terms of the number of bee colonies and the number of apiculturist practitioners. The country is also ranked number 1 in the production and export of bee products [1]. Bee products can be divided into 3 categories according to their formation and source: (1) products from bees (eg, honey, propolis, bee pollen); (2) bee secretions (eg, royal jelly, beeswax, bee venom); and (3) bodies of various insect states grown and developed by bees, such as bee pupae and bee larva, which are used as food accompaniment, bubble liquor, or processed into dry powder (capsules) [2]. Honey is produced by bees in honeycomb from nectar acquired from flowering plants. It is produced by worker bees through the action of amylase in salivary glands, and its main components are carbohydrates, proteins, minerals, vitamins, and phenols [3]. Royal jelly is a honey bee secretion used in the nutrition of larvae and adult queens. It is secreted by the hypopharyngeal glands and mandible glands of worker bees. Its active ingredients are more complex, among which 10-hydroxy-2-decanoic acid (10-HDA) is a unique unsaturated fatty acid, also known as royal jelly acid, which plays an immunosuppressive role by inhibiting the proliferation of splenic T cells and reducing the production of interleukin (IL)-12 by splenic dendritic cells [4].

Royal jelly protein is one of the important biologically active components during the development of queen bees, which can in vitro promote the expression of superoxide dismutase-1 (SOD1), and has an antiaging effect on human embryonic lung fibroblast (HFL-I) [5]. In addition, 3,10-dihydroxy decanoic acid, a fatty acid isolated from royal jelly, promotes IL-12 and IL-18, and inhibits IL-10, affecting the maturation and function of human monocyte-derived dendritic cells, contributing to the imbalance of antitumor and antiviral immune responses [6]. Other active ingredients, such as polypeptides, vitamins, flavonoids, and phytochemicals, can not only affect the cell metabolism process, but also provide important raw materials for the brain to synthesize glial cells, and also play a certain role in tissue damage repair [7]. However, most of the aforesaid studies are either animal experiments or in vitro cell experiments, and there is no clear medical evidence on whether royal jelly has an antidisease role after ingestion and how it is absorbed and utilized by the human body.

Hubei Province is located in the south of Central China and its middle region expands up to the Yangtze River. It is mainly distributed in the western mountainous area and the central and eastern plains. The climate is subtropical monsoon, with abundant heat and rainfall, sufficient illumination, distinct 4 seasons, and a long frost-free period [8]. In the plains, rapeseed and other crops are planted in a large area, and there are seasonal plants that provide a plentiful source of nectar, which is collected

by honeybees [9]. The region has a long history of beekeeping which is handed down from one generation to another. It is a typical beekeeping province. In 2019, the total number of beekeeping colonies in Hubei Province was nearly 768,000. It is also the main province for processing and exporting bee products, with the intensive processing enterprises of bee products in Wuhan as the center, forming a sound production, processing, and marketing management system [9]. Huangpi District belongs to 1 of the 6 remote urban districts of Wuhan City, Hubei Province. Sanliqiao Street is located in the southern lakeside area of the district, where the cultivated land is deep, the soil is fertile, and the drainage and irrigation conditions are favorable. A number of farmers are converting the land to grow vegetables, which has become the “vegetable basket” of Wuhan citizens [10].

The author’s team found in the preliminary survey that because of the easy accessibility of work, more than half of the population regularly consume royal jelly. To explore the effects that differences in lifestyle and dietary structures have on the health status, this study compares beekeepers in Huangpi district with other regional vegetable farmers. Variables such as dietary structure, body composition, hematology indices, cognitive factors, and nutrition levels were compared and analyzed. This study provides the theoretical basis for health education and disease prevention for beekeepers’ community.

## **Methods**

### **Survey Participants**

This study adopts the method of cluster sampling, from February to April 2016. The study site is Huangpi district in Wuhan. A total of 191/236 beekeepers (80.9% of the total beekeepers) with large-scale breeding (300-500 colonies) and 182 vegetable farmers in the same area were sampled by the cluster sampling method. All participants were administered different questionnaires to collect demographic and nutritional information and underwent a physical examination to understand their current health status. A total of 362 questionnaires were collected (beekeepers group: 185; vegetable-farmers group: 177). The effective response rate is 97.1% (beekeepers group: 185/191, 96.9%; vegetable farmers group: 177/182, 97.3%). The criteria for inclusion were large-scale beekeeping with at least five years of practice, and no serious illness or communication problems. Informed consent was received from all participants in this study, and the consent form was signed.

### **Survey Contents and Methods**

#### **Demographic Information**

Data on age, gender, education level, years of royal jelly consumption, disease history (including self-reported disease history of respondents and diagnosis records of community health service centers/township health centers or medical and health institutions), and activities were collected.

### Body Composition Analysis

The analysis was performed using the Eco I-BCA10 body composition analyzer (Beijing Sihai Huachen Science and Technology Co., Ltd.), and included physical examination of the participants (measurement of height, weight, waist circumference, hip circumference, grip strength, fatless weight, body fat percentage, bone mass, and muscle mass). Because of gender differences in body composition and grip strength, an intergroup comparison was conducted on the physical examination results of the beekeepers group and the vegetable-farmers group after adjusting gender factors.

### Blood Index Test

For this purpose, whole blood samples from both groups were collected and stored at 4°C, and samples were sent to the Laboratory of Peking University People's Hospital for unified testing within 1 week. Indicators included biochemical whole items (blood lipid, liver and kidney function, blood glucose, electrolytes, etc.), trace elements (iron, magnesium, copper, zinc), ferritin, folic acid, vitamin B12, and homocysteine. Ferritin, folic acid, and vitamin B12 were detected by a Roche E601 immunoanalyzer; trace elements by a Beckman AU5800 biochemical analyzer, and other indices by a Hitachi LST008 biochemical analyzer. The reagents were all tested using the original detection reagents by matching with the corresponding model.

### Dietary Survey

The respondents were interviewed face to face by using a simplified version of the Food Frequency Inquiry questionnaire. The content of the questionnaire included the frequency and amount of food consumed ([Multimedia Appendix 1](#)).

### Cognitive State Investigation

The Mini-Mental State Examination (MMSE) was developed in 1975, and is a standardized tool to rapidly screen individuals for cognitive dysfunction [11]. It includes 11 questions involving orientation, attention, immediate and short-term recall, language, and the ability to follow simple verbal and written commands. The total score is 30 points, and it takes only about 5-10 minutes to administer.

## Data Collection and Statistical Methods

### Data Types

Descriptive epidemiological analysis methods include calculation rate, mean, etc. A *P* value of less than .05 indicates statistically significant differences. Among them, quantitative data such as waist circumference, bone mass, and grip strength (part of the physical examination index) after gender discrimination met the normal distribution and homogeneity of variance. Two independent samples *t* test (unpaired) were used to compare the differences in continuous variables between the beekeepers group and the vegetable-farmers group, whereas the chi-square test was used to compare the dichotomous variables. Blood index results (biochemical whole items, serum vitamins, and minerals, etc.) and cognitive function survey results were also compared using 2 independent samples *t* test (unpaired) without gender discrimination, and cognitive function differences were compared using regular intake of royal jelly

as a grouping variable. To estimate food consumption frequency and intake, the recommended amount based on the Chinese balanced diet pagoda was taken as the standard [12] and its level was compared with the corresponding reference value. The data were statistically analyzed using SPSS software (version 26.0; IBM), and EpiData software (version 3.2; Pascal) was used to establish a database for all the collected questionnaire responses and a parallel double entry was performed. MATLAB R2021 (MathWorks) was used to produce the volcano plot. The dimension reduction method principal component analysis was applied to reduce the dimensionality of the blood index data set, while retaining most of the information.

### Calculation of Daily Food Intake

The average daily intake of various kinds of food for each respondent in the past year was calculated according to the intake frequency and the amount of each intake. The basic formula is given as follows:

$$\text{Food intake (g/day)} = \{\text{intake frequency [times]/week} \times \text{intake amount (g)}\} / 7 \text{ days.}$$

### Calculation of Daily Nutrient Intake

Based on the Chinese Food Composition List 2009 (2nd Edition) compiled by the Nutrition and Food Safety of Chinese Center for Disease Control and Prevention [13], the average value of nutrients contained in the same category of food was taken to compile a food composition table, based on which the daily nutrient intake of each survey participant could be calculated. The formula is as follows:

$$\text{Daily nutrient intake (g/day)} = (\text{food intake [g/day]} \times \text{nutrient content in the cluster food composition table}) / 100 \text{ g.}$$

### Ethical Statement

This study passed the ethical review of the Medical Ethics Committee of Peking University People's Hospital (Approval Number: 2016PHB111-01). The research participants have been compensated with all tests free of charge and there were also gift compensations for daily supplies.

## Results

### General Results

There were 185 eligible individuals in the beekeepers group and 177 eligible individuals in the vegetable-farmers group. The smoking and drinking rates in the beekeepers group were higher than those in the vegetable-farmers group. More than half of the beekeepers have been consuming royal jelly for a long time or intermittently (55/185 beekeepers [29.7%] consumed royal jelly at least once a day for more than 10 years).

The prevalence of hyperlipidemia, stroke, and cardiovascular disease in the vegetable-farmers group was higher than that in the beekeepers group, and the prevalence of cardiovascular disease in the vegetable-farmers group (22/177, 12.4%) was 2.1 times higher than that in the beekeepers group (11/185, 6.0%). By contrast, the prevalence of hypertension and chronic gastritis was higher in the beekeepers group than that in the beekeepers

group. **Table 1** compares general results and the disease prevalence between the 2 groups.

**Table 1.** General results and disease prevalence rate between the beekeepers group and the vegetable-farmers group, sampled from Wuhan, China, between February and April 2016.

Characteristic	Beekeepers group (n=185)	Vegetable-farmers group (n=177)	P value
Male, n (%)	124 (67.0)	85 (48.0)	<.001
Female, n (%)	61 (33.0)	92 (52.0)	<.001
Mean (SD) age (years)	63.7 (7.9)	61.1 (9.8)	.39
Mean (SD) years of education	6.5 (0.8)	6.2 (0.8)	.28
Smoking, n (%)	62 (33.5)	45 (25.4)	.09
Drinking, n (%)	36 (19.5)	17 (9.6)	.008
Royal jelly consumption, n (%)	101 (54.6)	5 (2.8)	<.001
Hypertension, n (%)	80 (43.2)	70 (39.5)	.48
Hyperlipidemia, n (%)	11 (5.9)	20 (11.3)	.07
Cardiovascular disease, n (%)	11 (5.9)	22 (12.4)	.03
Stroke, n (%)	15 (8.1)	21 (11.9)	.23
Chronic gastritis, n (%)	40 (21.6)	25 (14.1)	.06

### Physical Examination Results

The hand grip strength of the beekeepers was much stronger than that of the vegetable farmers in both genders. Other physical examination indicators, such as height, weight, waist

circumference, hip circumference, body fat percentage, and bone mass, were not significantly different between the 2 groups (**Table 2**). The *P* values have been adjusted by false-discovery rate (FDR).

**Table 2.** Physical examination results of the beekeepers group and the vegetable-farmers group, sampled from Wuhan, China, between February and April 2016.

Characteristic	Male			Female		
	Beekeepers group (n=124)	Vegetable-farmers group (n=85)	<i>P</i> value <sup>a</sup>	Beekeepers group (n=61)	Vegetable-farmers group (n=92)	<i>P</i> value <sup>a</sup>
Height (cm), mean (SD)	166.1 (5.0)	165.4 (6.4)	.76	154.9 (5.0)	154.4 (5.8)	.84
Weight (kg), mean (SD)	67.9 (8.7)	65.2 (9.3)	.76	59.4 (8.2)	59.1 (9.4)	.84
BMI (kg/m <sup>2</sup> ), mean (SD)	24.6 (2.7)	23.8 (2.7)	.76	24.7 (3.3)	24.7 (3.5)	.54
Hip circumference (cm), mean (SD)	95.6 (4.7)	94.4 (9.5)	.48	95.7 (6.0)	97.1 (7.0)	.64
Fat-free mass (kg), mean (SD)	52.5 (5.6)	50.8 (9.3)	.70	39.4 (5.4)	39.7 (5.9)	.78
Waist circumference (cm), mean (SD)	85.7 (7.7)	86.2 (9.3)	.86	84.3 (8.5)	88.3 (8.1)	.84
Body fat rate (%), mean (SD)	21.4 (6.0)	19.7 (7.0)	.48	32.4 (6.6)	32.3 (6.8)	.78
Bone mass (kg), mean (SD)	2.8 (0.3)	2.8 (0.8)	.86	2.1 (0.3)	2.2 (0.3)	.84
Muscle mass (kg), mean (SD)	49.8 (5.4)	49.2 (5.7)	.86	37.3 (5.2)	37.4 (4.5)	.84
<b>Grip strength (kg)</b>						
Dominant hand, mean (SD)	24.2 (2.6)	10.6 (4.8)	<.001	20.9 (3.8)	10.2 (4.0)	<.001
Nondominant hand, mean (SD)	23.6 (2.7)	10.3 (4.8)	<.001	19.1 (4.4)	9.5 (3.7)	<.001

<sup>a</sup>False-discovery-rate adjusted *P* values; *P* values were obtained from *t* test.

### Blood Index Results

The main biochemical indices of the 2 groups were normal. Among them, the creatinine (*P*=.03) and uric acid (*P*=.02) levels of the beekeepers group were significantly higher than those of the vegetable-farmers group, and the total protein (*P*=.001) and albumin (*P*<.001) levels of the beekeepers group were significantly lower than those of the vegetable-farmers group.

The results of serum vitamins and minerals test showed that all indices of the 2 groups were normal. Among them, the blood copper level in the beekeepers group was higher than that in the vegetable-farmers group, whereas calcium, sodium, potassium, phosphorus, folic acid, and vitamin B12 were lower than those in the vegetable-farmers group, and the differences were statistically significant (*P*<.03 for potassium and *P*<.001 for all

others). Table 3 lists the main blood index results from both groups. Figure 1 is the volcano plot of the comparative results, showing the relative difference of each index between the 2 groups. We obtained the spread of points (beekeepers vs vegetable farmers) along the first 3 principal components in a

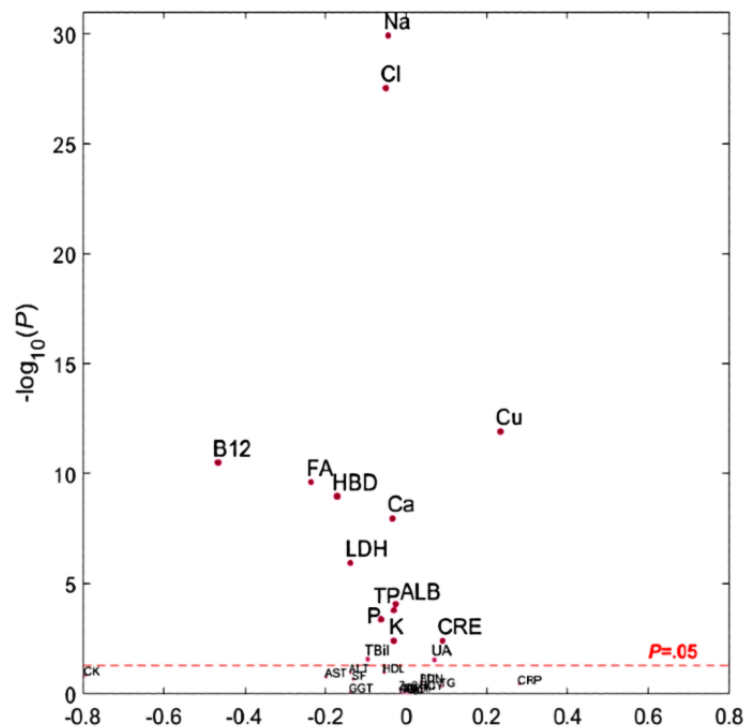
principal component analysis plot (Figure 2). This result shows that beekeepers have a much closer spread of points compared with vegetable farmers, which indicates that the blood indices of beekeepers are similar, whereas those of vegetable farmers have bigger variation in value.

**Table 3.** Main blood indices of beekeepers and vegetable farmers, sampled from Wuhan, China, between February and April 2016.

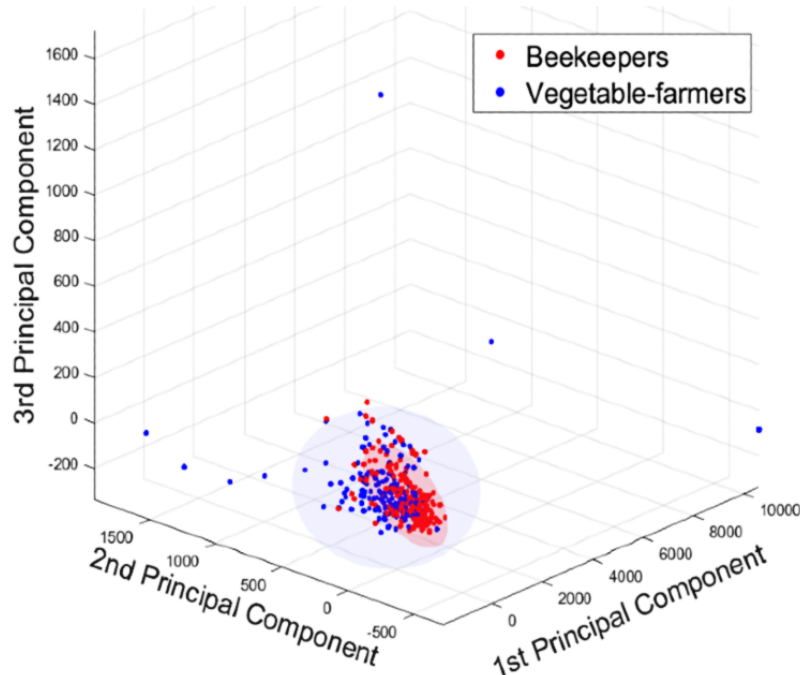
Characteristic	Reference value, range	Beekeepers, mean (SEM)	Vegetable farmers, mean (SEM)	<i>P</i> value <sup>a</sup>
Glucose (mmol/L)	3.3-6.1	5.7 (0.1)	5.7 (0.1)	.90
Total cholesterol (mmol/L)	2.9-6.2	5.1 (0.7)	5 (0.7)	.90
Total triglyceride (mmol/L)	0.45-1.7	1.6 (0.1)	1.5 (0.1)	.90
Creatinine (mmol/L)	59-104	72.7 (1.4)	66.5 (1.3)	.03
Uric acid (μmol/L)	208-428	358.7 (6.5)	334.3 (7.2)	.02
High-density lipoprotein cholesterol (mmol/L)	1.03-1.55	1.46 (0.03)	1.54 (0.03)	.90
Low-density lipoprotein cholesterol (mmol/L)	1.9-4.1	2.82 (0.06)	2.71 (0.06)	.90
Homocysteine (μmol/L)	0.0-15	14.4 (0.4)	13.8 (0.6)	.90
Potassium (mmol/L)	3.5-5.3	4.1 (0.03)	4.3 (0.03)	.03
Sodium (mmol/L)	137-147	137.1 (0.4)	143.4 (0.1)	<.001
Calcium (mmol/L)	2.2-2.65	2.27 (0.01)	2.35 (0.01)	<.001
Phosphorous (mmol/L)	0.81-1.45	1.02 (0.1)	1.01 (0.01)	<.001
Iron (μmol/L)	7.9-34.4	20.0 (0.5)	20.1 (0.5)	.90
Magnesium (mmol/L)	0.7-1.05	0.93 (0.01)	0.93 (0.01)	.90
Copper (μmol/L)	11-24	14.8 (0.3)	11.7 (0.3)	.001
Zinc (μmol/L)	10.7-17.7	14.5 (0.2)	14.8 (0.2)	.90
Serum ferritin (ng/mL)	30-400	137 (8)	157 (9)	.90
Total protein (g/L)	65-85	71.8 (0.4)	74.1 (0.4)	.001
Albumin (g/L)	40-55	44.0 (0.2)	45.2 (0.2)	<.001
Folic acid (ng/mL)	4.2-19.8	9.7 (0.3)	12.3 (0.3)	<.001
Vitamin B12 (pg/mL)	197-771	290 (11)	467 (22)	<.001

<sup>a</sup>False-discovery rate-adjusted values.

**Figure 1.** Volcano plot of blood index results, comparing between beekeepers group and vegetable-farmers group, sampled from Wuhan, China, between February and April 2016. Relative difference is positive if beekeepers group has higher value than vegetable-farmers group.



**Figure 2.** The first 3 principal components of blood index result, using PCA to compare between beekeepers group and vegetable-farmers group, sampled from Wuhan, China, between February and April 2016. Shaded areas represent two standard deviations of each population.



**Frequency of Distribution of Various Food Intake**

Among the surveyed beekeepers and vegetable farmers, the daily diet included grain cereals (185/185 [100%] and 177/177 [100%], respectively) and fresh vegetables (178/185 [96.2%] and 167/177 [94.4%], respectively). The frequency of intake of beef, mutton, and chicken was very low. About 63.2% (117/185) of beekeepers and 93.8% (166/177) of vegetable farmers never ate beef and mutton. At the same time, 68.1% (126/185) of

beekeepers and 72.3% (128/177) of vegetable farmers never drank milk.

**Daily Intake Results of Various Foods**

The intake of meat, fish, shrimp, eggs, milk, fruit, and bean products was lower than the recommended dietary pagoda for more than 50% of the individuals in both groups (92/185 beekeepers and 88/177 vegetable-farmers). About 70.3% (130/185) of the beekeepers and 82.5% (146/177) of the vegetable farmers consumed too much cooking oil (mean [SD]):



44.8 (25.0 g/day) in the beekeepers group and 55.2 (28.0 g/day) in the vegetable-farmers group.

### Daily Energy and Thermogenic Nutrient Intake Results

The daily energy and protein intake of beekeepers and vegetable farmers was low for both men and women (Table 4). The

beekeepers had a reasonable proportion of the 3 heat-producing nutrients, whereas the vegetable farmers had a low calorific proportion of protein and carbohydrate (the percentage of calories provided by protein and carbohydrate to total calories), and a high calorific proportion of fat.

**Table 4.** Mean daily energy and intake of 3 major heat-producing nutrients of beekeepers and vegetable farmers from Wuhan, China (sampled period February-April 2016).

Sex and characteristic	Energy (kilocalorie)		Protein (g)		Fat (g)		Carbohydrate (g)	
	Beekeepers	Vegetable farmers	Beekeepers	Vegetable farmers	Beekeepers	Vegetable farmers	Beekeepers	Vegetable farmers
<b>Male</b>								
Intake, mean (SD)	1567 (23)	1516 (39)	62 (1)	57 (2)	63 (1)	64 (3)	193 (4)	183 (5)
Calorific proportion (%)	N/A <sup>a</sup>	N/A	15.9	14.9	36	37.9	49.3	48.4
<b>Female</b>								
Intake, mean (SD)	1396 (25)	1754 (40)	53 (1)	56 (5)	60 (1)	85 (6)	166 (4)	196 (15)
Calorific proportion (%)	N/A	N/A	15.2	12.8	29.9	33.9	47.7	44.8
Reference calorific proportion (%)	N/A	N/A	15-20	N/A	25-30	N/A	50-60	N/A

<sup>a</sup>N/A: Not applicable

### Intake of Other Nutrients

The intake of vitamin A ( $P<.001$ ) and selenium ( $P<.001$ ) in the beekeepers group was higher than that in the vegetable-farmers

group, and the difference was statistically significant, whereas there was no significant difference in other nutrients between the 2 groups (Table 5).

**Table 5.** Comparing average daily intakes for other nutrients between beekeepers and vegetable farmers from Wuhan, China (sampled period February-April 2016).

Nutrient	Beekeeper male		Beekeeper female		Vegetable farmer male		Vegetable farmer female		P value
	Intake (g/day), mean (SD)	Dietary reference intakes, %	Intake (g/day), mean (SD)	Dietary reference intakes, %	Intake (g/day), mean (SD)	Dietary reference intakes, %	Intake (g/day), mean (SD)	Dietary reference intakes, %	
Cellulose (g)	18.2 (5.7)	72.8	17.5 (5.2)	70	18.4 (7.4)	74	20.4 (21.9)	82	.96
Vitamin A (µg)	249.2 (181.4)	44.5	165.6 (136.4)	28.4	194.8 (201.2)	24.2	127.3 (208.5)	18.1	<.001
Vitamin B1 (mg)	0.8 (0.2)	57.1	0.7 (0.2)	58.3	0.7 (0.2)	54.2	0.7 (0.8)	65.8	.39
Vitamin B2 (mg)	1.1 (0.3)	78.6	1.0 (0.3)	83.3	1.1 (0.4)	81	1.1 (1.2)	98.3	.14
Vitamin C (mg)	190.5 (90.1)	190.5	197.1 (80.8)	197.1	209.7 (107.0)	210	238.6 (258.5)	238	.77
Total vitamin E (mg)	32.1 (9.1)	N/A <sup>a</sup>	31.7 (7.7)	N/A	32.3 (15.3)	N/A	43.9 (41.6)	N/A	.96
Folic acid (µg)	634.2 (237.7)	158.6	623.4 (215.9)	155.9	666.9 (305.3)	167	737.5 (787.9)	184.2	.42
Potassium (mg)	2093.2 (649.4)	104.7	1988.4 (620.9)	99.4	2101.2 (889.2)	105	2265.6 (2432.6)	113.2	.53
Calcium (mg)	704.3 (255.2)	70.4	692.3 (237.2)	69.2	730.5 (339.6)	73	807.6 (860.5)	80.7	.68
Magnesium (mg)	348.9 (89.0)	105.7	319.3 (86.0)	96.7	341.8 (127.6)	103.3	368.1 (379.9)	111.5	.65
Iron (mg)	27.3 (7.4)	227.5	24.8 (6.7)	206.7	26.6 (10.0)	222	28.1 (29.4)	233.3	.66
Manganese (mg)	6.3 (1.6)	140	5.7 (1.5)	126.7	6.1 (2.2)	135.5	6.7 (6.7)	148.8	.88
Zinc (mg)	11.0 (2.5)	88	9.8 (2.5)	130.7	10.5 (3.7)	84	11.2 (11.5)	149.3	.39
Copper (mg)	1.9 (0.5)	237.5	1.7 (0.5)	212.5	1.7 (0.6)	221.2	1.6 (2.0)	237.5	.93
Phosphorus (mg)	904.1 (218.0)	125.6	791.6 (224.2)	109.9	860.1 (332.2)	119.4	887.0 (942.0)	123.1	.13
Selenium (µg)	41.8 (13.3)	69.7	35.0 (12.3)	58.3	38.8 (18.4)	64.6	38.3 (42.9)	63.3	<.001

<sup>a</sup>N/A: Not applicable.

## Results of Cognitive Function Survey

As presented in [Table 6](#), the total MMSE score of the beekeepers group was 28.1, which was significantly higher ( $P<.001$ ) than that of the vegetable-farmers group (23.3). Among them, the beekeepers group showed significantly better cognitive performance in Auditory Verbal Learning Test ( $P=.01$ ), Clock

Drawing Test ( $P=.005$ ), and Verbal Fluency Test ( $P=.005$ ). The 2 groups of people were further divided into 2 subgroups according to whether they regularly consumed royal jelly or not. It was concluded that the total MMSE score of the subgroup consuming royal jelly for several years was significantly higher than that of the subgroup not consuming royal jelly ( $P=.006$ ).

**Table 6.** Results of cognitive function survey in beekeepers and vegetable farmers from Wuhan, China (sampled between February and April 2016).

Test	Beekeepers		Vegetable farmers		P value	Royal jelly group		No royal jelly group		P value
	N	Score, mean (SD)	N	Score, mean (SD)		N	Score, mean (SD)	N	Score, mean (SD)	
Total Mini-Mental State Examination	180	28.1 (3.5)	165	23.3 (5.5)	<.001	100	25.5 (3.4)	245	23.7 (5.0)	.006
Rey Auditory Verbal Learning Test	185	30.7 (13.4)	177	26.1 (13.6)	.01	106	30.0 (14.5)	256	27.1 (13.4)	.07
Delayed word recall test	185	5.3 (3.8)	177	4.1 (3.6)	.15	106	4.9 (3.8)	256	5.0 (3.6)	.66
Clock drawing test	180	3.8 (1.5)	158	3.1 (1.9)	.005	99	3.9 (1.5)	239	3.3 (1.8)	<.001
Verbal fluency test	182	14.1 (4.7)	160	12.0 (3.9)	.005	101	14.5 (5.2)	241	12.5 (4.0)	<.001

## Discussion

### Principal Findings

This study is the first to carry out a comprehensive epidemiological investigation on beekeepers. This population has a unique dietary structure, living habits, and disease distribution characteristics; additionally, its overall cognitive level is significantly higher than that of vegetable farmers from the same area. It is worth noting that the average age of the beekeepers and vegetable farmers investigated in this study was over 60, indicating the aging population of beekeepers, which is consistent with the research results of the National Bee Industry Technology System [14].

It is difficult to attract young labor force into the beekeeping industry, possibly due to poor beekeeping conditions, the need to chase flowers in the wild for honey, beekeeping facilities that are relatively backward, a low degree of mechanization, and a high physical consumption. The results showed that the rates of smoking and drinking were higher among beekeepers than those among vegetable farmers, which may be related to the higher proportion of males in the beekeepers group, compared with that in the vegetable-farmers group. A large number of studies have shown that overweight and obesity are risk factors for hypertension and cardiovascular diseases in the elderly. The Chinese Hypertension Survey [15] showed that the prevalence of hypertension in people aged 55-64 was 44.3%, and other scholars have concluded through meta-analysis that the prevalence of hypertension in rural areas in southern China was 20.2% [16]. According to the BMI classification standard of adults in China, the BMI of the beekeepers group and that of the vegetable-farmers group was in the "overweight" category. Waist circumference and body fat rate also exceeded the standard of normal adults in China [17], but these did not reach the diagnostic standard of obesity. Thus, it is not difficult to understand the prevalence of hypertension in both groups, which was significantly higher than 20.2% (identified in 80/185 [43.2%] beekeepers and 70/177 [39.5%] vegetable farmers). As hypertension is an independent risk factor of stroke, the prevalence of stroke (identified in 15/185 [8.1%] beekeepers and 21/177 [11.9%] vegetable farmers) is also significantly higher than the national average (2.06%) [18]. At the same time, the physical examination results showed that both men and women in the beekeepers group had a much stronger hand grip than those in the vegetable-farmers group. This significant difference in grip strength is likely due to the difference in labor intensity between the 2 groups: beekeepers need to follow the blooming period all year round, with trucks used to carry beehives from one flower field to the next. This kind of work characteristic is also common among the beekeepers in other areas of China. As a result of convenient transportation and rapid development of agricultural mechanization modernization, the labor intensity of vegetable farmers in the flat terrains of Huangpi District is far lower than that of the beekeepers.

Nearly 29.7% (5/185) of beekeepers reported consuming royal jelly regularly for more than 10 years, which is significantly higher than the proportion consumed by the common population and vegetable farmers in the same area. This is no surprise, as

it is easier to obtain royal jelly due to the easy accessibility of work. Compared with vegetable farmers, beekeepers had higher intake of fish food, which mainly included preserved and dried fish. This might be mainly related to the special occupational requirements, whether fixed or transfer operations, of beekeepers, who need to work continuously in the rare natural environment for 5-8 months and keep up with the change in the flowering period [9]. The hard-working conditions in different provinces and regions might have resulted in the difficulty to obtain meat, soy products, eggs, milk, and other foods, while pickled vegetables, dried fish, cooking oil, and other food are easier to carry and eat over longer distances. This directly led to the insufficient intake of protein, most vitamins, calcium, zinc, and other nutrients in the beekeepers group. Moreover, salt in such preserved foods is well over standard limits. Long-term consumption of salted foods remains a risk factor for hypertension and chronic gastritis [19]. Whether this leads to a higher incidence of these 2 diseases among beekeepers remains to be further studied. In addition, the dietary structure has certain regional characteristics. Hubei is a land of fish and rice. Pickled fish, meat, rice, and other foods are popular in the province; however, seafood and dairy products are not popular enough [10,14]. Therefore, 68.1% (126/185) of the beekeepers and 72.3% (128/177) of the vegetable farmers in the study never drank milk. Although the average intake of cellulose in both groups were lower than the recommended amount (25 g) in China [12], it was significantly higher than the results of the epidemiological survey in the same gender and age group, which may be related to the fact that the vegetable supply is sufficient, and the daily diet of the residents mainly includes fresh vegetables and cereals [8].

The results of this study showed that the main biochemical indices of the 2 groups are normal, but the uric acid level of the beekeepers group was significantly higher than that of the vegetable-farmers group, and was close to the high uric acid level (360  $\mu\text{mol/L}$ ), which was speculated to be related to the long-term administration of royal jelly. In general, fructose and glucose account for 90% of total sugar in royal jelly. High consumption of fructose-containing products can lead to the accumulation of phosphorylated products and continuous consumption causes liver ATP (adenosine triphosphate) to produce a large amount of uric acid through metabolism. At the same time, the serum levels of folic acid (vitamin B9) and vitamin B12 in the beekeepers group were lower than those in the vegetable-farmers group, possibly because the B vitamins in royal jellies were mainly B5 (52.8 mg/100 g) and niacin (42.4 mg/100g), whereas the contents of folic acid (0.4 mg/100 g) and vitamin B12 (0.2 mg/100 g) were very low [20]. Although the mineral content in honey varies depending on plant sources, the mineral content in royal jelly is relatively stable, accounting for about 1.5% [21]. Royal jelly is considered to be a homeostasis-regulated larval lactation form that is generally harvested commercially after 4 days of age for queen bee larvae [22]. The blood indices of beekeepers were more concentrated than those of vegetable farmers, and the number of people exceeding the normal value was less, indicating that beekeepers were healthier than vegetable farmers. Possible reasons for this are the small lifestyle differences as well as more similar and healthier dietary structure and eating habits among beekeepers.

Whether it is related to the long-term consumption of royal jelly needs further study and verification. Al-Kahtani and Taha [23] found that, due to different harvesting times, royal jellies harvested 24 hours after the hatching of larvae had the highest contents of phosphorus and zinc; 48 hours later, the contents of calcium, potassium, and sodium were the highest; 96 hours later, the content of copper was higher. Combined with the findings of this study, we suggest that the levels of different mineral nutrients in the body can be improved by consuming royal jelly at different harvest times.

In addition, the intake of vitamin C and folic acid was significantly higher than that of dietary reference intakes, and the intake of vitamin A and selenium was significantly higher than that of vegetable farmers. The worker bees must use honey and pollen as raw materials to produce royal jelly. The nectar source and powder source plants (ie, plants that provide pollen, such as rape and locust flowers) vary based on regions and soil composition; consequently, the mineral types and contents in the royal jelly produced are also different [24]. There are many selenium-rich zones in Hubei Province [25], and oilseed rape, as a cruciferous plant, has a strong ability to enrich selenium [26]. Therefore, we speculated that the royal jelly eaten by beekeepers in this study may have a higher selenium content. Selenium plays a certain role in the nutritional value of royal jelly, but as a micronutrient, some scholars believe that compared with potassium (K), sodium (Na), calcium (Ca), magnesium (Mg), and other elements, the content of selenium in royal jelly is very low [27]. Therefore, with the development of instrumental analysis technology, it is necessary to further compare the selenium content of royal jelly produced in different regions in future studies.

When screening for cognitive function, the total MMSE score of the beekeepers group was significantly higher than that of the vegetable-farmers group, and the cognitive performance of the beekeepers who regularly consumed royal jelly on auditory word learning, clock drawing test, and language fluency was

better than that of the beekeepers and vegetable farmers who did not consume royal jelly. Studies have shown that brain-derived neurotrophic factor (BDNF), especially BDNF in the hippocampus, can regulate learning and memory processes through interaction with TrkB receptors, such as long-term enhancement, synaptic plasticity, axonal budding, and dendritic proliferation [28]. As a small unsaturated fatty acid, 10-HDA in royal jellies can pass through the blood-brain barrier and have effects similar to BDNF [29]. Alzheimer disease (AD) has complex causes, including nerve fiber tangles, amyloid beta deposition, inflammatory response, and oxidative stress response. In many animal experiments at home and abroad and in vitro cell experiments, it has been proved that royal jelly can improve the spatial learning and memory ability of AD model rats [30] by effectively alleviating the toxicity of  $\beta$ -amyloid in AD and significantly reducing  $\beta$ -amyloid species [31]. However, whether royal jelly and its functional components have a positive effect on the prevention and delaying of human AD and their possible mechanism of action remain to be further studied.

### Study Limitation

A limitation of this study is that only the beekeepers in a certain area of Central China were taken as the research subject, which has certain regional limitations and needs to be further investigated and studied in more areas. Moreover, the participants' recollections of how much they ate could be skewed.

### Conclusions

To sum up, combined with the results of this survey, beekeepers in Hubei Province have their special dietary structure, human body composition, and disease characteristics. The lifestyle and nutritional status of beekeepers, a special occupational group, are closely related to their chronic diseases, which need more attention and in-depth study. The role of royal jelly in the prevention and treatment of dementia and its related mechanisms will become the focus of our future research.

---

### Acknowledgments

We thank the relevant government departments of Huangpi District, Wuhan City, Hubei Province for their support and assistance, as well as the funding from Peking University People's Hospital (Project No. RDY2016-18). We thank the support from Guangzhou Yuan Gu Ji Technology Co., Ltd, China. This project was funded by Guangzhou Institute of Respiratory Health Open Project (Funds provided by China Evergrande Group) - Project No. 2020GIRHHMS04.

---

### Conflicts of Interest

None declared.

---

### Multimedia Appendix 1

Food frequency, intake, and lifestyle questionnaire.

[[DOCX File, 20 KB - publichealth\\_v7i5e28726\\_app1.docx](#)]

---

### References

1. Sun C, Zhang Z, Tang T, Yuan Y, Yang G, Zhen H. Analysis of technical trade measures for export of bee products in China. *Acta Agriculturae Zhejiangensis* 2012;24(06):1129-1133.
2. Qian Y. Determination of glucocorticoid residues in honey and royal jelly by liquid chromatography-tandem mass spectrometry. Zhejiang, China: Zhejiang university; 2017.

3. Feng X, Yang S, He L, Yang M, Zhao F, Li J, et al. Research progress on antioxidant activity of bee products. *Journal of Pu'er University* 2017;33(06):16-20.
4. Dzopalic T, Vucevic D, Tomic S, Djokic J, Chinou I, Colic M. 3,10-Dihydroxy-decanoic acid, isolated from royal jelly, stimulates Th1 polarising capability of human monocyte-derived dendritic cells. *Food Chemistry* 2011 Jun;126(3):1211-1217. [doi: [10.1016/j.foodchem.2010.12.004](https://doi.org/10.1016/j.foodchem.2010.12.004)]
5. Jiang C, Liu X, Li C, Qian H, Chen D, Lai C, et al. Anti-senescence effect and molecular mechanism of the major royal jelly proteins on human embryonic lung fibroblast (HFL-I) cell line. *J Zhejiang Univ Sci B* 2018;19(12):960-972 [FREE Full text] [doi: [10.1631/jzus.B1800257](https://doi.org/10.1631/jzus.B1800257)] [Medline: [30507079](https://pubmed.ncbi.nlm.nih.gov/30507079/)]
6. Ramadan MF, Al-Ghamdi A. Bioactive compounds and health-promoting properties of royal jelly: A review. *Journal of Functional Foods* 2012 Jan;4(1):39-52. [doi: [10.1016/j.jff.2011.12.007](https://doi.org/10.1016/j.jff.2011.12.007)]
7. Taniguchi Y, Kohno K, Inoue S, Koya-Miyata S, Okamoto I, Arai N, et al. Oral administration of royal jelly inhibits the development of atopic dermatitis-like skin lesions in NC/Nga mice. *International Immunopharmacology* 2003 Sep;3(9):1313-1324. [doi: [10.1016/s1567-5769\(03\)00132-2](https://doi.org/10.1016/s1567-5769(03)00132-2)]
8. Chen B. Study on the relationship between regional climate and agriculture in hubei province. *Chinese and foreign entrepreneurs* (04) 2019:238-239.
9. Guo Y, Yang H, Ye J. The Chinese bee industry in Hubei province promotes targeted poverty alleviation. *Journal of Bee* 2020;40(09):7-11.
10. Mei J, Li C, Li W, Mei L. Practice and thinking of vegetable industry development in huangpi district of wuhan. *Journal of Changjiang Vegetables* (01) 2013:58-61.
11. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". *Journal of Psychiatric Research* 1975 Nov;12(3):189-198. [doi: [10.1016/0022-3956\(75\)90026-6](https://doi.org/10.1016/0022-3956(75)90026-6)]
12. Chinese Society of Nutrition. Dietary Guidelines for Chinese Residents. In: *Dietary Guidelines for Chinese Residents*. Beijing: People's Medical Publishing House; 2016:2016.
13. Yang Y, Wang G, Pan X. Chinese food ingredients list. 2 ed. In: *Chinese food ingredients list*. 2 ed. Beijing: Peking University Medical Press; 2009.
14. Liu Z, Zhan-li S, She-mei Z. Transformation and development of characteristic agriculture under the background of supply-side reform: A case study of bee industry. *Research of Agricultural Modernization* 2019;40(01):A.
15. Wang Z, Chen Z, Zhang L, Wang X, Hao G, Zhang Z, China Hypertension Survey Investigators. Status of Hypertension in China: Results From the China Hypertension Survey, 2012-2015. *Circulation* 2018 May 29;137(22):2344-2356. [doi: [10.1161/CIRCULATIONAHA.117.032380](https://doi.org/10.1161/CIRCULATIONAHA.117.032380)] [Medline: [29449338](https://pubmed.ncbi.nlm.nih.gov/29449338/)]
16. Guo S. Meta-analysis of Prevalence of Hypertension in Rural China. Changsha: Central South University; 2014.
17. Shi H, Li W, Qi Y. Nutrition screening and evaluation. In: *Nutrition screening and evaluation*. Beijing: People's Medical Publishing House; 2014.
18. Hu S, Gao R, Liu L, Zhu M, Wang W, Wang Y. Summary of China Cardiovascular Disease Report 2018. *CHINESE CIRCULATION JOURNAL* 2019;34(03):209-220.
19. Mozaffarian D. Dietary and Policy Priorities for Cardiovascular Disease, Diabetes, and Obesity: A Comprehensive Review. *Circulation* 2016 Jan 12;133(2):187-225 [FREE Full text] [doi: [10.1161/CIRCULATIONAHA.115.018585](https://doi.org/10.1161/CIRCULATIONAHA.115.018585)] [Medline: [26746178](https://pubmed.ncbi.nlm.nih.gov/26746178/)]
20. Bărnuțiu L, Mărghitaș L, Dezmirean D, Mihai C, Bobiș O. CHEMICAL COMPOSITION AND ANTIMICROBIAL ACTIVITY OF ROYAL JELLY - REVIEW. *Animal Science and Biotechnologies* 2011;44(2):67-72.
21. Kocot J, Kielczykowska M, Luchowska-Kocot D, Kurzepa J, Musik I. Antioxidant Potential of Propolis, Bee Pollen, and Royal Jelly: Possible Medical Application. *Oxid Med Cell Longev* 2018;2018:7074209 [FREE Full text] [doi: [10.1155/2018/7074209](https://doi.org/10.1155/2018/7074209)] [Medline: [29854089](https://pubmed.ncbi.nlm.nih.gov/29854089/)]
22. Stocker A, Schramel P, Kettrup A, Bengsch E. Trace and mineral elements in royal jelly and homeostatic effects. *J Trace Elem Med Biol* 2005;19(2-3):183-189. [doi: [10.1016/j.jtemb.2005.08.004](https://doi.org/10.1016/j.jtemb.2005.08.004)] [Medline: [16325534](https://pubmed.ncbi.nlm.nih.gov/16325534/)]
23. Al-Kahtani SN, Taha EA. Post grafting time significantly influences royal jelly yield and content of macro and trace elements. *PLoS ONE* 2020 Sep 8;15(9):e0238751. [doi: [10.1371/journal.pone.0238751](https://doi.org/10.1371/journal.pone.0238751)]
24. Lou D, Wang G, Jiang F, Yu S, Liu X. Nutritional Regulation of Selenium in the Royal Jelly of *Apis occidentalis*. *Apiculture of China* 2017;68(06):25-26.
25. Zhu J, Wang N, Li S, Li L, Su H, Liu C. Distribution and transport of selenium in Yutangba, China: impact of human activities. *Sci Total Environ* 2008 Mar 25;392(2-3):252-261. [doi: [10.1016/j.scitotenv.2007.12.019](https://doi.org/10.1016/j.scitotenv.2007.12.019)] [Medline: [18215743](https://pubmed.ncbi.nlm.nih.gov/18215743/)]
26. Ming J, Hu C, Zhao X, Zheng Y, Liu X, Zhao Z. Effects of selenium on the content of mineral elements and migration characteristics in different parts of rapeseed. *Acta Agriculturae Zhejiangensis* 2016;28(09):1564-1571.
27. San H, Sun B, Huang J, Tong C, Feng C. Determination of selenium in royal jelly by DRC-ICP-MS. *Journal of Analytical Testing* 2016;35(09):1191-1194.
28. Tan CH, Low KA, Chiarelli AM, Fletcher MA, Navarra R, Burzynska AZ, et al. Optical measures of cerebral arterial stiffness are associated with white matter signal abnormalities and cognitive performance in normal aging. *Neurobiol Aging* 2019 Dec;84:200-207. [doi: [10.1016/j.neurobiolaging.2019.08.004](https://doi.org/10.1016/j.neurobiolaging.2019.08.004)] [Medline: [31500910](https://pubmed.ncbi.nlm.nih.gov/31500910/)]

29. Hattori N, Nomoto H, Fukumitsu H, Mishima S, Furukawa S. Royal jelly and its unique fatty acid, 10-hydroxy-trans-2-decenoic acid, promote neurogenesis by neural stem/progenitor cells in vitro. *Biomed Res* 2007 Oct;28(5):261-266 [FREE Full text] [doi: [10.2220/biomedres.28.261](https://doi.org/10.2220/biomedres.28.261)] [Medline: [18000339](https://pubmed.ncbi.nlm.nih.gov/18000339/)]
30. Reisi P, Pilehvarian A, Zamani Z, Alaei H. Effect of Royal Jelly on spatial learning and memory in rat model of streptozotocin-induced sporadic Alzheimer's disease. *Adv Biomed Res* 2012;1(1):26. [doi: [10.4103/2277-9175.98150](https://doi.org/10.4103/2277-9175.98150)]
31. Wang X, Cao M, Dong Y. Royal jelly promotes DAF-16-mediated proteostasis to tolerate  $\beta$ -amyloid toxicity in *C. elegans* model of Alzheimer's disease. *Oncotarget* 2016 Aug 23;7(34):54183-54193. [doi: [10.18632/oncotarget.10857](https://doi.org/10.18632/oncotarget.10857)] [Medline: [27472466](https://pubmed.ncbi.nlm.nih.gov/27472466/)]

## Abbreviations

- 10-HAD:** 10-hydroxy-2-decenoic acid  
**AD:** Alzheimer disease  
**BDNF:** brain-derived neurotrophic factor  
**FDR:** false-discovery rate  
**IL:** interleukin  
**MMSE:** Mini-Mental State Examination  
**SOD-1:** superoxide dismutase-1

*Edited by T Sanchez, G Eysenbach; submitted 11.03.21; peer-reviewed by J Poppleton, Y Ouyang, N Pawar, P Kanzow; comments to author 24.03.21; revised version received 25.03.21; accepted 09.04.21; published 03.05.21.*

*Please cite as:*

Wang B, Cheng ZJ, Xu Q, Zhu T, Su L, Xue M, Pei L, Zhu L, Liu P  
*Dietary Structure and Nutritional Status of Chinese Beekeepers: Demographic Health Survey*  
*JMIR Public Health Surveill* 2021;7(5):e28726  
URL: <https://publichealth.jmir.org/2021/5/e28726>  
doi: [10.2196/28726](https://doi.org/10.2196/28726)  
PMID: [33938812](https://pubmed.ncbi.nlm.nih.gov/33938812/)

©Boshi Wang, Zhangkai Jason Cheng, Qian Xu, Tiangang Zhu, Lin Su, Mingshan Xue, Lin Pei, Li Zhu, Peng Liu. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 03.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# Development of an Index for the Inspection of *Aedes aegypti* Breeding Sites in Brazil: Multi-criteria Analysis

Yuri Lima<sup>1</sup>, DSC; Wallace Pinheiro<sup>1,2</sup>, DSC; Carlos Eduardo Barbosa<sup>1,3</sup>, DSC; Matheus Magalhães<sup>1,3</sup>, MSc; Miriam Chaves<sup>4</sup>, DSC; Jano Moreira de Souza<sup>1</sup>, PhD; Sérgio Rodrigues<sup>5</sup>, DSC; Geraldo Xexéo<sup>1</sup>, DSC

<sup>1</sup>Graduate School of Engineering (COPPE), Federal University of Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil

<sup>2</sup>Military School of Engineering (IME), Rio de Janeiro, Brazil

<sup>3</sup>Center of Analysis of Naval Systems (CASNAV), Brazilian Navy, Rio de Janeiro, Brazil

<sup>4</sup>National Laboratory of Scientific Computation, Brazilian Ministry of Science, Technology, Innovation, and Communications, Petrópolis, Brazil

<sup>5</sup>Lemobs, Rio de Janeiro, Brazil

**Corresponding Author:**

Yuri Lima, DSC

Graduate School of Engineering (COPPE)

Federal University of Rio de Janeiro (UFRJ)

Rua Horácio Macedo, Bloco G, 2030 - 101 - Cidade Universitária da Universidade Federal do Rio de Janeiro

Rio de Janeiro, 21941-450

Brazil

Phone: 55 21995716204

Email: [yuriodelima@cos.ufrj.br](mailto:yuriodelima@cos.ufrj.br)

## Abstract

**Background:** *Aedes aegypti* is a vector for the transmission of diseases such as dengue fever, chikungunya, Zika fever, and yellow fever. In 2016, over 1 million cases of these diseases were reported in Brazil, which is an alarming public health issue. One of the ways of controlling this disease is by inspecting and neutralizing the places where *A. aegypti* lays its eggs. The Ministry of Planning, Development, and Administration of Brazil maintains the inspection statistics.

**Objective:** We propose a multi-criteria analysis to create an index for *A. aegypti* inspections reported through the Ministry of Planning, Development, and Administration system of Brazil.

**Methods:** Based on the repository from urban cleaning services combined with data on inspections conducted by government agencies in several Brazilian cities and municipalities, we selected and combined metrics, which we further ranked using the analytic hierarchy process methodology. We also developed risk maps based on the analytic hierarchy process ranking of the *A. aegypti* breeding sites.

**Results:** Based on our analysis and the available data, the priority for inspections should consider the number of sick people (weight 0.350), medical evaluations (weight 0.239), inspections (weight 0.201), mosquito breeding sites (weight 0.126), and days of absence from work (weight 0.096).

**Conclusions:** The proposed index could aid public health practitioners in preventing the appearance of new *A. aegypti* breeding sites. This information technology application can help solve such public health challenges.

(*JMIR Public Health Surveill* 2021;7(5):e19502) doi:[10.2196/19502](https://doi.org/10.2196/19502)

## KEYWORDS

multi-criteria analysis; public health; human sensors; vector surveillance; tropical diseases

## Introduction

### Background

*Aedes aegypti* is a vector for many diseases such as chikungunya, dengue fever, yellow fever, and Zika virus. The control of these diseases is difficult as there are several

hard-to-find mosquito breeding places (eg, empty bottles, plant vases, car tires) that can be found at any abandoned lot or in any house. In Brazil, *A. aegypti* is the main vector for dengue fever. However, *Aedes albopictus* is also a vector of such arboviruses [1] and have been reported in Brazil since 1986 [2]. *A. aegypti* and *A. albopictus* tend to breed in similar sites, and researchers have documented competition between these species.

*A. aegypti* is more prevalent in densely populated highly urbanized areas, while *A. albopictus* is more prevalent in rural, suburban, and forested urban areas [2].

Although *A. albopictus* is still regarded as the potential vector of arboviruses in most countries of the Americas [3], our work focused mostly in urban areas, and the objective of this study is the control of the breeding of *A. aegypti*. Nevertheless, our work can be applied with minor modifications to the control of breeding of *A. albopictus*. The challenge in controlling this vector is one of the reasons for the significant numbers associated with the outbreaks of the diseases, which shows how important it is as a public health issue. There are approximately 390 million cases estimated each year for dengue alone [4]. In Brazil, in 2016, there were over 1 million cases of diseases caused by *A. aegypti* [5].

There are currently several methods to control the breeding of *A. aegypti*, which has led to a reduction in the cases of disease related to it. These methods are usually combined and include contaminating the female mosquitoes with *Wolbachia* strains so that they cannot spread diseases [6,7], eliminating mosquitoes using poison, controlling breeding sites through inspections and simple measures (eg, putting sand in vases, covering water recipients, storing empty bottles upside down), and neutralizing the breeding sites found.

In Brazil, the *A. aegypti* infestation index rapid survey (*Levantamento Rápido de Índices para Aedes aegypti*) is a simplified entomological surveillance method adopted by the Ministry of Health to determine the infestation rates of *A. aegypti*. Municipalities perform larval surveys through systematic sampling of buildings to calculate the Breteau index and the building infestation index. The sample depends on the population density and the number of buildings. The indexes predominantly identify breeding sites and are used as indicators to initiate actions to neutralize these sites and reduce the use of larvicides [8].

Controlling *A. aegypti* is a transdisciplinary effort, and information technology plays a role, mainly in the creation of a data repository to support analysis and decision making. An example of information technology is the Sigelu Aedes software developed by the Brazilian company Lemobs as commissioned by the Brazilian Ministry of Planning, Development, and Administration. This software helps public workers to inspect government buildings reporting *Aedes* breeding sites and the actions taken to control them.

### Goal of This Study

Given this context, the goal of our work is to contribute to the effort of controlling *A. aegypti* breeding sites by proposing a georeferenced index that helps decision makers to identify places where mosquitoes could breed. We used a multi-criteria analysis, more specifically the analytic hierarchy process (AHP), to develop such an index. We tested our index by using real data from the Ministry of Planning, Development, and Administration of Brazil to produce a risk map layer in a multidimensional data model.

### Multi-criteria Analysis in Disease Vector Surveillance

Multi-criteria analysis has been used previously in disease vector surveillance literature for supporting decision making. We review such related literature with a special focus on the methodology and outcomes of each study. Aenishaenslin et al [9] identified, evaluated, and ranked different strategies for Lyme disease management in Quebec. They identified 3 intervention areas (preventive communication strategies, surveillance strategies, and control strategies) but focused on the latter two. They defined a multi-criteria decision analysis (MCDA) process with 10 steps—the first 7 focus on problem structuring and the last 3 on the decision analysis. Stakeholders were involved in the identification of issues, definition of criteria, selection of interventions, and individual weighting of the criteria defined. The authors used DSight software to perform the Preference Ranking Organization Method for Enrichment of Evaluations (PROMETHEE) and produce a visual model (geometrical analysis for interactive aid [GAIA]) to display the analysis results. Finally, they produced group rankings analysis and assessed the performance of the selected interventions.

In a second study, Aenishaenslin et al [10] adapted and evaluated the decision model, which had been constructed to rank interventions for Lyme disease prevention in Quebec [9] for a different epidemiological context in Switzerland, where Lyme disease has been endemic for over 30 years. They used a group of Swiss stakeholders to define a new set of criteria to evaluate the problem. The stakeholders kept the original criteria from Quebec but added 4 new criteria. They subsequently performed the analysis by comparing the resulting criteria sets; however, the original criteria had their weights normalized so that their relative importance was in line with the Swiss stakeholders.

Cox et al [11] designed a standardized method to prioritize infectious diseases of humans and animals that may emerge due to the climate change in Canada. They developed user-friendly tools to aid pathogen prioritization, which provided a structure for the study and enabled the decision-making process to be recorded. They identified 40 criteria (from the published literature and experts) that might be used to prioritize potential emerging pathogens in Canada and divided them into 5 groups—3 criterion groups measure the likelihood of pathogen emergence in Canada and 2 criterion groups measure the pathogen impact. Expert opinion was used in the criterion selection and weighting. The weights of all the criteria were standardized. Cox et al [11] then used 2 tools: a spreadsheet developed in Microsoft Excel and the MACBETH tool present in the M-MACBETH software [12]. Santos et al [13] developed a knowledge-driven spatial model to identify risk areas for foot-and-mouth disease (FMD) occurrence—this disease affects cloven-hoofed livestock and wildlife. They evaluated the FMD surveillance performance in the southern Brazilian state of Rio Grande do Sul by using MCDA. Thirteen experts analyzed 18 variables associated with FMD introduction and dissemination pathways. For each pathway, experts defined several risk factors—variables associated with FMD introduction and dissemination. In the next step, the authors requested the experts to weigh each risk factor and pathway following the AHP methodology. The introduction risk and the dissemination risk



were calculated separately, and they were then combined multiplicatively, thereby providing the likelihood of FMD occurrence. Finally, the authors built the spatial model using Idrisi 17.0 Selva GIS and Image Processing Software, with raster layers of 1 km × 1 km resolution.

Fruean and East [14] assessed Australia's targeted surveillance for detecting incursions of the screw-worm fly. Screw-worm fly abundance and survival are affected by—among various criteria—the vegetation type and moisture levels. The authors made a grid of the territory in a map, and to each square, they assigned numeric values for each criterion. They used the multi-criteria analysis shell for spatial decision support package [15], which includes raster maps for feral animal distribution, land use, land cover, and climate data. The authors invited 20 experts to answer a questionnaire in order to assess the relative importance of the potential pathways for the introduction of the screw-worm fly into Australia. Finally, they produced maps of the relative likelihood for the introduction and establishment of the screw-worm fly and considered the seasonal effect of climate. Gosselin et al [16] discussed the implementation of the Integrated System for Public Health Monitoring of West Nile Virus, a real-time geographic information system for public health surveillance of the West Nile virus, in Quebec, Canada. This system gathers information on Corvidae, mosquitoes, humans, horses, climate, and larvicide interventions. It was designed to support the collection, localization, management, and analysis of monitoring data, and presents the results of analyses on maps, tables, and statistical diagrams. Ho et al [17] used a raster-based model to map heat health risks, and they compared this to the traditional vector-based model. Among their goals was the use of the proposed framework to predict and map the heat risk hotspots at multiple spatial scales for the Vancouver area. Heat exposure was estimated using land surface temperature. They used MCDA with 2 different data resampling approaches to visualize the influence of the modifiable areal unit problem (MAUP) issue on heat health risk maps. MAUP is a common source of bias in the results of statistical hypothesis tests in the aggregation of point-based measures. Ho et al [17] used 2 groups of layers: vulnerability layers and heat exposure layers. All vulnerability layers were associated with values ranging from 1 (lowest) to 9 (highest). Each group of layers was combined into a composite layer by assigning equal weights to each layer and normalizing the result. Finally, the composite heat exposure layer was combined with the composite vulnerability layer using the same process. After the modeling, they used the Getis-Ord  $G_i^*$  index [18] to mitigate the problems caused by the MAUP problem.

Hongoh et al [19] ranked possible risk reduction measures for the management of the West Nile virus in Quebec. This study used the methodology presented by Aenishaenslin et al [9]; however, they produced 6 scenarios of increasing potential risk, from low risk (current state) to high risk (epidemics). Hongoh et al [19] elaborated a preliminary list of 15 evaluation criteria in 5 categories. Hongoh et al [19] also used the D-Sight software, the PROMETHEE method, and GAIA maps, and they analyzed interventions at the individual and regional level. Finally, sensitivity analyses were performed on all criteria and for all stakeholders. Sarkar et al [20] performed a five-stage

risk assessment for Chagas disease in Texas. First, using Maxent software, they built distribution models for the triatomine species. The environmental layers used were composed of 4 topographical variables and 15 bioclimatic variables. The output of this step was the likelihood of the presence of triatomine. They then did a risk assessment, defining sets of ecological risks and incidence-based risks, which were analyzed using multi-criteria analysis to generate a composite risk. Finally, they combined the composite risk and the population that would be exposed to Chagas disease to produce a relative expected exposure rate.

Thanapongtharm et al [21] characterized the spatial habitat of the flying fox bat, which is a vector of the Nipah virus, in populations along Thailand's central plain and the mapping zones for potential contact between flying fox bat habitats, pig farms, and human settlements. They collected geographic information about flying fox colonies—generally located in areas such as Buddhist temples, surrounded by bodies of water and vegetation—and combined them with the following layers: water bodies, human population density, elevation, and land cover. Thanapongtharm et al [21] used 7 species distribution models to map the ecological suitability for flying fox colonies. Their models were subject to 10 bootstraps to prevent overfitting and due to their very low proportion of positive samples in the data set. Finally, they applied potential surface analysis to map the risk area for the Nipah virus, assuming 2 potential scenarios for human infections: humans directly infected from the bats and humans infected through an intermediate pig host.

Vinhaes et al [22] analyzed data on the occurrence of domiciled triatomines—vectors of Chagas disease—in non-Amazonian regions of Brazil. MCDA was used to assess municipalities' vulnerability based on socioeconomic, demographic, entomological, and environmental indicators. The program to support decision making based on indicators (PRADIN) software [23], which implements the PROMETHEE II algorithm, was used for MCDA. The authors conducted 6 simulations using PRADIN, in which the municipalities were ranked and classified into quintiles, and their geographic coordinates were then used in the TerraView [24] software to produce vulnerability maps for the occurrence of Chagas disease transmission via domiciled triatomines that were compared to acute vector-borne Chagas disease cases between 2001 and 2012.

## Methods

Our proposed approach involves performing an analysis to create an index of the inspections to find places where *A. aegypti* lays their eggs. The data source for this study is the Ministry of Planning, Development, and Administration of Brazil through the Sigelu Aedes software. Like Santos et al [13], we adopted MCDA because such methods are widely used in the literature. Among MCDA methodologies, we chose to specifically use the AHP methodology. Similar to many other related works [3,6-9,11-14], we produced risk maps, which are useful for disease surveillance and prevention. The proposed approach does not use environmental variables that affect the density and distribution of the mosquito, such as temperature, precipitation, air humidity, and availability of water tanks. Instead, we used

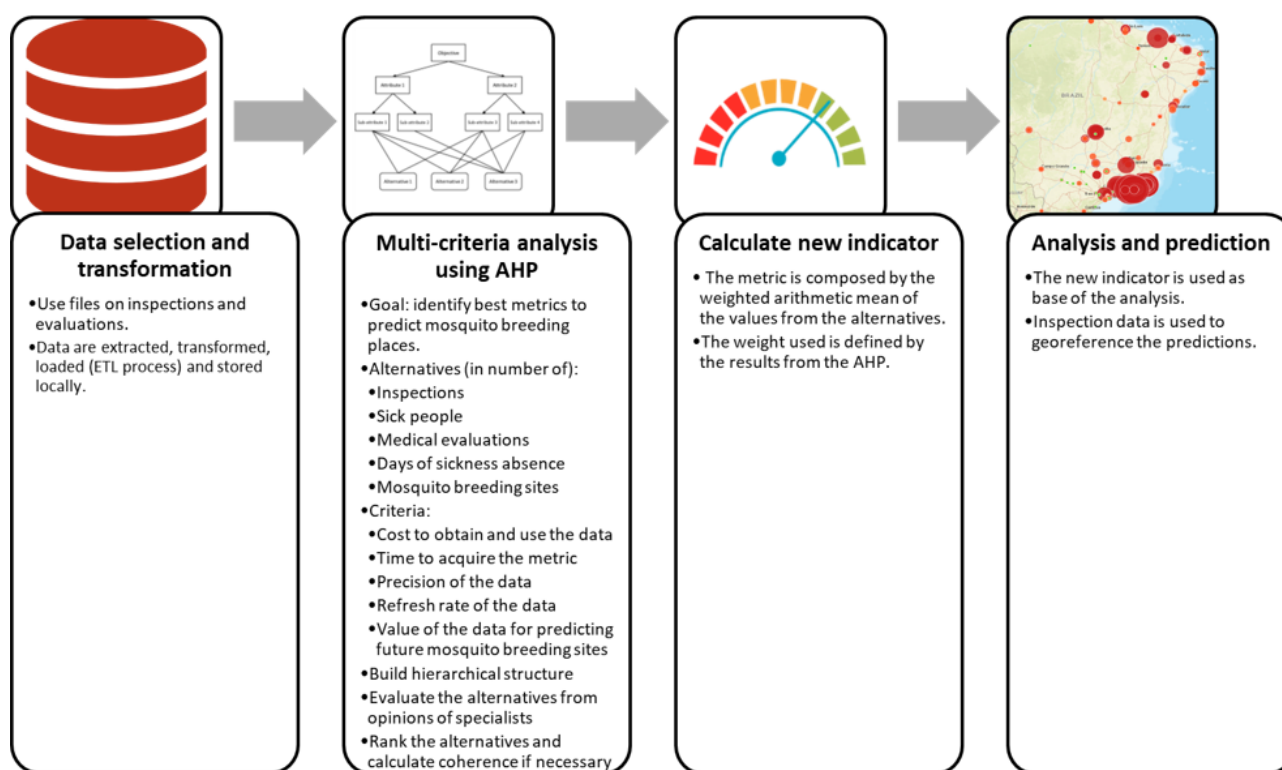
indirect indicators, that is, number of inspections, number of sick people, number of medical evaluations, number of days of sickness absence, and number of mosquito breeding sites found. Although the use of nontraditional data sources to trace arbovirus transmission can be found in the literature [25], our approach provides a novel paradigm, since these governmental data can provide an independent indicator, which may be applied in conjunction with the current methodologies. The proposed approach also takes into account that mosquitoes can repopulate sites that have been inspected. We also consider that information about inspections may indicate regions where it is more likely to find mosquitoes. A new index based on this information may help to plan actions to fight against this vector of many diseases in cities. We created the new index using some metrics extracted from the repository.

Managers of urban cleaning services provide data to form a repository. Given that the main breeding sites of *A. aegypti* are abandoned sites that can be used as garbage dumps, the developers of this software decided to integrate resources to combat this mosquito species. Thus, this system contains data on inspections conducted by government agencies in several Brazilian cities and municipalities. However, the metrics used

do not indicate possible future mosquito breeding sites—they only record the work done by government agents in the field.

Our proposed solution is presented in Figure 1. We compared each of the following alternatives: number of inspections, number of sick people, number of medical evaluations, number of days of sickness absence, and number of mosquito breeding sites. In our comparison, we selected the following criteria to use in the AHP: cost to obtain and use the data, time to acquire the metric, precision of the data, refresh rate of the data, and value of the data for predicting future mosquito breeding sites. For gathering the opinions of specialists about criteria and metrics (alternatives), in accordance with the AHP method, we used the AHP Excel template, with multiple inputs from Goepel [26]. To calculate the matrix for the criteria metrics and matrices for alternatives, we adapted a solution from Griffith [27]. The other calculations are shown in this paper. All inconsistencies related to coherence were less than 0.10, in accordance with the level suggested by Saaty [28]. After determining the final priorities, we assembled the new index, considering the data model that was populated using the repository presented in Figure 1. This set of metrics is used to calculate the new index of an inspection. It is crucial to note that only the metrics related to inspections were used as georeferenced metrics.

Figure 1. Proposed approach to assist in the prediction of *Aedes aegypti* breeding sites.



## Results

The AHP criteria matrix is shown in Table 1. The prioritization of the criteria is shown in the last column (AHP values are

shown in parentheses). The most important criterion was “value,” while the least important was “cost.” The priority value of the “value” criterion was almost double that of the next most important criterion (precision), which indicates the importance

of analyzing each metric according to its value. The inconsistency was 0.093.

The matrix for the alternatives with respect to each criterion is presented in [Table 2](#). In the “cost” section, lower values correspond to higher costs. The last column of “priority” shows the ranking of the alternatives. “Number of inspections” was considered the least important, while the “number of sick people” was the most important alternative for costs. In the “time” section, lower values correspond to a longer time. The least important criterion was “number of sick people” and the most important was “number of inspections” (we note that the least and most important criteria are inverted when compared to section “cost”). In the “precision” section, lower values correspond to lower precision. “Number of inspections” occupied the first position again, “number of medical

evaluations” was second, and “sick people” was third. In the “value” section, lower values correspond to lower value. The “value” section is the most relevant, because the “value” criterion has higher priority according to [Table 2](#). “Number of sick people” was the most important alternative followed by the “number of medical evaluations.” Finally, in the “refresh rate” section, lower values correspond to lower refresh rates. The alternative “number of days absent” is the most relevant metric.

At this point, it is possible to calculate the final priorities of the alternatives. Firstly, we must multiply the criterion values by the values for the alternatives, as shown in [Table 3](#).

We then obtained the final priorities, which are shown in [Table 4](#). We ended up calculating the weighted arithmetic mean by considering the priorities of the alternatives.

**Table 1.** The analytic hierarchy process criteria matrix.<sup>a</sup>

Criteria	Cost	Time	Precision	Value	Refresh rate	Priority (AHP <sup>b</sup> )
Cost	1	1	0.16	0.11	0.27	5 (0.042)
Time	1	1	0.24	0.17	0.52	4 (0.056)
Precision	1/0.16 <sup>c</sup>	1/0.24	1	0.26	7	2 (0.292)
Value	1/0.11	1/0.17	1/0.26	1	4.72	1 (0.516)
Refresh rate	1/0.27	1/0.52	1/7	1/4.72	1	3 (0.094)

<sup>a</sup>The values in this table are the results of a pairwise comparison between each one of the criteria to determine the relative priority of each one.

<sup>b</sup>AHP: analytic hierarchy process value.

<sup>c</sup>The fractions in this table are the result of the pairwise comparisons, which generates a triangular matrix.

**Table 2.** Matrix for alternatives with respect to cost, time, precision, value, and refresh rate.<sup>a</sup>

Alternatives for	Inspections	Sick people	Medical evaluations	Days of absence	Mosquito breeding	Priority (AHP <sup>b</sup> )	Inconsistency <sup>c</sup>
<b>Cost</b>							0.055
Inspections	1	1/7 <sup>d</sup>	1/7	1/7	1/5	5 (0.034)	
Sick people	1	1	3	3	5	1 (0.459)	
Medical evaluations	7	1/3	1	1	3	2 (0.207)	
Days of absence	7	1/3	1	1	3	3 (0.207)	
Mosquito breeding	5	1/5	1/3	1/3	1	4 (0.094)	
<b>Time</b>							0.090
Inspections	1	7	3	5	3	1 (0.472)	
Sick people	1/7	1	1/3	1/3	1/3	5 (0.051)	
Medical evaluations	1/3	3	1	1	3	2 (0.235)	
Days of absence	1/5	3	1/3	1	3	3 (0.142)	
Mosquito breeding	1/3	3	1/3	1/3	1	4 (0.099)	
<b>Precision</b>							0.095
Inspections	1	5	3	3	5	1 (0.454)	
Sick people	1/5	1	1/5	3	1	3 (0.102)	
Medical evaluations	1/3	5	1	5	3	2 (0.288)	
Days of absence	1/3	1/3	1/5	1	1	5 (0.074)	
Mosquito breeding	1/5	1	1/3	1	1	4 (0.082)	
<b>Value</b>							0.084
Inspections	1	1/9	1/7	1/5	1/7	5 (0.029)	
Sick people	9	1	3	5	5	1 (0.494)	
Medical evaluations	7	1/3	1	3	3	2 (0.244)	
Days of absence	5	1/5	1/3	1	1/3	4 (0.086)	
Mosquito breeding	7	1/5	1/3	3	1	3 (0.147)	
<b>Refresh rate</b>							0.055
Inspections	1	3	1/7	3	1/7	5 (0.042)	
Sick people	1/3	1	1/3	1/3	1/3	4 (0.056)	
Medical evaluations	1	3	1	3	3	2 (0.292)	
Days of absence	1/3	3	1/3	1	1	1 (0.516)	

Alternatives for	Inspections	Sick people	Medical evaluations	Days of absence	Mosquito breeding	Priority (AHP <sup>b</sup> )	Inconsistency <sup>c</sup>
Mosquito breeding	1	3	1/3	1	1	3 (0.094)	

<sup>a</sup>The values in this table are the results of a pairwise comparison between each one of the criteria to determine the relative priority of each one.

<sup>b</sup>AHP: analytic hierarchy process value.

<sup>c</sup>The inconsistency value refers to how consistent the opinion of the AHP participants is. If the value is lower than 0.1 or 10%, the inconsistency is acceptable.

<sup>d</sup>The fractions in this table are the results of the pairwise comparisons, which generate a triangular matrix.

**Table 3.** Candidates considering the criteria.<sup>a</sup>

Criterion (A), alternative (B)	A × B	Total
<b>Cost (0.042)</b>		0.042
Inspections (0.034)	$0.042 \times 0.034 = 0.001$	
Sick people (0.459)	$0.042 \times 0.459 = 0.019$	
Medical evaluations (0.207)	$0.042 \times 0.207 = 0.009$	
Days of absence (0.207)	$0.042 \times 0.207 = 0.009$	
Mosquito breeding (0.094)	$0.042 \times 0.094 = 0.004$	
<b>Time (0.056)</b>		0.056
Inspections (0.472)	$0.056 \times 0.472 = 0.026$	
Sick people (0.051)	$0.056 \times 0.051 = 0.003$	
Medical evaluations (0.235)	$0.056 \times 0.235 = 0.013$	
Days of absence (0.142)	$0.056 \times 0.142 = 0.008$	
Mosquito breeding (0.099)	$0.056 \times 0.099 = 0.006$	
<b>Precision (0.292)</b>		0.293
Inspections (0.454)	$0.292 \times 0.454 = 0.133$	
Sick people (0.102)	$0.292 \times 0.102 = 0.030$	
Medical evaluations (0.288)	$0.292 \times 0.288 = 0.084$	
Days of absence (0.074)	$0.292 \times 0.074 = 0.022$	
Mosquito breeding (0.082)	$0.292 \times 0.082 = 0.024$	
<b>Value (0.516)</b>		0.516
Inspections (0.029)	$0.516 \times 0.029 = 0.015$	
Sick people (0.494)	$0.516 \times 0.494 = 0.255$	
Medical evaluations (0.244)	$0.516 \times 0.244 = 0.126$	
Days of absence (0.086)	$0.516 \times 0.086 = 0.044$	
Mosquito breeding (0.147)	$0.516 \times 0.147 = 0.076$	
<b>Refresh rate (0.094)</b>		0.105
Inspections (0.272)	$0.094 \times 0.272 = 0.026$	
Sick people (0.459)	$0.094 \times 0.459 = 0.043$	
Medical evaluations (0.073)	$0.094 \times 0.073 = 0.007$	
Days of absence (0.141)	$0.094 \times 0.141 = 0.013$	
Mosquito breeding (0.175)	$0.094 \times 0.175 = 0.016$	

<sup>a</sup>The final priorities of each alternative in terms of the chosen criteria. We multiply the value of the priority column from [Table 2](#) by the value of the priority of the criteria in [Table 1](#).

**Table 4.** The final ranks of the alternatives.<sup>a</sup>

Alternatives	Criteria					
	Cost	Time	Precision	Value	Refresh rate	Priority (AHP <sup>b</sup> )
Inspections	0.001	0.026	0.133	0.015	0.026	3 (0.201)
Sick people	0.019	0.003	0.030	0.255	0.043	1 (0.350)
Medical evaluations	0.009	0.013	0.084	0.126	0.007	2 (0.239)
Days of absence	0.009	0.008	0.022	0.044	0.013	5 (0.096)
Mosquito breeding	0.004	0.006	0.024	0.076	0.016	4 (0.126)

<sup>a</sup>The values for each alternative are repeated and the final priority of each one is calculated by the total sum for each row.

<sup>b</sup>AHP: analytic hierarchy process value.

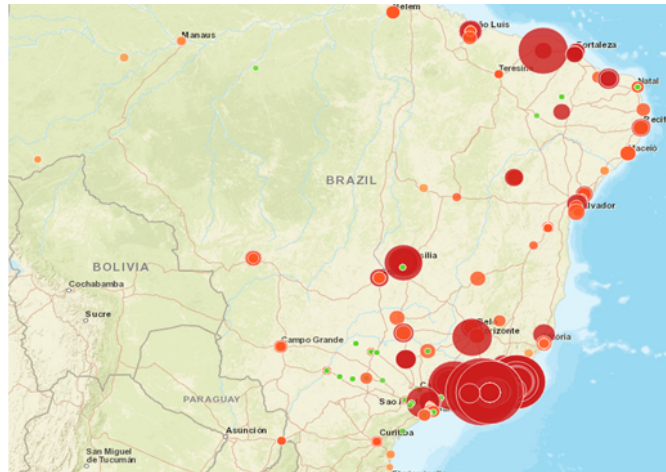
This new index is georeferenced by the inspection places retrieved from the data source, as seen in [Figure 1](#). We used the results of inspections to indicate the future risk of mosquito breeding. The map of risks, considering the new index for 2016, 2017, and 2018, is presented in [Figure 2](#). The visualization component lets specific regions be selected. The risk map considering only the number of mosquito breeding sites for the same period is shown in [Figure 3](#). We note that the relevant regions in the graphs are strikingly different when comparing the maps. In both figures, the size of the bubble (the greater the risk, the larger the bubble) and its color (red indicates the highest risk) refer to the risk. The new index shows that the risk is not only concentrated in the southeast region (a richer region, where the number of inspections is higher) of Brazil but also is widely

distributed across the country. However, the new index gives higher priority to the central region of Brazil, near Brasília. The extra data show that mosquito-breeding sites may be insufficient to provide a reliable index, and extra data may improve the risk prediction accuracy.

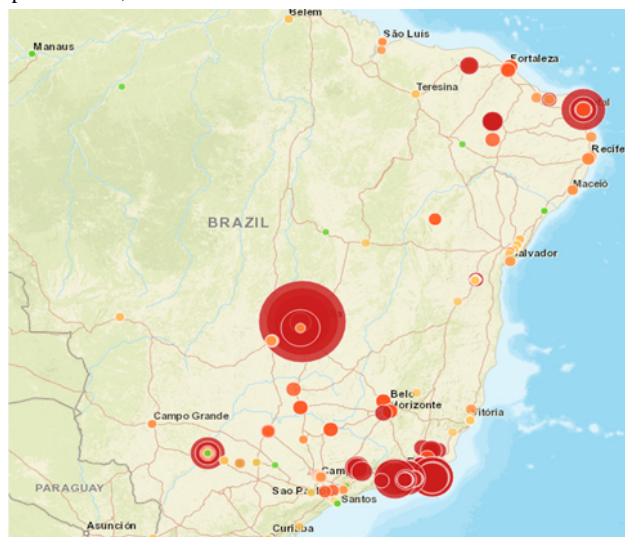
Another interesting result is that a map elaborated with the new index can be more useful than the current map used by the decision makers ([Figure 3](#)) in predicting where the number of infections will be higher. This can be seen by analyzing [Figure 4](#), which shows our proposed index considering data from 2016 and 2017, as well as [Figure 5](#), which presents the number of cases in 2018. The regions where our index showed higher risks for 2016 and 2017 were mostly the same areas with the highest concentration of sick people in 2018.

**Figure 2.** Risk map, considering the proposed index, for 2016, 2017, and 2018.

**Figure 3.** Risk map, considering only the number of mosquito breeding sites, for 2016, 2017, and 2018.



**Figure 4.** Risk map, considering the proposed index, for 2016 and 2017.



**Figure 5.** Number of sick people, considering only 2018.



## Discussion

### Contributions of This Study

In this work, we proposed a georeferenced index to help in the identification of likely risk areas for the proliferation of *A.*

*aegypti* breeding sites in Brazil. We applied multi-criteria analysis, specifically AHP, to prioritize the metric alternatives based on 5 criteria. By using this methodology, we were able to produce risk maps for *A. aegypti* disease control. This is a well-established approach as shown by the related works [3,6-9,11-14]. We then compared the map currently produced

for the Ministry of Planning, Development, and Administration of Brazil with the one created by our proposed index. The information shown by these maps was entirely different, given that we sought to indicate which areas have a higher risk of *A. aegypti* breeding sites, instead of the places with more inspections or breeding sites already identified. We also tested the index's capacity for identifying areas affected by the diseases caused by *A. aegypti* and showed that it can help in identifying these areas. It is our understanding that the proposed index—with its future orientation—could be another tool to public health practitioners in preventing the appearance of new *A. aegypti* breeding sites and in showing how information technology can be applied to help solve public health challenges. Other initiatives such as participatory disease surveillance [29-31] can be used to provide additional data to be used as analysis source.

## Limitations

This work does not use environmental variables that affect the density and distribution of the mosquitoes (such as temperature, precipitation, air humidity, availability of water tanks), which can be added in further versions of this study. In this work, we were only able to georeference the index that resulted from the first AHP, which only involved the opinion of 3 of the authors. After presenting the results of this work as a poster at the Workshop on Big Social Data and Urban Computing that was held in the Very Large Databases Conference, we consulted a group of 3 experts on diseases caused by *A. aegypti*, regarding the use of AHP in conjunction with their opinions. A form was created to help fill out the AHP spreadsheet with the pairwise comparisons. The result of this effort, as well as a comparison between the executions of the AHP by the authors and experts, can be seen in Table 5. This new AHP with a group of experts on diseases caused by *A. aegypti* will allow us to improve our research.

**Table 5.** The final ranking of the alternatives by the experts and the authors.

Alternatives	Ranking by experts (AHP <sup>a</sup> )	Ranking by authors (AHP)	Difference
Inspections	3 (0.215)	3 (0.201)	0.014
Sick people	2 (0.254)	1 (0.350)	-0.096
Medical evaluations	5 (0.091)	2 (0.239)	-0.148
Days of absence	4 (0.123)	5 (0.096)	0.027
Mosquito breeding	1 (0.316)	4 (0.126)	0.19

<sup>a</sup>AHP: analytic hierarchy process value.

## Conclusions

The proposed approach uses unconventional indicators based on the presence of mosquitoes: number of inspections, number of sick people, number of medical evaluations, number of days of sickness absence, and number of mosquito breeding sites found. Thus, this work provides a novel paradigm for public health practitioners in preventing the appearance of new *A.*

*aegypti* breeding sites. This new index may also be applied in conjunction with the current methodologies. Besides the criteria we used in our index proposal, we will explore environmental criteria that affect the density and distribution of the mosquitoes (such as temperature, precipitation, air humidity, availability of water tanks), which are the standard variables in the identification of *A. aegypti* breeding sites.

## Acknowledgments

We would like to thank Lemobs, especially Jacson Hwang, and the Ministry of Planning, Development, and Administration of Brazil, especially Eduardo Cesar Gomes, for making the data available for this research. We also thank the experts who provided their input for the second AHP: Sonia Brucki, Ana Paula de Andrade Lima Viana, and Lena Peres. This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior-Brasil (CAPES)-Finance Code 001.

## Conflicts of Interest

None declared.

## References

1. Ricas Rezende H, Malta Romano C, Morales Claro I, Santos Caleiro G, Cerdeira Sabino E, Felix AC, et al. First report of *Aedes albopictus* infected by Dengue and Zika virus in a rural outbreak in Brazil. *PLoS One* 2020;15(3):e0229847 [FREE Full text] [doi: [10.1371/journal.pone.0229847](https://doi.org/10.1371/journal.pone.0229847)] [Medline: [32163449](https://pubmed.ncbi.nlm.nih.gov/32163449/)]
2. Honório NA, Castro MG, Barros FSMD, Magalhães MDAFM, Sabroza PC. The spatial distribution of *Aedes aegypti* and *Aedes albopictus* in a transition zone, Rio de Janeiro, Brazil. *Cad Saude Publica* 2009 Jun;25(6):1203-1214 [FREE Full text] [doi: [10.1590/s0102-311x2009000600003](https://doi.org/10.1590/s0102-311x2009000600003)] [Medline: [19503951](https://pubmed.ncbi.nlm.nih.gov/19503951/)]



3. Ferreira-de-Lima VH, Lima-Camara TN. Natural vertical transmission of dengue virus in *Aedes aegypti* and *Aedes albopictus*: a systematic review. *Parasit Vectors* 2018 Feb 01;11(1):77 [FREE Full text] [doi: [10.1186/s13071-018-2643-9](https://doi.org/10.1186/s13071-018-2643-9)] [Medline: [29391071](https://pubmed.ncbi.nlm.nih.gov/29391071/)]
4. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature* 2013 Apr 25;496(7446):504-507 [FREE Full text] [doi: [10.1038/nature12060](https://doi.org/10.1038/nature12060)] [Medline: [23563266](https://pubmed.ncbi.nlm.nih.gov/23563266/)]
5. Secretaria de Vigilância em Saúde. Monitoramento dos casos de dengue, febre de chikungunya e febre pelo vírus Zika até a Semana Epidemiológica 7 de 2018 Internet. Ministério da Saúde. 2018. URL: <https://portalarquivos2.saude.gov.br/images/pdf/2018/marco/06/2018-008-Publicacao.pdf> [accessed 2020-06-05]
6. Rancès E, Ye YH, Woolfit M, McGraw EA, O'Neill SL. The relative importance of innate immune priming in Wolbachia-mediated dengue interference. *PLoS Pathog* 2012 Feb 23;8(2):e1002548 [FREE Full text] [doi: [10.1371/journal.ppat.1002548](https://doi.org/10.1371/journal.ppat.1002548)] [Medline: [22383881](https://pubmed.ncbi.nlm.nih.gov/22383881/)]
7. Schultz MJ, Isern S, Michael SF, Corley RB, Connor JH, Frydman HM. Variable Inhibition of Zika Virus Replication by Different Wolbachia Strains in Mosquito Cell Cultures. *J Virol* 2017 Jul 15;91(14):e00339-17 [FREE Full text] [doi: [10.1128/JVI.00339-17](https://doi.org/10.1128/JVI.00339-17)] [Medline: [28446677](https://pubmed.ncbi.nlm.nih.gov/28446677/)]
8. Azil AH, Li M, Williams CR. Dengue vector surveillance programs: a review of methodological diversity in some endemic and epidemic countries. *Asia Pac J Public Health* 2011 Nov;23(6):827-842. [doi: [10.1177/1010539511426595](https://doi.org/10.1177/1010539511426595)] [Medline: [22144710](https://pubmed.ncbi.nlm.nih.gov/22144710/)]
9. Aenishaenslin C, Hongoh V, Cissé HD, Hoen AG, Samoura K, Michel P, et al. Multi-criteria decision analysis as an innovative approach to managing zoonoses: results from a study on Lyme disease in Canada. *BMC Public Health* 2013 Sep 30;13:897 [FREE Full text] [doi: [10.1186/1471-2458-13-897](https://doi.org/10.1186/1471-2458-13-897)] [Medline: [24079303](https://pubmed.ncbi.nlm.nih.gov/24079303/)]
10. Aenishaenslin C, Gern L, Michel P, Ravel A, Hongoh V, Waub J, et al. Adaptation and Evaluation of a Multi-Criteria Decision Analysis Model for Lyme Disease Prevention. *PLoS One* 2015;10(8):e0135171 [FREE Full text] [doi: [10.1371/journal.pone.0135171](https://doi.org/10.1371/journal.pone.0135171)] [Medline: [26295344](https://pubmed.ncbi.nlm.nih.gov/26295344/)]
11. Cox R, Sanchez J, Revie CW. Multi-criteria decision analysis tools for prioritising emerging or re-emerging infectious diseases associated with climate change in Canada. *PLoS One* 2013;8(8):e68338 [FREE Full text] [doi: [10.1371/journal.pone.0068338](https://doi.org/10.1371/journal.pone.0068338)] [Medline: [23950868](https://pubmed.ncbi.nlm.nih.gov/23950868/)]
12. Bana Consulting. A multiple criteria decision support system. M-MACBETH. URL: <http://m-macbeth.com/> [accessed 2019-12-05]
13. Santos DVD, Silva GSE, Weber EJ, Hasenack H, Groff FHS, Todeschini B, et al. Identification of foot and mouth disease risk areas using a multi-criteria analysis approach. *PLoS ONE* 2017 May 26;12(5):e0178464. [doi: [10.1371/journal.pone.0178464](https://doi.org/10.1371/journal.pone.0178464)]
14. Fruean S, East I. Spatial analysis of targeted surveillance for screw-worm fly (*Chrysomya bezziana* or *Cochliomyia hominivorax*) in Australia. *Aust Vet J* 2014 Jul;92(7):254-262. [doi: [10.1111/avj.12197](https://doi.org/10.1111/avj.12197)] [Medline: [24964835](https://pubmed.ncbi.nlm.nih.gov/24964835/)]
15. Department of Agriculture. MCAS-S tool. Australian Government, Department of Agriculture, Water, and the Environment. URL: <https://www.agriculture.gov.au/abares/aclump/multi-criteria-analysis/mcas-s-tool> [accessed 2019-05-02]
16. Gosselin P, Lebel G, Rivest S, Douville-Fradet M. The Integrated System for Public Health Monitoring of West Nile Virus (ISPHM-WNV): a real-time GIS for surveillance and decision-making. *Int J Health Geogr* 2005 Sep 13;4:21 [FREE Full text] [doi: [10.1186/1476-072X-4-21](https://doi.org/10.1186/1476-072X-4-21)] [Medline: [16159403](https://pubmed.ncbi.nlm.nih.gov/16159403/)]
17. Ho HC, Knudby A, Huang W. A Spatial Framework to Map Heat Health Risks at Multiple Scales. *Int J Environ Res Public Health* 2015 Dec 18;12(12):16110-16123 [FREE Full text] [doi: [10.3390/ijerph121215046](https://doi.org/10.3390/ijerph121215046)] [Medline: [26694445](https://pubmed.ncbi.nlm.nih.gov/26694445/)]
18. Getis A, Ord J. The analysis of spatial association by use of distance statistics. *Geographical analysis* 1992;24(3):206. [doi: [10.1111/j.1538-4632.1992.tb00261.x](https://doi.org/10.1111/j.1538-4632.1992.tb00261.x)]
19. Hongoh V, Campagna C, Panic M, Samuel O, Gosselin P, Waub J, et al. Assessing Interventions to Manage West Nile Virus Using Multi-Criteria Decision Analysis with Risk Scenarios. *PLoS One* 2016;11(8):e0160651 [FREE Full text] [doi: [10.1371/journal.pone.0160651](https://doi.org/10.1371/journal.pone.0160651)] [Medline: [27494136](https://pubmed.ncbi.nlm.nih.gov/27494136/)]
20. Sarkar S, Strutz SE, Frank DM, Rivaldi C, Sissel B, Sánchez-Cordero V. Chagas Disease Risk in Texas. *PLoS Negl Trop Dis* 2010 Oct 5;4(10):e836. [doi: [10.1371/journal.pntd.0000836](https://doi.org/10.1371/journal.pntd.0000836)]
21. Thanapongtharm W, Linard C, Wiriyarat W, Chinsorn P, Kanchanasaka B, Xiao X, et al. Spatial characterization of colonies of the flying fox bat, a carrier of Nipah virus in Thailand. *BMC Vet Res* 2015 Mar 28;11:81 [FREE Full text] [doi: [10.1186/s12917-015-0390-0](https://doi.org/10.1186/s12917-015-0390-0)] [Medline: [25880385](https://pubmed.ncbi.nlm.nih.gov/25880385/)]
22. Vinhaes MC, de Oliveira SV, Reis PO, de Lacerda Sousa AC, Silva RAE, Obara MT, et al. Assessing the vulnerability of Brazilian municipalities to the vectorial transmission of *Trypanosoma cruzi* using multi-criteria decision analysis. *Acta Trop* 2014 Sep;137:105-110 [FREE Full text] [doi: [10.1016/j.actatropica.2014.05.007](https://doi.org/10.1016/j.actatropica.2014.05.007)] [Medline: [24857942](https://pubmed.ncbi.nlm.nih.gov/24857942/)]
23. Associação Nacional das Instituições de Planejamento, Pesquisa e Estatística. ANIPES. URL: <http://www.anipes.org.br/> [accessed 2020-04-05]
24. TerraLib and TerraView. DPI/INPE. URL: <http://www.dpi.inpe.br/terralib5/wiki/doku.php> [accessed 2020-05-04]
25. Majumder MS, Santillana M, Mekaru SR, McGinnis DP, Khan K, Brownstein JS. Utilizing Nontraditional Data Sources for Near Real-Time Estimation of Transmission Dynamics During the 2015-2016 Colombian Zika Virus Disease Outbreak. *JMIR Public Health Surveill* 2016 Jun 01;2(1):e30 [FREE Full text] [doi: [10.2196/publichealth.5814](https://doi.org/10.2196/publichealth.5814)] [Medline: [27251981](https://pubmed.ncbi.nlm.nih.gov/27251981/)]

26. Goepel K. New AHP Excel template with multiple inputs. Business Performance Management Singapore. URL: <https://bpmmsg.com/new-ahp-excel-template-with-multiple-inputs/> [accessed 2018-06-01]
27. Griffith P. A python implementation of the analytic hierarchy process. GitHub. URL: <https://github.com/PhilipGriffith/AHP> [accessed 2018-06-01]
28. Saaty TL. Decision Making for Leaders: The Analytic Hierarchy Process for Decisions in a Complex World. USA: University of Pittsburgh; 2013.
29. Smolinski MS, Crawley AW, Olsen JM, Jayaraman T, Libel M. Participatory Disease Surveillance: Engaging Communities Directly in Reporting, Monitoring, and Responding to Health Threats. *JMIR Public Health Surveill* 2017 Oct 11;3(4):e62 [FREE Full text] [doi: [10.2196/publichealth.7540](https://doi.org/10.2196/publichealth.7540)] [Medline: [29021131](https://pubmed.ncbi.nlm.nih.gov/29021131/)]
30. Lwin MO, Vijaykumar S, Rathnayake VS, Lim G, Panchapakesan C, Foo S, et al. A Social Media mHealth Solution to Address the Needs of Dengue Prevention and Management in Sri Lanka. *J Med Internet Res* 2016 Jul 01;18(7):e149 [FREE Full text] [doi: [10.2196/jmir.4657](https://doi.org/10.2196/jmir.4657)] [Medline: [27369296](https://pubmed.ncbi.nlm.nih.gov/27369296/)]
31. Lwin MO, Jayasundar K, Sheldenkar A, Wijayamuni R, Wimalaratne P, Ernst KC, et al. Lessons From the Implementation of Mo-Buzz, a Mobile Pandemic Surveillance System for Dengue. *JMIR Public Health Surveill* 2017 Oct 02;3(4):e65 [FREE Full text] [doi: [10.2196/publichealth.7376](https://doi.org/10.2196/publichealth.7376)] [Medline: [28970191](https://pubmed.ncbi.nlm.nih.gov/28970191/)]

## Abbreviations

**AHP:** analytic hierarchy process

**FMD:** foot-and-mouth disease

**GAIA:** geometrical analysis for interactive aid

**MAUP:** modifiable areal unit problem

**MCDA:** multi-criteria decision analysis

**PRADIN:** program to support decision making based on indicators

**PROMETHEE:** Preference Ranking Organization Method for Enrichment of Evaluations

*Edited by Y Khader; submitted 20.04.20; peer-reviewed by S Oliveira, D Montenegro; comments to author 14.06.20; revised version received 20.02.21; accepted 19.03.21; published 10.05.21.*

*Please cite as:*

*Lima Y, Pinheiro W, Barbosa CE, Magalhães M, Chaves M, de Souza JM, Rodrigues S, Xexéo G*

*Development of an Index for the Inspection of Aedes aegypti Breeding Sites in Brazil: Multi-criteria Analysis*

*JMIR Public Health Surveill* 2021;7(5):e19502

URL: <https://publichealth.jmir.org/2021/5/e19502>

doi: [10.2196/19502](https://doi.org/10.2196/19502)

PMID: [33970118](https://pubmed.ncbi.nlm.nih.gov/33970118/)

©Yuri Lima, Wallace Pinheiro, Carlos Eduardo Barbosa, Matheus Magalhães, Miriam Chaves, Jano Moreira de Souza, Sérgio Rodrigues, Geraldo Xexéo. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 10.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# Geographical Disparities in HIV Seroprevalence Among Men Who Have Sex with Men and People Who Inject Drugs in Nigeria: Exploratory Spatial Data Analysis

Amobi Onovo<sup>1,2</sup>, BTech, MPH; Abiye Kalaiwo<sup>2</sup>, MPH, MD; Moses Katbi<sup>2</sup>, MBA, MD; Otse Ogorry<sup>3</sup>, BSc, MPH; Antoine Jaquet<sup>4</sup>, PhD; Olivia Keiser<sup>1</sup>, PhD

<sup>1</sup>Institute of Global Health, University of Geneva, Geneva, Switzerland

<sup>2</sup>U S Agency for International Development, Abuja, Nigeria

<sup>3</sup>The President's Emergency Plan For AIDS Relief Coordination Office, Abuja, Nigeria

<sup>4</sup>Institut de Santé Publique d'épidémiologie et de développement, University of Bordeaux, Bordeaux, France

**Corresponding Author:**

Amobi Onovo, BTech, MPH

US Agency for International Development

HIV/AIDS & TB Office, US Embassy Abuja

1075 Diplomatic Drive, Central Business District

Abuja, 900211

Nigeria

Phone: 234 7030538954

Email: [amobiandrewonovo@gmail.com](mailto:amobiandrewonovo@gmail.com)

## Abstract

**Background:** The assessment of geographical heterogeneity of HIV among men who have sex with men (MSM) and people who inject drugs (PWID) can usefully inform targeted HIV prevention and care strategies.

**Objective:** We aimed to measure HIV seroprevalence and identify hotspots of HIV infection among MSM and PWID in Nigeria.

**Methods:** We included all MSM and PWID accessing HIV testing services across 7 prioritized states (Lagos, Nasarawa, Akwa Ibom, Cross Rivers, Rivers, Benue, and the Federal Capital Territory) in 3 geographic regions (North Central, South South, and South West) between October 1, 2016, and September 30, 2017. We extracted data from national testing registers, georeferenced all HIV test results aggregated at the local government area level, and calculated HIV seroprevalence. We calculated and compared HIV seroprevalence from our study to the 2014 integrated biological and behavioural surveillance survey and used global spatial autocorrelation and hotspot analysis to highlight patterns of HIV infection and identify areas of significant clustering of HIV cases.

**Results:** MSM and PWID had HIV seroprevalence rates of 12.14% (3209/26,423) and 11.88% (1126/9474), respectively. Global spatial autocorrelation Moran I statistics revealed a clustered distribution of HIV infection among MSM and PWID with a <5% and <1% likelihood that this clustered pattern could be due to chance, respectively. Significant clusters of HIV infection (Getis-Ord-Gi\* statistics) confined to the North Central and South South regions were identified among MSM and PWID. Compared to the 2014 integrated biological and behavioural surveillance survey, our results suggest an increased HIV seroprevalence among PWID and a substantial decrease among MSM.

**Conclusions:** This study identified geographical areas to prioritize for control of HIV infection among MSM and PWID, thus demonstrating that geographical information system technology is a useful tool to inform public health planning for interventions targeting epidemic control of HIV infection.

(*JMIR Public Health Surveill* 2021;7(5):e19587) doi:[10.2196/19587](https://doi.org/10.2196/19587)

**KEYWORDS**

key population; MSM; PWID; HIV seroprevalence; HIV testing modality; hotspots; geospatial; Getis-Ord-Gi\*; IBBSS; Nigeria

## Introduction

Geographic variation in HIV seroprevalence has been demonstrated in many sub-Saharan African countries [1-7]. According to the Nigeria AIDS Indicator and Impact Survey (NAIIS) 2018, HIV seroprevalence in Nigeria among adults aged 15-64 years was 1.5% (1.9% among females and 1.1% among males), ranging from 0.6% in the North West to 3.1% in the South South zone [8]. The spatial distribution of HIV infection in key populations (KPs), including in men who have sex with men (MSM) and people who inject drugs (PWID), is much less understood. Nigeria has a mixed epidemic, meaning that while HIV prevalence among the general population is high, certain groups still carry a far more significant HIV burden than the rest of the population. Men who have sex with men are the only group in Nigeria where HIV prevalence is still rising. In 2017, this group's prevalence stood at 23%, significantly more than the next highest prevalence group—sex workers—at 14.4% [9]. Of all new HIV infections in the country, 10% occur among MSM [10]. HIV prevalence among people who inject drugs (sometimes referred to as PWID) in Nigeria was 3.4% in 2017 [11]. Women who inject drugs are particularly affected, with a prevalence of 13.9% compared to 2.6% among men [9]. Female sex workers who inject drugs face the highest HIV prevalence at around 43% [9]. According to the 2010 integrated biological and behavioral surveillance survey (IBBSS) in Nigeria, female injecting drug users had a 7-fold higher HIV prevalence than male injecting drug users [12].

In, sub-Saharan Africa, MSM are at increased risk for HIV infection compared to men in the general population [13]. The HIV epidemic in West Africa is mainly heterosexually driven, but recent data suggest that anal sex plays a significant independent role in HIV infection [14]. In the 2015 the Joint United Nations Programme on HIV/AIDS (UNAIDS) report, studies in sub-Saharan Africa indicated prevalence rates of HIV infection ranging from 6% to 37% among MSM [15]. According to the progress reports on the global AIDS response, the highest prevalence rates of HIV infection among MSM were as follows: 19% in Central and Western Africa, 15% in Southern and Eastern Africa, 12% in Latin America, 11% in the Asia-Pacific region, and 8% in Central and Western Europe and North America [16]. A recent study conducted among MSM across India reported a relatively high HIV prevalence of 7% [17]. These reports indicate that a substantial number of infections occur among MSM, many of whom also have sex with women [18]. Other studies have confirmed that MSM who engage in transactional sex have an increased HIV prevalence compared to MSM who do not engage in transactional sex [17,19]. The variability in HIV prevalence may be attributed to individual, social, and structural level factors. MSM who engage in transactional sex may not be responsive to HIV prevention services designed explicitly for gay-identified MSM. These men are affected by similar multilevel factors, such as stigma and discrimination, inability to negotiate condom use, substance use and misuse, and psychological distress [20]. MSM across many countries in sub-Saharan Africa face stigma and discrimination [21]. Stahlman et al's [22] study revealed that stigmatization as gay and fear of being HIV positive present

barriers to accessing available voluntary HIV testing, counseling, and treatment services. In Nigeria, the Same-Sex Marriage Prohibition law was passed by the Senate in 2011 and was implemented in January 2014. The new law criminalized same-sex practices, prohibiting participation in organizations, service provision, or meetings that support gay people, and instituting punishments for attempts to enter civil unions or publicly show same-sex relationships [23].

About one-third of global HIV infections outside sub-Saharan Africa are related to PWID, who account for a growing proportion of persons living with HIV. It is estimated that PWID are 22 times more likely to acquire HIV than those among the rest of the population [24]. This risk arises from sharing needles and injection equipment but is reinforced through criminalization, marginalization, and poverty. HIV prevalence among PWID in Nigeria was 3.4% in 2017 [10]. Women who inject drugs are particularly affected, with a prevalence of 13.9% compared to 2.6% among men [10]. Seroprevalence ranges from 3.4% in Nigeria to 8.5% in Sierra Leone [10]. However, Nigeria has the highest number of PWID in the West African region, estimated at 45,000 in 2017 [10]. A recent study in 2015 among PWID showed that the estimated HIV prevalence was 18.1% [25]. HIV seroprevalence among women who inject drugs is much higher than among men who inject drugs. For example, in Senegal, the HIV seroprevalence among women and men who inject drugs is 28% and 7%, respectively [26].

Previous studies, have focused on developing statistical models to predict the seroprevalence of HIV among KPs in sub-Saharan Africa [27,28]. These models included multiple risk factors (eg, circumcision, distance to road, and condom usage). They have shown that there can be considerable small-scale heterogeneity in HIV seroprevalence and risk behaviors. However, none of these models have tested whether there is a spatial pattern of HIV infection among KPs, and the size of the studies has been limited. In our study, we examined the spatial pattern of HIV prevalence among MSM and PWID in Nigeria. There is currently great interest amongst public health planners concerning whether this geographic variation of HIV could be used to improve the effectiveness of targeted HIV prevention interventions by focusing on areas of highest need [29-31]. The study is divided roughly into 3 phases, each of which covers a particular study objective. The first phase used an HIV testing program data to estimate the seroprevalence of HIV between MSM and PWID, the second phase used geographic information system techniques to assess the infection pattern and classify HIV infection hot spots, and the third phase compared the outcomes of HIV seroprevalence from program data and the last IBBSS 2014 [32] carried out in Nigeria by the Federal Ministry of Health.

Therefore, we aimed to quantify the geographic variation of HIV seroprevalence among MSM and PWID by age and sex through using georeferenced HIV testing services data aggregated at the level of local government areas (LGAs). We planned to detect hot spots and compare HIV seroprevalence from our study to that of the 2014 IBBSS. We defined HIV seroprevalence as the overall occurrence of HIV within a defined population at a particular time, as measured by blood or serologic tests. The IBBSS was scheduled to occur every 5

years, with the last one taking place in 2014. The survey results served as the primary data source for the national response to AIDS among KPs in Nigeria. To track changes in HIV infection among MSM and PWID in the selected study and survey states, we compared HIV seroprevalence from our study with HIV prevalence from the 2014 IBBSS.

## Methods

### Study Setting and Data Source

Nigeria is organized into 36 federating states and the Federal Capital Territory, which hosts the national government. The states are further subdivided into 774 LGAs. The study was conducted in 93 LGAs spread across 7 prioritized states (Akwa Ibom, Rivers, Cross Rivers, Benue, Nasarawa, Lagos, and the Federal Capital Territory) in the 3 geographic regions of North Central, South South, and the South West. Under the national KP program, these states were prioritized for prevention and comprehensive HIV/AIDS treatment interventions due to their high population density and the high number of people living with HIV. The national KP program consists of an integrated HIV prevention and treatment program that identifies HIV-positive KPs in the community and links them to care and treatment at the LGA level. The primary source of data for this study was the performance HIV testing services data (disaggregated by fine age bands and sex) obtained from a Nigerian KP program, the Integrated Most-At-Risk Populations HIV/AIDS Prevention Program [33].

### HIV Testing Algorithm

HIV testing delivery services to KPs in the target communities adopted a 2-step HIV rapid testing serial algorithm testing strategy. Fourth generation rapid test kits were used for HIV testing (Alere Determine HIV-1/2 Ag/Ab Combo, Alere Scarborough, Inc). A nonreactive HIV test result after the first test was considered HIV negative. A reactive result was tested with a second test. When the result was reactive again, it was considered HIV positive, and when it was nonreactive, it was considered HIV negative. All HIV test results were documented using the national HIV testing and counseling register. Based on program design and data reporting requirements, the HIV test results of each KP (MSM and PWID) were aggregated up by the program level performance indicator, “Number of individuals who received HIV Testing Services and received their test result,” and linked to the location or LGA where the KP was tested.

### HIV Testing Modalities for KPs

The national HIV/AIDS program provides targeted HIV testing services to KP and their high-risk contacts. The following services are provided: index partner or index testing (also referred to as partner testing or partner notification) in which exposed contacts of an HIV-positive index case are offered HIV testing; KP testing in mobile or temporary testing locations, such as community centers, schools, workplaces, hotels, clubs, tents, and vans; and voluntary counseling and testing, which includes testing in voluntary counseling and testing centers outside of a health facility (ie, “one-stop shops”). The one-stop shop model for KP establishes safe spaces in the communities

for HIV prevention and treatment interventions. It integrates differentiated strategies that optimize efficiency along the 90-90-90 cascade [34]. HIV test results are aggregated by the KP group and the LGA where the test is conducted. To reduce double-counting of individuals and to account for retesters in a reporting period, tracking systems, such as “unique identifiers”, are established and used to monitor the frequency of contact or outreach of the KPs over time. A unique ID is generated and assigned to a KP group before HIV testing commences, and the results collected are entered into an electronic database. Data validation is conducted every quarter by running a query of all individual-level KP data on HIV testing using IDs to determine first-time testers and repeat testers. All duplicated KP data within the reporting period are deduplicated before data transmission. This is accomplished by community-level data review and reconciliation exercises between testing counselors and monitoring and evaluation officers to ensure that the first-time testers and repeat testers are adequately tracked. We divided the total number of KPs who tested HIV positive (numerator: first-time testers + previously known HIV-positive testers) by the total number of KP who received HIV testing services between October 1, 2016, and September 30, 2017, to measure the HIV prevalence.

### The 2014 Integrated Biological Behavioral Sentinel Survey

The 2014 IBBSS was conducted by the Federal Ministry of Health through the National AIDS & STIs Control Programme (NASCP) and other stakeholders and used respondent-driven sampling, a modified form of snowball sampling to identify hard to reach populations [32], to select MSM and PWID. The 2014 IBBSS was conducted in 14 states, and only 4 of the 7 states in our study (ie, Lagos, Rivers, Federal Capital Territory, and Cross River) had data on seroprevalence for MSM and PWID recorded in the 2014 IBBSS report. The goal of the IBBSS is to obtain serological, behavioral, and HIV service coverage data on key and vulnerable populations. Members of the communities, nongovernmental organizations working with the target populations, and key informants for each target group (recruited as seeds) helped identify various locations where the target groups could be found. Seeds were identified through the nongovernmental organizations’ networks that historically provide support and services for MSM and PWID. A list of sites where the population groups were located, how and when they can be reached for information and services, and the essential distinguishing characteristics of these sites were prepared and used for the 2014 IBBSS. All eligible key and vulnerable populations were tested for HIV, and results were documented in survey forms.

### Study Population

All MSM and PWID aged  $\geq 15$  years with a documented HIV test result were included. At the time of analysis and in line with the Nigeria KP program, HIV testing data were disaggregated into 4 age categories, 15-19, 20-24, 25-49, and 50+ years. The age classification for the HIV test data was based solely on the nature of the KP program. MSM was defined as self-identification as male and report of oral or anal sex with a man in the previous 12 months [35]. A PWID was defined as

an individual meeting one of the following conditions: self-reporting ever injecting any illicit drug and having a visible injection site on the body and self-reporting injecting illicit drugs in the past month [36]. All KP groups were screened before enrollment by known MSM or PWID recruited as peer navigators by the national KP program to ensure clients were members of the target population.

### Statistical Analyses

We analyzed aggregate-level data from index testing, mobile, and voluntary counseling and testing modalities by counting the number of KPs who received HIV testing services via the The President's Emergency Plan for AIDS Relief (PEPFAR) and the Nigerian KP program between October 1, 2016, and September 30, 2017, at the LGA level. We georeferenced all MSM and PWID who accessed HIV testing services at the LGA level and performed 4 analyses. First, we constructed maps of HIV seroprevalence among MSM and PWID. Second, we used spatial autocorrelation (global Moran I) statistics to measure the degree to which HIV seroprevalence was clustered, dispersed, or randomly distributed. Under the null hypothesis, the expected value is that there is no pattern of HIV infection in selected LGAs. Moran I values range from  $-1$  (indicating perfect dispersion) to  $1$  (indicating perfect spatial clustering). Third, we used hot spot analysis in the ArcGIS software (Environmental Systems Research Institute) to calculate the Getis-Ord  $G_i^*$  statistic for each LGA. The resultant  $z$  score identified where LGAs with either high or low HIV seroprevalence cluster spatially. Each LGA was analyzed within the context of neighboring LGAs: the larger the  $z$  score, the more intense the clustering of high seroprevalences or hot spots. Similarly, smaller  $z$  scores indicated clustering of low seroprevalences. To be a statistically significant hot spot, an LGA required a high HIV seroprevalence and to be surrounded by other LGAs with high HIV seroprevalence. For the 2 study groups, the map scale used varied: 1:25,000 was used for MSM and 1:42,000 for PWID. A resolution of 300 dpi was consistent throughout the 2 maps. Fourth, our study's calculated HIV

seroprevalence was compared to the HIV seroprevalence among MSM and PWID from the 2104 IBBSS. Using Stata 14 (StataCorp) we developed 95% CIs of HIV seroprevalence by state with the normal approximation. We created dot plots to compare the distribution of the 2 different HIV seroprevalence results (study vs IBBSS) between MSM and PWID in Lagos, Rivers, the Federal Capital Territory, and Cross River.

### Ethical Reviews

This analysis was conducted with routine data gathered through the national KP program. Informed consent was obtained for all clients who were tested for HIV in line with the HIV testing service policy of Nigeria. Ethical approval was obtained from the Federal Capital Territory, Health Research Ethics Committee, Nigeria (approval no. FHREC/2019/01/122/23-12-19). This study only analyzed anonymized and deidentified data. The 2014 IBBSS received appropriate ethical clearance from the National Health Research and Ethics Committee before the commencement of the survey.

## Results

### Overall HIV Seroprevalence by Age and Sex

Of the 26,423 MSMs and 9474 PWID who received HIV testing between October 1, 2016, and September 30, 2017, a total of 3209 MSM and 1126 PWID tested HIV positive for an overall seroprevalence of 12.1% (95% CI 9.7-13.1) and 11.8% (95% CI 9.3-12.7), respectively (Table 1). MSM aged 50 years and older had a considerably higher HIV seroprevalence (43/126, 34.1%,) than those aged 15-19 years (190/2648, 7.17%,). Middle-aged PWID (25-49 years old) had the highest HIV seroprevalence (905/6203, 14.58%,) over other PWID age groups. HIV seroprevalence among female PWID was twice as high as that among male PWID (female: 467/2485, 18.79%; male 659/6989, 9.42%). Female PWID aged 25-49 years had the highest HIV seroprevalence (345/1399, 24.66%,), while the seroprevalence among male PWID in the same age group was 11.65% (560/4804; Table 1).

**Table 1.** HIV Seroprevalence among MSM and PWID by age, sex, and study locations in Nigeria, September 30, 2017.

State by age group	No. of individuals tested for HIV			No. of individuals who tested HIV positive			SP <sup>a</sup> (%) among MSM (n=26423)	SP (%) among male PWID (n=6989)	SP (%) among female PWID (n=2485)
	MSM <sup>b</sup> (n=26,423)	PWID <sup>c</sup>		MSM (n=3209)	PWID				
		Male (n=6989)	Female (n=2485)		Male (n=659)	Female (n=467)			
<b>Akwa Ibom State</b>									
15-19 y	227	75	29	25	2	3	11.0	2.7	10.3
20-24 y	1134	281	82	53	13	20	4.7	4.6	24.4
25-49 y	2242	1033	188	490	159	66	21.9	15.4	35.1
50+ y	32	13	3	13	4	2	40.6	30.8	66.7
<b>Benue State</b>									
15-19 y	264	42	14	16	6	3	6.1	14.3	21.4
20-24 y	1093	251	66	70	10	10	6.4	4.0	15.2
25-49 y	1117	875	117	282	85	40	25.2	9.7	34.2
50+ y	4	31	5	4	6	1	100.0	19.4	20.0
<b>Cross River State</b>									
15-19 y	327	100	64	30	3	11	9.2	3.0	17.2
20-24 y	1495	358	176	145	11	27	9.7	3.1	15.3
25-49 y	2193	946	344	349	149	122	15.9	15.8	35.5
50+ y	31	9	1	11	4	0	35.5	44.4	0.0
<b>Federal Capital Territory</b>									
15-19 y	753	28	41	21	0	0	2.8	0.0	0.0
20-24 y	2401	318	280	154	6	19	6.4	1.9	6.8
25-49 y	2332	677	293	243	24	26	10.4	3.5	8.9
50+ y	10	2	1	5	1	1	50.0	50.0	100.0
<b>Lagos State</b>									
15-19 y	496	6	23	34	0	5	6.9	0.0	21.7
20-24 y	1375	44	76	167	2	5	12.1	4.5	6.6
25-49 y	731	278	219	99	4	26	13.5	1.4	11.9
50+ y	10	96	23	2	1	1	20.0	1.0	4.3
<b>Nasarawa State</b>									
15-19 y	227	51	21	7	1	1	3.1	2.0	4.8
20-24 y	1294	369	181	97	8	13	7.5	2.2	7.2
25-49 y	1193	668	238	153	68	65	12.8	10.2	27.3
50+ y	6	3	0	2	1	0	33.3	33.3	— <sup>d</sup>
<b>Rivers State</b>									
15-19 y	354	7	0	57	2	0	16.1	28.6	—
20-24 y	1929	88	0	268	15	0	13.9	17.0	—
25-49 y	3120	327	0	406	71	0	13.0	21.7	—
50+ y	33	13	0	6	3	0	18.2	23.1	—
<b>Overall</b>									
15-19 y	2648	309	192	190	14	23	7.2	4.5	12.0

State by age group	No. of individuals tested for HIV			No. of individuals who tested HIV positive			SP <sup>a</sup> (%) among MSM (n=26423)	SP (%) among male PWID (n=6989)	SP (%) among female PWID (n=2485)
	MSM <sup>b</sup> (n=26,423)	PWID <sup>c</sup>		MSM (n=3209)	PWID				
		Male (n=6989)	Female (n=2485)		Male (n=659)	Female (n=467)			
20-24 y	10,721	1709	861	954	65	94	8.9	3.8	10.9
25-49 y	12,928	4804	1399	2022	560	345	15.6	11.7	24.7
50+ y	126	167	33	43	20	5	34.1	12.0	15.2
Total	26,423	6989	2485	3209	659	467	12.1	9.4	18.8

<sup>a</sup>SP: seroprevalence.

<sup>b</sup>MSM: men who have sex with men.

<sup>c</sup>PWID: people who inject drugs.

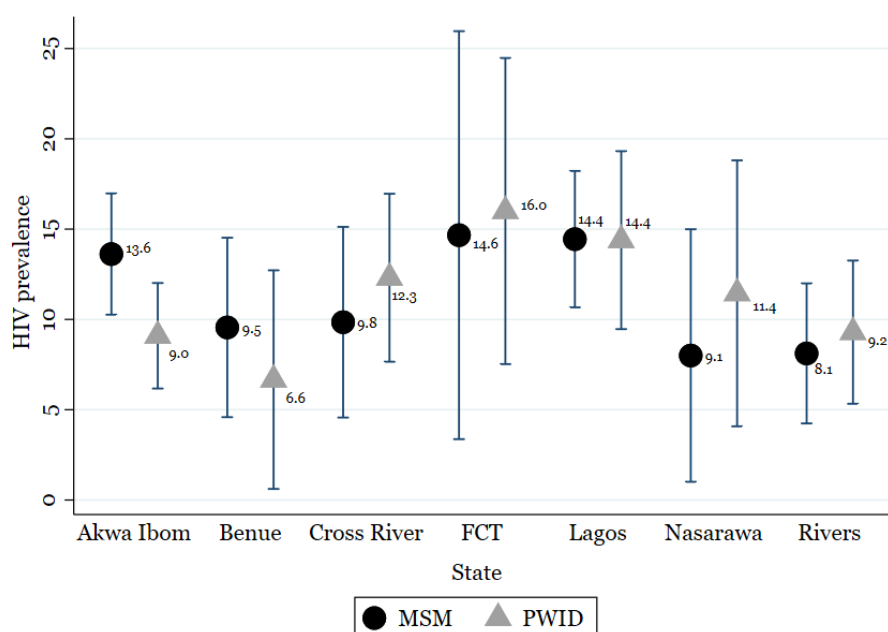
<sup>d</sup>Data not available.

### HIV Seroprevalence by State: Comparison to Previous Surveys

Figure 1 shows the mean HIV seroprevalence for the various states. Among MSM in all states, the mean HIV seroprevalence in the Federal Capital Territory was the highest (14.6%; 95% CI 3.4-25.9), followed by Lagos (14.4%; 95% CI 10.6-18.2), and Akwa Ibom state (13.6%; 95% CI 10.2-16.9). Mean HIV seroprevalence was lowest in Nasarawa (9.1%; 95% CI 1.0-14.9). Similarly, among PWID, mean HIV seroprevalence in the Federal Capital Territory was the highest (16.0%; 95%

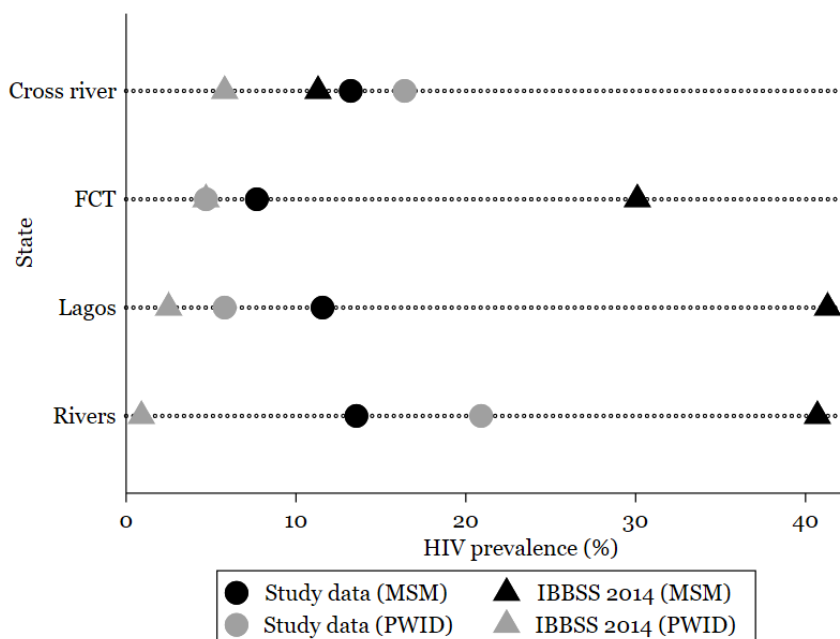
CI 7.5-24.5), followed by Lagos (14.4%; 95% CI 9.5-19.3). The mean seroprevalence in Cross River was 12.3% (95% CI 7.7-16.9), while that among PWID was the lowest in Benue (6.6%; 95% CI 0.6-12.7; Figure 1). Figure 2 shows HIV seroprevalence for the various states compared to previous estimates from the 2014 IBBSS. Findings from the 2014 IBBSS have demonstrated that HIV seroprevalence increased among MSM: from 13.5% in 2007 to 17.2% in 2010 to 23.0% in 2014. Simultaneously, the seroprevalence among PWID decreased from 5.6% in 2007 to 4.2% in 2010 to 3.4% in 2014.

**Figure 1.** HIV seroprevalence among MSM and PWID by state, September 30, 2017. Mean HIV seroprevalence with 95% CIs. FCT: Federal Capital Territory; MSM: men who have sex with men; PWID: people who inject drugs.





**Figure 2.** Comparison of HIV seroprevalence from the study to that in the 2014 IBBSS. The black circles and black triangles represent HIV seroprevalence among MSM as seen in our analysis and the 2014 IBBSS, respectively. The grey circles and grey triangles represent the PWID HIV seroprevalence as seen in our study and the 2014 IBBSS, respectively. FCT: Federal Capital Territory; IBSS: integrated biological and behavioural surveillance survey; MSM: men who have sex with men; PWID: people who inject drugs.

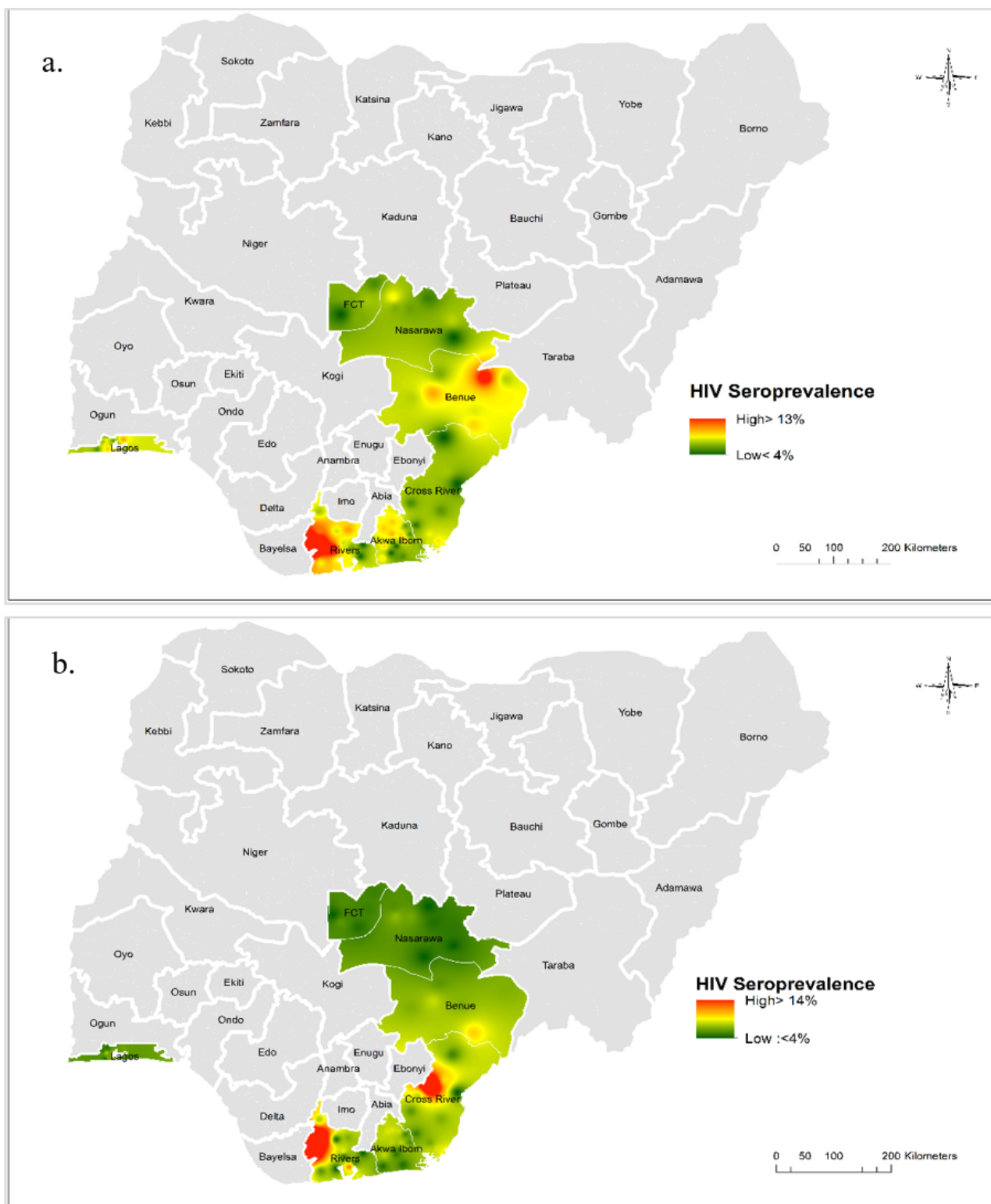


### Variability of HIV Seroprevalence Within Different States

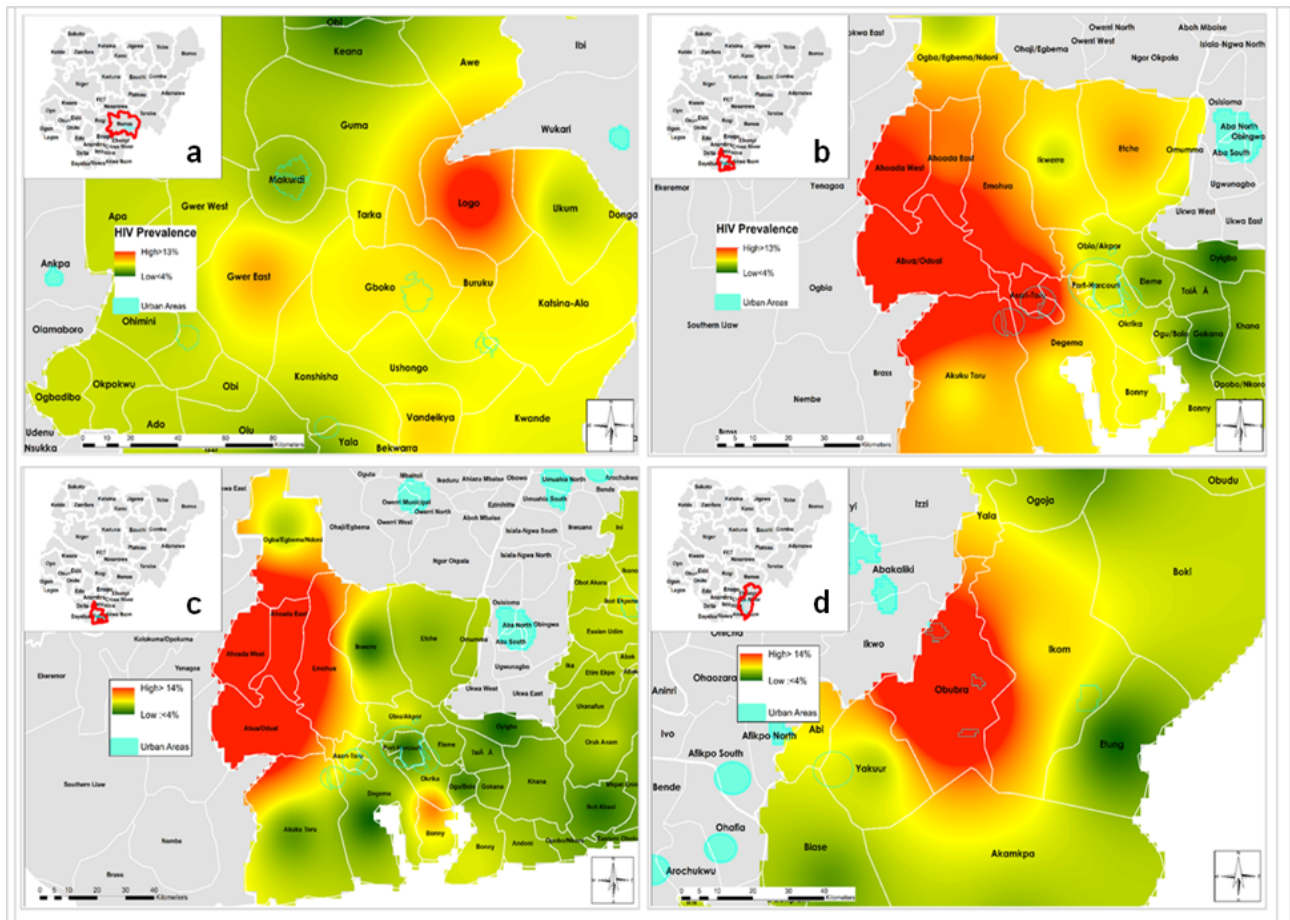
The interpolated HIV seroprevalence map reveals the geospatial distribution of HIV seroprevalence among MSM (Figure 3a, top panel) and PWID (Figure 3b, bottom panel) within various states. Seroprevalence in MSM was higher than in PWID. Large-scale spatial patterns are apparent, and they are more distinct for MSM than for PWID. Among MSM in Benue state, a high seroprevalence (>13%) was evident in the Logo community, while in the Gwer East and Vandeikya LGAs, the seroprevalence was below 10% (Figure 4a). HIV seroprevalence

among MSM in Rivers state was the highest in the Asari-Toru, Emohua, Ahoada East, Ahoada West, and Abua/Odual LGAs (Figure 4b). Similarly, HIV seroprevalence was relatively higher in Rivers among PWID who live outside the mapped urban area settlements in Ahoada East, Ahoada West, Emohua, Abua/Odual, and Bonny (Figure 4c). Notably, in Rivers state, high HIV seroprevalence among MSM was recorded in large urban area settlements in the Asari-Toru LGA. Seroprevalence in Cross River among PWID was highest in urban area settlements in the northern region of the Obubra LGA (Figure 4d).

**Figure 3.** Map of Nigeria showing the interpolated areas with high and low HIV seroprevalence on from October 1, 2016, to September 30, 2017, among men who have sex with men (a) and people who inject drugs (b). Seroprevalence >13% is shown in red, and seroprevalence <4% is shown in green.



**Figure 4.** State level map of Nigeria showing urban locations and interpolated areas with high and low HIV seroprevalence by local government area among men who have sex with men (a: Benue; b: Rivers), and people who inject drugs (c: Rivers; d: Cross River). Seroprevalence >13% is shown in red, and seroprevalence <4% is shown in green.



### Comparison of Program Data and the IBBSS 2014

Clear state differences in HIV seroprevalence between the 2014 IBBSS and our program data were observed for MSM in Lagos (41.3% vs 11.6%), Rivers (40.7% vs 13.6%), and the Federal Capital Territory (30.1% vs 7.7%). Seroprevalence from program data was higher than the seroprevalence from the 2014 IBBSS for MSM in the Cross River state (13.2% versus 11.3%). Seroprevalence among PWID was higher in our program data compared to the 2014 IBBSS data in Lagos (5.8% vs 2.5%), Rivers (20.9% vs 0.9%), and Cross River (16.4% vs 5.8%).

### Detection of Spatial Patterns and Hot Spots of HIV Seroprevalence

The global spatial autocorrelation Moran I statistics confirmed the clustered distribution of HIV seroprevalence among MSM and PWID. We found more significant clustering among PWID ( $z$  score=4.03;  $P<.001$ ) compared to MSM ( $z$  score=2.29;  $P<.02$ ). Getis-Ord-Gi\* statistics indicated significant clusters of HIV infection among MSM and PWID (Multimedia Appendix 1) that were confined to LGAs in the North Central (Abuja Municipal Area Council, Bwari, Karu, Keffi, and Gwer East) and South South (Calabar Municipal, Calabar South, Degema, Odukpani, and Akpabuyo) regions of the country.

## Discussion

### Principal Results

Our study shows a substantial geographic variation in the HIV seroprevalence of both MSM and PWID throughout the study areas. Similarly, mounting evidence suggests a large geographical variation in the sub-Saharan Africa HIV epidemic [37,38]. Although data on MSM in Eastern and Southern Africa are limited, HIV seroprevalence ranges from 2% in Angola to 31% in Zimbabwe [39]. The UNAIDS 2019 report suggests condom use by MSM exceeded 70% in South Africa, Kenya, and Rwanda, and was above 50% in Angola, Comoros, Eswatini, Madagascar, and Mauritius. Lesotho, Malawi, and Tanzania reported levels below 50% at 46%, 44%, and 14%, respectively [39]. Overall, around 1 in 5 (20%) MSM in the region are estimated to be living with HIV [36]. Evidence suggests the majority of the region's MSM engage in heterosexual sex, often with wives or other long-term female partners [39]. The HIV epidemic among MSM is therefore interlaced with the epidemic in the wider population [40]. Kenya, Madagascar, Mauritius, Mozambique, South Africa, Tanzania, and Uganda are all home to PWID populations. Overall, just under a third (30%) of people who inject drugs in these regions are believed to have HIV, and the proportion of new HIV infections arising from injection drug users is estimated to be as high as 75% to 80% percent in Eastern European countries and some areas of South and

Southeast Asia [41]. According to previous study, the majority of PWID in Kenya (89%) reported injecting in groups, and nearly a quarter (27.6%) of those who reported distributive syringe sharing (sharing used syringes with others) reported being infected with HIV [41]. In Tanzania, it is estimated that 15.5% of PWID are living with HIV, with HIV prevalence among women who inject drugs thought to be higher than among their male counterparts [42]. Between 85% to 96% of female PWID engage in transactional sex, and half of those working in transactional sex reported they had never used a condom in the previous 30 days, although just 23% said they still used condoms [43]. In 2018, an estimated 21.8% of people who inject drugs in South Africa lived with HIV [10]. A 2015 study in 5 South African cities found 32% of men and 26% of women who inject drugs regularly shared syringes and other injecting equipment, and nearly half reused needles [44]. Evidence from Kenya, Mauritius, Seychelles, and Tanzania suggests many PWID acquire HIV before the age of 25 years [26]. The interpolated maps in our analysis identified significant clustered patterns of the spatial distribution of HIV seroprevalence in Nigeria that would have been missed using macro-level national data. Spatial clustering of HIV seroprevalence, as shown in our study, can be due to geographic mobility trends, high rates of risky injection and sexual behaviors, and stigma and discrimination. Studies have consistently linked residential instability with high-risk behaviors (eg, syringe sharing and exchanging sex for drugs or money) and HIV infection [45]. Overall, HIV seroprevalence in our study ranged from 9.6% to 13.1% among MSM and from 9.3% to 12.7% among PWID. Seroprevalence was disproportionately distributed across the states. The median seroprevalence of 20.0% (95% CI 1.0-24.0) and 19.0% (95% CI 2.2-23.0) for MSM and PWID, respectively, in the Federal Capital Territory, and 18.5% (95% CI 3.0-23.0) for PWID in Lagos shows a concentrated epidemic among these KPs in Nigeria. Surveillance data have shown that women carry the highest burden of HIV on the African continent, with national-level statistics reporting that women have a higher HIV seroprevalence and incidence than men. These reports are substantiated by findings from our study, which showed that HIV seroprevalence among female PWID was twice as high as that in male PWID (female: 467/2485, 18.79%; male 659/6989, 9.42%).

Our study shows that, relative to the other age groups, MSM aged 50 years and older have higher HIV seroprevalence in all study areas. Our observation is consistent with previous studies suggesting a steady increase in the number of people living with HIV who are 50 years of age and older [46]. A study from Zimbabwe found that more than half of the adults aged 50 years and older included in the analysis had seroconverted after their 50th birthday [47]. Household survey results indicate that people 50 years of age and above are less likely than younger people 15-49 years old to have ever been tested for HIV [42]. In comparison, older persons were found to be less likely to use condoms during the most recent intercourse [48]. In our study, HIV seroprevalence among female PWID was twice as high as that in male PWID, with female PWID having higher HIV seroprevalence across all age groups. Data disaggregated by sex from PWID show considerable geographic variation in HIV prevalence among women who inject drugs (seroprevalence

range 0%-65%) [49]. In Tanzania, 55% of young women (aged 17-25 years) who injected drugs were HIV positive compared with 12% of young men who injected drugs [50]. In a review of sex differences in settings in which HIV seroprevalence among PWID is greater than 20%, women who inject drugs were more likely than their male counterparts to be living with HIV infection (pooled odds ratio 1.18; 95% CI 1.10-1.26) [51]. These findings indicate that the considerable heterogeneity in HIV seroprevalence between and within the study states may be clarified by sex and age-specific behaviors or characteristics.

Among MSM, the substantial decrease in HIV seroprevalence observed in our study data compared to the IBBSS 2014 could be attributed to better surveillance [52] and effectiveness of HIV interventions in the study states over 4 years. The minimum comprehensive package of HIV interventions implemented in these states and targeted at the general population and key population groups included community and facility testing for HIV, linkage of HIV-positive individuals to antiretroviral treatment, and HIV treatment retention to improve viral suppression. The findings from our study are substantiated by reports from the NAHS 2018, which showed a national HIV seroprevalence in Nigeria of 1.4% among adults aged 15-49 years compared to previous national seroprevalence estimates of 3.4% from the 2012 National HIV & AIDS and Reproductive Health Survey. The NAHS also showed that Nigeria had demonstrated steady progress on increasing access to treatment for people living with HIV, adopting a test and treat policy in 2016. Among PWID, our results indicated a higher seroprevalence compared to the 2014 IBBSS. The disproportionately high seroprevalence among PWID in our study compared to the 2014 IBBSS could be linked to the HIV infection distribution pattern among PWID that suggests overlapping risk groups with multiple transmission routes. For example, some PWID are sex workers, buy or trade drugs for sex, or are MSM, and may acquire HIV through sexual and injecting routes [53]. The differences between the program data and the IBBSS in HIV seroprevalence estimates may be due to differences in the sample size and HIV testing strategies. The differences in the proportion of the KPs tested for HIV by the state in the IBBSS suggests low participation in the survey mainly attributable to fear of stigma and criminalization by the Same-Sex Marriage Prohibition Act and discrimination against KPs. Although the IBBSS is implemented by the Federal Ministry of Health through NASCP, the national KP program is implemented by nongovernmental organizations through technical, logistics, and funding support from PEPFAR and bilateral development agencies (ie, United States Agency for International Development [USAID], Centers for Disease Control and Prevention, and the Department of Defense). The program provides all KP types with differentiated HIV testing and treatment services in a friendly and safe space at the community level. KP are extremely mobile [54], but they are more likely to participate in the program because of their regular involvement and consistent engagement with program personnel, i.e., program staff who are KP, and are hired as peer-outreach staff and HIV assessment counselors.

Recent studies outside sub-Saharan Africa have established a high seroprevalence of HIV among overlapping high-risk

populations such as PWID, MSM, and female sex workers. There are multiple transmission routes. Epidemiological studies from 2003 to 2015 in Tijuana, Mexico, reported a pooled HIV seroprevalence of 3.4% among male PWID, but 8% among male PWID who have sex with men, and 5% among male PWID who are clients of female sex workers [51]. Similarly, pooled studies from 2003 to 2015 reported a 5% HIV seroprevalence among female sex workers, indicating a rise from 6.7% among female PWID and 7.3% among female sex workers who inject drugs [51]. The 2018 National Survey on Drug Use and Health in Nigeria reported that PWID constitutes a sizeable proportion of high-risk drug users in Nigeria, with 1 in 5 high-risk drug users injecting drugs [55]. The most common drugs injected in the past year were pharmaceutical opioids, followed by cocaine and heroin. Women who injected drugs were more likely than men to engage in high-risk sexual behaviors, further compounding their risk for acquiring HIV, among other infections [55]. These results corroborate findings from our study that showed a higher seroprevalence of HIV among female PWID than among male PWID.

### Limitations

A fundamental limitation of our study was that criminalization through the Same-Sex Marriage Prohibition Act and discrimination against KPs has driven several KPs underground, limiting the study's overall representation. Consequently, continued discrimination and criminalization of KPs impede access to health services and willingness to participate in surveys. In 2014, the Nigerian government increased the punishment for homosexuality to 14 years in jail. Anyone who assists homosexual couples may face up to 10 years in prison [56]. Mass arrests of suspected gay men in Nigeria have followed. For example, in July 2017, the police arrested 40 men at a private house party [57]. Laws criminalizing homosexuality such as these have pushed MSM into hiding, making them more vulnerable to HIV [58].

At the time of analysis, and in line with the Nigeria KP program, HIV testing data was disaggregated into 4 age categories, 15-19, 20-24, 25-49, and 50+ years. The age range for HIV test results was based purely on the nature of the program, and thus the age range of 25-49 years could not be broken down into broader age categories, which might have influenced the variability of HIV seroprevalence in that age group between MSM and PWID. Given the length of the HIV testing data period (between October 2016 and September 2017), the analysis findings provide valid benchmark evidence for potential program reviews evaluating improvements in the adoption of HIV testing services and tracking practices relevant to the study of HIV seroprevalence variability among KPs. Program data used for this analysis were collected at an aggregate level and did not include individual or patient-level socioeconomic and clinical characteristics of the study population that might have provided further insights into the variation of HIV seropositivity. Due to the unavailability of individual-level data, spatial regression analysis could not be conducted.

Consequently, the unavailability of the individual-level variables might have influenced the spatial analysis results, but the study identified significant subnational clusters of HIV infection that

can be prioritized for tailored HIV prevention and treatment interventions. Identifying areas where the burden of HIV infection is concentrated might play a key role in identifying populations at higher risk of infection. Despite our study method of recruiting MSM and PWID for HIV testing being the same as that for the 2014 IBBSS, sample size variations might have influenced findings. Our study analyzed 89% of MSM and 84% of PWID compared with the 2014 IBBSS.

### Future Work

Further studies are recommended to determine the immediate effect of this prohibitive act on stigma, discrimination, and engagement among MSM in HIV prevention and treatment services in Nigeria. We suggest more studies to explore the risk factors associated with spatial clustering of HIV infection between MSM and PWID.

### Optimizing the Impact of the KP Program

The large sample of KP data collected and used in our study compared to other previous studies can be attributed to the peer outreach model. In this model, KPs are trained as peer-outreach workers to increase demand for tailored HIV services, improve the quality of behavior change communication, and increase access to HIV testing services—the starting point of the KP cascade—via social networks. This approach yielded veritable insights on the KP groups at the LGA level and offers a unique opportunity to estimate national and subnational key population size by scaling up the peer outreach method for data collection in HIV programming. As reflected in our study, the large sample of MSM and PWID data indicates that KPs can be effectively mobilized for HIV testing and treatment despite the legal, policy, and social barriers. Based on the 2018 national KP size estimation carried out by NASCP [59], the total KP in Nigeria is estimated to be 720,000. About three-quarters (69%) of the KP have been tested for HIV under the KP program. In our program, KP's high coverage in HIV testing offers an additional viewpoint on the access and uptake of HIV testing services at the community levels. We acknowledge that while a significant proportion of KPs living with HIV have been tested for HIV by the national program, the study sample might not be representative, as our study did not compare KP characteristics included or not included in the national program. In our study, this was another limitation.

Two studies in Uganda confirmed that program data routinely collected from the prevention of mother - to - child transmission programs can be used to monitor HIV prevalence trends [60,61]. Nigeria has a mixed epidemic, and HIV prevalence is disproportionality distributed among KPs. As we must wait for every 5-years to conduct an IBBSS, which depends entirely on the availability of funds, it is imperative to ensure frequent measurements to monitor changes in new HIV infections. The use of routine program data from groups with high-risk behaviors like MSM and PWID can help monitor trends in HIV seroprevalence at the community level. Identification of high HIV prevalence regions using routine program data can guide timely program management decisions on potential locations to scale up antiretroviral treatment interventions (the era of test and treat). Across several sub-Saharan Africa countries (including Nigeria), UNAIDS currently uses routine program

data in Spectrum Software to estimate the national HIV prevalence and people living with HIV burden. The Spectrum package uses the HIV prevalence over time from routine program data or survey data together with demographic information and epidemiological assumptions to model age-specific HIV prevalence, incidence and mortality rates, and the total number of people living with HIV [62].

## Conclusions

To our knowledge, this study represents the most extensive investigation on HIV seroprevalence among KPs in Sub-Saharan Africa. We showed that there is significant clustering and subnational variation in HIV seroprevalence among MSM and PWID. The geographical variations in HIV seroprevalence revealed by our analysis mean that HIV infection is disproportionately spread across Nigeria and confined to a particular region. To inform HIV prevention and care strategies in the more generalized HIV epidemics across sub-Saharan Africa, including in Nigeria, epidemiological assessment of the geographical heterogeneity of HIV among MSM and PWID is essential. Our results suggest that HIV seroprevalence among

middle-aged adult female PWID is disproportionately greater than among male PWID. PWID could transmit their HIV infection to their sexual contacts and injecting partners, which in turn may lead to the spread of HIV to the general population, particularly in the context of transactional sex. Interventions that significantly focus on women and their sexual and injecting partners are essential to address these high HIV acquisitions and transmission risks among KPs, particularly PWID. The substantial decrease in HIV seroprevalence among MSM as observed in our study data compared to the 2014 IBBSS suggests improvements in the national HIV prevention and treatment programs over the past 4 years. Understanding heterogeneity in mixing patterns among KPs in concentrated HIV epidemics may help in designing more effective interventions. We recommend the use of routine HIV testing service program data for the implementation of HIV infection surveillance among KPs. They should serve as an essential input for statistical models that estimate the national and subnational burden and incidence of HIV using estimation and projections tools.

## Acknowledgments

Data used for this study were collected from the KP program in Nigeria through PEPFAR/USAID. OK was supported by a professorship grant from the Swiss National Science Foundation (grant no. 163878) and a Swiss National Foundation project grant (320030\_192452). We thank the staff of Heartland Alliance Nigeria for their contribution to data collection and data transmission from program implementation states. We thank Ben Spycher for comments on an earlier version of this manuscript. We thank Sara Blough for proofreading the manuscript and providing English editing services.

## Authors' Contributions

AAO conceived of the study, including design and method. He was the principal contributor in the data management, performed the data analysis, and wrote the draft of the manuscript. OK performed critical reviews of the first and final version of the manuscript and provided input into the study and manuscript. AK, MK, UR, and OO provided reviews and feedback at the abstract phase. AJ reviewed and provided input on the final version of the manuscript. All authors approved the final version of the manuscript.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Hot spot analysis (Getis-Ord-Gi\*) of HIV infection distribution among men who have sex with men (a. left) and people who inject drugs (b. right).

[PDF File (Adobe PDF File), 50 KB - [publichealth\\_v7i5e19587\\_app1.pdf](#) ]

## References

1. Tanser F, Barnighausen T, Cooke GS, Newell M. Localized spatial clustering of HIV infections in a widely disseminated rural South African epidemic. *International Journal of Epidemiology* 2009 Mar 04;38(4):1008-1016. [doi: [10.1093/ije/dyp148](#)]
2. Smith AD, Tapsoba P, Peshu N, Sanders EJ, Jaffe HW. Men who have sex with men and HIV/AIDS in sub-Saharan Africa. *Lancet* 2009 Aug 01;374(9687):416-422. [doi: [10.1016/S0140-6736\(09\)61118-1](#)] [Medline: [19616840](#)]
3. Tanser F, de Oliveira T, Maheu-Giroux M, Barnighausen T. Concentrated HIV subepidemics in generalized epidemic settings. *Curr Opin HIV AIDS* 2014 Mar;9(2):115-125 [FREE Full text] [doi: [10.1097/COH.0000000000000034](#)] [Medline: [24356328](#)]
4. Wand H, Ramjee G. Targeting the hotspots: investigating spatial and demographic variations in HIV infection in small communities in South Africa. *J Int AIDS Soc* 2010 Oct 27;13:41 [FREE Full text] [doi: [10.1186/1758-2652-13-41](#)] [Medline: [20979651](#)]

5. Chimoyi LA, Musenge E. Spatial analysis of factors associated with HIV infection among young people in Uganda, 2011. *BMC Public Health* 2014 Jun 05;14:555 [FREE Full text] [doi: [10.1186/1471-2458-14-555](https://doi.org/10.1186/1471-2458-14-555)] [Medline: [24898872](https://pubmed.ncbi.nlm.nih.gov/24898872/)]
6. Local epidemic issues brief. UNAIDS. 2014. URL: [https://www.unaids.org/sites/default/files/media\\_asset/JC2559\\_local-epidemics\\_en.pdf](https://www.unaids.org/sites/default/files/media_asset/JC2559_local-epidemics_en.pdf) [accessed 2021-05-01]
7. Subnational Estimates Working Group of the HIV Modelling Consortium. Evaluation of geospatial methods to generate subnational HIV prevalence estimates for local level planning. *AIDS* 2016 Jun 01;30(9):1467-1474 [FREE Full text] [doi: [10.1097/QAD.0000000000001075](https://doi.org/10.1097/QAD.0000000000001075)] [Medline: [26919737](https://pubmed.ncbi.nlm.nih.gov/26919737/)]
8. Nigeria 2018 HIV/AIDS indicator and impact survey. NAIIS. URL: [naiis.ng/](http://naiis.ng/) [accessed 2021-05-01]
9. NACA. National strategic framework on HIV and AIDS 2017-2021. National Agency for the Control of Aids. URL: <https://naca.gov.ng/2013-national-hiv-validated-data-2-2/> [accessed 2021-05-01]
10. AIDS info. UNAIDS. URL: <http://aidsinfo.unaids.org/> [accessed 2021-05-01]
11. HIV and AIDS in Nigeria. Avert. URL: [www.avert.org/professionals/hiv-around-world/sub-saharan-africa/nigeria](http://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/nigeria) [accessed 2021-05-01]
12. UNAIDS. HIV integrated biological and behavioural surveillance survey 2010. Federal Ministry of Health; Abuja, Nigeria. URL: <https://naca.gov.ng/wp-content/uploads/2016/11/IBBSS-2010.pdf> [accessed 2021-05-01]
13. Hessou PHS, Glele-Ahanhanzo Y, Adekpedjou R, Ahouada C, Johnson RC, Boko M, et al. Comparison of the prevalence rates of HIV infection between men who have sex with men (MSM) and men in the general population in sub-Saharan Africa: a systematic review and meta-analysis. *BMC Public Health* 2019 Dec 04;19(1):1634 [FREE Full text] [doi: [10.1186/s12889-019-8000-x](https://doi.org/10.1186/s12889-019-8000-x)] [Medline: [31801503](https://pubmed.ncbi.nlm.nih.gov/31801503/)]
14. Nigeria GARPR 2015. National Agency for the Control of Aids. URL: [https://naca.gov.ng/nigeria\\_garpr\\_2015\\_report/](https://naca.gov.ng/nigeria_garpr_2015_report/) [accessed 2021-05-01]
15. Hessou PHS, Glele-Ahanhanzo Y, Adekpedjou R, Ahouada C, Johnson RC, Boko M, et al. Comparison of the prevalence rates of HIV infection between men who have sex with men (MSM) and men in the general population in sub-Saharan Africa: a systematic review and meta-analysis. *BMC Public Health* 2019 Dec 04;19(1):1634 [FREE Full text] [doi: [10.1186/s12889-019-8000-x](https://doi.org/10.1186/s12889-019-8000-x)] [Medline: [31801503](https://pubmed.ncbi.nlm.nih.gov/31801503/)]
16. Zeng X, Zhong X, Peng B, Zhang Y, Kong C, Liu X, et al. Prevalence and associated risk characteristics of HIV infection based on anal sexual role among men who have sex with men: a multi-city cross-sectional study in Western China. *Int J Infect Dis* 2016 Aug;49:111-118 [FREE Full text] [doi: [10.1016/j.ijid.2016.06.009](https://doi.org/10.1016/j.ijid.2016.06.009)] [Medline: [27312581](https://pubmed.ncbi.nlm.nih.gov/27312581/)]
17. Bangboye EA, Badru T, Bangboye A. Transactional sex between men and its implications on HIV and sexually transmitted infections in Nigeria. *J Sex Transm Dis* 2017;2017:1810346 [FREE Full text] [doi: [10.1155/2017/1810346](https://doi.org/10.1155/2017/1810346)] [Medline: [28845320](https://pubmed.ncbi.nlm.nih.gov/28845320/)]
18. Djomand G, Quaye S, Sullivan PS. HIV epidemic among key populations in west Africa. *Curr Opin HIV AIDS* 2014 Sep;9(5):506-513 [FREE Full text] [doi: [10.1097/COH.0000000000000090](https://doi.org/10.1097/COH.0000000000000090)] [Medline: [25010898](https://pubmed.ncbi.nlm.nih.gov/25010898/)]
19. Oldenburg CE, Perez-Brumer AG, Reisner SL, Mimiaga MJ. Transactional sex and the HIV epidemic among men who have sex with men (MSM): results from a systematic review and meta-analysis. *AIDS Behav* 2015 Dec;19(12):2177-2183 [FREE Full text] [doi: [10.1007/s10461-015-1010-5](https://doi.org/10.1007/s10461-015-1010-5)] [Medline: [25652233](https://pubmed.ncbi.nlm.nih.gov/25652233/)]
20. Sheehy M, Tun W, Vu L, Adebajo S, Obianwu O, Karlyn A. High levels of bisexual behavior and factors associated with bisexual behavior among men having sex with men (MSM) in Nigeria. *AIDS Care* 2014 Jan;26(1):116-122. [doi: [10.1080/09540121.2013.802281](https://doi.org/10.1080/09540121.2013.802281)] [Medline: [23742663](https://pubmed.ncbi.nlm.nih.gov/23742663/)]
21. Cloete A, Simbayi L, Kalichman S, Strebel A, Henda N. Stigma and discrimination experiences of HIV-positive men who have sex with men in Cape Town, South Africa. *AIDS Care* 2008 Oct;20(9):1105-1110 [FREE Full text] [doi: [10.1080/09540120701842720](https://doi.org/10.1080/09540120701842720)] [Medline: [18608067](https://pubmed.ncbi.nlm.nih.gov/18608067/)]
22. Stahlman S, Bechtold K, Sweitzer S, Mothopeng T, Tarubekera N, Nkonyana J, et al. Sexual identity stigma and social support among men who have sex with men in Lesotho: a qualitative analysis. *Reprod Health Matters* 2015 Nov;23(46):127-135. [doi: [10.1016/j.rhm.2015.11.017](https://doi.org/10.1016/j.rhm.2015.11.017)] [Medline: [26719004](https://pubmed.ncbi.nlm.nih.gov/26719004/)]
23. Same sex marriage prohibition act, 2014. Law Nigeria. URL: <https://lawnigeria.com/2020/01/same-sex-marriage-prohibition-act-2014/> [accessed 2021-05-01]
24. Miles to go—closing gaps, breaking barriers, righting injustices. UNAIDS. 2018. URL: <https://www.unaids.org/en/resources/documents/2018/global-aids-update> [accessed 2021-05-01]
25. Phanuphak N, Lo YR, Shao Y, Solomon SS, O'Connell RJ, Tovnanabutra S, et al. HIV epidemic in Asia: implications for HIV vaccine and other prevention trials. *AIDS Res Hum Retroviruses* 2015 Nov;31(11):1060-1076 [FREE Full text] [doi: [10.1089/aid.2015.0049](https://doi.org/10.1089/aid.2015.0049)] [Medline: [26107771](https://pubmed.ncbi.nlm.nih.gov/26107771/)]
26. Prevention gap report. UNAIDS. 2016. URL: <https://www.unaids.org/en/resources/documents/2016/prevention-gap> [accessed 2021-05-01]
27. Methods for modeling the HIV/AIDS epidemic in sub-Saharan Africa. World Health Organization. URL: <https://www.who.int/healthinfo/paper03.pdf> [accessed 2021-05-01]
28. Salomon JA, Murray CJ. Modelling HIV/AIDS epidemics in sub-Saharan Africa using seroprevalence data from antenatal clinics. *Bull World Health Organ* 2001;79(7):596-607 [FREE Full text] [Medline: [11477962](https://pubmed.ncbi.nlm.nih.gov/11477962/)]

29. Local epidemics issues brief. UNAIDS. 2016. URL: [https://www.unaids.org/en/resources/documents/2014/20140707\\_JC2559\\_local-epidemics](https://www.unaids.org/en/resources/documents/2014/20140707_JC2559_local-epidemics) [accessed 2021-05-01]
30. How AIDS changed everything. UNAIDS. URL: [https://www.unaids.org/en/resources/documents/2015/MDG6\\_15years-15lessonsfromtheAIDSresponse](https://www.unaids.org/en/resources/documents/2015/MDG6_15years-15lessonsfromtheAIDSresponse) [accessed 2021-05-01]
31. Weir SS, Pailman C, Mahlalela X, Coetzee N, Meidany F, Boerma JT. From people to places: focusing AIDS prevention efforts where it matters most. *AIDS* 2003;17(6):895-903. [doi: [10.1097/00002030-200304110-00015](https://doi.org/10.1097/00002030-200304110-00015)]
32. Final Nigeria IBBSS 2014 Report. National Agency for the Control of Aids. URL: <https://naca.gov.ng/final-nigeria-ibbss-2014-report/> [accessed 2021-05-01]
33. Heartland Alliance Nigeria. Integrated most at risk populations hiv prevention program (IMHIPP). Heartland Alliance International. URL: <https://www.heartlandalliance.org/wp-content/uploads/2019/10/About-IMHIPP-Nigeria-Oct2019.pdf> [accessed 2019-10-10]
34. Ending AIDS: progress towards the 90–90–90 targets. UNAIDS. 2017. URL: <http://www.refworld.org/docid/5971f3b24.html> [accessed 2018-10-14]
35. HIV and AIDS in East and Southern Africa regional overview. Avert. URL: <https://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/overview> [accessed 2020-08-25]
36. Nguyen, Bui D, Dinh T, Pham L, Nguyen V, Tran T, team for the implementation research project “Vietnam HIV early antiretroviral therapy with regular HIV testing (V-HEART)”. A prospective “test-and-treat” demonstration project among people who inject drugs in Vietnam. *J Int AIDS Soc* 2018 Jul;21(7):e25151 [FREE Full text] [doi: [10.1002/jia2.25151](https://doi.org/10.1002/jia2.25151)] [Medline: [29984473](https://pubmed.ncbi.nlm.nih.gov/29984473/)]
37. Zulu LC, Kalipeni E, Johannes E. Analyzing spatial clustering and the spatiotemporal nature and trends of HIV/AIDS prevalence using GIS: the case of Malawi, 1994-2010. *BMC Infect Dis* 2014 May 23;14:285 [FREE Full text] [doi: [10.1186/1471-2334-14-285](https://doi.org/10.1186/1471-2334-14-285)] [Medline: [24886573](https://pubmed.ncbi.nlm.nih.gov/24886573/)]
38. Cuadros DF, Awad SF, Abu-Raddad LJ. Mapping HIV clustering: a strategy for identifying populations at high risk of HIV infection in sub-Saharan Africa. *Int J Health Geogr* 2013 May 22;12:28 [FREE Full text] [doi: [10.1186/1476-072X-12-28](https://doi.org/10.1186/1476-072X-12-28)] [Medline: [23692994](https://pubmed.ncbi.nlm.nih.gov/23692994/)]
39. UNAIDS. Communities at the centre: Global AIDS Update 2019. <https://www.unaids.org/en/resources/documents/2019/2019-global-AIDS-update> 2019:12.
40. Getting to Zero: the HIV epidemic in the eastern and southern Africa. UNAIDS. 2013. URL: <https://reliefweb.int/report/world/getting-zero-hiv-epidemic-eastern-and-southern-africa> [accessed 2021-05-01]
41. Rhodes T, Stimson GV, Crofts N, Ball A, Dehne K, Khodakevich L. Drug injecting, rapid HIV spread, and the ‘risk environment’: implications for assessment and response. *AIDS* 1999;13 Suppl A:S259-S269. [Medline: [10885783](https://pubmed.ncbi.nlm.nih.gov/10885783/)]
42. Consensus estimates on key population size and HIV prevalence in Tanzania. National Aids Control Programme (NACP). 2014. URL: <https://www.healthpolicyproject.com/index.cfm?id=publications&get=pubID&pubId=391> [accessed 2021-05-01]
43. Williams ML, McCurdy SA, Bowen AM, Kilonzo GP, Atkinson JS, Ross MW, et al. HIV seroprevalence in a sample of Tanzanian intravenous drug users. *AIDS Educ Prev* 2009 Oct;21(5):474-483 [FREE Full text] [doi: [10.1521/aeap.2009.21.5.474](https://doi.org/10.1521/aeap.2009.21.5.474)] [Medline: [19842830](https://pubmed.ncbi.nlm.nih.gov/19842830/)]
44. Scheibe A, Makapela D, Brown B, dos Santos M, Hariga F, Virk H, et al. HIV prevalence and risk among people who inject drugs in five South African cities. *Int J Drug Policy* 2016 Apr;30:107-115. [doi: [10.1016/j.drugpo.2016.01.004](https://doi.org/10.1016/j.drugpo.2016.01.004)] [Medline: [26860326](https://pubmed.ncbi.nlm.nih.gov/26860326/)]
45. Communities at the centre: Global AIDS Update 2019. UNAIDS. URL: <https://www.unaids.org/en/resources/documents/2019/2019-global-AIDS-update> [accessed 2021-05-01]
46. UNAIDS. HIV And Aging: A Special Supplement to the UNAIDS Report on the Global Aids Epidemic Programme. Geneva: Joint UN Programme on HIV/AIDS; 2013.
47. Negin JCN, Eaton J, Schur N, Gregson S. HIV among older adults in Zimbabwe: Aging with HIV or seroconverting after age 50? 2012 Jul 31 Presented at: International AIDS Conference; 2014 July 20–25; Melbourne p. S1-S5.
48. The gap report. UNAIDS. 2014. URL: [https://www.unaids.org/en/resources/documents/2014/20140716\\_UNAIDS\\_gap\\_report](https://www.unaids.org/en/resources/documents/2014/20140716_UNAIDS_gap_report) [accessed 2021-05-01]
49. Des Jarlais DC, Feelemyer JP, Modi SN, Arasteh K, Hagan H. Are females who inject drugs at higher risk for HIV infection than males who inject drugs: an international systematic review of high seroprevalence areas. *Drug Alcohol Depend* 2012 Jul 01;124(1-2):95-107 [FREE Full text] [doi: [10.1016/j.drugalcdep.2011.12.020](https://doi.org/10.1016/j.drugalcdep.2011.12.020)] [Medline: [22257753](https://pubmed.ncbi.nlm.nih.gov/22257753/)]
50. Atkinson AJ, McCurdy S, Williams M, Mbwambo J, Kilonzo G. HIV risk behaviors, perceived severity of drug use problems, and prior treatment experience in a sample of young heroin injectors in Dar es Salaam, Tanzania. *Afr J Drug Alcohol Stud* 2011;10(1):1-9 [FREE Full text] [Medline: [23024611](https://pubmed.ncbi.nlm.nih.gov/23024611/)]
51. Strathdee SA, Magis-Rodriguez C, Mays VM, Jimenez R, Patterson TL. The emerging HIV epidemic on the Mexico-U.S. border: an international case study characterizing the role of epidemiology in surveillance and response. *Ann Epidemiol* 2012 Jun;22(6):426-438 [FREE Full text] [Medline: [22626001](https://pubmed.ncbi.nlm.nih.gov/22626001/)]
52. HIV and AIDS in Nigeria. Avert. 2019. URL: [avert.org/professionals/hiv-around-world/sub-saharan-africa/nigeria](https://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/nigeria) [accessed 2021-05-01]



53. Martin NK, Vickerman P, Hickman M, Patterson TL, Rand E, Abramovitz D, et al. Overlapping substance using high-risk groups and infectious diseases: how dynamic modelling can evaluate risk and target HIV prevention. *Addiction* 2016 Sep;111(9):1512-1515 [FREE Full text] [doi: [10.1111/add.13338](https://doi.org/10.1111/add.13338)] [Medline: [27075692](https://pubmed.ncbi.nlm.nih.gov/27075692/)]
54. HIV, AIDS and population mobility - overview of the IOM global hiv programme 2006. IOM. 2006. URL: <https://migrationhealthresearch.iom.int/hiv-aids-and-population-mobility-overview-iom-global-hiv-programme-2006> [accessed 2021-05-01]
55. Sylvester. Nigeria, EU and UNODC release first-ever national drug use survey. United Nations Office on Drugs and Crime. 2019. URL: <https://www.unodc.org/nigeria/en/nigeria--eu-and-unodc-release-first-ever-national-drug-use-survey.html> [accessed 2021-05-01]
56. Nigeria GARPR 2015 report. National Agency for the Control of Aids. URL: [https://naca.gov.ng/nigeria\\_garpr\\_2015\\_report/](https://naca.gov.ng/nigeria_garpr_2015_report/) [accessed 2021-05-01]
57. Mass arrest of 40 gay men in Nigeria may harm HIV fight: activist. Reuters. 2017 Jul 31. URL: <https://www.reuters.com/article/us-nigeria-gay-idUSKBN1AG21W> [accessed 2021-05-01]
58. HIV, the law and human rights in the African human rights system: key challenges and opportunities for rights-based responses. The African Commission on Human & Peoples' Rights. URL: [https://www.achpr.org/public/Document/file/English/africancommission\\_hiv\\_report\\_full\\_eng.pdf](https://www.achpr.org/public/Document/file/English/africancommission_hiv_report_full_eng.pdf) [accessed 2021-05-01]
59. McIntyre A, Mitchell A, Nwafor S, Sebastian V, Schwitters AM, Lo J, et al. Key population size estimation in nigeria: novel approaches to sampling and analysis. 2020 Presented at: CROI Conference; 2021 Mar 8-11; Boston URL: <https://www.croiconference.org/abstract/key-population-size-estimation-in-nigeria-novel-approaches-to-sampling-and-analysis/>
60. Mpairwe H, Muhangi L, Namujju PB, Kisitu A, Tumusiime A, Muwanga M, et al. HIV risk perception and prevalence in a program for prevention of mother-to-child HIV transmission: comparison of women who accept voluntary counseling and testing and those tested anonymously. *J Acquir Immune Defic Syndr* 2005 Jul 01;39(3):354-358. [doi: [10.1097/01.qai.0000148081.38331.92](https://doi.org/10.1097/01.qai.0000148081.38331.92)] [Medline: [15980698](https://pubmed.ncbi.nlm.nih.gov/15980698/)]
61. Fabiani M, Nattabi B, Ayella EO, Ogwang M, Declich S. Using prevalence data from the programme for the prevention of mother-to-child-transmission for HIV-1 surveillance in North Uganda. *AIDS* 2005 May 20;19(8):823-827. [doi: [10.1097/01.aids.0000168977.51843.d6](https://doi.org/10.1097/01.aids.0000168977.51843.d6)] [Medline: [15867497](https://pubmed.ncbi.nlm.nih.gov/15867497/)]
62. Stover J. Projecting the demographic consequences of adult HIV prevalence trends: the Spectrum Projection Package. *Sex Transm Infect* 2004 Aug;80 Suppl 1:i14-i18 [FREE Full text] [doi: [10.1136/sti.2004.010157](https://doi.org/10.1136/sti.2004.010157)] [Medline: [15249694](https://pubmed.ncbi.nlm.nih.gov/15249694/)]

## Abbreviations

**IBBSS:** integrated biological and behavioral surveillance survey

**KP:** key population

**LGA:** local government area

**MSM:** men who have sex with men

**NAIIS:** Nigeria AIDS Indicator and Impact Survey

**NASCP:** National AIDS & STIs Control Programme

**PEPFAR:** The President's Emergency Plan for AIDS Relief

**PWID:** people who inject drugs

**UNAIDS:** the Joint United Nations Programme on HIV/AIDS

**USAID:** United States Agency for International Development

*Edited by T Sanchez; submitted 23.04.20; peer-reviewed by A Algarin, R Poluru, T Torres; comments to author 15.05.20; revised version received 25.07.20; accepted 26.02.21; published 24.05.21.*

*Please cite as:*

Onovo A, Kalaiwo A, Katbi M, Ogorry O, Jaquet A, Keiser O

*Geographical Disparities in HIV Seroprevalence Among Men Who Have Sex with Men and People Who Inject Drugs in Nigeria: Exploratory Spatial Data Analysis*

*JMIR Public Health Surveill* 2021;7(5):e19587

URL: <https://publichealth.jmir.org/2021/5/e19587>

doi: [10.2196/19587](https://doi.org/10.2196/19587)

PMID: [34028360](https://pubmed.ncbi.nlm.nih.gov/34028360/)

©Amobi Onovo, Abiye Kalaiwo, Moses Katbi, Otse Ogorry, Antoine Jaquet, Olivia Keiser. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 24.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use,

distribution, and reproduction in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# Burden of Cervical Cancer in the Eastern Mediterranean Region During the Years 2000 and 2017: Retrospective Data Analysis of the Global Burden of Disease Study

Fereshteh Safaeian<sup>1\*</sup>, MPH; Shidrokh Ghaemimood<sup>1\*</sup>, MPH; Ziad El-Khatib<sup>2</sup>, MSc, EMBA, PhD; Sahba Enayati<sup>3</sup>, MD; Roksana Mirkazemi<sup>1</sup>, PhD; Bruce Reeder<sup>4</sup>, MD

<sup>1</sup>Public Health Graduate Studies, The Bahá'í Institute for Higher Education, Tehran, Iran

<sup>2</sup>World Health Programme, Université du Québec en Abitibi-Témiscamingue, Québec, QC, Canada

<sup>3</sup>Internal Medicine and Cardiology, Kompetenzcenter Gesundheit, St Stephan, Wels, Austria

<sup>4</sup>Department of Community Health and Epidemiology, University of Saskatchewan, Saskatoon, SK, Canada

\*these authors contributed equally

**Corresponding Author:**

Shidrokh Ghaemimood, MPH

Public Health Graduate Studies

The Bahá'í Institute for Higher Education

Tehran

Iran

Phone: 98 9388520250

Email: [shidrokh.ghaemi@gmail.com](mailto:shidrokh.ghaemi@gmail.com)

## Abstract

**Background:** Cervical cancer is a growing health concern, especially in resource-limited settings.

**Objective:** The objective of this study was to assess the burden of cervical cancer mortality and disability-adjusted life years (DALYs) in the Eastern Mediterranean Region (EMR) and globally between the years 2000 and 2017 by using a pooled data analysis approach.

**Methods:** We used an ecological approach at the country level. This included extracting data from publicly available databases and linking them together in the following 3 steps: (1) extraction of data from the Global Burden of Disease (GBD) study in the years 2000 and 2017, (2) categorization of EMR countries according to the World Bank gross domestic product per capita, and (3) linking age-specific population data from the Population Statistics Division of the United Nations (20-29 years, 30-49 years, and >50 years) and GBD's data with gross national income per capita and globally extracted data, including cervical cancer mortality and DALY numbers and rates per country. The cervical cancer mortality rate was provided by the GBD study using the following formula: number of cervical cancer deaths × 100,000/female population in the respective age group.

**Results:** The absolute number of deaths due to cervical cancer increased from the year 2000 (n=6326) to the year 2017 (n=8537) in the EMR; however, the mortality rate due to this disease decreased from the year 2000 (2.7 per 100,000) to the year 2017 (2.5 per 100,000). According to age-specific data, the age group ≥50 years showed the highest mortality rate in both EMR countries and globally, and the age group of 20-29 years showed the lowest mortality rate both globally and in the EMR countries. Further, the rates of cervical cancer DALYs in the EMR were lower compared to the global rates (2.7 vs 6.8 in 2000 and 2.5 vs 6.8 in 2017 for mortality rate per 100,000; 95.8 vs 222.2 in 2000 and 86.3 vs 211.8 in 2017 for DALY rate per 100,000; respectively). However, the relative difference in the number of DALYs due to cervical cancer between the year 2000 and year 2017 in the EMR was higher than that reported globally (34.9 vs 24.0 for the number of deaths and 23.5 vs 18.1 for the number of DALYs, respectively).

**Conclusions:** We found an increase in the burden of cervical cancer in the EMR as per the data on the absolute number of deaths and DALYs. Further, we found that the health care system has an increased number of cases to deal with, despite the decrease in the absolute number of deaths and DALYs. Cervical cancer is preventable if human papilloma vaccination is taken and early screening is performed. Therefore, we recommend identifying effective vaccination programs and interventions to reduce the burden of this disease.

**KEYWORDS**

cervical cancer; Eastern Mediterranean Region; burden of disease; cancer; burden; inequality; mortality; preventable disease

## Introduction

Globally, cervical cancer is one of the leading causes of mortality in women [1] mainly due to human papillomavirus (HPV) infection, smoking, and other risk factors [2]. Although cervical cancer is highly preventable [3], it contributes to the death of 260,000 women each year, of which nearly 85% occur in low- and middle-income countries (LMICs) [4]. Global cervical cancer incidence has increased from 378,000 cases in 1980 to 454,000 cases in 2010—an annual rate increase of 0.6% [5]. New cases of cervical cancer occur in all age groups more often in LMICs than in high-income countries (HICs), where 46,000 persons out of 200,000 persons are in the age range of 15-49 years [5]. Additionally, there is a link between cervical cancer and global inequalities, especially in the LMICs [6,7]. The cervical cancer mortality rate has decreased in HICs owing to effective screening, access to treatment, and vaccinations. Currently, the major burden of cervical cancer is present in the LMICs [8].

The Eastern Mediterranean Region (EMR) consists of 22 countries in the Middle East, North Africa, the Horn of Africa, and Central Asia. This region includes some of the greatest social inequalities within countries and between countries in the world [9]. Health disparities in this region are paralleled with disparities in socioeconomic development [10]. The profile of cancer prevalence in the EMR in 2017 showed that the highest proportions of cervical cancer were found in North Africa and the Horn of Africa [11]. In these countries, nationwide programs of cervical cancer screening do not exist or are based on a limited opportunistic cytology-based screening, which often lacks quality assurance [12].

This study examined the burden of cervical cancer and potential differences within the countries in the EMR in relation to the level of national economic development and age of the patients. The objective of this study was to assess the burden of cervical cancer mortality and disability-adjusted life years (DALYs) as the number of years lost due to disability or early death because of cervical cancer in countries of the EMR and globally. The following research questions were investigated:

1. What is the pattern of mortality and DALYs due to cervical cancer in the EMR and globally? Further, what changes in this pattern have occurred between the years 2000 and 2017?
2. Do these rates differ by the level of national economic development and age of the population?

## Methods

### Data Sources

This was an ecological study that was conducted at the country level. Three publicly available databases were linked together in a three-step process. The first step consisted of extracting

cervical cancer data at the country level from the Global Burden of Disease (GBD) study in 2000 and 2017 [13] to provide the numbers and rates of cervical cancer mortality as well as the numbers and rates of DALYs. We chose the data from the years 2000 and 2017 as the most recent data available from the cancer registry system.

### Measures and Analyses

The EMR consists of the following 22 countries: Afghanistan, Bahrain, Djibouti, Egypt, Iraq, Iran, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Palestine (West Bank and Gaza), Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, and the United Arab Emirates [14]. The cervical cancer mortality of 122 countries was expressed as the overall mortality and DALYs (number and rates) in the GBD study. As the countries vary significantly in terms of their levels of economic development, they were stratified, in the second step, to 3 standard world economy groups according to the World Bank definition based on the gross national income per capita in 2017: HICs at >US \$12,056, MICs at US \$996-12,055, and low-income countries (LICs) at <US \$995 [14]. The LICs are Afghanistan and Somalia. The MICs are Djibouti, Egypt, Iraq, Iran, Jordan, Lebanon, Libya, Morocco, Pakistan, Palestine (West Bank and Gaza), Sudan, Syria, Yemen, and Tunisia. The HICs are Bahrain, Saudi Arabia, Kuwait, Oman, Qatar, and the United Arab Emirates [14]. The third step included extracting age-specific population data (rate and frequency) from the Population Statistics Division of the United Nations [15]. This was necessary as the GBD study data were different from those of the Population Statistics Division and they provide no rates at regional or income level.

Cervical cancer mortality rates and DALY rates per 100,000 persons were extracted from the GBD database for people older than 20 years at the country level in the years 2000 and 2017 and then combined for an EMR average (n=22) and global average of EMR plus all other countries (n=122). The mortality rate formula was as follows: cervical cancer deaths (n) × 100,000/female population in the respective age group. The results were then stratified by the 3 income levels (high, middle, low) and 3 age groups (20-29 years, 30-49 years, ≥50 years). The burden of cervical cancer mortality was presented through the compilation of 3 variables: (1) average mortality rates per 100,000 with minimum and maximum values to provide the range as a measure of spread for cervical cancer mortality and mortality from other diseases, (2) DALYs as a measure of total burden, whereby 1 DALY represents 1 healthy year of life lost to cervical cancer; the GBD study did estimate DALYs by summing the fatal burden (years of life lost) and nonfatal burden (years of life with disability) due to cervical cancer [16], and (3) relative difference (%) and absolute difference between years 2000 and 2017 to show the comparative changes in deaths and DALY numbers. The absolute difference equals the difference between the 2 comparing numbers of years 2000 and 2017. The relative difference is equal to the value of the absolute

difference divided by the value in the year 2000, and then we multiplied it by 100 [17].

## Results

The rates of cervical cancer mortality and DALYs in the EMR were lower than the global rates; however, the relative difference in the number of deaths and DALYs due to cervical cancer between the years 2000 and 2017 in the EMR was higher than that of the global data. Further, according to age-specific data, the age group of  $\geq 50$  years had the highest mortality rates in both EMR countries and globally and the age group of 20-29 years had the lowest mortality rate both globally and in the EMR countries. The EMR average mortality rate due to cervical cancer was lower than the global average for both reference years and all 3 income levels (Table 1). Within income levels, the differences between EMR countries and the global average is the most remarkable in the HICs. During the period 2000-2017, there was a decline in the mortality rate in the

LMICs, both globally and in the EMR. Although there was a decline in the average mortality rate in the EMR, there was an increase in the mortality rates in Egypt, Iran, Libya, Morocco, Syria, Tunisia, and Yemen. Further, although the mortality rate in the EMR according to the 3 income levels compared to the global mortality rate was lower, the relative difference in the number of deaths compared to the global relative difference in the number of deaths was higher (Table 1). The relative change in the number of deaths due to cervical cancer in the EMR for all income levels over the course of 2000 and 2017 was greater than that seen globally (relative difference 34.9 vs 24.0, respectively) (Table 1). In the EMR, the HICs showed the greatest relative increase in the number of deaths (85.5%), and among LICs, Afghanistan had greater relative increase compared to Somalia. Among MICs, Iran had the greatest relative difference and Iraq had the lowest; among the HICs, United Arab Emirates showed the greatest relative increase and Bahrain the lowest (Table 1).

**Table 1.** Cervical cancer mortality among women older than 20 years in the Eastern Mediterranean Region by country and income level compared to the global average in the years 2000 and 2017.

Group by income level, country	Cervical cancer mortality rate per 100,000 women in year 2000, mean (min-max)	Cervical cancer deaths (n) in year 2000	Cervical cancer mortality rate per 100,000 women in year 2017, mean (min-max)	Cervical cancer deaths (n) in year 2017	Relative difference (%) in the number of deaths between years 2000 and 2017 <sup>a</sup>	Absolute difference in the number of deaths between years 2000 and 2017 <sup>b</sup>
Low-income countries globally	12.4 (9.1-16.2)	26,884	10.0 (7.1-13.6)	33,591	24.9	6707
<b>Low-income countries in the EMR<sup>c</sup></b>	10.7 (6.3-15.0)	1448	7.9 (4.7-11.5)	1930	33.3	482
Afghanistan	5.3 (1.9-7.9)	468	3.9 (1.7-5.7)	631	34.9	163
Somalia	20.9 (14.7-28.3)	980	15.8 (10.6-22.9)	1299	32.5	319
Middle-income countries globally	6.5 (5.7-7.7)	149,272	6.7 (5.4-8.0)	192,643	29.1	43,370
<b>Middle-income countries in the EMR</b>	2.3 (1.9-2.8)	4755	2.2 (1.6-2.8)	6380	34.2	1625
Djibouti	16.0 (10.6-22.9)	48	13.8 (8.7-21.8)	72	50.4	24
Egypt	0.9 (0.8-1.0)	292	1.0 (0.8-1.2)	449	53.6	157
Iran	1.2 (1.0-1.3)	397	1.8 (1.4-1.9)	726	82.7	329
Iraq	1.5 (1.0-2.1)	186	0.8 (0.7-0.9)	168	-9.4	-18
Jordan	1.5 (1.2-1.9)	35	1.0 (0.8-1.3)	48	37.2	13
Lebanon	2.4 (2.0-2.8)	63	2.0 (1.7-2.3)	82	31.2	20
Libya	2.5 (2.0-3.0)	61	3.2 (2.4-4.1)	106	74.4	45
Morocco	5.5 (4.5-6.4)	823	5.7 (4.1-7.5)	1011	22.8	187
Pakistan	3.3 (2.8-3.8)	2213	2.8 (2.0-3.8)	2886	30.4	673
Palestine	1.2 (1.0-1.4)	18	1.2 (0.9-1.4)	28	56.2	10
Syria	0.9 (0.8-1.1)	73	1.1 (0.8-1.4)	98	34.1	25
Tunisia	2.4 (2.0-2.9)	119	2.5 (1.8-3.4)	145	22.5	27
Sudan	1.8 (1.0-2.6)	242	1.4 (0.9-2.0)	281	15.9	39
Yemen	0.9 (0.8-1.1)	185	1.9 (1.2-2.6)	279	50.8	94
High-income countries globally	6.0 (5.8-6.2)	32,475	5.4 (5.0-5.9)	32,444	-0.1	-31
<b>High-income countries in the EMR</b>	1.0 (0.8-1.2)	123	1.0 (0.8-1.4)	227	85.5	105
Bahrain	1.9 (1.7-2.3)	5	1.5 (1.2-1.8)	8	51.1	3
Kuwait	1.1 (1.0-1.1)	8	0.7 (0.6-0.8)	14	59.5	5
Oman	1.7 (1.2-2.2)	17	1.5 (1.1-1.8)	23	35.9	6
Qatar	1.4 (1.1-1.8)	3	1.0 (0.7-1.2)	6	122.9	4
Saudi Arabia	0.7 (0.6-0.9)	68	0.8 (0.6-1.1)	117	71.1	49
United Arab Emirates	2.0 (1.5-2.4)	21	2.3 (1.7-3.1)	60	187.2	39
Global average (122 countries)	6.8 (6.4-7.6)	208,631	6.8 (6.3-7.1)	258,678	24.0	50,047
EMR average (22 countries)	2.7 (2.1-3.4)	6326	2.5 (1.8-3.4)	8537	34.9	2211

<sup>a</sup>Relative difference (%) in the number of deaths = (absolute difference in the number of deaths/number of cervical cancer deaths in 2000)\*100.

<sup>b</sup>Absolute difference in the number of deaths = number of cervical cancer deaths in 2017 – number of cervical cancer deaths in 2000.

<sup>c</sup>EMR: Eastern Mediterranean Region.

DALYs due to cervical cancer by income level globally and in EMR countries have been shown in Table 2. The LICs had the highest rates of DALYs both globally and in the EMR, with rates in the EMR exceeding those seen globally. Somalia had the highest rate of 761.5 DALYs in 2000 and 554.5 DALYs in

2017. The MICs in the EMR had a lower DALY rate than other countries globally in both reference years. Within this income level, Djibouti had the highest rate of 585.7 DALYs in 2000 and 497.6 DALYs in 2017. Globally, HICs showed a decline in the DALYs in 2017 whereas HICs in the EMR showed an

increase in 2017. Within this income level, Emirates and Bahrain had the highest rate of 65.6 DALYs per 100,000 in the year 2000 and Emirates had the highest rate of 81.9 DALYs per 100,000 in the year 2017 (Table 2). The relative difference in the number of DALYs in the EMR for the 3 income levels was higher than that in the DALYs globally (Table 2). Among LICs in the EMR, Afghanistan had the highest relative difference in

the number of DALYs and among the MICs in the EMR, Libya had the highest relative difference and Iraq had the lowest relative difference in the number of DALYs. Among the HICs in the EMR, Emirates had the highest relative difference in the number of DALYs and Oman had the lowest relative difference in the number of DALYs (Table 2).

**Table 2.** Disability-adjusted life years data due to cervical cancer among women older than 20 years in the Eastern Mediterranean Region by country and income level compared to the global average in the years 2000 and 2017.

Group by income level, country	Cervical cancer DALY <sup>a</sup> rate per 100,000 women in year 2000, mean (min-max)	DALY number in year 2000	Cervical cancer DALY rate per 100,000 women in year 2017, mean (min-max) <sup>c</sup>	DALY number in year 2017	Relative difference (%) in the number of DALYs between years 2000 and 2017 <sup>b</sup>	Absolute difference in the number of DALYs between years 2000 and 2017 <sup>c</sup>
Low-income countries globally	435.3 (312.8-566.6)	941,128	343.9 (239.4-472.8)	1,157,715	23.0	216,587
<b>Low-income countries in the EMR<sup>d</sup></b>	388.8 (227.8-553.0)	52,554	287.0 (162.8-424.4)	69,812	32.8	17,258
Afghanistan	191.2 (65.2-296.4)	16,895	150.6 (64.5-227.1)	24,265	43.6	7371
Somalia	761.5 (534.7-1037.1)	35,659	554.5 (355.7-811.5)	45,546	27.7	9887
Middle-income countries globally	217.4 (187.6-260.8)	5,003,701	213.0 (167.5-255.4)	6,086,292	21.6	1,082,592
<b>Middle-income countries in the EMR</b>	80.5 (64.7-97.8)	165,567	73.3 (52.9-98.2)	216,480	30.8	50,913
Djibouti	585.7 (389.7-840.8)	1754	497.6 (308.6-795.5)	2598	48.1	844
Egypt	31.2 (27.1-36.3)	10,191	32.3 (25.7-40.2)	15,065	47.8	4875
Iran	39.5 (33.3-43.3)	13,058	51.8 (41.6-55.6)	20,993	60.8	7936
Iraq	51.8 (32.5-74.8)	6619	26.8 (22.2-32.4)	5636	-14.9	-983
Jordan	52.2 (42.9-64.8)	1223	29.8 (22.9-39.4)	1482	21.2	259
Lebanon	77.4 (63.4-91.9)	2043	59.3 (49.4-72.1)	2505	22.6	461
Libya	85.0 (68.0-104.7)	2092	112.2 (81.8-145.0)	3758	79.7	1667
Morocco	182.7 (147.2-215.1)	27,265	181.1 (131.0-239.0)	31,984	17.3	4720
Pakistan	118.4 (100.9-139.9)	80,013	100.8 (71.4-141.5)	105,213	31.5	25,200
Palestine	36.6 (29.3-42.7)	545	34.7 (26.2-41.2)	825	51.5	280
Syria	32.0 (26.8-39.2)	2592	34.3 (25.1-44.2)	3051	17.7	459
Tunisia	73.4 (59.7-87.3)	3604	71.0 (50.7-94.7)	4075	13.1	471
Sudan	60.8 (31.9-90.8)	8142	48.5 (28.6-69.5)	9644	18.5	1502
Yemen	70.4 (38.8-105.6)	6426	64.1 (39.1-92.6)	9648	50.1	3222
High-income countries globally	158.4 (152.4-164.8)	854,589	131.7 (119.7-144.8)	787,560	-7.8	-67,028
<b>High-income countries in the EMR</b>	32.8 (26.7-41.1)	4193	38.0 (28.7-50.3)	8274	97.3	4081
Bahrain	65.6 (57.3-78.7)	183	46.8 (39.2-57.1)	261	42.9	78
Kuwait	39.3 (35.7-43.2)	315	26.5 (22.9-30.5)	515	63.5	200
Oman	58.9 (42.9-78.7)	598	50.6 (38.1-64.3)	790	32.2	193
Qatar	47.7 (37.6-61.5)	99	33.8 (25.5-44.0)	228	131.7	130
Saudi Arabia	24.4 (20.2-30.7)	2302	30.1 (22.8-40.4)	4348	88.9	2046
United Arab Emirates	65.6 (51.8-82.0)	697	81.9 (58.6-111.6)	2132	205.8	1435
Global average (122 countries)	222.2 (206.2-245.9)	6,799,418	211.8 (197.8-220.8)	8,031,567	18.1	1,232,149



Group by income level, country	Cervical cancer DALY <sup>a</sup> rate per 100,000 women in year 2000, mean (min-max)	DALY number in year 2000	Cervical cancer DALY rate per 100,000 women in year 2017, mean (min-max) <sup>c</sup>	DALY number in year 2017	Relative difference (%) in the number of DALYs between years 2000 and 2017 <sup>b</sup>	Absolute difference in the number of DALYs between years 2000 and 2017 <sup>c</sup>
EMR average (22 countries)	95.8 (72.1-121.2)	222,314	86.3 (59.2-118.4)	294,566	32.5	72,252

<sup>a</sup>DALY: disability-adjusted life year.

<sup>b</sup>Relative difference (%) in the number of DALYs = (absolute difference in the number of DALYs/number of cervical cancer DALYs in 2000)\*100.

<sup>c</sup>Absolute difference in the number of DALYs = number of cervical cancer DALYs in 2017 – number of cervical cancer DALYs in 2000.

<sup>d</sup>EMR: Eastern Mediterranean Region.

The age group of  $\geq 50$  years had the highest mortality rate in both EMR countries and globally and the age group of 20-29 years showed the lowest mortality rate both globally and in the EMR countries. Among EMR countries, Somalia and Djibouti showed the highest mortality rate in all the age groups. Kuwait had the lowest mortality rate for the age group of  $\geq 50$  years (5.9 per 100,000 in 2000 and 3.3 per 100,000 in 2017) and Qatar had the lowest mortality rate in the age group of 30-49 years (1.5 per 100,000 in 2000 and 0.7 per 100,000 in 2017). Oman had the lowest mortality rate of 0 per 100,000 in 2017 for the age group of 20-29 years (Table 3).

The relative difference in the number of deaths between 2000 and 2017 in EMR-LICs for age groups 20-29 years and 30-49 years was higher than the global difference (12.8% and 49.6%

vs 4.7% and 21.9, respectively), but it was lower for the age group  $>50$  years (25.1% vs 27.3%) (Table 3). In MICs, this variable in EMR countries was lower than that seen globally for the age groups 20-29 years and 30-49 years (13.5% and 27.4% vs -24.4% and 4.3%, respectively), but it was higher for the age group  $>50$  years (39.0% vs 43.7%). The relative difference in the number of deaths in EMR-HICs for the 3 age groups was higher than that reported globally (25.6%, 110%, and 74.8% vs -16.5%, -26.9%, and 6.7%, respectively). Among the EMR countries, the United Arab Emirates and Saudi Arabia showed an increase in the relative difference in the number of deaths in 2017. Further, in the EMR-MICs, Egypt, Iran, Libya, and Syria showed an increase in the relative difference in the number of deaths in 2017, while LICs showed a decrease in the relative difference in 2017 (Table 3).

**Table 3.** Cervical cancer mortality rates among women older than 20 years in the Eastern Mediterranean Region by age, country, and income level compared to the global average in the years 2000 and 2017.

Group by income level, country	Average cervical cancer mortality rate per 100,000 women by age range						Relative difference (%) in the number of deaths between years 2000 and 2017 <sup>a</sup>		
	Year 2000, mean (min-max)			Year 2017, mean (min-max)			20-29 years	30-49 years	≥50 years
	20-29 years	30-49 years	≥50 years	20-29 years	30-49 years	≥50 years			
Low-income countries globally	2.5 (1.3-4.2)	53.0 (32.3-79.4)	94.8 (67.8-127.6)	1.6 (0.8-2.9)	38.2 (22.6-59.8)	77.4 (53.7-107.7)	4.7	21.9	27.3
<b>Low-income countries in the EMR<sup>b</sup></b>	2.0 (0.8-3.7)	57.8 (28.7-96.4)	72.2 (42.6-101.8)	1.5 (0.7-2.9)	34.6 (16.1-59.7)	72.9 (44.5-106.7)	12.8	49.6	25.1
Afghanistan	1.3 (0.4-2.7)	31.1 (8.6-57.8)	34.8 (14.4-52.0)	1.1 (0.4-2.1)	20.6 (7.0-36.8)	31.9 (16.2-45.6)	19.7	105.0	-0.1
Somalia	3.3 (1.7-5.7)	90.8 (53.5-143.2)	153.2 (108.4-208.4)	2.4 (1.2-4.5)	65.6 (36.6-109.1)	135.3 (90.3-201.5)	7.1	26.1	37.5
Middle-income countries globally	1.0 (0.7-1.4)	16.9 (13.5-21.3)	31.8 (27.7-38.4)	0.6 (0.4-0.9)	13.0 (9.5-16.6)	26.6 (21.1-32.0)	-24.4	4.3	43.7
<b>Middle-income countries in the EMR</b>	0.5 (0.3-0.8)	7.7 (4.9-11.3)	15.9 (12.3-19.7)	0.4 (0.2-0.8)	5.7 (3.4-8.9)	13.3 (9.7-17.7)	13.5	27.4	39.0
Djibouti	2.1 (1.1-3.7)	63.2 (37.1-101.8)	113.9 (75.3-159.5)	1.3 (0.6-2.4)	41.8 (23.2-71.6)	78.7 (50.3-121.1)	8.1	49.1	53.1
Egypt	0.1 (0.1-0.2)	2.8 (1.9-4.0)	6.3 (5.1-7.6)	0.1 (0.1-0.2)	2.6 (1.6-3.8)	6.7 (5.1-8.6)	34.2	35.8	64.6
Iran	0.2 (0.2-0.3)	3.3 (2.7-3.8)	8.5 (7.2-9.5)	0.2 (0.1-0.2)	2.5 (2.0-2.8)	10.2 (7.9-11.1)	-21.4	37.3	109.0
Iraq	0.3 (0.5-0.1)	6.3 (3.1-10.3)	11.9 (9.0-16.4)	0.1 (0.1-0.2)	2.3 (3.3-1.6)	5.6 (4.6-6.7)	-23.3	-24.1	0.6
Jordan	0.2 (0.1-0.4)	5.8 (3.9-8.2)	12.4 (10.0-16.6)	0.1 (0.0-0.1)	1.9 (1.2-2.9)	7.5 (5.7-10.3)	-26.5	5.2	56.9
Lebanon	0.3 (0.2-0.5)	7.2 (4.7-10.5)	15.4 (12.3-19.0)	0.2 (0.1-0.3)	4.0 (2.6-5.8)	12.2 (9.6-15.2)	2.8	20.4	36.6
Libya	0.4 (0.2-0.7)	8.8 (5.7-12.9)	16.9 (13.1-22.2)	0.3 (0.2-0.6)	7.8 (4.7-11.9)	15.4 (11.3-20.6)	-0.3	97.8	65.9
Morocco	0.5 (0.3-0.9)	15.5 (9.9-22.1)	30.6 (23.5-37.0)	0.4 (0.2-0.7)	11.1 (6.6-17.3)	23.8 (17.3-31.2)	-12.6	1.8	32.8
Pakistan	1.1 (0.6-1.7)	11.8 (7.8-17.0)	20.8 (16.5-25.3)	0.8 (0.4-1.6)	9.0 (5.3-14.5)	17.1 (12.5-24.2)	24.3	37.6	27.1
Palestine	0.2 (0.1-0.2)	3.8 (2.5-5.4)	13.8 (11.0-16.5)	0.1 (0.1-0.2)	2.6 (1.7-3.8)	12.1 (8.8-14.7)	18.0	40.8	62.6
Syria	0.2 (0.1-0.3)	3.6 (2.5-5.1)	7.0 (5.8-8.9)	0.1 (0.1-0.2)	2.2 (1.4-3.6)	6.5 (5.0-8.1)	-48.4	-6.4	63.6
Tunisia	0.2 (0.1-0.3)	5.4 (3.5-7.7)	14.3 (11.6-18.0)	0.1 (0.1-0.2)	3.4 (2.0-5.3)	11.2 (8.0-15.3)	-33.2	-10.9	35.6

Group by income level, country	Average cervical cancer mortality rate per 100,000 women by age range						Relative difference (%) in the number of deaths between years 2000 and 2017 <sup>a</sup>		
	Year 2000, mean (min-max)			Year 2017, mean (min-max)			20-29 years	30-49 years	≥50 years
	20-29 years	30-49 years	≥50 years	20-29 years	30-49 years	≥50 years			
Sudan	0.4 (0.1-0.7)	7.2 (2.9-12.5)	14.6 (9.2-22.2)	0.2 (0.1-0.4)	5.2 (2.4-8.7)	11.3 (7.6-15.9)	-0.9	22.1	13.5
Yemen	0.4 (0.2-0.7)	9.5 (4.1-16.3)	18.8 (11.1-28.4)	0.3 (0.1-0.5)	7.1 (3.4-11.9)	15.5 (10.6-22.1)	30.3	49.0	52.9
High-income countries globally	0.4 (0.3-0.4)	8.2 (7.4-9.1)	19.5 (18.6-20.5)	0.3 (0.2-0.4)	5.6 (4.7-6.7)	14.9 (13.4-16.4)	-16.5	-26.9	6.7
<b>High-income countries in the EMR</b>	0.1 (0.1-0.2)	2.3 (1.6-3.4)	8.4 (6.7-10.7)	0.1 (0.0-0.1)	1.7 (1.0-2.6)	7.2 (5.4-9.2)	25.6	110.0	74.8
Bahrain	0.2 (0.1-0.4)	3.3 (2.3-4.7)	17.4 (14.4-22.6)	0.1 (0.1-0.2)	1.2 (0.8-1.7)	9.6 (7.7-12.3)	-6.8	7.2	75.5
Kuwait	0.1 (0.1-0.2)	2.5 (1.9-3.3)	5.9 (5.2-6.6)	0.1 (0.0-0.1)	1.5 (1.1-2.0)	3.3 (2.9-3.8)	-0.5	67.4	57.5
Oman	0.2 (0.1-0.4)	5.3 (3.3-8.1)	14.2 (10.9-18.8)	0.1 (0.0-0.1)	2.4 (1.5-3.8)	10.2 (7.6-13.0)	15.8	25.5	43.9
Qatar	0.1 (0.0-0.1)	1.5 (0.9-2.3)	15.2 (19.4-11.8)	0.0 (0.0-0.1)	0.7 (0.4-1.1)	8.0 (6.0-10.4)	184.6	125.6	120.7
Saudi Arabia	0.1 (0.1-0.1)	2.0 (1.4-2.8)	6.3 (5.2-7.8)	0.1 (0.0-0.1)	1.7 (1.1-2.6)	5.3 (4.1-6.6)	38.5	109.5	51.2
United Arab Emirates	0.1 (0.1-0.2)	2.5 (1.6-3.8)	26.6 (19.7-33.7)	0.1 (0.1-0.2)	1.7 (1.0-2.7)	21.2 (15.1-27.8)	2.3	256.5	165.6
Global average (122 countries)	1.0 (0.9-1.1)	16.7 (15.3-18.5)	29.9 (28.4-32.8)	0.7 (0.6-0.7)	13.3 (12.1-14.0)	24.9 (23.3-25.9)	-19.1	3.8	35.0
EMR average (22 countries)	0.6 (0.3-1.0)	9.2 (5.6-14.0)	18.9 (13.8-24.2)	0.4 (0.2-0.8)	6.7 (3.8-10.7)	15.6 (11.0-21.1)	13.5	34.5	36.6

<sup>a</sup>Relative difference (%) in the number of deaths = [(number of cervical cancer deaths in 2017 – number of cervical cancer deaths in 2000)/number of cervical cancer deaths in 2000]\*100.

<sup>b</sup>EMR: Eastern Mediterranean Region.

Both globally and in the EMR, DALYs declined for all age groups in the period of 2000-2017. The global average of DALYs for the 3 age groups was higher than the EMR average in both the reference years, and the age group of 30-49 years showed the highest number of DALYs (Table 4). The age group of 30-49 years showed the highest rate of DALYs both globally and in the EMR and for the 3 income levels. HICs in the EMR was the exception in this age group as they showed a lower rate of DALYs compared to the age group of ≥50 years. LICs, both globally and in the EMR, showed a decline in the DALYs for the 3 age groups in 2017 compared to 2000. Somalia had the highest number of DALYs for all 3 age groups and both reference years. MICs in the EMR showed lower rates of DALYs for the 3 age groups and in both reference years. Djibouti had the highest rates of DALYs for all age groups and in both reference years. Egypt had the lowest rates of DALYs

for all 3 age groups in 2000 and for the age group ≥50 years in 2017. Jordan had the lowest number of DALYs for the age groups of 20-29 years and 30-49 years in 2017 (Table 4). The distribution of the relative difference in the number of DALYs for the different age groups showed that the DALYs of EMR-LICs were higher than those of the global countries for the age groups of 20-29 years and 30-49 years (14% and 50.6% vs 5.5% and 21.8%, respectively). Further, it was lower for the age group >50 years (18.2% vs 26%, respectively). Afghanistan had the highest relative difference in the number of DALYs of 95.0% for the age group of 30-49 years (Table 4). EMR-MICs had higher relative difference in the number of DALYs than the global MICs for all 3 age groups (Table 4). The age group of 20-29 years in Egypt had the highest relative difference in the number of DALYs of 35.7%, and the age group of 30-49 years in Libya had the highest relative difference of 95.9%. For

the age group >50 years, Iran had the highest relative difference in the number of DALYs of 98.0%. Finally, EMR-HICs had higher relative difference in the number of DALYs than global HICs for all 3 age groups (28.1%, 111.6%, and 90.6% vs -15.4%, -26.2%, and 3.4%, respectively). Among EMR-HICs,

the age group of 20-29 years in Qatar had the highest relative difference in the number of DALYs of 192.8% and age groups of 30-49 years and >50 years in Emirates had the highest relative difference of 258.9% and 185.6%, respectively ([Table 4](#)).

**Table 4.** Disability-adjusted life years data due to cervical cancer among women older than 20 years in the Eastern Mediterranean Region by age, country, and income level compared to the global average in the years 2000 and 2017.

Group by income level, country	Average cervical cancer DALY <sup>a</sup> rate per 100,000 women by age range						Relative difference (%) in number of DALYs <sup>b</sup> (2000 vs 2017)		
	Year 2000, mean (min-max)			Year 2017, mean (min-max)			20-29 years	30-49 years	≥50 years
	20-29 years	30-49 years	≥50 years	20-29 years	30-49 years	≥50 years			
Low-income countries globally	161.5 (85.5-268.9)	2473.0 (1496.9-3715.7)	2062.9 (1466.6-2779.8)	106.7 (54.8-188.5)	1783.2 (1051.3-2807.4)	1641.5 (1128.3-2294.7)	5.5	21.8	26.0
<b>Low-income countries in the EMR<sup>c</sup></b>	128.1 (53.6-235.7)	2637.7 (1294.6-4425.8)	1689.7 (986.3-2398.2)	97.3 (43.3-187.5)	1628.2 (754.6-2815.3)	1617.3 (972.9-2364.2)	14.0	50.6	18.2
Afghanistan	85.8 (25.8-169.6)	1456.7 (402.8-2719.2)	783.9 (300.6-1183.2)	69.9 (25.8-136.6)	971.6 (331.2-1749.2)	697.3 (330.0-1001.0)	21.9	95.0	-1.8
Somalia	213.8 (109.5-370.0)	4186.9 (2458.3-6609.7)	3555.1 (2483.6-4884.5)	152.5 (77.2-294.0)	3022.9 (1679.8-5033.9)	3006.5 (1978.5-4457.5)	7.6	30.4	27.3
Middle-income countries globally	65.6 (47.3-88.9)	801.3 (638.8-1011.8)	642.6 (555.4-778.8)	43.1 (29.8-62.3)	628.7 (447.7-838.0)	532.0 (412.6-643.9)	-81.4	-86.1	17.6
<b>Middle-income countries in the EMR</b>	34.5 (19.7-55.9)	368.1 (232.7-542.7)	326.8 (249.3-407.8)	26.8 (13.7-50.3)	272.3 (162.1-429.7)	259.5 (185.7-345.1)	14.6	28.3	36.0
Djibouti	135.4 (69.1-237.0)	2907.3 (1707.0-4709.3)	2569.5 (1675.6-3674.6)	82.2 (39.0-155.3)	1940.6 (1076.8-3330.4)	1714.6 (1082.4-2677.9)	8.7	50.9	49.2
Egypt	8.9 (5.1-14.4)	134.6 (90.5-193.0)	120.5 (97.7-146.7)	8.3 (4.4-14.6)	122.7 (74.6-184.2)	122.4 (93.5-156.5)	35.7	36.9	61.2
Iran	16.7 (13.0-20.1)	158.8 (130.4-182.6)	163.1 (136.9-181.8)	10.6 (8.2-12.6)	121.3 (98.8-138.5)	176.2 (136.4-190.3)	-20.2	37.7	98.0
Iraq	17.4 (7.4-31.6)	298.5 (145.6-486.0)	237.4 (169.3-336.8)	8.4 (5.0-13.6)	110.8 (76.2-156.2)	106.1 (86.5-128.0)	-22.0	-24.4	-2.9
Jordan	15.2 (8.9-24.0)	274.6 (185.5-394.6)	251.4 (200.0-334.0)	5.5 (3.1-9.3)	92.1 (59.4-139.5)	136.0 (102.9-186.6)	-25.2	3.5	44.5
Lebanon	21.5 (12.3-35.3)	348.6 (225.5-506.7)	302.1 (239.3-374.7)	13.8 (7.9-23.6)	194.7 (124.4-285.3)	222.5 (174.9-279.2)	6.0	22.0	24.9
Libya	24.5 (13.0-44.1)	420.5 (267.5-618.9)	340.0 (261.3-438.7)	22.0 (11.6-39.0)	373.2 (225.4-575.0)	309.4 (224.1-416.2)	1.4	95.9	73.6
Morocco	34.5 (18.9-56.0)	717.9 (458.0-1030.1)	668.3 (488.1-820.3)	26.2 (13.1-46.9)	517.7 (306.5-812.3)	494.1 (344.1-647.7)	-11.3	1.9	31.2
Pakistan	70.2 (40.3-115.1)	565.8 (372.8-824.1)	443.3 (352.6-543.4)	52.1 (25.5-103.3)	433.4 (255.2-704.4)	350.3 (250.5-491.3)	25.4	38.7	25.6
Palestine	10.7 (6.5-16.3)	182.8 (119.6-261.9)	245.2 (194.7-297.8)	6.9 (3.9-11.4)	127.2 (83.3-184.1)	202.4 (153.0-245.4)	18.9	39.1	64.0
Syria	12.0 (7.1-19.0)	173.2 (117.2-243.8)	140.7 (115.5-183.0)	8.8 (4.4-15.1)	107.1 (64.6-171.8)	123.7 (91.8-158.2)	-47.4	-7.7	58.6

Group by income level, country	Average cervical cancer DALY <sup>a</sup> rate per 100,000 women by age range						Relative difference (%) in number of DALYs <sup>b</sup> (2000 vs 2017)		
	Year 2000, mean (min-max)			Year 2017, mean (min-max)			20-29 years	30-49 years	≥50 years
	20-29 years	30-49 years	≥50 years	20-29 years	30-49 years	≥50 years			
Tunisia	13.2 (7.6-20.9)	259.1 (168.2-375.4)	269.5 (216.5-339.7)	8.3 (4.2-15.4)	165.5 (95.9-259.7)	199.6 (141.2-274.6)	-32.1	-11.3	34.8
Sudan	23.7 (9.4-43.9)	339.9 (134.9-595.9)	284.8 (173.1-430.4)	15.1 (7.2-26.8)	248.1 (113.8-415.3)	217.8 (140.3-309.9)	0.1	22.5	16.7
Yemen	25.2 (10.3-45.3)	448.1 (192.1-769.9)	381.2 (217.9-575.2)	17.9 (8.4-30.8)	335.1 (157.4-561.7)	311.5 (208.3-450.8)	31.5	51.2	51.7
High-income countries globally	24.6 (20.6-29.7)	399.8 (357.9-445.7)	339.4 (321.9-357.8)	20.7 (16.4-26.2)	275.5 (228.7-331.6)	249.9 (224.1-278.0)	-15.4	-26.2	3.4
<b>High-income countries in the EMR</b>	7.6 (4.5-12.1)	112.0 (75.3-162.9)	154.4 (121.5-199.7)	5.3 (2.8-9.0)	76.9 (46.7-121.4)	124.9 (92.9-161.6)	28.1	111.6	90.6
Bahrain	16.1 (8.0-25.3)	160.0 (109.8-226.1)	333.0 (271.0-424.9)	9.7 (4.7-16.3)	56.5 (37.6-83.6)	166.5 (132.9-214.7)	-5.5	5.7	86.7
Kuwait	8.6 (5.9-12.1)	121.8 (90.5-158.9)	115.5 (100.4-131.5)	4.8 (3.0-7.3)	72.0 (52.0-99.3)	62.6 (52.7-73.8)	1.1	66.3	71.4
Oman	14.7 (8.1-24.9)	254.5 (157.3-388.9)	268.9 (201.6-361.8)	115.1 (84.6-149.4)	72.4 (44.4-112.7)	121.4 (81.0-174.6)	17.3	28.0	40.3
Qatar	5.4 (3.1-8.9)	72.0 (45.5-111.6)	266.4 (202.6-346.4)	2.2 (1.2-3.6)	34.7 (21.4-53.7)	135.6 (100.0-177.5)	192.8	130.9	129.8
Saudi Arabia	6.1 (3.7-9.6)	95.8 (66.6-135.4)	111.4 (89.8-143.0)	4.4 (2.3-7.6)	82.0 (50.7-127.8)	95.0 (72.7-119.9)	41.8	111.9	68.5
United Arab Emirates	9.1 (5.0-15.6)	113.7 (72.8-176.0)	486.3 (356.1-624.4)	6.9 (12.2-3.7)	80.4 (46.5-129.8)	354.4 (250.7-472.1)	3.7	258.9	185.6
Global average (122 countries)	65.8 (57.2-73.7)	795.3 (726.2-874.5)	596.3 (562.2-655.4)	44.6 (40.0-49.1)	631.5 (575.4-669.8)	491.6 (456.4-512.0)	-18.3	3.2	35.7
EMR average (22 countries)	29.9 (21.0-42.1)	413.6 (340.7-501.7)	349.1 (317.9-381.6)	25.2 (16.1-40.1)	299.1 (218.8-405.3)	261.2 (223.5-303.5)	-2.0	-11.8	8.0

<sup>a</sup>DALY: disability-adjusted life year.

<sup>b</sup>Relative difference (%) in the number of DALYs = [(number of cervical cancer DALYs in 2017 – number of cervical cancer DALYs in 2000)/number of cervical cancer DALYs in 2000]\*100.

<sup>c</sup>EMR: Eastern Mediterranean Region.

## Discussion

### Principal Findings

In this study, we report the results of the data analysis on both mortality and DALYs associated with cervical cancer in 22 countries in the EMR. We found a change in the number of deaths and mortality rates from the year 2000 to the year 2017. Although the number of deaths due to cervical cancer has

increased in the year 2017 (n=8537) compared to that in the year 2000 (n=6326) in the EMR, the mortality rate decreased in 2017 (2.5 per 100,000) compared to that in 2000 (2.7 per 100,000). The population expansion in the younger age groups may have contributed to the reduction in the mortality rates. For example, the population size in EMR-LICs in 2017 increased two-fold in comparison to that in the year 2000. According to the causation and nature of cervical cancer, there exists 10-20 years of gap between HPV infection and the

development of cervical cancer. Thus, this disease is not seen in the younger generation; therefore, population expansion does not affect the number of deaths whereas mortality rate calculation under its influence decreases, as reported in previous studies [18]. Previous studies have shown that mortality rates and DALY rates are low in Saudi Arabia and Iran [18,19]; therefore, 1 study suggested that the cost-effectiveness of investment on HPV vaccination should be examined and if the incidence of cervical cancer is truly low, there is no reason for public health to institute either screening or vaccination [20].

Our results showed that large differences existed within the EMR in both deaths and DALYs. Considering the stratification by country income level, we found that HICs carried the largest burden of deaths and the number burden of DALYs for the 2 reference years (85.5%) compared to MICs and LICs (34.2% and 33.3%, respectively) and for all the 3 age groups (25.6%, 110%, and 74.8% vs 13.5%, 27.4%, and 39% vs 12.8%, 49.6%, and 25.1%, respectively). The EMR-HICs, unlike the HICs globally, may have higher relative difference even in comparison to LICs. This might have different causes apart from their economic level that are common in countries of the EMR.

In our study, we consider that one cause that may be relevant is the economic development of the Gulf region in the last 3 decades. This development may have improved the access to health care services, education, and changes in lifestyle and nutrition and traditional social and family structures [11]. For example, marriage in some areas includes the practice of either polygamy or temporary marriage, known by the names of “mesiar and mesfar”; this may contribute to the increase in the prevalence of HPV infections [21]. The first notable factor in this region is the lack of a reliable system of registry for diseases, including cervical cancer. According to the World Health Organization (WHO) cancer country profiles, Afghanistan [22], Somalia [23], Djibouti [24], Libya [25], and Pakistan [26] do not have a cancer registry. As per the WHO, the situation of cervical cancer in EMR should be assessed and improved [1]. The WHO’s first step is related to primary prevention through immunization against HPV of all 9-13-year-old girls before their sexual debut. HPV in almost all of the cases is the main attributable risk factor for cervical cancer, and the risk of developing cervical cancer is highly associated with the age of first intercourse; the younger the individual, the more is the probability of developing infection into papillomavirus-associated cancer [27]. All the countries in the EMR report the prevalence of HPV strains 16 and 18 (the most oncogenic subtypes of HPV) in women with normal cytology—from 0.2% in Kuwait [28] up to 4.8% in Somalia [29] and Djibouti [30], which has the potential to progress to cervical precancer and cancer in 10-20 years. The prevalence of HPV strains 16 and 18 in low-grade lesions was from 20.8% in Morocco [31] and Libya [32] up to 42.9% in Iran [33] and that in high-grade lesions was from 45.7% in Somalia [29] and Djibouti [30] up to 63.4% in Afghanistan [34] and Pakistan [35]. In women with cervical cancer, the prevalence was from 58.6% in Iran [33] up to 92.7% in Jordan [36]. This shows the importance of HPV vaccination in these countries to ensure that the infection does not progress to cervical precancer and cancer. Among the EMR countries, Libya [31] has had a national HPV

vaccination program since 2013, and Emirates [37] had a partial program since 2008. In addition, in the EMR, education and knowledge on cervical cancer are reported as important determinative factors in primary prevention [38]. The increased education of women and their families about cervical cancer, its causes, signs, symptoms, and preventions will engage them more in the preventive and screening practices [38]. The WHO’s other primary preventive measures are “Girls and boys, as appropriate—Health information and warnings about tobacco use—Sexuality education tailored to age and culture—Condom promotion/provision for those engaged in sexual activity—Male circumcision” [1]. Almost all of the countries of the EMR report more than 80% male circumcision, and the usage of condom is low from 0.0% in Somalia [29] and Sudan [39] up to 13.8% in Iran [33]. With regard to the sexual education for girls and boys, a study conducted in Iran generalized the matter to all Muslim countries and reported the social unacceptability of sexual health education for unmarried people due to religious and cultural prohibition of extramarital sex, in particular, for girls. Further, sexual education highlights the effect of technology improvement and internet on the sexual behaviors of youth, including extramarital relationships, and this should not be denied [40]. The WHO’s second step to comprehensive prevention and control of cervical cancer is related to secondary prevention through effective screening of women older than 30 years and treatment as needed with low-cost technology, for example, visual inspection with acetic acid (VIA) followed by cryotherapy [1]. In the EMR, Somalia [29], Djibouti [30], Libya [32], Sudan [39], and Yemen [41] have no cervical cancer screening programs. Two countries, Tunisia [42] and Morocco [31], have quality assurance structures, which supervise and monitor the screening; however, none of them has an active invitation for screening. In Egypt, the cost of screening and treatment is not covered by public funding; therefore, this is considered as a nonaffordable service by over 40% of the Egyptian women [43]. Cytology is considered as the main screening test in EMR, except for Morocco [31] and Pakistan [35] where VIA is used. The VIA is suggested especially in LICs and rural areas that do not have access to health care facilities [44]. Further, women face additional challenges such as language, transportation, insurance, and family pressure as inhibitors for obtaining regular cervical cancer screening, especially in case it is perceived as a threat to their cultural and religious values [45]. The reported barriers in the rural areas are the financial costs, acceptance by husbands, and availability of a female health care provider [43].

The early detection of cancer reduces financial burdens, both on the health care system and economically [46]. Screening and vaccination programs are considered to be more accessible and effective than relying only on cancer treatment. For example, in Saudi Arabia, the pap test is fully subsidized in public hospitals, and it costs US \$50 in private clinics. Yet, these costs are negligible compared to the costs of cervical cancer treatment, where it can vary between US \$14,000-US \$30,000 during the first year of therapy [21].

The WHO recommends a comprehensive prevention and control of cervical cancer, which is related to tertiary prevention for women older than 30 years. This includes treating invasive

cancer at any age, including ablative surgery, radiotherapy, and chemotherapy palliative care [1]. However, radiotherapy is not generally available in Afghanistan [22], Somalia [23], Djibouti [24], Egypt [47], and Pakistan [26] and is generally available in other countries of the EMR. The availability of radiotherapy centers ranges from 1 center in Yemen [48], Bahrain [49], Kuwait [50], Oman [51], and Qatar [52] up to 40 centers in Iran [53]. The availability of radiation clinics ranges from 3 centers in Qatar [52] up to 237 centers in Egypt [47]. Chemotherapy is not available in Afghanistan [22], Somalia [23], Djibouti [24], Egypt [47], and Pakistan [26], but it is available in other countries of the EMR. Finally, community/home care for people with advanced-stage cancer is only available in 2 countries of the EMR, namely, Bahrain [49] and Kuwait [50].

### Study Limitations

The ongoing civil unrest may have affected the quality of the health data in the EMR, as the GBD study uses modelling techniques to generate the estimates based on other available variables or data from countries with a similar health profile in the neighboring region for countries that have insufficient data. In this study, we used data on the numbers of mortality, crude death rate, and DALY rate. Moreover, the incidence of cervical cancer was not examined.

### Conclusion

Cervical cancer is becoming a major problem in the EMR, and its burden might increase due to the population growth. There is a need for effective interventions to reduce the burden of cervical cancer. This includes prevention measures such as HPV vaccination, early detection of cervical cancer, and reducing the risk factors associated with cervical cancer.

---

### Authors' Contributions

FS, SG, ZEK, and SE conceived the study in the form of a master's thesis project. FS and SG conducted the analysis and wrote the first draft. BR supervised the process of the manuscript writing. All authors reviewed the draft and contributed to the revisions.

### Conflicts of Interest

None declared.

---

### References

1. WHO. Comprehensive Cervical Cancer Control: A Guide to Essential Practice - Second edition. Geneva: World Health Organization; 2014.
2. Tota J, Ramana-Kumar AV, El-Khatib Z, Franco E. The road ahead for cervical cancer prevention and control. *Curr Oncol* 2014 Apr;21(2):e255-e264 [FREE Full text] [doi: [10.3747/co.21.1720](https://doi.org/10.3747/co.21.1720)] [Medline: [24764711](https://pubmed.ncbi.nlm.nih.gov/24764711/)]
3. What you need to know about cervical cancer? Centers for Disease Control and Prevention. URL: <https://www.cdc.gov/cancer/cervical/accessible> [accessed 2020-06-15]
4. Nour N. Cervical cancer: a preventable death. *Rev Obstet Gynecol* 2009;2(4):240-244. [Medline: [20111660](https://pubmed.ncbi.nlm.nih.gov/20111660/)]
5. Forouzanfar M, Foreman K, Delossantos A, Lozano R, Lopez A, Murray C, et al. Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. *The Lancet* 2011 Oct;378(9801):1461-1484. [doi: [10.1016/s0140-6736\(11\)61351-2](https://doi.org/10.1016/s0140-6736(11)61351-2)]
6. Singh G, Azuine RE, Siahpush M. Global Inequalities in Cervical Cancer Incidence and Mortality are Linked to Deprivation, Low Socioeconomic Status, and Human Development. *Int J MCH AIDS* 2012;1(1):17-30 [FREE Full text] [doi: [10.21106/ijma.12](https://doi.org/10.21106/ijma.12)] [Medline: [27621956](https://pubmed.ncbi.nlm.nih.gov/27621956/)]
7. Parikh S, Brennan P, Boffetta P. Meta-analysis of social inequality and the risk of cervical cancer. *Int J Cancer* 2003 Jul 10;105(5):687-691 [FREE Full text] [doi: [10.1002/ijc.11141](https://doi.org/10.1002/ijc.11141)] [Medline: [12740919](https://pubmed.ncbi.nlm.nih.gov/12740919/)]
8. Wentzensen N, Schiffman M. Accelerating cervical cancer control and prevention. *The Lancet Public Health* 2018 Jan;3(1):e6-e7. [doi: [10.1016/s2468-2667\(17\)30242-6](https://doi.org/10.1016/s2468-2667(17)30242-6)]
9. Scenarios for the Mediterranean region. World Economic Forum. URL: [http://projects.mcrit.com/foresightlibrary/attachments/WEF\\_Scenario\\_MediterraneanRegion\\_Report\\_2011.pdf](http://projects.mcrit.com/foresightlibrary/attachments/WEF_Scenario_MediterraneanRegion_Report_2011.pdf) [accessed 2021-05-04]
10. World Health Organization. Noncommunicable diseases in the eastern Mediterranean region. EMRO Technical Publications Series. URL: [https://applications.emro.who.int/dsaf/EMROPUB\\_2016\\_EN\\_18977.pdf?ua=1](https://applications.emro.who.int/dsaf/EMROPUB_2016_EN_18977.pdf?ua=1) [accessed 2021-04-14]
11. Kulhánová I, Bray F, Fadhil I, Al-Zahrani AS, El-Basmy A, Anwar WA, et al. Profile of cancer in the Eastern Mediterranean region: The need for action. *Cancer Epidemiology* 2017 Apr;47:125-132. [doi: [10.1016/j.canep.2017.01.009](https://doi.org/10.1016/j.canep.2017.01.009)] [Medline: [28268206](https://pubmed.ncbi.nlm.nih.gov/28268206/)]
12. Vaccarella S, Bruni L, Seoud M. Burden of human papillomavirus infections and related diseases in the extended Middle East and North Africa region. *Vaccine* 2013 Dec 30;31 Suppl 6:G32-G44. [doi: [10.1016/j.vaccine.2012.06.098](https://doi.org/10.1016/j.vaccine.2012.06.098)] [Medline: [24331818](https://pubmed.ncbi.nlm.nih.gov/24331818/)]
13. Protocol for the global burden of diseases, injuries, and risk factors study (GBD). Institute for Health Metrics and Evaluation. URL: [http://www.healthdata.org/sites/default/files/files/Projects/GBD/GBD\\_Protocol.pdf](http://www.healthdata.org/sites/default/files/files/Projects/GBD/GBD_Protocol.pdf) [accessed 2019-06-15]
14. World Bank. World bank country and lending groups. The World Bank. URL: [https://datahelpdesk.worldbank.org/knowledgebase/articles/906519\(accessed\)](https://datahelpdesk.worldbank.org/knowledgebase/articles/906519(accessed)) [accessed 2018-08-05]



15. United Nations. World population prospects 2019. Department of Economic and Social Affairs Population Dynamics. URL: <https://esa.un.org/unpd/wpp/> [accessed 2019-12-16]
16. The global burden of disease concept. World Health Organization. URL: [https://www.who.int/quantifying\\_ehimpacts/publications/en/9241546204chap3.pdf](https://www.who.int/quantifying_ehimpacts/publications/en/9241546204chap3.pdf) [accessed 2019-11-16]
17. Institute for Health Metrics and Evaluation (IHME). Protocol for the Global burden of diseases, injuries, and risk factors study (GBD) Version 4. Global burden of diseases, injuries, and risk factors study. URL: [http://www.healthdata.org/sites/default/files/files/Projects/GBD/March2020\\_GBD%20Protocol\\_v4.pdf](http://www.healthdata.org/sites/default/files/files/Projects/GBD/March2020_GBD%20Protocol_v4.pdf) [accessed 2021-05-05]
18. Gynecological cancer in Saudi Arabia. Jeddah Cervical Screening Program. URL: <http://www.jcsp.sa.com/index.php?lang=en> [accessed 2019-10-16]
19. Momenimovahed Z, Salehiniya H. Cervical cancer in Iran: integrative insights of epidemiological analysis. *BioMedicine* 2018;37-44 [FREE Full text] [doi: [10.1051/bmdcn/2018080318](https://doi.org/10.1051/bmdcn/2018080318)]
20. Alsbeih G. HPV Infection in Cervical and Other Cancers in Saudi Arabia: Implication for Prevention and Vaccination. *Front Oncol* 2014 Mar 31;4:65 [FREE Full text] [doi: [10.3389/fonc.2014.00065](https://doi.org/10.3389/fonc.2014.00065)] [Medline: [24744990](https://pubmed.ncbi.nlm.nih.gov/24744990/)]
21. Alhamlan FS, AlAhdal MNA, Al-Zahrani AS, Almatrouk SA. Human papillomaviruses: The cervical cancer saga in developing countries. *J Infect Dev Ctries* 2017 Dec 10;11(11):819-825 [FREE Full text] [doi: [10.3855/jidc.9704](https://doi.org/10.3855/jidc.9704)] [Medline: [31618179](https://pubmed.ncbi.nlm.nih.gov/31618179/)]
22. Cancer country profile, Afghanistan. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/afg\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/afg_en.pdf?ua=1) [accessed 2019-06-06]
23. Cancer country profile, Somalia. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/som\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/som_en.pdf?ua=1) [accessed 2019-06-15]
24. Cancer country profile, Djibouti. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/dji\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/dji_en.pdf?ua=1) [accessed 2019-06-15]
25. Cancer country profile, Libya. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/lby\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/lby_en.pdf?ua=1) [accessed 2019-06-15]
26. Cancer country profile, Pakistan. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/pak\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/pak_en.pdf?ua=1) [accessed 2019-06-15]
27. de Quadros QC. Vaccines. PAHO. URL: <https://www.paho.org/hq/dmdocuments/2012/book-vaccines-dequadros.pdf> [accessed 2019-06-15]
28. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Kuwait. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/KWT.pdf> [accessed 2019-12-15]
29. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Somalia. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/SOM.pdf> [accessed 2019-06-15]
30. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Djibouti. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/DJI.pdf> [accessed 2019-06-15]
31. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Morocco. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/MAR.pdf> [accessed 2019-06-15]
32. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in Libya. URL: <https://hpvcentre.net/statistics/reports/LBY.pdf> [accessed 2019-06-15]
33. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Iran. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/IRN.pdf> [accessed 2019-06-15]
34. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Afghanistan. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/AFG.pdf> [accessed 2019-12-15]
35. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Pakistan. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/PAK.pdf> [accessed 2019-10-15]
36. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Jordan. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/JOR.pdf> [accessed 2019-10-15]
37. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in United Arab Emirates. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/ARE.pdf> [accessed 2019-11-15]

38. Al Sairafi M, Mohamed FA. Knowledge, attitudes, and practice related to cervical cancer screening among Kuwaiti women. *Med Princ Pract* 2009;18(1):35-42 [FREE Full text] [doi: [10.1159/000163044](https://doi.org/10.1159/000163044)] [Medline: [19060489](https://pubmed.ncbi.nlm.nih.gov/19060489/)]
39. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Sudan. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/SDN.pdf> [accessed 2019-10-15]
40. Latifnejad Roudsari R, Javadnoori M, Hasanpour M, Hazavehei SMM, Taghipour A. Socio-cultural challenges to sexual health education for female adolescents in Iran. *Iran J Reprod Med* 2013 Feb;11(2):101-110 [FREE Full text] [Medline: [24639734](https://pubmed.ncbi.nlm.nih.gov/24639734/)]
41. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Yemen. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/YEM.pdf> [accessed 2020-01-15]
42. Bruni L, Albero G, Serrano B, Mena M, Gomez D, Munoz J, et al. Human papillomavirus and related diseases in Tunisia. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpvcentre.net/statistics/reports/TUN.pdf> [accessed 2020-01-15]
43. Sancho-Garnier H, Khazraji YC, Cherif MH, Mahnane A, Hsairi M, El Shalakamy A, et al. Overview of cervical cancer screening practices in the extended Middle East and North Africa countries. *Vaccine* 2013 Dec 30;31 Suppl 6:G51-G57. [doi: [10.1016/j.vaccine.2012.06.046](https://doi.org/10.1016/j.vaccine.2012.06.046)] [Medline: [24331820](https://pubmed.ncbi.nlm.nih.gov/24331820/)]
44. Sankaranarayanan R, Anorlu R, Sangwa-Lugoma G, Denny LA. Infrastructure requirements for human papillomavirus vaccination and cervical cancer screening in sub-Saharan Africa. *Vaccine* 2013 Dec 29;31 Suppl 5:F47-F52. [doi: [10.1016/j.vaccine.2012.06.066](https://doi.org/10.1016/j.vaccine.2012.06.066)] [Medline: [24331747](https://pubmed.ncbi.nlm.nih.gov/24331747/)]
45. Matin M, LeBaron S. Attitudes Toward Cervical Cancer Screening Among Muslim Women: A Pilot Study. *Women & Health* 2004 Jun 30;39(3):63-77. [doi: [10.1300/j013v39n03\\_05](https://doi.org/10.1300/j013v39n03_05)]
46. Early cancer diagnosis saves lives, cuts treatment costs. World Health Organization. URL: <https://www.who.int/en/news-room/detail/03-02-2017-early-cancer-diagnosis-saves-lives-cuts-treatment-costs> [accessed 2019-06-15]
47. Cancer country profile, Egypt. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/egy\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/egy_en.pdf?ua=1) [accessed 2019-06-15]
48. Cancer country profile, Yemen. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/yem\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/yem_en.pdf?ua=1) [accessed 2019-06-15]
49. Cancer country profile, Bahrain. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/bhr\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/bhr_en.pdf?ua=1) [accessed 2019-06-15]
50. Cancer country profile, Kuwait. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/kwt\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/kwt_en.pdf?ua=1) [accessed 2019-06-15]
51. Cancer country profile, Oman. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/omn\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/omn_en.pdf?ua=1) [accessed 2019-06-15]
52. Cancer country profile, Qatar. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/qat\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/qat_en.pdf?ua=1) [accessed 2019-06-15]
53. Cancer country profile, Iran. World Health Organization. URL: [https://www.who.int/cancer/country-profiles/irn\\_en.pdf?ua=1](https://www.who.int/cancer/country-profiles/irn_en.pdf?ua=1) [accessed 2019-06-15]

## Abbreviations

- DALY:** disability-adjusted life year
- EMR:** Eastern Mediterranean Region
- GBD:** global burden of disease
- HIC:** high-income country
- HPV:** human papillomavirus
- LIC:** low-income country
- LMICs:** low- and middle-income countries
- MIC:** middle-income country
- VIA:** visual inspection with acetic acid
- WHO:** World Health Organization

*Edited by T Sanchez; submitted 07.07.20; peer-reviewed by F Lami, O Chimed-Ochir; comments to author 02.09.20; revised version received 27.10.20; accepted 19.03.21; published 12.05.21.*

*Please cite as:*

*Safaeian F, Ghaemimood S, El-Khatib Z, Enayati S, Mirkazemi R, Reeder B*

*Burden of Cervical Cancer in the Eastern Mediterranean Region During the Years 2000 and 2017: Retrospective Data Analysis of the Global Burden of Disease Study*

*JMIR Public Health Surveill 2021;7(5):e22160*

URL: <https://publichealth.jmir.org/2021/5/e22160>

doi: [10.2196/22160](https://doi.org/10.2196/22160)

PMID: [33978592](https://pubmed.ncbi.nlm.nih.gov/33978592/)

©Fereshteh Safaeian, Shidrokh Ghaemimood, Ziad El-Khatib, Sahba Enayati, Roksana Mirkazemi, Bruce Reeder. Originally published in JMIR Public Health and Surveillance (<https://publichealth.jmir.org>), 12.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Corrigenda and Addenda

# Correction: The Impact of COVID-19 Management Policies Tailored to Airborne SARS-CoV-2 Transmission: Policy Analysis

Charles Roberto Telles<sup>1\*</sup>, BSc; Archisman Roy<sup>2\*</sup>, BSc; Mohammad Rehan Ajmal<sup>3\*</sup>, PhD; Syed Khalid Mustafa<sup>4\*</sup>, PhD; Mohammad Ayaz Ahmad<sup>5\*</sup>, PhD; Juan Moises de la Serna<sup>6\*</sup>, PhD; Elisandro Pires Frigo<sup>7\*</sup>, PhD; Manuel Hernández Rosales<sup>8\*</sup>, PhD

<sup>1</sup>Internal Control Center, Secretary of State for Education and Sport of Paraná, Curitiba, Brazil

<sup>2</sup>Mathematics Group, Department of Physics, Faculty of Science, Institute of Science, Banaras Hindu University, Varanasi, India

<sup>3</sup>Department of Biochemistry, Faculty of Science, University of Tabuk, Tabuk, Saudi Arabia

<sup>4</sup>Department of Chemistry, Faculty of Science, University of Tabuk, Tabuk, Saudi Arabia

<sup>5</sup>Department of Physics, Faculty of Science, University of Tabuk, Tabuk, Saudi Arabia

<sup>6</sup>Universidad Internacional de la Rioja, Madrid, Spain

<sup>7</sup>Federal University of Paraná, Curitiba, Brazil

<sup>8</sup>Programa Universitario de Estudios Sobre la Ciudad, National Autonomous University of Mexico, Mexico City, Mexico

\* all authors contributed equally

**Corresponding Author:**

Charles Roberto Telles, BSc

Internal Control Center

Secretary of State for Education and Sport of Paraná

Av Água Verde, 2140

Curitiba, 80240-900

Brazil

Phone: 55 41996056321

Email: [charlestelles@seed.pr.gov.br](mailto:charlestelles@seed.pr.gov.br)

**Related Article:**

Correction of: <https://publichealth.jmir.org/2021/4/e20699/>

(*JMIR Public Health Surveill* 2021;7(5):e30007) doi:[10.2196/30007](https://doi.org/10.2196/30007)

In “The Impact of COVID-19 Management Policies Tailored to Airborne SARS-CoV-2 Transmission: Policy Analysis” (*JMIR Public Health Surveill* 2021;7(4):e20699), the authors noted one error.

The academic degree of author Archisman Roy has been corrected from “MSc” to “BSc.”

The correction will appear in the online version of the paper on the JMIR website on May 3, 2021, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

*Submitted 28.04.21; this is a non-peer-reviewed article; accepted 28.04.21; published 03.05.21.*

*Please cite as:*

*Telles CR, Roy A, Ajmal MR, Mustafa SK, Ahmad MA, de la Serna JM, Frigo EP, Rosales MH*

*Correction: The Impact of COVID-19 Management Policies Tailored to Airborne SARS-CoV-2 Transmission: Policy Analysis*

*JMIR Public Health Surveill* 2021;7(5):e30007

URL: <https://publichealth.jmir.org/2021/5/e30007>

doi:[10.2196/30007](https://doi.org/10.2196/30007)

PMID:[33939626](https://pubmed.ncbi.nlm.nih.gov/33939626/)

©Charles Roberto Telles, Archisman Roy, Mohammad Rehan Ajmal, Syed Khalid Mustafa, Mohammad Ayaz Ahmad, Juan Moises de la Serna, Elisandro Pires Frigo, Manuel Hernández Rosales. Originally published in JMIR Public Health and Surveillance (<https://publichealth.jmir.org>), 03.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# Evaluating the Consistency Between Conceptual Frameworks and Factors Influencing the Safe Behavior of Iranian Workers in the Petrochemical Industry: Mixed Methods Study

Azita Zahiri Harsini<sup>1,2</sup>, PhD; Philip Bohle<sup>3</sup>, PhD; Lynda R Matthews<sup>4</sup>, PhD; Fazlollah Ghofranipour<sup>1</sup>, PhD; Hormoz Sanaeinasab<sup>5</sup>, PhD; Farkhondeh Amin Shokravi<sup>1</sup>, PhD; Krishan Prasad<sup>6</sup>, PhD

<sup>1</sup>Department of Health Education, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

<sup>2</sup>Faculty of Medicine and Health, The University of Sydney, Sydney, Australia

<sup>3</sup>Tasmanian School of Business and Economics, University of Tasmania, Private Bag 84, Hobart, Tasmania, Australia

<sup>4</sup>Work and Health Research Team, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia

<sup>5</sup>Health Research Center, Lifestyle Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

<sup>6</sup>School of Business, School of Accounting, Western Sydney University, Sydney, Australia

**Corresponding Author:**

Farkhondeh Amin Shokravi, PhD

Department of Health Education, Faculty of Medical Sciences

Tarbiat Modares University

Jalal AleAhmad, Nasr

North Kargar St

Tehran, 14115-111

Iran

Phone: 98 912 250 5977

Email: [AMINSH\\_F@modares.ac.ir](mailto:AMINSH_F@modares.ac.ir)

## Abstract

**Background:** Unsafe worker behavior is often identified as a major cause of dangerous incidents in the petrochemical industry. Behavioral safety models provide frameworks that may help to prevent such incidents by identifying factors promoting safe or unsafe behavior. We recently conducted a qualitative study to identify factors affecting workers' unsafe behaviors in an Iranian petrochemical company.

**Objective:** The aims of this study were to (1) conduct a review of the relevant research literature between the years 2000 and 2019 to identify theoretical models proposed to explain and predict safe behavior in the workplace and (2) to select the model that best reflects our qualitative findings and other evidence about the factors influencing safe behaviors among petrochemical workers.

**Methods:** This research used mixed methods. Initially, we conducted a qualitative study of factors that Iranian petrochemical workers believed affected their safety behavior. Four themes emerged from the semistructured interviews: (1) poor direct safety management and supervision; (2) unsafe workplace conditions; (3) workers' perceptions, skills, and training; and (4) broader organizational factors. Electronic databases, including PubMed, Embase, Scopus, Google Scholar, EBSCOhost, and Science Direct, were then searched for eligible studies on models to explain and predict safe behaviors, which were published between the years 2000 and 2019. Medical subject headings were used as the primary analytical element. Medical subject headings and subheadings were then extracted from the literature. One researcher conducted the search and 3 researchers performed screening and data extraction. Then, constructs described in each study were assessed to determine which were the most consistent with themes derived from our qualitative analysis.

**Results:** A total of 2032 publications were found using the search strategy. Of these, 142 studies were assessed and 28 studies met the inclusion criteria and were included in the review. The themes identified in the qualitative study most closely matched 3 scales included in Wu et al's model that measured safety behavior and performance, safety leadership, and safety climate in petrochemical industries. Poor direct safety management and supervision matched with safety leadership and its subscales; unsafe workplace conditions matched with safety climate and its subscales; workers' perceptions, skills, and training matched with safety performance and its subscales; and broader organizational factors matched with some subscales of the model.

**Conclusions:** This is the first literature review to identify models intended to explain and predict safe behavior and select the model most consistent with themes elicited from a qualitative study. Our results showed that effective safety leadership and management and safety climate and culture systems are the most frequently identified factors affecting safe behaviors in the petrochemical industry. These results can further help safety researchers and professionals design effective behavior-based safety interventions, which can have a more sustainable and persistent impact on workers' safety behaviors.

**Trial Registration:** Iranian Registry of Clinical Trials IRCT20170515033981N2; <https://www.irct.ir/trial/26107>

**International Registered Report Identifier (IRRID):** RR2-10.1186/s12889-019-7126-1

(*JMIR Public Health Surveill* 2021;7(5):e22851) doi:[10.2196/22851](https://doi.org/10.2196/22851)

## KEYWORDS

safe behavior; petrochemical industry; conceptual frameworks; literature review; occupational health

## Introduction

The International Labor Organization estimates that 1 worker in the world dies every 15 seconds because of occupational injuries and 160 workers develop work-related illnesses [1,2]. Workplace accidents not only cause occupational injuries and illness but also lead to financial losses for organizations [3]. Most behavior-based safety researchers consider that dangerous incidents are principally caused by workers acting unsafely or inappropriately and many studies have focused on worker behaviors that promote safety and prevent injuries [4]. Workplace safety is not solely explained by human error, and many other factors may contribute to this [5].

A substantial body of research indicates that organizational factors, including managers' behavior and decisions, have a significant impact on safety-related attitudes and behaviors in industrial contexts [6]. Several studies, for example, indicate that safety performance is affected by leadership [6-8]. There is evidence that leadership and effective occupational health and safety management, particularly by direct managers and supervisors, is necessary to promote safe behavior [9,10]. Hald [11] noted that the role of leaders and managers typically involves various functions such as setting goals and monitoring and controlling workers' performance. Other evidence indicates that broader organizational variables such as work intensification arising from increases in expected output or extended working hours are associated with poorer safety outcomes [12,13]. Another organizational factor is the contextual impact of safety climate [14,15]. Several studies have found a significant positive relationship between safety climate and safe behavior [16-18]. Safety climate is usually regarded as a subset of organizational climate that shapes workers' behaviors through a coherent set of perceptions and expectations about an organization's values and reward systems [19,20]. Various studies indicate that a poor safety climate leads to a reduction in compliance with safety procedures, which, in turn, causes an increase in the potential for workplace injuries and incidents [7,21-23].

Reason [24] describes 2 different ways to understand human errors at work: the individual ("person") approach and the system approach. The first approach focusses on unsafe acts by workers, inappropriate ways of doing tasks that could result in a dangerous incident, for example, lack of or inappropriate use of personal protective equipment, operating equipment without qualification or authorization, or operating equipment at unsafe

speeds [24]. The second approach focusses on unsafe working conditions or the state of the workplace system that could result in a workplace accident. Examples include defective tools, equipment or supplies, lack of emergency exits, and inadequate warning systems. Recent studies have placed importance on psychosocial conditions in policy and demonstrated the value of workers' psychological well-being at work. Organizations that aim to concentrate on both physical and psychological factors together have safer working environments at lower risk of employee mental and physical health harm, and consequently, lead to positive workplace behaviors such as work engagement and safety incident reporting [25]. Many safe behavior studies have been based upon generic safety theories and models such as the Health Belief Model [26-29], the Theory of Planned Behavior [30-33], the Risk Perception Attitude Framework [34-36], and Social Cognitive Theory [37-39]. There is also a growing literature supporting the positive effects of safety behavior interventions on safety compliance and participation, injury rates, and near misses in various high-risk industries, including the oil, gas, and petrochemical industry [40-42].

A recent study by our research team [43] identified 4 sets of factors that workers believe discourage safe behaviors in an Iranian petrochemical company: (1) poor direct safety management and supervision, (2) unsafe workplace conditions, (3) workers' perceptions, skills, and training, and (4) broader organizational factors. The first aim of this study was to identify theoretical models proposed to explain and predict safe behavior in the workplace by reviewing relevant research studies published between the years 2000 and 2019. The second aim was to select the model that best reflects the results of our above-mentioned qualitative study [43] and other evidences on the factors influencing safe behaviors among petrochemical workers.

## Methods

### Study Design

The study protocol of this research has been published recently [44]. This study was a mixed methods research, which was carried out in 2 phases. In the first phase, semistructured interviews were conducted using a qualitative approach to gain detailed understanding of the factors associated with workers' unsafe behaviors in the petrochemical industry. In the second phase, models that have been applied to explain and predict safe behavior in the industrial settings were investigated. The

findings of the first phase were matched with the constructs of the reviewed models to select a well-suited theoretical model.

### Qualitative Data Analysis

The interviews were conducted between May and July 2017 at a mutually convenient time and private areas at the participants' workplaces. To obtain a broad cross-section of the worker opinions and experiences, multi-stage sampling was used. This approach involves a combination of 2 or more sampling techniques. By combining sampling methods at different stages of research, researchers can increase confidence that they are mitigating biases and engaging hard-to-reach, vulnerable participants [45]. In this study, purposive sampling was supplemented by snowball sampling to enhance recruitment. Purposive and snowball sampling approaches were selected because the research team considered the combination of the two was the most practical means to secure a representative sample of the company employees. The research team utilized purposive sampling, also known as judgmental sampling, to recruit particular interview subjects deliberately in order to provide important information and then snowball sampling to seek out further potential interviewees from the social network of the initial respondents [43]. Both techniques are used to achieve hard-to-reach participants in qualitative research studies [45].

Members of the company's Safety, Health, and Environment unit, who were not part of the research team, assisted with the sampling process. They invited workers, supervisors, and safety managers from various occupational groups working in the operations department and the maintenance and repair department who had experienced accidents and injuries or had witnessed colleagues' accidents to participate in the study (purposive sampling). Workers were eligible to participate if they had worked in the petrochemical industry for at least 2 years. All workers in the petrochemical industry were males. During the interviews, respondents identified employees who had information about workplace accidents in the company and were key informants (snowball sampling). These employees were also invited to participate in the study. Before the start of each interview, a member of the safety staff introduced the participant to the first author, who provided clear verbal information about the study [43].

Data saturation is a criterion that is used to justify adequate sample sizes in qualitative studies. Data saturation is reached when the final interviews do not reveal any new themes or introduce new elements of an existing theme. When saturation is achieved, additional interviews only generate redundant data rather than novel findings. A total of 20 interviews were conducted before saturation was reached. The 20 participants consisted of workers, supervisors, and safety staff members. For the analysis of the responses from Iranian petrochemical workers [43], conventional content analysis, described by Graneheim and Lundman [46], was used to interpret the content of the interview transcripts through a systematic classification process involving coding and identifying themes [47]. A team of 6 coders (4 in Iran and 2 in Australia) reviewed the transcripts and conducted analysis in both languages. Open coding was carried out to allow codes to emerge from the qualitative data

and avoid codes based on preconceptions of the authors. Codes were repeatedly discussed and revised by the authors to achieve consensus and memos written to explain the analysis [48]. To increase interrater coding reliability, only the codes and themes that were validated by at least 2 of the 3 coders (the first author, an Iranian and 2 Australian authors) were included in the results. Immersion in the data was an important first stage in the analysis process during which transcripts were read and reread many times to ensure familiarity with the data. Repeated reading and rereading of transcripts without coding helped identify emergent themes from the data without losing the connections between key concepts and their context.

Content analysis was performed using MAXQDA (version 2018) software (VERBI Software GmbH) to facilitate and document the coding process and retrieve codes afterwards. While software can assist researchers in organizing qualitative data, computer software for qualitative analysis do not analyze data and the researcher makes decisions about the coding participants' responses and the relationships between codes, coding categories, and broader themes. MAXQDA allows the researcher to upload raw data such as transcribed interviews that can be then coded and cross-referenced in ways that facilitate organizing the data for easy retrieval.

### Literature Search Sources and Strategy

A literature search of publications in academic journals and conference papers covering the period 2000-2019 was conducted using the following web-based databases: PubMed, Embase, Scopus, Google Scholar, EBSCOhost, and Science Direct. A review of the literature revealed a lack of consensus among research studies regarding factors that discourage safe work behaviors and the risk of incidents occurring in industrial settings. The gap in the literature was identified in the 2000s. These eligibility dates were chosen to provide a sample of studies, including the constructs to explain and predict safe behavior using models. The reference lists of the included studies were also searched to identify additional relevant studies. We applied a predefined search strategy by using free terms and medical subject heading terms. Terms referring to safety were combined with OR, terms referring to safe behavior were combined with OR, and terms referring to both were combined with AND. The following free terms were used in all electronic databases: safety, behavior, worker, and workplace. The following medical subject heading terms were employed: safety, safety behavior, safe work behavior, behavior-based safety, workers' behavior, safety models, and workplace safety. The references provided in the publications identified were also examined. When full-text publications were not available directly from electronic databases, the authors of the studies were contacted and copies of their articles were requested. The search results were updated using Google alerts.

The publications were filtered using a set of inclusion and exclusion criteria. Inclusion criteria were that the publication described the (1) development of a theoretical model as a tool to assess safe work behavior, (2) application of a theoretical approach and method that had been used to assess workplace safety, or (3) definitions used to describe and evaluate safe work behaviors. Publications that did not describe the development



or application of a safe work behavior model were excluded. Non-English papers, conference abstracts, literature reviews, editorials, commentaries, letters to the editor, theses, and full texts that were not accessible were also excluded.

### Investigation Models

Publications were reviewed to identify theoretical models that have been used to explain and predict safe behavior in the petrochemical industry or other industrial settings. The key constructs in the models were then evaluated for consistency with the themes identified in our qualitative study of workers in the Iranian petrochemical industry [43]: *poor direct safety management and supervision; unsafe workplace conditions; workers' perceptions, skills, and training; and broader organizational factors*. The model including constructs that were the most consistent with the qualitative findings was then identified.

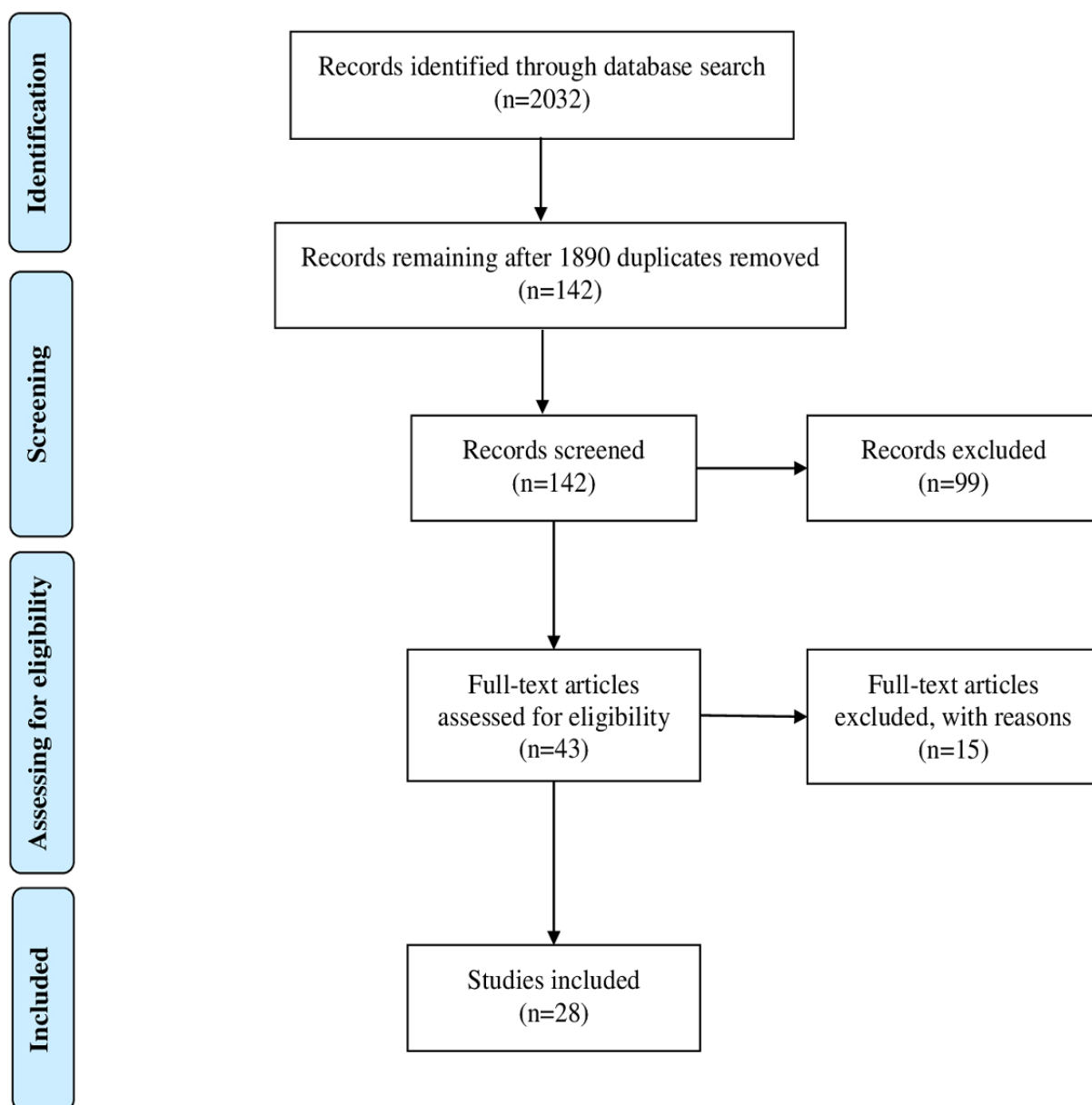
## Results

### Study Selection

This review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and

Meta-Analyses) statement [49]. A flow diagram describing the process for reviewing the studies is provided in [Figure 1](#). In total, 2032 publications were retrieved from the databases listed in the Methods section. Duplicate publications were removed, and 142 (84 academic journal articles, 55 reports and other publications, and 3 PhD theses) were screened by reading the title, abstract, and key words. By using the inclusion and exclusion criteria, 99 studies were excluded from the review, leaving 43 studies eligible for full-text review. During this review, 15 publications were excluded, because they did not meet the inclusion criteria. Ultimately, 28 studies were included in this review. The themes, categories, and codes that emerged from the content analysis of the semistructured interviews are listed in Table S1 of [Multimedia Appendix 1](#). An overview of the final chosen set of publications eligible for review and the constructs used in each of them is provided in [Table 1](#). All study selection processes were performed using EndNote X8.1 (Clarivate Analytics).

Figure 1. Flow diagram of the search results and the study selection process using the PRISMA template.



**Table 1.** Description of the included studies (listed by the year of publication) and the constructs used in each of them.

Study	Country of origin	Industry context	Constructs included in the model
Griffin and Neal (2000) [50]	Australia	A range of manufacturing and mining organizations	Manager values, safety inspections <sup>a</sup> , personal training <sup>a</sup> , safety communication <sup>b</sup> , safety knowledge <sup>a</sup> , safety compliance <sup>c</sup> , safety participation <sup>c</sup>
Brown et al (2000) [51]	United States of America	Steel industry	Safety hazards, safety climate <sup>b</sup> , pressure <sup>b</sup> , cavalier attitudes <sup>d</sup> , safety-efficacy <sup>c</sup> , safe behavior <sup>c</sup>
Hong et al (2004) [52]	Taiwan	Petrochemical industry	Training courses <sup>a</sup> , workers' cognition and attitude <sup>d</sup> , behavior and normative belief, behavior attitude <sup>d</sup> , subjective norm, behavior <sup>c</sup>
Seo (2005) [53]	United States of America	Grain industry	Perceived safety climate <sup>b</sup> , perceived hazard level, perceived work pressure <sup>b</sup> , perceived risk, perceived barriers, unsafe work behavior <sup>c</sup>
Pousette et al (2008) [54]	Sweden	Construction	Safety climate <sup>b</sup> , safety motivation <sup>b</sup> , safety knowledge <sup>a</sup> , self-rated safety behavior <sup>c</sup>
Larsson et al (2008) [55]	Sweden	Construction	Psychological climate <sup>b</sup> , job situation, workplace commitment <sup>b</sup> , safety motivation <sup>b</sup> , safety knowledge <sup>a</sup> , safety behavior <sup>c</sup>
Zhou et al (2008) [56]	China	Construction	Safety climate <sup>b</sup> , safety management <sup>a</sup> , management commitments <sup>a</sup> , safety attitudes <sup>c</sup> , workmate's influence, employee's involvement <sup>b</sup> , personal experience, safety knowledge <sup>a</sup> , education experience <sup>a</sup> , work experience <sup>a</sup> , drinking habits, safety behavior <sup>c</sup>
Lu and Yang (2010) [57]	Taiwan	Container terminal companies	Safety motivation <sup>b</sup> , safety policy, safety concern, safety compliance <sup>c</sup> , safety participation <sup>c</sup>
Martínez-Córcoles et al (2011) [6]	Spain	Nuclear power plant	Empowerment leadership <sup>a</sup> , safety culture <sup>d</sup> , safety climate <sup>d</sup> , safety behaviors <sup>c</sup>
Wu et al (2011) [42] <sup>e</sup>	Taiwan	Petrochemical company	<i>Safety leadership</i> <sup>a</sup> : safety coaching <sup>a</sup> , safety caring <sup>d</sup> , safety controlling <sup>a</sup> <i>Safety climate</i> <sup>b</sup> : workers' commitment to safety <sup>b</sup> , perceived risk <sup>b</sup> , emergency response <sup>b</sup> <i>Safety performance</i> <sup>c</sup> : safety inspection <sup>a</sup> , accident investigation <sup>c</sup> , safety training <sup>d</sup> , safety motivation <sup>b</sup>
Li et al (2013) [58]	China	Oil company	Job demands <sup>b</sup> , job resources, emotional exhaustion, safety compliance <sup>c</sup> , safety outcomes
Qinqin et al (2014) [59]	China	Petrochemical industry	Hazardous materials, production process, equipment condition <sup>a</sup> , environmental safety and health <sup>b</sup> , vulnerability of receptor <sup>c</sup>
Shin et al (2015) [60]	South Korea	Construction	Management values, safety climate <sup>b</sup> , stress response <sup>b</sup> , safety motivation <sup>b</sup> , safety knowledge <sup>a</sup> , safety behavior <sup>c</sup>
Wu et al (2015) [61]	China	Railway construction	Safety leadership <sup>a</sup> , design and planning for safety, preconstruction hazard inspection <sup>a</sup> , construction process safety, emergency preparedness <sup>b</sup> , management auditing and organizational learning, safety performance <sup>c</sup>

Study	Country of origin	Industry context	Constructs included in the model
Azadeh et al (2015) [62]	Iran	Petrochemical plant	Physical factors of workplace <sup>b</sup> , environmental features and issues <sup>b</sup> , management systems and control <sup>a</sup> , individual protection tools <sup>a</sup> , workplace safety actions, on-the-job training <sup>a</sup> , passing ways, monitors and displays <sup>a</sup> , muscular and skeletal disorders <sup>c</sup> , anthropometric features and issues, job characteristics, layout feature and issues, job and environmental satisfactions, overall health, safety, and environment management and performance <sup>a</sup> , mental workload and stress <sup>b</sup>
Alshahrani et al (2015) [63]	Saudi Arabia	Petrochemical industry	Safety culture <sup>d</sup> , safety attitudes <sup>b</sup> , safety and health requirements to circumvent accidents at workplace, safety behavior <sup>c</sup> , safety performance <sup>c</sup>
Wang et al (2016) [64]	China	Construction	Personal subjective perception <sup>b</sup> , work knowledge and experiences <sup>c</sup> , work characteristics, safety management <sup>a</sup> , workers' safety risk tolerance
Zhang et al (2016) [65]	China	Coal mining	Safety management agency <sup>a</sup> , rules and regulations of safety production <sup>a</sup> , defect of technology and design <sup>b</sup> , lack of safety education and training <sup>a</sup> , incomplete or poor execution of rules and regulations, rules and regulations and inspection <sup>a</sup> , safety culture <sup>d</sup> , operator error, venturing into dangerous places, protections, device signal deficiencies <sup>a</sup> , equipment, facilities and tools <sup>a</sup> , poor workplace environment <sup>b</sup>
Petitta et al (2017) [14]	Italy	Manufacturing, construction, transportation, military, energy, health care, and distribution/service	Safety compliance <sup>c</sup> , supervisor enforcement <sup>d</sup> , organizational safety climate <sup>b</sup> , organizational safety culture <sup>d</sup>
Zaira and Hadikusumo (2017) [66]	Malaysia	Construction	Management safety intervention <sup>a</sup> , human safety intervention, technical safety intervention, safety behavior <sup>c</sup>
Jafari et al (2017) [67]	Iran	Petrochemical company	Management commitment <sup>a</sup> , workers' empowerment, communication <sup>b</sup> , blame culture, safety training <sup>a</sup> , safety supervision <sup>a</sup> , interpersonal relationship <sup>b</sup> , continuous improvement, reward system <sup>b</sup> , job satisfaction
Razmara et al (2018) [27]	Iran	Taxi stations	Perceived susceptibility, perceived severity, perceived benefits <sup>c</sup> , perceived barriers <sup>c</sup> , self-efficacy <sup>c</sup> , cues to action, safe driving behavior <sup>c</sup>
Nioi et al (2018) [30]	United Kingdom	Construction	Behavioral beliefs <sup>c</sup> , normative beliefs, control beliefs, attitudes toward the behavior <sup>d</sup> , subjective norms, perceived control <sup>c</sup> , behavioral intention <sup>c</sup> , behavior <sup>c</sup>
Hald (2018) [11]	China	Electronics industry	Safety climate <sup>b</sup> , safety hazards, experience with safety and health problems <sup>c</sup> , pressure <sup>b</sup> , employees' knowledge of the factory <sup>a</sup> , cavalier attitudes toward safety <sup>b</sup> , safety efficacy <sup>c</sup> , safe workplace behavior <sup>c</sup>
Zhang et al (2018) [68]	China	Petrochemical enterprise	Personnel training <sup>a</sup> , fire facilities, fire management, technical level

Study	Country of origin	Industry context	Constructs included in the model
Newaz et al (2019) [19]	Australia	Construction	Management safety commitment <sup>a</sup> , supervisor safety behavior <sup>a</sup> , coworker safety behavior <sup>b</sup> , psychological contract of safety <sup>b</sup> , worker safety behavior <sup>c</sup>
Gao et al (2019) [41]	China	Oil industry	Leadership/management commitment <sup>a</sup> , organizing responsibilities/procedures, communication and coordination <sup>b</sup> , safety training <sup>a</sup> , inspection and monitoring <sup>a</sup> , employee involvement <sup>b</sup>
Wang et al (2019) [69]	China	Coal mining	Workers' characteristics, workers' perception of safety, working pressure <sup>b</sup> , leader's attitude in meeting, inspectors' quality <sup>a</sup> , management system's integrity <sup>a</sup> , management system's stringency <sup>a</sup>

<sup>a</sup>Matches with the theme of poor direct safety management and supervision in our qualitative study.

<sup>b</sup>Matches with the theme of unsafe workplace conditions in our qualitative study.

<sup>c</sup>Matches with the theme of workers' perceptions, skills, and training in our qualitative study.

<sup>d</sup>Matches with the theme of broader organizational factors in our qualitative study.

<sup>e</sup>The italicized constructs identified in the model most closely matched those identified in our qualitative study.

## Study Characteristics

Eleven (39%) out of 28 studies were conducted in a single industry (steel [51], grain [53], container terminal companies [22], nuclear power [6], oil [41,58], railway construction [61], coal mining [65,69], taxi stations [27], electronics [11]), and 2 studies (7%) included multiple industries [50,57]. Industries attracting the most studies were the construction (8/28, 29%) and petrochemical (7/28, 25%) industries. Ten studies were conducted in China (36%). Many regulations, occupational health and safety laws, and documents have been issued to help industries establish a positive safety culture in China. According to the Unemployment by Country 2021 [70], 23 out of 28 studies (82%) were conducted in countries with low unemployment (Malaysia, South Korea, Taiwan, China, United States, the United Kingdom, Australia, Saudi Arabia, and Sweden) and 5 studies (18%) were conducted in countries with high unemployment (Italy, Iran, and Spain).

## Contributing Factors

Elements of the models presented in the 28 selected studies were evaluated for consistency with the 4 factors identified in our previous study: *poor direct safety management and supervision*; *unsafe workplace conditions*; *workers' perceptions, skills, and training*; and *broader organizational factors*. All the emergent themes, categories, and codes matched up directly with each of the constructs included in the models in the general industrial settings and petrochemical industry. Concept matches in each of the studies are highlighted in Table 1 by labelling each match as "a," "b," "c," or "d" to indicate which of our 4 contributing factors it corresponds with. Based on the number of these matches, the model most consistent with the 4 contributing factors was identified.

The *poor direct safety management and supervision* theme combines 2 categories, namely, ineffective safety system and poor safety monitoring. Concepts in the reviewed models that correspond with these categories have been labelled as "a" (Table 1). Of the 28 studies evaluated, the model constructs of

20 (71%) studies were matched with categories and codes of theme "a" [6,11,19,41,42,50,52,54-56,59-62,64-69].

The *unsafe workplace conditions* theme consists of 2 categories: unsafe physical environment and unsafe psychological environment. The codes of these categories have been matched with concepts in the reviewed models by using the character "b" in Table 1. Of the 28 assessed studies, constructs included in the models of 22 (78%) studies were matched with categories and codes of theme "b" [11,14,19,41,42,50,51,53-65,67,69,71].

The *workers' perceptions, skills, and training* theme consists of 2 categories: workers not skilled enough to deal with safety issues and active errors. The codes of these categories have been matched with concepts in the reviewed models by using the character "c" in Table 1. Of the 28 assessed studies, 23 (82%) found constructs included in the model and matches with categories and codes of theme "c" [6,11,14,19,27,30,42,50-64,66].

The *broader organizational factors* theme includes unsafe management culture and organizational impact on workers' safety categories. The codes of these categories have been matched with concepts in the reviewed models by using the character "d" in Table 1. Constructs applied in 8 (28%) of the 28 studies included in the literature review were matched with categories and codes of theme "d" [6,14,30,42,51,52,63,65].

## Selection of the Theoretical Model

The purpose of reviewing the models of safe work behaviors was to (1) identify constructs included in the selected models and (2) identify the model that included constructs most consistent with the findings of the preceding qualitative study of Iranian petrochemical workers' perceptions of factors affecting safe work behaviors [43]. The constructs identified in the model described by Wu et al (see Table 1 [42]) most closely matched those identified in our qualitative study. Wu et al [42] proposed a theoretical model relating to safety behaviors in a petrochemical company and explored 3 major factors, namely, *safety leadership*, *safety climate*, and *safety performance*. Safety

leadership consists of 3 subscales: *safety coaching, safety caring, and safety controlling*. Safety climate also consists of 3 subscales: *workers' commitment to safety, perceived risk, and emergency response*. Safety performance consists of 4 subscales: *safety inspection, accident investigation, safety training, and safety motivation*. The constructs described by Wu et al [42] were well matched to the contributing factors identified in our qualitative study: safety leadership and its subscales matched with poor direct safety management and supervision; safety climate and its subscales matched with unsafe workplace conditions; safety performance and its subscales matched with workers' perceptions, skills, and training; and codes from several subscales matched with broader organizational factors.

## Discussion

### Principal Findings

This study evaluated the consistency between 28 theoretical models proposed to explain and predict safe behaviors in industrial settings and qualitative findings of our previous study examining the factors that petrochemical workers perceived to affect safe behaviors. The first aim of this study was to identify the theoretical models that were developed to explain and predict safe behavior in both the petrochemical industry and general industrial settings. The second aim was to select the model that corresponds most closely with our qualitative findings. The majority of the included studies were found to focus on some aspects of our qualitative data. Most of the studies were conducted in various industrial domains. Our findings indicate that the key elements of the model described by Wu et al [42] corresponded most strongly with the themes derived from our qualitative interview study. Several of the other models identified in the review also included elements that corresponded closely with the themes identified in our interview study.

### Comparison With Previous Studies

Based on the findings from our review, the safety concern of managers and supervisors was identified as the most key factor affecting the workers' risk perception and their understanding of safety issues [19,42,56,62,72]. In addition, supervisors' safe behaviors such as regular safety inspection, motivating and supporting the subordinates, and providing resources for appropriate training of the workforce can motivate safety performance, encourage workers' participation as well as reporting potential incidents and unsafe behaviors [41,50,61,64,69,71]. Managers have a crucial role in the success of workplace health promotion activities and changing employee health behavior. Managers and supervisors are able to create a safe organizational climate and positively influence employees' healthy and safe work behavior by providing necessary resources for planning, implementing, and evaluating workplace health promotion interventions. Supporting workplace health promotion programs can enhance the engagement of the employees and benefit both organizations and employees in the long run [73]. These findings are consistent with the *poor direct safety management and supervision* theme of our qualitative study. The included studies assessed the relationship between safety climate and workers' perceptions of safety issues and various aspects of safety-related behavior. These studies examined work

safety climate and aspects of working conditions and their associations with occupational safety and work-related injuries among various workplace settings [11,42,51,53,69]. They focus mainly on improving working conditions and its organizational and psychological aspects such as perceived work pressure, emergency response, physical and psychosocial hazards at work, job demands, physical factors of workplace, mental workload and stress, and defect of technology and design [42,53,58,62,65,72]. A Korean study reported that working conditions are important key factors that could influence workers' behavior at the workplace. The employment status of workers impacts the organizational commitment and safety performance. Even within the same organization, workers in different employment statuses are treated differently. Because of the health inequalities of temporary employment such as workers' compensation and welfare programs, employment status affects workers' health and causes disparities in safety, which is compounded by unsafe workplace settings. In fact, occupational injury rates for part-time and temporary contract workers are significantly higher than those for regular and permanent workers in the same occupation [74]. These results support our qualitative findings related to the *unsafe workplace conditions* theme. According to the review of 28 studies, adequate and appropriate job training, workers' perception of risk, and their knowledge of health and safety issues were negatively correlated with occupational accident rates [50,52,71]. Workers' skills and perceptions of their own behavior plays a significant role in producing better safety outcomes [27,30,42,64,75]. These findings are also consistent with the *workers' perceptions, skills, and training* theme of the qualitative study. The findings of the included studies also focused on the importance of management culture and organizational impact on workers' safety. These findings highlight that workers' cognition and attitude, safety culture, and prioritizing safety can influence workers to adopt positive behavioral intentions toward safety at workplace [6,14,42,52,56,63,72,76]. These findings also support the fourth theme of our qualitative findings: *broader organizational factors*.

Nixon and Braithwaite [77] in their detailed qualitative investigation suggest that a well-developed conceptual model can be employed to train employees, manage their progress, and develop high work performance culture. Wu et al's [42] model suggests that 2 important prior causes greatly affect safe behaviors and performance: safety leadership and safety climate. In this context, the role of managers and supervisors in shaping subordinates' safe behaviors is likely to be considerably greater than that of managers and supervisors in work settings with routine production processes [78]. Consistent with our qualitative findings, the results of a sample of 103 industrial organizations located in Spain indicated that supervisor enforcement and managers' commitment to safety is significantly related to workers' safety compliance [79]. Supervisors have the most frequent contact with employees and workers among the hierarchical levels of an organization and are directly responsible for guaranteeing safety performance at the workplace. Managers' responses to safety are a key determinant in the creation of subordinates' beliefs about the importance of safety to the work settings [80,81]. As expected, a positive safety culture will be developed when managers commit to the priority

of safety [41]. In addition, workers perceive that the role of both the managers and supervisors in combination with their safety commitments enables workers to develop a mutual obligation with them and these obligations will lead to safer behavior of workers [82].

The findings of our qualitative study indicated that unsafe workplace conditions may be a particularly strong influence on whether work is done safely or not. Wu et al [42] defined safety climate as “employees' perception, attitudes, beliefs, and values of safety of an environment or organization, which is affected by personal and organizational factors, and affects employees' safety performance.” The relationship between safety climate and safe work behavior has been well established in safety research, and safety climate has been identified as a critical indicator for enhanced safety, which has been linked to increased safe behaviors and decreased injury severity in industrial settings [83-85]. Safety climate is therefore related to how workers perceive organizational priorities in their workplace and has a major role in motivating workers to work safely [86]. Safety climate is indicated by the perceptions of norms and actions that help to prevent unsafe acts [20]. Furthermore, Beus et al [87] reported that a supportive safety climate is associated with higher rule compliance and fewer work-related injuries. A positive organization's safety climate provides workers with cues and vital information regarding the extent to which safe behaviors are valued, supported, and rewarded in the workplace [88]. Studies have shown that safety climate scores are significantly predictive of worker safety attitudes, safety compliance and performance, workplace accidents, injuries, near misses, safety knowledge, and safety motivation [89-91].

Another factor identified in our qualitative study was workers' perceptions, skills, and training. Occupational hazards and safety performances are affected by factors, including workers' safety attitude and knowledge [42]. Findings indicate that workers with more knowledge of the products, work environment, and objectives of the organization demonstrated a higher level of safe behaviors in their contexts as compared to their ignorant colleagues [92]. Workers' knowledge, skills, and competence with regard to safety are the required content of safety training [93,94]. Workers who do not fully understand the safety and health instructions that are related to their jobs tend to experience higher accident rates. In addition, owing to differences in the education level, safety training should be provided separately according to workers' education levels and ages. Therefore, safety training should be designed in accordance with the requirements for workers to be aware of safety at work [75,95]. Korkmaz and Park [75] also agreed that workers who are familiar with their job tasks could help by being involved in the risk assessment in the workplace. Researchers [96,97] found that organizations can have low injury and accident rates when they predict and implement practical safety training regularly.

In Wu et al's model [42], safety performance reflects the workers' perceptions, skills, and training. Safety leadership has been associated with safety management and supervision, in general. Further, the dimensions of safety climate (workers' commitment to safety, perceived risk, and emergency response) are consistent with categories and codes of the unsafe workplace

conditions theme. Since our qualitative findings align with the dimensions of the established model by Wu et al [42], we evaluate this model as applicable in order to design educational interventions for petrochemical workers. Technical intervention safety practices have a positive effect on safe work behaviors. In addition, the management safety intervention plays a significant role in the implementation of safety practices. Therefore, this model provides some guidance to industrial companies to better focus on specific safety intervention practices that improve workers' safe behaviors and their safety awareness to work safely.

### Implications for Research and Practice

The current literature search identified 28 studies that served as examples for the translation of a safety model into intervention efforts, which can guide workplaces to improve their safety conditions and reduce accident rates. When reviewing the models in the 28 selected studies, the main feature of the model was assumed from the assessment of general levels of safety and major components of conceptualizing safety (eg, safety management, safety climate) to special and detailed latent hazard conditions such as levels of organizational support, and risk perceptions might be seen to imply that safety models are seen as ways to assess the wider and bigger picture of how safety promotion might work in industrial contexts.

### Limitations of This Study

This study enhances understanding of the factors affecting safe work behavior and highlights directions for further research. However, some important limitations should be recognized. A key limitation, which was difficult to avoid, is the exclusive focus on published research. This review included studies published in peer-reviewed journals. Although this was done to provide a high quality of evidence and findings, the criteria excluded a number of potentially valuable research and industry reports or unpublished studies. Evidence suggests that use of workplace safety models may be underreported. The studies identified, which were drawn from a variety of settings (eg, petrochemical, construction, oil and gas), indicated that safety models are widely used by organizations that are eager to develop better understanding of safety risks in their workplaces. A key weakness of the safety model approach may be that results obtained at one point in time may not prove to be repeatable at another. The studies reviewed in this paper do not allow firm conclusions to be drawn about the reliability, validity, and overall robustness of using safety models in practice. Deeper investigation into these issues would be a valuable focus for future research. The aim of the improvement plan is to have a better safety status by making suggestions for the Iranian petrochemical industry for workers. However, this may be applied in other countries. Nevertheless, this subject should be studied more for other industrial settings and countries in order to reach a more generalized result.

### Conclusions

This study is the first, to the best of our knowledge, to examine the key variables in theoretical frameworks designed to explain safety behaviors in industrial settings, identify potentially relevant theoretical models, and evaluate the suitability and

applicability of the models identified to explaining the safety of petrochemical workers based on independent qualitative findings about the factors that discourage safe work behaviors. The findings indicate growth in terms of the use of safety models to assess workers' safe behaviors and significant variation in the ways in which they are used and reported in the safety literature. For safety researchers and practitioners, the results are important because the models provide guidance on how workers may be influenced to work more safely. By identifying the conditions in which workers can be encouraged to change unsafe behaviors to safe ones, integrated safety intervention models can provide a valuable tool for enhancing safety performance. Lastly, this study has implications for leadership

at both the supervisory and management levels by identifying the effects of supervisor' behaviors and safety climate as determinants of safety performance. Taken as a whole, our findings encourage a holistic approach that takes into account both safety management and climate to comprehensively understand the individual and contextual factors that shape safe work behaviors in the petrochemical industry. It is important that future theoretical and conceptual frameworks address the inconsistencies identified in this study to enable the adoption and replication of safe behavior interventions in industries, thereby preventing workplace injuries and fatalities and making workplaces healthier and safer.

---

## Acknowledgments

The authors would like to thank all the participating interview workers, supervisors, managers, and safety staff members involved in this study.

---

## Authors' Contributions

AZH was the main investigator who collected and analyzed the qualitative data, conducted a literature review to identify theoretical models, and wrote the first draft of this manuscript. FG is the dissertation supervisor who contributed to the conception and design of this study. HS, FAS, and PB were the study advisors. AZH spent her sabbatical leave as a Visiting Researcher in the Faculty of Medicine and Health, The University of Sydney, under the supervision of PB and LM. FG, HS, FAS, PB, and LM were involved in revising the manuscript for intellectual content and AZH, PB, LM, and KP finalized the manuscript. AZH, FG, HS, and FAS contributed to analyzing qualitative data. Qualitative findings were repeatedly discussed and revised, and the theoretical models were investigated by AZH, PB, and LM. PB, LM, and KP made significant contributions to the critical editing of English grammar. All authors have read and approved the final manuscript.

---

## Conflicts of Interest

None declared.

---

## Multimedia Appendix 1

Themes, categories, and codes from the qualitative analysis.

[DOC File, 20 KB - [publichealth\\_v7i5e22851\\_app1.doc](#) ]

---

## References

1. Sanders NR, Wood JD. Foundations of Sustainable Business: Theory, Function, and Strategy, 2nd Edition. United States: Wiley; Dec 12, 2019:1-352.
2. The prevention of occupational diseases. International Labor Organization. 2013 Apr 28. URL: [https://www.ilo.org/wcmsp5/groups/public/---ed\\_protect/---protrav/---safework/documents/publication/wcms\\_208226.pdf](https://www.ilo.org/wcmsp5/groups/public/---ed_protect/---protrav/---safework/documents/publication/wcms_208226.pdf) [accessed 2013-03-25]
3. Aburumman M, Newnam S, Fildes B. Evaluating the effectiveness of workplace interventions in improving safety culture: A systematic review. *Safety Science* 2019 Jun 01;115:376-392. [doi: [10.1016/j.ssci.2019.02.027](https://doi.org/10.1016/j.ssci.2019.02.027)]
4. Hermann JA, Ibarra GV, Hopkins BL. A Safety Program That Integrated Behavior-Based Safety and Traditional Safety Methods and Its Effects on Injury Rates of Manufacturing Workers. *Journal of Organizational Behavior Management* 2010 Mar 25;30(1):6-25. [doi: [10.1080/01608060903472445](https://doi.org/10.1080/01608060903472445)]
5. Mattson Molnar M, Von Thiele Schwarz U, Hellgren J, Hasson H, Tafvelin S. Leading for Safety: A Question of Leadership Focus. *Saf Health Work* 2019 Jun;10(2):180-187 [FREE Full text] [doi: [10.1016/j.shaw.2018.12.001](https://doi.org/10.1016/j.shaw.2018.12.001)] [Medline: [31297280](https://pubmed.ncbi.nlm.nih.gov/31297280/)]
6. Martínez-Córcoles M, Gracia F, Tomás I, Peiró JM. Leadership and employees' perceived safety behaviours in a nuclear power plant: A structural equation model. *Safety Science* 2011 Oct;49(8-9):1118-1129. [doi: [10.1016/j.ssci.2011.03.002](https://doi.org/10.1016/j.ssci.2011.03.002)]
7. Parker SK, Axtell CM, Turner N. Designing a safer workplace: Importance of job autonomy, communication quality, and supportive supervisors. *Journal of Occupational Health Psychology* 2001;6(3):211-228. [doi: [10.1037//1076-8998.6.3.211](https://doi.org/10.1037//1076-8998.6.3.211)]
8. Mearns K, Flin R, Fleming M. Human and organisational factors in offshore safety. *Offshore Technology Report-Health and Safety*. Aberdeen (United Kingdom): The Robert Gordon University; 1997. URL: <https://www.osti.gov/etdeweb/biblio/595349> [accessed 1998-02-01]
9. Flin R. Leadership for safety: industrial experience. *Quality and Safety in Health Care* 2004 Dec 01;13(suppl\_2):ii45-ii51. [doi: [10.1136/qshc.2003.009555](https://doi.org/10.1136/qshc.2003.009555)]



10. Simard M, Marchand A. The behaviour of first-line supervisors in accident prevention and effectiveness in occupational safety. *Safety Science* 1994 Mar;17(3):169-185. [doi: [10.1016/0925-7535\(94\)90010-8](https://doi.org/10.1016/0925-7535(94)90010-8)]
11. Hald KS. Social influence and safe behavior in manufacturing. *Safety Science* 2018 Nov;109:1-11. [doi: [10.1016/j.ssci.2018.05.008](https://doi.org/10.1016/j.ssci.2018.05.008)]
12. Spurgeon A, Harrington JM, Cooper CL. Health and safety problems associated with long working hours: a review of the current position. *Occup Environ Med* 1997 Jun;54(6):367-375 [FREE Full text] [doi: [10.1136/oem.54.6.367](https://doi.org/10.1136/oem.54.6.367)] [Medline: [9245942](https://pubmed.ncbi.nlm.nih.gov/9245942/)]
13. Lee J, Lee Y. Can working hour reduction save workers? *Labour Economics* 2016 Jun;40:25-36. [doi: [10.1016/j.labeco.2016.02.004](https://doi.org/10.1016/j.labeco.2016.02.004)]
14. Petitta L, Probst TM, Barbaranelli C, Ghezzi V. Disentangling the roles of safety climate and safety culture: Multi-level effects on the relationship between supervisor enforcement and safety compliance. *Accid Anal Prev* 2017 Feb;99(Pt A):77-89. [doi: [10.1016/j.aap.2016.11.012](https://doi.org/10.1016/j.aap.2016.11.012)] [Medline: [27883895](https://pubmed.ncbi.nlm.nih.gov/27883895/)]
15. Ashkanasy NM, Jackson CRA. Organizational culture and climate. In: Anderson N, Ones DS, Sinangil HK, Viswesvaran C, editors. *Handbook of Industrial, Work and Organizational Psychology*. United States: Sage Publications; 2002:398-415.
16. Givhchi S, Hemmativaghef E, Hoveidi H. Association between safety leading indicators and safety climate levels. *J Safety Res* 2017 Sep;62:23-32. [doi: [10.1016/j.jsr.2017.05.003](https://doi.org/10.1016/j.jsr.2017.05.003)] [Medline: [28882271](https://pubmed.ncbi.nlm.nih.gov/28882271/)]
17. Zohar D. Safety climate in industrial organizations: Theoretical and applied implications. *Journal of Applied Psychology* 1980;65(1):96-102. [doi: [10.1037/0021-9010.65.1.96](https://doi.org/10.1037/0021-9010.65.1.96)]
18. Smith TD, DeJoy DM. Safety climate, safety behaviors and line-of-duty injuries in the fire service. *Int J Emerg Serv* 2014 Mar 04;3(1):49-64. [doi: [10.1108/ijes-04-2013-0010](https://doi.org/10.1108/ijes-04-2013-0010)]
19. Newaz MT, Davis P, Jefferies M, Pillay M. The psychological contract: A missing link between safety climate and safety behaviour on construction sites. *Safety Science* 2019 Feb;112:9-17. [doi: [10.1016/j.ssci.2018.10.002](https://doi.org/10.1016/j.ssci.2018.10.002)]
20. Zohar D, Luria G. A multilevel model of safety climate: cross-level relationships between organization and group-level climates. *J Appl Psychol* 2005 Jul;90(4):616-628. [doi: [10.1037/0021-9010.90.4.616](https://doi.org/10.1037/0021-9010.90.4.616)] [Medline: [16060782](https://pubmed.ncbi.nlm.nih.gov/16060782/)]
21. Neal A, Griffin MA. A study of the lagged relationships among safety climate, safety motivation, safety behavior, and accidents at the individual and group levels. *J Appl Psychol* 2006 Jul;91(4):946-953. [doi: [10.1037/0021-9010.91.4.946](https://doi.org/10.1037/0021-9010.91.4.946)] [Medline: [16834517](https://pubmed.ncbi.nlm.nih.gov/16834517/)]
22. Hofmann DA, Stetzer A. A cross-level investigation of factors influencing unsafe behaviors and accidents. *Personnel Psychology* 1996 Jun;49(2):307-339. [doi: [10.1111/j.1744-6570.1996.tb01802.x](https://doi.org/10.1111/j.1744-6570.1996.tb01802.x)]
23. Guo BH, Yiu TW, González VA. Predicting safety behavior in the construction industry: Development and test of an integrative model. *Safety Science* 2016 Apr;84:1-11. [doi: [10.1016/j.ssci.2015.11.020](https://doi.org/10.1016/j.ssci.2015.11.020)]
24. Reason J. Human error: models and management. *BMJ* 2000 Mar 18;320(7237):768-770 [FREE Full text] [doi: [10.1136/bmj.320.7237.768](https://doi.org/10.1136/bmj.320.7237.768)] [Medline: [10720363](https://pubmed.ncbi.nlm.nih.gov/10720363/)]
25. Potter RE, Dollard MF, Owen MS, O'Keeffe V, Bailey T, Leka S. Assessing a national work health and safety policy intervention using the psychosocial safety climate framework. *Safety Science* 2017 Dec;100:91-102. [doi: [10.1016/j.ssci.2017.05.011](https://doi.org/10.1016/j.ssci.2017.05.011)]
26. Haghghi M, Taghdisi MH, Nadrian H, Moghaddam HR, Mahmoodi H, Alimohammadi I. Safety Culture Promotion Intervention Program (SCPIP) in an oil refinery factory: An integrated application of Geller and Health Belief Models. *Safety Science* 2017 Mar;93:76-85. [doi: [10.1016/j.ssci.2016.11.019](https://doi.org/10.1016/j.ssci.2016.11.019)]
27. Razmara A, Aghamolaei T, Madani A, Hosseini Z, Zare S. Prediction of safe driving Behaviours based on health belief model: the case of taxi drivers in Bandar Abbas, Iran. *BMC Public Health* 2018 Mar 20;18(1):380 [FREE Full text] [doi: [10.1186/s12889-018-5300-5](https://doi.org/10.1186/s12889-018-5300-5)] [Medline: [29558924](https://pubmed.ncbi.nlm.nih.gov/29558924/)]
28. Fallah Zavareh M, Mohamadi Hezaveh A, Nordfjærn T. Intention to use bicycle helmet as explained by the Health Belief Model, comparative optimism and risk perception in an Iranian sample. *Transportation Research Part F: Traffic Psychology and Behaviour* 2018 Apr;54:248-263. [doi: [10.1016/j.trf.2018.02.003](https://doi.org/10.1016/j.trf.2018.02.003)]
29. Zhang L, Dalal K, Wang S. Injury related risk behaviour: a Health belief model-based study of primary school students in a safe community in Shanghai. *PLoS One* 2013;8(8):e70563 [FREE Full text] [doi: [10.1371/journal.pone.0070563](https://doi.org/10.1371/journal.pone.0070563)] [Medline: [23950963](https://pubmed.ncbi.nlm.nih.gov/23950963/)]
30. Nioi A, Wendelboe-Nelson C, Cowan S, Cowie H, Rashid S, Ritchie P, et al. A randomised control crossover trial of a theory based intervention to improve sun-safe and healthy behaviours in construction workers: study protocol. *BMC Public Health* 2018 Feb 15;18(1):259 [FREE Full text] [doi: [10.1186/s12889-018-5164-8](https://doi.org/10.1186/s12889-018-5164-8)] [Medline: [29448922](https://pubmed.ncbi.nlm.nih.gov/29448922/)]
31. Moeini B, Hazavehei SMM, Zareban I, Mousali A, Bashiriyani S, Soltanian AR, et al. Effectiveness of an Educational Program Based on the Theory of Planned Behavior for Improving Safe Sexual Behaviors Intention among Addicted Males: A Quasi Experimental Study. *Int J High Risk Behav Addict* 2017 Jun 01;6(2):1-7 Article number e32432 [FREE Full text] [doi: [10.5812/ijhrba.32432](https://doi.org/10.5812/ijhrba.32432)]
32. White KM, Starfelt LC, Young RM, Hawkes AL, Leske S, Hamilton K. Predicting Australian adults' sun-safe behaviour: examining the role of personal and social norms. *Br J Health Psychol* 2015 May;20(2):396-412. [doi: [10.1111/bjhp.12108](https://doi.org/10.1111/bjhp.12108)] [Medline: [24917299](https://pubmed.ncbi.nlm.nih.gov/24917299/)]

33. Ledesma RD, Tosi JD, Díaz-Lázaro CM, Poó FM. Predicting road safety behavior with implicit attitudes and the Theory of Planned Behavior. *J Safety Res* 2018 Sep;66:187-194. [doi: [10.1016/j.jsr.2018.07.006](https://doi.org/10.1016/j.jsr.2018.07.006)] [Medline: [30121105](https://pubmed.ncbi.nlm.nih.gov/30121105/)]
34. Real K. Information Seeking and Workplace Safety: A Field Application of the Risk Perception Attitude Framework. *Journal of Applied Communication Research* 2008 Aug;36(3):339-359. [doi: [10.1080/00909880802101763](https://doi.org/10.1080/00909880802101763)]
35. Rimal RN, Real K. Perceived Risk and Efficacy Beliefs as Motivators of Change. *Human Comm Res* 2003 Jul;29(3):370-399. [doi: [10.1111/j.1468-2958.2003.tb00844.x](https://doi.org/10.1111/j.1468-2958.2003.tb00844.x)]
36. Barry P, Fleur DC, Su Mon KM. Asbestos exposure and compliance study of construction and maintenance workers. *Safe Work Australia*, Canberra. 2010 Feb 01. URL: <https://www.safeworkaustralia.gov.au/doc/asbestos-exposure-and-compliance-study-construction-and-maintenance-workers-follow-report> [accessed 2010-02-01]
37. Clissold G, Buttigieg DM, De Cieri H. A psychological approach to occupational safety. *Asia Pacific Journal of Human Resources* 2012 Jan 11;50(1):92-109. [doi: [10.1111/j.1744-7941.2011.00002.x](https://doi.org/10.1111/j.1744-7941.2011.00002.x)]
38. Cooper M. Towards a model of safety culture. *Safety Science* 2000 Nov;36(2):111-136. [doi: [10.1016/s0925-7535\(00\)00035-7](https://doi.org/10.1016/s0925-7535(00)00035-7)]
39. Lee J, Jeong S, Ko G, Park H, Ko Y. Development of a Food Safety and Nutrition Education Program for Adolescents by Applying Social Cognitive Theory. *Osong Public Health Res Perspect* 2016 Aug;7(4):248-260 [FREE Full text] [doi: [10.1016/j.phrp.2016.05.005](https://doi.org/10.1016/j.phrp.2016.05.005)] [Medline: [27635375](https://pubmed.ncbi.nlm.nih.gov/27635375/)]
40. Stackhouse M, Turner N. How do organizational practices relate to perceived system safety effectiveness? Perceptions of safety climate and co-worker commitment to safety as workplace safety signals. *J Safety Res* 2019 Sep;70:59-69. [doi: [10.1016/j.jsr.2019.04.002](https://doi.org/10.1016/j.jsr.2019.04.002)] [Medline: [31848010](https://pubmed.ncbi.nlm.nih.gov/31848010/)]
41. Gao Y, Fan Y, Wang J, Li X, Pei J. The mediating role of safety management practices in process safety culture in the Chinese oil industry. *Journal of Loss Prevention in the Process Industries* 2019 Jan;57:223-230. [doi: [10.1016/j.jlp.2018.11.017](https://doi.org/10.1016/j.jlp.2018.11.017)]
42. Wu T, Chang S, Shu C, Chen C, Wang C. Safety leadership and safety performance in petrochemical industries: The mediating role of safety climate. *Journal of Loss Prevention in the Process Industries* 2011 Nov;24(6):716-721. [doi: [10.1016/j.jlp.2011.04.007](https://doi.org/10.1016/j.jlp.2011.04.007)]
43. Zahiri Harsini A, Ghofranipour F, Sanaeinasab H, Amin Shokravi F, Bohle P, Matthews LR. Factors associated with unsafe work behaviours in an Iranian petrochemical company: perspectives of workers, supervisors, and safety managers. *BMC Public Health* 2020 Jul 31;20(1):1192 [FREE Full text] [doi: [10.1186/s12889-020-09286-0](https://doi.org/10.1186/s12889-020-09286-0)] [Medline: [32736619](https://pubmed.ncbi.nlm.nih.gov/32736619/)]
44. Zahiri Harsini A, Ghofranipour F, Sanaeinasab H, Amin Shokravi F. A randomised controlled trial of an educational intervention to promote safe behaviours in petrochemical workers: a study protocol. *BMC Public Health* 2019 Jun 18;19(1):776 [FREE Full text] [doi: [10.1186/s12889-019-7126-1](https://doi.org/10.1186/s12889-019-7126-1)] [Medline: [31215406](https://pubmed.ncbi.nlm.nih.gov/31215406/)]
45. Valerio MA, Rodriguez N, Winkler P, Lopez J, Dennison M, Liang Y, et al. Comparing two sampling methods to engage hard-to-reach communities in research priority setting. *BMC Med Res Methodol* 2016 Oct 28;16(1):146 [FREE Full text] [doi: [10.1186/s12874-016-0242-z](https://doi.org/10.1186/s12874-016-0242-z)] [Medline: [27793191](https://pubmed.ncbi.nlm.nih.gov/27793191/)]
46. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today* 2004 Feb;24(2):105-112. [doi: [10.1016/j.nedt.2003.10.001](https://doi.org/10.1016/j.nedt.2003.10.001)] [Medline: [14769454](https://pubmed.ncbi.nlm.nih.gov/14769454/)]
47. Hsieh H, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res* 2005 Nov;15(9):1277-1288. [doi: [10.1177/1049732305276687](https://doi.org/10.1177/1049732305276687)] [Medline: [16204405](https://pubmed.ncbi.nlm.nih.gov/16204405/)]
48. Loerbros A, Nguyen XQ, Vu-Eickmann P, Krichbaum M, Kulzer B, Icks A, et al. Psychosocial working conditions and diabetes self-management at work: A qualitative study. *Diabetes Res Clin Pract* 2018 Jun;140:129-138. [doi: [10.1016/j.diabres.2018.03.023](https://doi.org/10.1016/j.diabres.2018.03.023)] [Medline: [29608978](https://pubmed.ncbi.nlm.nih.gov/29608978/)]
49. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009 Jul 21;6(7):e1000100 [FREE Full text] [doi: [10.1371/journal.pmed.1000100](https://doi.org/10.1371/journal.pmed.1000100)] [Medline: [19621070](https://pubmed.ncbi.nlm.nih.gov/19621070/)]
50. Griffin MA, Neal A. Perceptions of safety at work: A framework for linking safety climate to safety performance, knowledge, and motivation. *Journal of Occupational Health Psychology* 2000;5(3):347-358. [doi: [10.1037/1076-8998.5.3.347](https://doi.org/10.1037/1076-8998.5.3.347)]
51. Brown KA, Willis P, Prussia GE. Predicting safe employee behavior in the steel industry: Development and test of a sociotechnical model. *Journal of Operations Management* 2000 Sep 29;18(4):445-465. [doi: [10.1016/S0272-6963\(00\)00033-4](https://doi.org/10.1016/S0272-6963(00)00033-4)]
52. Hong Y, Lin Y, Pai H, Lai Y, Lee I. Developing a Safety and Health Training Model for Petrochemical Workers. *The Kaohsiung Journal of Medical Sciences* 2004 Feb;20(2):56-61. [doi: [10.1016/s1607-551x\(09\)70085-3](https://doi.org/10.1016/s1607-551x(09)70085-3)]
53. Seo D. An explicative model of unsafe work behavior. *Safety Science* 2005 Mar;43(3):187-211. [doi: [10.1016/j.ssci.2005.05.001](https://doi.org/10.1016/j.ssci.2005.05.001)]
54. Pousette A, Larsson S, Törner M. Safety climate cross-validation, strength and prediction of safety behaviour. *Safety Science* 2008 Mar;46(3):398-404. [doi: [10.1016/j.ssci.2007.06.016](https://doi.org/10.1016/j.ssci.2007.06.016)]
55. Larsson S, Pousette A, Törner M. Psychological climate and safety in the construction industry-mediated influence on safety behaviour. *Safety Science* 2008 Mar;46(3):405-412. [doi: [10.1016/j.ssci.2007.05.012](https://doi.org/10.1016/j.ssci.2007.05.012)]
56. Zhou Q, Fang D, Wang X. A method to identify strategies for the improvement of human safety behavior by considering safety climate and personal experience. *Safety Science* 2008 Dec;46(10):1406-1419. [doi: [10.1016/j.ssci.2007.10.005](https://doi.org/10.1016/j.ssci.2007.10.005)]

57. Lu C, Yang C. Safety leadership and safety behavior in container terminal operations. *Safety Science* 2010 Feb;48(2):123-134. [doi: [10.1016/j.ssci.2009.05.003](https://doi.org/10.1016/j.ssci.2009.05.003)]
58. Li F, Jiang L, Yao X, Li Y. Job demands, job resources and safety outcomes: The roles of emotional exhaustion and safety compliance. *Accid Anal Prev* 2013 Mar;51:243-251. [doi: [10.1016/j.aap.2012.11.029](https://doi.org/10.1016/j.aap.2012.11.029)] [Medline: [23274477](https://pubmed.ncbi.nlm.nih.gov/23274477/)]
59. Qinqin C, Jia Q, Yuan Z, Huang L. Environmental risk source management system for the petrochemical industry. *Process Safety and Environmental Protection* 2014 May;92(3):251-260. [doi: [10.1016/j.psep.2013.01.004](https://doi.org/10.1016/j.psep.2013.01.004)]
60. Shin DP, Gwak HS, Lee DE. Modeling the predictors of safety behavior in construction workers. *Int J Occup Saf Ergon* 2015;21(3):298-311. [doi: [10.1080/10803548.2015.1085164](https://doi.org/10.1080/10803548.2015.1085164)] [Medline: [26414618](https://pubmed.ncbi.nlm.nih.gov/26414618/)]
61. Wu C, Fang D, Li N. Roles of owners' leadership in construction safety: The case of high-speed railway construction projects in China. *International Journal of Project Management* 2015 Nov;33(8):1665-1679. [doi: [10.1016/j.jproman.2015.07.005](https://doi.org/10.1016/j.jproman.2015.07.005)]
62. Azadeh A, Saberi M, Rouzbahman M, Valianpour F. A neuro-fuzzy algorithm for assessment of health, safety, environment and ergonomics in a large petrochemical plant. *Journal of Loss Prevention in the Process Industries* 2015 Mar;34:100-114. [doi: [10.1016/j.jlp.2015.01.008](https://doi.org/10.1016/j.jlp.2015.01.008)]
63. Alshahrani A, Panuwatwanich K, Mohamed S. Relationship between national culture and safety behavior: evidence from petrochemical employees in Saudi Arabia. 2014 Nov 28 Presented at: The 2014 (5th) international conference on engineering, project, and production management; 26-28 November 2014; South Africa p. 312-321. [doi: [10.32738/ceppm.201411.0032](https://doi.org/10.32738/ceppm.201411.0032)]
64. Wang J, Zou PX, Li PP. Critical factors and paths influencing construction workers' safety risk tolerances. *Accid Anal Prev* 2016 Aug;93:267-279. [doi: [10.1016/j.aap.2015.11.027](https://doi.org/10.1016/j.aap.2015.11.027)] [Medline: [26775077](https://pubmed.ncbi.nlm.nih.gov/26775077/)]
65. Zhang Y, Shao W, Zhang M, Li H, Yin S, Xu Y. Analysis 320 coal mine accidents using structural equation modeling with unsafe conditions of the rules and regulations as exogenous variables. *Accid Anal Prev* 2016 Jul;92:189-201. [doi: [10.1016/j.aap.2016.02.021](https://doi.org/10.1016/j.aap.2016.02.021)] [Medline: [27085591](https://pubmed.ncbi.nlm.nih.gov/27085591/)]
66. Mazlina Zaira M, Hadikusumo B. Structural equation model of integrated safety intervention practices affecting the safety behaviour of workers in the construction industry. *Safety Science* 2017 Oct;98:124-135. [doi: [10.1016/j.ssci.2017.06.007](https://doi.org/10.1016/j.ssci.2017.06.007)]
67. Jafari MJ, Eskandari D, Valipour F, Mehrabi Y, Charkhand H, Mirghotbi M. Development and validation of a new safety climate scale for petrochemical industries. *Work* 2017;58(3):309-317. [doi: [10.3233/WOR-172623](https://doi.org/10.3233/WOR-172623)] [Medline: [29036870](https://pubmed.ncbi.nlm.nih.gov/29036870/)]
68. Zhang Y, Zhang M, Qian C. System dynamics analysis for petrochemical enterprise fire safety system. *Procedia Engineering* 2018;211:1034-1042. [doi: [10.1016/j.proeng.2017.12.107](https://doi.org/10.1016/j.proeng.2017.12.107)]
69. Wang C, Wang J, Wang X, Yu H, Bai L, Sun Q. Exploring the impacts of factors contributing to unsafe behavior of coal miners. *Safety Science* 2019 Jun;115:339-348. [doi: [10.1016/j.ssci.2019.02.003](https://doi.org/10.1016/j.ssci.2019.02.003)]
70. Unemployment by country 2021. *World Population Review*. 2021. URL: <https://worldpopulationreview.com/country-rankings/unemployment-by-country> [accessed 2021-02-01]
71. Godbey, Jessie. The effects of behavior-based safety techniques on behavior variation, targeted and non-targeted safe behaviors, and productivity and quality in manufacturing facilities. Auburn University Electronic Theses and Dissertations. 2006 Dec 15. URL: <http://hdl.handle.net/10415/1297> [accessed 2006-12-15]
72. Isha ASN. Occupational health and safety practices in the petrochemical industries of Malaysia. eTheses Online Service. 2012 Mar. URL: <https://ethos.bl.uk/OrderDetails.do?uin=uk.bl.ethos.587829> [accessed 2012-03-01]
73. Jimenez P, Bregenzer A. Integration of eHealth Tools in the Process of Workplace Health Promotion: Proposal for Design and Implementation. *J Med Internet Res* 2018 Feb 23;20(2):e65 [FREE Full text] [doi: [10.2196/jmir.8769](https://doi.org/10.2196/jmir.8769)] [Medline: [29475828](https://pubmed.ncbi.nlm.nih.gov/29475828/)]
74. Min K, Song S, Min J. Topic Modeling of Social Networking Service Data on Occupational Accidents in Korea: Latent Dirichlet Allocation Analysis. *J Med Internet Res* 2020 Aug 13;22(8):e19222 [FREE Full text] [doi: [10.2196/19222](https://doi.org/10.2196/19222)] [Medline: [32663156](https://pubmed.ncbi.nlm.nih.gov/32663156/)]
75. Korkmaz S, Park DJ. Comparison of Safety Perception between Foreign and Local Workers in the Construction Industry in Republic of Korea. *Saf Health Work* 2018 Mar;9(1):53-58 [FREE Full text] [doi: [10.1016/j.shaw.2017.07.002](https://doi.org/10.1016/j.shaw.2017.07.002)] [Medline: [30363074](https://pubmed.ncbi.nlm.nih.gov/30363074/)]
76. Nedzamba G. Safety perceptions on productivity in the petrochemical industry. North-West University Repository. 2018 May. URL: <http://hdl.handle.net/10394/31029> [accessed 2018-09-13]
77. Nixon J, Braithwaite GR. What do aircraft accident investigators do and what makes them good at it? Developing a competency framework for investigators using grounded theory. *Safety Science* 2018 Mar;103:153-161. [doi: [10.1016/j.ssci.2017.11.017](https://doi.org/10.1016/j.ssci.2017.11.017)]
78. Cooke T, Lingard H, Blismas N. Multi-level safety climates: An investigation into the health and safety of workgroups in road construction. 2008 Jun Presented at: Proceedings of CIB W099 International Conference on "Global Unity for Safety and Health in Construction; 28-30 June; Beijing, China.
79. Fernández-Muñiz B, Montes-Peón JM, Vázquez-Ordás CJ. The role of safety leadership and working conditions in safety performance in process industries. *Journal of Loss Prevention in the Process Industries* 2017 Nov;50:403-415. [doi: [10.1016/j.jlp.2017.11.001](https://doi.org/10.1016/j.jlp.2017.11.001)]
80. Fang D, Wu C, Wu H. Impact of the Supervisor on Worker Safety Behavior in Construction Projects. *J. Manage. Eng* 2015 Nov;31(6):04015001. [doi: [10.1061/\(asce\)me.1943-5479.0000355](https://doi.org/10.1061/(asce)me.1943-5479.0000355)]

81. Lingard H, Cooke T, Blismas N. Do Perceptions of Supervisors' Safety Responses Mediate the Relationship between Perceptions of the Organizational Safety Climate and Incident Rates in the Construction Supply Chain? *J. Constr. Eng. Manage* 2012 Feb;138(2):234-241. [doi: [10.1061/\(asce\)co.1943-7862.0000372](https://doi.org/10.1061/(asce)co.1943-7862.0000372)]
82. Zhou Z, Goh YM, Li Q. Overview and analysis of safety management studies in the construction industry. *Safety Science* 2015 Feb;72:337-350. [doi: [10.1016/j.ssci.2014.10.006](https://doi.org/10.1016/j.ssci.2014.10.006)]
83. Dedobbeleer N, Béland F. A safety climate measure for construction sites. *Journal of Safety Research* 1991 Jun;22(2):97-103. [doi: [10.1016/0022-4375\(91\)90017-p](https://doi.org/10.1016/0022-4375(91)90017-p)]
84. Liu X, Huang G, Huang H, Wang S, Xiao Y, Chen W. Safety climate, safety behavior, and worker injuries in the Chinese manufacturing industry. *Safety Science* 2015 Oct;78:173-178. [doi: [10.1016/j.ssci.2015.04.023](https://doi.org/10.1016/j.ssci.2015.04.023)]
85. Newaz MT, Davis PR, Jefferies M, Pillay M. Developing a safety climate factor model in construction research and practice. *ECAM* 2018 Jul 16;25(6):738-757. [doi: [10.1108/ecam-02-2017-0038](https://doi.org/10.1108/ecam-02-2017-0038)]
86. Mearns K, Kirwan B, Reader TW, Jackson J, Kennedy R, Gordon R. Development of a methodology for understanding and enhancing safety culture in Air Traffic Management. *Safety Science* 2013 Mar;53:123-133. [doi: [10.1016/j.ssci.2012.09.001](https://doi.org/10.1016/j.ssci.2012.09.001)]
87. Beus JM, Payne SC, Bergman ME, Arthur W. Safety climate and injuries: an examination of theoretical and empirical relationships. *J Appl Psychol* 2010 Jul;95(4):713-727. [doi: [10.1037/a0019164](https://doi.org/10.1037/a0019164)] [Medline: [20604591](https://pubmed.ncbi.nlm.nih.gov/20604591/)]
88. Probst TM, Goldenhar LM, Byrd JL, Betit E. The Safety Climate Assessment Tool (S-CAT): A rubric-based approach to measuring construction safety climate. *J Safety Res* 2019 Jun;69:43-51. [doi: [10.1016/j.jsr.2019.02.004](https://doi.org/10.1016/j.jsr.2019.02.004)] [Medline: [31235234](https://pubmed.ncbi.nlm.nih.gov/31235234/)]
89. Clarke S. An integrative model of safety climate: Linking psychological climate and work attitudes to individual safety outcomes using meta-analysis. *J Occup Organ Psychol* Sep 2010 Sep;83(3):553-578. [doi: [10.1348/096317909x452122](https://doi.org/10.1348/096317909x452122)]
90. Christian MS, Bradley JC, Wallace JC, Burke MJ. Workplace safety: a meta-analysis of the roles of person and situation factors. *J Appl Psychol* 2009 Sep;94(5):1103-1127. [doi: [10.1037/a0016172](https://doi.org/10.1037/a0016172)] [Medline: [19702360](https://pubmed.ncbi.nlm.nih.gov/19702360/)]
91. Jiang L, Lavaysse LM, Probst TM. Safety climate and safety outcomes: A meta-analytic comparison of universal vs. industry-specific safety climate predictive validity. *Work & Stress* 2018 Apr 08;33(1):41-57. [doi: [10.1080/02678373.2018.1457737](https://doi.org/10.1080/02678373.2018.1457737)]
92. Nesheim T, Gressgård LJ. Knowledge sharing in a complex organization: Antecedents and safety effects. *Safety Science* 2014 Feb;62:28-36. [doi: [10.1016/j.ssci.2013.07.018](https://doi.org/10.1016/j.ssci.2013.07.018)]
93. Burke MJ, Chan-Serafin S, Salvador R, Smith A, Sarpy SA. The role of national culture and organizational climate in safety training effectiveness. *European Journal of Work and Organizational Psychology* 2008 Mar;17(1):133-152. [doi: [10.1080/13594320701307503](https://doi.org/10.1080/13594320701307503)]
94. Wachter JK, Yorio PL. A system of safety management practices and worker engagement for reducing and preventing accidents: an empirical and theoretical investigation. *Accid Anal Prev* 2014 Jul;68:117-130 [FREE Full text] [doi: [10.1016/j.aap.2013.07.029](https://doi.org/10.1016/j.aap.2013.07.029)] [Medline: [23993683](https://pubmed.ncbi.nlm.nih.gov/23993683/)]
95. Cheng C, Wu T. An investigation and analysis of major accidents involving foreign workers in Taiwan's manufacture and construction industries. *Safety Science* 2013 Aug;57:223-235. [doi: [10.1016/j.ssci.2013.02.008](https://doi.org/10.1016/j.ssci.2013.02.008)]
96. Lee T. Assessment of safety culture at a nuclear reprocessing plant. *Work & Stress* 1998 Jul;12(3):217-237. [doi: [10.1080/02678379808256863](https://doi.org/10.1080/02678379808256863)]
97. Jiang L, Yu G, Li Y, Li F. Perceived colleagues' safety knowledge/behavior and safety performance: safety climate as a moderator in a multilevel study. *Accid Anal Prev* 2010 Sep;42(5):1468-1476. [doi: [10.1016/j.aap.2009.08.017](https://doi.org/10.1016/j.aap.2009.08.017)] [Medline: [20538103](https://pubmed.ncbi.nlm.nih.gov/20538103/)]

*Edited by G Eysenbach; submitted 24.07.20; peer-reviewed by J Li, A Rosman; comments to author 21.09.20; revised version received 16.11.20; accepted 11.04.21; published 27.05.21.*

*Please cite as:*

Zahiri Harsini A, Bohle P, Matthews LR, Ghofranipour F, Sanaeinasab H, Amin Shokravi F, Prasad K  
*Evaluating the Consistency Between Conceptual Frameworks and Factors Influencing the Safe Behavior of Iranian Workers in the Petrochemical Industry: Mixed Methods Study*  
*JMIR Public Health Surveill* 2021;7(5):e22851  
URL: <https://publichealth.jmir.org/2021/5/e22851>  
doi: [10.2196/22851](https://doi.org/10.2196/22851)  
PMID: [34042605](https://pubmed.ncbi.nlm.nih.gov/34042605/)

©Azita Zahiri Harsini, Philip Bohle, Lynda R Matthews, Fazlollah Ghofranipour, Hormoz Sanaeinasab, Farkhondeh Amin Shokravi, Krishan Prasad. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 27.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium,

provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# Increases in Naloxone Administrations by Emergency Medical Services Providers During the COVID-19 Pandemic: Retrospective Time Series Study

Dalia Khoury<sup>1</sup>, PhD; Alexander Preiss<sup>1</sup>, MS; Paul Geiger<sup>1</sup>, PhD; Mohd Anwar<sup>2</sup>, PhD; Kevin Paul Conway<sup>3</sup>, PhD

<sup>1</sup>Research Triangle Institute International, Research Triangle Park, NC, United States

<sup>2</sup>North Carolina Agricultural and Technical State University, Greensboro, NC, United States

<sup>3</sup>National Institute of Mental Health, Bethesda, MD, United States

**Corresponding Author:**

Dalia Khoury, PhD

Research Triangle Institute International

3040 East Cornwallis Road

Research Triangle Park, NC, 27709

United States

Phone: 1 9195411227

Email: [dkhoury@rti.org](mailto:dkhoury@rti.org)

## Abstract

**Background:** The opioid crisis in the United States may be exacerbated by the COVID-19 pandemic. Increases in opioid use, emergency medical services (EMS) runs for opioid-related overdoses, and opioid overdose deaths have been reported. No study has examined changes in multiple naloxone administrations, an indicator of overdose severity, during the COVID-19 pandemic.

**Objective:** This study examines changes in the occurrence of naloxone administrations and multiple naloxone administrations during EMS runs for opioid-related overdoses during the COVID-19 pandemic in Guilford County, North Carolina (NC).

**Methods:** Using a period-over-period approach, we compared the occurrence of opioid-related EMS runs, naloxone administrations, and multiple naloxone administrations during the 29-week period before (September 1, 2019, to March 9, 2020) and after NC's COVID-19 state of emergency declaration (ie, the *COVID-19 period* of March 10 to September 30, 2020). Furthermore, historical data were used to generate a quasi-control distribution of period-over-period changes to compare the occurrence of each outcome during the COVID-19 period to each 29-week period back to January 1, 2014.

**Results:** All outcomes increased during the COVID-19 period. Compared to the previous 29 weeks, the COVID-19 period experienced increases in the weekly mean number of opioid-related EMS runs (25.6, SD 5.6 vs 18.6, SD 6.6;  $P < .001$ ), naloxone administrations (22.3, SD 6.2 vs 14.1, SD 6.0;  $P < .001$ ), and multiple naloxone administrations (5.0, SD 1.9 vs 2.7, SD 1.9;  $P < .001$ ), corresponding to proportional increases of 37.4%, 57.8%, and 84.8%, respectively. Additionally, the increases during the COVID-19 period were greater than 91% of all historical 29-week periods analyzed.

**Conclusions:** The occurrence of EMS runs for opioid-related overdoses, naloxone administrations, and multiple naloxone administrations during EMS runs increased during the COVID-19 pandemic in Guilford County, NC. For a host of reasons that need to be explored, the COVID-19 pandemic appears to have exacerbated the opioid crisis.

(*JMIR Public Health Surveill* 2021;7(5):e29298) doi:[10.2196/29298](https://doi.org/10.2196/29298)

**KEYWORDS**

opioids; naloxone; EMS; emergency medical services; COVID-19; pandemic; medical services; overdose; outcomes; opioid crisis; public health

## Introduction

The United States remains in an unrelenting opioid crisis. According to the latest official mortality data from the Centers for Disease Control and Prevention (CDC), 49,860 Americans

died from an opioid-related overdose in 2019 (~137 per day), a substantial increase from 2018 [1]. Furthermore, there is mounting concern that the COVID-19 pandemic will exacerbate the crisis [2,3]. Provisional data indicate that 81,003 people died from a drug overdose during the 12 months ending in May 2020, the highest ever recorded in a 1-year period in the United

States and a trend driven largely by heroin and synthetic opioids [4].

The magnitude and volatility of the opioid crisis warrants up-to-date data to monitor and guide intervention in the quickest manner possible, especially during potentially aggravating circumstances such as the COVID-19 pandemic [5]. However, the primary data used to track the opioid crisis in the United States (ie, verified opioid-related deaths from the CDC) are outdated by at least a year, a lag that substantially limits their value for surveillance purposes. Alternative timelier data have been leveraged by several studies to explore the opioid crisis generally [6,7] and how it has shifted since the onset of the COVID-19 pandemic. Niles et al [8] analyzed national urine drug testing patterns before and during the pandemic, and reported a significant increase during the pandemic especially for fentanyl and heroin. Wainwright et al [9] similarly reported a significant increase in positive urine tests during the pandemic for all drugs tested among a convenience sample of patients with or at risk for substance use disorders. Like Niles et al [8], the proportional increase reported by Wainwright et al [9] was greatest for fentanyl and heroin. Using data from the National Emergency Medical Services (EMS) Information System, a national registry of EMS agencies representing 80% of EMS dispatches across 47 states, Friedman et al [10] reported an increase in overdose-related cardiac events from mid-March through August 1, 2020. This surge in cardiac events corresponded temporally with an increase in social distancing as measured by cell phone mobility. Slavova and colleagues [11] examined changes in the number of EMS runs 52 days before and after the declaration of a state of emergency in Kentucky on March 6, 2020, and reported a significant increase in EMS runs in response to opioid overdoses after the declaration. The increase in opioid overdose-related EMS runs during COVID-19 reported by both Friedman et al [10] and Slavova et al [11] is especially noteworthy in the context of an overall decrease in EMS responses across the United States during the early part of the COVID-19 outbreak [12].

In addition to their timeliness, EMS data are also potentially valuable for studying the opioid epidemic because EMS providers increasingly use naloxone, an opioid antagonist medication, to treat respiratory depression in patients with suspected opioid overdose [13-15]. Naloxone administrations have been shown to hold promise as a near real-time proxy of the opioid epidemic [16-20]. Positive associations between EMS naloxone administrations and fatal and nonfatal overdose events have been reported [13,21]. Furthermore, the percentage of patients receiving multiple naloxone administrations has increased over time and may reflect the increasing severity of the opioid epidemic [14,22,23]. Although these studies suggest that analyzing EMS data on naloxone administrations may be a viable approach to monitor opioid overdoses, we are aware of only two studies comparing EMS naloxone administrations before and during the COVID-19 pandemic. Guber et al [24] reported proportional increases in EMS runs for opioid overdoses (43%), EMS-administered naloxone for opioid overdoses (61%), and drug overdose deaths (47%) in Marion County (Indiana) as compared to either of two prepandemic periods. Ballesteros et al [25] reported increases in both

EMS-administered naloxone for opioid-related overdoses (28%) and opioid overdose deaths (15%) in Michigan from March 1 to September 2020, as compared with the same period in 2019. To our knowledge, no study has examined changes in multiple naloxone administrations during the COVID-19 pandemic.

This study examines changes in naloxone administrations during EMS runs for opioid-related overdoses during the COVID-19 pandemic in Guilford County, the third most populous county in North Carolina (NC). We focused on Guilford County for two reasons. First, the confluence of the opioid crisis and COVID-19 in Guilford County is evident. The number of opioid overdose deaths increased in the county during the study period (47 in 2015, 71 in 2016, 98 in 2017, 96 in 2018, and 108 in 2019) [1,26]. Likewise, COVID-19 deaths in the county increased and, by the end of the study period, recorded a fatality rate (35.3 per 100,000) resembling the rate for NC (34.9 per 100,000) [27]. Second, one of the study investigators secured an ongoing data use agreement with the Guilford County EMS department to regularly share EMS data. For these reasons, we compared opioid overdose-related EMS runs, naloxone administrations, and multiple naloxone administrations before and during the COVID-19 pandemic in Guilford County.

## Methods

### Data

This study used data from the Guilford County, NC EMS department on opioid overdose-related EMS runs from January 1, 2014, to September 30, 2020. These dates correspond respectively to the earliest and latest data available to us prior to manuscript submission. Opioid overdose-related runs were identified using the fields *primary impression* and *secondary impression*, as indicated by the EMS personnel for the reasons for the encounter. The data set also included an observation for each treatment (eg, naloxone) administered during an opioid overdose-related EMS run. Because the data set was deidentified, we used a combination of the incident date, patient's birth date, and patient's gender to generate a quasi-unique run identifier to identify runs that included multiple naloxone administrations. We then grouped the data set to the unit of analysis of opioid overdose-related EMS runs and calculated weekly counts by calendar week to allow for comparison over time.

### Outcomes

We studied three weekly count outcomes: (1) opioid overdose-related EMS runs, (2) naloxone administrations during opioid overdose-related EMS runs, and (3) multiple naloxone administrations during opioid overdose-related EMS runs. Together, these outcomes permit the analyses of change in the occurrence (1 and 2) and severity (3) of opioid overdoses [14,16-20,22,23].

To measure change in these outcomes in the 29 weeks following NC's COVID-19 state of emergency declaration on March 10, 2020 (ie, the COVID-19 period), we calculated the mean of each outcome during the 29-week COVID-19 period, then expressed it as a percent change from the mean of the outcome during a comparison period.

### Period-Over-Period Approach

We evaluated period-over-period change between the COVID-19 period and two other comparison periods. For the first, we compared the COVID-19 period to the 29 calendar weeks immediately preceding the state of emergency declaration (September 1, 2019, to March 9, 2020). For the second, we compared the COVID-19 period to the same 29 calendar weeks of the previous year (March 13 to October 5, 2019). The second comparison accounts for potential seasonality in opioid overdoses [28]. We chose to include the second comparison after time series decomposition showed yearly seasonality in opioid overdose-related EMS runs.

This period-over-period approach is a generalization of the year-over-year growth rate commonly used in finance and business analytics [29]. The period-over-period changes between the COVID-19 period and the comparison periods can be considered the absolute effect size. To test the hypothesis that the COVID-19 period and comparison periods had unequal means, we conducted Welch unequal variances *t* tests for each outcome and comparison period. We treated the means in each 29-week period as independent samples. We used a critical value of 0.05 and two-tailed tests. Although these comparisons depict the magnitude of change of the outcomes during the COVID-19 period, they alone cannot convey how unique such a change is compared to more distal past periods. What may seem like a large increase may not be noteworthy (nor connected to the COVID-19 pandemic) if changes of similar magnitude

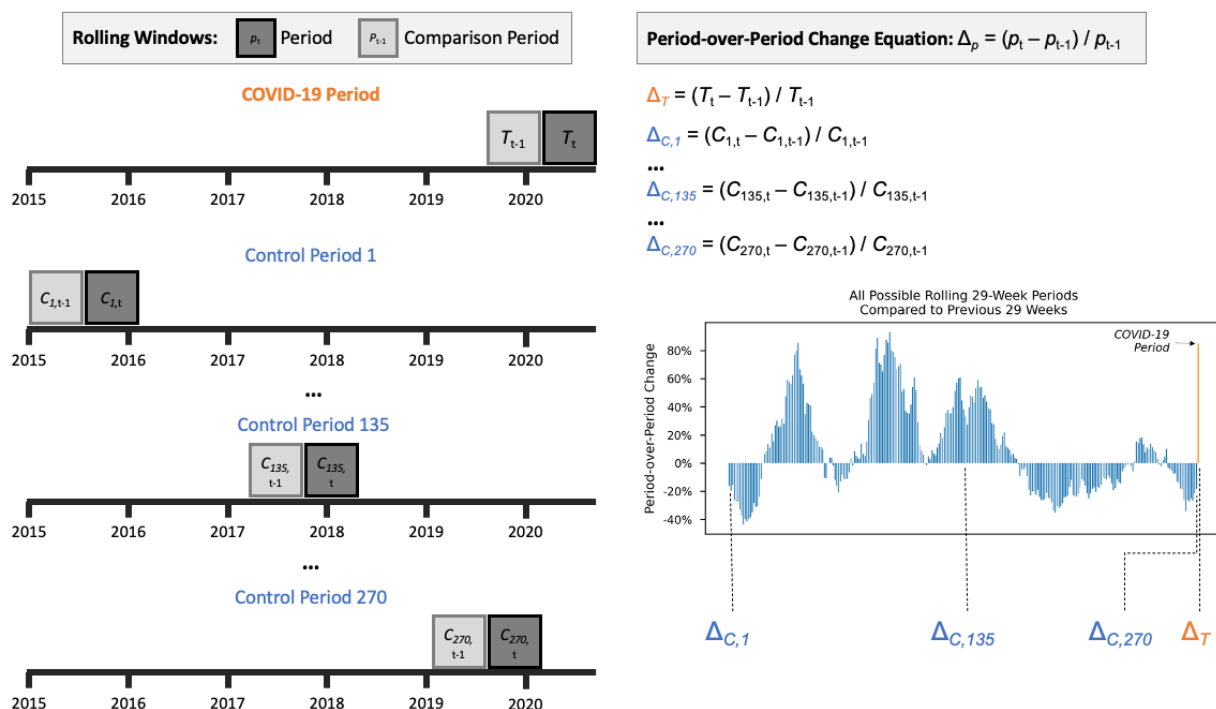
occurred frequently in the past. Therefore, we used historical data to generate a quasi-control distribution of period-over-period changes to compare to the change observed during the COVID-19 period.

This produced 270 possible comparisons of a 29-week period to the previous 29 weeks, and 246 possible comparisons of a 29-week period to the same 29 weeks of the previous year. We repeated this process for both comparison periods. We then compared the change during the COVID-19 period to the distribution of past period-over-period changes. This provides a measurement of how extreme the change in outcomes during the COVID-19 period was relative to past changes.

### Illustration of Period-Over-Period Approach

Figure 1 depicts the process used to calculate these period-over-period changes for the COVID-19 period (shown in orange) and the comparison periods (shown in blue). In the top timeline, the period-over-period change for the COVID-19 period is calculated by comparing the outcome from March 10 to September 30, 2020, to the outcome during the previous 29 weeks. The next three timelines depict how the quasi-control distribution was generated for more distal periods. In the second timeline (control period 1), the first control observation was calculated by comparing the outcome from January 1 to July 18, 2015, with the outcome from July 19, 2015, to January 30, 2016. The ellipses indicate that, from this starting point to the beginning of the COVID-19 state of emergency declaration, a control observation was calculated for each calendar week.

**Figure 1.** Illustration of period-over-period change method using previous 29 weeks as comparison period from January 1, 2015, to September 30, 2020.



### Statistical Analyses

The equations in Figure 1 show how period-over-period change was calculated for each period. This analytic approach is similar

in concept to the common difference in difference (DID) quasi-experimental research design [30]. In DID terms, we treated each possible 29-week period as a unit *p* that is observed



twice ( $t, t-1$ ). For each period,  $p_t$  is the mean of the outcome during the primary period and  $p_{t-1}$  is the mean of the outcome during the comparison period (either the previous 29 weeks or the same 29 weeks of the previous year). We calculated the percent change in period  $p$  as  $\Delta_p = (p_t - p_{t-1}) / p_{t-1}$ . We can consider the COVID-19 period to be the treatment group, which is exposed to the treatment condition (the COVID-19 pandemic) in  $t$  and to the control condition in  $t-1$ . The distribution of past period-over-period changes forms the control group, which is exposed to the control condition in both  $t$  and  $t-1$ . This results in a control group of  $n=270$  or  $n=246$  (depending on the comparison period used) and a treatment group of  $n=1$ .

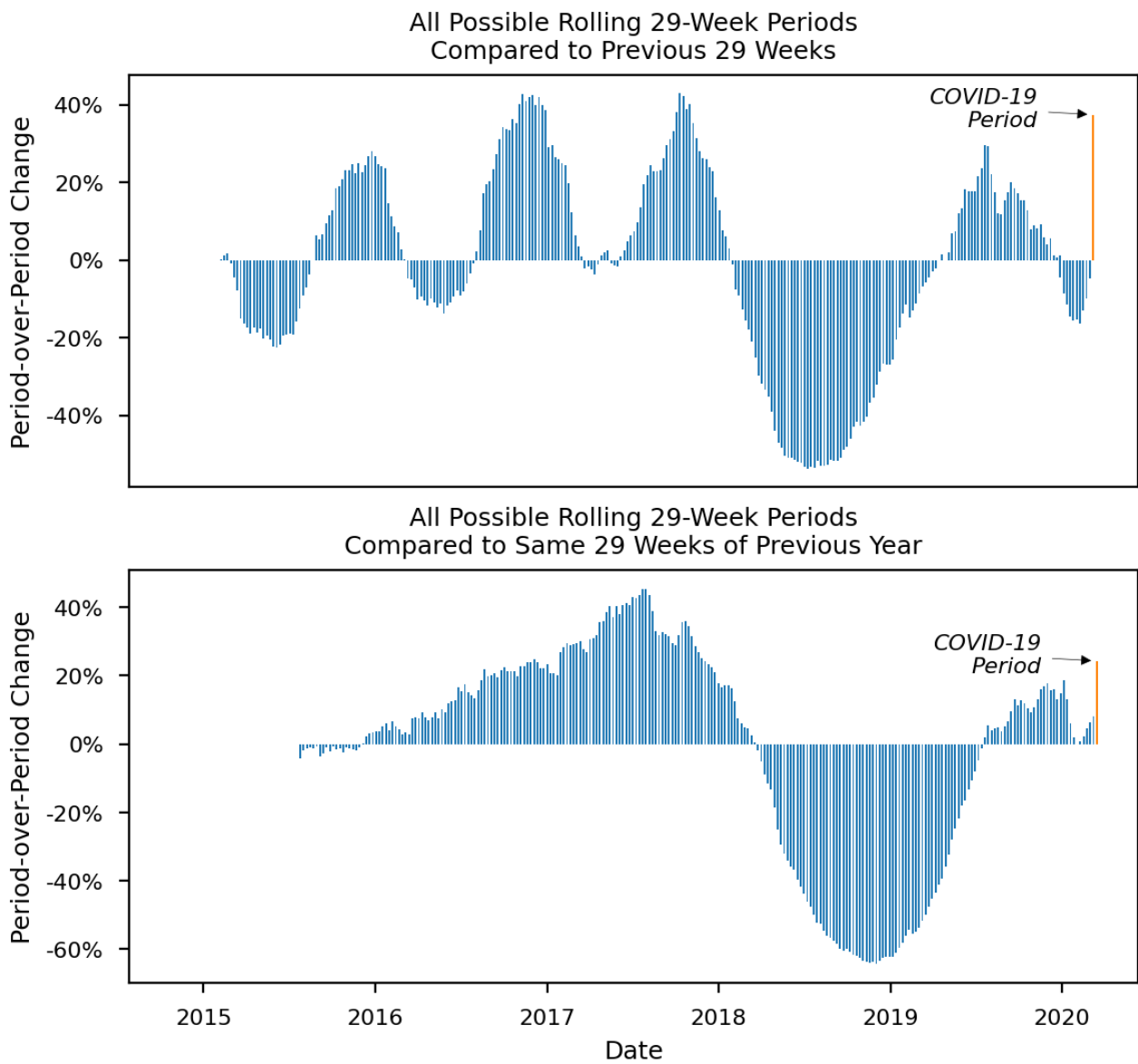
This treatment group of  $n=1$  precluded the usual regression analysis and statistical inference used with DID study data. Instead, we used two simple heuristics to express how extreme the change in outcomes during the COVID-19 period was relative to past changes. First, we calculated the percentile of the COVID-19 period ( $\Delta$ ) within the distribution of past changes. This allowed us to determine how often period-over-period changes of greater magnitude had occurred in the past. We then plotted period-over-period changes over time and graphically compared the change in outcomes during the COVID-19 period

to the recent trend. The plot shows how each period forms one observation in a timeline where period-over-period change is calculated for each calendar week.

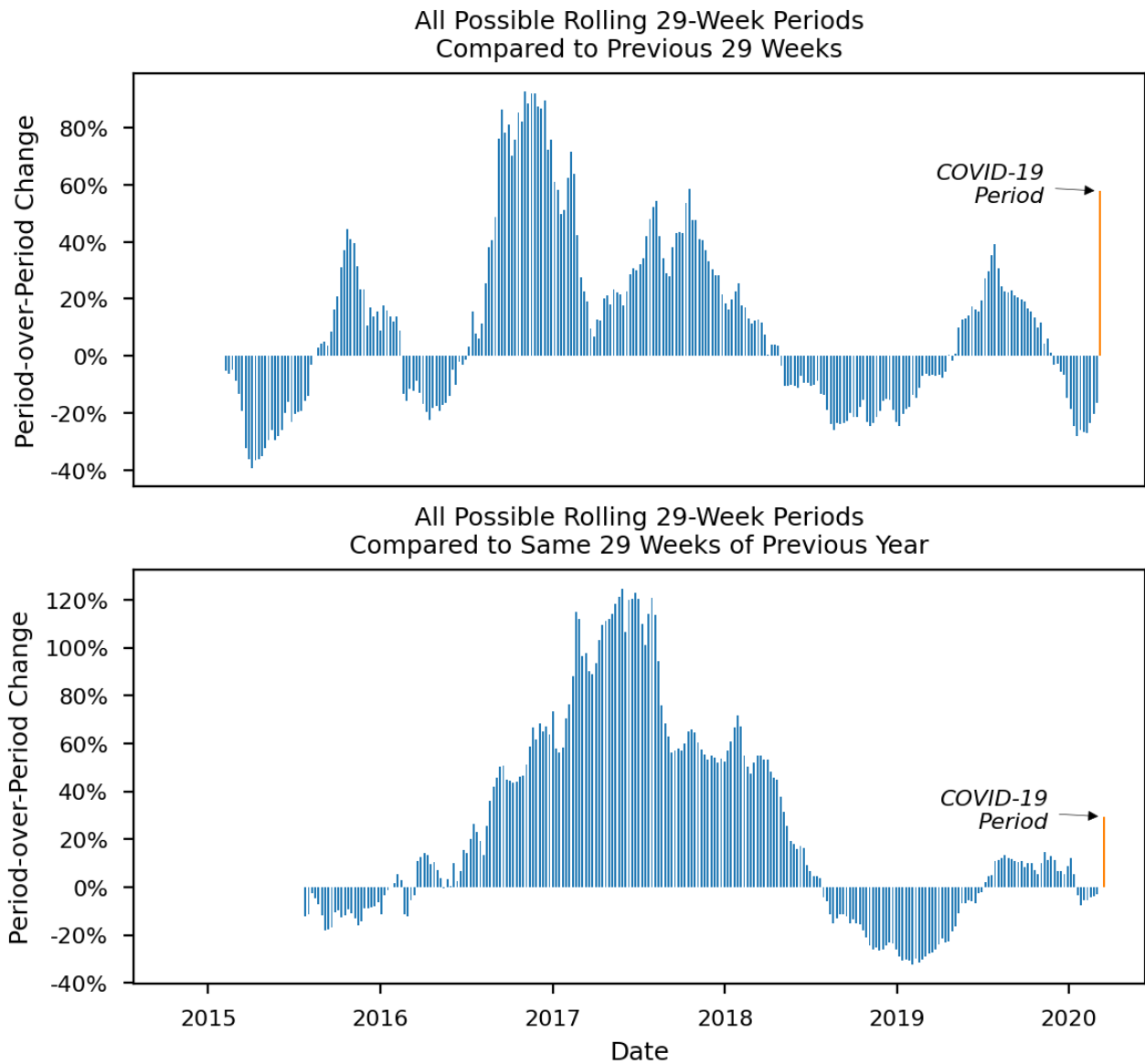
Finally, a series of figures further illustrates how the increases in outcomes during the COVID-19 period represent departures from historical trends. For each figure (Figures 2-4), the x-axis represents time from the first possible comparison period (February 8, 2015) since the beginning of the data set (January 1, 2014) to the end of the COVID-19 period (September 30, 2020). The y-axis represents period-over-period change or the percent change in each period relative to its comparison period. Each bar shows a 29-week period's change from its comparison period, 1 calendar week at a time as previously described. The furthest right bar (in orange) shows the outcome during the COVID-19 period. Period-over-period changes are shown for opioid overdose-related EMS runs (Figure 2), naloxone administrations (Figure 3), and multiple naloxone administrations (Figure 4).

All data analysis was conducted using Python 3.8 (Python Software Foundation) and the Python packages NumPy 1.19.0, SciPy 1.5.0, and pandas 1.0.5.

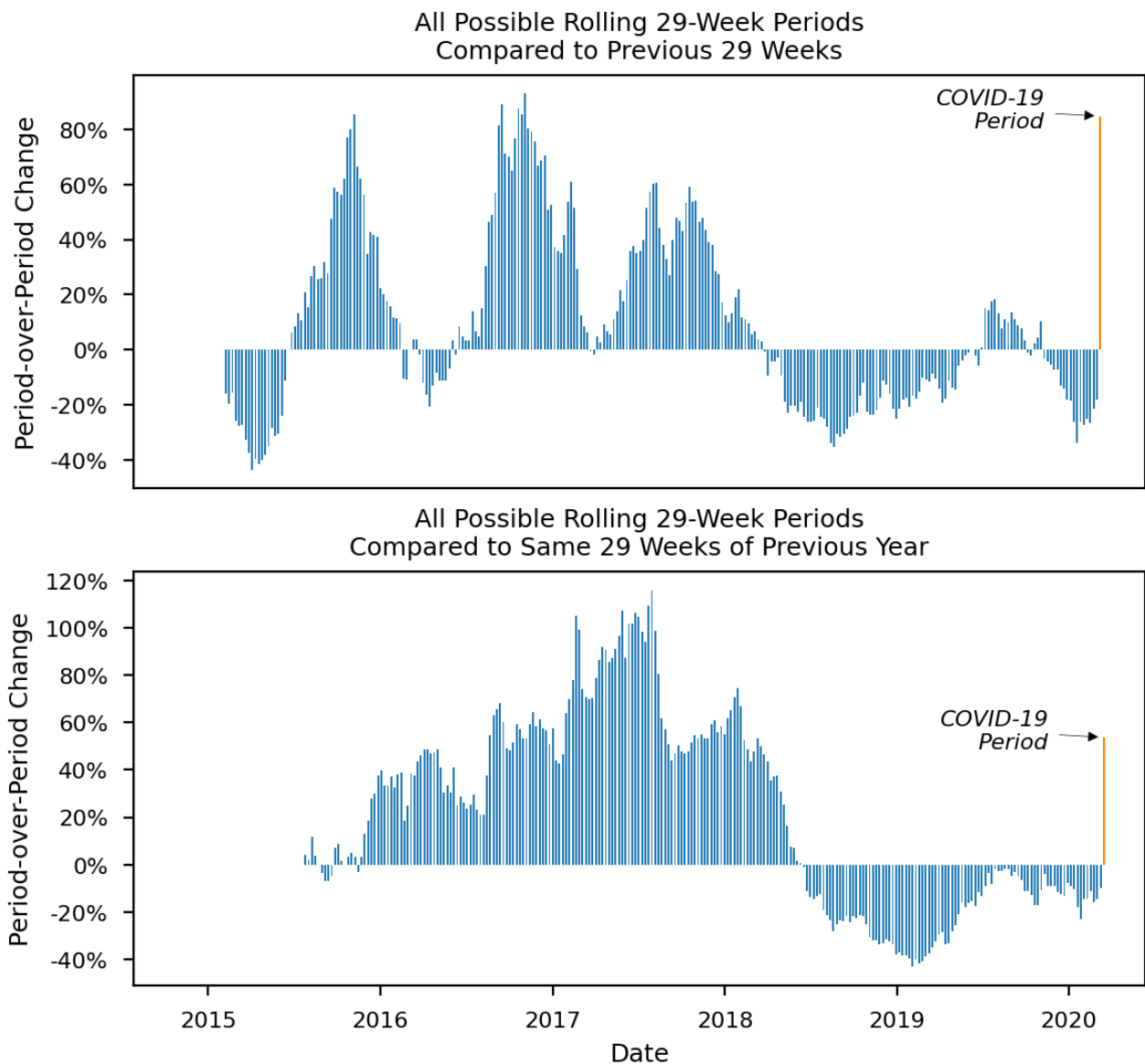
**Figure 2.** Historical period-over-period change in emergency medical services runs involving opioid overdoses in Guilford County, North Carolina before and after the COVID-19 state of emergency declaration.



**Figure 3.** Historical period-over-period change in emergency medical services runs involving naloxone administrations in Guilford County, North Carolina before and after the COVID-19 state of emergency declaration.



**Figure 4.** Historical period-over-period change in emergency medical services runs involving multiple naloxone administrations in Guilford County, North Carolina before and after the COVID-19 state of emergency declaration.



## Results

All three outcomes increased sharply and significantly during the COVID-19 period (Table 1).

Table 1 shows that, compared to either 29-week comparison period, the mean number of opioid overdose-related EMS runs, naloxone administrations, and multiple naloxone administrations increased during the COVID-19 period. For each outcome, the magnitude of change during the COVID-19 period was greater when compared to the previous 29 weeks than when compared to the same 29 weeks of the previous year. This suggests that

seasonality may account for some, but not all, of the increase from the previous 29 weeks.

Further, the increases in outcomes during the COVID-19 period were extreme historically. Table 2 shows, for both comparison periods, the COVID-19 period change expressed as a percentile of the quasi-control distribution of all past period-over-period changes. Across the three outcomes, the increase during the COVID-19 period was greater than 91% of all past 29-week period-over-period changes. When compared to the same 29 weeks of the previous year, the increase for each outcome during the COVID-19 period exceeded at least 63% of all past changes.

**Table 1.** Mean and percent change in EMS runs involving opioid overdoses, naloxone administrations, and multiple naloxone administrations in Guilford County, North Carolina before and after the COVID-19 state of emergency declaration.

Outcomes	COVID-19 period <sup>a</sup> , mean (SD) <sup>b</sup>	Comparison period					
		Previous 29 weeks <sup>c</sup>			Same 29 weeks of previous year <sup>d</sup>		
		Mean (SD) <sup>b</sup>	COVID-19 period change (%) <sup>e,f</sup>	<i>P</i> value	Mean (SD) <sup>b</sup>	COVID-19 period change (%) <sup>e</sup>	<i>P</i> value
Opioid overdose–related EMS <sup>g</sup> runs	25.6 (5.6)	18.6 (6.6)	37.4	<.001	20.6 (6.5)	24.3	.003
Naloxone administrations	22.3 (6.2)	14.1 (6.0)	57.8	<.001	17.2 (6.9)	29.7	.006
Multiple naloxone administrations	5.0 (1.9)	2.7 (1.9)	84.8	<.001	3.3 (1.8)	51.5	<.001

<sup>a</sup>March 10 to September 30, 2020.

<sup>b</sup>Weekly mean and SD of outcome during period.

<sup>c</sup>September 2, 2019, to March 9, 2020.

<sup>d</sup>March 13 to October 5, 2019.

<sup>e</sup>(COVID-19 period mean – comparison period mean) / comparison period mean.

<sup>f</sup>The percentage changes shown may not correspond exactly to the values shown due to rounding.

<sup>g</sup>EMS: emergency medical services.

**Table 2.** Magnitude of period-over-period change in EMS runs involving opioid overdoses, naloxone administrations, and multiple naloxone administrations in Guilford County, North Carolina before the COVID-19 state of emergency declaration.

Comparison period	Percentile (%) <sup>a</sup>
<b>Opioid overdose–related EMS<sup>b</sup> runs</b>	
Previous 29 weeks <sup>c</sup>	94.8
Same 29 weeks of previous year <sup>d</sup>	81.7
<b>Naloxone administrations</b>	
Previous 29 weeks <sup>c</sup>	91.1
Same 29 weeks of previous year <sup>d</sup>	63.0
<b>Multiple naloxone administrations</b>	
Previous 29 weeks <sup>c</sup>	98.1
Same 29 weeks of previous year <sup>d</sup>	76.8

<sup>a</sup>Percentile of COVID-19 period-over-period change within quasi-control distribution of all past period-over-period changes.

<sup>b</sup>EMS: emergency medical services.

<sup>c</sup>September 1, 2019, to March 9, 2020.

<sup>d</sup>March 13 to October 5, 2019.

All outcomes showed mostly positive period-over-period changes from 2015 to 2017. An inflection point occurred in mid to late 2017 when naloxone administrations and multiple naloxone administrations started to drop (in July 2017), followed by a drop in opioid overdose–related runs (in November 2017). From 2018 to 2020, the outcomes continued to decrease, and most period-over-period changes were negative. In the COVID-19 period, a sharp increase occurred for all outcomes. The large positive period-over-period changes in the COVID-19 period are thus an abrupt and large departure from the recent trend of mostly negative period-over-period changes. Most notably, multiple naloxone administrations increased by 84.8%

when compared to the previous 29 weeks and by 53.7% when compared to the same 29 weeks of 2019.

## Discussion

This study detected increases in the occurrence of EMS runs for opioid-related overdoses, naloxone administrations, and multiple naloxone administrations during EMS runs in the course of the COVID-19 pandemic in Guilford County, NC. The findings confirm and extend research on the convergence of the opioid epidemic and the COVID-19 pandemic. The study replicates previous research [11,24,25] by showing increases in opioid overdose–related EMS runs and EMS-administered

naloxone during the COVID-19 pandemic in a large metropolitan county in NC. The sharp increase in multiple naloxone administrations, an indicator of the potential lethality of opioid overdoses [13,21,22], constitutes new evidence linking COVID-19 to an increase in the severity of the overdose crisis. Moreover, the period-over-period analytic approach demonstrates unequivocally that the increases observed for each outcome were historically uncharacteristic of prior periods dating back to 2014 and not explained by seasonality effects. Together, these findings indicate that opioid overdoses have increased in occurrence and severity in Guilford County during COVID-19 to a great extent, thereby contributing to growing empirical support for the hypothesis that the COVID-19 pandemic exacerbates the opioid epidemic [31,32].

To help interpret the findings reported here and elsewhere, we refer to a host-agent-vector-environment model to synthesize the multifactorial evolution of the opioid overdose crisis in the United States [33]. Based upon a modification of the epidemiological triangle model of disease for chronic health conditions [34-36], the model posits that the risk of opioid overdose results from an interaction of risk factors associated with the *host* (ie, individual-level factors such as addiction susceptibility or opioid tolerance), the *agent* (ie, external factors such as heroin or fentanyl), the *vector* (ie, purveyors of licit and illicit drugs), and the environment (ie, contextual external factors such as the economy or geography). With this model in mind, this study offers compelling evidence that the COVID-19 pandemic serves as a potent environmental factor that increases the risk of opioid overdoses, perhaps by augmenting the risk-conferring nature of other factors in the model.

There are a variety of ways by which the environmental strain of the COVID-19 pandemic could interact with host, agent, and vector factors to potentiate opioid overdose risk. Host factors (eg, central nervous system depression) associated with overdose risk may intensify under conditions of social isolation by using opioids alone and without the availability of a bystander to administer naloxone [3]. Indeed, Friedman et al [10] reported increases in EMS runs for opioid overdose cardiac arrests that corresponded with decreases in mobility, an indicator of social isolation. Other host factors (eg, tolerance to opioids) may temporarily decrease due to pandemic-related barriers that limit acquiring and using opioids, only to be supplanted with an escalation of overdose risk when opioids become more available and used at prehiatus dosage [3,37]. Consistent with this notion, Currie et al [38] reported an initial fentanyl-fueled spike in opioid overdose deaths in Ohio approximately 6 weeks following the declaration of a national public health emergency on March 13, 2020. Notably, opioid overdose deaths returned to comparable historical levels within approximately 3 months. Regarding agent factors, it is evident that the COVID-19 pandemic began during the third wave of the opioid epidemic when overdoses were increasingly attributable to the use of heroin and fentanyl [39]. With its estimated 50 times potency of heroin, fentanyl and other synthetic opioids substantially intensify the risk of fatal and nonfatal overdoses [40]. Additionally, polysubstance abuse increases overdose risk [41] and has now been empirically linked to risk of opioid overdoses during COVID-19 [26]. Regarding vector factors, COVID-19

may potentiate supply-side pressures that intensify overdose risk [3,42]. Fentanyl increasingly dominates the illegal drug market [43] and remains highly prevalent in drugs tested during the pandemic [9]. National drug positivity rates increased especially for fentanyl and heroin despite a decrease in overall positivity during the study period [8], suggesting a net increase in lethality due to greater exposure of fentanyl in the drugs that were used.

Regarding specific environmental factors, reduced access to treatment and other services for opioid use disorders likely contributed to overdoses [44]. Opioid use disorder treatment and harm reduction services have been substantially impacted by COVID-19 social distancing regulations due to limits on face-to-face contact [45]. Historically, harm reduction services such as syringe exchange programs, drug consumption rooms, naloxone distribution, and fentanyl test strips have been provided in an in-person capacity. In fact, Schlosser and Harris [46] argue that harm reduction services are predicated on the “physical, social, and emotional intimacies” associated with drug use, conditions that were limited after social distancing regulations were introduced. Bartholomew et al [47] found that 15% of needle and syringe programs across nine states closed during COVID-19, 72% were operating at limited capacity, and 25% eventually pivoted to provide virtual harm reduction services. These trends in closures, reduced hours, and service modifications are reflected across the United States [48] and 25 countries in Europe [49].

Our study has several limitations. The use of a convenience sample of EMS records in a single county limits the generalizability of the findings. Although our finding of increased naloxone administrations during COVID-19 replicates a study conducted in Marion County (Indiana) [24], investigations in other geographical locations are needed. By using only EMS data, the use of naloxone by bystanders or other first respondents (eg, law enforcement) are not included. Furthermore, part of the increase in opioid-related EMS runs during the pandemic may be driven by temporary redirection of other treatment access points, perhaps due to a disincentive to seek care at hospitals during the pandemic. There is also a potential for misclassification of overdose events, as EMS responders may overuse naloxone in some cases. Because of their anonymized nature, EMS data were not linked to death records; doing so would help verify multiple naloxone administration as a proxy for severity. It also remains unclear the extent that the increases in naloxone administrations and multiple naloxone administrations reported here are attributable to the COVID-19 pandemic independent of fentanyl’s effect; research on this is needed.

To our knowledge, this study is the first to report an increase in both occurrence and severity of opioid overdoses during the COVID-19 pandemic. Our study also encourages additional research on the use of EMS data on naloxone administrations and multiple naloxone administrations to monitor opioid overdoses. The timeliness, ubiquity, and specificity to the opioid crisis make EMS data on naloxone administrations especially viable proxy measures of the evolving opioid epidemic, even during public health disasters such as the COVID-19 pandemic. More broadly, our study reiterates the value of data sharing

among public health and safety, research, community, and academic organizations for tracking the opioid crisis [5,7,50,51]. The global sharing of COVID-19 data clearly shows that this is possible.

## Acknowledgments

This research was supported by funding from the Research Triangle Institute Opioid Strategic Investment Fund. The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. This study was also supported in part by the Intramural Research Program of the National Institute of Mental Health (ZIAMH002953). The views and opinions expressed in this paper are those of the authors and should not be construed to represent the views of any of the sponsoring organizations, agencies, or US Government.

The authors would like to thank the Guilford County, NC EMS Department for sharing more than 6 years of EMS data, making this research possible.

## Conflicts of Interest

None declared.

## References

1. National Center for Health Statistics Mortality Data on CDC WONDER. CDC WONDER. URL: <https://wonder.cdc.gov/mcd.html> [accessed 2021-01-15]
2. Becker W, Fiellin D. When epidemics collide: coronavirus disease 2019 (COVID-19) and the opioid crisis. *Ann Intern Med* 2020 Jul 07;173(1):59-60 [FREE Full text] [doi: [10.7326/M20-1210](https://doi.org/10.7326/M20-1210)] [Medline: [32240291](https://pubmed.ncbi.nlm.nih.gov/32240291/)]
3. Wakeman SE, Green TC, Rich J. An overdose surge will compound the COVID-19 pandemic if urgent action is not taken. *Nat Med* 2020 Jun;26(6):819-820. [doi: [10.1038/s41591-020-0898-0](https://doi.org/10.1038/s41591-020-0898-0)] [Medline: [32555514](https://pubmed.ncbi.nlm.nih.gov/32555514/)]
4. Ahmad FB, Rossen LM, Sutton P. Provisional drug overdose death counts. Centers for Disease Control and Prevention. 2021. URL: <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm> [accessed 2021-01-15]
5. Blanco C, Compton WM, Volkow ND. Opportunities for research on the treatment of substance use disorders in the context of COVID-19. *JAMA Psychiatry* 2020 Sep 01;177(9):811-812. [doi: [10.1001/jamapsychiatry.2020.3177](https://doi.org/10.1001/jamapsychiatry.2020.3177)] [Medline: [32870241](https://pubmed.ncbi.nlm.nih.gov/32870241/)]
6. Anwar M, Khoury D, Aldridge AP, Parker SJ, Conway KP. Using Twitter to surveil the opioid epidemic in North Carolina: an exploratory study. *JMIR Public Health Surveill* 2020 Jun 24;6(2):e17574 [FREE Full text] [doi: [10.2196/17574](https://doi.org/10.2196/17574)] [Medline: [32469322](https://pubmed.ncbi.nlm.nih.gov/32469322/)]
7. Zibbell JE, Aldridge AP, Cauchon D, DeFiore-Hymer J, Conway KP. Association of law enforcement seizures of heroin, fentanyl, and carfentanil with opioid overdose deaths in Ohio, 2014-2017. *JAMA Netw Open* 2019 Nov 01;2(11):e1914666 [FREE Full text] [doi: [10.1001/jamanetworkopen.2019.14666](https://doi.org/10.1001/jamanetworkopen.2019.14666)] [Medline: [31702795](https://pubmed.ncbi.nlm.nih.gov/31702795/)]
8. Niles JK, Gudim J, Radcliff J, Kaufman HW. The opioid epidemic within the COVID-19 pandemic: drug testing in 2020. *Popul Health Manag* 2021 Feb;24(S1):S43-S51 [FREE Full text] [doi: [10.1089/pop.2020.0230](https://doi.org/10.1089/pop.2020.0230)] [Medline: [33031013](https://pubmed.ncbi.nlm.nih.gov/33031013/)]
9. Wainwright JJ, Mikre M, Whitley P, Dawson E, Huskey A, Lukowiak A, et al. Analysis of drug test results before and after the US declaration of a national emergency concerning the COVID-19 outbreak. *JAMA* 2020 Oct 27;324(16):1674-1677 [FREE Full text] [doi: [10.1001/jama.2020.17694](https://doi.org/10.1001/jama.2020.17694)] [Medline: [32945855](https://pubmed.ncbi.nlm.nih.gov/32945855/)]
10. Friedman J, Beletsky L, Schriger DL. Overdose-related cardiac arrests observed by emergency medical services during the US COVID-19 epidemic. *JAMA Psychiatry* 2021 May 01;78(5):562-564. [doi: [10.1001/jamapsychiatry.2020.4218](https://doi.org/10.1001/jamapsychiatry.2020.4218)] [Medline: [33270086](https://pubmed.ncbi.nlm.nih.gov/33270086/)]
11. Slavova S, Rock P, Bush HM, Quesinberry D, Walsh SL. Signal of increased opioid overdose during COVID-19 from emergency medical services data. *Drug Alcohol Depend* 2020 Sep 01;214:108176 [FREE Full text] [doi: [10.1016/j.drugalcdep.2020.108176](https://doi.org/10.1016/j.drugalcdep.2020.108176)] [Medline: [32717504](https://pubmed.ncbi.nlm.nih.gov/32717504/)]
12. Lerner E, Newgard C, Mann N. Effect of the coronavirus disease 2019 (COVID-19) pandemic on the U.S. Emergency Medical Services System: a preliminary report. *Acad Emerg Med* 2020 Aug;27(8):693-699 [FREE Full text] [doi: [10.1111/acem.14051](https://doi.org/10.1111/acem.14051)] [Medline: [32557999](https://pubmed.ncbi.nlm.nih.gov/32557999/)]
13. Cash RE, Kinsman J, Crowe RP, Rivard MK, Faul M, Panchal AR. Naloxone administration frequency during emergency medical service events - United States, 2012-2016. *MMWR Morb Mortal Wkly Rep* 2018 Aug 10;67(31):850-853. [doi: [10.15585/mmwr.mm6731a2](https://doi.org/10.15585/mmwr.mm6731a2)] [Medline: [30091966](https://pubmed.ncbi.nlm.nih.gov/30091966/)]
14. Faul M, Lurie P, Kinsman JM, Dailey MW, Crabaugh C, Sasser SM. Multiple naloxone administrations among emergency medical service providers is increasing. *Prehosp Emerg Care* 2017;21(4):411-419 [FREE Full text] [doi: [10.1080/10903127.2017.1315203](https://doi.org/10.1080/10903127.2017.1315203)] [Medline: [28481656](https://pubmed.ncbi.nlm.nih.gov/28481656/)]
15. Rzasz Lynn R, Galinkin JL. Naloxone dosage for opioid reversal: current evidence and clinical implications. *Ther Adv Drug Saf* 2018 Jan;9(1):63-88 [FREE Full text] [doi: [10.1177/2042098617744161](https://doi.org/10.1177/2042098617744161)] [Medline: [29318006](https://pubmed.ncbi.nlm.nih.gov/29318006/)]

16. Faul M, Dailey MW, Sugerman DE, Sasser SM, Levy B, Paulozzi LJ. Disparity in naloxone administration by emergency medical service providers and the burden of drug overdose in US rural communities. *Am J Public Health* 2015 Jul;105 Suppl 3:e26-e32. [doi: [10.2105/AJPH.2014.302520](https://doi.org/10.2105/AJPH.2014.302520)] [Medline: [25905856](https://pubmed.ncbi.nlm.nih.gov/25905856/)]
17. Knowlton A, Weir BW, Hazzard F, Olsen Y, McWilliams J, Fields J, et al. EMS runs for suspected opioid overdose: implications for surveillance and prevention. *Prehosp Emerg Care* 2013;17(3):317-329 [FREE Full text] [doi: [10.3109/10903127.2013.792888](https://doi.org/10.3109/10903127.2013.792888)] [Medline: [23734988](https://pubmed.ncbi.nlm.nih.gov/23734988/)]
18. Lindstrom HA, Clemency BM, Snyder R, Consiglio JD, May PR, Moscati RM. Prehospital naloxone administration as a public health surveillance tool: a retrospective validation study. *Prehosp Disaster Med* 2015 Aug;30(4):385-389. [doi: [10.1017/S1049023X15004793](https://doi.org/10.1017/S1049023X15004793)] [Medline: [26061280](https://pubmed.ncbi.nlm.nih.gov/26061280/)]
19. Moore PQ, Weber J, Cina S, Aks S. Syndrome surveillance of fentanyl-laced heroin outbreaks: Utilization of EMS, Medical Examiner and Poison Center databases. *Am J Emerg Med* 2017 Nov;35(11):1706-1708. [doi: [10.1016/j.ajem.2017.05.003](https://doi.org/10.1016/j.ajem.2017.05.003)] [Medline: [28506507](https://pubmed.ncbi.nlm.nih.gov/28506507/)]
20. Ray BR, Lowder EM, Kivisto AJ, Phalen P, Gil H. EMS naloxone administration as non-fatal opioid overdose surveillance: 6-year outcomes in Marion County, Indiana. *Addiction* 2018 Dec;113(12):2271-2279. [doi: [10.1111/add.14426](https://doi.org/10.1111/add.14426)] [Medline: [30255531](https://pubmed.ncbi.nlm.nih.gov/30255531/)]
21. Lasher L, Rhodes J, Viner-Brown S. Identification and description of non-fatal opioid overdoses using Rhode Island EMS data, 2016-2018. *R I Med J* (2013) 2019 Mar 01;102(2):41-45. [Medline: [30823701](https://pubmed.ncbi.nlm.nih.gov/30823701/)]
22. Klebacher R, Harris M, Ariyaprakai N, Tagore A, Robbins V, Dudley LS, et al. Incidence of naloxone redosing in the age of the new opioid epidemic. *Prehosp Emerg Care* 2017;21(6):682-687. [doi: [10.1080/10903127.2017.1335818](https://doi.org/10.1080/10903127.2017.1335818)] [Medline: [28686547](https://pubmed.ncbi.nlm.nih.gov/28686547/)]
23. Somerville NJ, O'Donnell J, Gladden RM, Zibbell JE, Green TC, Younkin M, et al. Characteristics of fentanyl overdose - Massachusetts, 2014-2016. *MMWR Morb Mortal Wkly Rep* 2017 Apr 14;66(14):382-386. [doi: [10.15585/mmwr.mm6614a2](https://doi.org/10.15585/mmwr.mm6614a2)] [Medline: [28406883](https://pubmed.ncbi.nlm.nih.gov/28406883/)]
24. Glober N, Mohler G, Huynh P, Arkins T, O'Donnell D, Carter J, et al. Impact of COVID-19 pandemic on drug overdoses in Indianapolis. *J Urban Health* 2020 Dec;97(6):802-807 [FREE Full text] [doi: [10.1007/s11524-020-00484-0](https://doi.org/10.1007/s11524-020-00484-0)] [Medline: [33005988](https://pubmed.ncbi.nlm.nih.gov/33005988/)]
25. Ballesteros A, Roche J, Myers M, Carter P, Cunningham R, Goldstick J. 0058 Changes in suspected overdoses following the start of the COVID-19 pandemic: results from the michigan system for opioid overdose surveillance. *Inj Prev* 2021;27(Suppl 3):A1. [doi: [10.1136/injuryprev-2021-SAVIR.38](https://doi.org/10.1136/injuryprev-2021-SAVIR.38)]
26. COVID-19 North Carolina Dashboard. NCDHHS COVID-19 Response. URL: <https://covid19.ncdhhs.gov/dashboard#by-counties-map> [accessed 2021-02-28]
27. Precision for COVID. URL: <https://www.precisionforcoviddata.org/> [accessed 2021-04-22]
28. Dasgupta N. Opioid analgesic prescribing and overdose mortality in North Carolina. Carolina Digital Repository. 2013. URL: <https://cdr.lib.unc.edu/downloads/8623hz362> [accessed 2021-04-17]
29. Amadeo K. Year-over-year explained with its pros and cons. *The Balance*. 2020 May 28. URL: <https://www.thebalance.com/year-over-year-yoy-growth-calculation-definition-3305970> [accessed 2021-03-03]
30. Wing C, Simon K, Bello-Gomez RA. Designing difference in difference studies: best practices for public health policy research. *Annu Rev Public Health* 2018 Apr 01;39:453-469. [doi: [10.1146/annurev-publhealth-040617-013507](https://doi.org/10.1146/annurev-publhealth-040617-013507)] [Medline: [29328877](https://pubmed.ncbi.nlm.nih.gov/29328877/)]
31. Kuehn BM. Accelerated overdose deaths linked with COVID-19. *JAMA* 2021 Feb 09;325(6):523. [doi: [10.1001/jama.2021.0074](https://doi.org/10.1001/jama.2021.0074)] [Medline: [33560330](https://pubmed.ncbi.nlm.nih.gov/33560330/)]
32. Alexander G, Stoller K, Haffajee R, Saloner B. An epidemic in the midst of a pandemic: opioid use disorder and COVID-19. *Ann Intern Med* 2020 Jul 07;173(1):57-58 [FREE Full text] [doi: [10.7326/M20-1141](https://doi.org/10.7326/M20-1141)] [Medline: [32240283](https://pubmed.ncbi.nlm.nih.gov/32240283/)]
33. Compton W, Jones C. Epidemiology of the U.S. opioid crisis: the importance of the vector. *Ann N Y Acad Sci* 2019 Sep;1451(1):130-143 [FREE Full text] [doi: [10.1111/nyas.14209](https://doi.org/10.1111/nyas.14209)] [Medline: [31378974](https://pubmed.ncbi.nlm.nih.gov/31378974/)]
34. Giovino GA. Epidemiology of tobacco use in the United States. *Oncogene* 2002 Oct 21;21(48):7326-7340. [doi: [10.1038/sj.onc.1205808](https://doi.org/10.1038/sj.onc.1205808)] [Medline: [12379876](https://pubmed.ncbi.nlm.nih.gov/12379876/)]
35. Merikangas K, McClair V. Epidemiology of substance use disorders. *Hum Genet* 2012 Jun;131(6):779-789 [FREE Full text] [doi: [10.1007/s00439-012-1168-0](https://doi.org/10.1007/s00439-012-1168-0)] [Medline: [22543841](https://pubmed.ncbi.nlm.nih.gov/22543841/)]
36. Merikangas KR, Nakamura EF, Kessler RC. Epidemiology of mental disorders in children and adolescents. *Dialogues Clin Neurosci* 2009;11(1):7-20 [FREE Full text] [Medline: [19432384](https://pubmed.ncbi.nlm.nih.gov/19432384/)]
37. Binswanger I, Stern M, Deyo R, Heagerty PJ, Cheadle A, Elmore JG, et al. Release from prison--a high risk of death for former inmates. *N Engl J Med* 2007 Jan 11;356(2):157-165 [FREE Full text] [doi: [10.1056/NEJMsa064115](https://doi.org/10.1056/NEJMsa064115)] [Medline: [17215533](https://pubmed.ncbi.nlm.nih.gov/17215533/)]
38. Currie JM, Schnell MK, Schwandt H, Zhang J. Trends in drug overdose mortality in Ohio during the first 7 months of the COVID-19 pandemic. *JAMA Netw Open* 2021 Apr 01;4(4):e217112 [FREE Full text] [doi: [10.1001/jamanetworkopen.2021.7112](https://doi.org/10.1001/jamanetworkopen.2021.7112)] [Medline: [33852004](https://pubmed.ncbi.nlm.nih.gov/33852004/)]
39. Dasgupta N, Beletsky L, Ciccarone D. Opioid crisis: no easy fix to its social and economic determinants. *Am J Public Health* 2018 Feb;108(2):182-186. [doi: [10.2105/AJPH.2017.304187](https://doi.org/10.2105/AJPH.2017.304187)] [Medline: [29267060](https://pubmed.ncbi.nlm.nih.gov/29267060/)]



40. O'Donnell J, Gladden RM, Goldberger BA, Mattson CL, Kariisa M. Notes from the field: opioid-involved overdose deaths with fentanyl or fentanyl analogs detected - 28 States and the District of Columbia, July 2016-December 2018. *MMWR Morb Mortal Wkly Rep* 2020 Mar 13;69(10):271-273. [doi: [10.15585/mmwr.mm6910a4](https://doi.org/10.15585/mmwr.mm6910a4)] [Medline: [32163382](https://pubmed.ncbi.nlm.nih.gov/32163382/)]
41. Compton W, Valentino R, DuPont R. Polysubstance use in the U.S. opioid crisis. *Mol Psychiatry* 2021 Jan;26(1):41-50 [FREE Full text] [doi: [10.1038/s41380-020-00949-3](https://doi.org/10.1038/s41380-020-00949-3)] [Medline: [33188253](https://pubmed.ncbi.nlm.nih.gov/33188253/)]
42. Ciccarone D. The triple wave epidemic: supply and demand drivers of the US opioid overdose crisis. *Int J Drug Policy* 2019 Sep;71:183-188 [FREE Full text] [doi: [10.1016/j.drugpo.2019.01.010](https://doi.org/10.1016/j.drugpo.2019.01.010)] [Medline: [30718120](https://pubmed.ncbi.nlm.nih.gov/30718120/)]
43. Althoff KN, Leifheit KM, Park JN, Chandran A, Sherman SG. Opioid-related overdose mortality in the era of fentanyl: monitoring a shifting epidemic by person, place, and time. *Drug Alcohol Depend* 2020 Nov 01;216:108321. [doi: [10.1016/j.drugalcdep.2020.108321](https://doi.org/10.1016/j.drugalcdep.2020.108321)] [Medline: [33007700](https://pubmed.ncbi.nlm.nih.gov/33007700/)]
44. The Global State of Harm Reduction 2020. Harm Reduction International. 2021. URL: <https://www.hri.global/global-state-of-harm-reduction-2020> [accessed 2021-03-01]
45. Dietze PM, Peacock A. Illicit drug use and harms in Australia in the context of COVID-19 and associated restrictions: anticipated consequences and initial responses. *Drug Alcohol Rev* 2020 May;39(4):297-300 [FREE Full text] [doi: [10.1111/dar.13079](https://doi.org/10.1111/dar.13079)] [Medline: [32445265](https://pubmed.ncbi.nlm.nih.gov/32445265/)]
46. Schlosser A, Harris S. Care during COVID-19: drug use, harm reduction, and intimacy during a global pandemic. *Int J Drug Policy* 2020 Sep;83:102896 [FREE Full text] [doi: [10.1016/j.drugpo.2020.102896](https://doi.org/10.1016/j.drugpo.2020.102896)] [Medline: [32768156](https://pubmed.ncbi.nlm.nih.gov/32768156/)]
47. Bartholomew TS, Nakamura N, Metsch LR, Tookes HE. Syringe services program (SSP) operational changes during the COVID-19 global outbreak. *Int J Drug Policy* 2020 Sep;83:102821 [FREE Full text] [doi: [10.1016/j.drugpo.2020.102821](https://doi.org/10.1016/j.drugpo.2020.102821)] [Medline: [32591222](https://pubmed.ncbi.nlm.nih.gov/32591222/)]
48. Glick N, Prohaska S, LaKosky P, Juarez AM, Corcorran MA, Des Jarlais DC. The impact of COVID-19 on syringe services programs in the United States. *AIDS Behav* 2020 Sep;24(9):2466-2468 [FREE Full text] [doi: [10.1007/s10461-020-02886-2](https://doi.org/10.1007/s10461-020-02886-2)] [Medline: [32333209](https://pubmed.ncbi.nlm.nih.gov/32333209/)]
49. EMCDDA trendspotter briefing - impact of COVID-19 on drug services and help-seeking in Europe. European Monitoring Centre for Drugs and Drug Addiction. 2020. URL: [https://www.emcdda.europa.eu/publications/ad-hoc/impact-of-covid-19-on-drug-services-and-help-seeking-in-europe\\_en](https://www.emcdda.europa.eu/publications/ad-hoc/impact-of-covid-19-on-drug-services-and-help-seeking-in-europe_en) [accessed 2021-02-28]
50. Alter A, Yeager C. The consequences of COVID-19 on the overdose epidemic: overdoses are increasing. Overdose Detection Mapping Application Program. 2020. URL: <http://odmap.org/Content/docs/news/2020/ODMAP-Report-May-2020.pdf> [accessed 2021-04-30]
51. Guilford County Solution to the Opioid Problem. 2019. URL: <https://gcstop.uncg.edu/> [accessed 2021-04-30]

## Abbreviations

**CDC:** Centers for Disease Control and Prevention

**DID:** difference in difference

**EMS:** emergency medical services

**NC:** North Carolina

*Edited by T Sanchez; submitted 01.04.21; peer-reviewed by A Naser, S Linder; comments to author 14.04.21; revised version received 06.05.21; accepted 10.05.21; published 27.05.21.*

*Please cite as:*

*Khoury D, Preiss A, Geiger P, Anwar M, Conway KP*

*Increases in Naloxone Administrations by Emergency Medical Services Providers During the COVID-19 Pandemic: Retrospective Time Series Study*

*JMIR Public Health Surveill* 2021;7(5):e29298

URL: <https://publichealth.jmir.org/2021/5/e29298>

doi: [10.2196/29298](https://doi.org/10.2196/29298)

PMID: [33999828](https://pubmed.ncbi.nlm.nih.gov/33999828/)

©Dalia Khoury, Alexander Preiss, Paul Geiger, Mohd Anwar, Kevin Paul Conway. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 27.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# SARS-CoV-2 Surveillance System in Canada: Longitudinal Trend Analysis

Lori Post<sup>1</sup>, PhD; Michael J Boctor<sup>2</sup>, BSc; Tariq Z Issa<sup>2</sup>, BA; Charles B Moss<sup>3</sup>, PhD; Robert Leo Murphy<sup>4</sup>, MD; Chad J Achenbach<sup>5</sup>, MD, MPH; Michael G Ison<sup>5</sup>, MD, MSc; Danielle Resnick<sup>6</sup>, PhD; Lauren Singh<sup>1</sup>, MPH; Janine White<sup>1</sup>, MA; Sarah B Welch<sup>1</sup>, MPH; James F Oehmke<sup>1</sup>, PhD

<sup>1</sup>Buehler Center for Health Policy and Economics, Feinberg School of Medicine, Northwestern University, Chicago, IL, United States

<sup>2</sup>Feinberg School of Medicine, Northwestern University, Chicago, IL, United States

<sup>3</sup>Institute of Food and Agricultural Sciences, University of Florida, Gainesville, FL, United States

<sup>4</sup>Institute of Global Health, Feinberg School of Medicine, Northwestern University, Chicago, IL, United States

<sup>5</sup>Division of Infectious Disease, Feinberg School of Medicine, Northwestern University, Chicago, IL, United States

<sup>6</sup>International Food Policy Research Institute, Washington, DC, United States

**Corresponding Author:**

Lori Post, PhD

Buehler Center for Health Policy and Economics

Feinberg School of Medicine

Northwestern University

420 E Superior

Chicago, IL, 60611

United States

Phone: 1 203 980 7107

Email: [lori.post@northwestern.edu](mailto:lori.post@northwestern.edu)

## Abstract

**Background:** The COVID-19 global pandemic has disrupted structures and communities across the globe. Numerous regions of the world have had varying responses in their attempts to contain the spread of the virus. Factors such as public health policies, governance, and sociopolitical climate have led to differential levels of success at controlling the spread of SARS-CoV-2. Ultimately, a more advanced surveillance metric for COVID-19 transmission is necessary to help government systems and national leaders understand which responses have been effective and gauge where outbreaks occur.

**Objective:** The goal of this study is to provide advanced COVID-19 surveillance metrics for Canada at the country, province, and territory level that account for shifts in the pandemic including speed, acceleration, jerk, and persistence. Enhanced surveillance identifies risks for explosive growth and regions that have controlled outbreaks successfully.

**Methods:** Using a longitudinal trend analysis study design, we extracted 62 days of COVID-19 data from Canadian public health registries for 13 provinces and territories. We used an empirical difference equation to measure the daily number of cases in Canada as a function of the prior number of cases, the level of testing, and weekly shift variables based on a dynamic panel model that was estimated using the generalized method of moments approach by implementing the Arellano-Bond estimator in R.

**Results:** We compare the week of February 7-13, 2021, with the week of February 14-20, 2021. Canada, as a whole, had a decrease in speed from 8.4 daily new cases per 100,000 population to 7.5 daily new cases per 100,000 population. The persistence of new cases during the week of February 14-20 reported 7.5 cases that are a result of COVID-19 transmissions 7 days earlier. The two most populous provinces of Ontario and Quebec both experienced decreases in speed from 7.9 and 11.5 daily new cases per 100,000 population for the week of February 7-13 to speeds of 6.9 and 9.3 for the week of February 14-20, respectively. Nunavut experienced a significant increase in speed during this time, from 3.3 daily new cases per 100,000 population to 10.9 daily new cases per 100,000 population.

**Conclusions:** Canada excelled at COVID-19 control early on in the pandemic, especially during the first COVID-19 shutdown. The second wave at the end of 2020 resulted in a resurgence of the outbreak, which has since been controlled. Enhanced surveillance identifies outbreaks and where there is the potential for explosive growth, which informs proactive health policy.

**KEYWORDS**

global COVID surveillance; COVID-19; COVID-21; new COVID strains; Canada Public Health Surveillance; Great COVID Shutdown; Canadian COVID-19; surveillance metrics; wave 2 Canada COVID-19; dynamic panel data; generalized method of the moments; Canadian econometrics; Canada SARS-CoV-2; Canadian COVID-19 surveillance system; Canadian COVID transmission speed; Canadian COVID transmission acceleration; COVID transmission deceleration; COVID transmission jerk; COVID 7-day lag; Alberta; British Columbia; Manitoba; New Brunswick; Newfoundland and Labrador; Northwest Territories; Nova Scotia; Nunavut; Ontario; Prince Edward Island; Quebec; Saskatchewan; Yukon

**Introduction****Background**

On January 30, 2020, the World Health Organization officially declared the outbreak of SARS-CoV-2, the virus that causes COVID-19, a public health emergency of international concern [1]. The virus has disrupted communities across the globe [2]. Numerous factors, including public health policies, climate, population characteristics, governance, and sociopolitical factors, led to varying levels of success at controlling the spread of SARS-CoV-2 [3-7]. Despite sharing many similarities, COVID-19 could not have played out more differently between Canada and the United States [8]. Canada reported a total of 849,517 COVID-19 infections or 2235 cases per 100,000 population and 21,723 COVID-19 deaths or 57 deaths per 100,000 population as of February 22, 2021 [9,10]. In comparison, as of February 22, 2021, the United States had a total of 28,221,129 COVID-19 infections or 8598 per 100,000 population and 501,663 COVID-19 deaths or 153 deaths per 100,000 population [9,10]. The COVID-19 infection and death rates of the United States are 3.8 times and 2.7 times those of Canada's, respectively. Understanding the context in which the COVID-19 pandemic occurs and the dynamics of the pandemic will inform not only Canada but also those nations struggling to control the multiple outbreaks, such as the United States. Unfortunately, existing surveillance suffers from reporting biases, undercounts, missing data, and data contamination.

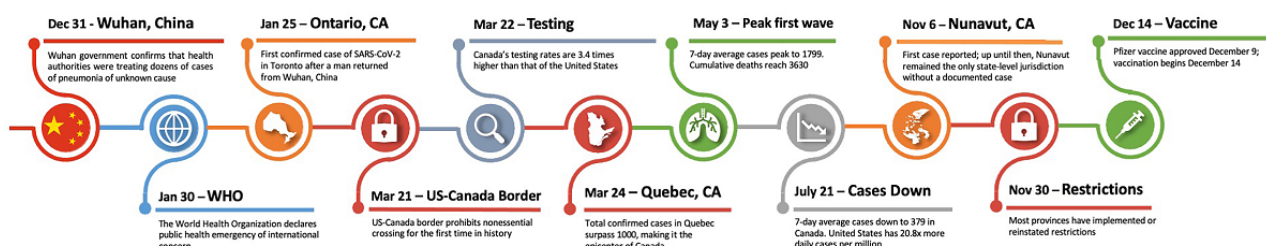
**How the Pandemic Unfolded in Canada**

On January 25, 2020, Canada saw its first case of SARS-CoV-2 after a man returned to Toronto from Wuhan, China [11]. Cases in Ontario rose a month later [12]. Quebec soon became Canada's first epicenter, likely due to southern travel into the United States during its winter school break, which occurred two weeks prior to lockdown measures implemented in

mid-March [5]. [Figure 1](#) shows the timeline of COVID-19 in Canada.

Fast forward one year later, Canada has had a resurgence of COVID-19 infections and has reimplemented public health guidelines to control the COVID-19 epidemic. As of February 22, 2021, Ontario and Quebec account for 68% of confirmed cases and 79% of deaths in Canada [10]. Nunavut, with a population of 38,780, remained the only geographical jurisdiction in North America without a single confirmed case of SARS-CoV-2 until early November 2020, when it began to see cases accelerate quickly [13]. Nunavut has one hospital and struggles with food security [14] and tuberculosis outbreaks [15]. Nunavut faced potentially catastrophic consequences from the introduction of SARS-CoV-2 to its region. Strict prevention measures barred anyone but residents and critical workers from entering—with required self-isolation for 14 days prior to entering [16]. The measures put in place by the Nunavut government were not entirely unique among its neighboring provinces and territories. The Northwest Territories had even stricter isolation measures, barring all travel to the territory except for residents, who were required to quarantine for 14 days in a government-run location [16]. Despite the substantial administrative authority each province possesses, Canadian leaders worked well together, constructing a unified response [17-19]. Across the country, mass gatherings were prohibited, schools and nonessential businesses were required to close, and fines were implemented for failing to follow social distancing policies [18,19]. Furthermore, there has been consistent messaging in regard to public health guidelines such as mask wearing [18]. This is in stark contrast to the United States, which has no national policies and failed to issue clear guidance on mask wearing, quarantines, hand hygiene, and social distancing, as many states have not implemented public health guidelines or supported the benefits of mask wearing [20-23].

**Figure 1.** Timeline of major COVID-19 events for Canada. WHO: World Health Organization.



## Politics

Furthermore, Canada's response to the COVID-19 pandemic and social unity in public health adherence has likely benefited from the country's experience with the 2003 severe acute respiratory syndrome (SARS) epidemic that killed 44 Canadians [17]. A number of improvements were made in response to the SARS dress rehearsal in 2003, creating better federal-provincial collaboration and more effective public health communication strategies [17].

Canadian Prime Minister Justin Trudeau did not downplay the SARS-CoV-2 threat [18,24]. Trudeau began wearing a mask in May 2020 and practiced self-isolation for several weeks following his wife's diagnosis with SARS-CoV-2 in March [24,25]. Adherence to evidence-based guidelines that prevent the transmission of SARS-CoV-2 by political leaders is a critical component to promoting safe behavior and cooperation in the general population with public health guidelines [26]. Furthermore, in Canada, provincial leaders on polar ends of the political spectrum shared a cross-partisan consensus on how to manage the COVID-19 pandemic [18,19], whereas in the United States, political leaders of each political party have found little agreement on standard pandemic control measures including stay-at-home orders and mask mandates.

## Significance

Ideally, the development of a more advanced methodology for tracking and estimating COVID-19 transmission in regions within Canada will allow for more reliable analysis of which policies are effective and what other factors may be associated with transmission rates. Public health departments, as well as several universities and media outlets, are tracking the novel coronavirus using raw data including the number of new infections, testing, positivity, Rho, and deaths, in addition to other measures such as local hospital capacity [27-36]. To remove temporal effects, many surveillance systems have shifted to 7-day moving averages to counter the dearth of reporting during holidays and weekends. Although moving averages temper volatility of data and testing/reporting affects, surveillance still suffers from missing cases. General public health surveillance is helpful and provides a proxy of the pandemic, but surveillance data still suffer from significant bias due to undercounts, reporting delays, testing errors, dearth of testing, asymptomatic carriers, and other types of data contamination. In fact, surveillance systems are limited by the fact that they tend to include only the more severe cases while missing the mild cases and undiagnosed infections and deaths [37,38].

## Objective

To that end, the objective of our research is to provide standard surveillance metrics, which are necessary but not sufficient to detect the dynamics of the pandemic at the province level, even though they are limited to more severe cases and suffer from incomplete case ascertainment and data contamination. To address these data limitations, we validated additional novel surveillance metrics: (1) speed, (2) acceleration, (3) jerk (change in acceleration), (4) 7-day lag, and (5) 7-day persistence effect [39-43].

The basic question we are trying to inform is the following: how are we doing this week relative to previous weeks? From a public health perspective, in the midst of a pandemic, we would like (at least) three affirmative responses: (1) there are fewer new cases per day this week than last week, (2) the number of new cases is declining from day to day, and (3) the day-to-day decline in the number of cases is even bigger this week than last week. Additionally, we would like some indicative information about significant shifts in how the pandemic is progressing—positive shifts could be the first indicators of the emergence of a new or recurrent hotspot, and negative shifts could be the first indicators of successful public health policy.

We use a longitudinal trend analysis study design in concert with dynamic panel modeling and the method of moments to correct for existing surveillance data limitations [39,40]. Specifically, we will measure significant weekly shifts in the transmission of COVID-19 (ie, increase, decrease, or plateau). Our study will measure the underlying causal effect from a given prior week that persists through the following week, with a 7-day persistence rate to explain a clustering/declustering effect. The 7-day persistence represents an underlying disease transmission wave, where a large number of transmissions in a given prior week that results in a large number of infections the following week then “echoes” forward into a large number of new transmissions and hence a large number of new cases 7 days forward.

In summary, we will measure negative and positive shifts in the transmission of SARS-CoV-2 and the dynamics of the pandemic with acceleration/deceleration and jerk. Our novel indicator of persistence does not suffer from sampling bias. Our surveillance system measures the dynamics of the pandemic so that provincial governments can be proactive rather than reactive to outbreaks at the subnational level. This informs decision making regarding disease control, mitigation strategies, and reopening policies as Canada continues to manage this pandemic.

## Methods

The Government of Canada compiles data from each of the provinces and territories. Data have been accessed daily through their official government website [44] since January 2020 and static measures are updated. Persistence and shifts in the pandemic are calculated biweekly. The current panel included 13 provinces and territories to include the entire country of Canada, with 62 days in each panel ( $n=806$ ). An empirical difference equation was specified in which the number of new positive cases in each province each day is a function of the prior number of cases, the level of testing, and weekly shift variables that measure whether the outbreak was growing faster than, slower than, or at the same rate as the previous weeks. This resulted in a dynamic panel model that was estimated using the generalized method of moments (GMM) approach by implementing the Arellano-Bond estimator in R [45].

Dynamic panel models allow us to derive novel metrics of COVID-19 transmissions by using data collected from the government. Hence, we can provide additional useful metrics

that are less labor intensive. Although this is less of a benefit for Canada because of the notable health system and immense resources, dynamic panel models are useful in low-income countries that do not have the resources to have teams of epidemiologists model COVID-19. Dynamic panel data using GMM are the same methods used to measure the expansion and contraction of the economy. These methods lend themselves well to measuring the pandemic. Given the extensive detail necessary to derive novel metrics that are necessary for this study, we refer to original works by Oehmke and colleagues [40], followed by a proof of concept of a surveillance system with enhanced surveillance techniques to measure the dynamics of the pandemic [39].

Existing surveillance metrics are helpful at gauging the spread of COVID-19 and to that end, we provide traditional measures that include the number of new COVID-19 cases, cumulative cases since the outbreak began, a 7-day moving average to control for temporal effects such as dearth of reporting during weekends and holidays, the rate of infection per 100,000 population, new daily number of deaths, cumulative number of deaths, the 7-day moving average of deaths, and the death rate per 100,000 population. We consider these metrics as a proxy for the ongoing epidemic as surveillance systems tend to pick up on the more severe cases.

The dynamic measures include a temporal element to better understand how past cases affect the present and present cases affect the future. Dynamic measures include the following: (1)

speed (the number of new observed COVID-19 cases per day per 100,000, averaged over a week), (2) acceleration (the change in speed from the prior week to the current week), (3) jerk (the week-over-week change in acceleration as a function of time over the course of 2 weeks), and (4) 7-day persistence effect on speed (the average of the number of new cases per day in a given week that are statistically attributable to new cases seven days earlier). We compare the week of February 7-13, 2021, with the week of February 14-20, 2021.

## Results

### Country Regression Results

Regression results for 13 Canadian provinces and territories are presented in [Table 1](#). Weekly surveillance data in [Tables 2-6](#) are based on these regressions. The regression Wald statistic is significant ( $\chi^2_{8}=615.617, P<.001$ ). The Sargan test is not significant, failing to reject the validity of overidentifying restrictions, which further supports our model ( $\chi^2_{511}=13, P=.99$ ). The coefficient on the 7-day lag was both positive and statistically significant ( $P=.01$ ), demonstrating that the number of infections one week prior to data collection had a significant effect on number of infections at the point of data collection. The shift parameter coefficient 14 days prior was positive but not significant (.116,  $P=.49$ ), suggesting that exogenous shift events did not have an effect on cases. The cumulative number of tests administered was significant (coefficient .001,  $P=.02$ ).

**Table 1.** Arellano-Bond dynamic panel data model of COVID-19 dynamics at the province level in Canada.

Variable	Coefficient	Chi-square (df)	P value
7-day lag	.332	N/A <sup>a</sup>	.01
Cumulative tests	.001	N/A	.02
7-day lag shift	.116	N/A	.49
Wald statistic for regression	N/A	615.617 (2, 8)	<.001
Sargan statistic for validity	N/A	13 (2, 511)	.99

<sup>a</sup>N/A: not applicable.

[Tables 2-5](#) show static and novel dynamic surveillance measures for the weeks of February 7-13 and February 14-20, 2021. Additional weeks can be found in [Tables S1-S10](#) in the [Multimedia Appendix 1](#). Canada as a whole had a decrease in 7-day average COVID-19 cases from 2728 per 100,000 during the week of February 7-13 to 2502 per 100,000 during the week of February 14-20 ([Tables 2](#) and [3](#)). As of February 20, 2021,

Canada had a relatively low caseload of 843,284 infections and 21,630 deaths. There are 37,742,154 people that reside in Canada and relative to the United States, their rate of infection is much lower.

Between the weeks of February 7-13 and February 14-20, 2021, we found indicators demonstrating an increase from the first to the second week of 19,947 cumulative cases ([Tables 2](#) and [3](#)).

**Table 2.** Static surveillance metrics for the week of February 7-13, 2021.

Province	New cases	Cumulative cases	7-day moving average	Infection rate	Deaths	Cumulative deaths	7-day moving average of death	Death rate
Alberta	305	128,532	303.43	6.90	15	1775	10	0.34
British Columbia	0	72,750	433.43	0	0	1288	6.00	0
Manitoba	99	30,687	75.57	7.18	0	866	3.43	0
New Brunswick	16	1398	8.71	2.05	0	22	0.29	0
Newfoundland and Labrador	26	686	38.71	4.98	0	4	0	0
Northwest Territories	0	43	1	0	0	0	0	0
Nova Scotia	2	1592	1.14	0.20	0	65	0	0
Nunavut	5	308	1.29	12.71	0	1	0	0
Ontario	1300	284,887	1167.00	8.82	19	6651	24	0.13
Prince Edward Island	0	114	0.29	0	0	0	0	0
Quebec	1049	275,880	986.14	12.23	28	10,201	28.86	0.33
Saskatchewan	244	26,389	168.57	20.70	4	354	2.57	0.34
Yukon	0	71	0.14	0	0	1	0	0
Canada	3046	823,337	2727.86	8.01	66	21,228	75.14	0.17

**Table 3.** Static surveillance metrics for the week of February 14-20, 2021.

Province	New cases	Cumulative cases	7-day moving average	Infection rate	Deaths	Cumulative deaths	7-day moving average of death	Death rate
Alberta	380	130,727	313.57	8.59	6	1818	6.14	0.14
British Columbia	0	75,835	440.71	0	0	1327	5.57	0
Manitoba	94	31,329	91.71	6.82	3	882	2.29	0.22
New Brunswick	3	1420	3.14	0.38	0	24	0.29	0
Newfoundland and Labrador	38	901	30.71	7.28	0	4	0	0
Northwest Territories	0	47	0.57	0	0	0	0	0
Nova Scotia	4	1608	2.29	0.41	0	65	0	0
Nunavut	6	338	4.29	15.25	0	1	0	0
Ontario	1228	291,999	1016	8.33	28	6848	28.14	0.19
Prince Edward Island	0	114	0	0	0	0	0	0
Quebec	769	281,456	796.57	8.97	14	10,292	13	0.16
Saskatchewan	193	27,438	149.86	16.37	3	368	2	0.25
Yukon	0	72	0.14	0	0	1	0	0
Canada	2715	843,284	2502.14	7.14	54	21,630	57.43	0.14

Canada's speed of infection decreased from 8.38 new cases per 100,000 per week the week of February 7-13, 2021, to 7.5 new cases per 100,000 per week the week of February 14-20, 2021. Nunavut's speed increased dramatically from 3.3 to 10.9 per 100,000; Quebec's speed decreased from 11.5 to 9.3 per 100,000; Saskatchewan decreased from 14.3 to 12.7 per 100,000 over the two-week period from February 7-20. Saskatchewan's

persistent rate decreased from 8.6 to 6.4 between February 7 and February 20, 2021 (Table 6). Canada had deceleration in new cases and a negative jerk from February 7 to February 20 (Tables 4 and 5). Looking at provinces individually, the overall countrywide pattern holds, as all provinces had acceleration of <1 or deceleration and jerk of <1 or negative jerk from February 7-20.

**Table 4.** Novel surveillance metrics for the week of February 7-13, 2021.

Province	Speed: daily positives per 100,000 (weekly average of new daily cases per 100,000)	Acceleration: day-to-day change in the number of positives per day, weekly average, per 100,000	Jerk: week-over-week change in acceleration, per 100,000	7-day persistence effect on speed (number of new cases per day per 100,000 attributed to new cases 7 days ago)
Alberta	6.86	-0.14	0.13	3.86
British Columbia	8.42	0	0.07	3.65
Manitoba	5.48	0.20	0.50	3.30
New Brunswick	1.12	0.07	0.11	0.88
Newfoundland and Labrador	7.42	0.63	-0.71	0.09
Northwest Territories	2.21	0	0	0.14
Nova Scotia	0.12	0.03	0.03	0.03
Nunavut	3.27	0.73	0.73	2.44
Ontario	7.92	-0.09	0.49	4.49
Prince Edward Island	0.18	0	0	0.04
Quebec	11.50	-0.26	-0.06	5.68
Saskatchewan	14.30	-0.23	0.72	8.58
Yukon	0.34	0	-0.34	0
Canada	8.38	-0.10	0.23	4.37

**Table 5.** Novel surveillance metrics for the week of February 14-20, 2021.

Province	Speed: daily positives per 100,000 (weekly average of new daily cases per 100,000)	Acceleration: day-to-day change in the number of positives per day, weekly average, per 100,000	Jerk: week-over-week change in acceleration, per 100,000	7-day persistence effect on speed (number of new cases per day per 100,000 attributed to new cases 7 days ago)
Alberta	7.09	0.24	0.21	3.07
British Columbia	8.56	0	-0.17	3.77
Manitoba	6.65	-0.05	-0.15	2.45
New Brunswick	0.40	-0.24	-0.26	0.50
Newfoundland and Labrador	5.88	0.33	0.05	3.32
Northwest Territories	1.27	0	0	0.99
Nova Scotia	0.23	0.03	0	0.05
Nunavut	10.89	0.36	-0.36	1.46
Ontario	6.90	-0.07	-0.14	3.54
Prince Edward Island	0	0	0	0.08
Quebec	9.29	-0.47	-0.16	5.15
Saskatchewan	12.71	-0.62	-0.11	6.40
Yukon	0.34	0	0.34	0.15
Canada	7.50	-0.12	-0.10	3.75

In general, between February 7, 2021, and February 20, 2021, the speed of the COVID-19 pandemic slowed slightly in Canada as it went from 8.4 to 7.5 cases per day per 100,000 population. The pandemic was decelerating during the week of February 13, 2021, by -0.1 cases per day per 100,000 population and

maintained that minor deceleration the following week at -0.1 per day per 100,000 population. Moreover, comparing the acceleration week over week, the rate of acceleration jerked downward by -0.1 per day per 100,000 population.

**Table 6.** Provinces with the highest 7-day persistence.

Date and provinces	7-day persistence values
<b>February 13, 2021</b>	
Saskatchewan	8.58
Quebec	5.68
Ontario	4.49
Alberta	3.86
British Columbia	3.65
<b>February 20, 2021</b>	
Saskatchewan	6.40
Quebec	5.15
British Columbia	3.77
Ontario	3.54
Newfoundland and Labrador	3.32

The persistence rate, which is the number of cases this week that are statistically linked to novel infections a week ago, shows the pandemic shifting downward with the exception of British Columbia, which had a modest increase (Table 6). Less densely populated areas of Newfoundland and Labrador, the Northwest Territories, Nova Scotia, and Prince Edward Island experienced modest increases in the persistence of infections during the week of February 20, 2021.

The most populous provinces and their populations are shown in Table 7. Of the most populous provinces, Ontario and Quebec both had a decrease in speed, deceleration, and negative jerk during February 7-20, 2021. All dynamic indicators of the two largest provinces show that the pandemic is slowing. Of concern are British Columbia, Alberta, and Manitoba because they are headed in the opposite direction. Specifically, the speed of the pandemic is increasing in these three provinces. Acceleration of the daily speed, which is the week-to-week change in the number of new daily cases per 100,000 population increased for Alberta, remained at 0 for British Columbia, and decreased

slightly for Manitoba the week of February 20, 2021. Although the speed is increasing, the day-to-day increase in COVID-19 transmissions jerked downward for British Columbia and Manitoba, with Alberta's jerk slightly increasing (Tables 4 and 5). Jerk can be interpreted as a given week's acceleration minus the prior week's acceleration. Jerk helps us to understand how the pandemic is increasing or decreasing relative to last week. Nunavut's rates indicated an outbreak between the weeks of February 7-13 and February 14-20, 2021, when the rate of speed increased from 3.3 to 10.9 new infections per day per 100,000 population. Fortunately, there is evidence that this outbreak is slowing. The acceleration of speed slowed during this time, down from 0.7 per 100,000 per day during the week of February 7-13 to 0.4 per 100,000 per day during the week of February 14-20. The persistence rate also decreased from 2.4 to 1.5 cases that are directly attributable to the number of new infections 7 days earlier. Although Nunavut experienced an outbreak, we also see the pandemic slowing, indicating a favorable response to mitigation efforts.

**Table 7.** Most populous Canadian provinces.

Province	Population as of 2020
Ontario	14,734,014
Quebec	8,574,571
British Columbia	5,147,712
Alberta	4,421,876
Manitoba	1,379,263

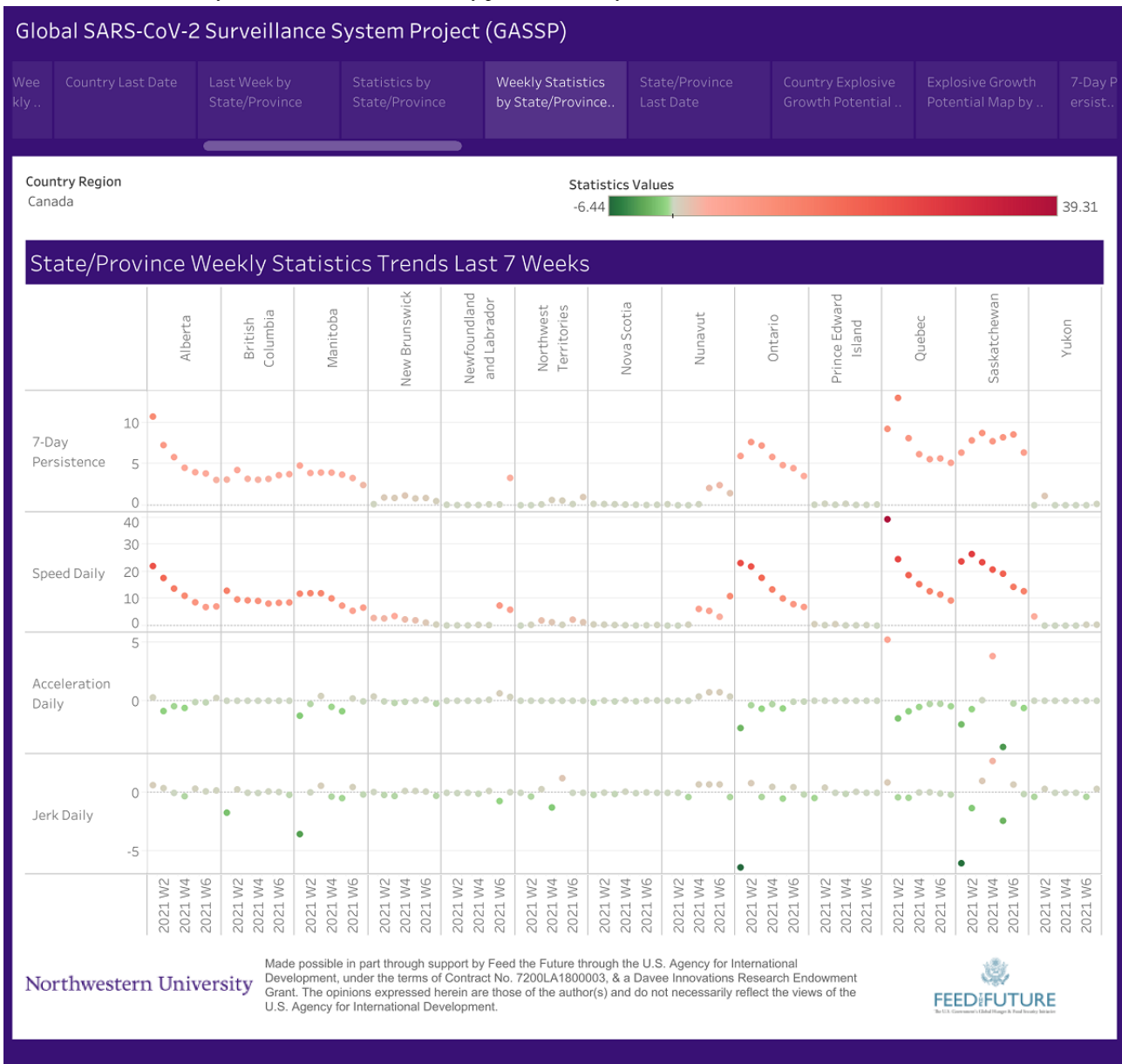
## Province Regression Results

Due to the nature of publications, the moment we publish our research findings, the data become outdated. To that end, the

active surveillance system that informed this study, which contains more recent data, can be accessed online [46]. Figure 2 provides a visualization of our novel metrics over a 3-week period.



Figure 2. Screenshot of weekly Canada SARS-CoV-2 trends by province/territory.



## Discussion

### Principal Findings

The novel metrics applied in this paper advance Canada’s surveillance capacity for monitoring the COVID-19 pandemic. In particular, acceleration and jerk provide a more complete picture of day-to-day and week-to-week changes in the pandemic than do traditional surveillance measures. The 7-day persistence rate helps identify areas where a high incidence of cases one week is passed forward to create a high incidence of cases the next week, and high persistence rates indicate an underlying problem with pandemic control. These measures, available through an online data dashboard, provide valuable information to Canada (as well as other countries) to monitor the pandemic.

Canada initially had an outbreak of COVID-19 around the same time as the initial outbreak in the United States. At many levels, the United States and Canada are similar in that they are both

located in North America and both are developed, high-income countries, with vast geographical areas and heterogeneous populations. Beyond this, the similarities end between the United States and Canada as it relates to COVID-19 transmissions.

Canada developed a coordinated national plan between political parties and among its provinces and territories. First and foremost, Canada successfully implemented a widespread shutdown, which led to the initial reduction in COVID-19 transmissions. In addition, social isolation, distancing, masking, testing, and contact tracing have resulted in a coordinated effort that has mitigated the pandemic. Fortunately, this has worked well for a number of provinces and territories. Though Canada overall still has new daily cases, the pandemic is slowing based on measures of acceleration, jerk, and 7-day persistence rate, meaning cases and transmission were trending downward during the week of February 14-20. These rates were trending upward the week before. The most alarming metric is that speed in Nunavut increased from 3.3 new cases per day per 100,000 population to 10.9 cases per day per 100,000 population, which

is a three-fold increase. This is indicative of an outbreak; however, the Canadian response to novel infections in Nunavut resulted in the speed decelerating, which is evident in the decrease in the acceleration rate as well as a negative jerk during the week of February 14-20, 2021.

Canada is successfully tamping down the pandemic, evident by the decrease in daily cases of daily transmissions from 3046 to 2715, concurrent with a decrease in the 7-day moving average, decrease in deaths, and decrease in death rates. Regardless, the weekly number of new cases remains at 2715 for the week of February 20, 2021. Such a large caseload could quickly escalate to a large outbreak if prevention efforts wane.

## Conclusion

Canada has maintained good COVID-19 control policies that resulted in fewer transmissions for the week of February 14-20, 2021, compared to the previous week; however, it is not time for Canada to declare victory over COVID-19 transmissions or to be complacent. The opposite is necessary. Canada must remain vigilant and continue implementing those policies that caused the Canadian outbreak to reverse course and decrease. In summary, we understand what causes COVID-19 and how it is transmitted. We also understand how to control outbreaks. Enhanced surveillance is the first indicator that an outbreak is occurring and that immediate action is needed. Conversely, enhanced surveillance also informs policy makers when policies put into place to control the COVID-19 pandemic are successfully decreasing the spread of disease.

## Acknowledgments

This study and the resulting surveillance system were funded in part by the Davee Innovations Research Endowment for North America. Any opinions, findings, conclusions, or recommendations expressed here are those of the authors alone and do not necessarily reflect the opinions of funders or authors' employers. The opinions expressed in this paper are those of the authors and do not necessarily represent the opinions of the US Agency for International Development.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Static and novel surveillance metrics for weeks between 1/3/2021-2/6/2021.

[[DOCX File, 42 KB - publichealth\\_v7i5e25753\\_app1.docx](#)]

## References

1. Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *Int J Surg* 2020 Apr;76:71-76 [FREE Full text] [doi: [10.1016/j.ijssu.2020.02.034](https://doi.org/10.1016/j.ijssu.2020.02.034)] [Medline: [32112977](https://pubmed.ncbi.nlm.nih.gov/32112977/)]
2. Nicola M, Alsafi Z, Sohrabi C, Kerwan A, Al-Jabir A, Iosifidis C, et al. The socio-economic implications of the coronavirus pandemic (COVID-19): A review. *Int J Surg* 2020 Jun;78:185-193 [FREE Full text] [doi: [10.1016/j.ijssu.2020.04.018](https://doi.org/10.1016/j.ijssu.2020.04.018)] [Medline: [32305533](https://pubmed.ncbi.nlm.nih.gov/32305533/)]
3. Pennycook G, McPhetres J, Bago B, Rand DG. Predictors of attitudes and misperceptions about COVID-19 in Canada, the UK, and the USA. *PsyArXiv*. Preprint posted online on April 14, 2020.
4. Husain I, Briggs B, Lefebvre C, Cline DM, Stopyra JP, O'Brien MC, et al. Fluctuation of Public Interest in COVID-19 in the United States: Retrospective Analysis of Google Trends Search Data. *JMIR Public Health Surveill* 2020 Jul 17;6(3):e19969 [FREE Full text] [doi: [10.2196/19969](https://doi.org/10.2196/19969)] [Medline: [32501806](https://pubmed.ncbi.nlm.nih.gov/32501806/)]
5. Baniamin HM, Rahman M, Hasan MT. The COVID-19 pandemic: why are some countries coping more successfully than others? *Asia Pacific Journal of Public Administration* 2020 Jul 15;42(3):153-169. [doi: [10.1080/23276665.2020.1784769](https://doi.org/10.1080/23276665.2020.1784769)]
6. Wang D, Marmo-Roman S, Krase K, Phanord L. Compliance with preventative measures during the COVID-19 pandemic in the USA and Canada: Results from an online survey. *Soc Work Health Care* 2021 Jan 06:1-16. [doi: [10.1080/00981389.2020.1871157](https://doi.org/10.1080/00981389.2020.1871157)] [Medline: [33407057](https://pubmed.ncbi.nlm.nih.gov/33407057/)]
7. Agle J, Xiao Y. Misinformation about COVID-19: evidence for differential latent profiles and a strong association with trust in science. *BMC Public Health* 2021 Jan 07;21(1):89 [FREE Full text] [doi: [10.1186/s12889-020-10103-x](https://doi.org/10.1186/s12889-020-10103-x)] [Medline: [33413219](https://pubmed.ncbi.nlm.nih.gov/33413219/)]
8. Béland D, Marchildon GP, Medrano A, Rocco P. COVID-19, Federalism, and Health Care Financing in Canada, the United States, and Mexico. *Journal of Comparative Policy Analysis: Research and Practice* 2021 Jan 07;23(2):143-156. [doi: [10.1080/13876988.2020.1848353](https://doi.org/10.1080/13876988.2020.1848353)]
9. Johns Hopkins University. COVID-19 Dashboard. 2021. URL: <https://coronavirus.jhu.edu/map.html> [accessed 2021-02-22]
10. Government of Canada. Coronavirus disease (COVID-19): Outbreak update. URL: <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection.html> [accessed 2021-02-22]

11. Neustaeter B. Emerging from coronavirus: Reopening plans province-by-province. CTV News. URL: <https://www.ctvnews.ca/health/coronavirus/emerging-from-coronavirus-reopening-plans-province-by-province-1.4913652> [accessed 2020-08-09]
12. Wise J. Covid-19: Risk of second wave is very real, say researchers. BMJ 2020 Jun 09;369:m2294. [doi: [10.1136/bmj.m2294](https://doi.org/10.1136/bmj.m2294)] [Medline: [32518177](https://pubmed.ncbi.nlm.nih.gov/32518177/)]
13. Nunavut Department of Health. Confirmed case of COVID-19 in Nunavut. 2020 Nov 06. URL: <https://gov.nu.ca/executive-and-intergovernmental-affairs/news/confirmed-case-covid-19-nunavut-0> [accessed 2021-05-05]
14. Ford JD, Berrang-Ford L. Food security in Igloolik, Nunavut: an exploratory study. Polar Record 2009 Jul 01;45(3):225-236. [doi: [10.1017/s0032247408008048](https://doi.org/10.1017/s0032247408008048)]
15. Orr P. Tuberculosis in Nunavut: looking back, moving forward. CMAJ 2013 Mar 05;185(4):287-288 [FREE Full text] [doi: [10.1503/cmaj.121536](https://doi.org/10.1503/cmaj.121536)] [Medline: [23382256](https://pubmed.ncbi.nlm.nih.gov/23382256/)]
16. Boyd A, Ferguson R, McKeen A, McKinley S. How each province and territory has shaped Canada's fight against the coronavirus. 2020 Apr 13. URL: <https://www.thestar.com/news/canada/2020/04/11/how-each-province-and-territory-has-shaped-canadas-fight-against-the-coronavirus.html> [accessed 2020-08-09]
17. Webster P. Canada and COVID-19: learning from SARS. The Lancet 2020 Mar;395(10228):936-937. [doi: [10.1016/s0140-6736\(20\)30670-x](https://doi.org/10.1016/s0140-6736(20)30670-x)]
18. Merkley E, Bridgman A, Loewen PJ, Owen T, Ruths D, Zhilin O. A Rare Moment of Cross-Partisan Consensus: Elite and Public Response to the COVID-19 Pandemic in Canada. Can J Pol Sci 2020 Apr 16;53(2):311-318. [doi: [10.1017/S0008423920000311](https://doi.org/10.1017/S0008423920000311)]
19. Turnbull S. COVID-19 in Canada: This is how each province is handling the pandemic. CTV News. 2020. URL: <https://www.ctvnews.ca/politics/covid-19-in-canada-this-is-how-each-province-is-handling-the-pandemic-1.4867626> [accessed 2021-05-05]
20. Lyu W, Wehby GL. Community Use Of Face Masks And COVID-19: Evidence From A Natural Experiment Of State Mandates In The US. Health Aff (Millwood) 2020 Aug 01;39(8):1419-1425. [doi: [10.1377/hlthaff.2020.00818](https://doi.org/10.1377/hlthaff.2020.00818)] [Medline: [32543923](https://pubmed.ncbi.nlm.nih.gov/32543923/)]
21. Maxouris C. Half of US states are reporting increased Covid-19 cases and some leaders push new measures. CNN. 2020 Oct 07. URL: <https://www.cnn.com/2020/10/07/health/us-coronavirus-wednesday/index.html> [accessed 2021-05-05]
22. Guzman J. Fauci says new coronavirus actions by Florida governor are 'very concerning'. The Hill. 2020 Sep 28. URL: <https://thehill.com/changing-america/well-being/prevention-cures/518577-fauci-says-new-coronavirus-actions-by-florida> [accessed 2021-05-05]
23. Eggert D, White E. Michigan Governor's Virus Powers Upended With Court Ruling. US News. 2020 Oct 02. URL: <https://www.usnews.com/news/best-states/michigan/articles/2020-10-02/539k-signatures-submitted-to-repeal-whitmer-emergency-powers> [accessed 2021-05-05]
24. Beauchamp Z. Canada succeeded on coronavirus where America failed. Why? Vox. 2020 May 04. URL: <https://www.vox.com/2020/5/4/21242750/coronavirus-covid-19-united-states-canada-trump-trudeau> [accessed 2020-08-05]
25. Fong BYF, Law VTS. COVID-19 – A Tale of Two Cities: Seattle and Vancouver. APJHM 2020 Jul 26;15(3):39-44. [doi: [10.24083/apjhm.v15i3.455](https://doi.org/10.24083/apjhm.v15i3.455)]
26. Van Bavel JJ, Baicker K, Boggio PS, Capraro V, Cichocka A, Cikara M, et al. Using social and behavioural science to support COVID-19 pandemic response. Nat Hum Behav 2020 May;4(5):460-471. [doi: [10.1038/s41562-020-0884-z](https://doi.org/10.1038/s41562-020-0884-z)] [Medline: [32355299](https://pubmed.ncbi.nlm.nih.gov/32355299/)]
27. CoronaTracker. URL: <https://www.coronatracker.com/about> [accessed 2020-08-16]
28. Ministry of Health of Ukraine. Ukraine COVID Dashboard. URL: <https://covid19.gov.ua/> [accessed 2020-08-16]
29. Busquets Guàrdia A, Pawelec H, Hirsch C. Coronavirus in Europe: Live Data Tracker. Politico. 2020 Mar 13. URL: <https://www.politico.eu/article/coronavirus-in-europe-by-the-numbers/> [accessed 2020-08-16]
30. Coronavirus Pandemic: Tracking the Global Outbreak. BBC News. URL: <https://www.bbc.com/news/world-51235105> [accessed 2020-08-16]
31. Coronavirus tracker: the latest figures as countries fight the Covid-19 resurgence. Financial Times. URL: <https://www.ft.com/content/a2901ce8-5eb7-4633-b89c-cbdf5b386938> [accessed 2020-08-16]
32. Coronavirus Disease 2019 (COVID-19) - Situation Report of the Robert Koch Institute. Robert Koch Institute. URL: [https://www.rki.de/EN/Content/infections/epidemiology/outbreaks/COVID-19/Situationsberichte\\_Tab.html](https://www.rki.de/EN/Content/infections/epidemiology/outbreaks/COVID-19/Situationsberichte_Tab.html) [accessed 2021-05-05]
33. Italian Ministry of Health. New coronavirus. URL: <http://www.salute.gov.it/portale/nuovocoronavirus/homeNuovoCoronavirus.jsp> [accessed 2021-05-05]
34. Government of Spain Ministry of Health. Current situation. URL: <https://www.mscbs.gob.es/en/profesionales/saludPublica/ccayes/alertasActual/nCov-China/situacionActual.htm> [accessed 2020-08-16]
35. European Centre for Disease Prevention and Control. COVID-19 Country Overviews. URL: <https://covid19-country-overviews.ecdc.europa.eu/> [accessed 2020-08-03]
36. Government of the United Kingdom. Coronavirus (COVID-19) in the UK. 2020. URL: <https://coronavirus.data.gov.uk/> [accessed 2020-08-16]
37. Teutsch SM. Considerations in Planning a Surveillance System. In: Lee LM, Teutsch SM, Thacker SB, St. Louis ME, editors. Principles & Practice of Public Health Surveillance. Oxford, UK: Oxford University Press; 2010:18.

38. Thacker SB, Berkelman RL. Public health surveillance in the United States. *Epidemiol Rev* 1988;10:164-190. [doi: [10.1093/oxfordjournals.epirev.a036021](https://doi.org/10.1093/oxfordjournals.epirev.a036021)] [Medline: [3066626](https://pubmed.ncbi.nlm.nih.gov/3066626/)]
39. Oehmke JF, Moss CB, Singh LN, Oehmke TB, Post LA. Dynamic Panel Surveillance of COVID-19 Transmission in the United States to Inform Health Policy: Observational Statistical Study. *J Med Internet Res* 2020 Oct 5;22(10):e21955. [doi: [10.2196/21955](https://doi.org/10.2196/21955)]
40. Oehmke JF, Oehmke TB, Singh LN, Post LA. Dynamic Panel Estimate-Based Health Surveillance of SARS-CoV-2 Infection Rates to Inform Public Health Policy: Model Development and Validation. *J Med Internet Res* 2020 Sep 22;22(9):e20924 [FREE Full text] [doi: [10.2196/20924](https://doi.org/10.2196/20924)] [Medline: [32915762](https://pubmed.ncbi.nlm.nih.gov/32915762/)]
41. Oehmke JF, Moss CB, Singh LN, Oehmke TB, Post LA. Dynamic Panel Surveillance of COVID-19 Transmission in the United States to Inform Health Policy: Observational Statistical Study. *J Med Internet Res* 2020 Oct 5;22(10):e21955. [doi: [10.2196/21955](https://doi.org/10.2196/21955)]
42. Post LA, Issa TZ, Boctor MJ, Moss CB, Murphy RL, Ison MG, et al. Dynamic Public Health Surveillance to Track and Mitigate the US COVID-19 Epidemic: Longitudinal Trend Analysis Study. *J Med Internet Res* 2020 Dec 03;22(12):e24286 [FREE Full text] [doi: [10.2196/24286](https://doi.org/10.2196/24286)] [Medline: [33216726](https://pubmed.ncbi.nlm.nih.gov/33216726/)]
43. Post L, Marogi E, Moss CB, Murphy RL, Ison MG, Achenbach CJ, et al. SARS-CoV-2 Surveillance in the Middle East and North Africa: Longitudinal Trend Analysis. *J Med Internet Res* 2021 Jan 15;23(1):e25830 [FREE Full text] [doi: [10.2196/25830](https://doi.org/10.2196/25830)] [Medline: [33302252](https://pubmed.ncbi.nlm.nih.gov/33302252/)]
44. Government of Canada. Interactive data visualizations of COVID-19. Public Health Infobase. URL: <https://health-infobase.canada.ca/covid-19/> [accessed 2021-02-22]
45. Hansen LP. Large Sample Properties of Generalized Method of Moments Estimators. *Econometrica* 1982 Jul;50(4):1029. [doi: [10.2307/1912775](https://doi.org/10.2307/1912775)]
46. The Global SARS-CoV-2 Surveillance Project. Northwestern University. URL: <https://sites.northwestern.edu/covidglobalsurveillance/> [accessed 2021-05-06]

## Abbreviations

**GMM:** generalized method of moments

**SARS:** severe acute respiratory syndrome

*Edited by G Eysenbach; submitted 13.11.20; peer-reviewed by B Dixon; comments to author 04.12.20; revised version received 25.02.21; accepted 09.04.21; published 10.05.21.*

*Please cite as:*

*Post L, Boctor MJ, Issa TZ, Moss CB, Murphy RL, Achenbach CJ, Ison MG, Resnick D, Singh L, White J, Welch SB, Oehmke JF SARS-CoV-2 Surveillance System in Canada: Longitudinal Trend Analysis*

*JMIR Public Health Surveill* 2021;7(5):e25753

URL: <https://publichealth.jmir.org/2021/5/e25753>

doi: [10.2196/25753](https://doi.org/10.2196/25753)

PMID: [33852410](https://pubmed.ncbi.nlm.nih.gov/33852410/)

©Lori Post, Michael J Boctor, Tariq Z Issa, Charles B Moss, Robert Leo Murphy, Chad J Achenbach, Michael G Ison, Danielle Resnick, Lauren Singh, Janine White, Sarah B Welch, James F Oehmke. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 10.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

## Original Paper

# Protective Behaviors and Secondary Harms Resulting From Nonpharmaceutical Interventions During the COVID-19 Epidemic in South Africa: Multisite, Prospective Longitudinal Study

Guy Harling<sup>1,2,3,4,5,6</sup>, ScD; Francesc Xavier Gómez-Olivé<sup>3,7</sup>, MBMCh, PhD; Joseph Tlouyamma<sup>8,9</sup>, MSc; Tinofa Mutevedzi<sup>10</sup>, MSc; Chodziwadziwa Whiteson Kabudula<sup>3</sup>, PhD; Ruth Mahlako<sup>8</sup>, BSc (Hons); Urisha Singh<sup>1</sup>, PhD; Daniel Ohene-Kwofie<sup>3</sup>, MSc; Rose Buckland<sup>2</sup>, MSc; Pedzisai Ndagurwa<sup>3</sup>, PhD; Dickman Gareta<sup>1</sup>, MSc; Resign Gunda<sup>1,6</sup>, PhD; Thobeka Mngomezulu<sup>1</sup>, DipM; Siyabonga Nxumalo<sup>1</sup>, BSc; Emily B Wong<sup>1,11</sup>, MD; Kathleen Kahn<sup>3,7</sup>, MBBCh, PhD; Mark J Siedner<sup>1,12</sup>, MD; Eric Maimela<sup>8,13</sup>, PhD; Stephen Tollman<sup>3,7</sup>, MBBCh, PhD; Mark Collinson<sup>3,10</sup>, PhD; Kobus Herbst<sup>1,10</sup>, MBBCh, MSc

<sup>1</sup>Africa Health Research Institute, KwaZulu-Natal, South Africa

<sup>2</sup>Institute for Global Health, University College London, London, United Kingdom

<sup>3</sup>Medical Research Council/Wits Rural Public Health and Health Transitions Research Unit (Agincourt), School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

<sup>4</sup>Department of Epidemiology, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, United States

<sup>5</sup>Center for Population and Development Studies, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, United States

<sup>6</sup>School of Nursing and Public Health, University of KwaZulu-Natal, Durban, South Africa

<sup>7</sup>International Network for the Demographic Evaluation of Populations and Their Health Network, Accra, Ghana

<sup>8</sup>Dikgale-Mamabolo-Mothiba Population Health Research Centre, School of Health Care Sciences, Faculty of Health Sciences, University of Limpopo, Mankweng, South Africa

<sup>9</sup>Department of Computer Science, School of Mathematical and Computer Sciences, Faculty of Science and Agriculture, University of Limpopo, Mankweng, South Africa

<sup>10</sup>Department of Science and Innovation-Medical Research Council South African Population Research Infrastructure Network, Johannesburg, South Africa

<sup>11</sup>Division of Infectious Diseases, University of Alabama, Birmingham, Birmingham, AL, United States

<sup>12</sup>Harvard Medical School and the Medical Practice Evaluation Center, Massachusetts General Hospital, Boston, MA, United States

<sup>13</sup>Department of Public Health, School of Health Care Sciences, Faculty of Health Sciences, University of Limpopo, Mankweng, South Africa

## Corresponding Author:

Guy Harling, ScD

Africa Health Research Institute

P.O. Box 198, Mtubatuba 3935

KwaZulu-Natal

South Africa

Phone: 27 0355507500

Email: [guy.harling@ahri.org](mailto:guy.harling@ahri.org)

## Abstract

**Background:** In March 2020, South Africa implemented strict nonpharmaceutical interventions (NPIs) to contain the spread of COVID-19. Over the subsequent 5 months, NPI policies were eased in stages according to a national strategy. COVID-19 spread throughout the country heterogeneously; the disease reached rural areas by July and case numbers peaked from July to August. A second COVID-19 wave began in late 2020. Data on the impact of NPI policies on social and economic well-being and access to health care are limited.

**Objective:** We aimed to determine how rural residents in three South African provinces changed their behaviors during the first COVID-19 epidemic wave.

**Methods:** The South African Population Research Infrastructure Network nodes in the Mpumalanga (Agincourt), KwaZulu-Natal, (Africa Health Research Institute) and Limpopo (Dikgale-Mamabolo-Mothiba) provinces conducted up to 14 rounds of longitudinal telephone surveys among randomly sampled households from rural and periurban surveillance populations every 2-3 weeks.

Interviews included questions on the following topics: COVID-19–related knowledge and behaviors, the health and economic impacts of NPIs, and mental health. We analyzed how responses varied based on NPI stringency and household sociodemographics.

**Results:** In total, 5120 households completed 23,095 interviews between April and December 2020. Respondents' self-reported satisfaction with their COVID-19–related knowledge and face mask use rapidly rose to 85% and 95%, respectively, by August. As selected NPIs were eased, the amount of travel increased, economic losses were reduced, and the prevalence of anxiety and depression symptoms fell. When the number of COVID-19 cases spiked at one node in July, the amount of travel dropped rapidly and the rate of missed daily medications doubled. Households where more adults received government-funded old-age pensions reported concerns about economic matters and medication access less often.

**Conclusions:** South Africans complied with stringent, COVID-19–related NPIs despite the threat of substantial social, economic, and health repercussions. Government-supported social welfare programs appeared to buffer interruptions in income and health care access during local outbreaks. Epidemic control policies must be balanced against the broader well-being of people in resource-limited settings and designed with parallel support systems when such policies threaten peoples' income and access to basic services.

(*JMIR Public Health Surveill* 2021;7(5):e26073) doi:[10.2196/26073](https://doi.org/10.2196/26073)

## KEYWORDS

behaviour change; COVID-19; economic well-being; health care access; health knowledge; mental health; South Africa; surveillance; nonpharmaceutical interventions

## Introduction

Since the emergence of COVID-19 in humans in late 2019, the epidemic has spread to every country in the world, resulting in direct mortality and morbidity [1] and indirect impacts on physical and mental health and economic well-being [2-4]. Shortly after COVID-19 was declared a Public Health Emergency of International Concern on January 30, 2020, South Africa was identified as a highly vulnerable country due to (1) its extensive internal and international transportation links [5]; (2) its burden of infectious and noncommunicable health conditions [6,7]; and (3) its large, socioeconomically vulnerable population [8]. The national government rapidly announced strict, nationwide nonpharmaceutical interventions (NPIs; Level 5 lockdown) on March 26, 2020. Under these NPIs, leaving home was only allowed for grocery shopping, obtaining medicine and medical care, or conducting permitted essential work. Furthermore, tobacco and alcohol sales were banned, and from May 1 onward, face mask use was mandatory in public spaces. These regulations were accompanied with guidance on enhanced handwashing, sanitizer use, and surface cleaning.

The lockdown was intended to (1) reduce COVID-19 transmission through strictly restricting physical interactions; (2) prevent rapid epidemic growth and allow health care providers to prepare for a subsequent rise in the demand for care; (3) promote widespread educational campaigns to reduce COVID-19 transmission; and (4) initiate an ambitious, country-wide, community-based COVID-19 screening and testing program [9]. Between May and September 2020, the lockdown was gradually eased, allowing people to return work and school and engage in limited public gatherings. For example, under Level 4 lockdown, restrictions were eased to allow the restarting of work in high-value sectors, meal deliveries, and nongroup daytime exercise. Under Level 3 lockdown, limited religious gatherings, professional noncontact sports, and sit-down meals were allowed.

Although the cumulative number of COVID-19 cases slowly grew during April 2020, the disease incidence curve rapidly rose from May onward, peaking between June and August. By September 1, 2020, South Africa had reported over 625,000 confirmed COVID-19 cases and over 14,000 deaths [10]; the COVID-19 epidemic in South Africa was among the 10 largest epidemics reported worldwide by that date [11]. The true impact of the epidemic appears to be even greater, with an excess of 42,396 deaths reported in South Africa between January and August 2020 compared to those reported in the same period in 2018 and 2019 [12].

The relaxation of lockdown regulations, which occurred even as the epidemic grew, reflected competing health and economic vulnerabilities and priorities as well as sustained popular pressures [13-15]. There was widespread concern that the lockdown was substantially affecting the national economy; individual household livelihoods; and access to education, health care, and medication [8,16]. Additionally, some expected the lockdown to be futile, since much of the population could neither maintain physical distancing nor implement NPIs due to household and community overcrowding and limited access to running water and sanitation [17].

Robust data are essential for evaluating the hypotheses that lockdowns cause substantial harm or are futile and for targeting locations that are the most in need of resources. The impact of NPIs has been evaluated in various low- and middle-income countries, generating evidence of early reductions in income and food security and the rapid, substantial uptake of protective behaviors [18-22].

Although South Africa has effective national health care surveillance systems, there is limited capacity for monitoring the social and behavioral effects of NPIs on the COVID-19 epidemic at a local level. NPIs, such as those implemented in South Africa, might be expected to generate differing risks and benefits across socioeconomic settings. For example, there was unease in rural areas regarding water access for hand hygiene and *imilindo* (funeral night vigils held in crowded rooms) [23],

while people from urban areas worried about dwelling proximity and shared ablutions [24]. The number of robust comparisons between urban and rural settings has been limited, but such comparisons are vital if public sector responses are to be effectively aligned with prevailing conditions.

To date, most evaluations of the impact of COVID-19 in South Africa have been limited to web-based or urban settings [25-27]. Studies on the initial weeks of lockdown reported that although people had substantial concerns about the disease and its economic impact, they also had a strong willingness to abide by travel restrictions and other measures [26,27]. To date, the most comprehensive longitudinal study of the impact of the COVID-19 epidemic in South Africa on behavior is the National Income Dynamics Study (NIDS)-Coronavirus Rapid Mobile Survey (CRAM). The NIDS is an ongoing panel survey that began in 2008 and follows a nationally representative sample of households and their members [28]. The NIDS-CRAM recontacted NIDS respondents from the most recent interview wave in 2017 [29]. In 2020, 3 rounds of telephonic data collection were completed (first round: May and June; second round: July and August; third round: November and December), and data on a wide range of social and economic impacts of the epidemic were captured [25,30,31]. Employment dropped sharply after lockdown was imposed, but by October 2020 the overall employment rate appeared to have recovered, although not for women or respondents with low levels of education. The provision of increased government support, including top-ups for existing unconditional grants (which ended after October) and the new, temporary Social Relief of Distress grant for working-aged adults with no other sources of support appeared to aid households, particularly those in rural areas [32]. However, the withdrawal of these grants has caused concern. Mental health concerns remained substantial throughout the year and were positively associated with household child hunger [33].

The NIDS-CRAM has substantial strengths in terms of its national reach and wide-ranging topic coverage. However, it only provides sporadic snapshots of the epidemic. We therefore used an existing research infrastructure in three South African provinces to evaluate how health, social, and economic behaviors continuously changed between April and December 2020. We used a high-frequency survey of a panel of households for which substantial, pre-epidemic data were already available. Our first hypothesis was that behaviors would change as regulations and the national epidemic changed. Our second hypothesis was that these changes would vary based on socioeconomic characteristics (those that reflected households' ability to maintain their compliance with NPI and social distancing policies) and households' needs and resources.

## Methods

### Study Site

The South African Population Research Infrastructure Network (SAPRIN)—an initiative that is hosted by the South African Medical Research Council and receives long-term from the National Department of Science and Innovation—integrates three Health and Demographic Surveillance System (HDSS)

nodes for population and health surveillance: (1) the Medical Research Council (MRC)/Wits Rural Public Health and Health Transitions Research Unit (Agincourt) in Ehlanzeni district, Mpumalanga [34]; (2) the Dikgale-Mamabolo-Mothiba (DIMAMO) Population Health Research Centre in Capricorn district, Limpopo [35]; and (3) the Africa Health Research Institute (AHRI) in uMkhanyakude district, KwaZulu-Natal [36]. Other urban nodes are under development. The nodes, which each contain over 100,000 individuals residing in approximately 20,000 households, vary in settlement structure and density. The three districts are rural or periurban areas that are located on the east side of South Africa (Figure S1 in [Multimedia Appendix 1](#)) and have low average income levels relative to the rest of the country. Nodes conduct multiple in-person and telephonic surveys per year to update health and sociodemographic data. However, DIMAMO had only partially captured socioeconomic data for the first time before the COVID-19 epidemic began in South Africa.

### Study Design and Implementation

In March 2020, SAPRIN initiated plans for each HDSS node to implement a high-intensity, longitudinal telephonic survey that covered at least 750 randomly selected households in each province, by using telephone numbers extracted from each node's most recent census. This sample was selected to obtain estimates of survey- and wave-specific proportions with a precision of no less than 4 percentage points, under the assumption of an 80% response rate based on past SAPRIN surveys. Every 2-3 weeks, a central call center at each node contacted households and asked a primary respondent to answer questions on behalf of the household. Primary respondents had to be resident adult members of the household (aged  $\geq 18$  years). To combat survey fatigue, from mid-September onward or after the seventh survey wave (whichever was earlier), one-third of the cohort was rotated out at each subsequent wave, and a new random sample that included the same number of households was rotated in for 4-6 survey waves. Details for each node are shown in Figure S2 in [Multimedia Appendix 1](#).

The questionnaire included both household-level and individual-specific questions; the latter could be directly answered by other household members if they were present. Otherwise, the primary respondent served as a proxy. The questionnaire included COVID-19 symptom screening; individuals who met the Department of Health's COVID-19 symptom criteria were referred for further investigation, possible testing, and care. Data were captured on laptop computers by call center interviewers who used electronic data capture software, including automated skip patterns and validation checks. Telephone calls continued from April to December 2020 with continuous quality monitoring. The survey implementation process at one node (AHRI) is described in detail elsewhere [37]. The study questionnaire is provided in [Multimedia Appendix 1](#).

### Outcomes

Our outcomes for this study were based on answers to questions related to COVID-19 and NPIs in three key domains: (1) COVID-19-related knowledge and behavior; (2) the health and economic impacts of NPIs; and (3) mental health. For behavior,

the primary respondent was asked to rate their perceived knowledge about COVID-19 on a 5-point scale; we classified respondents as (1) those who self-reported that they did not have enough knowledge or (2) those who reported that they had enough or more than enough knowledge. Respondents were then asked about household behavior changes that they made in response to the COVID-19 epidemic. They were asked whether any resident household member had left the house in the past 7 days and whether any nonhousehold members had visited the house during the preceding day; we classified respondents as either (1) those who reported any number of household or nonhousehold members or (2) those who reported “none” for each question. Respondents were also asked if household members had, over the past 7 days, avoided crowded areas or social events, travelled (using local minibus taxis or long-distance travel methods), or used face masks when going out.

For health and economic impacts, primary respondents were asked about household members' ability to (1) access all needed daily medications, (2) access needed health care, and (3) earn money. Finally, for mental health, we asked primary respondents to answer the Generalized Anxiety Disorder 2-item (GAD-2) and Patient Health Questionnaire 2-item (PHQ-2) scales. GAD-2 and PHQ-2 scores of  $\geq 3$  were considered positive, as per the standard, South African-validated cutoffs [38]. The Cronbach  $\alpha$  values in this study were .85 for the PHQ-2 and .91 for the GAD-2.

### Statistical Analysis

We linked data from the high-intensity SAPRIN survey to the following routine individual and household sociodemographic data, which were collected from households in 2019: the number of children, working-aged adults, and pension-aged adults; the maximum education level attained; node-specific asset index quintiles; levels of employment; and the receipt of unconditional social grants. South African noncontributory pensions are available to all citizens, permanent residents, or documented refugees aged  $>60$  years, although pension applications require proof of status.

In this study, we included anyone who was interviewed in 2020. First, we described survey response rates at each node and time period as well as key, pre-COVID-19 epidemic household characteristics. Second, we described changes in each of the 11 measures across the three domains (behavior, health and economic impact, and mental health) based on node and month of data collection. Third, we used multivariable regression models to assess independent predictors of our outcomes of interest via complete case analysis. For each outcome, we fitted a Poisson model with household-level random effects and robust SEs to calculate prevalence ratios. All models included variables for node, interview round number, month of the interview, and household characteristics. Data analysis was conducted with Stata version 15.1 (StataCorp LLC) and R version 4.0.2 (The R Foundation) [39]. Results were considered statistically significant at the .05 level.

### Ethical Considerations

All households previously provided consent to be contacted by phone and each primary respondent provided recorded, verbal consent. Households were not directly compensated for study participation; however, one node annually provided a shopping voucher (value of around US \$3) to each participating household to thank them for their participation in all SAPRIN-related activities. Responses to questions were electronically captured in secure, on-premise databases with role-based security. Personally identifiable data were sequestered in separate database tables with restricted access, and all analytic data sets were pseudonymized prior to analysis. All study procedures were approved by Limpopo, Mpumalanga, and KwaZulu-Natal's provincial Department of Health Research Ethics Committees (RECs), the University of KwaZulu-Natal's Biomedical REC, the University of the Witwatersrand's Human REC (Medical), and the University of Limpopo's Turfloop REC.

### Patient and Public Involvement

The adaptation of the existing SAPRIN surveillance program was discussed with and approved by each nodes' existing community advisory groups prior to the finalization of the study protocol. The results of the studies were routinely shared with the community through a range of engagement activities that were conducted by the teams at each node.

### Data Availability

The data collected in the SAPRIN COVID-19 surveillance survey, including those reported in this paper, will be made available in pseudonymized form through the SAPRIN data repository [40].

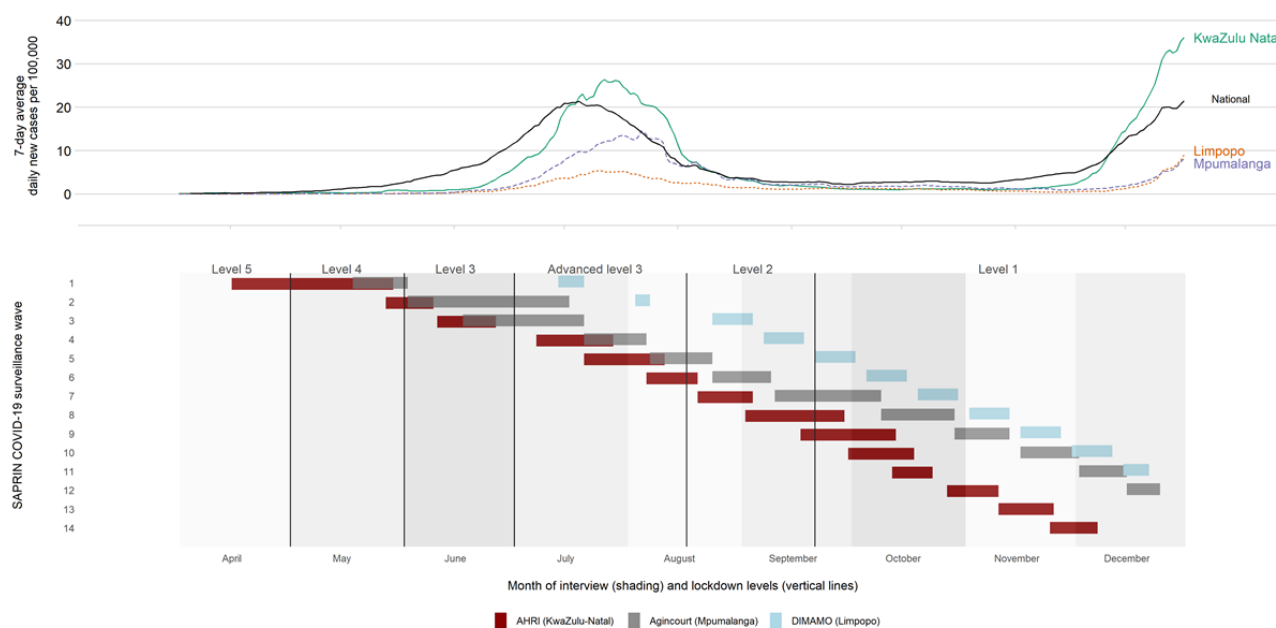
## Results

### Study Implementation

Between April 15 and December 24, 2020, AHRI (in KwaZulu-Natal) completed 14 waves of data collection, Agincourt (in Mpumalanga) completed 12 waves of data collection, and DIMAMO (in Limpopo) completed 11 waves of data collection (Figure 1). These waves covered the entire period of the first COVID-19 epidemic wave in South Africa, including outbreaks of varying sizes that occurred in the three provinces under observation, and part of the early phase of the second national wave. The average response rate was 71% (23,095/31,643), and response rates varied from 56.9% (427/750) to 90.3% (1013/1122) depending on wave and node. Direct refusal was rare (1242/31,643, 3.8%), while unanswered calls were more common (4304/31,643, 13.2%). Phone numbers were quite often out of service or claimed to be wrong numbers (3002/31,643, 9.2%; Table S1 in Multimedia Appendix 1). Nonresponding households had lower levels of maximum education and fewer employed members, but responding and nonresponding households did not differ greatly based on household wealth or grant receipt (based on 2019 data; Table S2 in Multimedia Appendix 1). In total, 23,095 household interviews were completed with 5120 unique households in 2020.



**Figure 1.** Epidemic curve and interview rounds across SAPRIN nodes in 2020. AHRI: Africa Health Research Institute; DIMAMO: Dikgale-Mamabolo-Mothiba; SAPRIN: South African Population Research Infrastructure Network.



## Descriptive Results

Descriptive statistics for all respondent households with valid telephone numbers and members who consented to and completed an interview are shown in Table 1. In one-sixth (894/3932, 21.7%) of the households, no one had completed secondary education, while 19.3% (797/3932) included a household member who had completed a postsecondary

qualification. Wealthier households were more likely to have a valid telephone number; at the AHRI and Agincourt nodes they were also more likely to participate in study surveys. Households were large (median of 5 resident and nonresident members, of whom 2 were aged <18 years). Households had a mean of 1.2 employed members. In total, 38.9% (1979/5083) of all households received 1 or more old-age pensions and 66.2% (3364/5083) received other government grants.

**Table 1.** Descriptive statistics for participating households at South African Population Research Infrastructure Network nodes from April to December 2020.

Characteristics	Total <sup>a</sup>	Node <sup>b</sup>			P value <sup>e</sup>
		AHRI <sup>c</sup>	Agincourt	DIMAMO <sup>d</sup>	
Number of households	5120	1608	1797	1715	N/A <sup>f</sup>
<b>Highest education attained, %<sup>g</sup></b>					<.001
Less than complete secondary education	21.7	23.4	22.5	16.3	
Complete secondary education	59	59.7	77.3	17.3	
Diploma/certificate/degree	19.3	16.9	0.2	66.4	
<b>Node-specific household wealth quintile, %<sup>h</sup></b>					<.001
Lowest	14	16.3	9.6	18.1	
Second lowest	18.2	19.8	16.5	18.4	
Middle	20.9	20.1	20.8	22.6	
Second highest	22.8	20.4	25.4	22.2	
Highest	24.1	23.5	27.7	18.6	
<b>Household size in 2020<sup>i</sup>, median (IQR)</b>					<.001
Number of children	2 (1-3)	2 (1-4)	2 (1-3)	1 (0-3)	<.001
Number of working age adults	3 (2-4)	2 (1-4)	3 (2-5)	3 (2-4)	<.001
Number of people aged over 60	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)	.79
Number of full-time or part-time employed people, median (IQR) <sup>j</sup>	1 (0-2)	1 (0-2)	1 (0-2)	0 (0-1)	<.001
Number of pension grant receivers, median (IQR) <sup>j</sup>	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)	.06
Number of nonpension grant receivers, median (IQR) <sup>j</sup>	1 (0-3)	1 (0-3)	2 (0-3)	1 (0-2)	<.001

<sup>a</sup>Percentages refer to all participating households.

<sup>b</sup>Percentages refer to all households with nonmissing values.

<sup>c</sup>AHRI: Africa Health Research Institute.

<sup>d</sup>DIMAMO: Dikgale-Mamabolo-Mothiba

<sup>e</sup>P values were based on the differences in characteristics between groups and were calculated from Chi-square tests for categorical variables and Wilcoxon rank-sum tests (participation comparison) or Kruskal-Wallis tests (node comparisons) for continuous variables.

<sup>f</sup>N/A: not applicable.

<sup>g</sup>Data are missing from 1.4% (22/1608) of households surveyed by AHRI, 4.8% (86/1797) of households surveyed by Agincourt, and 48.3% (828/1715) of households surveyed by DIMAMO.

<sup>h</sup>Data are missing from 0.5% (8/1608) of households surveyed by AHRI, 6.6% (118/1797) households surveyed by Agincourt, and 47.7% (818/1715) of households surveyed by DIMAMO.

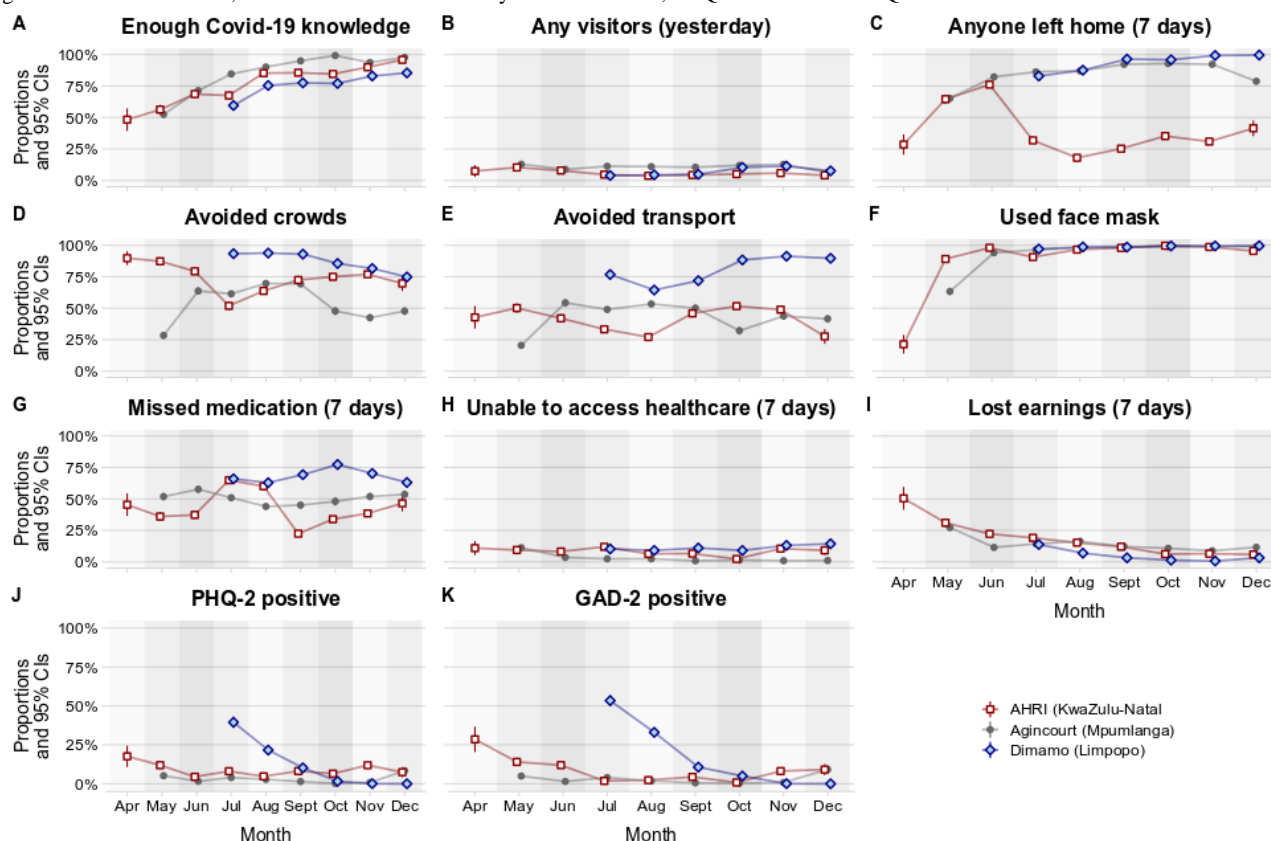
<sup>i</sup>Household sizes in 2020 were only determined for participating households.

<sup>j</sup>Data are missing from 23 households surveyed by AHRI, 10 households surveyed by Agincourt, and 4 households surveyed by DIMAMO.

Figure 2 describes the questionnaire responses across time and location. Respondents' self-reported satisfaction with their knowledge about COVID-19 rose over time at all three nodes from 53.7% (972/1811) in April and May 2020 to 92.1% (1997/2169) in December 2020. The number of daily visitors to households was consistently low; the proportion of households that had 1 or more visitors on the day before the survey peaked in May (202/1693, 11.9%). The proportion of households with members who left home increased over time,

ranging from 28.2% (33/117) in April to a peak of 79.5% (1459/1836) in June. There was however a notable drop in this proportion at AHRI in KwaZulu-Natal (June: 641/842, 76.1%; August: 192/1064, 18%) that occurred concurrently with reports of local COVID-19 transmission. The proportion somewhat increased again by October (400/1133, 35.3%). Face mask use rose rapidly and became almost universal at all three nodes by June.

**Figure 2.** Knowledge about, behavior relating to, and impact of COVID-19 and related regulations at South African Population Research Infrastructure Network nodes from April to December 2020. Graphs A, D, E, F, J, and K reflect individual-level responses of the primary household respondents. Graphs B, C, G, H, and I reflect household-level responses reported by the primary household respondents. Values are proportions of household primary respondents and 95% CIs. Precise values are provided in Table S3 in [Multimedia Appendix 1](#). AHRI: Africa Health Research Institute; DIMAMO: Dikgale-Mamabolo-Mothiba; GAD-2: Generalized Anxiety Disorder 2-item; PHQ-2: Patient Health Questionnaire 2-item.



Respondents' reported inability to access health care remained low and relatively stable over time. However, households reported that members missed daily medications in the past week at 52.9% (12,155/22,974) of interviews. Although rates of missed daily medications were stable over time at Agincourt and DIMAMO, they almost doubled at AHRI from 37.4% (315/843) in June to 64.9% (634/979) in July, as the epidemic arrived in the local area. The proportion of households that reported that members lost earnings due to COVID-19 regulations dropped substantially as the lockdown was reduced from Level 5 to Level 4. This proportion dropped again when the lockdown was lowered to Level 3 and remained steadily low thereafter. Finally, the proportion of individuals who screened positive for possible anxiety and depression fell over

time at AHRI and DIMAMO and stayed low at Agincourt throughout the period studied.

### Multivariable Results

After accounting for study node and month of interview, and despite variation in household composition, no household characteristics were substantively associated with (1) respondents self-reporting satisfaction with their COVID-19-related knowledge; (2) residents leaving their homes in the week before the interview; or (3) residents avoiding travel or face mask use (Tables 2 and 3). Households with individuals who had attained more education were more likely to report that they had had visitors on the day before the interview and less likely to report that they had avoided crowded spaces. These associations may reflect that more educated individuals are likelier to live in more urban locations.

**Table 2.** COVID-19–related knowledge and home behaviors in South Africa from April to August 2020<sup>a</sup>.

Variable	Individual has enough knowledge (n=17,292), prevalence ratio (95% CI)	Household had any visitors (n=17,282), prevalence ratio (95% CI)	Any member left home (n=17,164), prevalence ratio (95% CI)
<b>Node</b>			
AHRI <sup>b</sup> (KwaZulu-Natal)	1.00 (N/A <sup>c</sup> )	1.00 (N/A)	1.00 (N/A)
Agincourt (Mpumalanga)	1.09 (1.07-1.11)	2.07 (1.76-2.43)	2.26 (2.18-2.35)
DIMAMO <sup>d</sup> (Limpopo)	0.91 (0.88-0.95)	1.42 (1.07-1.88)	2.58 (2.46-2.72)
<b>Month of interview</b>			
April	0.93 (0.77-1.13)	1.08 (0.57-2.04)	0.76 (0.57-1.02)
May	1.00 (N/A)	1.00 (N/A)	1.00 (N/A)
June	1.32 (1.25-1.39)	0.72 (0.59-0.88)	1.29 (1.24-1.35)
July	1.45 (1.38-1.52)	0.71 (0.60-0.84)	0.98 (0.94-1.03)
August	1.64 (1.56-1.71)	0.64 (0.53-0.77)	0.91 (0.87-0.96)
September	1.69 (1.62-1.77)	0.69 (0.57-0.83)	1.00 (0.95-1.04)
October	1.71 (1.63-1.79)	0.79 (0.65-0.96)	1.05 (1.00-1.10)
November	1.72 (1.64-1.80)	0.87 (0.72-1.05)	1.03 (0.98-1.08)
December	1.80 (1.71-1.88)	0.48 (0.37-0.62)	0.98 (0.93-1.03)
<b>Household members (per person)</b>			
Children	1.00 (1.00-1.01)	0.96 (0.91-1.01)	1.02 (1.02-1.03)
Working-aged adults	1.00 (1.00-1.00)	0.99 (0.96-1.03)	1.02 (1.01-1.02)
Pension-aged adults	0.98 (0.96-1.00)	1.09 (0.95-1.26)	1.01 (0.98-1.04)
<b>Maximum education of household members</b>			
Less than complete secondary education	1.00 (N/A)	1.00 (N/A)	1.00 (N/A)
Complete secondary education	1.02 (1.00-1.04)	0.92 (0.78-1.08)	1.00 (0.97-1.03)
Diploma/certificate/degree	1.02 (0.98-1.06)	1.06 (0.80-1.39)	1.01 (0.96-1.07)
<b>Household income sources in 2019</b>			
Full-time and part-time employees	1.01 (1.00-1.01)	1.06 (1.01-1.11)	1.01 (1.00-1.02)
Pension grants	0.99 (0.97-1.01)	0.96 (0.83 - 1.11)	0.97 (0.94 - 1.00)
Nonpension grants	1.00 (1.00-1.01)	0.99 (0.94-1.04)	0.99 (0.99-1.00)
Household asset index quintiles	1.00 (0.99-1.01)	0.99 (0.94-1.03)	1.00 (1.00-1.01)

<sup>a</sup>Each column (knowledge, the number of visitors, and members leaving home) is a single Poisson regression with household-level random effects and robust SEs for calculating prevalence ratios and 95% CIs. In total, 17,384 observations have complete covariate data and 5704 observations from 1475 households have missing covariate values; 33 households surveyed by AHRI, 103 surveyed by Agincourt, and 1339 surveyed by DIMAMO are missing data. The remaining missing observations reflect missing outcome values.

<sup>b</sup>AHRI: Africa Health Research Institute.

<sup>c</sup>N/A: not applicable.

<sup>d</sup>DIMAMO: Dikgale-Mamabolo-Mothiba

**Table 3.** Beyond-home behavior regarding COVID-19 at South African Population Research Infrastructure Network nodes from April to August 2020<sup>a</sup>.

Variable	Individual avoided crowds (n=17,043), prevalence ratio (95% CI)	Individual avoided transport (n=17,043), prevalence ratio (95% CI)	Individual used face mask (n=17,043), prevalence ratio (95% CI)
<b>Node</b>			
AHRI <sup>b</sup> (KwaZulu-Natal)	1.00 (N/A <sup>c</sup> )	1.00 (N/A)	1.00 (N/A)
Agincourt (Mpumalanga)	0.77 (0.75-0.79)	1.05 (1.01-1.10)	0.98 (0.97-0.99)
DIMAMO <sup>d</sup> (Limpopo)	1.24 (1.19-1.29)	1.87 (1.76-1.98)	1.00 (0.98-1.01)
<b>Month of interview</b>			
April	1.51(1.39-1.63)	1.40 (1.12-1.75)	0.28 (0.20-0.40)
May	1.00 (N/A)	1.00 (N/A)	1.00 (N/A)
June	1.36 (1.29-1.43)	1.54 (1.41-1.68)	1.30 (1.26-1.34)
July	1.15 (1.09-1.22)	1.37 (1.26-1.49)	1.28 (1.24-1.32)
August	1.30 (1.23-1.38)	1.31 (1.20-1.43)	1.32 (1.28-1.36)
September	1.35 (1.28-1.42)	1.48 (1.36-1.60)	1.33 (1.30-1.37)
October	1.18 (1.12-1.25)	1.40 (1.29-1.52)	1.34 (1.31-1.38)
November	1.13 (1.07-1.19)	1.48 (1.36-1.61)	1.34 (1.30-1.38)
December	1.08 (1.01-1.15)	1.30 (1.19-1.43)	1.34 (1.30-1.39)
<b>Household members (per person)</b>			
Children	1.00 (1.00-1.01)	1.01 (1.00-1.02)	1.00 (1.00-1.00)
Working-aged adults	1.02 (1.01-1.02)	1.02 (1.01-1.03)	1.00 (1.00-1.00)
Pension-aged adults	1.02 (1.00-1.05)	1.00 (0.96-1.04)	1.00 (0.99-1.01)
<b>Maximum education of household members</b>			
Less than complete secondary education	1.00 (N/A)	1.00 (N/A)	1.00 (N/A)
Complete secondary education	1.00 (0.97-1.03)	1.02 (0.98-1.07)	1.00 (0.99-1.01)
Diploma/certificate/degree	0.96 (0.92-1.00)	1.00 (0.94-1.07)	1.00 (0.98-1.01)
<b>Household income sources in 2019</b>			
Full-time and part-time employees	0.99 (0.98-1.00)	0.99 (0.98-1.00)	1.00 (1.00-1.00)
Pension grants	1.00 (0.97-1.02)	1.00 (0.97-1.05)	1.00 (0.99-1.01)
Nonpension grants	1.00 (0.99-1.00)	0.99 (0.98-1.00)	1.00 (1.00-1.00)
Household asset index quintiles	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (1.00-1.00)

<sup>a</sup>Each column (knowledge, the number of visitors, and members leaving home) is a single Poisson regression with household-level random effects and robust SEs for calculating prevalence ratios and 95% CIs. In total, 17,384 observations have complete covariate data and 5704 observations from 1475 households have missing covariate values; 33 households surveyed by AHRI, 103 surveyed by Agincourt, and 1339 surveyed by DIMAMO are missing data. The remaining missing observations reflect missing outcome values.

<sup>b</sup>AHRI: Africa Health Research Institute.

<sup>c</sup>N/A: not applicable.

<sup>d</sup>DIMAMO: Dikgale-Mamabolo-Mothiba

Households with a higher number of older individuals and pension recipients were more likely to have a recent unmet health need (nonsignificantly for older members;  $P=.55$ ) but were less likely to have been unable to access medicine (Table 4). These same two factors predicted a lower prevalence of lost earnings, as did having a household member who had completed secondary education; having a household member who had completed postsecondary education was not predictive of lost

earnings. Finally, the prevalence of depression and anxiety symptoms was higher in households with a member that had a postsecondary qualification, and the prevalence of depression symptoms was nonsignificantly ( $P=.18$ ) greater in households that received pension grants compared to those that did not receive pension grants (either due to households having no eligible members or not having applied for such grants; Table 5).

**Table 4.** Health care and economic behaviors at South African Population Research Infrastructure Network nodes from April to August 2020<sup>a</sup>.

Variable	Any member missed daily medication (n=17,277), prevalence ratio (95% CI)	Any member unable to access health care (n=17,272), prevalence ratio (95% CI)	Any member lost earnings (n=17,256), prevalence ratio (95% CI)
<b>Node</b>			
AHRI <sup>b</sup> (KwaZulu-Natal)	1.00 (N/A <sup>c</sup> )	1.00 (N/A)	1.00 (N/A)
Agincourt (Mpumalanga)	1.20 (1.14-1.27)	0.34 (0.29-0.40)	0.90 (0.80-1.01)
DIMAMO <sup>d</sup> (Limpopo)	1.60 (1.48-1.74)	1.66 (1.31-2.09)	0.27 (0.19-0.38)
<b>Month of interview</b>			
April	1.08 (0.88-1.33)	0.64 (0.38-1.09)	1.56 (1.29-1.89)
May	1.00 (N/A)	1.00 (N/A)	1.00 (N/A)
June	1.06 (0.99-1.13)	0.51 (0.41-0.64)	0.58 (0.52-0.66)
July	1.22 (1.15-1.28)	0.52 (0.42-0.64)	0.57 (0.52-0.64)
August	1.10 (1.04-1.17)	0.35 (0.28-0.44)	0.57 (0.51-0.64)
September	0.81 (0.76-0.87)	0.33 (0.26-0.42)	0.42 (0.37-0.48)
October	0.93 (0.87-1.00)	0.17 (0.13-0.23)	0.27 (0.23-0.33)
November	0.98 (0.92-1.05)	0.48 (0.39-0.59)	0.27 (0.22-0.32)
December	1.02 (0.94-1.10)	0.48 (0.37-0.63)	0.37 (0.31-0.45)
<b>Household members (per person)</b>			
Children	0.99 (0.98-1.01)	1.00 (0.96-1.04)	1.01 (0.97-1.04)
Working-aged adults	0.98 (0.96-0.99)	1.03 (0.99-1.07)	1.07 (1.04-1.10)
Pension-aged adults	0.81 (0.76-0.86)	1.04 (0.91-1.20)	0.82 (0.72-0.92)
<b>Maximum education of household members</b>			
Less than complete secondary education	1.00 (N/A)	1.00 (N/A)	1.00 (N/A)
Complete secondary education	1.07 (1.00-1.14)	0.98 (0.82-1.16)	1.15 (1.00-1.32)
Diploma/certificate/degree	1.08 (0.99-1.18)	1.02 (0.82-1.28)	1.03 (0.83 - 1.28)
<b>Household income sources in 2019</b>			
Full-time and part-time employees	1.02 (1.00-1.04)	1.01 (0.96-1.05)	1.04 (1.00-1.08)
Pension grants	0.92 (0.86-0.98)	1.21 (1.05-1.40)	0.92 (0.81-1.05)
Nonpension grants	1.01 (0.99-1.02)	0.98 (0.94-1.02)	1.04 (1.00-1.07)
Household asset index quintiles	1.01 (0.99-1.03)	1.00 (0.95-1.05)	0.99 (0.95-1.03)

<sup>a</sup>Each column (knowledge, the number of visitors, and members leaving home) is a single Poisson regression with household-level random effects and robust SEs for calculating prevalence ratios and 95% CIs. In total, 17,384 observations have complete covariate data and 5704 observations from 1475 households have missing covariate values; 33 households surveyed by AHRI, 103 surveyed by Agincourt, and 1339 surveyed by DIMAMO are missing data. The remaining missing observations reflect missing outcome values.

<sup>b</sup>AHRI: Africa Health Research Institute.

<sup>c</sup>N/A: not applicable.

<sup>d</sup>DIMAMO: Dikgale-Mamabolo-Mothiba

**Table 5.** Mental health impacts of COVID-19 and household characteristics at South African Population Research Infrastructure Network nodes from April to August 2020<sup>a</sup>.

Variable	Individual PHQ-2 <sup>b</sup> screened positive (n=17,257), prevalence ratio (95% CI)	Individual GAD-2 <sup>c</sup> screened positive (n=17,256), prevalence ratio (95% CI)
<b>Node</b>		
AHRI <sup>d</sup> (KwaZulu-Natal)	1.00 (N/A <sup>e</sup> )	1.00 (N/A)
Agincourt (Mpumalanga)	0.35 (0.30-0.41)	0.46 (0.39-0.54)
DIMAMO <sup>f</sup> (Limpopo)	1.16 (0.93-1.44)	2.83 (2.23-3.60)
<b>Month of interview</b>		
April	1.34 (0.87-2.05)	2.15 (1.55-2.99)
May	1.00 (N/A)	1.00 (N/A)
June	0.37 (0.27-0.50)	0.72 (0.57-0.91)
July	0.93 (0.76-1.14)	0.61 (0.50-0.75)
August	0.59 (0.47-0.74)	0.41 (0.33-0.51)
September	0.56 (0.44-0.71)	0.25 (0.19-0.33)
October	0.34 (0.26-0.46)	0.06 (0.04-0.10)
November	0.60 (0.47-0.77)	0.32 (0.25-0.43)
December	0.88 (0.67-1.16)	0.63 (0.47-0.84)
<b>Household members (per person)</b>		
Children	1.01 (0.97-1.05)	1.03 (0.98-1.07)
Working-aged adults	1.03 (0.99-1.07)	1.01 (0.97-1.05)
Pension-aged adults	0.88 (0.76-1.02)	0.91 (0.78-1.07)
<b>Maximum education of household members</b>		
Less than complete secondary	1.00 (N/A)	1.00 (N/A)
Complete secondary	1.07 (0.91-1.27)	0.89 (0.75-1.07)
Diploma/certificate/degree	1.33 (1.08-1.65)	1.16 (0.92-1.46)
<b>Household income sources in 2019</b>		
Full/part-time employees	0.97 (0.92-1.02)	0.98 (0.93-1.03)
Pension grants	1.11 (0.95-1.29)	0.99 (0.84-1.16)
Non-pension grants	0.98 (0.94-1.02)	0.99 (0.95-1.03)
<b>Household asset index quintiles</b>	1.01 (0.96-1.06)	1.06 (1.00-1.11)

<sup>a</sup>Each column (knowledge, the number of visitors, and members leaving home) is on a single Poisson regression with household-level random effects and robust SEs for calculating prevalence ratios and 95% CIs. In total, 17,384 observations have complete covariate data and 5704 observations from 1475 households have missing covariate values; 33 households surveyed by AHRI, 103 surveyed by Agincourt, and 1339 households surveyed by DIMAMO are missing data. The remaining missing observations reflect missing outcome values.

<sup>b</sup>PHQ-2: Patient Health Questionnaire 2-item.

<sup>c</sup>GAD-2: Generalized Anxiety Disorder 2-item.

<sup>d</sup>AHRI: Africa Health Research Institute.

<sup>e</sup>N/A: not applicable.

<sup>f</sup>DIMAMO: Dikgale-Mamabolo-Mothiba

## Discussion

### Principal Findings

By conducting rapid, repeated telephonic interviews at sites in three provinces in South Africa, we observed how households in rural and periurban areas responded to and were affected by national NPIs that were enacted to minimize the epidemic spread

of COVID-19. As both NPIs and the epidemic spread across the country, our longitudinal surveillance program captured the impact of both processes.

Our first key finding was that the South African national public health measures and messages implemented were effective in several ways. Respondents across three provinces showed consistent improvements over time in satisfaction with their

understanding of the epidemic. There was early concern that South Africa's public health messages were insufficiently contextualized to the country's varying social and economic conditions. Both politicians and scientists conducted televised national press conferences that were supported by provincial and local follow-up events. Although causality cannot be proven between these events and changes in behavior, in line with other evidence from South Africa and other countries [21,31], our respondents reported that they rapidly and comprehensively complied with public health messages, including those about face mask use, and actively avoided crowds and public transport. Several of these protective behaviors remained prevalent even as formal, lockdown-related NPIs were relaxed and even after the first national epidemic wave had passed. This continued adherence to policies, which persisted even after they were no longer formally required, highlights the importance of considering how infection-related fears and prosocial desires to protect others can drive epidemic dynamics [41-43]; formal lockdowns may be less vital than carefully crafted public health communication.

Second, we identified substantial behavior changes as the COVID-19 epidemic arrived in the local study areas. This was particularly noticeable at the KwaZulu-Natal node, where rapid epidemic growth in the local district during early July coincided with a rapid decline in the proportion of household members leaving home and concomitant increases in levels of missed daily medications and the inability to access needed health care. There were also smaller behavior changes that occurred after mid-December at the Mpumalanga and Limpopo nodes (the KwaZulu-Natal node stopped data collection early in the month) as the second epidemic wave spread across the country.

These behavioral responses reflected local epidemic dynamics. The first national epidemic started in the Western Cape and spread first to the adjacent Eastern Cape before spreading to the densely populated Gauteng province and urban eThekweni in KwaZulu-Natal and then finally reaching the rural eastern and northern areas of South Africa, which were analyzed in this study. The second wave began in the Eastern Cape during November before spreading nationwide. The patterns of rapid behavior change in the face of a rising epidemic wave seen in this study were congruent with those seen worldwide. However, there are limited data on behavior in low- and middle-income countries either after first waves have receded or during subsequent waves. The impact of regulations and epidemic trajectories on travel is particularly pertinent in our study settings, as medium- and long-distance circular labor migration to urban areas is highly prevalent and vital to the economic well-being of rural and periurban South African households [44]. Bans on long-distance travel have potentially substantial economic implications for people who are not able to return to work, although such travel bans might also partially explain the limited epidemics that were seen in these rural areas even as NPIs were relaxed.

Third, our mental health findings are reassuring. At all three nodes, we observed declines over time in the prevalence of depression and anxiety symptoms (based on validated screening scales). The prevalence of such symptoms was notably higher at the DIMAMO periurban node in Limpopo earlier in the year.

This higher prevalence perhaps reflected concerns of being at greater risk of SARS-CoV-2 infection due to respondents' proximity to the nearby city of Polokwane. However, it was encouraging that even when the COVID-19 epidemic arrived at AHRI in KwaZulu-Natal during July 2020, depression and anxiety prevalence did not increase, though the uptick in these rates that occurred late in the year as the second wave arrived at Agincourt in Mpumalanga may be concerning. Mental health concerns were much more prevalent at some sites than at others, particularly earlier in the year, but it is also notable that households with postsecondary-educated members were significantly more likely to report depression (prevalence ratio: 1.33; 95% CI 1.08-1.65;  $P=.008$ ) and nonsignificantly more likely to report anxiety (prevalence ratio: 1.16; 95% CI 0.92-1.46;  $P=.21$ ). Comparisons are complex, but our findings align with national South African data, which suggest that COVID-19-related mental health impacts were more limited in low-income and rural areas [31]. Longitudinal surveillance across a range of settings via harmonized measures will help determine the extent to which mental health is directly affected by COVID-19-related fears and indirectly affected by secondary social and economic effects.

Fourth, our analysis raises concern about unmet needs for health care. Households reported that members had recently missed daily medication doses at almost half of all interviews (10,819/22,974, 47.1%) and that a member had wanted but was unable to access health care in the 7 days before the interview 6.7% (1538/22,967) of the time. These levels are similar to those of other South African surveys [25]. Notably, the epidemic's arrival at AHRI had diverging effects; unmet health care needs did not change much, but missed medication rates almost doubled. These patterns suggest that household members may be calculating the trade-offs between COVID-19 and non-COVID-19 risks and are potentially willing to risk physical proximity to others to attend clinics [45] but not to collect medicine [46]. However, unmet health care and medication needs at the other study sites were stable throughout the observation period. Additional information is needed to determine (1) whether unmet health care needs are indicative of operational, mobility, transport cost, and transport availability issues or other issues; and (2) the extent to which such needs were the result of or were exacerbated by the COVID-19 epidemic or related regulations. Data that cover the pre-epidemic and postepidemic periods would help identify these effects, as would qualitative investigations of household decision making during lockdowns.

Finally, we found that households with higher numbers of older members and pension recipients reported more unmet health care needs but fewer instances of missed daily medication or lost earnings. South African noncontributory pensions—broad national government support schemes that are often the largest household income source in these relatively rural settings with very high unemployment rates—have previously been linked to positive physical and mental health outcomes [47,48]. Our study suggests that such government support structures likely play an essential role in maintaining household security in crisis contexts such as the COVID-19 epidemic by providing a guaranteed income to vulnerable populations. The government's



temporary supplementation of grant programs through top-up payments and novel noncontributory unemployment support early in the epidemic may have also helped [13]. However, it will be important to observe if the ending of income supplementation (grant top-ups ended in October 2020; unemployment payments have continued in 2021) reverses these supplements' beneficial effects. The lack of substantive associations between household characteristics and social distancing measures is also noteworthy. In some instances, such as mask use, this likely reflects an overwhelming uptake of protective behaviors, which made statistically significant associations impossible. In other instances, our results suggest either that behavior was primarily driven by the epidemic cycle—as measured by interview month—or that key drivers of household behavior were not included in our analysis. Further investigations of this and other data sources may help determine which (if any) characteristics predict changes in protective behaviors during the COVID-19 epidemic.

This study presents an overview of key insights across time from multiple sites across South Africa. However, there are several additional analyses that could further contextualize our findings. First, data can be longitudinally analyzed at the household or individual level to evaluate trajectories of behavior and impact as the COVID-19 epidemic continues to affect rural and periurban environments. For example, it will be important to evaluate the impact of new government policies, such as the ending of temporary increases in noncontributory grants. Second, these behavior-related data can be linked to COVID-19 symptoms and individual and population health outcomes to evaluate how risk perceptions and reactions are associated with health outcomes. Third, a more in-depth analysis of how household members' historical and current age, gender, employment status, and migration composition, as well as preexisting comorbidities, affect the impacts of COVID-19 and NPIs will help identify those who are most in need of support during such crises. The ongoing SAPRIN COVID-19 surveillance program will enable the longitudinal measurement of these factors throughout the epidemic's course.

### Strengths and Limitations

This study has limitations. As with all observational studies, the generalizability of our results to those outside our study population—in this case, households in rural and periurban areas of eastern South Africa—is uncertain. This concern was tempered by our ability to compare and combine data across multiple sites and compare our results to those of other studies on the COVID-19 epidemic's impact in South Africa and Sub-Saharan African. Additionally, while household cellphone ownership was high, there was evidence that lower-wealth households in these areas were somewhat less likely to participate in the survey. Although nonrandom response may have affected prevalence measures, it should have very limited scope to affect the trend measures we focused on. Further, our data were self-reported and thus represented perceived needs and impacts, and changes in reported behavior may have reflected desirability biases. However, even with such biases, our findings provide insight into the perceptions and lived experiences of these communities. Comparing our findings to digital data sources can help alleviate such biases. Finally, we

did not have data on identical questions from the pre-epidemic period; however, we were able to include similar information on many topics from earlier surveillance studies.

This study also has several strengths, including a clearly defined sampling base, high response rates, low attrition rates, frequent follow-up, and linkages to pre-epidemic household data. Although we were not able to interview the same people in every survey wave, our longitudinal household cohort design, which allowed for repeated interviews with the same households over multiple months, reduced the risk of confounding by time-invariant household factors that could have arisen if we had used multiple cross-sectional surveys. Many of these benefits arise from the nature of the existing SAPRIN surveillance infrastructure, which reinforces the importance of long-term, population-based surveillance systems that collect social, demographic, and health data. This study demonstrates that surveillance systems can be rapidly repurposed to respond to emergency health needs, including (1) rapid pathogen data acquisition; (2) the identification of susceptible populations; (3) the assessment of behavioral and biomedical interventions; and (4) the development of mitigation strategies [49].

SAPRIN nodes have been working with their local communities for 20-28 years. Such long-term engagement promotes deep understanding and community buy-in, which in turn enables rapid implementation and sustained, high-intensity follow-ups with minimal dropout. The network nature of SAPRIN also allowed each node to flexibly implement an overarching protocol. Furthermore, the use of telephonic call centers at each node allowed for rapid survey rollout that was based on previously provided informed consent for personal calls and substantially reduced the risk of SARS-CoV-2 infection among study staff and research participants. Since these call centers employed locally recruited staff, we were able to reach population segments that web-based surveys (in a country with rural areas that have limited access to internet) and even random-digit dialing approaches (in a country with 11 official spoken languages and numerous dialects) struggle to capture. Additionally, we could link self-response survey data to other data sources within the SAPRIN databases. These include the previously collected sociodemographic data used in this study and biological samples that were collected as part of the COVID-19 surveillance project. SAPRIN data can also be linked to data on public sector health care use and laboratory test results through memoranda of understanding with government departments. SAPRIN's ongoing expansion will also allow comparisons with well-characterized urban sites to be made in the future.

### Conclusion

South Africans in three rural and periurban areas were largely willing and able to comply with national government regulations and recommendations regarding social interaction and other risk behaviors related to COVID-19, despite limited resources and the substantial economic need to travel. This rapid uptake of preventative behaviors reflects the clarity of government messages and the population's willingness to comply with such measures, even in settings where enforcement measures were limited. Even as official NPIs were relaxed, the arrival of the

epidemic in local areas led to further self-imposed behavioral restrictions, several of which led to difficulties in accessing health care. However, the economic and mental health effects of NPIs continued to decline as the measures were eased. Our findings highlight the importance of monitoring the possibly deleterious secondary impacts of NPIs in epidemic situations. Our results reinforce the principle that NPIs should be adjusted

based on epidemic cycles and show that mitigation measures will be required to combat anticipated and unanticipated secondary impacts. All of these factors should be considered when setting, adjusting, and relaxing NPIs in low-income settings, especially as urgently established national policies give way to differentiated, decentralized approaches across diverse subnational environments.

## Acknowledgments

We gratefully acknowledge the enormous efforts of all the call center agents at the three study sites who worked intensively throughout the COVID-19 epidemic and the participants who responded multiple times despite the difficult social and economic conditions. Core surveillance activities, including the telephonic surveillance of COVID-19 at all three nodes, are wholly or in part funded by the South African Department of Science and Innovation through the SAPRIN, which is hosted by the South African Medical Research Council. The MRC/Wits Rural Public Health and Health Transitions Research Unit, which hosts the Agincourt Health and Socio-Demographic Surveillance System, is also supported by the University of the Witwatersrand and Medical Research Council of South Africa. DIMAMO Population Health Research Centre receives funding from the National Institutes of Health and is supported by the Human Heredity and Health in Africa Consortium. The African Health Research Institute receives funding from the Wellcome Trust (grant number: 201433/Z/16/Z) for the aspects of its health and demographic surveillance. GH is supported by a fellowship from the Royal Society and the Wellcome Trust (grant number: 210479/Z/18/Z). EBW is supported by the National Institutes of Health (grant numbers: NIAID K08AI118538 and FIC R21TW011687). This research was funded in whole, or in part, by the Wellcome Trust (grant numbers: 201433/Z/16/Z and 210479/Z/18/Z). For the purpose of open access, the author has applied a CC-BY public copyright license to any Author Accepted Manuscript version arising from this submission.

## Conflicts of Interest

None declared.

Multimedia Appendix 1

Supplementary materials.

[[DOCX File , 235 KB - publichealth\\_v7i5e26073\\_app1.docx](#) ]

## References

1. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis* 2020 May;20(5):533-534 [FREE Full text] [doi: [10.1016/S1473-3099\(20\)30120-1](https://doi.org/10.1016/S1473-3099(20)30120-1)] [Medline: [32087114](https://pubmed.ncbi.nlm.nih.gov/32087114/)]
2. Jackson JK, Weiss MA, Schwarzenberg AB, Nelson RM, Sutter KM, Sutherland MD. Global economic effects of COVID-19. Congressional Research Service. URL: <https://fas.org/sgp/crs/row/R46270.pdf> [accessed 2021-04-16]
3. Xiong J, Lipsitz O, Nasri F, Lui LMW, Gill H, Phan L, et al. Impact of COVID-19 pandemic on mental health in the general population: A systematic review. *J Affect Disord* 2020 Dec 01;277:55-64 [FREE Full text] [doi: [10.1016/j.jad.2020.08.001](https://doi.org/10.1016/j.jad.2020.08.001)] [Medline: [32799105](https://pubmed.ncbi.nlm.nih.gov/32799105/)]
4. Hogan AB, Jewell BL, Sherrard-Smith E, Vesga JF, Watson OJ, Whittaker C, et al. Potential impact of the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income countries: a modelling study. *Lancet Glob Health* 2020 Sep;8(9):e1132-e1141 [FREE Full text] [doi: [10.1016/S2214-109X\(20\)30288-6](https://doi.org/10.1016/S2214-109X(20)30288-6)] [Medline: [32673577](https://pubmed.ncbi.nlm.nih.gov/32673577/)]
5. Gilbert M, Pullano G, Pinotti F, Valdano E, Poletto C, Boëlle PY, et al. Preparedness and vulnerability of African countries against importations of COVID-19: a modelling study. *Lancet* 2020 Mar 14;395(10227):871-877 [FREE Full text] [doi: [10.1016/S0140-6736\(20\)30411-6](https://doi.org/10.1016/S0140-6736(20)30411-6)] [Medline: [32087820](https://pubmed.ncbi.nlm.nih.gov/32087820/)]
6. Nojilana B, Bradshaw D, Pillay-van Wyk V, Msemburi W, Laubscher R, Somdya NIM, et al. Emerging trends in non-communicable disease mortality in South Africa, 1997 - 2010. *S Afr Med J* 2016 Apr 01;106(5):58. [doi: [10.7196/SAMJ.2016.v106i5.10674](https://doi.org/10.7196/SAMJ.2016.v106i5.10674)] [Medline: [27138667](https://pubmed.ncbi.nlm.nih.gov/27138667/)]
7. Oni T, Berkowitz N, Kubjane M, Goliath R, Levitt NS, Wilkinson RJ. Trilateral overlap of tuberculosis, diabetes and HIV-1 in a high-burden African setting: implications for TB control. *Eur Respir J* 2017 Jul 20;50(1):1700004 [FREE Full text] [doi: [10.1183/13993003.00004-2017](https://doi.org/10.1183/13993003.00004-2017)] [Medline: [28729474](https://pubmed.ncbi.nlm.nih.gov/28729474/)]
8. Sekyere E, Bohler-Muller N, Hongoro C, Makoe M. The impact of COVID-19 in South Africa. Wilson Center. 2020 Apr. URL: [https://www.wilsoncenter.org/sites/default/files/media/uploads/documents/The%20Impact%20of%20COVID-19%20in%20South%20Africa\\_0.pdf](https://www.wilsoncenter.org/sites/default/files/media/uploads/documents/The%20Impact%20of%20COVID-19%20in%20South%20Africa_0.pdf) [accessed 2021-04-16]
9. Abdool Karim SS. The South African Response to the Pandemic. *N Engl J Med* 2020 Jun 11;382(24):e95 [FREE Full text] [doi: [10.1056/NEJMc2014960](https://doi.org/10.1056/NEJMc2014960)] [Medline: [32469479](https://pubmed.ncbi.nlm.nih.gov/32469479/)]

10. National COVID-19 daily report, 1 September 2020. National Institute for Communicable Diseases. URL: [https://www.nicd.ac.za/wp-content/uploads/2020/09/COVID-19-National-Daily-Report\\_Public\\_01092020.pdf](https://www.nicd.ac.za/wp-content/uploads/2020/09/COVID-19-National-Daily-Report_Public_01092020.pdf) [accessed 2020-09-19]
11. Coronavirus disease (COVID-19) : weekly epidemiological update, 30 August 2020. World Health Organization. URL: [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200831-weekly-epi-update-3.pdf?sfvrsn=d7032a2a\\_4](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200831-weekly-epi-update-3.pdf?sfvrsn=d7032a2a_4) [accessed 2021-04-16]
12. Bradshaw D, Laubscher R, Dorrington RE, Groenewald P, Moultrie T. Report on weekly deaths in South Africa: 1 January - 1 September 2020 (Week 35). South African Medical Research Council. URL: <https://www.samrc.ac.za/sites/default/files/files/2020-09-09/weekly1September2020.pdf> [accessed 2021-04-16]
13. Seekings J, Nattrass N. Covid vs. democracy: South Africa's lockdown misfire. *Journal of Democracy* 2020;31(4):106-121. [doi: [10.1353/jod.2020.0059](https://doi.org/10.1353/jod.2020.0059)]
14. Lancaster L, Mulaudzi G. Rising protests are a warning sign for South Africa's government. 2020 Aug 06. URL: <https://issafrica.org/iss-today/rising-protests-are-a-warning-sign-for-south-africas-government> [accessed 2021-04-16]
15. Staunton C, Swanepoel C, Labuschaigne M. Between a rock and a hard place: COVID-19 and South Africa's response. *J Law Biosci* 2020 Jul 07;7(1):lsaa052 [FREE Full text] [doi: [10.1093/jlb/lsaa052](https://doi.org/10.1093/jlb/lsaa052)] [Medline: [32908671](https://pubmed.ncbi.nlm.nih.gov/32908671/)]
16. Nyasulu J, Pandya H. The effects of coronavirus disease 2019 pandemic on the South African health system: A call to maintain essential health services. *Afr J Prim Health Care Fam Med* 2020 Jul 22;12(1):e1-e5 [FREE Full text] [doi: [10.4102/phcfm.v12i1.2480](https://doi.org/10.4102/phcfm.v12i1.2480)] [Medline: [32787396](https://pubmed.ncbi.nlm.nih.gov/32787396/)]
17. Nkengasong JN, Mankoula W. Looming threat of COVID-19 infection in Africa: act collectively, and fast. *Lancet* 2020 Mar 14;395(10227):841-842 [FREE Full text] [doi: [10.1016/S0140-6736\(20\)30464-5](https://doi.org/10.1016/S0140-6736(20)30464-5)] [Medline: [32113508](https://pubmed.ncbi.nlm.nih.gov/32113508/)]
18. Quaife M, van Zandvoort K, Gimma A, Shah K, McCreesh N, Prem K, CMMID COVID-19 Working Group, et al. The impact of COVID-19 control measures on social contacts and transmission in Kenyan informal settlements. *BMC Med* 2020 Oct 05;18(1):316 [FREE Full text] [doi: [10.1186/s12916-020-01779-4](https://doi.org/10.1186/s12916-020-01779-4)] [Medline: [33012285](https://pubmed.ncbi.nlm.nih.gov/33012285/)]
19. Egger D, Miguel E, Warren SS, Shenoy A, Collins E, Karlan D, et al. Falling living standards during the COVID-19 crisis: Quantitative evidence from nine developing countries. *Sci Adv* 2021 Feb 05;7(6):eabe0997 [FREE Full text] [doi: [10.1126/sciadv.abe0997](https://doi.org/10.1126/sciadv.abe0997)] [Medline: [33547077](https://pubmed.ncbi.nlm.nih.gov/33547077/)]
20. Pinchoff J, Austrian K, Rajshekhar N, Abuya T, Kangwana B, Ochako R, et al. Gendered economic, social and health effects of the COVID-19 pandemic and mitigation policies in Kenya: evidence from a prospective cohort survey in Nairobi informal settlements. *BMJ Open* 2021 Mar 03;11(3):e042749 [FREE Full text] [doi: [10.1136/bmjopen-2020-042749](https://doi.org/10.1136/bmjopen-2020-042749)] [Medline: [33658260](https://pubmed.ncbi.nlm.nih.gov/33658260/)]
21. Banda J, Dube A, Brumfield S, Amoah A, Crampin A, Reniers G, et al. Knowledge, risk perceptions, and behaviors related to the COVID-19 pandemic in Malawi. *Demogr Res* 2021 Mar 10;44:459-480 [FREE Full text] [doi: [10.4054/demres.2021.44.20](https://doi.org/10.4054/demres.2021.44.20)]
22. Banda J, Dube AN, Brumfield S, Crampin AC, Reniers G, Amoah AS, et al. Controlling the first wave of the COVID-19 pandemic in Malawi: results from a panel study. medRxiv. Preprint posted online on February 23, 2021. [FREE Full text] [doi: [10.1101/2021.02.21.21251597](https://doi.org/10.1101/2021.02.21.21251597)]
23. Macupe B. The Covid-19 view from rural Eastern Cape: 'The virus is still far from us'. *Mail & Guardian*. 2020 Mar 27. URL: <https://mg.co.za/article/2020-03-27-the-covid-19-view-from-rural-eastern-cape-the-virus-is-still-far-from-us/> [accessed 2021-04-16]
24. Gibson L, Rush D. Novel coronavirus in Cape Town informal settlements: Feasibility of using informal dwelling outlines to identify high risk areas for COVID-19 transmission from a social distancing perspective. *JMIR Public Health Surveill* 2020 Apr 06;6(2):e18844 [FREE Full text] [doi: [10.2196/18844](https://doi.org/10.2196/18844)] [Medline: [32250283](https://pubmed.ncbi.nlm.nih.gov/32250283/)]
25. Spaul N, Ardington C, Bassier I, Bhorat H, Bridgman G, Brophy T, et al. Overview and findings: NIDS-CRAM synthesis report wave 1. National Income Dynamics Study – Coronavirus Rapid Mobile Survey. 2020 Jul 15. URL: <https://cramsurvey.org/wp-content/uploads/2020/07/Spaul-et-al.-NIDS-CRAM-Wave-1-Synthesis-Report-Overview-and-Findings-1.pdf> [accessed 2021-04-16]
26. Behavioural and health impacts of the COVID-19 pandemic in South Africa: Report-00-80-02. Statistics South Africa. URL: <http://www.statssa.gov.za/publications/Report-00-80-02/Report-00-80-022020.pdf> [accessed 2021-04-16]
27. Reddy SP, Sewpaul R, Mabaso M, Parker S, Naidoo I, Jooste S, et al. South Africans' understanding of and response to the COVID-19 outbreak: An online survey. *S Afr Med J* 2020 Aug 11;110(9):894-902 [FREE Full text] [Medline: [32880275](https://pubmed.ncbi.nlm.nih.gov/32880275/)]
28. Leibbrandt M, Woolard I, de Villiers VL. Methodology: Report on NIDS wave 1. National Income Dynamics Study. 2009 Jul. URL: <http://www.nids.uct.ac.za/publications/technical-papers/108-nids-technical-paper-no1/file> [accessed 2021-04-16]
29. Kerr A, Ardington C, Burger R. Sample design and weighting in the NIDS-CRAM survey. National Income Dynamics Study – Coronavirus Rapid Mobile Survey. 2020 Jul 15. URL: [https://cramsurvey.org/wp-content/uploads/2020/07/REPORT-B-CRAM-Sample-Design-and-Weighting-in-the-NIDS-CRAM-survey\\_v7.pdf](https://cramsurvey.org/wp-content/uploads/2020/07/REPORT-B-CRAM-Sample-Design-and-Weighting-in-the-NIDS-CRAM-survey_v7.pdf) [accessed 2021-04-16]
30. Spaul N, Daniels RC, Ardington C, Bassier I, Benhura M, Bridgman G, et al. Synthesis Report: NIDS-CRAM wave 3. National Income Dynamics Study – Coronavirus Rapid Mobile Survey. 2021 Feb 17. URL: <https://cramsurvey.org/wp-content/uploads/2021/02/1.-Spaul-N.-Daniels-R.-C-et-al.-2021-NIDS-CRAM-Wave-3-Synthesis-Report.pdf> [accessed 201-04-21]

31. Spaul N, Oyenubi A, Kerr A, Maughan-Brown B, Ardington C, Christian C, et al. Synthesis Report: NIDS-CRAM wave 2. National Income Dynamics Study – Coronavirus Rapid Mobile Survey. 2020 Aug 30. URL: <https://cramsurvey.org/wp-content/uploads/2020/10/1.-Spaul-etal.-NIDS-CRAM-Wave-2-Synthesis-Report.pdf> [accessed 2021-04-16]
32. Visagie J, Turok I. Rural–urban inequalities amplified by COVID-19: evidence from South Africa. *Area Development and Policy* 2021 Jan 18;6(1):50-62 [FREE Full text] [doi: [10.1080/23792949.2020.1851143](https://doi.org/10.1080/23792949.2020.1851143)]
33. van der Berg S, Patel L, Bridgman G. Hunger in South Africa during 2020: Results from wave 3 of NIDS-CRAM. National Income Dynamics Study – Coronavirus Rapid Mobile Survey. 2021 Feb 17. URL: <https://cramsurvey.org/wp-content/uploads/2021/02/10.-Van-der-Berg-S.-Patel-L.-Bridgman-G.-2021-Hunger-in-South-Africa-during-2020-Results-from-Wave-3-of-NIDS-CRAM-1.pdf> [accessed 2021-04-16]
34. Kahn K, Collinson MA, Gómez-Olivé FX, Mokoena O, Twine R, Mee P, et al. Profile: Agincourt health and socio-demographic surveillance system. *Int J Epidemiol* 2012 Aug;41(4):988-1001 [FREE Full text] [doi: [10.1093/ije/dys115](https://doi.org/10.1093/ije/dys115)] [Medline: [22933647](https://pubmed.ncbi.nlm.nih.gov/22933647/)]
35. Alberts M, Dikotope SA, Choma SR, Masemola ML, Modjadji SEP, Mashinya F, et al. *Int J Epidemiol* 2015 Oct;44(5):1565-1571. [doi: [10.1093/ije/dyv157](https://doi.org/10.1093/ije/dyv157)] [Medline: [26275454](https://pubmed.ncbi.nlm.nih.gov/26275454/)]
36. Gareta D, Baisley K, Mngomezulu T, Smit T, Khoza T, Nxumalo S, et al. Cohort Profile Update: Africa Centre Demographic Information System (ACDIS) and population-based HIV survey. *Int J Epidemiol* 2021 Mar 03;50(1):33-34 [FREE Full text] [doi: [10.1093/ije/dyaa264](https://doi.org/10.1093/ije/dyaa264)] [Medline: [33437994](https://pubmed.ncbi.nlm.nih.gov/33437994/)]
37. Siedner MJ, Harling G, Derache A, Smit T, Khoza T, Gunda R, et al. Protocol: Leveraging a demographic and health surveillance system for Covid-19 Surveillance in rural KwaZulu-Natal. *Wellcome Open Res* 2020 Aug 25;5:109 [FREE Full text] [doi: [10.12688/wellcomeopenres.15949.2](https://doi.org/10.12688/wellcomeopenres.15949.2)] [Medline: [32802963](https://pubmed.ncbi.nlm.nih.gov/32802963/)]
38. Bhana A, Mntambo N, Gigaba SG, Luvuno ZPB, Grant M, Ackerman D, et al. Validation of a brief mental health screening tool for common mental disorders in primary healthcare. *S Afr Med J* 2019 Mar 29;109(4):278-283 [FREE Full text] [doi: [10.7196/SAMJ.2019.v109i4.13664](https://doi.org/10.7196/SAMJ.2019.v109i4.13664)] [Medline: [31084695](https://pubmed.ncbi.nlm.nih.gov/31084695/)]
39. The R Project for statistical computing. The R Foundation. URL: <http://www.R-project.org/> [accessed 2021-04-16]
40. Central data catalog. SAPRIN Data Repository. URL: <http://saprindata.samrc.ac.za/index.php/catalog> [accessed 2021-04-19]
41. Epstein JM, Parker J, Cummings D, Hammond RA. Coupled contagion dynamics of fear and disease: mathematical and computational explorations. *PLoS One* 2008;3(12):e3955. [doi: [10.1371/journal.pone.0003955](https://doi.org/10.1371/journal.pone.0003955)] [Medline: [19079607](https://pubmed.ncbi.nlm.nih.gov/19079607/)]
42. Weitz JS, Park SW, Eksin C, Dushoff J. Awareness-driven behavior changes can shift the shape of epidemics away from peaks and toward plateaus, shoulders, and oscillations. *Proc Natl Acad Sci U S A* 2020 Dec 22;117(51):32764-32771 [FREE Full text] [doi: [10.1073/pnas.2009911117](https://doi.org/10.1073/pnas.2009911117)] [Medline: [33262277](https://pubmed.ncbi.nlm.nih.gov/33262277/)]
43. Lin Q, Zhao S, Gao D, Lou Y, Yang S, Musa SS, et al. A conceptual model for the coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China with individual reaction and governmental action. *Int J Infect Dis* 2020 Apr;93:211-216. [doi: [10.1016/j.ijid.2020.02.058](https://doi.org/10.1016/j.ijid.2020.02.058)] [Medline: [32145465](https://pubmed.ncbi.nlm.nih.gov/32145465/)]
44. Collinson MA. Striving against adversity: the dynamics of migration, health and poverty in rural South Africa. *Glob Health Action* 2010 Jun 03;3(1):5080 [FREE Full text] [doi: [10.3402/gha.v3i0.5080](https://doi.org/10.3402/gha.v3i0.5080)] [Medline: [20531981](https://pubmed.ncbi.nlm.nih.gov/20531981/)]
45. Siedner MJ, Kraemer JD, Meyer MJ, Harling G, Mngomezulu T, Gabela P, et al. Access to primary healthcare during lockdown measures for COVID-19 in rural South Africa: an interrupted time series analysis. *BMJ Open* 2020 Oct 05;10(10):e043763 [FREE Full text] [doi: [10.1136/bmjopen-2020-043763](https://doi.org/10.1136/bmjopen-2020-043763)] [Medline: [33020109](https://pubmed.ncbi.nlm.nih.gov/33020109/)]
46. Hofman K, Madhi S. The unanticipated costs of COVID-19 to South Africa's quadruple disease burden. *S Afr Med J* 2020 Jul 16;110(8):698-699 [FREE Full text] [Medline: [32880282](https://pubmed.ncbi.nlm.nih.gov/32880282/)]
47. Schatz E, Gómez-Olivé X, Ralston M, Menken J, Tollman S. The impact of pensions on health and wellbeing in rural South Africa: does gender matter? *Soc Sci Med* 2012 Nov;75(10):1864-1873 [FREE Full text] [doi: [10.1016/j.socscimed.2012.07.004](https://doi.org/10.1016/j.socscimed.2012.07.004)] [Medline: [22884944](https://pubmed.ncbi.nlm.nih.gov/22884944/)]
48. Duflo E. Child health and household resources in South Africa: Evidence from the old age pension program. *Am Econ Rev* 2000;90(2):393-398. [doi: [10.1257/aer.90.2.393](https://doi.org/10.1257/aer.90.2.393)] [Medline: [29053233](https://pubmed.ncbi.nlm.nih.gov/29053233/)]
49. Lee A. Wuhan novel coronavirus (COVID-19): why global control is challenging? *Public Health* 2020 Feb;179:A1-A2 [FREE Full text] [doi: [10.1016/j.puhe.2020.02.001](https://doi.org/10.1016/j.puhe.2020.02.001)] [Medline: [32111295](https://pubmed.ncbi.nlm.nih.gov/32111295/)]

## Abbreviations

- AHRI:** Africa Health Research Institute
- CRAM:** Coronavirus Rapid Mobile Survey
- DIMAMO:** Dikgale-Mamabolo-Mothiba
- HDSS:** Health and Demographic Surveillance System
- GAD-2:** Generalized Anxiety Disorder 2-item
- MRC:** Medical Research Council
- NIDS:** National Income Dynamics Study
- NPI:** nonpharmaceutical intervention
- PHQ-2:** Patient Health Questionnaire 2-item

**REC:** Research Ethics Committee

**SAPRIN:** South African Population Research Infrastructure Network

*Edited by T Sanchez; submitted 26.11.20; peer-reviewed by C Mavrot, C Entwistle; comments to author 12.02.21; revised version received 25.03.21; accepted 31.03.21; published 13.05.21.*

*Please cite as:*

*Harling G, Gómez-Olivé FX, Tlouyamma J, Mutevedzi T, Kabudula CW, Mahlako R, Singh U, Ohene-Kwofie D, Buckland R, Ndagurwa P, Gareta D, Gunda R, Mngomezulu T, Nxumalo S, Wong EB, Kahn K, Siedner MJ, Maimela E, Tollman S, Collinson M, Herbst K Protective Behaviors and Secondary Harms Resulting From Nonpharmaceutical Interventions During the COVID-19 Epidemic in South Africa: Multisite, Prospective Longitudinal Study*

*JMIR Public Health Surveill* 2021;7(5):e26073

URL: <https://publichealth.jmir.org/2021/5/e26073>

doi: [10.2196/26073](https://doi.org/10.2196/26073)

PMID: [33827046](https://pubmed.ncbi.nlm.nih.gov/33827046/)

©Guy Harling, Francesc Xavier Gómez-Olivé, Joseph Tlouyamma, Tinofa Mutevedzi, Chodziwadziwa Whiteson Kabudula, Ruth Mahlako, Urisha Singh, Daniel Ohene-Kwofie, Rose Buckland, Pedzisai Ndagurwa, Dickman Gareta, Resign Gunda, Thobeka Mngomezulu, Siyabonga Nxumalo, Emily B Wong, Kathleen Kahn, Mark J Siedner, Eric Maimela, Stephen Tollman, Mark Collinson, Kobus Herbst. Originally published in JMIR Public Health and Surveillance (<https://publichealth.jmir.org>), 13.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# The Differential Effects of Social Media on Depressive Symptoms and Suicidal Ideation Among the Younger and Older Adult Population in Hong Kong During the COVID-19 Pandemic: Population-Based Cross-sectional Survey Study

Xue Yang<sup>1,2</sup>, PhD; Benjamin H K Yip<sup>1</sup>, PhD; Arthur D P Mak<sup>3</sup>, MBChB, FRCPsych; Dexing Zhang<sup>1</sup>, PhD; Eric K P Lee<sup>1</sup>, MSc; Samuel Y S Wong<sup>1</sup>, MD, MPH

<sup>1</sup>Jockey Club School of Public Health and Primary Care, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, Hong Kong

<sup>2</sup>The Chinese University of Hong Kong Shenzhen Research Institute, Shenzhen, China

<sup>3</sup>Department of Psychiatry, The Chinese University of Hong Kong, Hong Kong, Hong Kong

**Corresponding Author:**

Samuel Y S Wong, MD, MPH

Jockey Club School of Public Health and Primary Care

Faculty of Medicine

The Chinese University of Hong Kong

School of Public Health Building, Prince of Wales Hospital

30-32 Ngan Shing Street, Shatin, New Territories

Hong Kong

Hong Kong

Phone: 852 2252 8488

Email: [yeungshanwong@cuhk.edu.hk](mailto:yeungshanwong@cuhk.edu.hk)

## Abstract

**Background:** Social media has become a ubiquitous part of daily life during the COVID-19 pandemic isolation. However, the role of social media use in depression and suicidal ideation of the general public remains unclear. Related empirical studies were limited and reported inconsistent findings. Little is known about the potential underlying mechanisms that may illustrate the relationship between social media use and depression and suicidal ideation during the COVID-19 pandemic.

**Objective:** This study tested the mediation effects of social loneliness and posttraumatic stress disorder (PTSD) symptoms on the relationship between social media use and depressive symptoms and suicidal ideation, as well as the moderation effect of age on the mediation models.

**Methods:** We administered a population-based random telephone survey in May and June 2020, when infection control measures were being vigorously implemented in Hong Kong. A total of 1070 adults (658 social media users and 412 nonusers) completed the survey. Structural equation modeling (SEM) and multigroup SEM were conducted to test the mediation and moderation effects.

**Results:** The weighted prevalence of probable depression was 11.6%; 1.6% had suicidal ideation in the past 2 weeks. Both moderated mediation models of depressive symptoms ( $\chi^2_{62}=335.3$ ;  $P<.05$ ; comparative fit index [CFI]=0.94; nonnormed fit index [NNFI]=0.92; root mean square error of approximation [RMSEA]=0.06) and suicidal ideation ( $\chi^2_{34}=50.8$ ;  $P<.05$ ; CFI=0.99; NNFI=0.99; RMSEA=0.02) showed acceptable model fit. There was a significantly negative direct effect of social media use on depressive symptoms among older people ( $\beta=-.07$ ;  $P=.04$ ) but not among younger people ( $\beta=.04$ ;  $P=.55$ ). The indirect effect via PTSD symptoms was significantly positive among both younger people ( $\beta=.09$ ;  $P=.02$ ) and older people ( $\beta=.10$ ;  $P=.01$ ). The indirect effect via social loneliness was significant among older people ( $\beta=-.01$ ;  $P=.04$ ) but not among younger people ( $\beta=.01$ ;  $P=.31$ ). The direct effect of social media use on suicidal ideation was not statistically significant in either age group ( $P>.05$ ). The indirect effects via PTSD symptoms were statistically significant among younger people ( $\beta=.02$ ;  $P=.04$ ) and older people ( $\beta=.03$ ;  $P=.01$ ). Social loneliness was not a significant mediator between social media use and suicidal ideation among either age group ( $P>.05$ ).

**Conclusions:** Social media may be a “double-edged sword” for psychosocial well-being during the COVID-19 pandemic, and its roles vary across age groups. The mediators identified in this study can be addressed by psychological interventions to prevent severe mental health problems during and after the COVID-19 pandemic.

(*JMIR Public Health Surveill* 2021;7(5):e24623) doi:[10.2196/24623](https://doi.org/10.2196/24623)

## KEYWORDS

social media; depression; suicidal ideation; social loneliness; posttraumatic stress; suicide; mental health; COVID-19; loneliness; age; mediation

## Introduction

Unprecedented control measures, such as lockdown, quarantine, social distancing, and home confinement, have been implemented to contain the spread of COVID-19, an infectious disease caused by a coronavirus that was newly discovered in 2019 [1,2]. These measures have brought marked changes in our social worlds and digital lifestyles within a short time frame. As a large proportion of the global population hunkers down in isolation away from their family and friends, social media and social networking sites (SNSs) have become a crutch for human connection and information sharing [3]. Although the World Health Organization (WHO) has expressed support for the gaming industry’s online social media campaign #PlayApartTogether, which incorporates WHO guidelines on coronavirus prevention [4], the role of social media use in the mental health of the general public during the COVID-19 pandemic remains unclear. Related empirical studies have been limited and have reported inconsistent findings [5-8]. The inconsistent results highlight the need to explore the potential underlying mechanisms that may illustrate the link between social media use and mental health during the COVID-19 pandemic; however, we did not identify such studies. In addition, there have been growing concerns about people experiencing increased suicidal ideation or self-harming behavior during the COVID-19 pandemic isolation [9]. No study tested whether or how social media use status may influence suicidal ideation during the COVID-19 pandemic.

Reduced social loneliness and increased trauma-related stress (eg, posttraumatic stress disorder [PTSD] symptoms) may serve as two important psychosocial mechanisms that explain the relationship between social media use and depression and suicidal ideation. Social loneliness refers to the situation where an individual has a smaller number of relationships, stemming from the absence of a broader group of contacts or an engaging social network, such as friends, colleagues, and neighbors. Meanwhile, social media has been demonstrated to play an important role in forming and maintaining social networks and social capital, which may counter social loneliness [10-12]. While isolation during the COVID-19 pandemic may have reduced physical interpersonal encounters and increased social loneliness, social media can maintain social connections (eg, Shah et al [13]). Thus, social media may help to reinforce interpersonal resources and ameliorate social loneliness, which may help people cope with stress and mitigate the adverse impact of the COVID-19 pandemic on mental health [14,15].

On the other hand, intensified trauma-related stress and PTSD symptoms may explain the positive association between social

media use and mental health (eg, Chao et al [5] and Riehm et al [6]). Social media may allow for the spread of rumors, fake news, and negative emotions, such as hopelessness, anxiety, and fear (eg, Depoux et al [16] and Kramer et al [17]). Ubiquitous and repeated social media exposure to anxiety-provoking topics related to the health crisis can also lead users to inaccurately estimate the threat of infection within their communities [18]. This can trigger acute and posttraumatic stress responses as well as panic responses during collective traumatic events, which may, in turn, aggravate depressive symptoms and suicidal ideation during a pandemic [19].

Theoretically, the proposed mediation effects of social loneliness and PTSD symptoms can be supported by the conservation of resources (COR) theory [20]. This theory suggests that perceived and actual loss or gain of interpersonal resources (eg, social connection and loneliness) and personal resources (eg, perceived stress and self-efficacy) serves as the central mechanism that explains how people may develop psychological distress. This theory has been applied to explain the relationships between the use of digital technology and psychological well-being; that is, social media can significantly affect the psychosocial resources of users, which, in turn, affect their mental health and distress (eg, Feldman et al [21] and van der Velden et al [22]). Social loneliness and perceived trauma-related stress are well-documented interpersonal and personal factors of severe mental health problems [23,24]. However, we have not identified any studies that tested their mediation effects on the relationship between social media use and mental health during collective traumatic events.

Furthermore, an increasing number of older adults have been using the internet and social media. In Hong Kong, people aged 45 years or above have caught up rapidly with their social media participation rate (ie, 78% in 2018) [25]. Social media applications are considered helpful in reducing loneliness and enhancing well-being among older adults, while concerns about the negative consequences on well-being have been highlighted in some studies (eg, Leist [26] and Berryman et al [27]). Most research on the effects of social media use has focused on younger people only, with few studies conducted among older people (eg, van der Velden et al [22]). It is unclear how age may moderate the effect of social media use on psychosocial status during the COVID-19 pandemic.

In this study, we randomly recruited both social media users and nonusers to create a representative sample of the Hong Kong population; we examined whether and how social media use is associated with depressive symptoms and suicidal ideation through two psychosocial processes: social loneliness and PTSD symptoms. We hypothesized the following:

1. Social media use would be negatively associated with social loneliness; in turn, loneliness would be positively associated with depressive symptoms and suicidal ideation.
2. Social media use would be positively associated with PTSD symptoms; in turn, PTSD symptoms would be positively associated with depressive symptoms and suicidal ideation.

In addition, we also tested whether these mediation effects would be constant among younger and older people.

## Methods

### Recruitment of Participants

We administered a population-based, random telephone survey between May 14 and June 4, 2020, when infection control measures (eg, social distancing, business restrictions, and border control) were being vigorously implemented in Hong Kong. Participant inclusion criteria included the following: (1) Chinese speaking, (2) 18 years old or above, and (3) Hong Kong resident (ie, holder of a Hong Kong identification card). The telephone interviews were conducted between 6 PM and 10 PM in order to avoid undersampling working individuals. The interviewers were well trained and had at least 6 months of interviewing experience. They were supervised on site by a senior project coordinator. Telephone numbers were randomly drawn from the latest residential telephone directory by a random phone number generator program. Telephone numbers were selected randomly from an updated landline telephone directory as seed numbers. Another three sets of numbers were then generated using the randomization of the last two digits to recruit unlisted numbers. Eligible household members whose day and month of birth was closest to the survey date were invited to join the study. Two follow-up calls were conducted for unanswered calls before a telephone number was considered invalid. Verbal informed consent was obtained from the participants. The anonymous interview took 10 to 15 minutes. No incentive was given to the participants. Of the 1882 eligible participants identified and invited, 1070 completed the interviews, resulting in a modest response rate (56.9%).

### Ethical Approval

The study was approved by the Survey and Behavioural Research Ethics Committee of the corresponding author's affiliated university, the Chinese University of Hong Kong (reference No. SBRE-19-645). The study followed the ethical standards of the responsible committee on human experimentation, institutional and national, and of the Helsinki Declaration of 1975, as revised in 2000.

### Measures

#### *Status of Social Media Use*

The participants were asked whether they had used an SNS in the past 12 months, such as Facebook, Twitter, WhatsApp, or WeChat, which are platforms for communicating with one another [28]. Those who said "yes" to the question were further asked how many hours per day they had spent, on average, on these SNSs during the COVID-19 pandemic. Similar questions were used in previous studies on social media use [8,29,30].

#### *PTSD Symptoms*

The 8-item Posttraumatic Stress Disorder scale (PTSD-8) [31] was used to assess posttraumatic stress responses and symptoms in the past month. The items correspond to the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) criteria for PTSD. They are answered on a 4-point Likert scale, ranging from 1 (not at all) to 4 (all the time). Higher summed scores indicate greater symptoms of PTSD. The internal consistency as measured by Cronbach  $\alpha$  was .76 and was acceptable in the current sample.

#### *Social Loneliness*

The 3-item social loneliness subscale of the De Jong Gierveld Loneliness Scale [32] was used to assess social loneliness during the COVID-19 pandemic. Response options include *no, more or less, and yes*. Summed scores range from 3 to 9. Higher scores suggest higher levels of loneliness. The Cronbach  $\alpha$  for this scale was .94.

#### *Depressive Symptoms*

The 10-item Center for Epidemiologic Studies Depression Scale (CESD-10) assessed depressive symptoms during the past week [33]. This is a short version of the CESD-20 and has good reliability and validity [33]. A cutoff point of 10 or higher denotes probable depression; this was predictive of a depression diagnosis [34,35]. Items are rated on a 4-point Likert scale, ranging from 0 (less than 1 day) to 3 (5 to 7 days). The Chinese version of the scale was validated in the Hong Kong population [36]. The Cronbach  $\alpha$  was .78 in the current sample.

#### *Suicidal Ideation*

Item 9 of the 9-item Patient Health Questionnaire (PHQ-9) [37] (ie, "How often have you been bothered by the following problem: Thoughts that you would be better off dead, or thoughts of hurting yourself in some way?") was used to assess the frequency of suicidal ideation in the past 2 weeks. Participants rated the question on a 4-point Likert scale, ranging from 0 (not at all) to 3 (almost every day). A score of 0 indicates having no suicidal ideation, while a score of 1 or higher indicates having suicidal ideation in the past 2 weeks. The Chinese version has been used in previous studies [38].

The participants were also asked to report their sociodemographic information, including sex, age, current marital status, educational level, income, health status, and mandatory quarantine status (ie, whether one had been subjected to compulsory quarantine at designated places—home, hotel, or other accommodation—under government order for COVID-19 infection control).

#### *Statistical Analyses*

Descriptive statistics were computed for both background and psychological variables. Age-standardized weighted prevalence of probable depression was calculated by the direct method and the age distribution for the 2020 census population. Simple logistic regression analyses were conducted to test the associations between background, independent, and mediation variables and probable depression and suicidal ideation. Odds ratios and 95% CIs were reported. Structural equation modeling (SEM) was conducted to test the proposed mediation models



of depressive symptoms and suicidal ideation. For the variables of PTSD symptoms and depressive symptoms, indicators were created by the item parceling method. Since the two scales are unidimensional, the random method of combining items was used to create item parcels. For the latent factors of social loneliness, all three individual items of the scale were used as indicators. The observed variable of suicidal ideation was created by using item 9 of the PHQ-9. Goodness of fit was tested by using the chi-square test, the comparative fit index (CFI), the nonnormed fit index (NNFI), and the root mean square error of approximation (RMSEA). Standardized regression coefficients ( $\beta$ ) and 95% CIs were reported. Bootstrapping based on 5000 bootstrap samples was performed to test for indirect effects. A statistically significant indirect effect would be observed when the CI did not include zero. Multigroup SEM analyses were conducted to test the moderation effect of age on the mediation models. The age of retirement of most people in Hong Kong ranges from 55 to 65 years [39]. Hence, participants aged 18 to 55 years were classified as younger adults and those older than 55 years were classified as older adults. The level of statistical significance was .05. SPSS, version 21.0, and Amos (IBM Corp) were used to conduct statistical analysis.

## Results

The background characteristics of the participants are presented in Table 1. The sample of 1070 participants included 367 (34.3%) young adults and 684 (63.9%) older adults; 60.4% (646/1070) of the participants reported that they used social media in the past year and were classified as social media users. The weighted prevalence of probable depression was 11.6%. Younger adults (14.8%) had higher weighted prevalence of probable depression than older adults (8.4%). A total of 1.6% (17/1070) of the participants had suicidal ideation in the past 2 weeks (younger adults: 10/367, 2.7%; older adults: 7/684, 1.0%).

Associations between the background or mediator variables and probable depression and suicidal ideation are presented in Table 2. The significant background variables of probable depression included age, current marital status, educational level, monthly household income, and mental health status before and during the COVID-19 pandemic. Social media use status, time spent on social media, PTSD symptoms, and social loneliness were significantly and positively associated with depressive symptoms. Income, being diagnosed with mental health problems before or during the COVID-19 pandemic, mandatory quarantine status, and PTSD symptoms were positively associated with suicidal ideation.

**Table 1.** Background characteristics of the participants recruited from the adult population in Hong Kong during the COVID-19 pandemic.

Background characteristic	All participants (N=1070)	Younger adults (aged 18-55 years; n=367)	Older adults (older than 55 years; n=684)	P value <sup>a</sup>
<b>Sex, n (%)</b>				.01
Male	346 (32.3)	137 (37.3)	204 (29.8)	
Female	724 (67.7)	230 (62.7)	480 (70.2)	
<b>Age group (years), n (%)</b>				N/A <sup>b</sup>
18-35	115 (10.7)	N/A	N/A	
36-55	252 (23.6)	N/A	N/A	
56-65	301 (28.1)	N/A	N/A	
>65	383 (35.8)	N/A	N/A	
Refused to answer	19 (1.8)	N/A	N/A	
<b>Current marital status, n (%)</b>				<.001
Single	201 (18.8)	148 (40.3)	50 (7.3)	
Cohabiting or married	745 (69.6)	209 (56.9)	528 (77.2)	
Separated, divorced, or widowed	107 (10.0)	5 (1.4)	101 (14.8)	
Refused to answer or missing value	17 (1.6)	5 (1.4)	5 (0.7)	
<b>Educational level, n (%)</b>				<.001
Primary school or below	355 (33.2)	7 (1.9)	345 (50.4)	
Secondary school	384 (35.9)	139 (37.9)	239 (34.9)	
College or above	294 (27.5)	211 (57.5)	81 (11.8)	
Refused to answer	37 (3.5)	10 (2.7)	19 (2.8)	
<b>Monthly household income (HK \$<sup>c</sup>), n (%)</b>				<.001
≤20,000	627 (58.6)	92 (25.1)	526 (76.9)	
20,001-30,000	124 (11.6)	77 (21.0)	47 (6.9)	
30,001-50,000	103 (9.6)	64 (17.4)	39 (5.7)	
>50,000	84 (7.9)	62 (16.9)	22 (3.2)	
Refused to answer or missing value	132 (12.3)	72 (19.6)	50 (7.3)	
<b>Have chronic diseases<sup>d</sup>, n (%)</b>				<.001
No	716 (66.9)	334 (91.0)	369 (53.9)	
Yes	354 (33.1)	33 (9.0)	315 (46.1)	
<b>Diagnosed with mental health problems<sup>e</sup> before the pandemic, n (%)</b>				.25
No	1045 (97.7)	361 (98.4)	665 (97.2)	
Yes	25 (2.3)	6 (1.6)	19 (2.8)	
<b>Diagnosed with mental health problems<sup>e</sup> during the pandemic, n (%)</b>				.64
No	1050 (98.1)	361 (98.4)	670 (98.0)	
Yes	20 (1.9)	6 (1.6)	14 (2.0)	
<b>Subjected to mandatory quarantine, n (%)</b>				.02
No	1055 (98.6)	358 (97.5)	679 (99.3)	
Yes	15 (1.4)	9 (2.5)	5 (0.7)	
<b>Social media user in the past year, n (%)</b>				<.001
No	412 (38.5)	25 (6.8)	379 (55.4)	

Background characteristic	All participants (N=1070)	Younger adults (aged 18-55 years; n=367)	Older adults (older than 55 years; n=684)	<i>P</i> value <sup>a</sup>
Yes	658 (61.5)	342 (93.2)	305 (44.6)	
<b>Hours spent per day on social media during the pandemic (n=658) , n (%)</b>				<.001
0.0-2.0	232 (35.3)	89 (26.0)	137 (44.9)	
2.5-4.0	261 (39.7)	133 (38.9)	126 (41.3)	
4.5-6.0	110 (16.7)	77 (22.5)	30 (9.8)	
>6.0	55 (8.4)	43 (12.6)	12 (3.9)	
Posttraumatic stress disorder symptoms, mean (SD) <sup>f</sup>	4.2 (3.8)	4.7 (3.6)	4.0 (3.9)	.008
Social loneliness, mean (SD) <sup>g</sup>	4.4 (1.7)	4.4 (1.8)	4.3 (1.7)	.76

<sup>a</sup>Based on chi-square tests or independent-samples *t* tests where appropriate.

<sup>b</sup>N/A: not applicable; the number of participants in each age group was reported for the total sample only (hence, the *P* value was not calculated).

<sup>c</sup>A currency exchange rate of HK \$1=US \$0.1287 is applicable.

<sup>d</sup>Chronic diseases included hypertension, diabetes, cancer, etc.

<sup>e</sup>Mental health problems included depression, anxiety, insomnia, etc.

<sup>f</sup>The 8-item Posttraumatic Stress Disorder scale (PTSD-8) was used to assess posttraumatic stress responses and symptoms in the past month. Summed scores range from 0 to 23; higher summed scores indicate greater symptoms of PTSD.

<sup>g</sup>The 3-item social loneliness subscale of the De Jong Gierveld Loneliness Scale was used to assess social loneliness. Summed scores range from 3 to 9; higher scores suggest higher levels of loneliness.

**Table 2.** Associations between the background or mediator variables and depressive symptoms and suicidal ideation among the adult population in Hong Kong during the COVID-19 pandemic (N=1070).

Variable	Probable depression OR <sup>a</sup> (95% CI)	P value	Suicidal ideation OR (95% CI)	P value
<b>Sex</b>				
Male	1 <sup>b</sup>		1	
Female	1.09 (0.71-1.67)	.69	0.68 (0.26-1.80)	.44
<b>Age (years)</b>				
18-35	1		1	
36-55	0.90 (0.49-1.66)	.73	0.68 (0.19-2.45)	.55
56-65	0.55 (0.29-1.04)	.07	0.37 (0.09-1.52)	.17
>65	0.39 (0.21-0.75)	.004	0.22 (0.05-0.99)	.049
<b>Current marital status (n=1053)</b>				
Single	1		1	
Cohabiting or married	0.61 (0.39-0.96)	.03	0.53 (0.18-1.58)	.26
Separated, divorced, or widowed	0.46 (0.20-1.04)	.06	0.75 (0.14-3.91)	.73
<b>Educational level (n=1033)</b>				
Primary school or below	1		1	
Secondary school	1.41 (0.83-2.39)	.21	2.18 (0.56-8.49)	.26
College or above	2.45 (1.46-4.09)	.001	2.86 (0.73-11.17)	.13
<b>Monthly household income (HK \$<sup>c</sup>; n=938)</b>				
≤20,000	1		1	
20,001-30,000	2.41 (1.38-4.18)	.002	1.45 (0.30-7.07)	.64
30,001-50,000	1.56 (0.80-3.04)	.20	2.66 (0.68-10.45)	.16
>50,000	2.78 (1.50-5.15)	.001	4.43(1.27-15.46)	.02
<b>Have chronic diseases<sup>d</sup></b>				
No	1		1	
Yes	0.84 (0.55-1.29)	.43	0.84 (0.29-2.41)	.75
<b>Diagnosed with mental health problems<sup>e</sup> before the pandemic</b>				
No	1		1	
Yes	12.44 (5.50-28.15)	<.001	15.12 (4.55-50.26)	<.001
<b>Diagnosed with mental health problems<sup>e</sup> during the pandemic</b>				
No	1		1	
Yes	40.21 (13.18-122.72)	<.001	28.83 (9.03-92.08)	<.001
<b>Subjected to mandatory quarantine</b>				
No	1		1	
Yes	2.19 (0.61-7.89)	.23	10.67 (2.21-51.45)	.003
<b>Social media use in the past year</b>				
No	1		1	
Yes	1.98 (1.27-3.10)	.003	2.96 (0.85-10.38)	.09
<b>Hours spent per day on social media during the pandemic (n=658)</b>				
0.0-2.0	1		1	
2.5-4.0	1.29 (0.72-2.29)	.39	0.29 (0.08-1.08)	.06

Variable	Probable depression OR <sup>a</sup> (95% CI)	<i>P</i> value	Suicidal ideation OR (95% CI)	<i>P</i> value
4.5-6.0	2.12 (1.10-4.08)	.02	0.23 (0.03-1.82)	.16
>6.0	2.12 (0.94-4.79)	.07	0.46 (0.06-3.70)	.46
Posttraumatic stress disorder symptoms	1.38 (1.31-1.46)	<.001	1.21 (1.11-1.31)	<.001
Social loneliness	1.17 (1.05-1.30)	.004	1.20 (0.93-1.54)	.16

<sup>a</sup>OR: odds ratio; based on logistic regression analyses.

<sup>b</sup>Variable items with a value of 1 are the reference items.

<sup>c</sup>A currency exchange rate of HK \$1=US \$0.1287 is applicable.

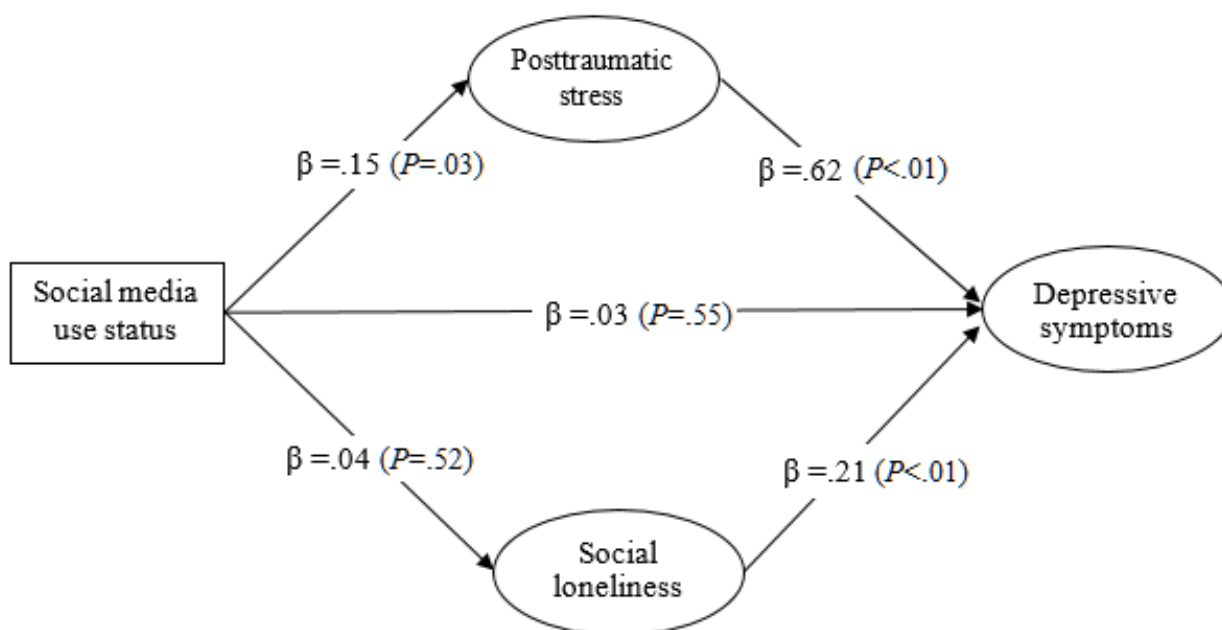
<sup>d</sup>Chronic diseases included hypertension, diabetes, cancer, etc.

<sup>e</sup>Mental health problems included depression, anxiety, insomnia, etc.

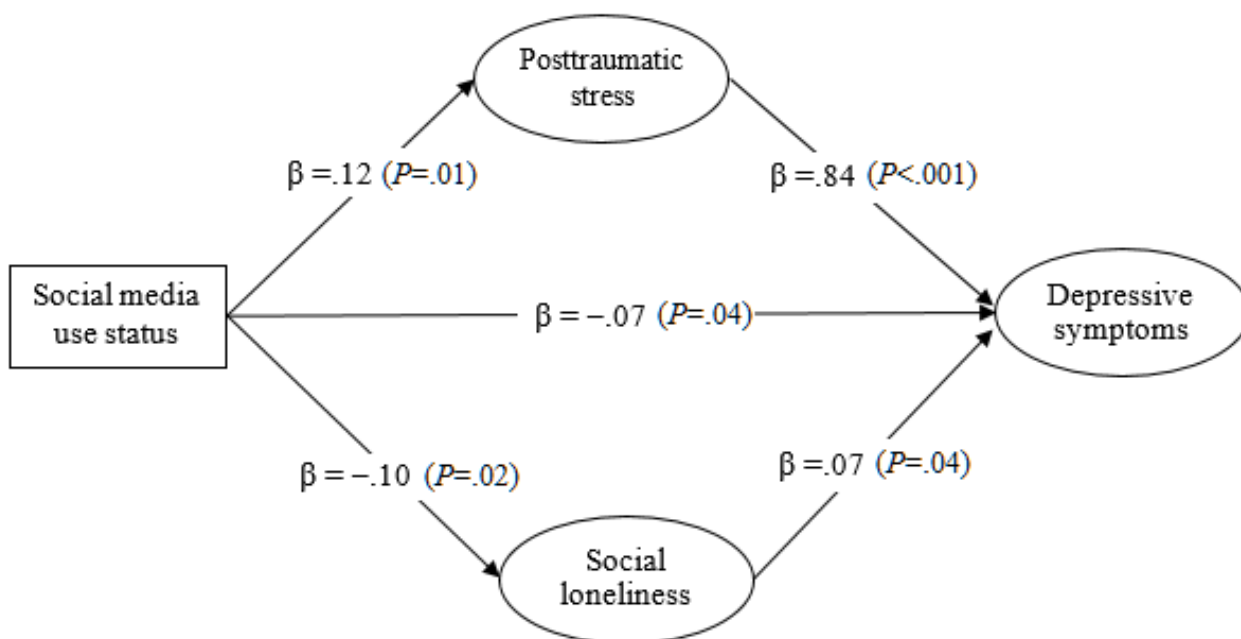
Both the measurement model ( $\chi^2_{30}=294.3$ ;  $P<.05$ ; CFI=0.95; NNFI=0.92; RMSEA=0.08) and the structural model of depressive symptoms ( $\chi^2_{31}=294.6$ ;  $P<.05$ ; CFI=0.95; NNFI=0.92; RMSEA=0.08) showed acceptable model fit. Multigroup SEM analyses further revealed that the mediation model fitted the data well across younger and older adults ( $\chi^2_{62}=335.3$ ;  $P<.05$ ; CFI=0.94; NNFI=0.92; RMSEA=0.06). As Figures 1 and 2 show, there was a significantly negative

direct effect of social media use on depressive symptoms among older people ( $\beta=-.07$ ;  $P=.04$ ) (Figure 2) but not among younger people ( $\beta=.03$ ;  $P=.55$ ) (Figure 1). The indirect effect via PTSD symptoms was significantly positive among both younger people ( $\beta=.09$ , 95% CI .02-.14;  $P=.02$ ) (Figure 1) and older people ( $\beta=.10$ , 95% CI .05-.16;  $P=.01$ ) (Figure 2). The indirect effect via social loneliness was significant among older people ( $\beta=-.01$ , 95% CI -.02 to -.001;  $P=.04$ ) (Figure 2) but not among younger people ( $\beta=.01$ , 95% CI -.01 to .03;  $P=.31$ ) (Figure 1).

**Figure 1.** The proposed mediation model of depressive symptoms with standardized regression coefficients ( $\beta$ ) among younger adults in Hong Kong during the COVID-19 pandemic (n=367).



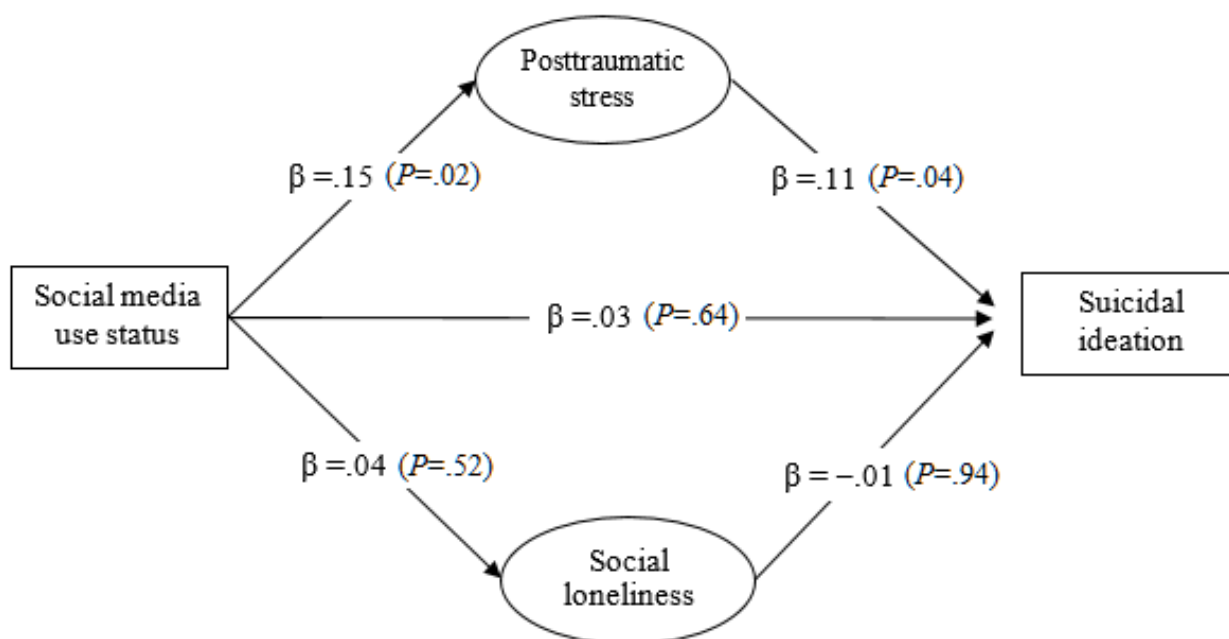
**Figure 2.** The proposed mediation model of depressive symptoms with standardized regression coefficients ( $\beta$ ) among older adults in Hong Kong during the COVID-19 pandemic (n=684).



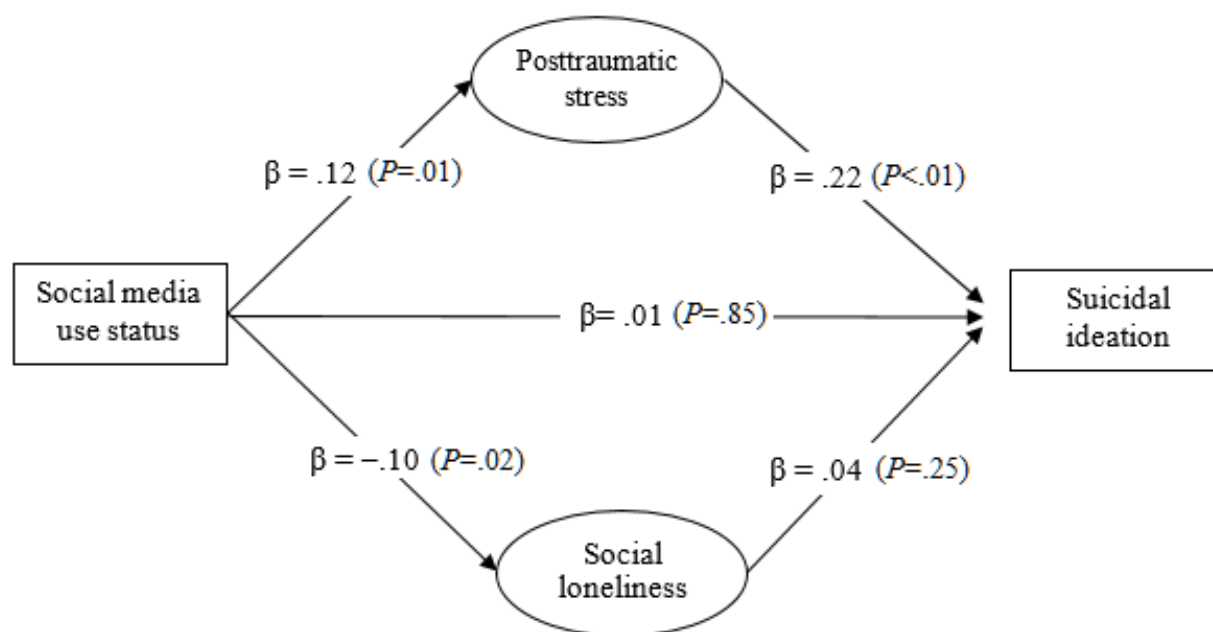
Both the measurement model ( $\chi^2_{16}=34.4$ ;  $P<.05$ ; CFI=0.99; NNFI=0.99; RMSEA=0.03) and the structural model of suicidal ideation ( $\chi^2_{17}=34.7$ ;  $P<.05$ ; CFI=0.99; NNFI=0.99; RMSEA=0.03) showed excellent model fit. Multigroup SEM analyses showed that the mediation model fitted the data well across age groups ( $\chi^2_{34}=50.8$ ;  $P<.05$ ; CFI=0.99; NNFI=0.99; RMSEA=0.02). As Figures 3 and 4 show, the direct effect of

social media use on suicidal ideation was not statistically significant in either age group ( $P>.05$ ). The indirect effects via PTSD symptoms were statistically significant among younger people ( $\beta=.02$ , 95% CI .001-.06;  $P=.04$ ) (Figure 3) and older people ( $\beta=.03$ , 95% CI .01-.06;  $P=.01$ ) (Figure 4). Social loneliness was not a significant mediator between social media use and suicidal ideation among younger and older adults.

**Figure 3.** The proposed mediation model of suicidal ideation with standardized regression coefficients ( $\beta$ ) among younger adults in Hong Kong during the COVID-19 pandemic (n=367).



**Figure 4.** The proposed mediation model of suicidal ideation with standardized regression coefficients ( $\beta$ ) among older adults in Hong Kong during the COVID-19 pandemic (n=684).



## Discussion

### Principal Findings

This population-based study investigated the prevalence of probable depression and suicidal ideation in Hong Kong adults during the COVID-19 pandemic. Furthermore, the study tested a complex relationship between social media use and mental health (ie, depressive symptoms and suicidal ideation). Findings suggest that this relationship could be explained by the mediation effects of PTSD symptoms and social loneliness and moderated by age. Specifically, social media use was indirectly and positively associated with depressive symptoms and suicidal ideation through PTSD symptoms in both younger and older adults. In addition, social media use was directly and indirectly associated with depressive symptoms through social loneliness in older adults.

The weighted prevalence of probable depression was higher than that reported in pre-COVID-19 research conducted in 2007 (11.6% versus 8.6%) [40]. It may suggest an increase in mental distress among the Hong Kong population during the COVID-19 pandemic. Some subgroups may need particular attention, as they showed higher risks of depression or suicidal ideation, including those who were younger or single, had higher educational levels, had higher household incomes, had been diagnosed with mental health problems before or during the COVID-19 pandemic, had been under mandatory quarantine, used social media, or spent more hours on social media during the COVID-19 pandemic. Higher scores of depression among the younger sample seem to confirm findings from both COVID-19 and pre-COVID-19 studies [41,42]: the younger participants tended to obtain a large amount of information from social media that could easily trigger stress. Interestingly, the results appear to suggest that people with higher social capital, such as having higher educational levels, having higher household incomes, or using social media, may be more

vulnerable to mental distress during the COVID-19 pandemic. Recent studies reported similar findings and suggested that it may be because these groups tend to have higher self-awareness of, and concern about, their health [41,43]. Time spent on social media was positively associated with depressive symptoms during the COVID-19 pandemic, consistent with recently published studies [5-7]. It may be due to the fact that during the COVID-19 pandemic, spending excessive time on social media implies more social media exposure to COVID-19 news and greater likelihood of experiencing the infodemic and emotional contagion through online social networks [44]. These findings are susceptible to reverse causality, whereby mental distress might lead to rumination on social media.

Furthermore, this study brings novel information to the field about the underlying mechanisms of the relationships between social media use and depression and suicidal ideation. The proposed mediation models based on the COR theory were well supported by the acceptable model fit. This is the first study that applied this theory to understand the roles of social media use in the context of the COVID-19 pandemic. From the COR perspectives, people strive to develop, maintain, or restore important resources, such as social relationships, well-being, and a low state of stress, and a loss of these resources can, in turn, lead to mental health problems [20,45]. Our SEM results suggest that during the COVID-19 crisis, social media use might intensify PTSD symptoms, which were, in turn, associated with more depressive symptoms and suicidal ideation; these mediation effects are broadly applicable to both younger and older adults. Our findings support the assertion that the heightened PTSD symptoms due to media exposure to collective crises may have profound repercussions for mental health [46]. Consistently, recent studies also suggested that social media use, especially long times spent on social media for COVID-19-related information, was positively associated with a range of negative psychological statuses, including negative

affect, mental distress, anxiety, and depression [5-7]. Previous studies in the contexts of other infectious diseases and traumatic events (eg, the Ebola virus disease outbreak) also argued that a state of stress could be triggered and intensified by social media exposure [16,17,47]. Reverse causality may also be applicable, as people experiencing more stress and mental health problems may tend to use social media to escape from the real world, which is stressful during the COVID-19 pandemic. Follow-up studies are warranted to better understand their dynamic relationships at different stages of the COVID-19 pandemic and to monitor whether social media exposure during the crisis would lead to PTSD in the long run. Other personal resources, such as information deficiency as well as positive and negative affect, may also serve as mediators between social media use and mental health. In addition, other mental and emotional statuses, such as anxiety, can be induced by the false, fearful, and anxiety-increasing messages—due to politicization, rumination, sensationalizing, or catastrophizing—spread by social media, and can explain the development of depression and suicidal ideation [48]. Pervasive uncertainty and hopelessness increased by repeated exposures to online information related to the health crisis may also be a robust predictor of suicidal ideation and suicide, especially for vulnerable groups (eg, people who need ongoing mental health care) [49]. These potential mediators should be explored in future work.

On the other hand, social media use might indirectly reduce depression because it can provide opportunities to maintain and enhance interpersonal resources (eg, reduced social loneliness) by using SNSs, such as Facebook, WeChat, and WhatsApp, during the COVID-19 pandemic isolation. This result provides preliminary empirical evidence for the assertion of recently published commentaries [50]. However, such mediation effects might vary across age groups. We found that social media use might only benefit older adults' mental health by ameliorating their social loneliness, as the negative direct and indirect effects of social media use on depressive symptoms through social loneliness were statistically significant among older adults but not among younger adults. Consistently, a study by Cotten et al, which was conducted among retired residents, estimated that internet use reduced depression (CESD-8 score  $\geq 4$ ) by about 30% among this older group [51]; in addition, van Ingen et al found that social media use was predictive of social loneliness among older adults [52]. The age differences may be due to the fact that for younger people, social media is the "real" and default mode of social networks, which is less likely to change because of the COVID-19 pandemic. However, older adults might have taken up social media because of the COVID-19 pandemic—or the 2019-2020 social movement in Hong Kong—and that would have a more dynamic implication for older adults than for younger adults. The life span theory of selective optimization with compensation [53] can also be used to explain such age differences. This theory suggests that older people may experience various age-related losses, including those in social reserves [54]. Thus, social media use may be a particularly useful strategy that older adults can use to compensate for reduced mobility and social connection and that can contribute to their own successful aging and well-being [55]. Social media use may help to gain other interpersonal and

social resources, such as social support, timely health communication, and access to and utilization of technology-based health care services, which may explain the relationship between social media use and mental health.

Unexpectedly, social loneliness was not a significant mediator between social media use and suicidal ideation because it was not significantly associated with suicidal ideation. Inconsistently, previous studies found that loneliness and social connection were significant interpersonal factors of suicidal ideation [23,24]. The insignificant association in our study may be because the lack of social networks during the COVID-19 pandemic isolation has been seen as normal, which may temporally mitigate its harmful effect on hopelessness and suicidal ideation. However, given that social connection is a basic human psychological need [56], the long-term effects of social loneliness on suicidal ideation should be investigated.

### Implications

The positive mediation effect of PTSD symptoms among younger and older people and the negative mediation effect of social loneliness among older people suggest that social media use may have both beneficial and harmful effects on mental health during the COVID-19 pandemic, and that age plays a significant role. Notably, the mediation effect of PTSD symptoms was larger than that of social loneliness. This is consistent with the principle of the COR theory, in that resource loss is disproportionately more salient than resource gain [20]. The effect sizes of both mediation effects were relatively small. Hence, the results should be interpreted with caution. Nevertheless, these findings highlight the importance of further exploration of underlying mechanisms in understanding the complex relationship between social media use and mental health during different times across the life span and in different social contexts.

Such results have important practical and political implications. First, the high prevalence of mental health problems during the COVID-19 pandemic is a significant public health concern, and high-risk groups (eg, younger people) need particular attention from health care service providers. From a public health perspective, there are effective mental health interventions (eg, cognitive behavioral therapy and mindfulness-based interventions) available, which can be delivered via the internet during the COVID-19 pandemic isolation. Second, since the COVID-19 pandemic might persist and a digital lifestyle could become inevitable, it is important to understand the psychological mechanisms that may explain how digital technology users and nonusers may be different in psychosocial status and mental health. Our studied psychosocial mediators can be modified by interventions and can be used to guide prevention programs for mental health problems. For example, health education programs and public health strategies are recommended to enhance awareness of digital literacy, strategic social media use, and potential harms of social media use in the general public to reduce their trauma-related stress. A large-scale online relaxation training program is also feasible to help the general public manage their trauma-related stress [57,58]. Efforts at the environmental, political, and structural levels, such as timely and accurate information of the pandemic from official



sources (eg, local health agencies and the WHO), may also help to reduce individuals' stress and panic responses to the COVID-19 pandemic. It is imperative that trusted sources are available to provide risk assessments and recommendations for the general public [59]. Last but not least, promoting healthy use of social media among older people may be particularly beneficial for their social and mental well-being. This population has been vulnerable during the COVID-19 pandemic isolation. Community services should be provided to teach older adults how to use new technology. Policy makers should also pay attention to the potential digital inequality and inequity between generations and should improve accessibility of social media for the older generations.

### Limitations and Future Research

This study has several limitations. First, it was cross-sectional in nature. It is plausible that people with the greatest concerns and depressive symptoms may be more likely to seek out media coverage of the event. Longitudinal studies to monitor the trajectories of social media use and psychological responses are warranted. Second, we recruited the participants via landline telephone numbers, and this sampling method might exclude those without landline telephones or those who were not at home during the survey period (eg, younger adults who are more likely to use mobile phones and less likely to have landline telephones). Thus, this sampling method might also have

influenced the representativeness of the sample. Third, this study only focused on the use of SNSs that people use to build social networks or social relationships with other people. We did not investigate the content and functions of the SNSs in this study, or those of other types of SNSs, that may cause different psychological responses to the COVID-19 pandemic [5]. Future studies should investigate these domains of social media use to better understand its impacts on mental health during the COVID-19 pandemic. Fourth, this study used self-reported measures. Thus, the results might be subject to social desirability or recall bias. Fifth, we did not look at other mental health variables, such as anxiety, which may play a role in the mechanisms analyzed in this study. Last but not least, we used item 9 of the PHQ-9 to measure suicidal ideation. Future studies need to validate the results using well-validated scales of suicidal ideation, such as the Suicidal Ideation Questionnaire.

### Conclusions

The findings suggest that social media may be a "double-edged sword" for psychosocial well-being during the COVID-19 pandemic and its roles vary across age groups. The mediators identified in this study should be further validated through qualitative inquiry and longitudinal cohort studies and can be addressed by psychological interventions to prevent severe mental health problems.

### Authors' Contributions

XY conceived the research questions, conducted the statistical analysis, drafted the manuscript, and supervised the project's implementation. XY, BY, and SW designed this study, assembled the team of collaborators, and gave comments regarding the intellectual content of the manuscript. All authors assisted in questionnaire design, data collection, and data interpretation, and gave comments regarding the intellectual content of the manuscript.

### Conflicts of Interest

None declared.

### References

1. Wong SY, Kwok KO, Chan FK. What can countries learn from Hong Kong's response to the COVID-19 pandemic? *CMAJ* 2020 May 11;192(19):E511-E515 [FREE Full text] [doi: [10.1503/cmaj.200563](https://doi.org/10.1503/cmaj.200563)] [Medline: [32332040](https://pubmed.ncbi.nlm.nih.gov/32332040/)]
2. Quarantine and isolation. Centers for Disease Control and Prevention. URL: <https://www.cdc.gov/quarantine/index.html> [accessed 2021-03-12]
3. Coronavirus Research | March 2020 Release 3: Multi-market research. London, UK: GlobalWebIndex; 2020. URL: [https://www.globalwebindex.com/hubfs/1.%20Coronavirus%20Research%20PDFs/GWI%20coronavirus%20findings%20March%202020%20-%20Multi-Market%20data%20\(Release%203\).pdf](https://www.globalwebindex.com/hubfs/1.%20Coronavirus%20Research%20PDFs/GWI%20coronavirus%20findings%20March%202020%20-%20Multi-Market%20data%20(Release%203).pdf) [accessed 2021-03-12]
4. Snider M. Video games can be a healthy social pastime during coronavirus pandemic. *USA Today*. 2020 Mar 28. URL: <https://www.usatoday.com/story/tech/gaming/2020/03/28/video-games-whos-prescription-solace-during-coronavirus-pandemic/2932976001/> [accessed 2021-03-12]
5. Chao M, Xue D, Liu T, Yang H, Hall BJ. Media use and acute psychological outcomes during COVID-19 outbreak in China. *J Anxiety Disord* 2020 Aug;74:102248 [FREE Full text] [doi: [10.1016/j.janxdis.2020.102248](https://doi.org/10.1016/j.janxdis.2020.102248)] [Medline: [32505918](https://pubmed.ncbi.nlm.nih.gov/32505918/)]
6. Riehm KE, Holingue C, Kalb LG, Bennett D, Kapteyn A, Jiang Q, et al. Associations between media exposure and mental distress among US adults at the beginning of the COVID-19 pandemic. *Am J Prev Med* 2020 Nov;59(5):630-638 [FREE Full text] [doi: [10.1016/j.amepre.2020.06.008](https://doi.org/10.1016/j.amepre.2020.06.008)] [Medline: [33011008](https://pubmed.ncbi.nlm.nih.gov/33011008/)]
7. Ni MY, Yang L, Leung CMC, Li N, Yao XI, Wang Y, et al. Mental health, risk factors, and social media use during the COVID-19 epidemic and cordon sanitaire among the community and health professionals in Wuhan, China: Cross-sectional survey. *JMIR Ment Health* 2020 May 12;7(5):e19009 [FREE Full text] [doi: [10.2196/19009](https://doi.org/10.2196/19009)] [Medline: [32365044](https://pubmed.ncbi.nlm.nih.gov/32365044/)]

8. Gao J, Zheng P, Jia Y, Chen H, Mao Y, Chen S, et al. Mental health problems and social media exposure during COVID-19 outbreak. *PLoS One* 2020;15(4):e0231924 [FREE Full text] [doi: [10.1371/journal.pone.0231924](https://doi.org/10.1371/journal.pone.0231924)] [Medline: [32298385](https://pubmed.ncbi.nlm.nih.gov/32298385/)]
9. Iob E, Steptoe A, Fancourt D. Abuse, self-harm and suicidal ideation in the UK during the COVID-19 pandemic. *Br J Psychiatry* 2020 Oct;217(4):543-546 [FREE Full text] [doi: [10.1192/bjp.2020.130](https://doi.org/10.1192/bjp.2020.130)] [Medline: [32654678](https://pubmed.ncbi.nlm.nih.gov/32654678/)]
10. Pittman M, Reich B. Social media and loneliness: Why an Instagram picture may be worth more than a thousand Twitter words. *Comput Human Behav* 2016 Sep;62:155-167. [doi: [10.1016/j.chb.2016.03.084](https://doi.org/10.1016/j.chb.2016.03.084)]
11. Halston A, Iwamoto D, Junker M, Chun H. Social media and loneliness. *Int J Psychol Stud* 2019 Jul 13;11(3):27. [doi: [10.5539/ijps.v11n3p27](https://doi.org/10.5539/ijps.v11n3p27)]
12. Sohn Y, Woo S, Jo D, Yang E. The role of the quality of college - based relationship on social media in college - to - work transition of Korean college students: The longitudinal examination of intimacy on social media, social capital, and loneliness. *Jpn Psychol Res* 2018 Oct 25;61(4):236-248. [doi: [10.1111/jpr.12234](https://doi.org/10.1111/jpr.12234)]
13. Shah SGS, Nogueras D, van Woerden HC, Kiparoglou V. The COVID-19 pandemic: A pandemic of lockdown loneliness and the role of digital technology. *J Med Internet Res* 2020 Nov 05;22(11):e22287 [FREE Full text] [doi: [10.2196/22287](https://doi.org/10.2196/22287)] [Medline: [33108313](https://pubmed.ncbi.nlm.nih.gov/33108313/)]
14. Liu BF, Kim S. How organizations framed the 2009 H1N1 pandemic via social and traditional media: Implications for US health communicators. *Public Relat Rev* 2011 Sep;37(3):233-244. [doi: [10.1016/j.pubrev.2011.03.005](https://doi.org/10.1016/j.pubrev.2011.03.005)]
15. Zhou X, Snoswell CL, Harding LE, Bambling M, Edirippulige S, Bai X, et al. The role of telehealth in reducing the mental health burden from COVID-19. *Telemed J E Health* 2020 Apr;26(4):377-379. [doi: [10.1089/tmj.2020.0068](https://doi.org/10.1089/tmj.2020.0068)] [Medline: [32202977](https://pubmed.ncbi.nlm.nih.gov/32202977/)]
16. Depoux A, Martin S, Karafillakis E, Preet R, Wilder-Smith A, Larson H. The pandemic of social media panic travels faster than the COVID-19 outbreak. *J Travel Med* 2020 May 18;27(3):taaa031 [FREE Full text] [doi: [10.1093/jtm/taaa031](https://doi.org/10.1093/jtm/taaa031)] [Medline: [32125413](https://pubmed.ncbi.nlm.nih.gov/32125413/)]
17. Kramer ADI, Guillory JE, Hancock JT. Experimental evidence of massive-scale emotional contagion through social networks. *Proc Natl Acad Sci U S A* 2014 Jun 17;111(24):8788-8790 [FREE Full text] [doi: [10.1073/pnas.1320040111](https://doi.org/10.1073/pnas.1320040111)] [Medline: [24889601](https://pubmed.ncbi.nlm.nih.gov/24889601/)]
18. Thompson RR, Jones NM, Holman EA, Silver RC. Media exposure to mass violence events can fuel a cycle of distress. *Sci Adv* 2019 Apr;5(4):eaav3502 [FREE Full text] [doi: [10.1126/sciadv.aav3502](https://doi.org/10.1126/sciadv.aav3502)] [Medline: [31001584](https://pubmed.ncbi.nlm.nih.gov/31001584/)]
19. Ahmad AR, Murad HR. The impact of social media on panic during the COVID-19 pandemic in Iraqi Kurdistan: Online questionnaire study. *J Med Internet Res* 2020 May 19;22(5):e19556 [FREE Full text] [doi: [10.2196/19556](https://doi.org/10.2196/19556)] [Medline: [32369026](https://pubmed.ncbi.nlm.nih.gov/32369026/)]
20. Hobfoll SE. Conservation of resources: A new attempt at conceptualizing stress. *Am Psychol* 1989;44(3):513-524. [doi: [10.1037/0003-066x.44.3.513](https://doi.org/10.1037/0003-066x.44.3.513)]
21. Feldman DB, Davidson OB, Margalit M. Personal resources, hope, and achievement among college students: The conservation of resources perspective. *J Happiness Stud* 2014 Feb 25;16(3):543-560. [doi: [10.1007/s10902-014-9508-5](https://doi.org/10.1007/s10902-014-9508-5)]
22. van der Velden PG, Setti I, van der Meulen E, Das M. Does social networking sites use predict mental health and sleep problems when prior problems and loneliness are taken into account? A population-based prospective study. *Comput Human Behav* 2019 Apr;93:200-209. [doi: [10.1016/j.chb.2018.11.047](https://doi.org/10.1016/j.chb.2018.11.047)]
23. Zhang D, Wang R, Zhao X, Zhang J, Jia J, Su Y, et al. Role of resilience and social support in the relationship between loneliness and suicidal ideation among Chinese nursing home residents. *Aging Ment Health* 2020 Jun 30:1-11. [doi: [10.1080/13607863.2020.1786798](https://doi.org/10.1080/13607863.2020.1786798)] [Medline: [32602736](https://pubmed.ncbi.nlm.nih.gov/32602736/)]
24. Teo AR, Marsh HE, Forsberg CW, Nicolaidis C, Chen JJ, Newsom J, et al. Loneliness is closely associated with depression outcomes and suicidal ideation among military veterans in primary care. *J Affect Disord* 2018 Apr 01;230:42-49. [doi: [10.1016/j.jad.2018.01.003](https://doi.org/10.1016/j.jad.2018.01.003)] [Medline: [29407537](https://pubmed.ncbi.nlm.nih.gov/29407537/)]
25. Social media usage in Hong Kong. Hong Kong Legislative Council Secretariat. 2019. URL: <https://www.legco.gov.hk/research-publications/english/1920issh15-social-media-usage-in-hong-kong-20191212-e.pdf> [accessed 2021-03-12]
26. Leist AK. Social media use of older adults: A mini-review. *Gerontology* 2013;59(4):378-384 [FREE Full text] [doi: [10.1159/000346818](https://doi.org/10.1159/000346818)] [Medline: [23594915](https://pubmed.ncbi.nlm.nih.gov/23594915/)]
27. Berryman C, Ferguson CJ, Negy C. Social media use and mental health among young adults. *Psychiatr Q* 2018 Jun;89(2):307-314. [doi: [10.1007/s11126-017-9535-6](https://doi.org/10.1007/s11126-017-9535-6)] [Medline: [29090428](https://pubmed.ncbi.nlm.nih.gov/29090428/)]
28. Perrin A. Social media usage: 2005-2015. Pew Research Center. Washington, DC: Pew Research Center; 2015 Oct 08. URL: <https://www.pewresearch.org/internet/2015/10/08/social-networking-usage-2005-2015/> [accessed 2021-03-12]
29. Cellini N, Canale N, Mioni G, Costa S. Changes in sleep pattern, sense of time and digital media use during COVID-19 lockdown in Italy. *J Sleep Res* 2020 Aug;29(4):e13074 [FREE Full text] [doi: [10.1111/jsr.13074](https://doi.org/10.1111/jsr.13074)] [Medline: [32410272](https://pubmed.ncbi.nlm.nih.gov/32410272/)]
30. Sun Y, Li Y, Bao Y, Meng S, Sun Y, Schumann G, et al. Brief report: Increased addictive internet and substance use behavior during the COVID-19 pandemic in China. *Am J Addict* 2020 Jul;29(4):268-270 [FREE Full text] [doi: [10.1111/ajad.13066](https://doi.org/10.1111/ajad.13066)] [Medline: [32500608](https://pubmed.ncbi.nlm.nih.gov/32500608/)]
31. Hansen M, Andersen TE, Armour C, Elklit A, Palic S, Mackrill T. PTSD-8: A short PTSD inventory. *Clin Pract Epidemiol Ment Health* 2010 Sep 28;6:101-108 [FREE Full text] [doi: [10.2174/1745017901006010101](https://doi.org/10.2174/1745017901006010101)] [Medline: [21253461](https://pubmed.ncbi.nlm.nih.gov/21253461/)]

32. Leung GTY, de Jong Gierveld J, Lam LCW. Validation of the Chinese translation of the 6-item De Jong Gierveld Loneliness Scale in elderly Chinese. *Int Psychogeriatr* 2008 Jul 1;20(06):1262. [doi: [10.1017/s1041610208007552](https://doi.org/10.1017/s1041610208007552)]
33. Amtmann D, Kim J, Chung H, Bamer AM, Askew RL, Wu S, et al. Comparing CESD-10, PHQ-9, and PROMIS depression instruments in individuals with multiple sclerosis. *Rehabil Psychol* 2014 May;59(2):220-229 [FREE Full text] [doi: [10.1037/a0035919](https://doi.org/10.1037/a0035919)] [Medline: [24661030](https://pubmed.ncbi.nlm.nih.gov/24661030/)]
34. Campo Arias A, Díaz Martínez LA, Rueda Jaimes GE, Cadena Afanador LDP, Hernández NL. Psychometric properties of the CES-D scale among Colombian adults from the general population. *Rev Colomb Psiquiatr* 2007;36(4):664-674 [FREE Full text]
35. Björgvinsson T, Kertz SJ, Bigda-Peyton JS, McCoy KL, Aderka IM. Psychometric properties of the CES-D-10 in a psychiatric sample. *Assessment* 2013 Aug;20(4):429-436. [doi: [10.1177/1073191113481998](https://doi.org/10.1177/1073191113481998)] [Medline: [23513010](https://pubmed.ncbi.nlm.nih.gov/23513010/)]
36. Cheung C, Bagley C. Validating an American scale in Hong Kong: The Center for Epidemiological Studies Depression Scale (CES-D). *J Psychol* 1998 Mar;132(2):169-186. [doi: [10.1080/00223989809599157](https://doi.org/10.1080/00223989809599157)] [Medline: [9529665](https://pubmed.ncbi.nlm.nih.gov/9529665/)]
37. Kroenke K, Spitzer RL. The PHQ-9: A new depression diagnostic and severity measure. *Psychiatr Ann* 2002 Sep;32(9):509-515. [doi: [10.3928/0048-5713-20020901-06](https://doi.org/10.3928/0048-5713-20020901-06)]
38. Tsai F, Huang Y, Liu H, Huang K, Huang Y, Liu S. Patient health questionnaire for school-based depression screening among Chinese adolescents. *Pediatrics* 2014 Feb;133(2):e402-e409. [doi: [10.1542/peds.2013-0204](https://doi.org/10.1542/peds.2013-0204)] [Medline: [24446447](https://pubmed.ncbi.nlm.nih.gov/24446447/)]
39. Youth IDEAS. Encouraging the Employment of Seniors. Hong Kong, China: The Hong Kong Federation of Youth Groups; 2018. URL: [https://yrc.hkfyg.org.hk/wp-content/uploads/sites/56/2018/06/YI031\\_powerpoint.pdf](https://yrc.hkfyg.org.hk/wp-content/uploads/sites/56/2018/06/YI031_powerpoint.pdf) [accessed 2021-03-12]
40. Lee S, Guo W, Tsang A, Mak AD, Wu J, Ng KL, et al. Evidence for the 2008 economic crisis exacerbating depression in Hong Kong. *J Affect Disord* 2010 Oct;126(1-2):125-133. [doi: [10.1016/j.jad.2010.03.007](https://doi.org/10.1016/j.jad.2010.03.007)] [Medline: [20381157](https://pubmed.ncbi.nlm.nih.gov/20381157/)]
41. Qiu J, Shen B, Zhao M, Wang Z, Xie B, Xu Y. A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: Implications and policy recommendations. *Gen Psychiatr* 2020;33(2):e100213 [FREE Full text] [doi: [10.1136/gpsych-2020-100213](https://doi.org/10.1136/gpsych-2020-100213)] [Medline: [32215365](https://pubmed.ncbi.nlm.nih.gov/32215365/)]
42. Cheng C, Huang J, Liang B. Psychological health diathesis assessment system: A nationwide survey of resilient trait scale for Chinese adults. *Stud Psychol Behav* 2014;12(6):735-742.
43. Roberts T, Miguel Esponda G, Krupchanka D, Shidhaye R, Patel V, Rathod S. Factors associated with health service utilisation for common mental disorders: A systematic review. *BMC Psychiatry* 2018 Aug 22;18(1):262 [FREE Full text] [doi: [10.1186/s12888-018-1837-1](https://doi.org/10.1186/s12888-018-1837-1)] [Medline: [30134869](https://pubmed.ncbi.nlm.nih.gov/30134869/)]
44. Kramer ADI, Guillory JE, Hancock JT. Experimental evidence of massive-scale emotional contagion through social networks. *Proc Natl Acad Sci U S A* 2014 Jun 17;111(24):8788-8790 [FREE Full text] [doi: [10.1073/pnas.1320040111](https://doi.org/10.1073/pnas.1320040111)] [Medline: [24889601](https://pubmed.ncbi.nlm.nih.gov/24889601/)]
45. Hobfoll SE. Social and psychological resources and adaptation. *Rev Gen Psychol* 2002 Dec 01;6(4):307-324. [doi: [10.1037/1089-2680.6.4.307](https://doi.org/10.1037/1089-2680.6.4.307)]
46. Holman EA, Garfin DR, Silver RC. Media's role in broadcasting acute stress following the Boston Marathon bombings. *Proc Natl Acad Sci U S A* 2014 Jan 07;111(1):93-98 [FREE Full text] [doi: [10.1073/pnas.1316265110](https://doi.org/10.1073/pnas.1316265110)] [Medline: [24324161](https://pubmed.ncbi.nlm.nih.gov/24324161/)]
47. Fung IC, Tse ZTH, Cheung C, Miu AS, Fu K. Ebola and the social media. *Lancet* 2014 Dec;384(9961):2207. [doi: [10.1016/s0140-6736\(14\)62418-1](https://doi.org/10.1016/s0140-6736(14)62418-1)]
48. Pahayahay A, Khalili-Mahani N. What media helps, what media hurts: A mixed methods survey study of coping with COVID-19 using the media repertoire framework and the appraisal theory of stress. *J Med Internet Res* 2020 Aug 06;22(8):e20186 [FREE Full text] [doi: [10.2196/20186](https://doi.org/10.2196/20186)] [Medline: [32701459](https://pubmed.ncbi.nlm.nih.gov/32701459/)]
49. Thakur V, Jain A. COVID 2019-suicides: A global psychological pandemic. *Brain Behav Immun* 2020 Aug;88:952-953 [FREE Full text] [doi: [10.1016/j.bbi.2020.04.062](https://doi.org/10.1016/j.bbi.2020.04.062)] [Medline: [32335196](https://pubmed.ncbi.nlm.nih.gov/32335196/)]
50. Orben A, Tomova L, Blakemore S. The effects of social deprivation on adolescent development and mental health. *Lancet Child Adolesc Health* 2020 Aug;4(8):634-640. [doi: [10.1016/s2352-4642\(20\)30186-3](https://doi.org/10.1016/s2352-4642(20)30186-3)]
51. Cotten SR, Ford G, Ford S, Hale TM. Internet use and depression among retired older adults in the United States: A longitudinal analysis. *J Gerontol B Psychol Sci Soc Sci* 2014 Sep;69(5):763-771. [doi: [10.1093/geronb/gbu018](https://doi.org/10.1093/geronb/gbu018)] [Medline: [24671896](https://pubmed.ncbi.nlm.nih.gov/24671896/)]
52. van Ingen E, Rains SA, Wright KB. Does social network site use buffer against well-being loss when older adults face reduced functional ability? *Comput Human Behav* 2017 May;70:168-177. [doi: [10.1016/j.chb.2016.12.058](https://doi.org/10.1016/j.chb.2016.12.058)]
53. Baltes PB, Baltes MM. Psychological perspectives on successful aging: The model of selective optimization with compensation. In: Baltes PB, Baltes MM, editors. *Successful Aging: Perspectives from the Behavioral Sciences*. Cambridge, UK: Cambridge University Press; 1990:1-34.
54. Freund AM, Baltes PB. Selection, optimization, and compensation as strategies of life management: Correlations with subjective indicators of successful aging. *Psychol Aging* 1998;13(4):531-543. [doi: [10.1037/0882-7974.13.4.531](https://doi.org/10.1037/0882-7974.13.4.531)]
55. Fang Y, Chau AKC, Wong A, Fung HH, Woo J. Information and communicative technology use enhances psychological well-being of older adults: The roles of age, social connectedness, and frailty status. *Aging Ment Health* 2018 Nov;22(11):1516-1524. [doi: [10.1080/13607863.2017.1358354](https://doi.org/10.1080/13607863.2017.1358354)] [Medline: [28777010](https://pubmed.ncbi.nlm.nih.gov/28777010/)]
56. Vansteenkiste M, Ryan RM, Soenens B. Basic psychological need theory: Advancements, critical themes, and future directions. *Motiv Emot* 2020 Jan 21;44(1):1-31. [doi: [10.1007/s11031-019-09818-1](https://doi.org/10.1007/s11031-019-09818-1)]

57. Ahtinen A, Mattila E, Väikkynen P, Kaipainen K, Vanhala T, Ermes M, et al. Mobile mental wellness training for stress management: Feasibility and design implications based on a one-month field study. *JMIR Mhealth Uhealth* 2013 Jul 10;1(2):e11 [FREE Full text] [doi: [10.2196/mhealth.2596](https://doi.org/10.2196/mhealth.2596)] [Medline: [25100683](https://pubmed.ncbi.nlm.nih.gov/25100683/)]
58. Brown JSL, Cochrane R, Hancox T. Large-scale health promotion stress workshops for the general public: A controlled evaluation. *Behav Cogn Psychother* 2000 Apr 01;28(2):139-151. [doi: [10.1017/s1352465800001053](https://doi.org/10.1017/s1352465800001053)]
59. Lachlan KA, Spence PR, Lin X, Najarian K, Del Greco M. Social media and crisis management: CERC, search strategies, and Twitter content. *Comput Human Behav* 2016 Jan;54:647-652. [doi: [10.1016/j.chb.2015.05.027](https://doi.org/10.1016/j.chb.2015.05.027)]

## Abbreviations

**CESD-10:** 10-item Center for Epidemiologic Studies Depression Scale  
**CFI:** comparative fit index  
**COR:** conservation of resources  
**DSM-IV:** Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition  
**NNFI:** nonnormed fit index  
**PHQ-9:** 9-item Patient Health Questionnaire  
**PTSD:** posttraumatic stress disorder  
**PTSD-8:** 8-item Posttraumatic Stress Disorder scale  
**RMSEA:** root mean square error of approximation  
**SEM:** structural equation modeling  
**SNS:** social networking site  
**WHO:** World Health Organization

*Edited by T Sanchez; submitted 28.09.20; peer-reviewed by K Kryszynska, J Han; comments to author 06.11.20; revised version received 27.11.20; accepted 02.04.21; published 25.05.21.*

*Please cite as:*

*Yang X, Yip BHK, Mak ADP, Zhang D, Lee EKP, Wong SYS*

*The Differential Effects of Social Media on Depressive Symptoms and Suicidal Ideation Among the Younger and Older Adult Population in Hong Kong During the COVID-19 Pandemic: Population-Based Cross-sectional Survey Study*

*JMIR Public Health Surveill* 2021;7(5):e24623

URL: <https://publichealth.jmir.org/2021/5/e24623>

doi: [10.2196/24623](https://doi.org/10.2196/24623)

PMID: [33835937](https://pubmed.ncbi.nlm.nih.gov/33835937/)

©Xue Yang, Benjamin H K Yip, Arthur D P Mak, Dexing Zhang, Eric K P Lee, Samuel Y S Wong. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 25.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# The Association of Unfairness with Mental and Physical Health in a Multiethnic Sample of Adults: Cross-sectional Study

Ken Resnicow<sup>1,2</sup>, PhD; Minal Patel<sup>1,3</sup>, MPH, PhD; Molly Green<sup>1</sup>, MPH; Alyssa Smith<sup>1</sup>, MPH; Elizabeth Bacon<sup>2</sup>, MPH; Stefanie Goodell<sup>2</sup>, BS; Dylan Kilby<sup>1</sup>, MPH; Madiha Tariq<sup>4</sup>, MPH; Asraa Alhawli<sup>4</sup>, BS; Nadia Syed<sup>4</sup>, MPH; Jennifer Griggs<sup>3</sup>, MPH, MD; Matthew Stiffler<sup>4</sup>, PhD

<sup>1</sup>Department of Health Behavior & Health Education, University of Michigan School of Public Health, Ann Arbor, MI, United States

<sup>2</sup>Center for Health Communications Research, Rogel Cancer Center, University of Michigan, Ann Arbor, MI, United States

<sup>3</sup>Rogel Cancer Center, University of Michigan, Ann Arbor, MI, United States

<sup>4</sup>Arab Community Center for Economic and Social Services, Dearborn, MI, United States

**Corresponding Author:**

Ken Resnicow, PhD

Department of Health Behavior & Health Education

University of Michigan School of Public Health

109 Observatory Street

Room 3867 SPH I

Ann Arbor, MI, 48109

United States

Phone: 1 734 764 9494

Email: [kresnic@umich.edu](mailto:kresnic@umich.edu)

## Abstract

**Background:** Two psychosocial constructs that have shown consistent associations with negative health outcomes are discrimination and perceived unfairness.

**Objective:** The current analyses report the effects of discrimination and unfairness on medical, psychological, and behavioral outcomes from a recent cross-sectional survey conducted in a multiethnic sample of adults in Michigan.

**Methods:** A cross-section survey was collected using multiple approaches: community settings, telephone-listed sample, and online panel. Unfairness was assessed with a single-item previously used in the Whitehall study, and everyday discrimination was assessed with the Williams 9-item scale. Outcomes included mental health symptoms, past-month cigarette use, past-month alcohol use, past-month marijuana use, lifetime pain medication use, and self-reported medical history.

**Results:** A total of 2238 usable surveys were collected. In bivariate analyses, higher unfairness values were significantly associated with lower educational attainment, lower age, lower household income, and being unmarried. The highest unfairness values were observed for African American and multiracial respondents followed by Middle Eastern or North African participants. Unfairness was significantly related to worse mental health functioning, net adjustment for sociodemographic variables, and everyday discrimination. Unfairness was also related to self-reported history of depression and high blood pressure although, after including everyday discrimination in the model, only the association with depression remained significant. Unfairness was significantly related to 30-day marijuana use, 30-day cigarette use, and lifetime opiate use.

**Conclusions:** Our findings of a generally harmful effect of perceived unfairness on health are consistent with prior studies. Perceived unfairness may be one of the psychological pathways through which discrimination negatively impacts health. Future studies examining the relationships we observed using longitudinal data and including more objective measures of behavior and health status are needed to confirm and extend our findings.

(*JMIR Public Health Surveill* 2021;7(5):e26622) doi:[10.2196/26622](https://doi.org/10.2196/26622)

**KEYWORDS**

unfairness; discrimination; health disparities; social determinants; substance use; mental health; physical health; disparity; ethnicity; health outcome; behavior; outcome; cross-sectional; survey

## Introduction

There has been considerable interest on the part of researchers and policy makers in understanding the social, economic, psychological, and behavioral factors that account for the many health disparities that are evident in the United States and the world [1-5]. Although socioeconomic factors are the most commonly examined drivers of disparities, social and interpersonal factors have also received considerable attention [3,6-9]. Two psychosocial constructs that have shown consistent associations with health outcomes are discrimination and perceived unfairness. The former has been extensively examined in both the United States [3,9-13] and globally [8,9,14], while studies of unfairness and health have been limited to a handful of studies in the United Kingdom and the Netherlands [15-17]. No studies have reported the joint effects of these 2 constructs.

In perhaps the first published study on unfairness, DeVogli et al [16] used the prospective data of 8298 individuals from The Whitehall II study, who were civil servants originally ages 35-55 at the study onset in 1985 through 1998. Baseline unfairness data were collected between 1991 and 1993 (during phase 3 of the study), and respondents were tracked for health outcomes on average 11 years through 2003 to 2004 (phase 7 of the study). The authors found that their single-item unfairness measure was associated with higher odds of clinically verified heart disease as well as worse physical and mental functioning, with the latter being assessed with the 36-Item Short Form Survey (SF-36) questionnaire [18,19] adjusted for sociodemographic and other risk factors. Unfairness was also positively related with being female, obese, and less physically active. Higher unfairness was associated with higher cigarette use but also higher rates of alcohol abstinence.

In a second study [15], again based on the Whitehall study, phase 3 data on unfairness were used to predict cardiovascular risk factors, over the subsequent 6 years through phase 5. The authors found that baseline unfairness was significantly associated with higher rates of low serum high-density lipoprotein, high serum triglycerides, hypertension, high fasting blood glucose, and elevated waist circumference.

A third study, conducted in the Netherlands, used a 9-item perception of unfairness scale, administered in 2008 [17]. Of those completing this unfairness questionnaire, 1282 adults also completed the SF-36 [18,19] in 2003, 2008, and 2010, which was used to classify respondents as experiencing either physical or mental health decline between 2003 and 2010 and between 2008 and 2010, with unfairness scores from 2008 being used as the predictor. In general, higher scores on unfairness were associated with significantly higher odds of both physical and mental health decline. Higher scores on the unfairness measure were also associated with lower socioeconomic position (eg, a composite of income and education).

The health effects of discrimination have been reported in hundreds of studies. One measure of discrimination that has been particularly popular is the Everyday Discrimination Scale developed by Williams and others [3,10,11]. The Everyday Discrimination Scale focuses on what are sometimes referred to as microaggressions, smaller acts of discrimination, racism,

or prejudice; for example, the scale includes items such as “people act as if you are inferior,” “you are treated with less respect than others,” and “people act as if you are dishonest.” Everyday discrimination is distinguished from more major experiences of discrimination, such as being unfairly fired from a job, maltreated by the police, or denied a bank loan.

The everyday discrimination scale has been associated with a wide range of adverse mental and physical health outcomes including depression, anxiety, distress [8,9,12-14], and overall well-being [9,13], breast cancer among women under the age of 50 years [20], and high blood pressure, although the relationship with the latter is often conditional on other variables [9]. Some studies have used unfair treatment as the measure of discrimination [21], although the 2 constructs likely represent different psychological and social phenomena [22]. One distinction between the 2 constructs is that everyday discrimination measures the occurrence of events, whereas unfairness can be thought of as more related to the perception of such events. Additionally, while discrimination measures multiple potential events, unfairness in the Whitehall studies and in the current investigation was measured with a single global item.

No study has reported the relationship of both discrimination and unfairness with either mental or physical health outcomes. The current analyses from a recent cross-sectional survey conducted in a multiethnic sample of adults in the state of Michigan provide insight into the effects of discrimination and unfairness on medical, psychological, and behavioral outcomes.

## Methods

### Measures

#### *Independent Variables*

##### **Unfairness**

Unfairness was assessed with a single-item from the Whitehall study [15,16], which was worded as follows: “I often have the feeling that I am being treated unfairly.” Participants rated their response on a 6-point scale (1, strongly disagree; 2, moderately disagree; 3, slightly disagree; 4, slightly agree; 5, moderately agree; and 6, strongly agree). We analyzed unfairness both as a continuous variable and as a categorical variable recoded into 3 levels low (responses 1 and 2), medium (responses 3 and 4), and high (responses 5 and 6) to facilitate data presentation.

##### **Discrimination**

We used the 9-item Everyday Discrimination scale developed by Williams [3,11]. Respondents indicated how often they experience 9 types of discrimination with responses ranging from “Never” to “Almost Everyday.” We computed a mean across the 9 items, which resulted in a score range of 1-6. Respondents were required to answer at least 5 of the 9 items to be included in the analyses.

#### *Dependent Variables*

Mental health symptoms were assessed with the Patient Health Questionnaire-4 (PHQ-4) [23] which asks how often over the past 2 weeks participants have experienced the following

problems: little interest or pleasure in doing things; feeling down, depressed, or hopeless; feeling nervous, anxious, or on edge; and not being able to stop or control worrying. All items were answered with a 1-4 scale, with 4 being “not at all” and 1 being “nearly every day”. Higher scores are indicative of better mental health status. The Cronbach  $\alpha$  for the 4 items in our sample was .91.

Health behaviors assessed included current cigarette use, defined as consuming at least 100 cigarettes all time and having smoked on at least some days in the past month [24]; past month alcohol, defined as having consumed at least one drink of any alcoholic beverage at least once in the past 30 days [24]; past month marijuana, defined as any use in the past 30 days; lifetime pain medication, which was queried with an item from the 2017 Youth Risk Behavior Survey [25]: “During your life, how many times have you taken prescription pain medicine without a doctor’s prescription or differently than how a doctor told you

to use it? (Count drugs such as codeine, Vicodin, OxyContin, Hydrocodone, and Percocet.)” Use was considered more than 2 times in one’s lifetime.

Self-reported medical history was assessed by asking if the respondent had ever been diagnosed with cancer; diabetes or high blood sugar; high blood pressure or hypertension; depression; or a heart condition, such as heart attack, angina, or congestive heart failure. Each variable was answered with 0 (no) or 1 (yes).

Demographic variables assessed included age (collapsed into 4 groups: 18-35, 30-45, 45-65, and >65 years), household income (collapsed into 4 groups: under US \$10,000, US \$10,000 to US \$49,999, US \$50,000 to US \$99,999, and >US \$100,000), education (collapsed into 4 groups: high school or lower, some college, college graduate, graduate school or higher), gender, country of birth (United States vs not United States), and marital status (no or yes). These are presented in [Table 1](#).

**Table 1.** Sample demographics (N=2238).

Variable	Respondents, n (%)
<b>Gender</b>	
Male	726 (32.50)
Female	1508 (67.50)
<b>Education</b>	
High school or lower	558 (25.04)
Some college	690 (30.97)
College graduate	659 (29.58)
Graduate school	321 (14.41)
<b>Age (years)</b>	
18-35	566 (25.76)
30-45	493 (22.44)
45-65	881 (40.10)
> 65	257 (11.70)
<b>Income (US\$)</b>	
Under \$10,000	227 (10.79)
\$10,000 to \$49,999	887 (42.18)
\$50,000 to \$99,999	611 (29.05)
\$>100,000	378 (17.97)
<b>Born in the United States</b>	
Yes	1902 (85.29)
No	328 (14.71)
<b>Race</b>	
White	1183 (53.00)
African American	525 (23.52)
Middle Eastern	403 (18.06)
Multiracial	105 (4.70)
Other	16 (0.72)
<b>Marital status</b>	
Married/living as married	1134 (50.90)
Not married	1094 (49.10)
<b>Modality</b>	
Online	1415 (63.23)
Telephone	496 (22.16)
Paper	327 (14.61)

## Procedures

Surveys were collected in 2019 using multiple methodologies including community settings, telephone, and online panel. The community sample was a convenience sample, whereas the telephone and online sample was built to match the demographic representation of the University of Michigan Rogel Cancer Center catchment area.

## *Community Administration for Middle Eastern and North African Participants*

The Middle Eastern and North African (MENA) sample was collected at community settings across 3 Michigan counties that included 2 supermarkets frequented by the MENA community, 1 health clinic serving a predominantly Arab American population, 1 health clinic serving a predominantly Chaldean population, a state university with a high number of Arab American students, 4 mosques with a high proportion of Yemeni



and Lebanese worshippers, 2 Chaldean churches, and a recreation center frequented by Lebanese youth.

Participants were given the option of completing surveys using pen and paper or online forms (tablet provided), with or without assistance, in English or Arabic. For those opting to complete surveys at home, we provided a self-addressed stamped envelopes or a web address to complete the online version. Both paper and electronic surveys required active consent and testament that the respondent was over 18 and self-identified as Arab or Chaldean. Data collectors, many of whom were fluent in both English and Arabic, were trained in interviewing by study staff. Participants received a US \$25 gift card after completing their survey. A total of 406 participants were accrued through this method, 87 of whom completed their survey in Arabic.

### **Community Administration for White and African American Participants**

We distributed surveys at 5 community-based educational events sponsored by the University of Michigan Rogel Cancer Center. Participants were able to complete surveys using printed forms or online with provided tablets, and they received a US \$25 gift card after completing their survey. A total of 214 participants were accrued through this method.

### **Telephone**

The telephone survey, conducted by Harris Interactive Inc, used a quota sample to reach 501 adults who indicated that they were aged 18 years or over, living in zip codes serviced by the University of Michigan Rogel Cancer Center, and self-identified as either White/Caucasian or Black/African American. The survey, conducted in English, averaged about 23 minutes and consisted of 44 substantive questions and 18 demographic questions. The survey was fielded from May 1, 2019, to July 9, 2019.

Known landline and cell phone numbers were obtained from Dynata, formerly Survey Sampling International. Numbers were randomly selected from within identified zip codes. We oversampled (with a target of at least 40% of the final sample) African American participants by selecting telephone exchanges that were estimated to have an at least 50% African American population.

A maximum of 8 contacts were attempted for each number: the initial dialing attempt plus up to 7 subsequent dialing attempts. A US \$10 incentive was offered to the survey participants. The overall response rate was 9%: 8% for landline numbers and 9% from cell phone numbers. A total of 496 participants were accrued through this method, approximately half through landline and half through cell phone.

### **Online**

A quota sample was recruited via an online panel through a commercial survey research organization (Dynata), which maintains a demographically diverse web panel of people who opt in to taking selected surveys. Panel members who log on to Dynata's site are routed (in a randomized fashion) to available surveys based on their demographic characteristics and needs of open surveys. We provided specific county level quotas for

individuals aged 18-80 years in 40 Michigan counties served by the University of Michigan Rogel Cancer Center. We oversampled African American participants so that they would comprise at least 20% of the sample. Additional details about Dynata can be found at their website [26]. A total of 1122 participants were accrued through this method. It is possible that participants could have appeared in both the telephone and online panels; however, given the anonymous nature of the data collection and the fact they were conducted independently, we cannot determine how many might have been duplicated. Based on the number of participants available in the targeted zip codes and the number that completed the surveys, the likelihood is small.

### **Analyses**

We first present mean unfairness and discrimination values by sociodemographic variables (Table 2). For mental health symptoms, we present (labeled Model 1) linear regression results for the association of unfairness (trichotomized into low, medium, and high to facilitate data presentation) with mental health symptoms, adjusting for income, education, age, gender, and marital status (this is Model 1 referenced in Table 3, Table 4, and Table 5). We then present results (labeled Model 2) with discrimination added to the regression model (this is Model 2 referenced in Table 3, Table 4, and Table 5).

For health behaviors and medical history, we first report multivariate logistic regression (ORs and 95% CIs), using unfairness (trichotomized) as the primary independent variable, adjusting for income, education, age, gender, and marital status, and then we report a model adding discrimination (labeled Model 2).

### **Results**

A total of 2238 usable surveys were collected, of which two-thirds (n=1508) were completed by females. A little less than half (980/2228, 43.79%) had college or higher educational attainment, and about half were aged 45 or higher, married, and reported a household income above US \$50,000 per year. Most, (1902/2230, 85.29%), were born in the United States. About half (1183/2232, 53.00%) were White, 23.52% (2232/2238) were African American, 18.06% (403/2232) were MENA, and 4.70% (105/2232) were multiracial.

As shown in Table 2, the mean value for the unfairness item was 2.62 (SD 1.61), with a range of 1-6; meanwhile, the mean for everyday discrimination was 1.87 (SD 1.06) with a range of 1-6. The 2 variables were moderately correlated ( $r=0.54$ ;  $P<.001$ ).

In bivariate analyses, higher unfairness values were significantly associated with lower educational attainment, lower age, lower household income, and being unmarried. Birthplace was unrelated to unfairness. For race, the highest values were observed for African American and multiracial respondents followed by MENA respondents. White respondents reported the lowest values, and they were significantly lower than African American, multiracial, and MENA respondents in pairwise comparisons.

**Table 2.** Mean scores for unfairness and everyday discrimination by demographic variables.

Variable	Unfairness, mean (SD)	Everyday discrimination, mean (SD)
<b>Gender</b>		
Male	2.62 (1.66)	1.88 (1.12)
Female	2.63 (1.59)	1.87 (1.03)
<b>Education<sup>a</sup></b>		
High school or less	2.82 (1.67) <sup>b,c</sup>	1.97 (1.18) <sup>b,c</sup>
Some college	2.76 (1.59) <sup>d,e</sup>	1.94 (1.06) <sup>d,e</sup>
College graduate	2.42 (1.53) <sup>b,d</sup>	1.79 (1.03) <sup>b,d</sup>
Graduate school	2.43 (1.63) <sup>c,e</sup>	1.72 (0.90) <sup>c,e</sup>
<b>Age<sup>a</sup></b>		
18-35	2.94 (1.58) <sup>b,c,d</sup>	2.27 (1.18) <sup>b,c,d</sup>
30-45	2.71 (1.61) <sup>b,e,f</sup>	2.05 (1.17) <sup>b,e,f</sup>
45-65	2.45 (1.58) <sup>c,e</sup>	1.66 (0.89) <sup>c,e,g</sup>
>65	2.31 (1.63) <sup>d,f</sup>	1.40 (0.70) <sup>d,f,g</sup>
<b>Income<sup>a</sup> (US \$)</b>		
Under 10,000	2.97 (1.68) <sup>b,c</sup>	2.12 (1.24) <sup>b,c,d</sup>
10,000 to 49,999	2.85 (1.62) <sup>d,e</sup>	1.95 (1.07) <sup>b,e,f</sup>
50,000 to 99,999	2.43 (1.51) <sup>b,d</sup>	1.81 (0.97) <sup>c,e</sup>
>100,000	2.26 (1.55) <sup>c,e</sup>	1.75 (1.08) <sup>d,f</sup>
<b>Born in the United States<sup>h</sup></b>		
Yes	2.62 (1.61)	1.92 (1.08)
No	2.68 (1.61)	1.56 (0.89)
<b>Race</b>		
White	2.25 (1.48) <sup>b,c,d</sup>	1.75 (0.97) <sup>b,c</sup>
African American	3.27 (1.67) <sup>b,e</sup>	2.12 (1.15) <sup>b,d,e</sup>
Middle Eastern	2.73 (1.58) <sup>c,e,f</sup>	1.69 (0.97) <sup>d,f</sup>
Multiracial	3.20 (1.69) <sup>d,f</sup>	2.55 (1.36) <sup>c,e,f</sup>
Other	2.75 (1.39)	2.17 (1.04)
<b>Marital status<sup>a</sup></b>		
Married/living as married	2.38 (1.56) <sup>b</sup>	1.72 (0.97) <sup>b</sup>
Not married	2.87 (1.62) <sup>b</sup>	2.03 (1.12) <sup>b</sup>
Total	2.62 (1.61)	1.87 (1.06)

<sup>a</sup>Group means differ  $P < .01$ .

<sup>b-g</sup>Rows with common superscript differ  $P < .05$

<sup>h</sup>Group means in everyday discrimination differ  $P < .01$ .

As shown in [Table 3](#), unfairness was significantly related to mental health symptoms, after adjustment for sociodemographic variables (Model 1), with higher unfairness values associated with worse (lower scores) mental health status. In addition to an overall significant effect, all pairwise contrasts were

significant. The association, both overall and pairwise, remained significant after inclusion of everyday discrimination scores in the regression model (Model 2). The  $R^2$  increased from 0.17 to 0.22 when everyday discrimination was added to the model.

**Table 3.** Adjusted least squares mean mental health symptoms by unfairness and discrimination<sup>a</sup>.

Model values	Mental health symptoms, mean (SE)
<b>Model 1<sup>b,c</sup></b>	
Low unfairness	13.70 (0.23) <sup>d,e</sup>
Medium unfairness	12.45 (0.23) <sup>d,f</sup>
High unfairness	10.80 (0.30) <sup>e,f</sup>
<b>Model 2<sup>c,g</sup></b>	
Low unfairness	13.43 (0.22) <sup>d,e</sup>
Medium unfairness	12.84 (0.24) <sup>d,f</sup>
High unfairness	11.70 (0.30) <sup>e,f</sup>

<sup>a</sup>Lower scores indicate worse mental health status.

<sup>b</sup>Model 1: adjusted for age, gender, race, income, education, and marital status;  $R^2=0.17$ .

<sup>c</sup>Group means differ  $P<.01$ .

<sup>d-f</sup>Rows with common superscript differ  $P<.05$ .

<sup>g</sup>Model 2: adjusted for age, gender, race, income, education, marital status, and everyday discrimination;  $R^2=0.22$ .

As shown in Table 4, unfairness was significantly related to self-reported history of depression and high blood pressure, after adjustment for sociodemographic variables (Model 1). Higher unfairness values were significantly associated with higher odds of depression, when both the middle and high groups were compared to the lowest group, and for high blood pressure, when the highest group was compared to the lowest

group. After inclusion of everyday discrimination scores in the model (Model 2), there was still an overall association with depression, and the pairwise contrast of highest to lowest remained significant. In Model 2, the effect of unfairness on high blood pressure disappeared. The addition of everyday discrimination to the model increased the  $R^2$  value by 0.01% to 0.02%.

**Table 4.** Adjusted odds of self-reported history of illness by unfairness and discrimination<sup>a</sup>.

Predictor	History of depression <sup>b</sup>	History of diabetes	History of heart disease	History of high blood pressure	History of cancer
<b>Model 1<sup>c</sup> unfairness (<math>R^2</math>)</b>	0.12	0.09	0.05	0.20	0.06
Low	REF <sup>d</sup>	REF	REF	REF	REF
Middle	<i>1.57 (1.24-1.98)</i> <sup>e</sup>	1.21 (0.92-1.58)	1.01 (0.69-1.48)	1.11 (0.87-1.42)	1.18 (0.82-1.69)
High	<i>2.93 (2.18-3.95)</i>	1.03 (0.72-1.45)	1.31 (0.84-2.06)	<i>1.49 (1.08-2.05)</i>	1.14 (0.71-1.82)
<b>Model 2<sup>f</sup> unfairness (<math>R^2</math>)</b>	0.14	0.10	0.07	0.21	0.07
Low	REF	REF	REF	REF	REF
Middle	1.19 (0.92-1.54)	1.15 (0.82-1.54)	0.80 (0.52-1.22)	1.00 (0.761-1.309)	0.99 (0.67-1.48)
High	<i>1.89 (1.35-2.64)</i>	0.84 (0.57-1.234)	0.87 (0.52-1.45)	1.22 (0.85-1.74)	0.78 (0.46-1.32)

<sup>a</sup>Unless otherwise stated, the data are reported as OR (95% CI).

<sup>b</sup>Overall variable  $P<.01$ .

<sup>c</sup>Model 1: adjusted for age, gender, race, income, education, and marital status.

<sup>d</sup>REF: reference group.

<sup>e</sup>Italicized CIs indicate statistically significant ORs.

<sup>f</sup>Model 2: adjusted for age, gender, race, income, education, marital status, and everyday discrimination.

As shown in Table 5, unfairness was significantly related to 30-day marijuana use, 30-day cigarette use, and lifetime opiate use, after adjustment for sociodemographic variables (Model 1). There was no association with 30-day alcohol use. Specifically, higher unfairness values, when both the middle and highest groups were compared to the lowest group, were associated with significantly higher odds of cigarette and opiate

use, whereas for marijuana, the contrast was significant only for the highest compared to the lowest group. When everyday discrimination scores were added to the model (model 2), the effect on marijuana was no longer significant and the effect on cigarettes was only significant for the comparison of the middle to the lowest group. In addition, the effect on alcohol use became significant. However, the effect was in the opposite direction

than with the other substances. That is, higher unfairness was significantly associated with lower odds of 30-day alcohol use.

The addition of everyday discrimination to the model increased the  $R^2$  value by 0.01% to 0.02%.

**Table 5.** Adjusted odds of self-reported substance use by unfairness<sup>a</sup>.

Predictor	30-day alcohol	30-day marijuana	30-day cigarettes	Lifetime opiates
<b>Model 1<sup>b</sup> unfairness (<math>R^2</math>)</b>	0.14	0.08	0.05	0.07
Low	REF <sup>c</sup>	REF	REF	REF
Middle	0.82 (0.64-1.04)	1.14 (0.82-1.59) <sup>d</sup>	<i>1.69 (1.28-2.23)</i> <sup>e,f</sup>	<i>1.37 (1.07-1.74)</i> <sup>d</sup>
High	0.76 (0.54-1.07)	<i>1.74 (1.17-2.57)</i> <sup>d</sup>	<i>1.96 (1.39-2.76)</i> <sup>f</sup>	<i>1.41 (1.03-1.92)</i> <sup>d</sup>
<b>Model 2<sup>g</sup> unfairness (<math>R^2</math>)</b>	0.14 <sup>f</sup>	0.09	0.08	0.08
Low	REF	REF	REF	REF
Middle	<i>0.73 (0.56-0.96)</i> <sup>d</sup>	0.89 (0.62-1.28)	<i>1.38 (1.01-1.87)</i>	1.00 (0.76-1.30)
High	<i>0.65 (0.45-0.95)</i> <sup>d</sup>	1.22 (0.79-1.89)	1.42 (0.972-2.10)	0.84 (0.59-1.19)

<sup>a</sup>Unless otherwise stated, the data are reported as OR (95% CI).

<sup>b</sup>Model 1: adjusted for age, gender, race, income, education, and marital status.

<sup>c</sup>REF: reference group.

<sup>d</sup> $P < .05$ .

<sup>e</sup>Italicized CIs indicate statistically significant ORs.

<sup>f</sup> $P < .01$ .

<sup>g</sup>Model 2: adjusted for age, gender, race, income, education, marital status, and everyday discrimination.

## Discussion

Unfairness was significantly related to worse mental health functioning, net adjustment for sociodemographic variables, and everyday discrimination. Unfairness was related to self-reported history of depression and high blood pressure after an adjustment for sociodemographic variables was made although after including everyday discrimination in the model, only the association with depression remained significant.

Unfairness was also significantly related to 30-day marijuana use, 30-day cigarette use, and lifetime opiate use. Adding everyday discrimination scores to the model attenuated these effects, with the association with marijuana no longer being significant and the effect on cigarettes only being significant for the comparison of the middle group to the lowest group.

Our findings of a generally harmful effect of perceived unfairness on health are consistent with prior studies [15-17]. Perceived unfairness, although moderately correlated with everyday discrimination, appears to serve as a unique predictor of health status and health behavior. Alternatively, given that, in some instances, adding everyday discrimination to the model attenuated the impact of unfairness on outcomes, unfairness may also serve as a partial mediator of discrimination; that is, it may be one of the psychological pathways through which discrimination negatively impacts health: it may be a consequence of discrimination. On the other hand, adding discrimination to the model (except for mental health) generally only increased the  $R^2$  value by 1% or 2%, suggesting that unfairness captures most of the same variance in health outcomes as does discrimination.

In our study, we found that higher unfairness was associated with lower educational attainment, lower age, lower household income, and being unmarried. The higher rates of unfairness observed for individuals with lower education and income is consistent with both UK [15,16] and Dutch studies [17]. Age was unrelated to unfairness in the Whitehall study [16], which differs from our findings. We found no differences by gender, which is inconsistent with the Whitehall study, where women had higher levels of reported unfairness [16].

With regard to race, we found the highest unfairness values were observed among African American and multiracial respondents, followed by MENA respondents. White respondents reported the lowest values, and they were significantly lower than African American, multiracial, and MENA respondents in pairwise comparisons. Prior studies did not report race effects, as their samples were more homogeneous than that of this study. The Whitehall study sample, for example, consisted of 90% White and 5% South Asian participants [27].

We found that the effect of unfairness on 30-day alcohol was in the opposite direction to the other substances we examined. That is, higher unfairness was associated with lower odds of 30-day alcohol use. The protective effect of unfairness on alcohol intake was not entirely unexpected. A few previous studies have found that higher levels of unfairness and discrimination were not associated with increased alcohol use [9,16,28]. In our study, this relationship was in part confounded by religiosity, as more religious respondents were both more likely to abstain from alcohol and to report higher levels of unfairness (data not shown). Controlling for religion reduced the protective effect of unfairness on alcohol use.

The study has several limitations. First, the data were all cross sectional, which limits our ability to determine causation; reverse causality cannot be excluded. For example, higher rates of illness or substance use could drive higher perceptions of unfairness or discrimination, rather than the inverse.

Secondly, unfairness may be caused by everyday discrimination. Experiencing discrimination could lead one to perceive life as unfair. Given the 2 variables were moderately correlated ( $r=0.54$ ) and that the effects of unfairness on health outcomes generally remained after adjustment for discrimination, it appears that unfairness may function as a unique contributor to health outcomes, above that of discrimination. It should also be noted that while the 9-item everyday discrimination scale assesses various types of discriminatory behaviors, the single-item unfairness measure we used only assesses global perceptions. Perhaps more granular assessment of unfairness, more akin to how discrimination is typically assessed, would yield more robust findings.

Furthermore, illness outcomes were all self-reported, which likely increased the error of these measures. Given this, the analyses might have underestimated the association of unfairness on health, unless they share a common reporting bias, which then would have spuriously inflated their association. Finally, our sample was recruited in Michigan, so the generalizability of our findings to other populations is unclear.

Our findings have implications for both research and practice. With regard to research, our results indicate that unfairness should be included as a potential variable in studies of health and health disparities in addition to the standard set of socioeconomic and social indicators. Unfairness may also be more amenable to intervention than discrimination and other disparity drivers. Because unfairness relates more to the perception or perseveration of events rather than simply their occurrence, cognitive interventions that help individuals cope with these perceptions may merit investigation.

---

## Acknowledgments

This work was supported by the National Cancer Institute (grant no. P30CA046592-29-S4).

---

## Conflicts of Interest

None declared.

---

## References

1. Braveman P. What are health disparities and health equity? We need to be clear. *Public Health Rep* 2014;129 Suppl 2:5-8 [FREE Full text] [doi: [10.1177/00333549141291S203](https://doi.org/10.1177/00333549141291S203)] [Medline: [24385658](https://pubmed.ncbi.nlm.nih.gov/24385658/)]
2. 2018 National healthcare quality and disparities report. Agency for Healthcare Research and Quality. Rockville, MD; 2020 Apr. URL: <https://www.ahrq.gov/research/findings/nhqrdr/nhqrdr18/index.html> [accessed 2020-02-01]
3. Williams DR, Yan Yu, Jackson JS, Anderson NB. Racial differences in physical and mental health: socio-economic status, stress and discrimination. *J Health Psychol* 1997 Jul;2(3):335-351. [doi: [10.1177/135910539700200305](https://doi.org/10.1177/135910539700200305)] [Medline: [22013026](https://pubmed.ncbi.nlm.nih.gov/22013026/)]
4. Ahmed AT, Mohammed SA, Williams DR. *Indian J Med Res* 2007 Oct;126(4):318-327. [Medline: [18032807](https://pubmed.ncbi.nlm.nih.gov/18032807/)]
5. Williams DR. Race, socioeconomic status, and health. The added effects of racism and discrimination. *Ann N Y Acad Sci* 1999;896:173-188. [doi: [10.1111/j.1749-6632.1999.tb08114.x](https://doi.org/10.1111/j.1749-6632.1999.tb08114.x)] [Medline: [10681897](https://pubmed.ncbi.nlm.nih.gov/10681897/)]
6. Williams DR, Collins C. US socioeconomic and racial differences in health: patterns and explanations. *Annu. Rev. Sociol* 1995 Aug;21(1):349-386. [doi: [10.1146/annurev.so.21.080195.002025](https://doi.org/10.1146/annurev.so.21.080195.002025)]
7. Borrell LN, Kiefe CI, Williams DR, Diez-Roux AV, Gordon-Larsen P. Self-reported health, perceived racial discrimination, and skin color in African Americans in the CARDIA study. *Soc Sci Med* 2006 Sep;63(6):1415-1427. [doi: [10.1016/j.socscimed.2006.04.008](https://doi.org/10.1016/j.socscimed.2006.04.008)] [Medline: [16750286](https://pubmed.ncbi.nlm.nih.gov/16750286/)]
8. Williams DR, Gonzalez HM, Williams S, Mohammed SA, Moomal H, Stein DJ. Perceived discrimination, race and health in South Africa. *Soc Sci Med* 2008 Aug;67(3):441-452 [FREE Full text] [doi: [10.1016/j.socscimed.2008.03.021](https://doi.org/10.1016/j.socscimed.2008.03.021)] [Medline: [18486292](https://pubmed.ncbi.nlm.nih.gov/18486292/)]
9. Williams DR, Mohammed SA. Discrimination and racial disparities in health: evidence and needed research. *J Behav Med* 2009 Feb;32(1):20-47 [FREE Full text] [doi: [10.1007/s10865-008-9185-0](https://doi.org/10.1007/s10865-008-9185-0)] [Medline: [19030981](https://pubmed.ncbi.nlm.nih.gov/19030981/)]
10. Williams DR, Neighbors HW, Jackson JS. Racial/ethnic discrimination and health: findings from community studies. *Am J Public Health* 2003 Feb;93(2):200-208. [doi: [10.2105/ajph.93.2.200](https://doi.org/10.2105/ajph.93.2.200)] [Medline: [12554570](https://pubmed.ncbi.nlm.nih.gov/12554570/)]
11. Krieger N, Smith K, Naishadham D, Hartman C, Barbeau EM. Experiences of discrimination: validity and reliability of a self-report measure for population health research on racism and health. *Soc Sci Med* 2005 Oct;61(7):1576-1596. [doi: [10.1016/j.socscimed.2005.03.006](https://doi.org/10.1016/j.socscimed.2005.03.006)] [Medline: [16005789](https://pubmed.ncbi.nlm.nih.gov/16005789/)]
12. Kessler RC, Mickelson KD, Williams DR. The prevalence, distribution, and mental health correlates of perceived discrimination in the United States. *J Health Soc Behav* 1999 Sep;40(3):208-230. [Medline: [10513145](https://pubmed.ncbi.nlm.nih.gov/10513145/)]
13. Schulz AJ, Gravelle CC, Williams DR, Israel BA, Mentz G, Rowe Z. Discrimination, symptoms of depression, and self-rated health among african american women in detroit: results from a longitudinal analysis. *Am J Public Health* 2006 Jul;96(7):1265-1270. [doi: [10.2105/AJPH.2005.064543](https://doi.org/10.2105/AJPH.2005.064543)] [Medline: [16735638](https://pubmed.ncbi.nlm.nih.gov/16735638/)]

14. Moomal H, Jackson PB, Stein DJ, Herman A, Myer L, Seedat S, et al. Perceived discrimination and mental health disorders: the South African Stress and Health study. *S Afr Med J* 2009 May;99(5 Pt 2):383-389. [Medline: [19588802](#)]
15. De Vogli R, Brunner E, Marmot MG. Unfairness and the social gradient of metabolic syndrome in the Whitehall II Study. *J Psychosom Res* 2007 Oct;63(4):413-419. [doi: [10.1016/j.jpsychores.2007.04.006](#)] [Medline: [17905050](#)]
16. De Vogli R, Ferrie JE, Chandola T, Kivimäki M, Marmot MG. Unfairness and health: evidence from the Whitehall II Study. *J Epidemiol Community Health* 2007 Jun;61(6):513-518. [doi: [10.1136/jech.2006.052563](#)] [Medline: [17496260](#)]
17. Bosma H, Gerritsma A, Klabbers G, van den Akker M. Perceived unfairness and socioeconomic inequalities in functional decline: the Dutch SMILE prospective cohort study. *BMC Public Health* 2012 Sep 22;12:818 [FREE Full text] [doi: [10.1186/1471-2458-12-818](#)] [Medline: [22998808](#)]
18. McHorney CA, Ware JE, Lu JF, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. *Med Care* 1994 Jan;32(1):40-66. [doi: [10.1097/00005650-199401000-00004](#)] [Medline: [8277801](#)]
19. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992 Jun;30(6):473-483. [Medline: [1593914](#)]
20. Taylor TR, Williams CD, Makambi KH, Mouton C, Harrell JP, Cozier Y, et al. Racial discrimination and breast cancer incidence in US Black women: the Black Women's Health Study. *Am J Epidemiol* 2007 Jul 01;166(1):46-54. [doi: [10.1093/aje/kwm056](#)] [Medline: [17400570](#)]
21. Emerson E, Milner A, Aitken Z, Krnjacki L, Vaughan C, Llewellyn G, et al. Overt acts of perceived discrimination reported by British working-age adults with and without disability. *J Public Health (Oxf)* 2021 Apr 12;43(1):e16-e23. [doi: [10.1093/pubmed/fdz093](#)] [Medline: [31876284](#)]
22. Kirkham R. Asking the wrong question? The difference between unfairness and discrimination. *J Public Health (Oxf)* 2019 Dec 02;2. [doi: [10.1093/pubmed/fdz153](#)] [Medline: [31789376](#)]
23. Kroenke K, Spitzer RL, Williams JB, Löwe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. *Psychosomatics* 2009;50(6):613-621. [doi: [10.1176/appi.psy.50.6.613](#)] [Medline: [19996233](#)]
24. Health Information National Trends Survey (HINTS). National Cancer Institute. 2018. URL: <https://hints.cancer.gov/data/survey-instruments.aspx#H5C2> [accessed 2019-01-03]
25. Youth Risk Behavior Survey. Centers for Disease Control and Prevention (CDC). 2017. URL: <https://www.cdc.gov/healthyyouth/data/yrbs/index.htm> [accessed 2019-01-03]
26. Dynata. URL: [www.dynata.com](http://www.dynata.com) [accessed 2021-04-09]
27. Britton A, Shipley M, Marmot M, Hemingway H. Does access to cardiac investigation and treatment contribute to social and ethnic differences in coronary heart disease? Whitehall II prospective cohort study. *BMJ* 2004 Aug 07;329(7461):318. [doi: [10.1136/bmj.381156.690150.AE](#)] [Medline: [15237088](#)]
28. Borrell L, Kiefe C, Diez-Roux A, Williams D, Gordon-Larsen P. Racial discrimination, racial/ethnic segregation, and health behaviors in the CARDIA study. *Ethn Health* 2013;18(3):227-243 [FREE Full text] [doi: [10.1080/13557858.2012.713092](#)] [Medline: [22913715](#)]

## Abbreviations

**MENA:** Middle Eastern and North African

**PHQ-4:** Patient Health Questionnaire-4

**SF-36:** 36-Item Short Form Survey

*Edited by G Eysenbach; submitted 18.12.20; peer-reviewed by L Marc; comments to author 23.02.21; revised version received 25.02.21; accepted 06.04.21; published 10.05.21.*

*Please cite as:*

Resnicow K, Patel M, Green M, Smith A, Bacon E, Goodell S, Kilby D, Tariq M, Alhawli A, Syed N, Griggs J, Stiffler M  
*The Association of Unfairness with Mental and Physical Health in a Multiethnic Sample of Adults: Cross-sectional Study*  
*JMIR Public Health Surveill* 2021;7(5):e26622

URL: <https://publichealth.jmir.org/2021/5/e26622>

doi: [10.2196/26622](#)

PMID: [33970121](#)

©Ken Resnicow, Minal Patel, Molly Green, Alyssa Smith, Elizabeth Bacon, Stefanie Goodell, Dylan Kilby, Madiha Tariq, Asraa Alhawli, Nadia Syed, Jennifer Griggs, Matthew Stiffler. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 10.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction

in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# Performance of the Neonatal Tetanus Surveillance System (NTSS) in Sana'a, Yemen: Evaluation Study

Khaled Mohammed Al-Jamrah<sup>1</sup>, MSc; Basheer Abdulgalil Al Nabehi<sup>2</sup>, PhD; Khaled Abdullah Almoayed<sup>1</sup>, MSc; Labiba Saeed Anam<sup>1</sup>, MD; Yousef S Khader<sup>3</sup>, SCD

<sup>1</sup>Yemen Field Epidemiology Training Program, Ministry of Public Health and Population, Sana'a, Yemen

<sup>2</sup>Neonatal Tetanus Surveillance Program, Ministry of Public Health and Population, Sana'a, Yemen

<sup>3</sup>Department of Public Health, Community Medicine, and Family Medicine, Faculty of Medicine, Jordan University of Science & Technology, Irbid, Jordan

**Corresponding Author:**

Khaled Mohammed Al-Jamrah, MSc  
Yemen Field Epidemiology Training Program  
Ministry of Public Health and Population  
Alhasabah Area  
Althawrah District  
Sana'a  
Yemen  
Phone: 967 777 950 053  
Email: [khjamrah2010@gmail.com](mailto:khjamrah2010@gmail.com)

## Abstract

**Background:** The Neonatal Tetanus Surveillance System (NTSS) in Yemen was established in 2009 to identify high-risk areas, determine trends, and evaluate elimination activities. Since its launch, the NTSS had never been evaluated.

**Objective:** This study aimed to assess the performance of NTSS and determine its strengths and weaknesses to recommend improvements.

**Methods:** The US Centers for Disease Control and Prevention (CDC) guidelines were used for evaluating the NTSS. Stakeholders at the central, district, and facility levels were interviewed to rate the attributes of the NTSS. The percentage scores for attributes were ranked as poor (<60%), average (≥60% to <80%) and good (≥80%).

**Results:** The overall usefulness score percentage was 38%, which indicates a poor performance. The performance of the NTSS was rated as average on flexibility (score percent: 68%) and acceptability (score percent: 64%) attributes and poor on stability (score percentage: 33%), simplicity (score percentage: 57%), and representativeness (score percentage: 39%) attributes. About 65% of investigation forms were completed within 48 hours of notification date. Data quality was poor, as 41% of the core variables were missing.

**Conclusions:** The overall performance of the NTSS was poor. Most of the system attributes require improvement, including stability, simplicity, quality of data, and completeness of investigation. To improve the performance of NTSS, the following are recommended: capacity building of staff (focal points), strengthening NTSS through technical support and government funding to ensure its sustainability, establishing electronic investigation forms for improving the system data quality, and expansion of NTSS coverage to include all private health care facilities.

(*JMIR Public Health Surveill* 2021;7(5):e27606) doi:[10.2196/27606](https://doi.org/10.2196/27606)

**KEYWORDS**

neonatal tetanus; evaluation; surveillance; CDC guidelines; Yemen

## Introduction

**Background**

Neonatal tetanus (NT) is a life-threatening vaccine-preventable disease and one of the most underreported diseases in many

developing countries. It is caused by the toxin of *Clostridium tetani*, a ubiquitous, spore-forming, gram-positive bacillus found in high concentrations in soil and animal excrement. The disease usually occurs in rural settings with poor access to health facilities, characterized by generalized rigidity and convulsive



spasms of skeletal muscles that usually involve the jaw and neck and then become generalized [1]. Newborns can become infected through contaminated instruments used to cut the umbilical cord or by improper handling of the umbilical stump [1,2].

NT remains a major cause of infant and neonatal mortality in many developing countries, but it is preventable by immunization and/or assuring clean delivery and postdelivery practices [2]. According to the World Health Organization (WHO), an NT case is defined as “a neonate with the normal ability to suck and cry during the first 2 days of life, between 3 to 28 days of age cannot suck normally and becomes stiff or has spasms” [3]. Global elimination is defined as an annual rate of <1 case of NT per 1000 live births at the district level [4].

Globally, good progress has been made in the last two decades. The number of reported NT cases worldwide declined by 90%, from 17,935 in 2000 to 1803 in 2018, and estimated NT deaths decreased by 85%, from 170,829 in 2000 to 25,000 in 2018 [4]. This disease accounts for 1% of worldwide neonatal mortality, compared with 7% in 2000 [5].

Despite the appreciable drop in the number of NT cases attributed to the global NT elimination strategies, NT still remains among the leading causes of death in 14 developing countries that have not yet eliminated NT [6]. The Eastern Mediterranean Region (EMR) has been ranked at the fourth position among WHO regions in term of NT burden. In 2018, 181 (10%) of NT cases were reported from 6 countries in the region: Afghanistan, Saudi Arabia, Iraq, Morocco, Egypt, and Yemen [4].

### Neonatal Tetanus Surveillance in Yemen

Yemen is one of the 5 remaining countries in the EMR that have not achieved the global elimination target set by WHO [6]. NT remains a public health problem in Yemen, where it is one of the major causes of neonatal mortality. In 2018, more than 64% of all NT cases in EMR were reported from Yemen. A total of 2069 NT cases were reported from 1980 to 2018 [4].

Tetanus immunization has been included in the national expanded program of immunization in Yemen since 1977, and includes 5 doses of tetanus toxoid vaccine for women of child-bearing age. Despite the availability of an inexpensive and effective tetanus vaccine, Yemen is far behind in tetanus toxoid vaccine coverage. Over the last decade, 17% to 21% of women received at least 2 doses of the tetanus toxoid vaccine in Yemen [7].

The Neonatal Tetanus Surveillance System (NTSS) was established in Yemen in 2009, with the objectives to identify high-risk areas, determine trends of NT, and evaluate tetanus elimination activities. NTSS in Yemen is a passive surveillance system that relies on the identification of NT cases collected at the health facility level and then reported to the next higher level at a specified frequency (weekly), even if there are zero cases (referred to as zero reporting). In addition, all NT cases are reported through community-based surveillance (CBS) and the Electronic Disease Early Warning System (eIDEWS). Particularly in high-risk areas, the NTSS relies on CBS through traditional birth attendants, community leaders, traditional

healers, or other community members who are sensitized to report NT cases and deaths to health authorities. The eIDEWS network of reporting sites includes both public and private health facilities.

### Objectives

High-quality NT surveillance is a key component of the NT elimination strategy, and its data are used to identify areas or subpopulations at high-risk for NT and guide effective public health response for NT elimination. However, since its launch in Yemen, NTSS had never been evaluated. Therefore, this study aimed to assess the level of usefulness and performance of the NTSS attributes, determine its strengths and weaknesses, and suggest recommendations for improvement.

### Methods

#### Study Design

A descriptive evaluation study was conducted to describe NTSS and its performance according to the Centers for Disease Control and Prevention (CDC) guideline for evaluating disease surveillance systems [8]. The study was performed in the city of Sana'a from October to December 2018.

#### Study Population and Sampling

The study population involved 31 stakeholders: 5 from the central level, 3 from governorate level, 3 from districts level, and 20 health facility focal points. At the district and health facility levels, samples were selected using a multistage sampling method. Using simple random sampling, 30% (3/10) of the districts—Assabain, Ma'ain, and Assafi'yah—were selected. A total of 33% (20/60) of health facilities were selected by stratified random sampling distributed proportionally among the chosen districts according to the curative services (public and private) in each district. The selection of health facilities from each chosen district was based on simple random sampling.

#### Data Collection

Desk review of the main NTSS documents and literature was conducted to describe the system. In depth interviews were conducted with NTSS stakeholders at the central and governorate levels to measure usefulness, flexibility, and stability. A semistructured questionnaire was used to collect data from surveillance coordinators of governorates, districts, and focal points at health facility levels to evaluate simplicity and acceptability (Multimedia Appendix 1). In addition, data registries from 2009 to 2018 were obtained to measure data quality, timeliness of investigation, completeness of investigation, and representativeness.

#### Performance of the System

The indicators of the level of usefulness, flexibility, and stability attributes were assessed using yes or no (yes = 1; no = 0) questions. The indicators of simplicity and acceptability were assessed using a 5-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, and 5 = strongly agree). Quality of data was assessed by measuring the percentages of missing variables. Timeliness of investigation was measured by the percentage of all suspected cases investigated within 48

hours of notification. Completeness of investigation was measured by the proportion of NT suspected cases reported that have been investigated. Representativeness was measured by the percentage of all public and private health facilities in Sana'a that were covered by NTSS.

### Data Analysis and Interpretation

The usefulness, flexibility, and stability indicators were scored as 0 or 1, whereas the simplicity and acceptability indicators were scored from 1 to 5. For each indicator, the score percentage was calculated as the following:



The overall attribute score percentage was calculated as the following:



Each indicator and overall attribute score percentage was represented as score rank and interpreted as poor <60%, average ≥60% to <80%, or good ≥80%. Missing data were measured by selecting 1-year data to calculate the percentage of the missed core variables. The core variables included case identification, date of birth, sex, place of usual residence, date of illness onset, date of notification, date of investigation, symptoms in case definition, outcome (alive/dead), maternal vaccination history, place/type of delivery, tool used for cutting cord, and material applied to cord. For any case, if information on any of the core variables is missing, the investigation was considered inadequate.

Timeliness of investigation was calculated by dividing the number of suspected NT cases investigated within 48 hours of

notification by the number of suspected NT cases investigated  $\times 100$ . Completeness of investigation was calculated by dividing the number of NT case investigations by the number of suspected NT cases reported  $\times 100$ . Representativeness was calculated by dividing the number of public and private health facilities in Sana'a that are covered by NTSS by the total number of public and private health facilities in Sana'a  $\times 100$ . Epi Info (version 7.2, Division of Health Informatics and Surveillance, CDC) was used for data entry and analysis. Data were described using frequencies, score percentages, and score rank.

## Results

### Participant Characteristics

A total of 31 participants (61% [19/31] male and 39% [12/31] female) were interviewed from 4 levels: central, governorate, district, and health facility. The median of their ages was 42 years (range 24 to 65 years) and the median years of their experience in surveillance systems was 4.0 years (range 1 to 20 years).

### Level of Usefulness

Based on 8 in-depth interviews with stakeholders at central and governorate levels, the overall usefulness score percentage was 38%, which indicates a poor performance. Only one usefulness indicator ("The system data are used to estimate NT magnitude, incidence, and mortality rates") was ranked as good (Table 1). One of the respondents said "Unfortunately, NT is neglected by researchers and the Ministry of Public Health and Population."

**Table 1.** The score, score percentage, and rank of usefulness indicators of the Neonatal Tetanus Surveillance System in Sana'a, 2018 (n=8).

Indicator	Score	Score percentage	Rank
The system data are used to estimate NT <sup>a</sup> magnitude, incidence, and mortality rates.	7	88	Good
The system data are used to monitor the trend of NT spread over time.	4	50	Poor
The system data are used to identify high-risk areas.	4	50	Poor
The system data are used to update and develop the national policy strategy for NT elimination.	1	13	Poor
The system data are used to assess the effect of interventions.	1	13	Poor
The system provides a basis for epidemiologic research.	1	13	Poor
Overall usefulness	18	38	Poor

<sup>a</sup>NT: neonatal tetanus.

### Flexibility

The overall score of flexibility was 68%, which reveals an average performance (Table 2). Three of the flexibility indicators ("The system can be adapted to accommodate new additional

information" [eg, change in case definition], "The system can be adapted to increases in the reporting sources," and "The system can be adapted to integrate with other surveillance") had good rank. One indicator ("The system is not affected by fund variation") was ranked as poor.

**Table 2.** The score, score percentage, and rank of flexibility indicators of the Neonatal Tetanus Surveillance System in Sana'a, 2018 (n=8).

Indicator	Score	Score percentage	Rank
The system can be adapted to accommodate new health-related events with little resources and time.	5	60	Average
The system can be adapted to accommodate new additional information (eg, change in case definition).	7	88	Good
The system is not affected by fund variation.	0	0	Poor
The system can be adapted to increases in the reporting sources.	7	88	Good
The system can be adapted to integrate with other surveillance.	8	100	Good
Overall flexibility	27	68	Average

### Stability

The overall stability of the system scored 33%, which reveals a poor performance. Of 5 stability indicators, only one (“The system does not require time for collecting, sending, receiving,

and managing data”) had a good rank (Table 3). One of the respondents said “There is no qualified coordinator capable of working continuously, and the most important obstacle is the lack of funding.”

**Table 3.** The score, score percentage, and rank of stability indicators of the Neonatal Tetanus Surveillance System in Sana'a, 2018 (n=8).

Indicator	Score	Score percentage	Rank
The system has funds from nongovernmental organizations.	0	0	Poor
The system has governmental funds.	1	13	Poor
The system is stable without sponsor funds.	0	0	Poor
The system does not require time for collecting, sending, receiving, and managing data.	8	100	Good
The reports are released regularly.	4	50	Poor
Overall stability	13	33	Poor

### Simplicity

A total of 26 stakeholders at governorate, district, and health facility levels rated the simplicity. Of 9 indicators, 5 had poor

ranking. Only one indicator had good ranking. The overall simplicity of the system scored 57%, which indicates a poor performance (Table 4).

**Table 4.** The score, score percentage, and rank of simplicity indicators of the Neonatal Tetanus Surveillance System in Sana'a, 2018 (n=26).

Indicator	Score	Score percentage	Rank
Case definition is available.	71	55	Poor
Case definition is easy to apply.	95	73	Average
Investigation forms are available.	48	37	Poor
Investigation forms are easy to complete.	52	40	Poor
Data collection does not require telephone contact or home visit.	84	65	Average
Data collection does not need much time.	99	76	Average
Data transportation to the central level is very easy.	108	83	Good
Received training on NT <sup>a</sup> .	35	27	Poor
Data updating and follow-up of cases are easy.	77	59	Poor
Overall simplicity	669	57	Poor

<sup>a</sup>NT: neonatal tetanus.

### Acceptability

The acceptability indicator related to willingness to participate in NTSS had good rank. However, satisfaction with NTSS was poor. The overall acceptability score percentage was 64%, which indicates an average performance.

### Timeliness and Completeness of Investigation

Of reported cases, the overall completeness of routine reporting under passive surveillance was only 23% (120/524), which indicates a poor performance. A total of 65% (340/524) of investigation forms were completed within 48 hours of the notification date, indicating an average timeliness performance, while 10% (53/524) of investigation forms were completed

more than 48 hours after the notification date. The remaining (131/524, 25%) had no investigation date.

### Data Quality

The data quality was poor, with 41% (645/1572) of the core variables missing. The highest percentage of data missing was in maternal vaccination history (96/131, 73%), followed by material applied to cord (72/131, 55%). The lowest percentage of missing was in date of birth (14/131, 11%) followed by sex variable (6/131, 5%).

### Representativeness

Almost all (64/66, 97%) public health facilities and 26.7% (80/300) of private health facilities were covered by NTSS. The overall representativeness score percentage was only 39%, that indicates a poor representativeness.

### Strengths and Weaknesses of the NTSS

The strengths of the system include easy data collection; transfer through eIDEWS; existence of surveillance staff in governorate, district, and health facility levels; several sources of reporting such as eIDEWS and CBS; and existence of new qualified leadership.

The weaknesses of the system include lack of investigation forms in the health facilities; no activities for the NTSS; lack of central supervision and communication; and no brochures, posters, or publications available on NT.

## Discussion

### Principal Findings

Every disease surveillance system should be analyzed and evaluated periodically to ensure it meet its objectives and improve performance wherever necessary. This evaluation revealed contradictory views about the usefulness of the NTSS, where it was generally considered poor. For example, the surveillance system did not play any role in assessing the effectiveness of the NT elimination strategy and was not capable of identifying areas at high risk. However, the surveillance data were useful to estimate NT magnitude, incidence, and mortality rates, which are the main goals for NTSS. The system might be considered useful if it satisfactorily addresses at least one of the usefulness indicators [8].

The NTSS demonstrated average flexibility. This result is reasonable, particularly with indicators related to the change in case definition, reporting sources, and integration with other surveillance. Receiving data from several sources such as eIDEWS and CBS may enhance the flexibility of the system. However, flexibility may be negatively affected by fund variation. Similar findings were reported by another study, which revealed its flexibility by incorporating information on measles and acute flaccid paralysis systems [9]. In the other hand, our finding disagrees with those of a previous evaluation performed in Baluchistan, Pakistan, which demonstrated that the system had poor flexibility [10].

Despite the ability of the system to collect, send, receive, and manage data with little resources and time, the stability of NTSS was poor. This poor stability of NTSS reflected the weak

capability of the system to release reports regularly and lack of funds, especially governmental funds, which affect the system activities implementation. Therefore, the system is unstable and its sustainability is in danger.

Concerning the simplicity, the study results showed that NTSS simplicity was generally poor. This result might be due to the unavailability of case definition and investigation forms, as well as poor training, which can be attributed to lack of funds necessary for implementation of system activities. However, the transfer of the data to the central level was simple.

The findings showed that the acceptability of NTSS was average, as the majority of respondents were willing to participate in the surveillance system. Nevertheless, about two-thirds of respondents were unsatisfied with NTSS. This might be due to lack of interaction between the central and health facility levels, and this may result in lack of communication. Similarly, previous evaluation performed in Baluchistan, Pakistan, found that the system was acceptable for all stockholders with average rank [10].

Completeness of reporting for NT depends on conscientious notification, use of health services, health-seeking behavior, access to health services, [11] and a sensitive surveillance system [3,12].

Our findings revealed the completeness of investigation forms was poor. This result was far from the WHO target for completeness of investigation ( $\geq 90\%$ ) [3]. It might be due to unavailability of investigation forms, registers, and case definitions in the health facilities as well as lack of central supervision, communication, and training courses for staff. A similar study suggested that the availability and widespread use of birth attendant logs, vital events registries, and standard case definitions in reporting sites may impact NT reporting and surveillance [13].

The NTSS has average timeliness of investigation within 48 hours after notification. This result was lower than the WHO target for timeliness of investigation, which is  $\geq 80\%$  [3]. This finding might be due to the investigation date being missing in a quarter of the investigation forms.

High-quality surveillance data and other key program indicators should be used to monitor the impact of interventions, achievement, and maintenance of NT elimination [3]. The findings of this evaluation showed poor quality of NTSS investigation-completed forms. In addition, the percentage of missing data was high, especially data related to the maternal vaccination history and material applied to cord. In contrast, the percentage of missing data was low on the date of birth and sex variables. This might be due to lack of staff training and incentives. In comparison, a previous evaluation in Baluchistan, Pakistan, also demonstrated that the system had poor data quality [10].

The representativeness of NTSS in general was poor in Sana'a, particularly among private health facilities. However, the representativeness of NTSS was good among public health facilities.

## Limitations

This evaluation has some limitations. This evaluation was limited to Sana'a due to time, budget, and security constraints. Moreover, arrival time of the investigation forms was not measured because it was not included in the investigation forms.

## Conclusion

The overall performance of the NTSS was poor, and it is not meeting its objectives. Most of the system attributes require improvement, such as usefulness, stability, simplicity, quality of data, and completeness of investigation. In contrast, the system flexibility, acceptability, and timeliness of investigation

were average. The representativeness of NTSS was poor in Sana'a, particularly among private health facilities. The most important reasons for system weakness were lack of governmental funds, program activities, staff training, central communication, and supervision. To improve the performance of NTSS, the following are recommended: capacity building of staff (focal points) by regular trainings, frequent quality checks through field visits, strengthening NTSS through technical support and government funding to ensure its sustainability, establishing electronic investigation forms for improving the system data quality, and expansion of NTSS coverage to include all private health care facilities.

## Acknowledgments

The authors would like to acknowledge the Global Health Development | Eastern Mediterranean Public Health Network for their technical support.

## Conflicts of Interest

None declared.

Multimedia Appendix 1

Data collection questionnaire.

[DOCX File, 67 KB - [publichealth\\_v7i5e27606\\_app1.docx](#)]

## References

1. Hamborsky J, Kroger A. Epidemiology and Prevention of Vaccine-Preventable Diseases, E-Book: The Pink Book, 15th Edition. Washington: Public Health Foundation; 2015.
2. Pan American Health Organization. Neonatal Tetanus Elimination Field Guide. Second Edition. Washington: Pan American Health Organization; 2005.
3. Neonatal Tetanus Surveillance Standards. Geneva: World Health Organization; 2018. URL: [https://www.who.int/immunization/monitoring\\_surveillance/burden/vpd/WHO\\_SurveillanceVaccinePreventable\\_14\\_NeonatalTetanus\\_R1.pdf](https://www.who.int/immunization/monitoring_surveillance/burden/vpd/WHO_SurveillanceVaccinePreventable_14_NeonatalTetanus_R1.pdf) [accessed 2019-09-15]
4. Njuguna HN, Yusuf N, Raza AA, Ahmed B, Tohme RA. Elimination of Maternal and Neonatal Tetanus, 2019. MMWR Morb Mortal Wkly Rep 2020;69:515-520 [FREE Full text] [doi: [10.15585/mmwr.mm6917a2](https://doi.org/10.15585/mmwr.mm6917a2)]
5. Levels and trends in child mortality 2019. UNICEF. URL: <https://www.unicef.org/media/60561/file/UN-IGME-child-mortality-report-2019.pdf> [accessed 2019-09-15]
6. Protecting all against tetanus: guide to sustaining maternal and neonatal tetanus elimination and broadening tetanus protection for all populations. World Health Organization. 2019. URL: <https://apps.who.int/iris/bitstream/handle/10665/329882/9789241515610-eng.pdf?ua=1> [accessed 2019-09-15]
7. World Health Organization. Vaccine-preventable diseases: monitoring system. Global summary—Yemen. 2018. URL: [http://apps.who.int/immunization\\_monitoring/globalsummary/countries?countrycriteria%5Bcountry%5D%5B%5D=YEM&commit=OK](http://apps.who.int/immunization_monitoring/globalsummary/countries?countrycriteria%5Bcountry%5D%5B%5D=YEM&commit=OK) [accessed 2019-01-15]
8. German RR, Lee LM, Horan JM, Milstein RL, Pertowski CA, Waller MN, Guidelines Working Group Centers for Disease Control/Prevention (CDC). Updated guidelines for evaluating public health surveillance systems: recommendations from the Guidelines Working Group. MMWR Recomm Rep 2001 Jul 27;50(RR-13):1-35. [Medline: [18634202](https://pubmed.ncbi.nlm.nih.gov/18634202/)]
9. Kakar A. Evaluation of acute flaccid paralysis (AFP) surveillance system in Balochistan. Int J Inf Dis 2014 Apr;21:239. [doi: [10.1016/j.ijid.2014.03.918](https://doi.org/10.1016/j.ijid.2014.03.918)]
10. Mengal AA, Safdar R, Asghar J. Evaluation of Neonatal Tetanus (NNT) Surveillance System in Baluchistan, Pakistan, 2009. 2011. URL: <https://www.tephinet.org/evaluation-of-neonatal-tetanus-nnt-surveillance-system-in-baluchistan%E2%80%93pakistan-2009> [accessed 2019-01-15]
11. World Health Organization. Expanded Programme on Immunization: the use of survey data to supplement disease surveillance. Wkly Epidemiol Rec 1982;57(47):361-362 [FREE Full text]
12. Vandelaer J, Birmingham M, Gasse F, Kurian M, Shaw C, Garnier S. Tetanus in developing countries: an update on the Maternal and Neonatal Tetanus Elimination Initiative. Vaccine 2003 Jul 28;21(24):3442-3445. [doi: [10.1016/s0264-410x\(03\)00347-5](https://doi.org/10.1016/s0264-410x(03)00347-5)] [Medline: [12850356](https://pubmed.ncbi.nlm.nih.gov/12850356/)]

13. Lambo JA, Khahro ZH, Memon MI, Lashari MI. Completeness of reporting and case ascertainment for neonatal tetanus in rural Pakistan. *Int J Infect Dis* 2011 Aug;15(8):e564-e568 [FREE Full text] [doi: [10.1016/j.ijid.2011.04.011](https://doi.org/10.1016/j.ijid.2011.04.011)] [Medline: [21683637](https://pubmed.ncbi.nlm.nih.gov/21683637/)]

## Abbreviations

**CBS:** community-based surveillance  
**CDC:** Centers for Disease Control and Prevention  
**eIDEWS:** Electronic Disease Early Warning System  
**EMR:** Eastern Mediterranean Region  
**NT:** neonatal tetanus  
**NTSS:** Neonatal Tetanus Surveillance System  
**WHO:** World Health Organization

*Edited by M Alyahya, T Sanchez; submitted 30.01.21; peer-reviewed by R Al-Dubaiee, H Mehdizadeh; comments to author 22.02.21; revised version received 28.02.21; accepted 03.03.21; published 04.05.21.*

*Please cite as:*

*Al-Jamrah KM, Al Nabehi BA, Almoayed KA, Anam LS, Khader YS  
Performance of the Neonatal Tetanus Surveillance System (NTSS) in Sana'a, Yemen: Evaluation Study  
JMIR Public Health Surveill 2021;7(5):e27606  
URL: <https://publichealth.jmir.org/2021/5/e27606>  
doi: [10.2196/27606](https://doi.org/10.2196/27606)  
PMID: [33944794](https://pubmed.ncbi.nlm.nih.gov/33944794/)*

©Khaled Mohammed Al-Jamrah, Basheer Abdulgalil Al Nabehi, Khaled Abdullah Almoayed, Labiba Saeed Anam, Yousef S Khader. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 04.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Viewpoint

# The Impact of Implementing the Egypt Pandemic Preparedness Plan for Acute Respiratory Infections in Combating the Early Stage of the COVID-19 Pandemic, February-July 2020: Viewpoint

Hanaa Abu El Sood<sup>1</sup>, MD; Shima Ali Abu Kamer<sup>1</sup>, MD; Reham Kamel<sup>1</sup>, MD; Hesham Magdy<sup>1</sup>, MD; Fatma S Osman<sup>1</sup>, MD; Manal Fahim<sup>1</sup>, MD; Amira Mohsen<sup>2</sup>, PhD; Mohamad AbdelFatah<sup>3</sup>, MD; Mohamed Hassany<sup>4</sup>, MD; Salma Afifi<sup>1</sup>, MD; Alaa Eid<sup>5</sup>, MD

<sup>1</sup>Department of Epidemiology and Surveillance, Preventive Sector, Ministry of Health and Population, Cairo, Egypt

<sup>2</sup>Egypt Country Office, World Health Organization, Cairo, Egypt

<sup>3</sup>Central Administration of Preventive Affairs, Ministry of Health and Population, Cairo, Egypt

<sup>4</sup>National Hepatology and Tropical Medicine Research Institute, Ministry of Health and Population, Vairo, Egypt

<sup>5</sup>Preventive Sector, Ministry of Health and Population, Cairo, Egypt

**Corresponding Author:**

Hanaa Abu El Sood, MD

Department of Epidemiology and Surveillance

Preventive Sector

Ministry of Health and Population

3 Magles Elshaab St

Cairo,

Egypt

Phone: 20 01282833078 ext 002

Fax: 20 27923683

Email: [hanaaabelsood@hotmail.com](mailto:hanaaabelsood@hotmail.com)

## Abstract

This article briefly describes Egypt's acute respiratory infection (ARI) epidemic preparedness and containment plan and illustrates the impact of implementation of the plan on combating the early stage of the COVID-19 epidemic in Egypt. Pillars of the plan include crisis management, enhancing surveillance systems and contact tracing, case and hospital management, raising community awareness, and quarantine and entry points. To identify the impact of the implementation of the plan on epidemic mitigation, a literature review was performed of studies published from Egypt in the early stage of the pandemic. In addition, data for patients with COVID-19 from February to July 2020 were obtained from the National Egyptian Surveillance system and studied to describe the situation in the early stage of the epidemic in Egypt. The lessons learned indicated that the single most important key to success in early-stage epidemic containment is the commitment of all partners to a predeveloped and agreed-upon preparedness plan. This information could be useful for other countries in the region and worldwide in mitigating future anticipated ARI epidemics and pandemics. Postepidemic evaluation is needed to better assess Egypt's national response to the COVID-19 epidemic.

(*JMIR Public Health Surveill* 2021;7(5):e27412) doi:[10.2196/27412](https://doi.org/10.2196/27412)

**KEYWORDS**

pandemic preparedness; Egypt; ARI; epidemic mitigation; COVID-19

## Introduction

### Country Profile

Egypt is a transcontinental country in the Middle East. Most of the country is situated in northeastern Africa, with the Sinai Peninsula located in Western Asia. The country covers an area of 1 million km<sup>2</sup> and has coastline on the Mediterranean Sea in

the north and the Red Sea in the east. Most of its population is concentrated along the banks of the Nile River and on the river's delta, and only approximately 3% of the territory is inhabited. The population of Egypt is greater than 100 million inhabitants, and the gross domestic product per capita in 2017 was US \$10,799. Life expectancy was 74.4 years in females and 68.0 in males, and the under-5 mortality rate was 19.2. The main causes of death in Egypt are ischemic heart disease, stroke, and

cirrhosis; the health care access and quality index was 58.0 and the governmental health spending per person was US \$39 in 2018 [1].

### The Beginning of the COVID-19 Epidemic in Egypt

On December 1, 2019, a cluster of pneumonia cases of unknown cause was noticed in Wuhan, China. On December 2019, China announced an epidemic of acute respiratory disease of unknown cause [2]. As soon as the COVID-19 epidemic was announced and before the World Health Organization (WHO) announced it to be a pandemic, the Egyptian Ministry of Health and Population (MoHP) started to adapt its acute respiratory infection (ARI) pandemic preparedness plan to apply it to the anticipated pandemic.

Egypt is considered to be one of the first countries to monitor infectious diseases through a national surveillance system for reporting infectious diseases; this system has been in operation for about a century. Egypt's national surveillance system was assessed, enhanced, and expanded to include all governmental health care facilities in 1999. The National Egyptian Electronic Disease Surveillance System (NEDSS) targets 40 communicable diseases, including ARIs, and it includes an electronic reporting element [3]. A comprehensive network of epidemiological and laboratory vertical systems for reporting ARIs was developed in 2009, along with an alert system for early detection of novel respiratory viruses. The network covers the entire country and comprises surveillance systems targeting severe acute respiratory infections (SARIs), influenza-like illness (ILI), pneumonia, avian influenza, and Middle East respiratory syndrome coronavirus (MERS-CoV). Event-based surveillance was introduced in Egypt in 2009 in response to the 2009 H1N1 pandemic to aid timely detection of and response to possible epidemics.

The aims of this viewpoint are to review and discuss the preventive and control measures that have been implemented by the Egyptian MoHP in response to the COVID-19 pandemic and to share Egypt's experience with public health practitioners and authorities to enable better response to such events in the future.

The specific objective of the preparedness plan for response to COVID-19 was to reduce morbidity and mortality in the event of a COVID-19 epidemic in Egypt.

### Methodology

In this report, we use two approaches: to discuss the interventions implemented in the COVID-19 epidemic in Egypt as a part of the preparedness plan and to describe the epidemic situation in its early stage in an attempt to link it to the interventions performed.

To describe the ARI epidemic preparedness and containment plan in Egypt, all documents addressing the ARI epidemic preparedness and response plan and their updates were reviewed, including the ARI case management plan, ARI and Influenza Pandemic Preparedness Plan, and national disease surveillance guidelines. In addition, the key studies and publications

describing the situation of the early stage of the COVID-19 epidemic were reviewed to describe the epidemic situation.

National surveillance data on all patients in Egypt with COVID-19 from February to July 2020 were obtained from the national disease surveillance database. Web-based data sources were consulted regularly to collect data published on the early stage of the epidemic in Egypt. Descriptive data analysis was performed to assess the response to the epidemic in Egypt.

### Egypt's ARI Pandemic Preparedness and Containment Plan

Egypt's ARI preparedness plan was first developed in 2007 in collaboration with WHO Egypt. It was activated in 2009 during the H1N1 pandemic, updated in 2019, and then adapted to the COVID-19 pandemic [4].

The pandemic preparedness plan was activated early, before the introduction of SARS-CoV-2 into the country, when the first positive case was identified among contacts of a Chinese woman who tested positive after returning to China from a short business trip to Cairo.

The plan includes five pillars:

1. Crisis management
2. Enhancing surveillance systems and contact tracing
3. Case and hospital management
4. Raising community awareness
5. Quarantine and entry points

### Crisis Management

A pre-established Supreme National Committee for crisis management was activated early in the pandemic. Members of the committee are Ministers of relevant Ministries, including the Ministry of Health, Ministry of Agriculture, Ministry of Local Development, Ministry of Environment, Ministry of Defense, Ministry of Foreign Affairs, Ministry of General Information Authority, General Administration of Veterinary Affairs, Crisis Management Room at Council of Ministers, and Ministry of the Interior, Preventive and Endemic Affairs of Ministry of Health. This committee was and is still responsible for deciding on the necessary preventive and control measures based on the rapid changes in the pandemic situation globally and in Egypt.

The crisis management committee of the MoHP was assembled before the introduction of the virus to Egypt. The committee included all sectors concerned within the ministry (preventive sector, curative sector, health care and nursing sector, general authority for health insurance, general authority for hospitals and educational institutes, central administration of medical medicine, central administration of preventive affairs, General Secretariat of Specialized Medical Centers, Central Administration of Pharmacy, General Directorate of Hospitals, General Department of Chest Diseases, General Department of Infectious Diseases, General Administration of Veterinary Affairs Mechanism, Epidemiology and Surveillance, the official spokesperson of the Ministry of Health, and a representative of the Supreme Council of Universities). The committee is



responsible for monitoring the epidemiologic situation on a 24-hour basis, implementing all preventive and curative measures to contain the disease, ensuring the preparedness and response of emergency teams 24 hours per day, establishing follow-up treatment protocols, and ensuring the availability of medical supplies necessary for prevention and case management and equipment and supplies for intensive care units.

## Enhancing ARI Surveillance Systems

### Case Definitions

NEDSS, ILI, SARI, and pneumonia and mortality surveillance systems were activated through 2 days of training for surveillance teams in all governmental health care facilities conducted at the central and regional levels. Guidelines for COVID-19 epidemic response were developed and distributed at all health system levels, and teams were instructed to report ARIs on a daily basis. Case definitions were developed using the WHO COVID-19 case definition [5] and distributed to all governmental and private health care facilities for reporting any suspected cases. The case definition was updated 3 times to increase the sensitivity for case detection as the epidemic progressed.

The updated COVID-19 case definitions as of June 2020 are outlined below.

A *suspected case* is defined as anyone who suffers from acute respiratory symptoms (cough, shortness of breath) or fever  $\geq 38$  °C or both with no other reasons, or anyone with any of the following conditions within 14 days before symptoms:

1. History of travel to a country or region that proves wide community spread or limited local transmission of COVID-19
2. Contact with a confirmed case with COVID-19
3. Contact with a person with acute respiratory symptoms (cough, shortness of breath) or a fever  $\geq 38$  °C and who is epidemiologically related to a place or region (locally or internationally) with epidemic outbreaks of COVID-19 but not yet confirmed by a laboratory
4. Health care workers or workers in a health care facility with reported confirmed cases of COVID-19 or a patient with SARI with fever  $\geq 38$  °C with one of the symptoms of acute respiratory disease (cough, shortness of breath) and the cause of the pathological condition could not be identified

If suspicion of the above is not verified, consider any person with at least two of the following clinical characteristics:

1. Fever, severe respiratory symptoms, or both
2. Computed tomography scan for chest (if not available; normal x-rays are performed on the chest) with diagnostic properties of COVID-19
3. Normal or low leukocyte count with lymphocytopenia

A *confirmed case* is defined as a person with laboratory confirmation of COVID-19 infection by real-time polymerase chain reaction (RT-PCR).

COVID-19 was added to the list of NEDSS-reportable diseases, and a data collection was developed and added to the web-based data screens. Suspected and confirmed cases of COVID-19 are

entered at all governmental hospitals to provide a regular description of the epidemic situation in Egypt, for contact tracing, and for future predictions. Daily reports are developed and shared with relevant stakeholders.

The International Health Regulations unit at MoHP is in direct contact with WHO Egypt and Eastern Mediterranean Regional (EMR) Office for daily reporting, regular sharing of global- and country-level information, updated recommendations, and viral genetic mutations.

The event-based surveillance was expanded to include the entire country, and teams at all levels are immediately reporting alert signals to the central level. Signal verification and case detection are performed for all received alert signals.

### The Role of Laboratories in Epidemic Mitigation

Specimens are collected from all suspected cases for testing at regional laboratories in governorates and central laboratories in Cairo. Testing results are monitored daily and distributed to affiliated governorates and hospitals. Genetic mutation is monitored regularly at the global and regional levels.

COVID-19 and influenza testing kits and reagents are secured at the Central Public Health Laboratory and regional laboratories. Training was provided to laboratory specialists and technicians at the governorate level in specimen collection, archiving, and transfer. Specimens are shared regularly with WHO reference laboratories.

### Contact Tracing

Evidence from the COVID-19 response in China has indicated that efficient contact tracing can enable early detection and isolation of cases and can substantially reduce disease transmission [6]. Because contact tracing is a crucial part of COVID-19 epidemic control in conjunction with case finding, Egypt was able to apply this strategy early in the pandemic, when the number of cases was small. In Egypt, contacts were classified as close and casual contacts according to the European Centers for Disease Control and Prevention definition and traced to provide contacts with information on self-quarantine, proper hand hygiene, and respiratory etiquette measures and to advise them on what to do if they developed symptoms. Contacts with symptoms undergo laboratory testing by PCR in a timely fashion for early case detection [7]. Responsibilities for contact tracing and management were developed and distributed at all levels of the health system.

### Case and Hospital Management

Intensive care units (adult and pediatric) and hospitals with ventilator capacity (adult and pediatric) were identified for the management of COVID-19 cases. A referral system between hospitals was defined, and information was distributed to all governorates and hospitals. Training was provided for all hospital physicians in case detection using the case definitions, triage, and protocol for management of acute respiratory infections. Continuous supervision and monitoring from the central level of assigned hospitals was performed to evaluate hospital performance in dealing with cases of acute respiratory symptoms. Chest consultants were assigned for management of severe cases. A manual was developed for treatment of

patients at different disease stages and severity. This manual is being revised and updated regularly as new information becomes available.

### **Raising Community Awareness**

A hotline was activated and WhatsApp was used 7 days per week to answer questions, respond to requests and complaints and coordinate patient transfer and hospital admissions. In addition, Facebook, radio, and television broadcasts were used to raise community awareness of the current status of the COVID-19 pandemic in Egypt, disease prevention, and home management of patients. Printed posters were developed and distributed at the intermediate and peripheral health system and hospital levels. The printed material included 3000 posters for case definition, 30,000 brochures of fact sheets, 2000 case management booklets, and 30,000 brochures on how to manage patients at home, in addition to >2 million posters on preventive measures at home, in the community, and at health care facilities. The printed materials were delivered to all governmental and private health facilities and communities.

### **Quarantine and Points of Entry**

Brochures were distributed to staff at all points of entry, including the definitions of suspected and confirmed cases of COVID-19. Travelers arriving to Egypt were assessed, and suspected cases were transferred to isolation hospitals as preventive measures. During the period from January to July 2020, 91,787 travelers arrived via different points of entry. Of these 91,787 travelers, 1616 (1.8%) had elevated temperature or respiratory symptoms detected at the checkpoints and were transferred to hospitals for evaluation and treatment. All asymptomatic arrivals (90,171) were tested by rapid testing. Of

them, 2329/90,171 (2.6%) tested positive and were sent for PCR confirmation testing. Of the 2329 persons who tested positive by rapid testing, 966 (41.5%) tested positive by PCR and were quarantined to prevent spread of the disease and for follow-up. All remaining travelers (87,842) were sent home for home isolation and were followed up on a daily basis by telephone to determine any symptoms appeared.

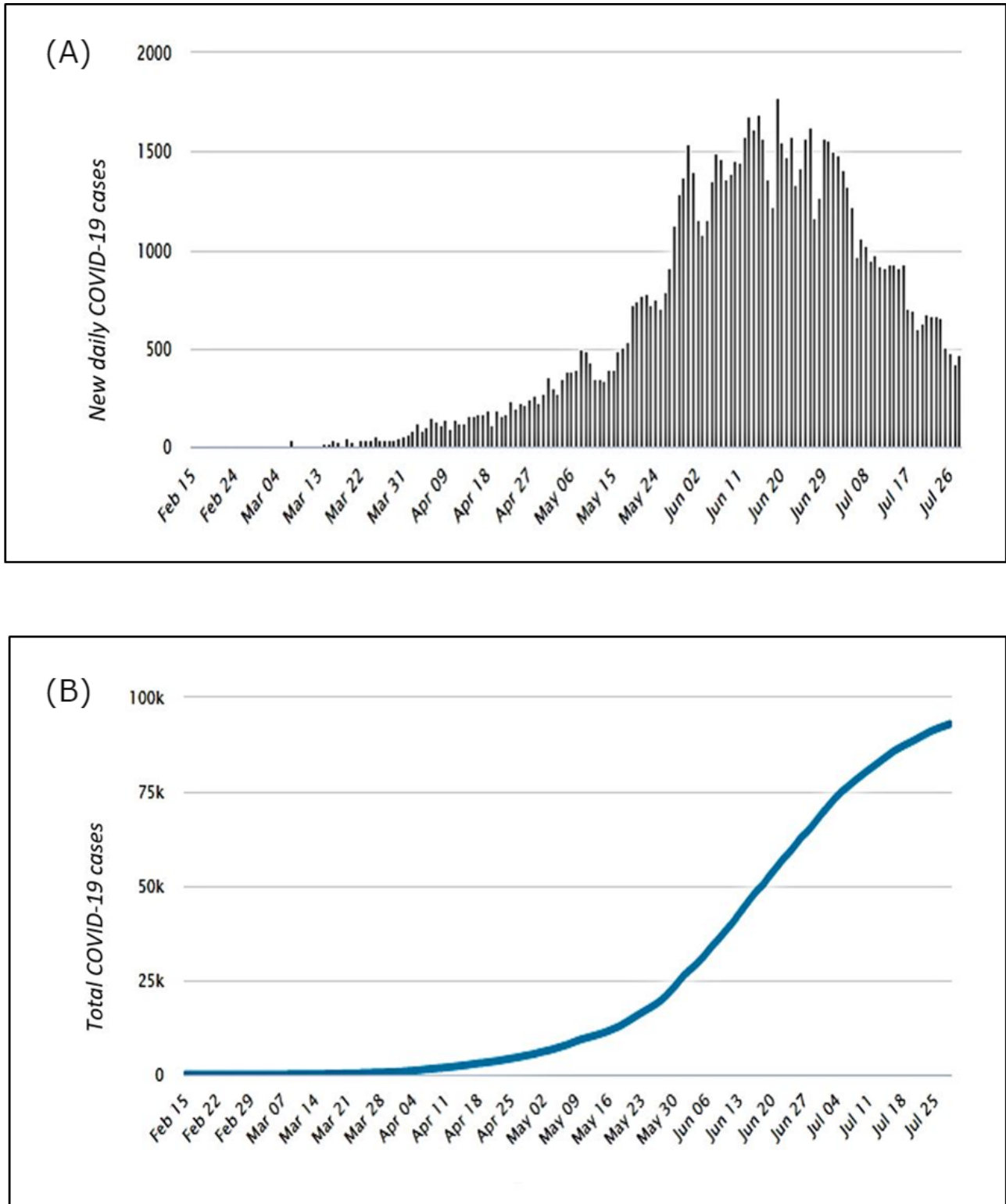
### **Source of Data**

We used data from the NEDSS from February to July 2020. Descriptive data analysis was performed by time, person, and place using Epi Info, version 7 (US Centers for Disease Control and Prevention). Attack rate was calculated as the total number of confirmed cases/100,000 population with the population data for 2020 obtained from the Department of Information Center at MoHP.

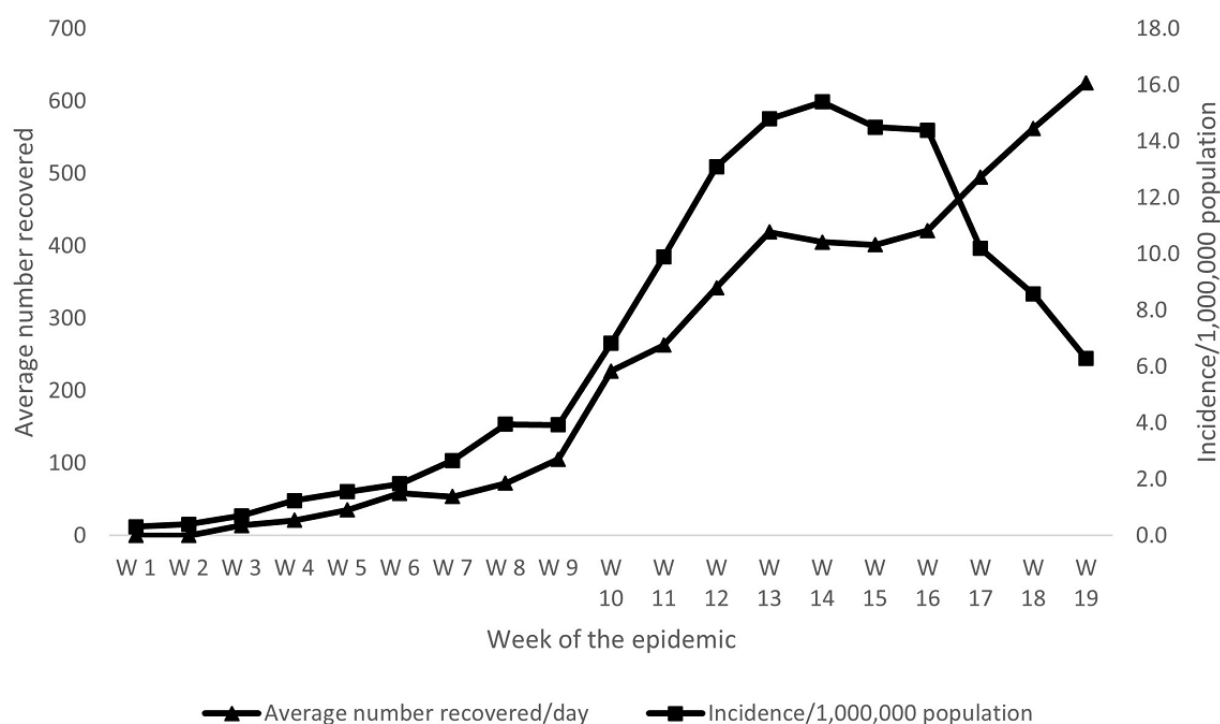
### **Situation During the Early Phase of the Epidemic**

According to MoHP senior officials, Egypt passed the first wave of the epidemic peak and entered the flattening phase of daily cases in mid-June 2020, with the highest number of cases in one day (1774) reported on June 20. The number of cases started to gradually drop during July, August, and possibly through September, with the lowest number of cases (112) reported on August 5 (Figures 1 and 2). Modeling studies suggested that Egypt had succeeded in delaying the peak of the COVID-19 curve after the seventh week, with no exponential growth of transmission rate identified [8].

Figure 1. (A) Daily new and (B) total numbers of COVID-19 cases in Egypt from February to July 2020 [9].



**Figure 2.** Incidence rate of COVID-19 and average number of recoveries in Egypt, February to July 2020. Source: Ministry of Health and Population daily COVID-19 report.



The overall number of cases by week started to rise in early May and peaked in mid-June, after which it started to decline but did not reach the baseline (Figure 1, A and B) [9]. The mean weekly growth rate from February to May 2020 was 0.35 (SD 0.33), which declined over time from 1.18 in early March to

0.13 at the end of May. Similarly, the reproductive number ( $R_0$ ) and herd immunity threshold declined from 6.5 to 1.6 and from 85% to 39%, respectively; meanwhile, the doubling time increased from 1.8 days to 15.6 days (Table 1) [10].

**Table 1.** Reproductive number ( $R_0$ ) and corresponding herd immunity threshold of COVID-19 in Egypt, February-May 2020 [10].

Date (2020)	Growth rate (weekly) <sup>a</sup>	Doubling time (days) <sup>b</sup>	Reproductive number <sup>c</sup>	Herd immunity threshold (%) <sup>d</sup>
February 28	0	0	1	0
March 7	1.18	1.8	6.5	85
March 14	0.79	2.7	4.7	79
March 21	0.44	4.8	3.1	67
March 28	0.29	7.4	2.3	57
April 7	0.34	6.3	2.6	61
April 14	0.31	6.8	2.5	59
April 21	0.18	11.6	1.9	46
April 28	0.16	13.4	1.7	42
May 7	0.2	10.5	1.9	49
May 14	0.14	15.2	1.6	39
May 21	0.13	15.6	1.6	39

<sup>a</sup>Mean 0.35 (SD 0.33).

<sup>b</sup>Mean 8.75 (SD 4.85).

<sup>c</sup>Mean 2.6 (SD 1.55).

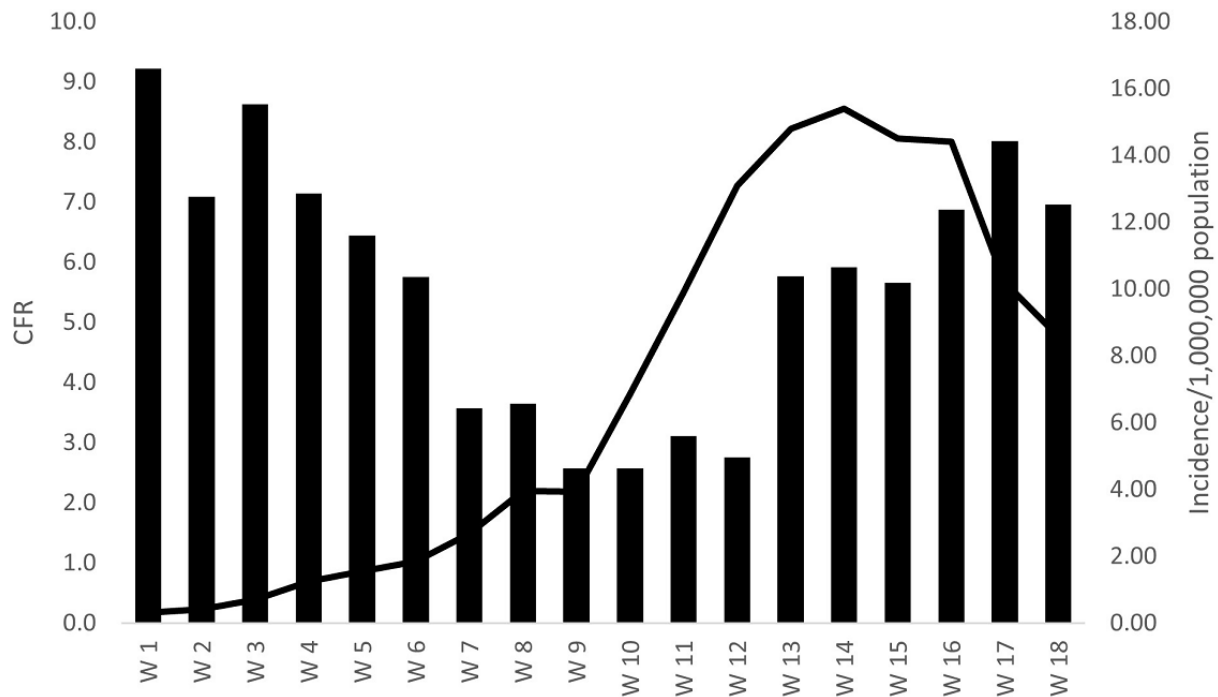
<sup>d</sup>Mean 52 (SD 22).

Incidence of COVID-19 in Egypt by week peaked in the 14th week after the first case was confirmed in Egypt (15.4/1,000,000 population) and declined to 6.29 in the 19th week after the first

case; meanwhile, the average number recovered per week constantly increased, reaching 625.0 by the 19th week after the first case was reported (Figure 2). The case fatality rate showed

a pattern of 2 peaks, 1 each in weeks 1-4 and weeks 16-18, with an increase after the decline in weeks 9-12, ranging from 2.57% in weeks 9-10 to 9.22% in week 1 (Figure 3).

**Figure 3.** COVID-19 incidence rate and case fatality rate in Egypt, February to July 2020. Source: Ministry of Health and Population daily COVID-19 report. CFR: case fatality rate.



Overall, 102,789 COVID-19 cases were reported to NEDSS in the study period, including 78,048 (43.2%) confirmed COVID-19 cases, giving an incidence of 77.0 cases/1,000,000 population, and 3457 (4.4%) deaths were reported due to COVID-19. Of the 78,048 case patients, 44,969 (57.6%) had mild symptoms and were identified in outpatient clinics. The middle age group (35-60 years) was the most affected; meanwhile, the disease was rare in people <15 years of age, representing 2.6% of all cases (2043/78,048), with slightly more male patients (40,621/78,048, 52%) than female (37,422/78,048, 48%). Of the 78,048 confirmed cases, 39,964 (51.2%) were

admitted to hospital for health care, while 33,037 (48.8%) were isolated at home or youth hostels for follow-up (Table 2).

Among the 54,300 cases for whom clinical data were available, the most prominent symptom was fever (45,188, 83.2%), followed by cough (39,549, 72.8%), dyspnea (27,009, 49.7%), and sore throat (26,330, 48.5%). Of the 12,661 confirmed cases for whom comorbidity data were available, 6845 (54.1%) had a history of diabetes and 5816 (45.9%) had cardiovascular disease, while only 274 (2.2%) were obese and 279 (2.2%) were pregnant (Table 2).

**Table 2.** Demographic, epidemiologic, and clinical characteristics of patients with confirmed COVID-19, National Egyptian Disease Surveillance, February to July 2020.

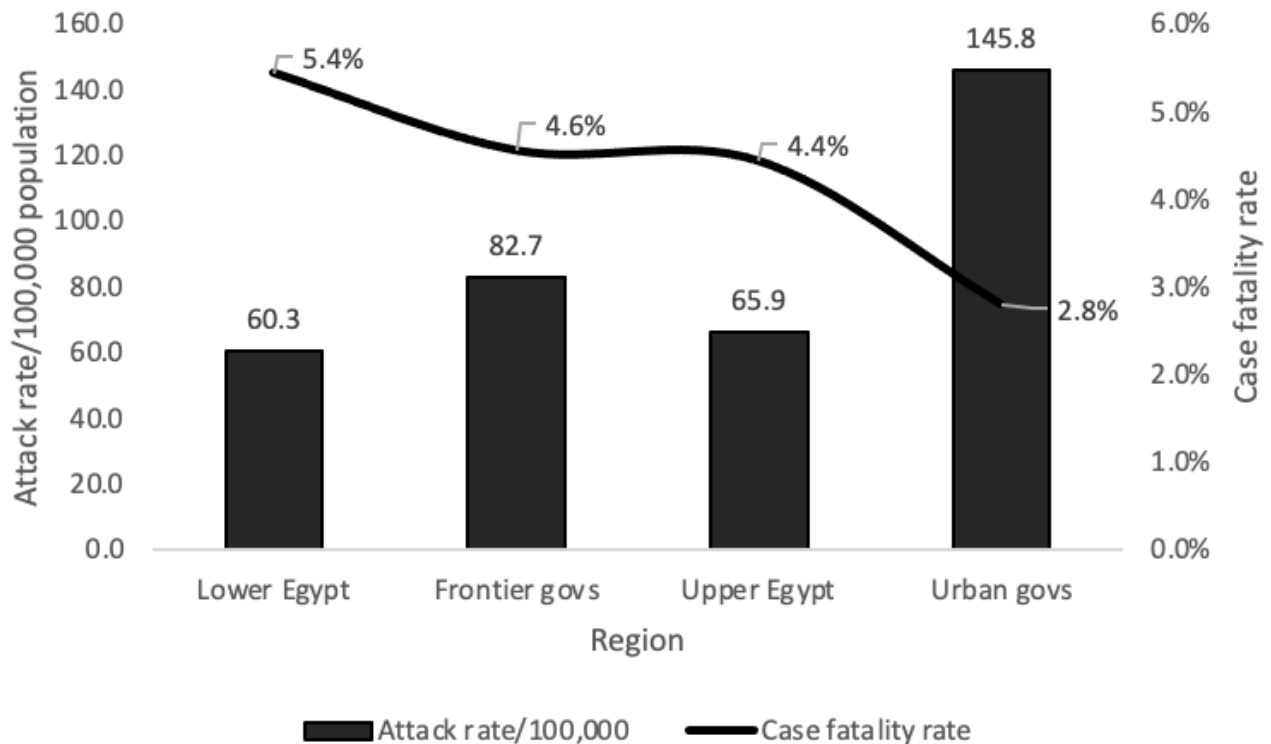
Characteristic	Value, n (%)
Suspected cases	102,789 (N/A) <sup>a</sup>
Confirmed cases	78,048 (43.2)
<b>Source</b>	
Inpatient	44,969 (57.6)
Outpatient	33,079 (42.4)
<b>Age group (years)</b>	
<1	223 (0.3)
1-4	552 (0.7)
5-14	1268 (1.6)
15-34	20,197 (25.9)
35-64	44,948 (57.6)
≥65	10,855 (13.9)
<b>Gender</b>	
Male	40,621 (52)
Female	37,422 (48)
<b>Clinical picture<sup>b</sup></b>	
Fever	45,188 (83.2)
Cough	39,549 (72.8)
Difficulty breathing	27,009 (49.7)
Sore throat	26,330 (48.5)
Joint pain	18,287 (33.7)
Diarrhea	6260 (11.5)
Vomiting	4730 (8.7)
Pneumonia	23,503 (43.3)
<b>Comorbidity<sup>c</sup></b>	
Diabetes	6845 (54.1)
Cardiovascular disease	5816 (45.9)
Chronic obstructive pulmonary disease	2620 (20.7)
Renal	630 (5.0)
Liver	491 (3.9)
Pregnant	279 (2.2)
Obese	274 (2.2)
Immunocompromised	226 (1.8)
<b>Isolation</b>	
Hospital isolation	39,964 (51.2)
Youth hostel	8380 (10.7)
Home isolation	29,704 (38.1)
Case fatality	3333 (4.3)

<sup>a</sup>N/A: not applicable.<sup>b</sup>Clinical data available for 54,300 cases.<sup>c</sup>Comorbidity data available for 12,661 cases.

Incidence rate differed by region of residence, ranging from 60.3 in Lower Egypt to 145.8/1,000,000 population in the urban governorates, while the case fatality rate (CFR) ranged from 2.8% in urban governorates to 5.4% in Lower Egypt

governorates. Data analysis indicated that highest incidence rate and lowest CFR were identified in the urban governorates (Figure 4).

**Figure 4.** Distribution of COVID-19 attack rates and case fatality rates by region, National Egyptian Disease Surveillance, February to July 2020. Govs: governorates.



## Conclusions

Egypt succeeded in containing the early stage of the COVID-19 epidemic. Containment measures taken in the early stage of the epidemic depended mainly on early case detection and tracing and isolation of infected persons as well as on raising community awareness to stop the disease from spreading. Strengthening of mitigation efforts began when community-wide

transmission occurred in the form of proper case management and coordination of different interventions to slow the spread of COVID-19 and mitigate its effects on the health care system and community. The ARI pandemic preparedness plan proved effective in epidemic mitigation, with high commitment from all partners. Postepidemic performance evaluation is needed to better assess Egypt's national response to the COVID-19 epidemic.

## Conflicts of Interest

None declared.

## References

1. Egypt. Institute for Health Metrics and Evaluation. URL: <http://www.healthdata.org/egypt> [accessed 2021-05-03]
2. She J, Jiang J, Ye L, Hu L, Bai C, Song Y. 2019 novel coronavirus of pneumonia in Wuhan, China: emerging attack and management strategies. *Clin Transl Med* 2020 Feb 20;9(1):19 [FREE Full text] [doi: [10.1186/s40169-020-00271-z](https://doi.org/10.1186/s40169-020-00271-z)] [Medline: [32078069](https://pubmed.ncbi.nlm.nih.gov/32078069/)]
3. Abdel-Razik MSM, Rizk HII, Hassan MHM. Surveillance of communicable diseases for decisionmaking in Egypt: 2006-2013. *East Mediterr Health J* 2017 Aug 20;23(6):395-403 [FREE Full text] [doi: [10.26719/2017.23.6.395](https://doi.org/10.26719/2017.23.6.395)] [Medline: [28836651](https://pubmed.ncbi.nlm.nih.gov/28836651/)]
4. Ministry OH. Preparedness Plan for Pandemic Influenza. Arab Republic of Egypt Ministry of Health and Population Preventive Sector. URL: <http://www.emro.who.int/images/stories/csr/documents/nipp-egypt-english-final-dec-2018.pdf?ua=1> [accessed 2021-05-03]
5. Public health surveillance for COVID-19: interim guidance. World Health Organization. URL: [https://www.who.int/publications/i/item/global-surveillance-for-human-infection-with-novel-coronavirus-\(2019-ncov\)](https://www.who.int/publications/i/item/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov)) [accessed 2021-05-03]

6. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020 Feb;395(10223):507-513. [doi: [10.1016/s0140-6736\(20\)30211-7](https://doi.org/10.1016/s0140-6736(20)30211-7)]
7. Contact tracing: public health management of persons, including healthcare workers, who have had contact with COVID-19 cases in the European Union – first update. European Center for Disease Control and Prevention. 2020 Mar 31. URL: <https://tinyurl.com/525zdzk5> [accessed 2021-05-03]
8. Hasab A, El-Ghitany E, Ahmed N. Situational Analysis and Epidemic Modeling of COVID-19 in Egypt. *JHIPH* 2020 Apr 25;50(1):46-51. [doi: [10.21608/jhiph.2020.87076](https://doi.org/10.21608/jhiph.2020.87076)]
9. Coronavirus: Egypt. Worldometer. URL: <https://www.worldometers.info/coronavirus/country/egypt/> [accessed 2021-05-03]
10. Radwan GN. Epidemiology of SARS-CoV-2 in Egypt. *East Mediterr Health J* 2020 Jul 23;26(7):768-773 [FREE Full text] [doi: [10.26719/emhj.20.084](https://doi.org/10.26719/emhj.20.084)] [Medline: [32794161](https://pubmed.ncbi.nlm.nih.gov/32794161/)]

## Abbreviations

**ARI:** acute respiratory infection

**CFR:** case fatality rate

**ILI:** influenza-like illness

**MERS-CoV:** Middle East respiratory syndrome coronavirus

**MoHP:** Ministry of Health and Population

**NEDSS:** National Egyptian Electronic Disease Surveillance System

**RT-PCR:** real-time polymerase chain reaction

**SARI:** severe acute respiratory illness

**WHO:** World Health Organization

*Edited by M Alyahya; submitted 26.01.21; peer-reviewed by S Samy, A Mansour; comments to author 30.03.21; revised version received 06.04.21; accepted 06.04.21; published 07.05.21.*

*Please cite as:*

Abu El Sood H, Abu Kamer SA, Kamel R, Magdy H, Osman FS, Fahim M, Mohsen A, AbdelFatah M, Hassany M, Afifi S, Eid A  
*The Impact of Implementing the Egypt Pandemic Preparedness Plan for Acute Respiratory Infections in Combating the Early Stage of the COVID-19 Pandemic, February-July 2020: Viewpoint*  
*JMIR Public Health Surveill* 2021;7(5):e27412  
URL: <https://publichealth.jmir.org/2021/5/e27412>  
doi: [10.2196/27412](https://doi.org/10.2196/27412)  
PMID: [33830932](https://pubmed.ncbi.nlm.nih.gov/33830932/)

©Hanaa Abu El Sood, Shimaa Ali Abu Kamer, Reham Kamel, Hesham Magdy, Fatma S Osman, Manal Fahim, Amira Mohsen, Mohamad AbdelFatah, Mohamed Hassany, Salma Afifi, Alaa Eid. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 07.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.



Original Paper

# Risk Factors of Extensively Drug Resistant Typhoid Fever Among Children in Karachi: Case-Control Study

Anum Vighio<sup>1\*</sup>, BDS, MScDPH; Muhammad Asif Syed<sup>1\*</sup>, PhD; Ishfaq Hussain<sup>1</sup>, MBBS; Syed Masroor Zia<sup>1</sup>, MBBS; Munaza Fatima<sup>1</sup>, MPH; Naveed Masood<sup>1</sup>, MPH; Ambreen Chaudry<sup>1</sup>, MSPH; Zakir Hussain<sup>1</sup>, MPH; Mirza Zeeshan Iqbal Baig<sup>1</sup>, MSPH; Mirza Amir Baig<sup>1</sup>, MPH, MHM; Aamer Ikram<sup>1</sup>, PhD; Yousef S Khader<sup>2</sup>, SCD

<sup>1</sup>Field Epidemiology and Laboratory Training Program Pakistan, Islamabad, Pakistan

<sup>2</sup>Department of Public Health, Community Medicine and Family Medicine, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan

\*these authors contributed equally

**Corresponding Author:**

Anum Vighio, BDS, MScDPH

Field Epidemiology and Laboratory Training Program Pakistan

National Institute of Health

Park Road, Chak Shahzad

Islamabad, 44000

Pakistan

Phone: 92 519255307

Email: [anumvighio@gmail.com](mailto:anumvighio@gmail.com)

## Abstract

**Background:** Extensively drug resistant typhoid fever (XDR-TF) has been responsible for an ongoing outbreak in Pakistan, which began in November 2016.

**Objective:** This study aimed to determine the risk factors associated with XDR-TF.

**Methods:** This age- and sex-matched case-control study was conducted during May-October 2018 in Karachi. All patients with XDR-TF were identified from the laboratory-based surveillance system data. Cases included patients aged <15 years living in Karachi with culture-positive *Salmonella enterica* serovar Typhi with resistance to chloramphenicol, ampicillin, trimethoprim/sulfamethoxazole, fluoroquinolones, and third-generation cephalosporins. Age- and sex-matched controls included children free from the symptoms of TF, aged under 15 years, and residing in Karachi. All controls were recruited from among those who attended outpatient clinics.

**Results:** A total of 75 cases and 75 controls were included in this study. On univariate analysis, the odds of having XDR-TF were 13-fold higher among participants who used piped municipal water than among those who did not (odds ratio [OR] 12.6, 95% CI 4.1-38.6). The use of bore water was significantly associated with XDR-TF (OR 5.1, 95% CI 1.4-19.0). Cases were more likely to report eating French fries with sauce (OR 13.5, 95% CI 3.9-47.0) and poppadum (OR 3.4, 95% CI 1.7-6.7) from street vendors than controls. Boiling water at home was negatively associated with XDR-TF (OR 0.3, 95% CI 0.2-0.7). On multivariate analysis, 2 factors were independently associated with XDR-TF. Using piped municipal water (OR 10.3, 95% CI 3.4-30.4) and eating French fries with sauce from street vendors (OR 8.8, 95% CI 2.1-36.2) were significantly associated with an increased odds of XDR-TF.

**Conclusions:** Community water supply and street food eating habits were implicated in the spread of the superbug *S typhi* outbreak, which continues to grow in Karachi. Therefore, it is recommended to improve the community water supply to meet recommended standards and to develop a policy to improve the safety of street food. In addition, health authorities are required to conduct mass vaccination for TF among high-risk groups.

(*JMIR Public Health Surveill* 2021;7(5):e27276) doi:[10.2196/27276](https://doi.org/10.2196/27276)

**KEYWORDS**

case-control study; drug resistance; extensively drug resistant typhoid fever; risk factors; typhoid fever

## Introduction

Typhoid fever is a preventable disease caused by *Salmonella enterica* serovar Typhi (*S* Typhi). A systematic review estimated an occurrence of 26.9 million culture-confirmed cases annually [1]. Typhoid fever affects high-risk populations in low- and middle-income countries [2]. Vaccination, access to clean water, and improved sanitation are effective means to prevent the spread of typhoid.

Antibiotics are vital to the treatment of typhoid. However, antibiotic-resistant pathogens have become increasingly prevalent [3]. Antibiotic resistance is an emerging public health threat worldwide. *S* Typhi resistant to first-line antibiotics (ampicillin, trimethoprim/sulfamethoxazole, and chloramphenicol) was initially considered multidrug-resistant. Reduced susceptibility to second-line drugs (ie, fluoroquinolones) has also been widely reported since these had then emerged as the preferred treatment for multidrug-resistant typhoid fever. Ceftriaxone and azithromycin are now used to treat patients with typhoid fever, who are nonresponsive to fluoroquinolones and first-line drug treatments [4].

In November 2016, the first ever recorded outbreak of extensively drug resistant typhoid fever (XDR-TF) (characterized by resistance to ampicillin, trimethoprim/sulfamethoxazole, chloramphenicol, fluoroquinolones, and ceftriaxone) was identified in the Sindh Province in Pakistan. Afterward, increased numbers of XDR-TF cases have been reported from different parts of the country, which were associated with abysmal sewage and water systems, coupled with low vaccination rates and overpopulated city dwellings [5]. Sporadic cases of XDR-TF have been reported worldwide, thus raising the fear of antibiotic failure at a global level [5].

A robust laboratory-based surveillance system for XDR-TF was established in Karachi (Sindh Province) in December 2018. This study aimed to determine factors associated with XDR-TF among children under 15 years of age in Karachi.

## Methods

### Study Design and Setting

This age- and sex-matched case-control study (75 cases and 75 controls) was conducted during May-October 2018 in Karachi, the capital city of Sindh Province in Pakistan. All patients with XDR-TF were identified from the laboratory-based surveillance system data through simple random sampling. If the patient provided incomplete information or did not agree to participate, another case was chosen at random. Cases included patients with culture-positive *S* Typhi resistant to chloramphenicol, ampicillin, trimethoprim-sulfamethoxazole, fluoroquinolones, and third-generation cephalosporins, who are aged <15 years

and living in Karachi. Cases aged over 15 years and those who are not permanent residents of Karachi were excluded. Age- and sex-matched controls included children who are free from the symptoms of typhoid fever, aged under 15 years, and residents of Karachi. Those who had experienced fever within the past 1 month were excluded. All controls were recruited from among those who attended outpatient clinics. This study was conducted after the formal approval of the Director General Health Services, Government of Sindh, and ethical approval was obtained from the ethics review board of Mohammad Medical College, Sindh. Verbal consent was obtained from the guardians or parents of the participants before obtaining data, and patient confidentiality was maintained by allotting a serial number to each participant.

### Data Collection

For both cases and controls, face-to-face interviews were conducted with caregivers or parents, using a standardized questionnaire. The questionnaire collected information about the participants' demographic and clinical characteristics and modifiable risk factors. For cases, information was sought for a period of exposure from 3 weeks prior to the onset of symptoms; for controls, information was sought for a period from 3 weeks prior to the date of the interview. Other questions included those related to sources of drinking water, boiling of water for domestic use, and street food eating habits among children, including the consumption of poppadum, French fries served by default with homemade sauce, and ice cream.

### Environmental Samples

Water samples were obtained from the houses of infected cases and sent to the Pakistan Council of Research in Water Resources (Karachi). All samples were tested for the presence of fecal coliform bacteria, turbidity, and pH. Samples were not obtained from the controls owing to the lack of resources.

### Statistical Analysis

Data are expressed as means and percentages. Univariate and multivariate analyses were conducted using binary logistic regression to determine factors associated with XDR-TF. Odds ratios (ORs) and their corresponding 95% CI values were reported. A *P* value of <.05 was considered significant. Epi Info (version 7, Centers for Disease Control and Prevention) was used for statistical analysis.

## Results

### Participants' Characteristics

A total of 75 cases and 75 controls were included in this study. Among cases, males were predominant (n=40, 53%). Almost half (n=34, 45%) of the cases aged 5-9 years (mean 6.5 years, range 1-177 months). The majority of cases (97%) and controls (96%) were not vaccinated against typhoid (Table 1).

**Table 1.** The characteristics of 75 cases of extensively drug resistant typhoid fever and 75 age- and sex-matched controls in Karachi, Pakistan, in 2018.

Characteristics	Cases (n=75), n (%)	Controls (n=75), n (%)
<b>Gender</b>		
Male	40 (53)	40 (53)
Female	35 (47)	35 (47)
<b>Age (years)</b>		
0-4	27 (36)	27 (36)
5-9	34 (45)	34 (45)
10-14	14 (19)	14 (19)
<b>Household income</b>		
<US \$125	60 (80)	50 (67)
≥US \$125	15 (20)	25 (33)
<b>Vaccinated for typhoid</b>		
Yes	2 (3)	3 (4)
No	73 (97)	72 (96)
<b>Residential area</b>		
Urban	54 (72)	40 (53)
Rural	21 (28)	35 (47)

### Univariate Analysis

On univariate analysis, the odds of having XDR-TF was 13-fold higher among participants who used piped municipal water than among those who did not (OR 12.6, 95% CI 4.1-38.6). The use of bore water was significantly associated with XDR-TF (OR

5.1, 95% CI 1.4-19.0). Cases were more likely to report eating French fries with sauce (OR 13.5, 95% CI 3.9-47.0) and poppadum (OR 3.4, 95% CI 1.7-6.7) from street vendors than controls. Boiling water at home was negatively associated with XDR-TF (OR 0.3, 95% CI 0.2-0.7) (Table 2).

**Table 2.** Univariate analysis of risk factors among 75 cases of extensively drug resistant typhoid fever and 75 age- and sex-matched controls enrolled in this study in Karachi, Pakistan, in 2018.

Factors	Odds ratio (95% CI)	P value
<b>Drinking water source</b>		
Bottled water	Ref <sup>a</sup>	N/A <sup>b</sup>
Piped municipal water	12.6 (4.1-38.6)	<.001
Bore water	5.1 (1.4-19.0)	.01
Tanker water	3.8 (0.8-17.6)	.08
Water treatment: boiling drinking water (yes vs no)	0.3 (0.2-0.7)	.003
<b>Common street food eating habits</b>		
French fries with sauce (yes vs no)	13.5 (3.9-47.0)	<.001
Ice cream (yes vs no)	2.3 (1.0-5.1)	.05
Poppadum (yes vs no)	3.4 (1.7-6.7)	<.001
Vaccination against typhoid (yes vs no)	0.7 (0.1-4.1)	.65

<sup>a</sup>Ref: reference for comparison.

<sup>b</sup>N/A: not applicable.

### Multivariate Analysis

On multivariate analysis, 2 factors were independently associated with XDR-TF. Using piped municipal water (OR 10.3, 95% CI 3.4-30.4) and eating French fries with sauce from

street vendors (OR 8.8, 95% CI 2.1-36.2) were significantly associated with increased odds of XDR-TF.

### Environmental Samples

Of the 75 water samples collected, 51 (68%) showed the presence of fecal coliform bacteria.

## Discussion

### Principal Findings

Previous studies, 2 of which were conducted in Pakistan, have suggested that children under 15 years of age are more likely to be affected by typhoid fever in endemic countries than those who are older than 15 years [6-9]. In this study, numerous cases were predominantly children aged under 15 years. This may be associated with high-risk eating behavior, poor hygiene practices in school and community settings, and lower immunity [10,11]. However, some studies have reported contrary findings and showed that the more likely affected age group involved those aged over 15 years [12,13].

Most of the XDR-TF cases were males, which is concurrent with previous reports from Pakistan and Uganda [7,12]. Although some studies found females to be predominant [13,14], which may be expected owing to different cultural and social norms in different countries.

Socioeconomic status has been discussed in the fundamental cause theory of health inequalities, stating it to be a risk factor for deteriorated health outcomes over time [15,16]. Furthermore, a low socioeconomic status is associated with higher odds of TF [17,18]. In this study, most cases belonged to a lower social background. Lower socioeconomic groups usually consume unsafe drinking water, are unable to purchase vaccines (because the typhoid vaccine is not included in the routine immunization schedule of Pakistan), have poor access to health care, and have less knowledge about the disease [19,20].

Urban regions of Karachi are highly populated and face multiple problems such as a poor drainage system that contaminates the water supply, poor garbage disposal, and environmental and sanitation problems. In this study, more cases were reported from the urban areas of Karachi. However, some studies have reported an even distribution of cases in urban and rural areas [21].

In this study, 3% of cases and 4% of controls were found to be vaccinated against TF. The low prevalence of vaccination is attributed to the high cost of the vaccine and absence of the vaccine in the Expanded Programme on Immunization. This small number of vaccinated individuals deterred us from establishing a relationship between a lower vaccination status and XDR-TF. A systematic review reported that typhoid vaccines are efficacious for the prevention of TF [22].

The use of piped municipal water was associated with increased odds of XDR-TF. Laboratory analysis of water samples revealed the presence of fecal coliform bacteria in the water supply in towns in Karachi, which indicates fecal contamination of water, which in turn suggests that the water supply may harbor *S Typhi* along with other pathogens transmitted through the fecal-oral route [23,24]. A meta-analysis reported that the risk of TF is 2-fold when using unsafe drinking water [17]. Furthermore, 2 outbreak investigation studies reported that contaminated or untreated water was the main contributor to the outbreak [12,21]. The other factor associated with the outbreak was the street food eating habits of children. In line with this finding, beverages from street vendors have also been implicated in an outbreak in Uganda [12].

### Limitations

One of the limitations of this study is that we were unable to acquire food samples from street food vendors. Future studies should include food sampling as well. We were able to detect fecal coliform bacteria in the water samples but were unable to isolate *S Typhi* because this facility is not available in water testing laboratories in Karachi.

### Conclusions

Community water supply and street food eating habits are implicated in the spread of the XDR-TF outbreak, which continues to grow in Karachi. Therefore, it is recommended to improve community water supply to meet recommended standards and to develop a policy to improve the safety of street food. In addition, health authorities should conduct mass vaccination against TF for high-risk groups.

### Acknowledgments

The authors would like to acknowledge the Global Health Development/Eastern Mediterranean Public Health Network for technical support.

### Conflicts of Interest

None declared.

### References

1. Buckle GC, Walker CLF, Black RE. Typhoid fever and paratyphoid fever: Systematic review to estimate global morbidity and mortality for 2010. *J Glob Health* 2012 Jun;2(1):010401 [FREE Full text] [doi: [10.7189/jogh.02.010401](https://doi.org/10.7189/jogh.02.010401)] [Medline: [23198130](https://pubmed.ncbi.nlm.nih.gov/23198130/)]
2. Mogasale V, Maskery B, Ochiai RL, Lee JS, Mogasale VV, Ramani E, et al. Burden of typhoid fever in low-income and middle-income countries: a systematic, literature-based update with risk-factor adjustment. *Lancet Glob Health* 2014 Oct;2(10):e570-e580 [FREE Full text] [doi: [10.1016/S2214-109X\(14\)70301-8](https://doi.org/10.1016/S2214-109X(14)70301-8)] [Medline: [25304633](https://pubmed.ncbi.nlm.nih.gov/25304633/)]
3. Klemm E, Shakoor S, Page A, Qamar F, Judge K, Saeed D, et al. Emergence of an Extensively Drug-Resistant Serovar Typhi Clone Harboring a Promiscuous Plasmid Encoding Resistance to Fluoroquinolones and Third-Generation

- Cephalosporins. *mBio* 2018 Feb 20;9(1):e00105-e00118 [FREE Full text] [doi: [10.1128/mBio.00105-18](https://doi.org/10.1128/mBio.00105-18)] [Medline: [29463654](https://pubmed.ncbi.nlm.nih.gov/29463654/)]
4. Crump JA, Sjölund-Karlsson M, Gordon MA, Parry CM. Epidemiology, Clinical Presentation, Laboratory Diagnosis, Antimicrobial Resistance, and Antimicrobial Management of Invasive Salmonella Infections. *Clin Microbiol Rev* 2015 Oct;28(4):901-937 [FREE Full text] [doi: [10.1128/CMR.00002-15](https://doi.org/10.1128/CMR.00002-15)] [Medline: [26180063](https://pubmed.ncbi.nlm.nih.gov/26180063/)]
  5. Rasheed MK, Hasan SS, Babar Z, Ahmed SI. Extensively drug-resistant typhoid fever in Pakistan. *Lancet Infect Dis* 2019 Mar;19(3):242-243. [doi: [10.1016/S1473-3099\(19\)30051-9](https://doi.org/10.1016/S1473-3099(19)30051-9)] [Medline: [30833059](https://pubmed.ncbi.nlm.nih.gov/30833059/)]
  6. Radhakrishnan A, Als D, Mintz E, Crump J, Stanaway J, Breiman R, et al. Introductory Article on Global Burden and Epidemiology of Typhoid Fever. *Am J Trop Med Hyg* 2018 Sep;99(3\_Suppl):4-9 [FREE Full text] [doi: [10.4269/ajtmh.18-0032](https://doi.org/10.4269/ajtmh.18-0032)] [Medline: [30047370](https://pubmed.ncbi.nlm.nih.gov/30047370/)]
  7. Yousafzai M, Qamar F, Shakoor S, Saleem K, Lohana H, Karim S, et al. Ceftriaxone-resistant Salmonella Typhi Outbreak in Hyderabad City of Sindh, Pakistan: High Time for the Introduction of Typhoid Conjugate Vaccine. *Clin Infect Dis* 2019 Feb 15;68(Suppl 1):S16-S21 [FREE Full text] [doi: [10.1093/cid/ciy877](https://doi.org/10.1093/cid/ciy877)] [Medline: [30767003](https://pubmed.ncbi.nlm.nih.gov/30767003/)]
  8. Bhunia R, Hutin Y, Ramakrishnan R, Pal N, Sen T, Murhekar M. A typhoid fever outbreak in a slum of South Dum Dum municipality, West Bengal, India, 2007: evidence for foodborne and waterborne transmission. *BMC Public Health* 2009 Apr 27;9:115 [FREE Full text] [doi: [10.1186/1471-2458-9-115](https://doi.org/10.1186/1471-2458-9-115)] [Medline: [19397806](https://pubmed.ncbi.nlm.nih.gov/19397806/)]
  9. Qamar FN, Yousafzai MT, Khalid M, Kazi AM, Lohana H, Karim S, et al. Outbreak investigation of ceftriaxone-resistant Salmonella enterica serotype Typhi and its risk factors among the general population in Hyderabad, Pakistan: a matched case-control study. *Lancet Infect Dis* 2018 Dec;18(12):1368-1376. [doi: [10.1016/S1473-3099\(18\)30483-3](https://doi.org/10.1016/S1473-3099(18)30483-3)] [Medline: [30507460](https://pubmed.ncbi.nlm.nih.gov/30507460/)]
  10. Simon AK, Hollander GA, McMichael A. Evolution of the immune system in humans from infancy to old age. *Proc Biol Sci* 2015 Dec 22;282(1821):20143085 [FREE Full text] [doi: [10.1098/rspb.2014.3085](https://doi.org/10.1098/rspb.2014.3085)] [Medline: [26702035](https://pubmed.ncbi.nlm.nih.gov/26702035/)]
  11. Prüss-Ustün A, Wolf J, Corvalán C, Bos R, Neira M. Preventing Disease Through Healthy Environments: A Global Assessment of the Burden of Disease from Environmental Risks. Geneva: World Health Organization; 2016.
  12. Kabwama SN, Bulage L, Nsubuga F, Pande G, Oguttu DW, Mafigiri R, et al. Correction to: A large and persistent outbreak of typhoid fever caused by consuming contaminated water and street-vended beverages: Kampala, Uganda, January - June 2015. *BMC Public Health* 2017 Oct 18;17(1):823 [FREE Full text] [doi: [10.1186/s12889-017-4801-y](https://doi.org/10.1186/s12889-017-4801-y)] [Medline: [29047373](https://pubmed.ncbi.nlm.nih.gov/29047373/)]
  13. Vollaard AM, Ali S, van Asten HAGH, Widjaja S, Visser LG, Surjadi C, et al. Risk factors for typhoid and paratyphoid fever in Jakarta, Indonesia. *JAMA* 2004 Jun 02;291(21):2607-2615. [doi: [10.1001/jama.291.21.2607](https://doi.org/10.1001/jama.291.21.2607)] [Medline: [15173152](https://pubmed.ncbi.nlm.nih.gov/15173152/)]
  14. Limpitikul W, Henpraserttae N, Saksawad R, Laoprasopwattana K. Typhoid outbreak in Songkhla, Thailand 2009-2011: clinical outcomes, susceptibility patterns, and reliability of serology tests. *PLoS One* 2014;9(11):e111768 [FREE Full text] [doi: [10.1371/journal.pone.0111768](https://doi.org/10.1371/journal.pone.0111768)] [Medline: [25375784](https://pubmed.ncbi.nlm.nih.gov/25375784/)]
  15. Phelan JC, Link BG, Tehranifar P. Social conditions as fundamental causes of health inequalities: theory, evidence, and policy implications. *J Health Soc Behav* 2010;51 Suppl:S28-S40. [doi: [10.1177/0022146510383498](https://doi.org/10.1177/0022146510383498)] [Medline: [20943581](https://pubmed.ncbi.nlm.nih.gov/20943581/)]
  16. Qasim M. Using the Theory of Fundamental Causes to Show the Potential Effects of Socioeconomic Status on Surgical Outcomes. *J Health Dispar Res Pract* 2016;9(2):143-153.
  17. Mogasale V, Ramani E, Mogasale V, Park J, Wierzba T. Estimating Typhoid Fever Risk Associated with Lack of Access to Safe Water: A Systematic Literature Review. *J Environ Public Health* 2018;2018:9589208 [FREE Full text] [doi: [10.1155/2018/9589208](https://doi.org/10.1155/2018/9589208)] [Medline: [30174699](https://pubmed.ncbi.nlm.nih.gov/30174699/)]
  18. Mutua J, Barker C, Vaidya N. Modeling impacts of socioeconomic status and vaccination programs on typhoid fever epidemics. *J Differ Equ* 2017;24:63-74.
  19. Ljung R, Peterson S, Hallqvist J, Heimerson I, Diderichsen F. Socioeconomic differences in the burden of disease in Sweden. *Bull World Health Organ* 2005 Feb;83(2):92-99 [FREE Full text] [Medline: [15744401](https://pubmed.ncbi.nlm.nih.gov/15744401/)]
  20. World Health Organization. Environmental burden of disease series. Virtual Health Library. 2005. URL: <https://pesquisa.bvsalud.org/portal/resource/pt/lis-18775?lang=en> [accessed 2021-05-04]
  21. Prasad N, Jenkins AP, Naucukidi L, Rosa V, Sahu-Khan A, Kama M, et al. Epidemiology and risk factors for typhoid fever in Central Division, Fiji, 2014-2017: A case-control study. *PLoS Negl Trop Dis* 2018 Jun;12(6):e0006571 [FREE Full text] [doi: [10.1371/journal.pntd.0006571](https://doi.org/10.1371/journal.pntd.0006571)] [Medline: [29883448](https://pubmed.ncbi.nlm.nih.gov/29883448/)]
  22. Anwar E, Goldberg E, Fraser A, Acosta CJ, Paul M, Leibovici L. Vaccines for preventing typhoid fever. *Cochrane Database Syst Rev* 2014 Jan 02;2(1):CD001261. [doi: [10.1002/14651858.CD001261.pub3](https://doi.org/10.1002/14651858.CD001261.pub3)] [Medline: [24385413](https://pubmed.ncbi.nlm.nih.gov/24385413/)]
  23. Mara D, Horan N. Handbook of Water and Wastewater Microbiology. London: Elsevier; Nov 04, 2003.
  24. Preventing travellers' diarrhoea: How to make drinking-water safe. World Health Organization. URL: [http://www.who.int/water\\_sanitation\\_health/publications/travel diarrhoea/en/](http://www.who.int/water_sanitation_health/publications/travel diarrhoea/en/) [accessed 2021-04-28]

## Abbreviations

**OR:** odds ratio

**XDR-TF:** extensively drug resistant typhoid fever

*Edited by M Algunaïd, T Sanchez; submitted 19.01.21; peer-reviewed by H Taha, H Bashier; comments to author 28.02.21; revised version received 10.03.21; accepted 10.03.21; published 11.05.21.*

*Please cite as:*

Vighio A, Syed MA, Hussain I, Zia SM, Fatima M, Masood N, Chaudry A, Hussain Z, Iqbal Baig MZ, Baig MA, Ikram A, S Khader Y  
*Risk Factors of Extensively Drug Resistant Typhoid Fever Among Children in Karachi: Case-Control Study*

*JMIR Public Health Surveill* 2021;7(5):e27276

URL: <https://publichealth.jmir.org/2021/5/e27276>

doi: [10.2196/27276](https://doi.org/10.2196/27276)

PMID: [33973861](https://pubmed.ncbi.nlm.nih.gov/33973861/)

©Anum Vighio, Muhammad Asif Syed, Ishfaque Hussain, Syed Masroor Zia, Munaza Fatima, Naveed Masood, Ambreen Chaudry, Zakir Hussain, Mirza Zeeshan Iqbal Baig, Mirza Amir Baig, Aamer Ikram, Yousef S Khader. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 11.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# Cutaneous Leishmaniasis Outbreak Investigation in Hajjah Governorate, Yemen, in 2018: Case-Control Study

Abdulkareem Ali Nassar<sup>1</sup>, MPH; Mahmood Hasan Abdelrazzaq<sup>2</sup>, MD; Ali Hamoud Almahaqri<sup>3</sup>, MCM; Mohammed Abdullah Al-Amad<sup>4</sup>, MPH; Abulwahed Abduljabbar Al Serouri<sup>4</sup>, PhD; Yousef Saleh Khader<sup>5</sup>, ScD

<sup>1</sup>Sana'a City's Public Health and Population Office, Yemen Ministry of Public Health and Population, Sana'a, Yemen

<sup>2</sup>Noncommunicable Diseases, World Health Organization, Sana'a, Yemen

<sup>3</sup>Leishmaniasis Control Program, Yemen Ministry of Public Health and Population, Sana'a, Yemen

<sup>4</sup>Field Epidemiology Training Program, Yemen Ministry of Public Health and Population, Sana'a, Yemen

<sup>5</sup>Department of Public Health, Community Medicine and Family Medicine, Faculty of Medicine, Jordan University of Science & Technology, Amman, Jordan

**Corresponding Author:**

Abdulkareem Ali Nassar, MPH  
Sana'a City's Public Health and Population Office  
Yemen Ministry of Public Health and Population  
Al-Thawra District  
Sana'a  
Yemen  
Phone: 967 777228977  
Email: [abdulkareemnassar@gmail.com](mailto:abdulkareemnassar@gmail.com)

## Abstract

**Background:** Cutaneous leishmaniasis (CL) is endemic in Yemen. About 4440 cases were reported in 2019. On July 23, 2018, a Hajjah governorate surveillance officer notified the Ministry of Public Health and Population about an increase in the number of CL cases in Bani-Oshb, Kuhlan district, Hajjah governorate. On July 24, 2018, Yemen Field Epidemiology Training Program sent a team to perform an investigation.

**Objective:** We aimed to describe a CL outbreak in Hajjah governorate and determine its risk factors.

**Methods:** A descriptive study and case-control study (1:1 ratio) were conducted. Cases included people who met the suspected or confirmed case definition of the World Health Organization and lived in Bani-Oshb subdistrict during the period from August 2017 to July 2018. Controls included people living for at least 1 year in Bani-Oshb without new or old skin lesions. Crude odds ratios (cORs) and adjusted odds ratios (aORs) with 95% CI were used to test the significance of associations.

**Results:** We identified 30 CL cases. Among the 30 patients, 7 (23%) were younger than 5 years, 17 (57%) were 5 to 14 years, 17 (57%) were females, and 23 (77%) had one lesion. The attack rate was 7 per 1000 population in the age group <15 years and 1 per 1000 population in the age group ≥15 years. On bivariate analysis, the following factors were significantly associated with CL: female gender (cOR 5.2, 95% CI 1.7-16.5), malnutrition (cOR 5.2, 95% CI 1.7-16.5), not using a bed net (cOR 14.5, 95% CI 1.7-122.4), poor house lighting (cOR 6.4, 95% CI 2.1-19.7), poor house hygiene (cOR 11.2, 95% CI 3.1-40.7), poor sanitation (cOR 14.5, 95% CI 1.7-122.4), living in houses without window nets (cOR 5.2, 95% CI 1.3-21.2), plantation around the house (cOR 6.5, 95% CI 2.1-20.5), animal barn inside or close to the house (cOR 9.3, 95% CI 1.9-46.7), raising animals (cOR 8.1, 95% CI 1.6-40.7), and having animal dung in or near the house (cOR 6.8, 95% CI 1.7-27.7). The following risk factors remained significant on multivariate stepwise analysis: female gender (aOR 22.7, 95% CI 1.6-320.5), malnutrition (aOR 17.2, 95% CI 1.3-225.8), poor house hygiene (aOR 45.6, 95% CI 2.5-846.4), plantation around the house (aOR 43.8, 95% CI 1.9-1009.9), and raising animals (aOR 287.1, 95% CI 5.4-15205.6).

**Conclusions:** CL was endemic in Hajjah governorate, and an increase in cases was confirmed. Many individual, housing, and animal related factors were shown to contribute to CL endemicity. Implementation of control measures directed toward altering the factors favoring contact among vectors, reservoirs, and susceptible humans is strongly recommended to control future outbreaks.

(*JMIR Public Health Surveill* 2021;7(5):e27442) doi:[10.2196/27442](https://doi.org/10.2196/27442)

**KEYWORDS**

cutaneous leishmaniasis; outbreak; risk factors; Yemen; Field Epidemiology Training Program

## Introduction

Leishmaniasis is a parasitic disease that is found in parts of the tropics, subtropics, and southern Europe. It is caused by infection with *Leishmania* parasites, which are spread by the bite of infected sand flies [1,2]. There are different forms of leishmaniasis. The most common form is cutaneous leishmaniasis (CL), which causes skin sores [1]. Most people have CL without any symptoms or signs [3]. People who develop clinical evidence of infection have one or more sores on their skin. The sores can change in size and appearance over time. The sores may start as nodules and may end up as ulcers like a volcano, with a raised edge and central crater [1].

Globally, approximately 700,000 to 1 million new cases and 26,000 to 65,000 deaths occur annually [4,5]. The disease is associated with malnutrition, population displacement, poor housing, a weak immune system, and poor socioeconomic status [4]. In the Eastern Mediterranean Region (EMR), it has been reported in many countries, including Afghanistan, Iran, Iraq, Pakistan, and Syria [4]. The EMR accounts for 70% of the CL cases worldwide [4].

CL is endemic in the north-western region of Yemen [6-8]. About 4440 CL cases were reported in 2019 [9]. On July 23, 2018, a Hajjah governorate surveillance officer notified the Ministry of Public Health and Population about an increase in the number of CL cases in Bani-Oshb, Kuhlan district, Hajjah governorate. On July 24, 2018, Yemen Field Epidemiology Training Program sent a team to perform an investigation.

This study aimed to confirm the existence of a CL outbreak in Bani-Oshb, describe the characteristics of CL by person, place, and time, and determine the risk factors of a CL outbreak.

## Methods

### Study Area

This study was conducted in Bani-Oshb subdistrict in Kuhlan Affar district, Hajjah governorate, Yemen. It has a population of 7453 persons (The Immunization Department of The Public Health and Population Office, Kuhlan Affar district, unpublished data, 2017). It has only one health unit, but it is not functional. It is rainy in summer and cold and dry in winter. Most people in Bani-Oshb have cattle and farms. They depend on raising animals and agricultural activities, and their houses are surrounded by farms and trees.

### Study Design

This investigation consisted of descriptive and analytic studies. A line list was developed to collect data, and an active house-to-house search was performed. The World Health Organization (WHO) case definition for CL was used [10]. A

suspected case was defined as the presence of clinical signs (skin lesions) without parasitological confirmation of the diagnosis. A confirmed case was defined as the presence of clinical signs with parasitological confirmation of the diagnosis (positive smear or culture from a skin lesion).

A case-control study design was used to determine the risk factors associated with CL (30 cases and 30 controls). Cases included people who met the suspected or confirmed case definition of the WHO and lived in Bani-Oshb subdistrict during the period from August 2017 to July 2018. Controls included people living in the house without any recorded new or old skin lesions among house members according to the household and examination of a medical doctor, and living for at least 1 year in Bani-Oshb without new or old skin lesions.

### Data Collection and Diagnosis

A structured questionnaire was used to collect data on individual, housing, and animal related characteristics. Data were collected on different variables, including age, gender, use of bed nets, house lighting, house hygiene (daily routine of cleaning rooms and disposal of garbage), sanitation (presence of a latrine with safe disposal of human waste), plantation around the house, animal barn inside or close to the house, raising of animals, and animal dung in or near the house. The data on these variables were self-reported by the participants or obtained by observation. One member of the research team collected 22 skin scrapings (small quantities of tissue) from cases. The tissues were directly smeared on glass slides, air dried, and fixed with methanol for a few seconds. After 20 minutes of staining, the slides were washed with water and left to dry in air. Then, the stained smears were sent to the National Central Public Health Laboratories. The laboratory result was considered positive if an amastigote was seen or negative if an amastigote was not seen after 15 minutes of inspection.

### Data Analysis

Data were analyzed using Epi Info version 7.2 [11]. Data were described using percentages. Crude odds ratios (cORs) or adjusted odds ratios (aORs) with 95% CIs were used to test the significance of associations in bivariate and multivariate stepwise analyses. A *P* value <.05 was considered statistically significant.

## Results

### Patient Characteristics

A total of 30 cases of leishmaniasis were found in Bani-Oshb subdistrict during the period from August 2017 to July 2018. The number of cases started to increase in January 2018 and reached a peak in July 2018 (Figure 1).



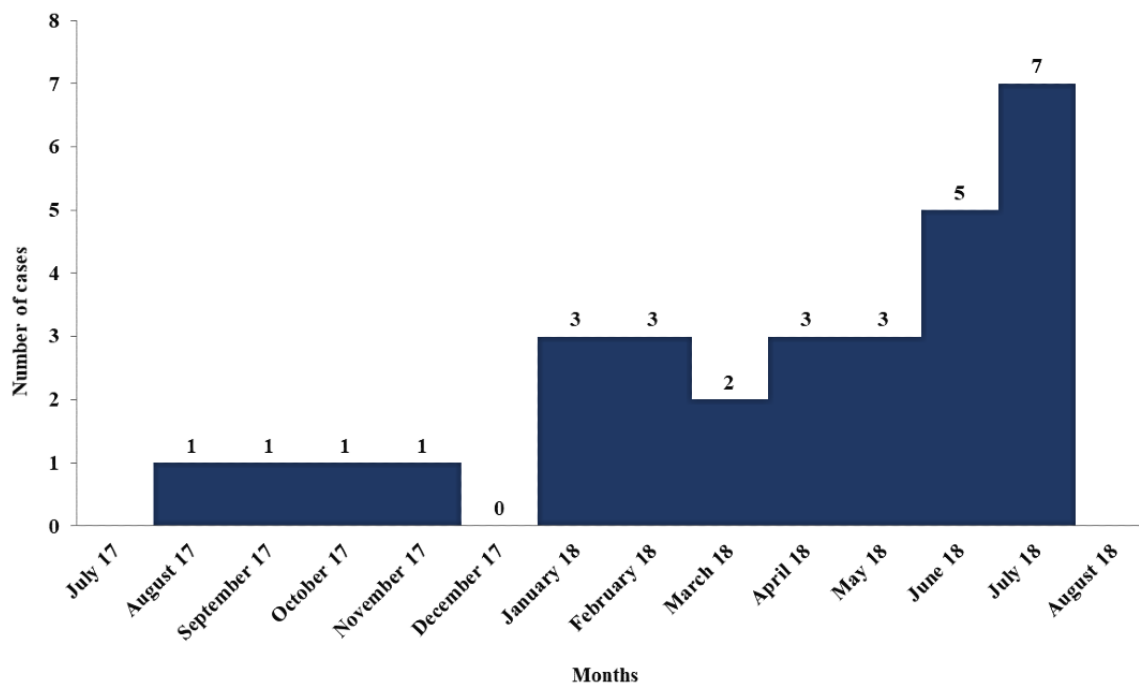
**Figure 1.** The distribution of cutaneous leishmaniasis cases by time in Bani-Oshb, Hajjah governorate from August 2017 to July 2018 (N=30).

Table 1 shows the characteristics of the CL cases. Of the 30 patients, 7 (23%) were younger than 5 years, 17 (57%) were aged 5 to 14 years, and 6 (20%) were older than 14 years. Additionally, females represented 17 (57%) cases. Moreover, 23 (76%) patients had one lesion, 4 (14%) had two to three lesions, and 3 (10%) had more than three lesions. The face was the most affected part of the body (20/30, 67%), followed by

the lower limbs (4/30, 13%) and upper limbs (3/30, 10%). In 10% (3/30) of cases, both the face and limbs were affected. Bait Rokn and Bait Alfrwi were the most affected villages with 12 (40%) cases. The attack rate was 7 per 1000 population in the age group <15 years and 1 per 1000 population in the age group ≥15 years. Among 22 skin scraping samples, 21 (96%) were positive, and leishmaniasis amastigotes were seen.

**Table 1.** Characteristics of cutaneous leishmaniasis cases (N=30).

Characteristic	Value, n (%)
<b>Age (years)</b>	
<5	7 (23%)
5-14	17 (57%)
≥15	6 (20%)
<b>Sex</b>	
Female	17 (57%)
Male	13 (43%)
<b>Village of residence</b>	
Bait Rokn	6 (20%)
Bait Alfrwi	6 (20%)
Bait Joma'an	4 (13%)
Al Wadi	3 (10%)
Fra'ah	3 (10%)
Al Obal	2 (7%)
Bani Bram	2 (7%)
Bait Za'abl	2 (7%)
Bait Alwali	1 (3%)
Arshan	1 (3%)
<b>Number of lesions</b>	
1	23 (76%)
2	2 (7%)
3	2 (7%)
>3	3 (10%)
<b>Site of lesions</b>	
Face	20 (67%)
Lower limbs	4 (13%)
Upper limbs	3 (10%)
Face and limbs	3 (10%)

### Factors Associated With CL

**Table 2** shows the bivariate analysis for associated risk factors of CL. Female gender (cOR 5.2, 95% CI 1.7-16.5), malnutrition (cOR 5.2, 95% CI 1.7-16.5), and not using a bed net (cOR 14.5, 95% CI 1.7-122.4) were associated with increased odds of CL. Poor house lighting (cOR 6.4, 95% CI 2.1-19.7), poor house hygiene (cOR 11.2, 95% CI 3.1-40.7), and poor sanitation (cOR 14.5, 95% CI 1.7-122.4) were associated with higher odds of CL. Moreover, other risk factors were identified, including living in houses without window nets (cOR 5.2, 95% CI

1.3-21.2), plantation around the house (cOR 6.5, 95% CI 2.1-20.5), animal barn inside or close to the house (cOR 9.3, 95% CI 1.9-46.7), raising animals (cOR 8.1, 95% CI 1.6-40.7), and having animal dung in or near the house (cOR 6.8, 95% CI 1.7-27.7).

The following risk factors remained significant on multivariate stepwise analysis (**Table 3**): female gender (aOR 22.7, 95% CI 1.6-320.5), malnutrition (aOR 17.2, 95% CI 1.3-225.8), poor house hygiene (aOR 45.6, 95% CI 2.5-846.4), plantation around the house (aOR 43.8, 95% CI 1.9-1009.9), and raising animals (aOR 287.1, 95% CI 5.4-15205.6).

**Table 2.** Bivariate analysis of associated risk factors of cutaneous leishmaniasis in Bani-Oshb, Hajjah governorate from August 2017 to July 2018.

Risk factor	Cases (n=30), n (%)	Controls (n=30), n (%)	cOR <sup>a</sup> (95% CI)	P value
<b>Age (years)</b>			0.8 (0.2-2.9)	.74
<15	24 (80%)	25 (83%)		
≥15	6 (20%)	5 (17%)		
<b>Sex</b>			5.2 (1.7-16.5)	.003
Female	17 (57%)	6 (20%)		
Male	13 (43%)	24 (80%)		
<b>Malnutrition</b>			5.2 (1.7-16.5)	.003
Yes	24 (80%)	13 (43%)		
No	6 (20%)	17 (57%)		
<b>Bed net use</b>			14.5 (1.7-122.4)	.002
Never	29 (97%)	20 (67%)		
Use	1 (3%)	10 (33%)		
<b>House lighting</b>			6.4 (2.1-19.7)	<.001
Poor	22 (73%)	9 (30%)		
Good	8 (27%)	21 (70%)		
<b>House hygiene</b>			11.2 (3.1-40.7)	<.001
Poor	26 (87%)	11 (37%)		
Good	4 (13%)	19 (63%)		
<b>Sanitation</b>			14.5 (1.7-122.4)	.003
Poor	29 (97%)	20 (67%)		
Good	1 (3%)	10 (33%)		
<b>Windows of the house</b>			5.2 (1.3-21.2)	.02
Without net	27 (90%)	19 (63%)		
With net	3 (10%)	11 (37%)		
<b>Plantation around the house</b>			6.5 (2.1-20.5)	<.001
Yes	20 (67%)	7 (23%)		
No	10 (33%)	23 (77%)		
<b>Animal barn inside or close to the house</b>			9.3 (1.9-46.7)	.002
Yes	28 (93%)	18 (60%)		
No	2 (7%)	12 (40%)		
<b>Raising animals</b>			8.1 (1.6-40.7)	.004
Yes	28 (93%)	19 (63%)		
No	2 (7%)	11 (37%)		
<b>Animal dung in or near the house</b>			6.8 (1.7-27.7)	.003
Yes	27 (90%)	17 (57%)		
No	3 (10%)	13 (43%)		

<sup>a</sup>cOR: crude odds ratio.

**Table 3.** Risk factors on multivariate stepwise analysis in Bani-Oshb, Hajjah governorate from August 2017 to July 2018.

Risk factor	Cases (n=30), n (%)	Controls (n=30), n (%)	aOR <sup>a</sup> (95% CI)	P value
<b>Sex</b>			22.7 (1.6-320.5)	.02
Female	17 (57%)	6 (20%)		
Male	13 (43%)	24 (80%)		
<b>Malnutrition</b>			17.2 (1.3-225.8)	.03
Yes	24 (80%)	13 (43%)		
No	6 (20%)	17 (57%)		
<b>House hygiene</b>			45.6 (2.5-846.4)	.01
Poor	26 (87%)	11 (37%)		
Good	4 (13%)	19 (63%)		
<b>Plantation around the house</b>			43.8 (1.9-1009.9)	.02
Yes	20 (67%)	7 (23%)		
No	10 (33%)	23 (77%)		
<b>Raising animals</b>			287.1 (5.4-15205.6)	.005
Yes	28 (93%)	19 (63%)		
No	2 (7%)	11 (37%)		

<sup>a</sup>aOR: adjusted odds ratio.

## Discussion

### Principal Findings

A total of 30 cases with leishmaniasis were found in Bani-Oshb subdistrict during the period from August 2017 to July 2018. Our results showed that most CL cases involved patients between the ages of 5 and 14 years and involved females. Additionally, most cases involved one lesion. The face was the most affected part of the body. We also observed that many individual, housing, and animal related factors, such as malnutrition, poor house hygiene, plantation around the house, and raising animals, were significantly associated with CL infection.

The number of cases showed an increase in January and reached a peak in July. This might be due to the rainy season, which is a favorable time for sand fly activity and breeding [8,12]. The age group less than 15 years was the most affected, with an attack rate of 7 per 1000 population. This finding might be explained by the fact that children are usually not aware about how to protect themselves from bites of sand flies. Besides, children spend most of their time outdoors. This finding is similar to the findings in other studies from Taiz and central Yemen governorates, as well as Iran [8,13,14].

Females were more likely to be infected than males. This might be explained by the fact that rural women in Hajjah governorate perform different tasks, including domestic animal care, getting water, and agricultural activities, which increase their probability of exposure to sand fly bites. This finding is consistent with findings in studies from Iran and Lebanon [14,15]. However, this finding disagrees with findings in other studies from Lahj, Hajjah, and Amran [6,7,12].

More than three-quarters of CL cases had one lesion. This finding confirms the findings of previous studies from Lahj, Hajjah, Taiz, and Nepal [6-8,16]. In agreement with the findings of other studies [6,7,12], two-thirds of cases had lesions on their faces, and this might be because the face is the most exposed part of the body.

Malnutrition was found to be significantly associated with increased risk of CL infection, which may be due to increased individual susceptibility to infection with CL. Few studies have confirmed the relationship between malnutrition and risk of CL [17,18].

Not using a bed net was significantly associated with increased risk of CL infection. This might be due to the absence of personal protection against the vector. This finding is consistent with the findings of studies from Ethiopia, Waziristan, and Turkey [5,19,20]. However, it is not consistent with the findings of other studies from Kenya, Bolivia, Thailand, and Afghanistan [2,21-23].

This investigation indicated that there was an association between CL infection and poor housing characteristics, including poor lighting, house hygiene, and sanitation. These findings might be explained by the fact that such conditions are favorable for the activity and breeding of sand flies. Similar findings have been reported in Amran governorate [12]. Moreover, living in houses without window nets was associated with an increased risk of CL, possibly because of increased exposure to sand flies. One study from Afghanistan did not report a significant association between living in houses without windows and CL [23]. Furthermore, there was an association between plantations around the house and CL. This finding is consistent with the findings of studies from Kenya, Amran, Waziristan, Sri Lanka, and Palestine [2,12,19,24,25] and is not consistent with the findings of a study from Thailand [22]. Additionally, having an

animal barn inside or close to the house was associated with CL, which has been reported in other studies from Taiz, Amran, and Turkey [8,12,20], but not in a study from Thailand in 2016 [22].

There was an association between animal-related factors and CL infection. Animals seem to be an important reservoir for maintaining the life cycle of many *Leishmania* species and transmission of infection. Similar findings were reported in studies from Taiz, Amran, Ethiopia, Turkey, and Palestine [5,8,12,20,25], but not in a study from Thailand [22]. Furthermore, animal dung in or close to the house increased the risk of CL infection because this creates a favorable environment to attract sand flies into human settlements. This finding agreed with the findings of a study from Turkey [20].

However, some of the abovementioned significant risk factors identified in bivariate analysis, which were also reported in previous studies, did not remain significant on multivariate stepwise analysis (eg, bed net use, house lighting, and sanitation). This may be because of the small sample size of this study or because those factors were not risk factors in the studied community.

This study has some limitations related to the study design and sample size. Recall bias might be present owing to the retrospective design of this study. The small sample size is possibly the most important limitation, which generated a wider CI. The study was performed in a subdistrict with mountainous terrain where communities are scattered and difficult to reach, and their work in agricultural activities during the day limited participation in this study. Moreover, difficulty in obtaining eligible controls in this endemic area was the main drawback of enrolling more controls.

## Conclusions

CL was endemic in Hajjah governorate, and an increase in cases was confirmed. Many individual, housing, and animal related factors were shown to contribute to CL endemicity. Implementation of control measures directed toward altering the factors favoring contact among vectors, reservoirs, and susceptible humans, such as malnutrition and plantation around the house, is recommended to control future outbreaks. Further studies focusing on the species of parasites, vectors, and reservoirs are recommended.

## Acknowledgments

The authors would like to acknowledge the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET) and the Global Health Development|Eastern Mediterranean Public Health Network (GHD|EMPHNET) for their support. We are grateful to Malak Al Sabahi for checking the English language of our manuscript.

## Conflicts of Interest

None declared.

## References

1. About Leishmaniasis. Centers for Disease Control and Prevention. URL: [https://www.cdc.gov/parasites/leishmaniasis/gen\\_info/faqs.html](https://www.cdc.gov/parasites/leishmaniasis/gen_info/faqs.html) [accessed 2020-03-14]
2. Ngere I, Gufu Boru W, Isack A, Muiruri J, Obonyo M, Matendechero S, et al. Burden and risk factors of cutaneous leishmaniasis in a peri-urban settlement in Kenya, 2016. *PLoS One* 2020;15(1):e0227697 [FREE Full text] [doi: [10.1371/journal.pone.0227697](https://doi.org/10.1371/journal.pone.0227697)] [Medline: [31971945](https://pubmed.ncbi.nlm.nih.gov/31971945/)]
3. Health Topic: Leishmaniasis. World Health Organization. URL: [https://www.who.int/health-topics/leishmaniasis#tab=tab\\_1](https://www.who.int/health-topics/leishmaniasis#tab=tab_1) [accessed 2020-03-14]
4. Fact Sheet: Leishmaniasis. World Health Organization. URL: <https://www.who.int/news-room/fact-sheets/detail/leishmaniasis> [accessed 2020-03-14]
5. Eshetu B, Mamo H. Cutaneous leishmaniasis in north-central Ethiopia: trend, clinical forms, geographic distribution, and determinants. *Trop Med Health* 2020;48:39 [FREE Full text] [doi: [10.1186/s41182-020-00231-w](https://doi.org/10.1186/s41182-020-00231-w)] [Medline: [32518497](https://pubmed.ncbi.nlm.nih.gov/32518497/)]
6. Muqbil N, Muqbel A. Cutaneous leishmaniasis in Al-Sawalha area, Lahj governorate, Yemen. *Micromedicine* 2016;4(1):37-42 [FREE Full text]
7. Khatri ML, Haider N, Di Muccio T, Gramiccia M. Cutaneous leishmaniasis in Yemen: clinicoepidemiologic features and a preliminary report on species identification. *Int J Dermatol* 2006 Jan;45(1):40-45. [doi: [10.1111/j.1365-4632.2004.02588.x](https://doi.org/10.1111/j.1365-4632.2004.02588.x)] [Medline: [16426374](https://pubmed.ncbi.nlm.nih.gov/16426374/)]
8. Asmaa Q, Al-Shamerii S, Al-Tag M, Al-Shamerii A, Li Y, Osman BH. Parasitological and biochemical studies on cutaneous leishmaniasis in Shara'b District, Taiz, Yemen. *Ann Clin Microbiol Antimicrob* 2017 Jul 04;16(1):47 [FREE Full text] [doi: [10.1186/s12941-017-0224-y](https://doi.org/10.1186/s12941-017-0224-y)] [Medline: [28676088](https://pubmed.ncbi.nlm.nih.gov/28676088/)]
9. Leishmaniasis: Status of endemicity of cutaneous leishmaniasis. World Health Organization. 2019. URL: [https://apps.who.int/neglected\\_diseases/ntddata/leishmaniasis/leishmaniasis.html](https://apps.who.int/neglected_diseases/ntddata/leishmaniasis/leishmaniasis.html) [accessed 2020-03-14]
10. Neglected tropical diseases: Cutaneous leishmaniasis factsheet. World Health Organization. URL: <http://www.emro.who.int/neglected-tropical-diseases/information-resources-leishmaniasis/cl-factsheet.html> [accessed 2021-05-06]
11. Epi Info. Centers for Disease Control and Prevention. URL: <https://www.cdc.gov/epiinfo/index.html> [accessed 2021-05-06]

12. Abdulmogni G, Al-Amad M, Anam L, Banower GM. Outbreak investigation of Cutaneous Leishmania in Yanaha village, Amran governorate, Yemen 2016. National Yemen Field Epidemiology Training Program. 2016. URL: <https://tinyurl.com/mufh7xmc> [accessed 2019-05-12]
13. Al-Kamel MA. Leishmaniasis in Yemen: a clinicoepidemiological study of leishmaniasis in central Yemen. *Int J Dermatol* 2016 Aug;55(8):849-855. [doi: [10.1111/ijd.13041](https://doi.org/10.1111/ijd.13041)] [Medline: [26547479](https://pubmed.ncbi.nlm.nih.gov/26547479/)]
14. Nikouee F, Soltanian M, Babae F, Motamed-Jahromi M. Cutaneous leishmaniasis: an epidemiological survey in Iran during 2013-2015. *JNMS* 2017 May 01;4(1):58-62. [doi: [10.18869/acadpub.jnms.4.1.58](https://doi.org/10.18869/acadpub.jnms.4.1.58)]
15. Alawieh A, Musharrafieh U, Jaber A, Berry A, Ghosn N, Bizri AR. Revisiting leishmaniasis in the time of war: the Syrian conflict and the Lebanese outbreak. *Int J Infect Dis* 2014 Dec;29:115-119 [FREE Full text] [doi: [10.1016/j.ijid.2014.04.023](https://doi.org/10.1016/j.ijid.2014.04.023)] [Medline: [25449245](https://pubmed.ncbi.nlm.nih.gov/25449245/)]
16. Ghimire P, Shrestha R, Pandey S, Pokhrel K, Pande R. Cutaneous Leishmaniasis: A Neglected Vector Borne Tropical Disease in Midwestern Region of Nepal. *Nepal J Dermatol Venereol & Leprol* 2018 Mar 29;16(1):41-44 [FREE Full text] [doi: [10.3126/njdvl.v16i1.19405](https://doi.org/10.3126/njdvl.v16i1.19405)]
17. Weigel MM, Armijos RX, Zurita C, Racines J, Reddy A, Mosquera J. Nutritional status and cutaneous leishmaniasis in rural Ecuadorian children. *J Trop Pediatr* 1995 Feb;41(1):22-28. [doi: [10.1093/tropej/41.1.22](https://doi.org/10.1093/tropej/41.1.22)] [Medline: [7723125](https://pubmed.ncbi.nlm.nih.gov/7723125/)]
18. Castro MDM, Cossio A, Velasco C, Osorio L. Risk factors for therapeutic failure to meglumine antimoniate and miltefosine in adults and children with cutaneous leishmaniasis in Colombia: A cohort study. *PLoS Negl Trop Dis* 2017 Apr;11(4):e0005515 [FREE Full text] [doi: [10.1371/journal.pntd.0005515](https://doi.org/10.1371/journal.pntd.0005515)] [Medline: [28379954](https://pubmed.ncbi.nlm.nih.gov/28379954/)]
19. Rehman I, Saleem M. Outbreak Investigation of Cutaneous Leishmaniasis (CL) in North Waziristan Agency, Federally Administered Tribal Area (FATA) - April 2016. *iproc* 2018 Mar 29;4(1):e10634 [FREE Full text] [doi: [10.2196/10634](https://doi.org/10.2196/10634)]
20. Votýpka J, Kasap OE, Volf P, Kodym P, Alten B. Risk factors for cutaneous leishmaniasis in Cukurova region, Turkey. *Trans R Soc Trop Med Hyg* 2012 Mar;106(3):186-190. [doi: [10.1016/j.trstmh.2011.12.004](https://doi.org/10.1016/j.trstmh.2011.12.004)] [Medline: [22284721](https://pubmed.ncbi.nlm.nih.gov/22284721/)]
21. Eid D, Guzman-Rivero M, Rojas E, Goicolea I, Hurtig A, Illanes D, et al. Risk factors for cutaneous leishmaniasis in the rainforest of Bolivia: a cross-sectional study. *Trop Med Health* 2018 Apr 17;46(1):9 [FREE Full text] [doi: [10.1186/s41182-018-0089-6](https://doi.org/10.1186/s41182-018-0089-6)] [Medline: [29692654](https://pubmed.ncbi.nlm.nih.gov/29692654/)]
22. Manomat J, Leelayoova S, Bualert L, Tan-Ariya P, Siripattanapipong S, Mungthin M, et al. Prevalence and risk factors associated with Leishmania infection in Trang Province, southern Thailand. *PLoS Negl Trop Dis* 2017 Nov;11(11):e0006095 [FREE Full text] [doi: [10.1371/journal.pntd.0006095](https://doi.org/10.1371/journal.pntd.0006095)] [Medline: [29155831](https://pubmed.ncbi.nlm.nih.gov/29155831/)]
23. Reithinger R, Mohsen M, Leslie T. Risk factors for anthroponotic cutaneous Leishmaniasis at the household level in Kabul, Afghanistan. *PLoS Negl Trop Dis* 2010 Mar 23;4(3):e639 [FREE Full text] [doi: [10.1371/journal.pntd.000639](https://doi.org/10.1371/journal.pntd.000639)] [Medline: [20351787](https://pubmed.ncbi.nlm.nih.gov/20351787/)]
24. Wijerathna T, Gunathilaka N, Gunawardena K, Rodrigo W. Socioeconomic, demographic and landscape factors associated with cutaneous leishmaniasis in Kurunegala District, Sri Lanka. *Parasit Vectors* 2020 May 12;13(1):244 [FREE Full text] [doi: [10.1186/s13071-020-04122-1](https://doi.org/10.1186/s13071-020-04122-1)] [Medline: [32398102](https://pubmed.ncbi.nlm.nih.gov/32398102/)]
25. Salah I, Davidovitch N, Kotler B. Risk factors of Cutaneous Leishmaniasis (CL) caused by *L. tropica*: a case-control study in Palestine: Ikram Salah. *European Journal of Public Health* 2016 Nov 02;26(1):95. [doi: [10.1093/eurpub/ckw166.055](https://doi.org/10.1093/eurpub/ckw166.055)]

## Abbreviations

- aOR:** adjusted odds ratio  
**cOR:** crude odds ratio  
**CL:** cutaneous leishmaniasis  
**EMR:** Eastern Mediterranean Region  
**WHO:** World Health Organization

*Edited by M Alyahya, T Sanchez; submitted 25.01.21; peer-reviewed by F Lami, A Sudaryanto; comments to author 28.02.21; revised version received 30.03.21; accepted 31.03.21; published 14.05.21.*

### *Please cite as:*

Nassar AA, Abdelrazzaq MH, Almahaqri AH, Al-Amad MA, Al Serouri AA, Khader YS  
*Cutaneous Leishmaniasis Outbreak Investigation in Hajjah Governorate, Yemen, in 2018: Case-Control Study*  
*JMIR Public Health Surveill* 2021;7(5):e27442  
URL: <https://publichealth.jmir.org/2021/5/e27442>  
doi: [10.2196/27442](https://doi.org/10.2196/27442)  
PMID: [33988521](https://pubmed.ncbi.nlm.nih.gov/33988521/)

©Abdulkareem Ali Nassar, Mahmood Hasan Abdelrazzaq, Ali Hamoud Almahaqri, Mohammed Abdullah Al-Amad, Abulwahed Abduljabbar Al Serouri, Yousef Saleh Khader. Originally published in JMIR Public Health and Surveillance (<https://publichealth.jmir.org>), 14.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

## Short Paper

# Morbidity and Mortality Associated with Typhoid Fever Among Hospitalized Patients in Hyderabad District, Pakistan, 2017-2018: Retrospective Record Review

Munaza Fatima<sup>1</sup>, MPhil; Santosh Kumar<sup>1</sup>, MPH; Mudassar Hussain<sup>1</sup>, MSPH; Naveed Masood Memon<sup>1</sup>, MPH; Anum Vighio<sup>1</sup>, MPH; Muhammad Asif Syed<sup>1</sup>, MPH; Ambreen Chaudhry<sup>2</sup>, MSPH, MSc; Zakir Hussain<sup>1</sup>, MPH; Zeeshan Iqbal Baig<sup>1</sup>, MSPH; Mirza Amir Baig<sup>1</sup>, MPH, MHM; Rana Jawad Asghar<sup>3</sup>, MPH; Aamer Ikram<sup>2</sup>, PhD; Yousef Khader<sup>4</sup>, SCD

<sup>1</sup>Field Epidemiology and Laboratory Training Program, Islamabad, Pakistan

<sup>2</sup>National Institute of Health Pakistan, Islamabad, Pakistan

<sup>3</sup>Global Health Strategists and Implementers, Islamabad, Pakistan

<sup>4</sup>Department of Public Health, Community Medicine and Family Medicine, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan

**Corresponding Author:**

Ambreen Chaudhry, MSPH, MSc  
National Institute of Health Pakistan  
Park Road, Chak Shehzad  
Islamabad, 44000  
Pakistan  
Phone: 92 519255302  
Email: [ambr.chaudhry@gmail.com](mailto:ambr.chaudhry@gmail.com)

## Abstract

**Background:** Hyderabad, Pakistan, was the first city to witness an outbreak of extensively drug resistant (XDR) typhoid fever. The outbreak strain is resistant to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, fluoroquinolones, and third-generation cephalosporin, thus greatly limiting treatment options. However, despite over 5000 documented cases, information on mortality and morbidity has been limited.

**Objective:** To address the existing knowledge gap, this study aimed to assess the morbidity and mortality associated with XDR and non-XDR *Salmonella* serovar Typhi infections in Pakistan.

**Methods:** We reviewed the medical records of culture-confirmed typhoid cases in 5 hospitals in Hyderabad from October 1, 2016, to September 30, 2018. We recorded data on age, gender, onset of fever, physical examination, serological and microbiological test results, treatment before and during hospitalization, duration of hospitalization, complications, and deaths.

**Results:** A total of 1452 culture-confirmed typhoid cases, including 947 (66%) XDR typhoid cases and 505 (34%) non-XDR typhoid cases, were identified. Overall,  $\geq 1$  complications were reported in 360 (38%) patients with XDR typhoid and 89 (18%) patients with non-XDR typhoid ( $P < .001$ ). Ileal perforation was the most commonly reported complication in both patients with XDR typhoid ( $n=210$ , 23%) and patients with non-XDR typhoid ( $n=71$ , 14%) ( $P < .001$ ). Overall, mortality was documented among 17 (1.8%) patients with XDR *S* Typhi infections and 3 (0.6%) patients with non-XDR *S* Typhi infections ( $P = .06$ ).

**Conclusions:** As this first XDR typhoid outbreak continues to spread, the increased duration of illness before hospitalization and increased rate of complications have important implications for clinical care and medical costs and heighten the importance of prevention and control measures.

(JMIR Public Health Surveill 2021;7(5):e27268) doi:[10.2196/27268](https://doi.org/10.2196/27268)

**KEYWORDS**

antimicrobial resistance; complications; control drug resistance; extensive drug resistance; hospitalization; Hyderabad; ileal perforation; medical records; microbiological; morbidity; mortality; Pakistan; prevention; typhoid



## Introduction

Typhoid fever is caused by *Salmonella enterica* serovar Typhi (hereinafter referred to as “Typhi”) and is characterized by prolonged fever, headache, nausea, loss of appetite, constipation, or diarrhea [1]. Globally, South Asia accounts for more typhoid fever cases each year than any other geographic region [2,3]. An estimated 11-21 million cases of typhoid fever and approximately 128,000-161,000 deaths are reported annually [3]. Among countries in South Asia, Pakistan has the highest estimated incidence rate of typhoid fever (493.5 per 100,000 persons/year) [4,5]. Treatment of enteric fever has been complicated by the development and rapid global spread of typhoidal organisms resistant to ampicillin, trimethoprim-sulfamethoxazole, and chloramphenicol. Additionally, the development of increasing resistance to fluoroquinolones is a growing challenge [6]. Since the extensively drug resistant (XDR) Typhi outbreak began in Hyderabad in late 2016 [7], typhoid fever cases in Pakistan increased, particularly in Hyderabad and other parts of Sindh province; this is attributed to the circulating XDR Typhi strain [8].

The most common serious and fatal complication of typhoid fever is intestinal perforation [9]. Even though many advancements have been made in patient care, morbidity and mortality rates remain high among patients with typhoid perforation, especially in low- and middle-income countries [10,11]. The high incidence of typhoid ileal perforations in developing countries is reportedly associated with delayed diagnosis and treatment and the emergence of antibiotic resistance. Once complications appear, patients require hospitalization and sometimes tertiary care [12]. Postoperative complications and mortality are common [13].

In November 2016, a multidrug-resistant Typhi strain that is resistant to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole and additionally to ciprofloxacin and ceftriaxone was identified in patients hospitalized in Hyderabad, Pakistan. This XDR Typhi strain belongs to the H58 lineage and includes a plasmid-mediated blaCTX-M-15 extended-spectrum  $\beta$ -lactamase [14]. Typhoid cases have since been identified in Hyderabad, Karachi, and in other districts of Sindh province, and over 5372 cases were reported by December 2018. As of that month, no isolates resistant to azithromycin or a carbapenem had been reported. Despite the large number of cases, little information on mortality and morbidity attributable to XDR Typhi infections has been available. To address this knowledge gap, this study aimed to assess the morbidity and mortality associated with XDR and non-XDR Typhi infections in Hyderabad, Pakistan.

## Methods

The medical records of all hospitalized patients with culture-confirmed typhoid fever between October 1, 2016, and September 30, 2018, at the 5 major hospitals in Hyderabad, including Liaquat University City, Jamshoro, Shah Bhattai, Qasimabad, and Peratabad Hospitals, were reviewed. Subsequently, the pediatric, medical, and surgical ward records of all identified cases were also reviewed. We obtained ethics approval from the institutional review board of Liaquat University of Medical Sciences, Jamshoro, and administrative approvals from all the participating hospitals.

We collected data on demographic characteristics, date of fever onset, illness duration and antibiotic history before hospitalization, physical examination findings, results of serological and microbiologic tests, treatments prescribed or administered in hospital, date of recovery, duration of hospitalization, complications (including ileal perforation, septicemia, cholecystitis, pneumonia, jaundice, encephalopathy, meningitis, and deaths), and antimicrobial susceptibility of Typhi isolates. XDR Typhi cases were defined as those whose isolates were resistant to the 5 aforementioned agents. Ileal perforations were diagnosed if biopsy reports indicated “a hollow viscous perforation of the terminal part of the ileal wall” and pus culture sensitivity reports indicated an XDR status among patients with ileal perforation.

Data were recorded using a specially designed questionnaire and transferred to a computerized database for statistical analysis in Epi Info (Centers for Disease Control and Prevention). The data are expressed as mean, median, and percentage values. The chi-square test was used to compare percentages and the Mann–Whitney *U* test was used to compare medians. A *P* value of <.05 was considered significant.

## Results

A total of 1452 cases of culture-confirmed typhoid fever were identified from in-patient departments of 5 hospitals in Hyderabad during the study period. Patient ages ranged 1-80 (mean 14, median 22) years. More than half (*n*=791, 55%) of the patients were aged between 2 and 10 years. Almost two-thirds (*n*=915, 63%) of patients were male. The total number of monthly cases ranged from 2 in October 2016 to 98 in May 2018. Typhi isolates from approximately two-thirds of cases (*n*=947, 66%) were XDR, while the remainder (*n*=505, 35%) were non-XDR. Patients with non-XDR typhoid belonged to a slightly younger age group. Males accounted for similar proportions of XDR and non-XDR cases (64% and 62%, respectively) (Table 1).

The signs and symptoms in patients with XDR typhoid and those with non-XDR typhoid on hospital presentation were very similar (Table 2).

**Table 1.** Age and gender distribution of hospitalized patients with XDR<sup>a</sup> typhoid and those with non-XDR typhoid in Hyderabad, Pakistan, from October 1, 2016, to September 30, 2018 (N=1452).

Characteristics	XDR typhoid cases (n=947), n (%)	Non-XDR typhoid cases (n=505), n (%)	All cases, n (%)
<b>Age (years)</b>			
0-5	308 (33)	209 (42)	517 (36)
6-10	236 (25)	134 (27)	370 (26)
11-15	72 (8)	47 (9)	119 (8)
16-25	142 (15)	43 (8)	185 (13)
>25	189 (20)	72 (14)	120 (8)
<b>Gender</b>			
Male	601 (54)	313 (62)	915 (63)
Female	345 (45)	192 (38)	537 (37)

<sup>a</sup>XDR: extensively drug resistant; resistant to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, ciprofloxacin, and ceftriaxone.

**Table 2.** Signs and symptoms of patients with XDR<sup>a</sup> typhoid and those with non-XDR typhoid on hospital admission in Hyderabad, Pakistan, from October 1, 2016, to September 30, 2018 (N=1452).

Signs and symptoms	XDR typhoid cases (n=947), n (%)	Non-XDR typhoid cases (n=505), n (%)	All cases, n (%)
Fever (body temperature of <40°C)	947 (100)	505 (100)	1452 (100)
Anorexia	947 (100)	505 (100)	1452 (100)
Headache	650 (68)	306 (60)	956 (65)
Abdominal pain	493 (52)	297 (58)	790 (54)
Diarrhea	488 (52)	297 (58)	785 (54)
Vomiting	385 (40)	196 (38)	581 (40)
Signs of anemia	360 (38)	89 (17)	449 (30)
Signs of toxicity	237 (25)	73 (14)	310 (21)
Constipation	210 (22)	71 (14)	281 (19)
Intestinal distension	218 (23)	72 (14)	290 (19)

<sup>a</sup>XDR: extensively drug resistant; resistant to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, ciprofloxacin, and ceftriaxone.

The duration of illness between fever onset and hospitalization ranged 5-28 (median 20) days for patients with XDR typhoid, and 5-30 (median 13) days for those with non-XDR typhoid ( $P<.001$ ). The conventional antibiotics taken before hospitalization among patients with XDR typhoid were ceftriaxone and ampicillin, whereas those among patients with non-XDR typhoid were cefixime, cephalosporin, and quinolones. In the hospitals, all patients with XDR typhoid were treated with a carbapenem or macrolides with a median hospitalization duration of 9.5 (range 2-25) days, while those with non-XDR typhoid were treated with cephalosporin and cefixime (n=483, 33%) and with ceftriaxone and ampicillin (n=22, 1.5%) with the median hospitalization duration of 6.5 (range 2-15) days.

Overall,  $\geq 1$  complications were reported in 360 (38%) patients with XDR and in 89 (18%) patients with non-XDR typhoid

( $P<.001$ ). Ileal perforation was the most commonly reported complication in both patients with XDR (n=210, 23%) and those with non-XDR (n=71, 14%) typhoid ( $P<.001$ ). Septicemia was the second-most commonly reported complication among both patients with XDR (n=97, 11%) and those with non-XDR (n=9, 1.7%) typhoid (Table 3).

The median duration of prehospitalization illness was longer among patients with complications (range 7-30 days, median 22 days) than among those without complications (range 5-25 days, median 6 days) ( $P<.001$ ). Overall, mortality was documented in 17 of 947 (1.8%) patients with XDR Typhi infections and 3 of 505 (0.6%) patients with non-XDR Typhi infections ( $P=.06$ ).

**Table 3.** Frequency of complications among hospitalized patients with XDR<sup>a</sup> typhoid and those with non-XDR typhoid in Hyderabad, Pakistan, from October 1, 2016, to September 30, 2018 (N=1452).

Complications	XDR typhoid cases (n=947), n (%)	Non-XDR typhoid cases (n=505), n (%)	P value
Ileal perforation	210 (23.0)	71 (11.0)	<.001
Septicemia	91 (14.0)	9 (1.7)	<.001
Cholecystitis	27 (2.8)	4 (0.7)	.008
Pneumonia	10 (1.0)	1 (0.1)	<.001
Jaundice	13 (1.3)	1 (0.1)	.001

<sup>a</sup>XDR: extensively drug resistant; resistant to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, ciprofloxacin, and ceftriaxone.

## Discussion

### Principal Findings

To our knowledge, this is the first study on the first major XDR typhoid outbreak worldwide and documenting mortality and morbidity in Pakistan. The delay in the initiation of appropriate antibiotic therapy is the leading cause of complications and deaths. XDR typhoid has reached alarmingly high levels, threatening to be potentially untreatable and leading to high morbidity and mortality in Hyderabad.

Our study reports a mean age was 15 years for patients with XDR typhoid and 12 years for those with non-XDR typhoid, the majority of our patients being male (n=915, 63%). In a study in Nepal, the mean age of patients with typhoid was 19 years, and 45% of them were male [15]. Typhi isolates from approximately two-thirds of cases (n=947, 66%) were XDR. A population-based study in 5 Asian countries reported that 23% of isolates were multidrug resistant [16].

Limited data on the case fatality rates of typhoid are available [17]. In this study, the case fatality rate was 1.8%. A study on the global burden of typhoid fever reported a case fatality rate of 1% [3].

Typhoid is an endemic disease in Pakistan. The major factors associated with its high prevalence rate include overcrowding, illiteracy, poverty, poor sanitation, and an unsafe supply of drinking water [18]. Early diagnosis and the use of appropriate antibiotics play a key role in reducing complications and deaths [19]. Poor sanitation and contaminated water supplies are serious infrastructure problems in Hyderabad, Karachi, and the rest of

Sindh province. The 2 main cities of this province are affected by XDR Typhi. Public health officials predict that XDR Typhi will also cross borders and start spreading outside of Pakistan [20].

### Limitations

Our study has limitations, given its retrospective manner of conducting reviews of medical records of in-hospital patients; this has yielded limited information regarding prior treatments, including antibiotic use prior to hospitalization. Patients who were admitted to hospitals do not represent those among the general population of Pakistan.

### Conclusions

As this first XDR typhoid outbreak continues to spread, the increased duration of illness before hospitalization and increased rate of complications has important implications for clinical care and medical costs, and heightens the importance of prevention and control measures. To ensure that the minimization of delay in treatment due to the lack of proper diagnoses and access to hospitals, the establishment of certified laboratories and the recruitment of trained, well-informed physicians in geographically strategic areas will help in improving the situation. The provision of safe drinking water and proper sanitation is the ultimate solution to prevent future outbreaks. Setting up of surveillance for typhoid in the province and the whole country is important to determine whether XDR typhoid is limited to only these 2 cities or it has widely spread in Pakistan. Further prospective studies are also required for understanding the factors that are leading to the spread of XDR typhoid in Pakistan.

### Acknowledgments

The authors would like to acknowledge the Global Health Development Eastern Mediterranean Public Health Network for their technical support.

### Conflicts of Interest

None declared.

### References

1. Wain J, Hendriksen RS, Mikoleit ML, Keddy KH, Ochiai RL. Typhoid fever. *Lancet* 2015 Mar 21;385(9973):1136-1145. [doi: [10.1016/S0140-6736\(13\)62708-7](https://doi.org/10.1016/S0140-6736(13)62708-7)] [Medline: [25458731](https://pubmed.ncbi.nlm.nih.gov/25458731/)]

2. Buckle GC, Walker CLF, Black RE. Typhoid fever and paratyphoid fever: Systematic review to estimate global morbidity and mortality for 2010. *J Glob Health* 2012 Jun;2(1):010401 [FREE Full text] [doi: [10.7189/jogh.02.010401](https://doi.org/10.7189/jogh.02.010401)] [Medline: [23198130](https://pubmed.ncbi.nlm.nih.gov/23198130/)]
3. Immunization, Vaccines and Biologicals. World Health Organization. URL: <https://www.who.int/immunization/diseases/typhoid/en/> [accessed 2021-04-26]
4. Das JK, Hasan R, Zafar A, Ahmed I, Ikram A, Nizamuddin S, et al. Trends, Associations, and Antimicrobial Resistance of Typhi and Paratyphi in Pakistan. *Am J Trop Med Hyg* 2018 Sep;99(3\_Suppl):48-54 [FREE Full text] [doi: [10.4269/ajtmh.18-0145](https://doi.org/10.4269/ajtmh.18-0145)] [Medline: [30047366](https://pubmed.ncbi.nlm.nih.gov/30047366/)]
5. Keddy KH. 21st-century typhoid fever—progression of knowledge but regression of control? *Lancet Infect Dis* 2018 Dec;18(12):1296-1298. [doi: [10.1016/S1473-3099\(18\)30515-2](https://doi.org/10.1016/S1473-3099(18)30515-2)] [Medline: [30507445](https://pubmed.ncbi.nlm.nih.gov/30507445/)]
6. Ryan ET, Andrews J, John J. Treatment and prevention of enteric (typhoid and paratyphoid) fever. UpToDate. URL: <https://www.uptodate.com/contents/treatment-and-prevention-of-enteric-typhoid-and-paratyphoid-fever> [accessed 2021-04-26]
7. Typhoid fever – Islamic Republic of Pakistan. World Health Organization. 2018. URL: <https://www.who.int/csr/don/27-december-2018-typhoid-pakistan/en> [accessed 2021-04-26]
8. Rasheed MK, Hasan SS, Babar Z, Ahmed SI. Extensively drug-resistant typhoid fever in Pakistan. *Lancet Infect Dis* 2019 Mar;19(3):242-243. [doi: [10.1016/S1473-3099\(19\)30051-9](https://doi.org/10.1016/S1473-3099(19)30051-9)] [Medline: [30833059](https://pubmed.ncbi.nlm.nih.gov/30833059/)]
9. Sharma AK, Sharma RK, Sharma SK, Sharma A, Soni D. Typhoid intestinal perforation: 24 perforations in one patient. *Ann Med Health Sci Res* 2013 Nov;3(Suppl 1):S41-S43 [FREE Full text] [doi: [10.4103/2141-9248.121220](https://doi.org/10.4103/2141-9248.121220)] [Medline: [24349848](https://pubmed.ncbi.nlm.nih.gov/24349848/)]
10. Qamar FN, Azmatullah A, Bhutta ZA. Challenges in measuring complications and death due to invasive Salmonella infections. *Vaccine* 2015 Jun 19;33 Suppl 3:C16-C20. [doi: [10.1016/j.vaccine.2015.03.103](https://doi.org/10.1016/j.vaccine.2015.03.103)] [Medline: [25921727](https://pubmed.ncbi.nlm.nih.gov/25921727/)]
11. Chalya PL, Mabula JB, Koy M, Kataraihya JB, Jaka H, Mshana SE, et al. Typhoid intestinal perforations at a University teaching hospital in Northwestern Tanzania: A surgical experience of 104 cases in a resource-limited setting. *World J Emerg Surg* 2012 Mar 08;7:4 [FREE Full text] [doi: [10.1186/1749-7922-7-4](https://doi.org/10.1186/1749-7922-7-4)] [Medline: [22401289](https://pubmed.ncbi.nlm.nih.gov/22401289/)]
12. Parry CM, Thompson C, Vinh H, Chinh NT, Phuong LT, Ho VA, et al. Risk factors for the development of severe typhoid fever in Vietnam. *BMC Infect Dis* 2014 Feb 10;14:73 [FREE Full text] [doi: [10.1186/1471-2334-14-73](https://doi.org/10.1186/1471-2334-14-73)] [Medline: [24512443](https://pubmed.ncbi.nlm.nih.gov/24512443/)]
13. Agu K, Nzegwu M, Obi E. Prevalence, morbidity, and mortality patterns of typhoid ileal perforation as seen at the University of Nigeria Teaching Hospital Enugu Nigeria: an 8-year review. *World J Surg* 2014 Oct;38(10):2514-2518 [FREE Full text] [doi: [10.1007/s00268-014-2637-5](https://doi.org/10.1007/s00268-014-2637-5)] [Medline: [24858189](https://pubmed.ncbi.nlm.nih.gov/24858189/)]
14. Qamar FN, Yousafzai MT, Khalid M, Kazi AM, Lohana H, Karim S, et al. Outbreak investigation of ceftriaxone-resistant Salmonella enterica serotype Typhi and its risk factors among the general population in Hyderabad, Pakistan: a matched case-control study. *Lancet Infect Dis* 2018 Dec;18(12):1368-1376. [doi: [10.1016/S1473-3099\(18\)30483-3](https://doi.org/10.1016/S1473-3099(18)30483-3)] [Medline: [30507460](https://pubmed.ncbi.nlm.nih.gov/30507460/)]
15. Kaljee L, Pach A, Garrett D, Bajracharya D, Karki K, Khan I. Social and Economic Burden Associated With Typhoid Fever in Kathmandu and Surrounding Areas: A Qualitative Study. *J Infect Dis* 2018 Nov 10;218(suppl\_4):S243-S249 [FREE Full text] [doi: [10.1093/infdis/jix122](https://doi.org/10.1093/infdis/jix122)] [Medline: [28973415](https://pubmed.ncbi.nlm.nih.gov/28973415/)]
16. Ochiai RL, Acosta CJ, Danovaro-Holliday MC, Baiqing D, Bhattacharya SK, Agtini MD, Domi Typhoid Study Group. A study of typhoid fever in five Asian countries: disease burden and implications for controls. *Bull World Health Organ* 2008 Apr;86(4):260-268 [FREE Full text] [doi: [10.2471/blt.06.039818](https://doi.org/10.2471/blt.06.039818)] [Medline: [18438514](https://pubmed.ncbi.nlm.nih.gov/18438514/)]
17. Klemm E, Shakoor S, Page A, Qamar F, Judge K, Saeed D, et al. Emergence of an Extensively Drug-Resistant Serovar Typhi Clone Harboring a Promiscuous Plasmid Encoding Resistance to Fluoroquinolones and Third-Generation Cephalosporins. *mBio* 2018 Feb 20;9(1):e00105-e00118 [FREE Full text] [doi: [10.1128/mBio.00105-18](https://doi.org/10.1128/mBio.00105-18)] [Medline: [29463654](https://pubmed.ncbi.nlm.nih.gov/29463654/)]
18. Naeem Khan M, Shafee M, Hussain K, Samad A, Arif Awan M, Manan A, et al. Typhoid fever in paediatric patients in Quetta, Balochistan, Pakistan. *Pak J Med Sci* 2013 Jul;29(4):929-932 [FREE Full text] [doi: [10.12669/pjms.294.3251](https://doi.org/10.12669/pjms.294.3251)] [Medline: [24353661](https://pubmed.ncbi.nlm.nih.gov/24353661/)]
19. Siddiqui FJ, Rabbani F, Hasan R, Nizami SQ, Bhutta ZA. Typhoid fever in children: some epidemiological considerations from Karachi, Pakistan. *Int J Infect Dis* 2006 May;10(3):215-222 [FREE Full text] [doi: [10.1016/j.ijid.2005.03.010](https://doi.org/10.1016/j.ijid.2005.03.010)] [Medline: [16431148](https://pubmed.ncbi.nlm.nih.gov/16431148/)]
20. Cohen J. 'Frightening' typhoid fever outbreak spreads in Pakistan. *Science* 2018 Jul 20;361(6399):214. [doi: [10.1126/science.361.6399.214](https://doi.org/10.1126/science.361.6399.214)] [Medline: [30026207](https://pubmed.ncbi.nlm.nih.gov/30026207/)]

---

## Abbreviations

**XDR:** extensively drug resistant

---

*Edited by M Alyahya, T Sanchez; submitted 19.01.21; peer-reviewed by A Allam, M Zinnah; comments to author 10.03.21; revised version received 12.03.21; accepted 12.03.21; published 17.05.21.*

*Please cite as:*

*Fatima M, Kumar S, Hussain M, Memon NM, Vighio A, Syed MA, Chaudhry A, Hussain Z, Baig ZI, Baig MA, Asghar RJ, Ikram A, Khader Y*

*Morbidity and Mortality Associated with Typhoid Fever Among Hospitalized Patients in Hyderabad District, Pakistan, 2017-2018: Retrospective Record Review*

*JMIR Public Health Surveill 2021;7(5):e27268*

*URL: <https://publichealth.jmir.org/2021/5/e27268>*

*doi: [10.2196/27268](https://doi.org/10.2196/27268)*

*PMID: [33999000](https://pubmed.ncbi.nlm.nih.gov/33999000/)*

©Munaza Fatima, Santosh Kumar, Mudassar Hussain, Naveed Masood Memon, Anum Vighio, Muhammad Asif Syed, Ambreen Chaudhry, Zakir Hussain, Zeeshan Iqbal Baig, Mirza Amir Baig, Rana Jawad Asghar, Aamer Ikram, Yousef Khader. Originally published in JMIR Public Health and Surveillance (<https://publichealth.jmir.org>), 17.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Viewpoint

# Pakistan's Response to COVID-19: Overcoming National and International Hypes to Fight the Pandemic

Hashaam Akhtar<sup>1</sup>, PhD; Maham Afridi<sup>2</sup>, MPhil; Samar Akhtar<sup>1</sup>, PhD; Hamaad Ahmad<sup>1</sup>, MPhil; Sabahat Ali<sup>3</sup>, MBBS; Sundas Khalid<sup>4</sup>, MSc; Sajid Mahmood Awan<sup>1</sup>, DPharm; Shahzaib Jahangiri<sup>1</sup>, DPharm; Yousef Saleh Khader<sup>5</sup>, PhD

<sup>1</sup>Yusra Institute of Pharmaceutical Sciences, Yusra Medical and Dental College, Islamabad, Pakistan

<sup>2</sup>Department of Biotechnology, Quaid-i-Azam University, Islamabad, Pakistan

<sup>3</sup>Department of Gynecology and Obstetrics, Paf Hospital, Islamabad, Pakistan

<sup>4</sup>School of Chemical and Materials Engineering, National University of Science and Technology, Islamabad, Pakistan

<sup>5</sup>Medical Education and Biostatistics, Department of Community Medicine, Public Health and Family Medicine, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan

**Corresponding Author:**

Hashaam Akhtar, PhD

Yusra Institute of Pharmaceutical Sciences

Yusra Medical and Dental College

Zaraj Housing Society, Opposite DHA Phase 2 Gate III, Main GT Road

Islamabad, 44000

Pakistan

Phone: 92 3165163945

Email: [hashaamakhtar@gmail.com](mailto:hashaamakhtar@gmail.com)

## Abstract

The COVID-19 outbreak started as pneumonia in December 2019 in Wuhan, China. The subsequent pandemic was declared as the sixth public health emergency of international concern on January 30, 2020, by the World Health Organization. Pakistan could be a potential hotspot for COVID-19 owing to its high population of 204.65 million and its struggling health care and economic systems. Pakistan was able to tackle the challenge with relatively mild repercussions. The present analysis has been conducted to highlight the situation of the disease in Pakistan in 2020 and the measures taken by various stakeholders coupled with support from the community to abate the risk of catastrophic spread of the virus.

(*JMIR Public Health Surveill* 2021;7(5):e28517) doi:[10.2196/28517](https://doi.org/10.2196/28517)

**KEYWORDS**

community health; coronavirus; COVID-19; epidemic; epidemiology; Pakistan; pandemic; public health emergency of international concern

## Introduction

COVID-19 started as an outbreak of a series of unusual pneumonia cases in Wuhan, China, with the earliest cases reported to the World Health Organization's country office in China on December 31, 2019. By January 12, 2020, the causative agent was identified as a novel coronavirus, initially termed "2019-nCoV," and up to 41 cases had been preliminarily diagnosed [1,2]. The virus has since been renamed as SARS-CoV-2 and spread drastically, and COVID-19 was declared as pandemic by the World Health Organization (WHO) on March 11, 2020 [3]. Having currently affected more than 210 countries and territories, with 19,550,650 active cases and a mortality rate of 2.85% as of December 31, 2020, the

COVID-19 pandemic continues to be a major global public health concern [4].

## Pakistan: Epidemiologic Profile

COVID-19 cases were reported from Islamabad and Karachi on February 26, 2020 [5]. Pakistan being one of the most densely populated countries in Asia, with a population of 204.65 million, and Karachi being the largest metropolitan city in Pakistan, has been greatly vulnerable to this outbreak [6]. Owing to its present economic condition, health care resources, and the occurrence of previous outbreaks, the Centers for Disease Control and Prevention had already issued a level 3 warning for international travelers to Pakistan [7]. The administration had a huge responsibility to constrain the spread through a timely response

and the adoption of appropriate measures to avoid any major catastrophe. The disease was initially difficult to contain, especially because of noncompliance of the general population to the necessary measures and timely reporting of symptoms. Within 45 days, on April 10, 2020, Pakistan reported 4601 confirmed cases with a death toll approaching 66 individuals [8].

## Public and Community Response to the COVID-19 Pandemic

There was a mixed response from the community. Few people paid attention to the news and some even considered it fake. News of the virus being a hoax or propaganda spread greatly worldwide and countered the efforts of governments and other agencies that made marked efforts to tackle the spread of the pandemic [9,10]. Common rumors on COVID-19 emergence and treatment through the media and social media resources are presented in Table 1.

**Table 1.** Rumors related to COVID-19 emergence and treatment.

Rumors	Source
The virus is no worse than the one that causes common cold	WHO's COVID-19 advice for the public: Mythbusters [9]
Hand dryers are effective in eliminating the coronavirus	Chinese social media pages [9,10]
Coronavirus originated with people eating bats in China	YouTube videos, conservative tabloids, blogs, and Twitter [9,10]
There is a vaccine or cure for coronavirus, which the government will not release	Facebook post containing a screenshot of a patent CO-V vaccine by the Centers for Disease Control and Prevention on January 22, 2020 [9,10]
Coronavirus will disappear by the summer	WHO's COVID-19 advice for the public: Mythbusters [9,11]
Vitamin C can help you ward off coronavirus	A popular social media post [12]
A "miracle" bleach product can cure coronavirus	Far-right conspiracy theory QAnon misinforming people to drink Miracle Mineral Solution, a bleach-based product [13]
Dean Koontz predicted the coronavirus in his 1981 novel <i>The Eyes of Darkness</i>	Dean Koontz's 1981 novel <i>The Eyes of Darkness</i> became very popular on Twitter [10]
Osaka flu shown in the television show <i>The Simpsons</i>	Screenshots allegedly from the "Marge in Chains" episode in 1993 on social media [10]
If you cannot hold your breath for 10 seconds without coughing, then you have coronavirus	Self-check coronavirus tests on social media originating in March 2020 [10]
The country will be placed in a nationwide quarantine effective immediately	Text messages claiming the implementation of a country-wide lockdown [10]

## Government's Initiatives to Tackle the Pandemic

The government of Pakistan has been lauded by international organizations including the WHO (and rightly so) for taking the necessary precautions and measures against the COVID-19 pandemic to guarantee not only the containment of disease spread but also to fulfill its responsibility as a state toward its people and their safety [14].

### Immediate Response to Contain Disease Spread

One of the first steps taken by the government was to develop functional emergency operations centers and to detect the route of disease spread in Pakistan. The origin of the virus was the first question; hence, detailed history-taking of patients was crucial not only in understanding the outbreak but also in determining the contacts of patients with other people in the community [15]. This helped in cordoning off areas or home-bounding people who came in close contact with a patient with COVID-19. In addition to this, patients with a recent international travel history were monitored closely. This made sense because many cases and massive spread was reported in the countries neighboring Pakistan [15-17].

### Containment Measures

Once primary and secondary contact-tracing was delineated, the foremost step taken by the government was to control the borders [18]. This was a crucial decision, owing to the consideration of a large number of Pakistani students and pilgrims studying in and travelling from China, Iran, and Europe. The government gained the confidence of the affected individuals and their families. It was almost unfeasible to restrict such individuals outside the country because of the strong public response; nonetheless, it was necessary if the spread of the virus was to be controlled quickly. To tackle this problem, the government took the initiative of designating quarantine houses near borders and airports to isolate people entering Pakistan for a short period to make sure they were not infected before they moved out in the community [19,20].

### Border Control

The WHO reported that the number of new cases increased by the minute, and disease spread was now not only limited to people who had a recent travel history in the regions highly affected by the pandemic. Disease spread within the community was alarming and called for drastic steps to be taken not only by local governments but also by countries and states at large.

All necessary services and measures are still being used in maximum capacity till date to ensure the safety of people's lives in the country. Since all cases initially had a history of recent travel, it was speculated that transmissions were imported from outside of the country. Therefore, travel restrictions were imposed to limit the spread of virus from other countries to Pakistan [21].

### Quarantine Houses

After the borders were contained, it was important for the government to provide a solution to all individuals stuck at the borders to enter the country without imposing a threat to the rest of the community [20]. It was crucial to quarantine the people at a specific location and either have them tested or wait for at least 2 weeks to ensure that they were not infected with SARS-CoV-2 before they travelled to their hometowns. People who did not show any symptoms after being quarantined for a certain duration could go to their cities and notify the authorities in case of any signs and symptoms after leaving the quarantine homes [19,20]. The development of these shelters was an economically and strategically massive task for the government. More than 3000 pilgrims arrived from Iran in the first week of March 2020 alone and were housed at quarantine shelters in Taftan and Chaman [22,23].

Toward the end of March 2020, the government decided to relocate the pilgrims to their respective provinces where quarantine centers were set up. Most news outlets and social media users condemned this step taken by the government. Many problems were faced by the pilgrims and other people who were quarantined at these centers, including included small, cramped spaces for people to live in, unhygienic conditions, shortage of food, water, medication, and unavailability of physicians [23].

### Country-Wide Lockdown

Many other steps were taken by the government to tackle disease spread and to minimize the damage caused by the pandemic in Pakistan [24,25].

One of the first steps that the government of Pakistan took to limit the spread of the virus within the community was to impose well-planned lockdowns in all major cities [20,26]. Lockdowns were imposed during different hours in different regions, and most of the public spaces were closed off except for grocery stores, pharmacies, and vegetable and fruit shops. All the eateries, parks, wedding halls, schools, and offices were closed until further notice by the federal government [27]. This led to retaliation from the provincial governments and opposition as it posed a great economic threat to the country's daily-wage workers and to the low-income population; however, this was a necessary measure to curtail disease spread. Another step that the government took, and faced major opposition, was the closure of prayers at mosques, including Friday prayers [26,28,29].

### Cordoning Off Areas

When reports of virus transmission started emerging, especially in the federal capital of Islamabad, the government took the initiative of sealing off areas that reported infections. According

to a notification issued by the District Magistrate Islamabad, the city administration decided to cordon off areas to ensure public safety after the number of infections increased [30]. Samples were tested by the National Institute of Health, Islamabad, and analyzed by epidemiologists of the deputy commissioner of the COVID-19 Nerve Centre after which the notification was issued. This helped in not only curbing the spread of the infection but also in contact-tracing and further testing of the public.

### Testing and Contact Tracing

The country's testing capacity was limited during the early months of the pandemic, and while high-income countries were conducting large-scale randomized tests to estimate the actual number of confirmed cases, Pakistan was forced to carry out priority-based testing and rely on the enforcement of strict quarantine and isolation strategies to contain the pandemic [31]. Contact-tracing, however, was an effective strategy that not only helped limit the spread of the virus but also helped predict its route through different regions of the country and across different age groups. Nevertheless, since large-scale testing was crucial to assess the severity of the pandemic, the testing capacity of laboratories and the availability of testing kits was gradually increased by the government, and in June 2020 up to 30,000 tests were conducted daily to ascertain the pace of spread and to formulate future strategies accordingly [32]. Both these strategies provided valuable insights on the differences in the clinical manifestation of COVID-19 in people with different demographic and health backgrounds.

### Field Epidemiology Laboratory Training Program

The Training Programs in Epidemiology and Public Health Interventions Network is a network of 75 field epidemiology training programs, which operate in >100 countries including Pakistan. After the WHO declared COVID-19 a public health emergency of international concern, alumni from the Field Epidemiology Training Program implemented standard operating procedures (SOPs) for COVID-19 screening at international airports in Pakistan. They also designed and implemented a real-time data entry system to screen travelers from high-risk countries [33].

### Implementation of SOPs: Masks, Sanitization, and Social Distancing

SOPs were devised for the public and were meant to be strictly followed in public areas. These included guidelines on social distancing; that is, avoiding crowded areas, maintaining a physical distance of 3 feet, wearing masks, maintaining hand hygiene, sanitizing frequently touched surfaces and areas, and following general hygiene rules such as avoiding touching the face, nose, or eyes, and coughing, or sneezing in the elbow or a paper napkin instead of the hands. The authorities started taking disciplinary action against those who violated the SOPs at public places in various parts of the country in accordance with the recommendations of the National Command and Control Centre of Pakistan. The focus of the National Command and Control Centre was on SOPs, compliance, strict administrative actions being implemented, and enforcement of various strands of the track, trace, and quarantine strategy [34].



### Initiation of Awareness Campaigns: Role of Community Health workers

Many campaigns were initiated by both local and federal governments in the interest of the general population to spread awareness about the risks, signs, and symptoms of COVID-19 [35]. Pakistan's extensive polio vaccination program, consisting of more than 265,000 community health workers and vaccinators, was mobilized with the help of the WHO [36]. This not only helped provide infrastructure to track and trace cases early during the epidemic but also helped spread awareness in the remote, underdeveloped rural regions of Pakistan. Another vital step was taken to spread awareness to the masses, where text messages were sent by the government of Pakistan on all mobile networks [37]. The daily reminders on following SOPs helped tackle those who did not take the necessary precautions and were unaware of the aforementioned information, and the imposition of fines and charges for noncompliance made risk and awareness campaigns a nationwide success [35,37].

Recorded voice messages in various local languages including Urdu, Pashto, and Sindhi, which warned against the risks of COVID-19, its spread, and its complications, and general awareness regarding the SOPs to help control its spread, were used as caller tunes before every phone call. The recorded messages were changed in accordance with the situation and ranged from guidelines on SOPs, warning noncompliers, and even congratulating efforts after successfully controlling disease spread during August 2020 [37].

### Economic Measures

On the emergence of COVID-19 in Pakistan, the entire system faced various problems owing to the limitations of the health care system, poor infrastructure, uneven access to health care, resistance from various social, political, cultural, and religious groups, political instability, economic fragilities, and mistrust among the public. Data of a web-based survey conducted by the Small and Medium Enterprises Development Authority from April 3-14, 2020, among 920 businesses revealed insufficient revenue generation, losses, and difficulty in survival among businesses [38]. Pakistan launched various schemes to tackle the economic crisis faced by many individuals during the pandemic. On May 2, 2020, Prime Minister Imran Khan launched a relief scheme for people who lost their jobs or whose source of income has been compromised owing to the lockdown. He launched a cash assistance program through the Ehsaas Cash Programme to support unemployed individuals [39].

After lifting the lockdown in some sectors, the government allowed construction and daily-wage workers to resume working while dutifully following the SOPs and taking necessary precautions. This helped ease some of the economic burdens of the government, especially in providing rations and relief packages for the daily-wage workers [40].

Furthermore, the government also requested people who had been diagnosed with mild or asymptomatic COVID-19 to quarantine at home as some of them did not require hospital care; this helped curb the patient influx in hospitals and at diagnostic centers, thus easing the burden on health workers and medical practitioners [41].

### Production of Ventilators

One of the largest concerns for the ministry of health and health departments in Pakistan and worldwide is coping with the continuously increasing demand of ventilators as the virus spreads and the number of cases increases. The shortage of ventilators is a major issue faced by Pakistan, especially because all the major medical equipment are imported and not produced locally. To tackle this problem, the National Radio and Telecommunication Corporation produced its first ventilator locally within a few months of the onset of the pandemic [42]. The National Radio and Telecommunications Corporation initially offered cost-free repairs for almost 109 ventilators throughout the country and later designed and produced its own ventilators. Initially, 8 ventilators were produced and handed over to the National Disaster Management Authority after which the prime minister formally inaugurated a facility for large-scale production of ventilators within Pakistan [43].

As a result of all the efforts made by the government of Pakistan, 6 months after reporting its first case, active cases in Pakistan are continuing to steadily decrease, with the number of deaths recorded in a day now often down to single-digit numbers. The country has had 312,263 confirmed cases of as on October 1, 2020, with 6479 COVID-19-related deaths, according to the official data [44]. Save for single-day glitches, active cases have been progressively declining since peaking in June 2020, currently standing at 8903, their lowest level since late April 2020.

### *Success Stories: Pakistan's Population Coming Together to Combat COVID-19*

Pakistan is currently faced with one of its toughest challenges since its establishment as an independent nation, and while COVID-19 has severely disrupted routines and led to intense fear among the public, efforts are still being made to bring together the expertise and knowledge of individuals from various fields to ensure combating this pandemic together. In addition to the government's efforts, many other organizations and individuals came forward to help against the pandemic in various capacities. From using social media to campaign for blood donations for patients with thalassemia nationwide to arranging food supplies and relief packages for those severely affected by the pandemic, the local people of Pakistan came forward and helped fellow citizens.

The Human Development Foundation Pakistan is one of the oldest nonprofit organizations in the country, and it estimated the provision and distribution of more than 14,000 ration packages containing food and medical supplies to the people of Karachi [45].

### Al-Khidmat Foundation Pakistan

Al-Khidmat Foundation Pakistan is one of the leading nonprofit foundations operating in Pakistan for the past 30 years. During the onset of the pandemic, it played a vital role in charity work including awareness campaigns, providing preventive equipment such as soap, sanitizers, masks, and relevant reading material to the general public, providing its services to government institutions including hospitals, Aghosh homes, ambulances,

and trained volunteers. Moreover, it carried out food drives, provided COVID-19 test facilities and antibody tests, and arranged for protective equipment to distribute among physicians and medical staff on the frontline [46]. Al-Khidmat Foundation Pakistan also played a vital role in arranging free plasma for patients with COVID-19 [47].

### Corona Recovered Warriors

The Facebook page titled “Corona Recovered Warriors” provided hope during the grim period of disease spread in Pakistan. Created by musician Zoraiz Riaz with the aim to help coordinate convalescent plasma donations for people with COVID-19 in Pakistan, this group quickly gained popularity and had 320,000 members in just 1 month, needing a team of 33 volunteers to manage the posts. People looking for plasma donors, medical supplies, oxygen cylinders, ventilators, injection drugs or other drugs, and leads on hospitals accepting new admittees posted all their queries on this group, and thousands of people came forward and offered help in all capacities to those in need [48]. The group then started organizing donation and food drives, providing personal protective equipment (PPE) to health care workers and delivering medical supplies to desperate families of patients with COVID-19 [49].

### Plasma Trials by Medical Professionals

In desperate times when everyone is seeking any cure to tackle the virus, many unapproved and untested remedies were used even by health care professionals to treat individuals with COVID-19. The most popular one was the use of plasma of a recovered patient to treat patients with COVID-19. Dr Shahid Junejo, a senior superintendent at a civil hospital, tested plasma therapy on a patient in Hyderabad. According to him, the decision for the trial was taken after consultation with the vice chancellor of the Liaquat University of Medical and Health Sciences Jamshoro, Prof Bikha Ram Devrajani [50]. Passive immunization is an old procedure used in the absence of a vaccine to treat infectious diseases; hence, the treatment was administered to many patients throughout the country without any strong evidence of its ability to neutralize the virus [51]. Even though the Ministry of National Health Services declared that plasma therapy is not a cure for COVID-19 as it is still undergoing a clinical trial on a global scale, there is still a high demand of plasma donors, and as of July 2020 approximately 750 donors were connected with critical patients through the Corona Recovered Warriors Facebook page alone.

### Availability of Scholars Against COVID-19 Pakistan

Scholars Against COVID-19 is a platform of over 3000 young scholars and researchers nationwide coming together as volunteers to assist the government and people through donations of equipment from laboratories and universities to scale up testing and experimentation related to the diagnosis and treatment of COVID-19 [52]. Their aim is to bridge the disconnect among various sectors in Pakistan, which makes executing such ideas challenging.

### Student Taskforce Against COVID-19

Student Taskforce Against COVID-19 is a group of final-year medical students from Aga Khan University Hospital who conceived the idea of creating a helpline for families and patients

affected by COVID-19 who have been looking for guidelines and help [53]. The taskforce is not only managing the helpline but also assisting the Aga Khan University Hospital and the Sindh government in contact-tracing and helping the Pakistan Medical Association in identifying and providing volunteers to help at Karachi's Expo Centre isolation ward for patients with COVID-19 [54].

### First Response Initiative of Pakistan

Over 400 medical students have come together through the Combat Corona campaign and are aiming to collect and provide PPE to health care workers. They have targeted hospitals in Karachi needing PPE and have collected hundreds of equipment for distribution through donations in all major hospitals of the city [54].

### Pakistan Against COVID-19 Volunteers Group

Pakistan Against COVID-19 Volunteers is a group of physicians and other professionals who have collaborated and aim to enable connections between manufacturers and suppliers of PPE, carry out innovation and experimentation for designing and manufacturing ventilators through 3D printing technology, and develop noncontact thermometers locally [55,56].

### Kwickdoctor.com

Kwickdoctor.com has been developed by 40-year-old information technology expert Salman Khan. He aims to connect the public to consultants, physicians, pharmacies, and laboratories and even delivers prescriptions at the doorstep. With the pandemic spreading, the need to avoid contact has increased and digital care is the need of the hour [57].

## Discussion

### Principal Findings

COVID-19, after being first reported in December 2019, is still swiftly spreading worldwide. Within 10 months, the mortality and morbidity rates have approached unexpected levels. Scientists, researchers, and clinicians have worked together with engineers to develop treatments, diagnostic kits, and vaccines to prevent this infection from spreading further; however, a third wave of COVID-19 is currently underway worldwide with numerous mutant strains. These mutations have rendered this virus either more virulent or resistant to previously used medications [58]. The second wave has been feared as the situation was reverting to normalcy and businesses, offices, and schools were reopening in late September or early October of 2020. The government of Pakistan started tackling COVID-19 on the basis of the experience of other countries as the disease approached Pakistan after having affected many other countries. Starting from preparing special wards, using all resources including polio and dengue teams and wards, respectively, preparing appropriate SOPs, conveying awareness messages to everyone through the television or mobile phones, updating everyone through special mobile apps and websites, showing hotspots, sharing the economic burden with the weak, and ending with smart lockdowns were some of the most impressive measures to handle the pandemic. The people of Pakistan also supported the government during this time, which is one of the

most prominent reasons Pakistan overcame the first 2 waves with minimal morbidities compared to other countries.

### Conclusions

Immunization and treatment of COVID-19 may still be questionable, but precautions and SOPs have undoubtedly been set by many. Technology has played its part in spreading awareness, but Pakistan is currently undergoing a third wave of infections. However, if precautions are taken and all SOPs

are followed, the entire community can be rescued and the risk of reinfection and further waves would decline immediately. This is a situation where everyone has a responsibility toward the community and must take steps to minimize the risk of further disease spread. Pakistan has shown tremendous potential in public health, and different government and nongovernment organizations can collaborate to address the challenges through the engagement of society and the community along with the introduction of new policies.

### Conflicts of Interest

None declared.

### References

1. Novel Coronavirus – China. World Health Organization. 2020 Jan 12. URL: <https://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/> [accessed 2021-05-04]
2. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis* 2020 Feb;91:264-266 [FREE Full text] [doi: [10.1016/j.ijid.2020.01.009](https://doi.org/10.1016/j.ijid.2020.01.009)] [Medline: [31953166](https://pubmed.ncbi.nlm.nih.gov/31953166/)]
3. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. *Acta Biomed* 2020 Mar 19;91(1):157-160 [FREE Full text] [doi: [10.23750/abm.v91i1.9397](https://doi.org/10.23750/abm.v91i1.9397)] [Medline: [32191675](https://pubmed.ncbi.nlm.nih.gov/32191675/)]
4. Coronavirus Worldwide Graphs. Worldometer. URL: <https://www.worldometers.info/coronavirus/worldwide-graphs/> [accessed 2020-12-31]
5. Pakistan Statistical Year Book 2018 (Provisional). Pakistan Bureau of Statistics: Government of Pakistan. URL: <https://www.pbs.gov.pk/sites/default/files/PAKISTAN%20STATISTICAL%20YEAR%20BOOK%202018.pdf> [accessed 2020-03-16]
6. Abid K, Bari YA, Younas M, Tahir Javaid S, Imran A. Progress of COVID-19 Epidemic in Pakistan. *Asia Pac J Public Health* 2020 May;32(4):154-156 [FREE Full text] [doi: [10.1177/1010539520927259](https://doi.org/10.1177/1010539520927259)] [Medline: [32429679](https://pubmed.ncbi.nlm.nih.gov/32429679/)]
7. COVID-19 in Pakistan. Centers for Disease Control and Prevention. URL: <https://wwwnc.cdc.gov/travel/notices/warning/coronavirus-pakistan> [accessed 2020-09-29]
8. See the Realtime Pakistan and Worldwide COVID-19 Situation!. Government of Pakistan. URL: <http://covid.gov.pk/> [accessed 2020-04-06]
9. Coronavirus disease (COVID-19) advice for the public: Mythbusters. World Health Organization. URL: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public/myth-busters> [accessed 2020-03-16]
10. Dickson EJ. Coronavirus Is Spreading — And So Are the Hoaxes and Conspiracy Theories Around It. *Rolling Stone*. 2020 Mar 18. URL: <https://www.rollingstone.com/culture/culture-news/coronavirus-china-bat-patent-conspiracy-theory-942416/> [accessed 2020-03-27]
11. 40 times Trump said the coronavirus would go away. *The Washington Post*. 2020 Nov 02. URL: [https://www.washingtonpost.com/video/politics/40-times-trump-said-the-coronavirus-would-go-away/2020/04/30/d2593312-9593-4ec2-aff7-72c1438fca0e\\_video.html](https://www.washingtonpost.com/video/politics/40-times-trump-said-the-coronavirus-would-go-away/2020/04/30/d2593312-9593-4ec2-aff7-72c1438fca0e_video.html) [accessed 2020-09-16]
12. Matt B. Fact Check: Could taking Vitamin C cure or prevent COVID-19. *USA Today*. 2020 Mar 24. URL: <https://www.usatoday.com/story/news/factcheck/2020/03/24/coronavirus-fact-check-could-vitamin-c-cure-covid-19/2904303001/> [accessed 2020-03-27]
13. Broderick R. QAnon Supporters And Anti-Vaxxers Are Spreading A Hoax That Bill Gates Created The Coronavirus. *BuzzFeed News*. 2020 Jan 23. URL: <http://www.buzzfeednews.com/articles/ryanhatesthis/qanon-supporters-and-anti-vaxxers-are-spreading-a-hoax> [accessed 2020-09-16]
14. Gul A. Pakistan Lifts Lockdowns, Top UN Diplomat Lauds Anti-Virus Gains. *Voice of America*. 2020 Aug 10. URL: <https://www.voanews.com/south-central-asia/pakistan-lifts-lockdowns-top-un-diplomat-lauds-anti-virus-gains> [accessed 2020-09-28]
15. Corona patients with travel history to be allocated tag numbers. *The Express Tribune*. 2020 Apr 19. URL: <https://tribune.com.pk/story/2201833/corona-patients-travel-history-allocated-tag-numbers> [accessed 2020-09-28]
16. Badshah SL, Ullah A, Badshah SH, Ahmad I. Spread of Novel coronavirus by returning pilgrims from Iran to Pakistan. *J Travel Med* 2020 May 18;27(3):taaa044 [FREE Full text] [doi: [10.1093/jtm/taaa044](https://doi.org/10.1093/jtm/taaa044)] [Medline: [32268358](https://pubmed.ncbi.nlm.nih.gov/32268358/)]
17. Pakistan on alert over deadly China virus. *The Express Tribune*. 2020 Jan 22. URL: <https://tribune.com.pk/story/2142464/pakistan-alert-deadly-china-virus> [accessed 2020-10-04]
18. Pakistan Travel Advisory. US Department of State - Bureau of Consular Affairs. URL: <https://travel.state.gov/content/travel/en/traveladvisories/traveladvisories/pakistan-travel-advisory.html> [accessed 2020-10-04]

19. Abid K, Bari YA, Younas M, Tahir Javaid S, Imran A. Progress of COVID-19 Epidemic in Pakistan. *Asia Pac J Public Health* 2020 May;32(4):154-156 [FREE Full text] [doi: [10.1177/1010539520927259](https://doi.org/10.1177/1010539520927259)] [Medline: [32429679](https://pubmed.ncbi.nlm.nih.gov/32429679/)]
20. Ahmad T. Pakistan: "Smart Lockdown" Imposed across Cities of Pakistan as Covid-19 Cases Grow Rapidly. Library of Congress. 2020 Jun 25. URL: <https://www.loc.gov/law/foreign-news/article/pakistan-smart-lockdown-imposed-across-cities-of-pakistan-as-covid-19-cases-grow-rapidly/> [accessed 2020-09-29]
21. Pakistan: Border closures extended for two weeks on April 13 /update 17. *Garda World*. 2020 Apr 14. URL: <https://www.garda.com/crisis24/news-alerts/332031/pakistan-border-closures-extended-for-two-weeks-on-april-13-update-17> [accessed 2020-10-08]
22. COVID-19: Number of quarantined people in Taftan reaches 4,000. *The Express Tribune*. 2020 Mar 11. URL: <https://tribune.com.pk/story/2173842/covid-19-number-quarantined-people-taftan-reaches-4000> [accessed 2020-09-30]
23. Ellis-Petersen H, Baloch SM. Pakistan coronavirus camp: 'No facilities, no humanity'. *The Guardian*. 2020 Mar 19. URL: <https://www.theguardian.com/world/2020/mar/19/pakistan-coronavirus-camp-no-facilities-no-humanity> [accessed 2020-10-03]
24. 'Pakistan's preparation, response to Covid-19 one of the best worldwide'. *The Express Tribune*. 2020 Jul 19. URL: <https://tribune.com.pk/story/2255603/pakistans-preparation-response-to-covid-19-one-of-the-best-worldwide> [accessed 2020-09-27]
25. Hashim A. Pakistan wins rare, fragile success against novel coronavirus. *Al Jazeera*. 2020 Aug 25. URL: <https://www.aljazeera.com/news/2020/08/25/pakistan-wins-rare-fragile-success-against-novel-coronavirus/> [accessed 2020-09-29]
26. Khan MI. Coronavirus updates: Pakistan imposes curfew to curtail Friday prayers. *BBC News*. 2020 Apr 03. URL: <https://www.bbc.com/news/world-asia-52149688> [accessed 2020-10-01]
27. Raza Z. Curfew remains only solution to keep people confined to home. *Daily Times*. 2020 Mar 31. URL: <https://dailymtimes.com.pk/586250/curfew-remains-only-solution-to-keep-people-confined-to-home> [accessed 2020-09-26]
28. Govt in limbo over banning congregation prayers in mosques amidst virus lockdown. *Dawn*. 2020 Mar 25. URL: <https://www.dawn.com/news/1543355> [accessed 2020-09-25]
29. Hassan SR. Pakistan's Sindh province bans prayer at mosques during Ramadan. *Reuters*. 2020 Apr 24. URL: <https://www.reuters.com/article/us-health-coronavirus-ramadan-pakistan/pakistans-sindh-province-bans-prayer-at-mosques-during-ramadan-idUSKCN226166> [accessed 2020-09-30]
30. Asghar I. Rawalpindi administration seals three neighbourhoods amid COVID-19 outbreak fears. *The Express Tribune*. 2020 Mar 28. URL: <https://tribune.com.pk/story/2186327/rawalpindi-administration-seals-three-neighbourhoods-amid-covid-19-outbreak-fears> [accessed 2020-10-01]
31. Contact Tracing. Centers for Disease Control and Prevention. URL: <https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/contact-tracing.html> [accessed 2020-10-02]
32. Daga N. Inside Pakistan's COVID-19 Contact Tracing. *The Diplomat*. 2020 Jul 01. URL: <https://thediplomat.com/2020/07/inside-pakistans-covid-19-contact-tracing/> [accessed 2020-09-29]
33. FELTP: The Frontline of Defense Against COVID-19 in Pakistan. Centers for Disease Control and Prevention. 2020 Jul 21. URL: <https://www.cdc.gov/globalhealth/healthprotection/fetp-40th-anniversary/stories/pakistan-fetp-covid.html> [accessed 2020-10-01]
34. NCOC to re-close public service sectors if SOPs compliance goes neglected. *Associated Press of Pakistan*. 2020. URL: <https://www.app.com.pk/national/ncoc-to-re-close-public-service-sectors-if-sops-compliance-goes-neglected/> [accessed 2020-10-01]
35. Corona Virus Public Awareness Campaign. *Reliefweb*. 2020 Mar 22. URL: <https://reliefweb.int/report/pakistan/corona-virus-public-awareness-campaign> [accessed 2020-09-26]
36. COVID-19 in Pakistan: WHO fighting tirelessly against the odds. *World Health Organization*. 2020 Nov 09. URL: <https://www.who.int/news-room/feature-stories/detail/covid-19-in-pakistan-who-fighting-tirelessly-against-the-odds> [accessed 2020-12-31]
37. Zong 4G and UNICEF Pakistan Partner to Create Awareness around COVID-19. *UNICEF*. 2020 Apr 28. URL: <https://www.unicef.org/pakistan/press-releases/zong-4g-and-unicef-pakistan-partner-create-awareness-around-covid-19> [accessed 2020-10-03]
38. Survey Report: Impact of COVID-19 on SMEs. *Small and Medium Enterprises Development Authority*. 2020 Apr. URL: [https://smeda.org/phocadownload/Research\\_Publications/SMEDA%20Survey%20Report%20-%20COVID-19%20Impact%20on%20SMEs%20reduce.pdf](https://smeda.org/phocadownload/Research_Publications/SMEDA%20Survey%20Report%20-%20COVID-19%20Impact%20on%20SMEs%20reduce.pdf) [accessed 2021-05-04]
39. Ehsaas Cash programme helped country respond to crisis successfully: Sania Nishtar. *The Nation*. 2020 Oct 09. URL: <https://nation.com.pk/09-Oct-2020/ehsaas-cash-programme-helped-country-respond-to-crisis-successfully-sania-nishtar> [accessed 2020-10-10]
40. PM Imran announces incentives for construction industry. *The Nation*. 2020 Apr 04. URL: <https://nation.com.pk/04-Apr-2020/pm-imran-announces-incentives-for-construction-industry> [accessed 2020-09-26]
41. Chaudhry A. Pakistan's guidelines on home isolation against WHO, Chinese recommendations. *Dawn*. 2020 Apr 10. URL: <https://www.dawn.com/news/1547879> [accessed 2020-09-25]
42. International Association of Science Parks and Areas of Innovation. URL: <https://www.iasp.ws/covid19/nrtc-ventilators> [accessed 2020-09-25]

43. PM inaugurates NRTC production facility: PMO. The Nation. 2020 Jul 06. URL: <https://nation.com.pk/06-Jul-2020/pm-inaugurates-nrtc-production-facility-pmo> [accessed 2020-09-24]
44. Pakistan Cases Details. Government of Pakistan. URL: <https://covid.gov.pk/stats/pakistan> [accessed 2020-10-01]
45. HDF distributes ration among 350 families in rural parts of the district – Daily Parliament Times. Human Development Foundation Pakistan. 2020 May 22. URL: <https://hdfpk.com/category/covid-19/> [accessed 2020-10-02]
46. Al-Khidmat Foundation plays leading role in fight against Covid-19. The News. URL: <https://www.thenews.com.pk/print/688169-al-khidmat-foundation-plays-leading-role-in-fight-against-covid-19> [accessed 2020-10-03]
47. Riaz R. Pakistani charity arranges free plasma for COVID-19 patients. Arab News. 2020 Jun 11. URL: <https://www.arabnews.pk/node/1688336/pakistan> [accessed 2020-10-02]
48. Tag: Corona Recovered Warriors - Pakistanis Turn To 'Corona Warriors' Facebook Group For Plasma Donations. When Where How. 2020 Jun 30. URL: <https://whenwherehow.pk/tag/corona-recovered-warriors/> [accessed 2020-10-01]
49. Ahmed A. These 'Corona Warriors' Are Countering Plasma Black Market by Connecting People with Volunteer Donors. ProPakistani. URL: <https://propakistani.pk/2020/07/07/these-corona-warriors-are-countering-plasma-black-market-by-connecting-people-with-volunteer-donors/> [accessed 2020-09-27]
50. Jamal S. Covid-19: Pakistani doctors get approval for plasma therapy clinical trial. Gulf News. 2020 Apr 15. URL: <https://gulfnews.com/world/asia/pakistan/covid-19-pakistani-doctors-get-approval-for-plasma-therapy-clinical-trial-1.70988056> [accessed 2020-10-02]
51. Latif A. Pakistan: COVID-19 patient recovers with plasma therapy. Anadolu Agency. 2020 May 09. URL: <https://www.aa.com.tr/en/asia-pacific/pakistan-covid-19-patient-recovers-with-plasma-therapy/1835196> [accessed 2020-09-30]
52. Ebrahim ZT. In the fight against Covid-19, these bright, young Pakistanis are coming together and improvising. Prism. 2020 Apr 07. URL: <https://www.dawn.com/news/1543349> [accessed 2020-09-29]
53. COVID-19: students assist with response. The Aga Khan University. 2020 Mar 20. URL: [https://www.aku.edu/news/Pages/News\\_Details.aspx?nid=NEWS-002113](https://www.aku.edu/news/Pages/News_Details.aspx?nid=NEWS-002113) [accessed 2020-10-01]
54. First Response Initiative of Pakistan. URL: <https://www.frip.org.pk/> [accessed 2020-09-28]
55. Ahmad Z. Pakistani volunteers 3D-print ventilators, join war against COVID-19. The Express Tribune. 2020 Mar 23. URL: <https://tribune.com.pk/story/2181993/pakistani-volunteers-3d-print-ventilators-join-war-covid-19> [accessed 2020-09-25]
56. Sandhu R. Pakistan may mass produce ventilators through 3D printing. News Lens Pakistan. 2020 Mar 23. URL: <https://www.newslens.pk/pakistan-may-mass-produce-ventilators-3d-printing/> [accessed 2020-10-03]
57. Ejaz R. Salman Khan suggests Kwick Doctor for better and affordable health care. Disrupt Magazine. URL: <https://disruptmag.pk/salman-khan-suggests-kwick-doctor-for-better-and-affordable-health-care/> [accessed 2020-09-25]
58. Wang P, Nair MS, Liu L, Iketani S, Luo Y, Guo Y, et al. Increased Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7 to Antibody Neutralization. bioRxiv. Preprint posted online January 26, 2021 [FREE Full text] [doi: [10.1101/2021.01.25.428137](https://doi.org/10.1101/2021.01.25.428137)] [Medline: [33532778](https://pubmed.ncbi.nlm.nih.gov/33532778/)]

## Abbreviations

**PPE:** personal protective equipment  
**SOP:** standard operating procedure  
**WHO:** World Health Organization

*Edited by DR Saadeh; submitted 05.03.21; peer-reviewed by M Faheem; comments to author 19.03.21; revised version received 08.04.21; accepted 09.04.21; published 19.05.21.*

### *Please cite as:*

Akhtar H, Afridi M, Akhtar S, Ahmad H, Ali S, Khalid S, Awan SM, Jahangiri S, Khader YS  
Pakistan's Response to COVID-19: Overcoming National and International Hypes to Fight the Pandemic  
JMIR Public Health Surveill 2021;7(5):e28517  
URL: <https://publichealth.jmir.org/2021/5/e28517>  
doi: [10.2196/28517](https://doi.org/10.2196/28517)  
PMID: [33877048](https://pubmed.ncbi.nlm.nih.gov/33877048/)

©Hashaam Akhtar, Maham Afridi, Samar Akhtar, Hamaad Ahmad, Sabahat Ali, Sundas Khalid, Sajid Mahmood Awan, Shahzaib Jahangiri, Yousef Saleh Khader. Originally published in JMIR Public Health and Surveillance (<https://publichealth.jmir.org>), 19.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic

information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# Impact of the Protracted War in Yemen on the Acute Flaccid Paralysis Surveillance System: Retrospective Descriptive Analysis

Riham Al-Dubaiee<sup>1</sup>, MSc; Mutaher AL Qassimi<sup>1</sup>, MD; Ahmed Al-Dar<sup>1</sup>, BSc; Abdulwahed Al Serouri<sup>1</sup>, PhD; Yousef Khader<sup>2</sup>, SCD

<sup>1</sup>Ministry of Public Health and Population, Sana'a, Yemen

<sup>2</sup>Jordan University of Science & Technology, Amman, Jordan

**Corresponding Author:**

Riham Al-Dubaiee, MSc

Ministry of Public Health and Population

Al-Hasaba, Mazda street

Sana'a

Yemen

Phone: 967 776417333

Email: [rihamm10@yahoo.com](mailto:rihamm10@yahoo.com)

## Abstract

**Background:** Highly sensitive acute flaccid paralysis (AFP) surveillance, which includes immediate case investigation and specimen collection, is critical for achieving global polio eradication. In Yemen, the Acute Flaccid Paralysis Surveillance System (AFPSS) was launched in 1998 to achieve the polio eradication target. Although Yemen was certified as a polio-free country in 2009, the protracted war since 2015 has placed the country at risk for polio reemergence.

**Objective:** The objectives of this analysis were to evaluate the performance of the Yemen AFPSS at both the national and governorate levels, and to assess the impact of the ongoing war on the performance.

**Methods:** Retrospective descriptive analysis was performed on Yemen secondary AFP surveillance data for the years 2014 (before the war) and 2015-2017 (during the war). Data comprising all children <15 years old reported as having AFP were included in the analysis. AFP surveillance performance was evaluated using World Health Organization-specified AFP surveillance indicators.

**Results:** At the national level, all indicators were met before and after the war except for "lab results received within  $\leq 28$  days," which was unmet since the war erupted. Furthermore, the indicator "stool specimens arriving at a central level within  $\leq 3$  days" was unmet after the war but only in 2017. At the governorate level, although the indicators "adequacy" and "stool specimens arriving at the laboratory in good condition" were met before the war in all governorates, the former indicator was unmet in 9 (41%) governorates since the war erupted and the latter indicator was also unmet in 9 governorates (41%) but only in 2017.

**Conclusions:** The findings show that some AFP surveillance indicators were negatively impacted by eruption of the war in Yemen due to closure of the Sana'a capital airport and postponement of sample shipment to the reference laboratory, which remained under long-term poor storage conditions. To ensure rapid detection of polio cases, improving specimen collection, storage, and transportation, together with proper and timely shipment of specimens to the reference laboratory should be considered.

(*JMIR Public Health Surveill* 2021;7(5):e27638) doi:[10.2196/27638](https://doi.org/10.2196/27638)

**KEYWORDS**

acute flaccid paralysis; surveillance indicators; war; Yemen

## Introduction

**Background**

Poliomyelitis is a highly infectious viral disease that affects children below the age of 15 years, and is transmitted from person to person via the feco-oral route [1]. Poliomyelitis is an

enteroviral disease that has an incubation period of 9-12 days, and presents as muscle weakness, headache, neck stiffness, fever, nausea, vomiting, and mostly flaccid paralysis [2].

The World Health Assembly adopted a resolution calling for the global eradication of poliomyelitis in 1988. In addition to routine polio immunization included in the Expanded Program of Immunization, two major activities were planned: mass polio

vaccination campaigns and surveillance of all cases of acute flaccid paralysis (AFP) [1]. Despite great achievement of polio eradication, transmission has never been stopped in two countries in the eastern Mediterranean region: Pakistan and Afghanistan [3].

In Yemen, AFP surveillance was launched in 1998 to achieve the polio eradication target, and there were no reported cases up to 2004. However, in 2005, 479 cases were reported; therefore, 10 immunization campaigns were launched to halt the outbreak. The last polio case was reported in February 2006, and Yemen was certified as a polio-free country in 2009. Yemen has also experienced three different outbreaks of circulating vaccine-derived polio viruses with 9 cases in April 2011, 4 cases in 2012, 1 case in 2016, and, most recently, one case reported in September 2020 [4-6]. Although the country is currently free of poliovirus, it is considered one of the high-risk countries for reemergence of the virus due to the current war situation.

### The Yemen Acute Flaccid Paralysis Surveillance System

The Yemen Acute Flaccid Paralysis Surveillance System (AFPSS) was launched in 1998 with strong support from the World Health Organization (WHO) to help in the early detection of any AFP case and to ensure immediate notification. The AFP surveillance data are regularly shared with the WHO country and regional offices, and with the Global Polio Eradication Initiative. As Yemen does not have a national polio laboratory, Kenya Medical Research Institute in Nairobi has served as a reference laboratory for Yemen since 2015. The AFP surveillance indicators were adapted from WHO certification standards [7].

Nationally, the AFPSS consists of a national AFP coordinator and four assistants. At the level of governorates, there are 35 coordinators and their assistants. In all districts, there are approximately 333 coordinators and 1980 officers in health facilities.

The purposes of the system include early detection of any AFP case and investigating it, evaluation of the polio eradication program performance, and certifying and confirming that Yemen is still free of poliovirus.

Since 2015, the war has affected the performance of the health system in Yemen, with nearly half of all health facilities suffering damage or unable to function because of severe

shortages of staff and equipment. Consequently, an estimated 56% of the population does not have regular access to basic health care [8].

### Aim

The objectives of this analysis were to evaluate the performance of the Yemen AFPSS at both the national and governorate levels, and to assess the impact of the ongoing Yemeni war on the performance.

### Methods

A retrospective descriptive analysis was performed on secondary AFP surveillance data for Yemen for the years 2014 (before the war) and 2015-2017 (during the war). The data included all children <15 years old who were reported in the AFPSS as an AFP case. AFP surveillance performance was evaluated using the following WHO-specified AFP surveillance indicators [7]: (1) nonpolio AFP rate in children  $\leq 15$  years of age (target:  $\geq 2/100,000$ ) annually and investigation within less than 48 hours of the report (target:  $\geq 80\%$ ); (2) two stool specimens collected at least 24 hours apart and within 14 days of paralysis onset (target:  $\geq 80\%$ ), reflecting the adequacy rate; (3) stool specimens arriving at the central level within  $\leq 3$  days (target:  $\geq 80\%$ ); (4) stool specimens arriving at the laboratory in "good condition" (target:  $\geq 80\%$ ); (5) notification within  $\leq 7$  days of paralysis onset (target:  $\geq 80\%$ ); (6) nonpolio enterovirus isolation rate (target:  $\geq 10\%$ ) to reflect the lab's performance level and virus detection sensitivity; and (7) lab results received within  $\leq 28$  days (target:  $\geq 80\%$ ).

The study was performed from October to January 2019, including data from 2014 to 2017. The data were entered and analyzed in Microsoft Excel.

### Results

#### AFP Surveillance Performance Indicators at the National Level

Table 1 shows the AFP surveillance performance indicators at the national level for 2014-2017. All indicators met the targets in 2014 before the war. After the war erupted, all indicators were met in 2015 and 2016 except for the "lab results received within  $\leq 28$  days." Furthermore, in 2017, the indicators "lab results received within  $\leq 28$  days" and "stool specimens arriving at the central level within  $\leq 3$  days" were not met.



**Table 1.** Acute flaccid paralysis (AFP) surveillance performance indicators at the national level, 2014-2017.

Indicator	Target	Reported value			
		2014	2015	2016	2017
Nonpolio AFP rate in children $\leq 15$ years old	$\geq 2/100,000$	4.6	4.2	5.2	5.2
Investigation within $\leq 48$ hours of the report	$\geq 80\%$	98%	99%	100%	100%
Two stool specimens collected at least 24 hours apart within 14 days of paralysis (adequacy)	$\geq 80\%$	95%	91%	91%	82%
Stool specimens arriving at a central level within $\leq 3$ days	$\geq 80\%$	88%	85%	83%	78% <sup>a</sup>
Stool specimens arriving at the reference laboratory in good condition	$\geq 80\%$	99%	99%	99%	81%
Notification within $\leq 7$ days of paralysis onset	$\geq 80\%$	86%	85%	85%	87%
Nonpolio enterovirus isolation rate	$\geq 10\%$	18%	19%	22%	15%
Lab results received within $\leq 28$ days	$\geq 80\%$	83%	48% <sup>a</sup>	24% <sup>a</sup>	33% <sup>a</sup>

<sup>a</sup>Did not meet target.

### AFP Surveillance Performance Indicators at the Governorate Level

The targets for the two indicators “nonpolio AFP rate in children  $\leq 15$  years” and “investigation within  $\leq 48$  hours of the report” were met in all governorates in all years both before and after the war. Although the adequacy indicator “two stool specimens collected at least 24 hours apart within 14 days of paralysis” met the target in all governorates in 2014 (before the war), the target was not met in two governorates in 2015 (Abyan and AlDhale’e) and 2016 (AlDhale’e and Socotra), and in seven governorates (AlBayda, AlJawf, Amran, Ibb, Raymah, Sana’a city, and Socotra) in 2017.

The target for the indicator “stool specimens arriving at the central level within  $\leq 3$  days” was not met in 5 governorates in 2014, 7 governorates in 2015, 11 governorates in 2016, and 14 governorates in 2017. The indicator “stool specimens arriving at the reference laboratory in good condition” met the target in all governorates in all years except for 2017, in which 9 governorates (AlBayda, AlJawf, Almahra, Amran, Dhamar, Lahj, Raymah, Sana’a city, and Taizz) did not meet the target for this indicator.

A total of 5 governorates in 2014 (AlHudaydah, Almahweet, Amran, Hajjah, and Sa’ada) and 2015 (Abyan, AlHudaydah, AlJawf, Hajjah, and Sa’ada), 6 governorates (Almahweet, Amran, Ibb, Sa’ada, Socotra, and Taizz) in 2016, and 7 governorates (AlBayda, AlHudaydah, AlJawf, Amran, Hajjah, Sa’ada, and Socotra) in 2017 did not meet the target of the indicator “notification within  $\leq 7$  days of paralysis onset.” The targets for the indicator “nonpolio enterovirus isolation rate” had not been met in 3 governorates (Abyan, Shabwah, and Taizz) in 2014, in 4 governorates (Aden, AlHudaydah, Almahra, and Sa’ada) in 2015, 5 governorates (Abyan, Almahra, Almahweet, Hadramaut Sayoun, and Shabwah) in 2016, and 4 governorates (AlBayda, Sa’ada, Sana’a city, and Socotra) in 2017. The target for the indicator “lab results received within  $\leq 28$  days” did not meet the target in 7 governorates only in 2014 (before the war) and in all governorates in all years after the war.

## Discussion

### Principal Findings

Evaluation of a surveillance system is important to examine the operation of the system and to show how it adheres to implementation protocols. Thus, the current AFPSS evaluation will help to identify whether the system met its target indicators properly.

This evaluation showed that at the national level, all indicators were met before the war erupted in 2014; however, the indicator “lab results received within  $\leq 28$  days” was not met through 2015-2017 after the war. This is because of closure of the main national airport in Sana’a in 2015, which remains closed to date [9]. Therefore, sending the samples to the reference laboratory in Kenya was not possible and the lab results were not received in a timely manner.

The indicator “stool specimens arriving at the central level within  $\leq 3$  days” was not met at the national level during 2017, which was most likely due to the lack of funding available for transporting specimens from the governorates to the national level, as well as the disruption and danger of some roads [8]. A similar result was reported from Iraq after the war erupted [10]. At the governorates level, we found that the number of governorates that did not meet this target increased as the war continued, which is attributed to the same reasons mentioned above.

The target for the indicator “nonpolio AFP rate in children  $\leq 15$  years old” was met at the national level and for all governorates in all years, and even exceeded the WHO-established minimum nonpolio AFP rate. Thus, the sensitivity of AFP surveillance has been good before and after the war. A similar finding was reported from Nigeria, the eastern Mediterranean region, and other WHO regions [10-13]. The lack of an effect of war on this indicator has been found for other countries in conflict, such as Iraq [10]. Similarly, the indicator “investigation within 48 hours of report of cases” met the target at the national level and in all governorates in all years, and was not affected by war in this study, in line with findings from other countries in conflict, such as Iraq [10].

The adequacy indicator also met the target in all years at the national level before and after the war erupted. The target of this indicator was met in similar evaluations in other countries, including Iraq and Nigeria [10-12]. This reflects a better awareness by patients' families and medical caregivers regarding the importance of early AFP case detection. Although this indicator was met at all governorates before the war, it was not met in some governorates after eruption of the war, which may be due to a discontinuation of training. Lack of training was also found to be the reason for not meeting the adequacy target in other countries such as Zimbabwe [14].

The indicator "stool specimen arriving at the reference laboratory in good condition" met the target at the national level in all years. This indicator also met the target in all governorates and all years of evaluation except for 2017. This was most likely due to suspension of the shipment of specimens to the reference laboratory for 3 months that were left under a poor storage condition in 2017. Furthermore, the indicator "notification within 7 days of paralysis onset" was met at the national level in all years. However, the target was not met in some governorates because of poor knowledge about the timeliness of notification and the lack of training at this time.

Although the indicator "nonpolio enterovirus isolation rate" met the target at the national level in all years, it was not met in some governorates before as well as after eruption of the war. This may reflect the poor collection and transport of specimens due to reduced training as well as accessibility and transport problems.

### Conclusions

The findings of this study showed that some AFP indicators were negatively impacted by eruption of the war in Yemen due to closure of the Sana'a capital airport and postponement of specimen shipment to the reference laboratory, leaving specimens in a poor storage condition. Therefore, proper and timely shipment of specimens to the reference laboratory in Kenya as well as ensuring receiving the lab results within 28 days is strongly recommended. It is also important to ensure the availability of funds for the transport of specimens from governorates to the national level, and to continuously train health workers on the proper collection and transport of specimens to ensure achievement of AFP indicators.

### Acknowledgments

The authors would like to acknowledge the support of the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET) and the Global Health Development| Eastern Mediterranean Public Health Network (GHD|EMPHNET).

### Conflicts of Interest

None declared.

### References

1. Rey M, Girard MP. The global eradication of poliomyelitis: progress and problems. *Comp Immunol Microbiol Infect Dis* 2008 Mar;31(2-3):317-325. [doi: [10.1016/j.cimid.2007.07.013](https://doi.org/10.1016/j.cimid.2007.07.013)] [Medline: [17923156](https://pubmed.ncbi.nlm.nih.gov/17923156/)]
2. Centers for Disease Control and Prevention. In: Hamborsky J, Kroger A, Wolfe C, editors. *Epidemiology and prevention of vaccine-preventable diseases* 13th edition. Washington, DC: Public Health Foundation; 2015.
3. Endemic countries. Polio global eradication initiative. URL: <https://polioeradication.org/where-we-work/polio-endemic-countries/> [accessed 2021-03-14]
4. World HO. Global Health Observatory visualizations. World Health Organization. URL: <https://apps.who.int/gho/data/view.wrapper> [accessed 2021-03-14]
5. Centers for Disease Control and Prevention. Update on vaccine-derived polioviruses--worldwide, April 2011-June 2012. *MMWR Morb Mortal Wkly Rep* 2012 Sep 21;61:741-746 [FREE Full text] [Medline: [22992572](https://pubmed.ncbi.nlm.nih.gov/22992572/)]
6. UNICEF, World Health Organization. EMR-MENA. URL: <https://www.unicef.org/mena/media/10071/file/EMR-MENA%20c> [accessed 2021-03-14]
7. WHO-recommended surveillance standard of poliomyelitis. World Health Organization. URL: [https://www.who.int/immunization/monitoring\\_surveillance/burden/vpd/surveillance\\_type/active/poliomyelitis\\_standards/en/](https://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/poliomyelitis_standards/en/) [accessed 2021-03-14]
8. Kozicharow A. WiRED Notes Humanitarian Crisis in Yemen Is Global Calamity. WiRED International. URL: [http://wiredinternational.org/wired\\_archive/Humanitarian\\_Crisis\\_in\\_Yemen\\_Is\\_Global\\_Calamity.html](http://wiredinternational.org/wired_archive/Humanitarian_Crisis_in_Yemen_Is_Global_Calamity.html) [accessed 2021-03-14]
9. Airport closure amounts to death sentence for thousands of sick Yemenis. Norwegian Refugee Council. URL: <https://www.nrc.no/news/2019/august2/airport-closure-amounts-to-death-sentence-for-thousands-of-sick-yemenis/> [accessed 2021-03-14]
10. Jasem JA, Marof K, Nawar A, Khalaf Y, Al-Hamdani F, Ali S, et al. An epidemiological analysis of acute flaccid paralysis and its surveillance system in Iraq, 1997-2011. *BMC Infect Dis* 2014 Aug 20;14(1):448 [FREE Full text] [doi: [10.1186/1471-2334-14-448](https://doi.org/10.1186/1471-2334-14-448)] [Medline: [25141887](https://pubmed.ncbi.nlm.nih.gov/25141887/)]
11. Almoayed KA, Bin Break A, Al-Qassimi M, Assabri A, Khader Y. The acute flaccid paralysis (AFP) surveillance system in Yemen, 2010-2015: descriptive study based on secondary data analysis. *JMIR Public Health Surveill* 2019 Dec 06;5(4):e14413 [FREE Full text] [doi: [10.2196/14413](https://doi.org/10.2196/14413)] [Medline: [31808749](https://pubmed.ncbi.nlm.nih.gov/31808749/)]

12. Bassey BE, Rui VG, Gasasira AN, Pascal M, Weldegbriel G, Mulum TJ, et al. Characteristics of acute flaccid paralysis reported by the surveillance system and verified by WHO Officer in Akwa Ibom State-Nigeria, 2006-2012. *Health* 2014;06(19):2602-2610. [doi: [10.4236/health.2014.619299](https://doi.org/10.4236/health.2014.619299)]
13. Centers for Disease Control and Prevention (CDC). Evaluating surveillance indicators supporting the Global Polio Eradication Initiative, 2011-2012. *MMWR Morb Mortal Wkly Rep* 2013 Apr 12;62(14):270-274 [FREE Full text] [Medline: [23575241](https://pubmed.ncbi.nlm.nih.gov/23575241/)]
14. Bangure D, Chirundu D, Nondo H, Tshimanga M, Gombe N, Takundwa L. Evaluation of Acute Flaccid Paralysis Surveillance System in Sanyati District, Zimbabwe, 2013. *Int J Epidem Infect* 2014;2(2):36. [doi: [10.12966/ije.05.04.2014](https://doi.org/10.12966/ije.05.04.2014)]

## Abbreviations

**AFP:** acute flaccid paralysis

**AFPSS:** Acute Flaccid Paralysis Surveillance System

**WHO:** World Health Organization

*Edited by M Algunaïd, T Sanchez; submitted 01.02.21; peer-reviewed by F Lami, K Almoayed, K Al-Jamrah; comments to author 01.03.21; revised version received 15.03.21; accepted 21.03.21; published 19.05.21.*

*Please cite as:*

*Al-Dubaiee R, AL Qassimi M, Al-Dar A, Al Serouri A, Khader Y*

*Impact of the Protracted War in Yemen on the Acute Flaccid Paralysis Surveillance System: Retrospective Descriptive Analysis*

*JMIR Public Health Surveill* 2021;7(5):e27638

URL: <https://publichealth.jmir.org/2021/5/e27638>

doi: [10.2196/27638](https://doi.org/10.2196/27638)

PMID: [34009132](https://pubmed.ncbi.nlm.nih.gov/34009132/)

©Riham Al-Dubaiee, Mutaher AL Qassimi, Ahmed Al-Dar, Abdulwahed Al Serouri, Yousef Khader. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 19.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Notes from the Field

# Notes From the Field: The Combined Effects of Tocilizumab and Remdesivir in a Patient With Severe COVID-19 and Cytokine Release Syndrome

Sabahat Ali<sup>1</sup>, MBBS, FCPS; Sundas Khalid<sup>2</sup>, MPhil; Maham Afridi<sup>3</sup>, MPhil; Samar Akhtar<sup>4</sup>, PhD; Yousef S Khader<sup>5</sup>, SCD; Hashaam Akhtar<sup>4</sup>, MPhil, PhD

<sup>1</sup>Department Of Gynecology And Obstetrics, Pakistan Air Force Hospital, Islamabad, Pakistan

<sup>2</sup>School of Chemical and Materials Engineering, National University of Science and Technology, Islamabad, Pakistan

<sup>3</sup>Department of Biotechnology, Quaid-i-Azam University, Islamabad, Pakistan

<sup>4</sup>Yusra Institute of Pharmaceutical Sciences, Islamabad, Pakistan

<sup>5</sup>Department of Community Medicine, Public Health and Family Medicine, Faculty of Medicine, Jordan University of Science & Technology, Irbid, Jordan

**Corresponding Author:**

Hashaam Akhtar, MPhil, PhD

Yusra Institute of Pharmaceutical Sciences

Zaraj Housing Society

Main GT Road

Islamabad, 44000

Pakistan

Phone: 92 3215272489

Email: [hashaamakhtar@gmail.com](mailto:hashaamakhtar@gmail.com)

## Abstract

SARS-CoV-2 is known to cause severe bilateral pneumonia and acute respiratory distress syndrome or COVID-19 in patients, which can be debilitating and even fatal. With no drugs or vaccines available yet, a wide range of treatment regimens used are being repurposed. The need of the hour is to analyze various currently available regimens and devise a treatment plan that is most effective for COVID-19. Here we describe the case of a 68-year-old man with hypertension and diabetes, exhibiting symptoms of cough and shortness of breath, who presented at the emergency department of our hospital. Chest computed tomography revealed bilateral ground glass opacities that were indicative of COVID-19, and a computed tomography score of 24 was indicative of severe pulmonary pneumonia. He tested positive for COVID-19. His treatment regimen included the use of convalescent plasma, oxygen therapy, steroids, high-dose antibiotics, broad-spectrum antiviral remdesivir, and anti-interleukin-6 monoclonal antibody (Tocilizumab) at various stages of the disease. Oxygen supplementation was required at the time of admission. The patient initially developed a cytokine release storm, and oxygen supplementation was initiated to manage his condition. Supportive care and multiple treatment regimens were used to successfully recover the patient's health. With a rapid increase in number of confirmed cases worldwide, COVID-19 has become a major challenge to our health care system. With no available vaccines currently, the establishment of a combination of therapeutic drugs that effectively reduce disease progression is of utmost importance.

(*JMIR Public Health Surveill* 2021;7(5):e27609) doi:[10.2196/27609](https://doi.org/10.2196/27609)

**KEYWORDS**

COVID-19; remdesivir; treatment; tocilizumab

## Introduction

COVID-19 is a severe acute respiratory infection that has spread worldwide since the first confirmed case in Wuhan (Hubei Province, China) on December 31, 2019 [1,2]. It has since affected 235 countries, areas, or territories, with 76,900,875

confirmed cases, including 1,696,401 deaths as of December 20, 2020 [3]. The causative infectious agent for COVID-19 is a novel encapsulated, positive sense RNA virus that belongs to family Coronaviridae, and has been named SARS-CoV-2 [4]. The gold standard for COVID-19 diagnosis is a positive finding on an RT-PCR test, which confirms the presence of viral nucleic acid in blood or respiratory swab samples of a patient. Initial

diagnosis of COVID-19 is based on (1) the patient's history, which may indicate possible contact with a patient with confirmed COVID-19; (2) clinical symptoms, which range from mild or moderate (cough, fever, tiredness, or shortness of breath) to severe (pulmonary pneumonia, acute respiratory distress syndrome [ARDS]); and (3) radiological findings consistent with COVID-19 [5,6]. The first 2 cases of COVID-19 in Pakistan were reported on February 26, 2020, with 457,288 confirmed cases and 9330 deaths as on December 20, 2020 [7].

Currently available treatment alternatives for hospitalized patients with COVID-19 with severe or critical disease presentation are limited to drugs that aid in the resolution of symptoms and provide supportive care. These include the use of convalescent plasma, oxygen therapy, steroids, and broad-spectrum, high-dose antivirals and antibiotics [8]. Here we report the case of an elderly male who presented with cough, shortness of breath, and severe pulmonary pneumonia at our hospital during the early months of the pandemic. The patient was admitted after an initial examination and later tested positive for COVID-19. The patient was treated with convalescent plasma, dexamethasone, high-dose antibiotics, broad-spectrum antiviral remdesivir, and anti-interleukin (IL)-6 monoclonal antibody Tocilizumab in addition to a number of other drugs. The patient's condition initially worsened after admission, from requiring a low flow of oxygen to developing ARDS, and required mechanical ventilation; thereafter, his condition improved, and he made full recovery and was discharged after 14 days. This case study is aimed to analyze the role of a combination of different drugs on the progression of COVID-19 in our patient and to highlight its life-saving potential.

## Case Presentation

On the evening of June 10, 2020, a 68-year-old Pakistani male physician with a history of hypertension and diabetes mellitus presented with fever, cough, and shortness of breath. Difficulty in breathing had started 3 days prior to reporting to the emergency department of our hospital and seemed to worsen with time. His vital parameters at the time of presentation included a temperature of 98.6°F, pulse rate of 85 beats per minute, blood pressure of 110/70 mmHg, and oxygen saturation (SpO<sub>2</sub>) of 87% in ambient air. After the initial physical examination, the on-duty physician admitted the patient to the intensive care unit for the management of possible pulmonary pneumonia and suspected COVID-19, an RT-PCR test, and chest computed tomography (CT). Chest CT revealed bilateral multifocal patchy and confluent areas of ground glass opacity (GGO) in the lungs. Associated interlobular septal thickening with an erratic paving appearance, subpleural fibrosis, and prominent lower lobe bronchi were also noted bilaterally, with more marked effects on the right side. The CT severity score was 24, which was indicative of severe disease. On admission to the intensive care unit (day 1), the patient was initially administered a one-time intravenous dose each of convalescent plasma (450 mL) and paracetamol (1 g) and administered supplemental oxygen through a non-rebreathable mask at 4 L O<sub>2</sub>/min to maintain an SpO<sub>2</sub> of >90%. He was also started on a regimen of intravenous methylprednisolone (60 mg, once

daily [OD]) and enoxaparin sodium (60 mg, OD). On Day 2, his laboratory findings indicated lymphopenia, neutrophilia, increased C reactive protein (CRP), and raised serum lactate dehydrogenase (LDH); hence, a 7-day course of two antibiotics, meropenem trihydrate (500 mg, thrice daily) and moxifloxacin (400 mg, OD), was also added to the regimen. On days 3 and 4, the patient's condition deteriorated considerably. He was semiconscious and developed ARDS. The flow velocity of oxygen had to be increased to 15 L O<sub>2</sub>/min, which was still insufficient to maintain an SpO<sub>2</sub> of 90%-91%. Serum ferritin levels of the patient increased, with a further increase in lymphopenia, CRP, and LDH, and as the patient developed signs of cytokine release syndrome (CRS), tocilizumab (80 mg) was administered intravenously with the dose repeated after 12 hours. On day 5, the patient was started on continuous positive airway pressure ventilation where an SpO<sub>2</sub> between 88%-92% was maintained, along with a 50% fraction of inspired oxygen (FiO<sub>2</sub>), positive end-expiratory pressure (PEEP) of 6 cmH<sub>2</sub>O, and pressure support ventilation (PSV) of 14 cmH<sub>2</sub>O. The patient was then maintained in a prone position for up to 12 hours to manage the respiratory distress. In addition to ventilator support, dexamethasone (8 mg, twice daily [BD]) was administered intravenously. On day 8, remdesivir (200 mg) was administered intravenously with a dose halved to 100 mg for the next 4 days. A one-time dose of 20% albumin infusion (50 mL) was also administered intravenously, and a regimen of intravenous linezolid (600 mg, BD) was added. On day 10, the patient's condition began to improve and an SpO<sub>2</sub> of 97% was achieved in the same ventilator setting. Serum ferritin, CRP, and LDH levels also reverted to baseline. On day 11, the patient displayed signs of recovery, having achieved an SpO<sub>2</sub> of 97%, FiO<sub>2</sub> reduced to 45%, PEEP of 6 cmH<sub>2</sub>O, and PSV of 14 cmH<sub>2</sub>O. On day 12, FiO<sub>2</sub> was further reduced to 40%, and the PEEP and PSV were 6 cmH<sub>2</sub>O and 14 cmH<sub>2</sub>O, respectively. The patient was advised to sit upright for 1 hour after regular intervals. Since the patient displayed signs of improvement, he was gradually weaned off the ventilator and instead provided an oxygen mask, which helped maintain an SpO<sub>2</sub> of 94%-96% at 2 L O<sub>2</sub>/min. On day 13, patient was prescribed oral doses of dexamethasone (5 mg, OD), moxifloxacin (400 mg, OD), and linezolid (600 mg, BD) for a 3-day course. Furthermore, a reduced intravenous dose of enoxaparin sodium (40 mg, OD) for the next 7 days was advised. The RT-PCR test for COVID-19 was repeated, which yielded a negative result, and the patient was discharged on day 14 of admission (June 24, 2020).

## Discussion

### Principal Findings

This case study summarizes the clinical characteristics upon presentation, diagnosis, and treatments administered to a 68-year-old male physician with diabetes and hypertension who presented with fever, cough, and shortness of breath at our hospital. Considering his age, history (potential exposure at his work place and the presence of underlying comorbidities including hypertension and diabetes), symptoms (fever, cough,

and shortness of breath), low SpO<sub>2</sub> (of 87%), and chest CT findings (CT severity score of 24), our patient was suspected with COVID-19 and was at the risk of developing severe disease. A positive RT-PCR finding for COVID-19 and later stages of disease progression during the course of his hospitalization confirmed this notion; however, timely recognition of risks and the provision of immediate, effective treatment most likely ensured his recovery and survival.

In a study describing the clinical characteristics, treatments, and outcomes of 138 confirmed COVID-19 cases, Wang et al [9] reported fever (98.6%), dry cough (59.4%), and dyspnea (31.2%) as the most common symptoms associated with COVID-19. Moreover, all their patients presented bilateral GGOs on chest CT. In another study, Zhu et al [10] analyzed the chest CT scans of 72 patients with COVID-19, who were divided into two age groups: ≤60 years (n=44) and >60 years (n=32). They reported GGOs in the peripheral areas accompanied by interlobular septal thickening, subpleural line, and pleural thickening. More extensive involvement of the lobes and subpleural line and pleural thickening in the patients older than 60 years was also observed. In another study involving 51 patients with COVID-19, Li and Xia [11] evaluated whether chest CT was a reliable tool for rapid diagnosis and management of patients with COVID-19. They concluded that chest CT had a low misdiagnosis rate for COVID-19, and common features characteristic of COVID-19 include the presence of GGOs and consolidation with or without vascular enlargement, interlobular septum thickening, and air bronchogram. Furthermore, older patients showed a greater degree of lung involvement than younger patients. The chest CT findings of our patient also indicated the presence of severe bilateral pneumonia, a high CT score 24, and characteristic imaging features reportedly consistent with COVID-19 (GGO, interlobular septal thickening, and subpleural fibrosis). In addition to presenting signs and symptoms characteristic to COVID-19, where shortness of breath is indicative of severe disease, several epidemiological studies have reported that old age, male gender, and the presence of underlying comorbidities including diabetes, hypertension, cardiovascular disease, and renal and liver diseases are risk factors for severe COVID-19 [12,13]. Our patient also had some of these risk factors (old age, hypertension, and diabetes), which indicated the possibility of progression to severe COVID-19.

As many of the factors were not indicative of a possibly favorable outcome, the patient was administered a number of therapeutic interventions including convalescent plasma, anticoagulants, antibiotics, corticosteroids, immunomodulatory drugs, and antivirals during the course of hospitalization.

Based on the hospital protocol at the time, one of the first interventions our patient received was intravenous convalescent plasma therapy (CPT). CPT is being used in different countries to provide passive immunization against SARS-CoV-2. It has been hypothesized that if CPT is administered in early stages of COVID-19, it reduces the overall viral load, improves disease prognosis, and increases the chances of survival among patients with COVID-19 [14]. In a retrospective study [15], the clinical outcomes of 37 critical patients with COVID-19 who received CPT were compared with controls who were simultaneously

hospitalized but did not receive CPT. Patients who received CPT displayed greater improvement in SpO<sub>2</sub> and had a better survival rate.

The pathogenesis of SARS-CoV-2 and its effect on host physiology is currently under intense investigation. In cases of severe COVID-19, the progression of viral infection manifests in the form of a massive inflammatory response termed as the cytokine storm or CRS, which initially affects the lungs, causing oxygen insufficiency and leading to ARDS, but can also spread to other organs such as the heart, kidneys, and liver, leading to multiple organ failure and eventually death [16,17].

The hallmarks of CRS include high serum levels of proinflammatory cytokines and chemokines, especially the IL-1 family and IL-6, which initiate the inflammatory cascade resulting in lung inflammation, fever, and fibrosis. These changes can be monitored through laboratory parameters including the lymphocyte count, which typically decreases (ie, lymphocytopenia), and an increase in serum levels of CRP, LDH, and ferritin [18]. The presence of these circulating biomarkers is considered predictive of the severity of COVID-19 and adverse outcomes such as death among patients with COVID-19 [19]. Hence, targeting them in order to reduce the overall inflammatory cascade (ie, the CRS) is the first logical step to control disease progression [16,20].

Use of glucocorticoid therapy for the management of CRS [21] has been explored and is associated with a reduction in respiratory inflammation and improvement in lung function, often eliminating the need for invasive ventilation in cases of severe or critical COVID-19. In a study by Liu et al [22], administration of a pulse dose of methylprednisolone to 101 patients with COVID-19 resulted in improved lung function among 15 patients who were critically affected, with only 1 patient requiring mechanical ventilation. In an open-label, controlled clinical trial [23] of 2014 patients with COVID-19 who received dexamethasone and 4321 patients who received usual care, the mortality rate was markedly reduced among patients who received dexamethasone. Moreover, among patients who received dexamethasone, mortality rates in patients who required invasive and noninvasive mechanical ventilation were significantly reduced, whereas no effect was observed among patients who received no respiratory support.

In our case, the initial use of CPT and methylprednisolone was unable to curtail the cytokine storm and effectively prevent the onset of ARDS. Consequently, the patient's condition deteriorated rapidly to the point where he was started on continuous positive airway pressure on day 5. The patient was then administered a regimen of combination therapy with 2 daily doses of dexamethasone and tocilizumab every 12 hours. Tocilizumab is an anti-IL-6 antibody preparation, which has been shown to be highly effective in improving disease severity by neutralizing IL-6, which plays a major role in inflammatory cascades and results in ARDS [24]. In a retrospective assessment of 21 critical patients with COVID-19, Xu et al [25] observed a resolution of lymphopenia in 85% of patients and a reduction in CRP levels in 84.25% of patients within 5 days of tocilizumab administration. Similarly, Guaraldi et al [26] reported that administration of tocilizumab was positively correlated with

recovery and reduced the requirement of invasive mechanical ventilation at later stages.

In addition to the aforementioned immunomodulatory therapies, our patient received remdesivir on day 8. Remdesivir is a broad-spectrum antiviral agent that has previously been investigated for its inhibitory effect on viral replication in the Ebola virus, severe acute respiratory syndrome coronavirus, and Middle East respiratory syndrome coronavirus. The double-blind, randomized, placebo-controlled trial by Beigel et al [27] concluded that 541 (of a total 1062) patients who received remdesivir had a shorter recovery time (10 days as compared to 15 days in control group). Their data also suggest that remdesivir may reduce the progression of the disease to a more severe stage. Since the results of the trial were made public, remdesivir has become the first antiviral to have been authorized by the Food and Drug Association for emergency use among hospitalized adult patients at the risk of severe disease [28]. The effects of the drug are, however, closely monitored and updated with the emergence of new evidence [29]. Thus far, the preliminary results of a more recent solidarity trial led by the World Health Organization recommended against the use of remdesivir for the treatment of COVID-19 owing to its limited efficacy [30]. Moreover, in addition to ambiguity regarding its efficacy, remdesivir is also associated with acute kidney and liver injury [31].

Furthermore, it has been suggested that remdesivir may be more effective in combination with an immunomodulator such as dexamethasone or tocilizumab. A number of trials investigating the use of remdesivir in combination with tocilizumab are

currently underway, and the final verdict regarding its efficacy is still pending [29,30,32,33].

In our patient, however, the combination of remdesivir, tocilizumab, and dexamethasone, administered at a favorable time (ie, during the early stages of the disease when the patient did not yet require mechanical intubation) resulted in timely resolution of the cytokine storm, resulting in an improvement in his ARDS symptoms and subsequent recovery. The underlying reason could be attributed to the effective recognition of risks and a timely administration of the available drugs.

## Conclusions

Despite being the focus of medical and scientific studies for more than a year, worldwide availability of a safe and effective COVID-19 vaccine still remains to be accomplished. Similarly, a number of antivirals and immunomodulators are being actively tested; however, an effective combination is still unavailable. Therefore, to effectively control COVID-19, there is a need to continuously explore and identify safe, effective combinations of the already available therapeutic agents. In order to ensure the safety and survival of patients, there is also a constant need to stay informed about the latest evidence. In our patient with CRS with normal liver and renal functions, combined treatment with tocilizumab, dexamethasone, and remdesivir helped reduce CRS and the subsequent requirement of mechanical ventilation. However, mixed evidence regarding the use of tocilizumab in combination with remdesivir suggests that caution should be exercised until more evidence is available for or against this combination for it to become a treatment regimen nationwide.

## Conflicts of Interest

None declared.

## References

1. Wang W, Tang J, Wei F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. *J Med Virol* 2020 Apr;92(4):441-447 [FREE Full text] [doi: [10.1002/jmv.25689](https://doi.org/10.1002/jmv.25689)] [Medline: [31994742](https://pubmed.ncbi.nlm.nih.gov/31994742/)]
2. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. *Acta Biomed* 2020 Mar 19;91(1):157-160 [FREE Full text] [doi: [10.23750/abm.v91i1.9397](https://doi.org/10.23750/abm.v91i1.9397)] [Medline: [32191675](https://pubmed.ncbi.nlm.nih.gov/32191675/)]
3. World H. Coronavirus Disease (COVID-19) Pandemic. World Health Organization. URL: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019> [accessed 2020-11-30]
4. Jebri N. World Health Organization declared a pandemic public health menace: a systematic review of the coronavirus disease 2019 "COVID-19". *Int J Psychosoc Rehabilitation* 2020;24(9):2784-2795 [FREE Full text] [doi: [10.37200/IJPR/V24I9/PR290311](https://doi.org/10.37200/IJPR/V24I9/PR290311)]
5. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020 Feb 15;395(10223):497-506 [FREE Full text] [doi: [10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)] [Medline: [31986264](https://pubmed.ncbi.nlm.nih.gov/31986264/)]
6. Alshami A, Douedi S, Varon J. Coronavirus in the Arena: One More Time. *CRMR* 2020 Sep 15;16(1):3-4. [doi: [10.2174/1573398X16999200302154418](https://doi.org/10.2174/1573398X16999200302154418)]
7. COVID-19 Coronavirus Pandemic. Worldometer. URL: <https://www.worldometers.info/coronavirus/> [accessed 2020-11-30]
8. Elhusseiny KM, Abd-Elhay FA, Kamel MG. Possible therapeutic agents for COVID-19: a comprehensive review. *Expert Rev Anti Infect Ther* 2020 Oct;18(10):1005-1020. [doi: [10.1080/14787210.2020.1782742](https://doi.org/10.1080/14787210.2020.1782742)] [Medline: [32538209](https://pubmed.ncbi.nlm.nih.gov/32538209/)]
9. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA* 2020 Mar 17;323(11):1061-1069 [FREE Full text] [doi: [10.1001/jama.2020.1585](https://doi.org/10.1001/jama.2020.1585)] [Medline: [32031570](https://pubmed.ncbi.nlm.nih.gov/32031570/)]

10. Zhu T, Wang Y, Zhou S, Zhang N, Xia L. A Comparative Study of Chest Computed Tomography Features in Young and Older Adults With Corona Virus Disease (COVID-19). *J Thorac Imaging* 2020 Jul;35(4):W97-W101 [FREE Full text] [doi: [10.1097/RTI.0000000000000513](https://doi.org/10.1097/RTI.0000000000000513)] [Medline: [32235187](https://pubmed.ncbi.nlm.nih.gov/32235187/)]
11. Li Y, Xia L. Coronavirus Disease 2019 (COVID-19): Role of Chest CT in Diagnosis and Management. *AJR Am J Roentgenol* 2020 Jun;214(6):1280-1286. [doi: [10.2214/AJR.20.22954](https://doi.org/10.2214/AJR.20.22954)] [Medline: [32130038](https://pubmed.ncbi.nlm.nih.gov/32130038/)]
12. Xu PP, Tian RH, Luo S, Zu ZY, Fan B, Wang XM, et al. Risk factors for adverse clinical outcomes with COVID-19 in China: a multicenter, retrospective, observational study. *Theranostics* 2020;10(14):6372-6383 [FREE Full text] [doi: [10.7150/thno.46833](https://doi.org/10.7150/thno.46833)] [Medline: [32483458](https://pubmed.ncbi.nlm.nih.gov/32483458/)]
13. Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. *Aging (Albany NY)* 2020 Apr 08;12(7):6049-6057 [FREE Full text] [doi: [10.18632/aging.103000](https://doi.org/10.18632/aging.103000)] [Medline: [32267833](https://pubmed.ncbi.nlm.nih.gov/32267833/)]
14. Xi Y. Convalescent plasma therapy for COVID-19: a tried-and-true old strategy? *Signal Transduct Target Ther* 2020 Sep 15;5(1):203 [FREE Full text] [doi: [10.1038/s41392-020-00310-8](https://doi.org/10.1038/s41392-020-00310-8)] [Medline: [32934211](https://pubmed.ncbi.nlm.nih.gov/32934211/)]
15. Liu STH, Lin H, Baine I, Wajnberg A, Gumprecht JP, Rahman F, et al. Convalescent plasma treatment of severe COVID-19: a propensity score-matched control study. *Nat Med* 2020 Nov;26(11):1708-1713. [doi: [10.1038/s41591-020-1088-9](https://doi.org/10.1038/s41591-020-1088-9)] [Medline: [32934372](https://pubmed.ncbi.nlm.nih.gov/32934372/)]
16. Moore JB, June CH. Cytokine release syndrome in severe COVID-19. *Science* 2020 May 01;368(6490):473-474. [doi: [10.1126/science.abb8925](https://doi.org/10.1126/science.abb8925)] [Medline: [32303591](https://pubmed.ncbi.nlm.nih.gov/32303591/)]
17. Jain U. Effect of COVID-19 on the Organs. *Cureus* 2020 Aug 03;12(8):e9540 [FREE Full text] [doi: [10.7759/cureus.9540](https://doi.org/10.7759/cureus.9540)] [Medline: [32905500](https://pubmed.ncbi.nlm.nih.gov/32905500/)]
18. Conti P, Ronconi G, Caraffa A, Gallenga C, Ross R, Frydas I, et al. Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies. *J Biol Regul Homeost Agents* 2020;34(2):327-331. [doi: [10.23812/CONTI-E](https://doi.org/10.23812/CONTI-E)] [Medline: [32171193](https://pubmed.ncbi.nlm.nih.gov/32171193/)]
19. Figliozzi S, Masci PG, Ahmadi N, Tondi L, Koutli E, Aimo A, et al. Predictors of adverse prognosis in COVID-19: A systematic review and meta-analysis. *Eur J Clin Invest* 2020 Oct;50(10):e13362. [doi: [10.1111/eci.13362](https://doi.org/10.1111/eci.13362)] [Medline: [32726868](https://pubmed.ncbi.nlm.nih.gov/32726868/)]
20. Hojyo S, Uchida M, Tanaka K, Hasebe R, Tanaka Y, Murakami M, et al. How COVID-19 induces cytokine storm with high mortality. *Inflamm Regen* 2020;40:37 [FREE Full text] [doi: [10.1186/s41232-020-00146-3](https://doi.org/10.1186/s41232-020-00146-3)] [Medline: [33014208](https://pubmed.ncbi.nlm.nih.gov/33014208/)]
21. Chrousos GP, Meduri GU. Critical COVID-19 disease, homeostasis, and the "surprise" of effective glucocorticoid therapy. *Clin Immunol* 2020 Oct;219:108550 [FREE Full text] [doi: [10.1016/j.clim.2020.108550](https://doi.org/10.1016/j.clim.2020.108550)] [Medline: [32745524](https://pubmed.ncbi.nlm.nih.gov/32745524/)]
22. Liu J, Zheng X, Huang Y, Shan H, Huang J. Successful use of methylprednisolone for treating severe COVID-19. *J Allergy Clin Immunol* 2020 Aug;146(2):325-327 [FREE Full text] [doi: [10.1016/j.jaci.2020.05.021](https://doi.org/10.1016/j.jaci.2020.05.021)] [Medline: [32479759](https://pubmed.ncbi.nlm.nih.gov/32479759/)]
23. RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, et al. Dexamethasone in Hospitalized Patients with Covid-19. *N Engl J Med* 2021 Feb 25;384(8):693-704 [FREE Full text] [doi: [10.1056/NEJMoa2021436](https://doi.org/10.1056/NEJMoa2021436)] [Medline: [32678530](https://pubmed.ncbi.nlm.nih.gov/32678530/)]
24. Khiali S, Khani E, Entezari-Maleki T. A Comprehensive Review of Tocilizumab in COVID-19 Acute Respiratory Distress Syndrome. *J Clin Pharmacol* 2020 Sep;60(9):1131-1146 [FREE Full text] [doi: [10.1002/jcph.1693](https://doi.org/10.1002/jcph.1693)] [Medline: [32557541](https://pubmed.ncbi.nlm.nih.gov/32557541/)]
25. Xu X, Han M, Li T, Sun W, Wang D, Fu B, et al. Effective treatment of severe COVID-19 patients with tocilizumab. *Proc Natl Acad Sci U S A* 2020 May 19;117(20):10970-10975 [FREE Full text] [doi: [10.1073/pnas.2005615117](https://doi.org/10.1073/pnas.2005615117)] [Medline: [32350134](https://pubmed.ncbi.nlm.nih.gov/32350134/)]
26. Guaraldi G, Meschiari M, Cozzi-Lepri A, Milic J, Tonelli R, Menozzi M, et al. Tocilizumab in patients with severe COVID-19: a retrospective cohort study. *Lancet Rheumatol* 2020 Aug;2(8):e474-e484 [FREE Full text] [doi: [10.1016/S2665-9913\(20\)30173-9](https://doi.org/10.1016/S2665-9913(20)30173-9)] [Medline: [32835257](https://pubmed.ncbi.nlm.nih.gov/32835257/)]
27. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, ACTT-1 Study Group Members. Remdesivir for the Treatment of Covid-19 - Final Report. *N Engl J Med* 2020 Nov 05;383(19):1813-1826 [FREE Full text] [doi: [10.1056/NEJMoa2007764](https://doi.org/10.1056/NEJMoa2007764)] [Medline: [32445440](https://pubmed.ncbi.nlm.nih.gov/32445440/)]
28. Lamb YN. Remdesivir: First Approval. *Drugs* 2020 Sep;80(13):1355-1363 [FREE Full text] [doi: [10.1007/s40265-020-01378-w](https://doi.org/10.1007/s40265-020-01378-w)] [Medline: [32870481](https://pubmed.ncbi.nlm.nih.gov/32870481/)]
29. Wilt TJ, Kaka AS, MacDonald R, Greer N, Obley A, Duan-Porter W. Remdesivir for Adults With COVID-19 : A Living Systematic Review for American College of Physicians Practice Points. *Ann Intern Med* 2021 Feb;174(2):209-220 [FREE Full text] [doi: [10.7326/M20-5752](https://doi.org/10.7326/M20-5752)] [Medline: [33017170](https://pubmed.ncbi.nlm.nih.gov/33017170/)]
30. WHO Solidarity Trial Consortium, Pan H, Peto R, Henao-Restrepo A, Preziosi M, Sathiyamoorthy V, et al. Repurposed Antiviral Drugs for Covid-19 - Interim WHO Solidarity Trial Results. *N Engl J Med* 2021 Feb 11;384(6):497-511 [FREE Full text] [doi: [10.1056/NEJMoa2023184](https://doi.org/10.1056/NEJMoa2023184)] [Medline: [33264556](https://pubmed.ncbi.nlm.nih.gov/33264556/)]
31. Rahimi MM, Jahantabi E, Lotfi B, Forouzes M, Valizadeh R, Farshid S. Renal and liver injury following the treatment of COVID-19 by remdesivir. *J Nephropathol* 2020 Aug 30;10(2):e10-e10. [doi: [10.34172/jnp.2021.10](https://doi.org/10.34172/jnp.2021.10)]
32. Abbaspour Kasgari H, Babamahmoodi F, Davoudi Badabi AR, Abbaskhani Davanloo A, Moradimajd P, Samaee H. Combination Therapy with Remdesivir and Tocilizumab for COVID-19: Lessons for Futures Studies. *Arch Clin Infect Dis* 2020 Jun 20;15(4) [FREE Full text] [doi: [10.5812/archcid.103537](https://doi.org/10.5812/archcid.103537)]



33. Akinosoglou K, Velissaris D, Ziazias D, Davoulos C, Tousis A, Tsiotsios K, et al. Remdesivir and tocilizumab: Mix or match. *J Med Virol* 2021 Jan;93(1):56-58 [FREE Full text] [doi: [10.1002/jmv.26117](https://doi.org/10.1002/jmv.26117)] [Medline: [32492200](https://pubmed.ncbi.nlm.nih.gov/32492200/)]

## Abbreviations

**ARDS:** acute respiratory distress syndrome  
**BD:** twice daily  
**CPT:** convalescent plasma therapy  
**CRP:** C reactive protein  
**CRS:** cytokine release syndrome  
**CT:** computed tomography  
**FiO<sub>2</sub>:** fraction of inspired oxygen  
**GGO:** ground glass opacity  
**IL:** interleukin  
**OD:** once daily  
**PEEP:** positive end-expiratory pressure  
**PSV:** pressure support ventilation.  
**RT-PCR:** reverse transcription-polymerase chain reaction  
**SpO<sub>2</sub>:** oxygen saturation

*Edited by M Alyahya, T Sanchez; submitted 30.01.21; peer-reviewed by Y Miao, M Popovic; comments to author 10.03.21; revised version received 29.03.21; accepted 29.03.21; published 19.05.21.*

*Please cite as:*

*Ali S, Khalid S, Afridi M, Akhtar S, Khader YS, Akhtar H*

*Notes From the Field: The Combined Effects of Tocilizumab and Remdesivir in a Patient With Severe COVID-19 and Cytokine Release Syndrome*

*JMIR Public Health Surveill* 2021;7(5):e27609

URL: <https://publichealth.jmir.org/2021/5/e27609>

doi: [10.2196/27609](https://doi.org/10.2196/27609)

PMID: [34009133](https://pubmed.ncbi.nlm.nih.gov/34009133/)

©Sabahat Ali, Sundas Khalid, Maham Afridi, Samar Akhtar, Yousef S Khader, Hashaam Akhtar. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 19.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# An Overview of the Treatment Options Used for the Management of COVID-19 in Pakistan: Retrospective Observational Study

Hashaam Akhtar<sup>1</sup>, PhD; Samar Akhtar<sup>1</sup>, PhD; Fazal-Ul Rahman<sup>2</sup>, MBBS, FCPS; Maham Afridi<sup>3</sup>, MPhil; Sundas Khalid<sup>4</sup>, MPhil; Sabahat Ali<sup>5</sup>, MBBS; Nasim Akhtar<sup>6</sup>, MBBS; Yousef S Khader<sup>7</sup>, BDS, MSc, MSPH, MHPE, FFPH, ScD; Hamaad Ahmad<sup>1</sup>, BPharm, MPhil; Muhammad Mujeeb Khan<sup>8</sup>, MBBS

<sup>1</sup>Yusra Institute of Pharmaceutical Sciences, Yusra Medical and Dental College, Islamabad, Pakistan

<sup>2</sup>Department of Medicine, Benazir Bhutto Hospital, Rawalpindi, Pakistan

<sup>3</sup>Department of Biotechnology, Quaid-i-Azam University, Islamabad, Pakistan

<sup>4</sup>School of Chemical and Materials Engineering, National University of Science and Technology, Islamabad, Pakistan

<sup>5</sup>Department of Gynecology and Obstetrics, Pakistan Air Force Hospital, Islamabad, Pakistan

<sup>6</sup>Department of Infectious Diseases, Pakistan Institute of Medical Sciences, Islamabad, Pakistan

<sup>7</sup>Medical Education and Biostatistics, Department of Community Medicine, Public Health and Family Medicine, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan

<sup>8</sup>Department of Infectious Diseases, Rawalpindi Medical University, Rawalpindi, Pakistan

**Corresponding Author:**

Hashaam Akhtar, PhD

Yusra Institute of Pharmaceutical Sciences

Yusra Medical and Dental College

Zaraj Housing Society

Opposite DHA Phase 2 Gate III, Main GT Road

Islamabad, 44000

Pakistan

Phone: 92 515709447

Email: [hashaamakhtar@gmail.com](mailto:hashaamakhtar@gmail.com)

## Abstract

**Background:** Since the first reports of COVID-19 infection, the foremost requirement has been to identify a treatment regimen that not only fights the causative agent but also controls the associated complications of the infection. Due to the time-consuming process of drug discovery, physicians have used readily available drugs and therapies for treatment of infections to minimize the death toll.

**Objective:** The aim of this study is to provide a snapshot analysis of the major drugs used in a cohort of 1562 Pakistani patients during the period from May to July 2020, when the first wave of COVID-19 peaked in Pakistan.

**Methods:** A retrospective observational study was performed to provide an overview of the major drugs used in a cohort of 1562 patients with COVID-19 admitted to the four major tertiary-care hospitals in the Rawalpindi-Islamabad region of Pakistan during the peak of the first wave of COVID-19 in the country (May-July 2020).

**Results:** Antibiotics were the most common choice out of all the therapies employed, and they were used as first line of treatment for COVID-19. Azithromycin was the most prescribed drug for treatment. No monthly trend was observed in the choice of antibiotics, and these drugs appeared to be a random but favored choice throughout the months of the study. It was also noted that even antibiotics used for multidrug resistant infections were prescribed irrespective of the severity or progression of the infection. The results of the analysis are alarming, as this approach may lead to antibiotic resistance and complications in immunocompromised patients with COVID-19. A total of 1562 patients (1064 male, 68.1%, and 498 female, 31.9%) with a mean age of 47.35 years (SD 17.03) were included in the study. The highest frequency of patient hospitalizations occurred in June (846/1562, 54.2%).

**Conclusions:** Guidelines for a targeted treatment regime are needed to control related complications and to limit the misuse of antibiotics in the management of COVID-19.

(JMIR Public Health Surveill 2021;7(5):e28594) doi:[10.2196/28594](https://doi.org/10.2196/28594)

**KEYWORDS**

COVID-19; antibiotics; Pakistan; multidrug resistant infections; antibiotic resistance; first wave

**Introduction**

In December 2019, a viral outbreak of pneumonia was reported in a city in China in December 2019 [1]; this outbreak would have a substantial impact worldwide. Shortly after the first reports of the disease, it rapidly spread globally and was declared a pandemic by the World Health Organization in 2020 [2]. The official name for this pneumonia-like disease is COVID-19, and the virus that causes it is called SARS-CoV-2 [3]. The pathological conditions of COVID-19 infection were classified into five categories, from asymptomatic to critical, according to clinical manifestations [4]. It has already been reported that approximately one-fifth of the hospitalized patients with COVID-19 are admitted to intensive care units due to difficulty in breathing or acute hypoxemic respiratory failure [5-8].

More than a year has passed since the initial outbreak, and SARS-CoV-2 continues to spread globally, crippling the economy, damaging health, and causing mortality each day; the current count has reached a staggering 112.65 million confirmed infections and 2.49 million deaths [9,10]. With the rapid spread of COVID-19 across the world, prompt diagnostic tools, readily available repurposable drugs, and effective containment measures to control SARS-CoV-2 infection are of paramount importance. The pandemic has also exposed inadequate research and health infrastructures globally, especially in countries such as Pakistan, where basic health care necessities were scarce when the infection reached its peak in June 2020 [11,12].

The second wave of COVID-19 infections being reported by various countries, including Pakistan, is proving to be even more challenging to address because of the severity of COVID-19-related complications, which vary with gender and age [13-15], underlying diseases and disorders, and even delay in hospital admissions [16,17]. Human behavior is also a major factor causing the resurgence in infections [18]. The relationship between adherence to precautions and cases of COVID-19 is clear: in areas where fewer people wear masks and more people gather indoors to eat, drink, celebrate, socialize, and observe religious practices, even if only with family, cases are on the rise [19-21].

With overburdened health care systems and an increasing number of infections among medical staff, the ultimate way to overcome this pandemic remains the discovery of an effective vaccine. Although pharmaceutical companies worldwide have introduced several vaccines to date [22,23], effectively vaccinating a sufficiently large number of people all over the world is a lengthy process [24,25]. Moreover, with reports of new strains from different regions, the effectiveness of some of these vaccines against multiple mutant strains shows mixed results [26]. As a result, repurposing existing drugs to target SARS-CoV-2 and treat COVID-19-associated symptoms still appears to be a logical scientific approach at the moment to contain this pandemic. Identifying and appropriating an effective combination of drugs from the available repertoire is a challenge in itself. The hit-and-trial method is dangerous but inevitable

in the current situation. Small-scale studies were performed in which a few drugs were reported to be effective; however, these drugs were later proved to result in no significant difference in clinical outcomes [27-29].

Currently, as observed in various reports globally as well as in Pakistan, supportive treatment, mechanical ventilation, and extracorporeal membrane oxygenation remain the primary treatment choices for medical practitioners. Therapeutic options that are being considered and used include antiviral, antiparasitic, and anti-inflammatory medications; interferon therapy; convalescent plasma therapy; hyperimmunoglobulin; oligonucleotide-based therapies; and, rarely, RNA interference and mesenchymal stem cell therapy [30-32].

In this study, we explored the use of antibiotic and antiviral drugs for the treatment of patients admitted during the peak of the first wave of COVID-19 in Pakistan (May-July 2020). Directions for treatment of the disease during the first wave phase were not very clear, and many necessities, including drugs, were out of stock in local markets due to lockdowns, high demand, limited stocks, and closure of borders.

**Methods****Study Design**

Clinical data from 1812 confirmed patients with COVID-19 admitted to four major tertiary care hospitals in Pakistan, that is, Pakistan Air Force Hospital, Islamabad, Pakistan Institute of Medical Sciences Hospital, Islamabad, Holy Family Hospital, Rawalpindi, and Benazir Bhutto Shaheed Hospital, Rawalpindi, were retrospectively collected during the period from February to August 2020.

**Patient Selection, Timeline, and Data Collection**

Confirmed COVID-19 cases were defined as patients with a positive polymerase chain reaction test for COVID-19 from nasal and oropharyngeal swab samples taken at the time of admission to the hospital. Patients with incomplete data were excluded. Descriptive data of 1562 patients admitted during the months of May to July 2020 were abstracted and analyzed accordingly. The data included information about the patients' age, gender, dates of admission and discharge (or death), medical history, presenting signs and symptoms, initial categorization of COVID-19 (mild, moderate, severe, and critical), and types of therapeutic agents (including but not limited to use of antibiotics, antimalarials, antivirals, antiparasitics, anticoagulants, and corticosteroids) used for treatment and management of COVID-19 during their hospital stay.

The statistical analysis was conducted using SPSS, version 24 (IBM Corporation) and Stata 16.1 (StataCorp LLC). Categorical variables were described using frequencies and percentages [33,34]. Chi-square tests and Fisher exact tests were used to compare percentages wherever appropriate. This retrospective cohort study was approved by the ethics review board of

Rawalpindi Medical University. Data were collected with approval of the National Institute of Health (NIH), Pakistan.

## Results

A total of 1562 patients were included in the study; 1064 (68.1%) were male and 498 (31.9%) were female, with a mean

age of 47.35 years (SD 17.03). The basic demographic characteristics of the hospitalized patients with COVID-19 and their distribution across the hospitals are shown in [Table 1](#). The frequencies of admission during the months of May, June, and July 2020 were 37.9% (592/1562), 54.2% (846/1562), and 7.9% (124/1562), respectively.

**Table 1.** Baseline characteristics of the study participants (N=1562).

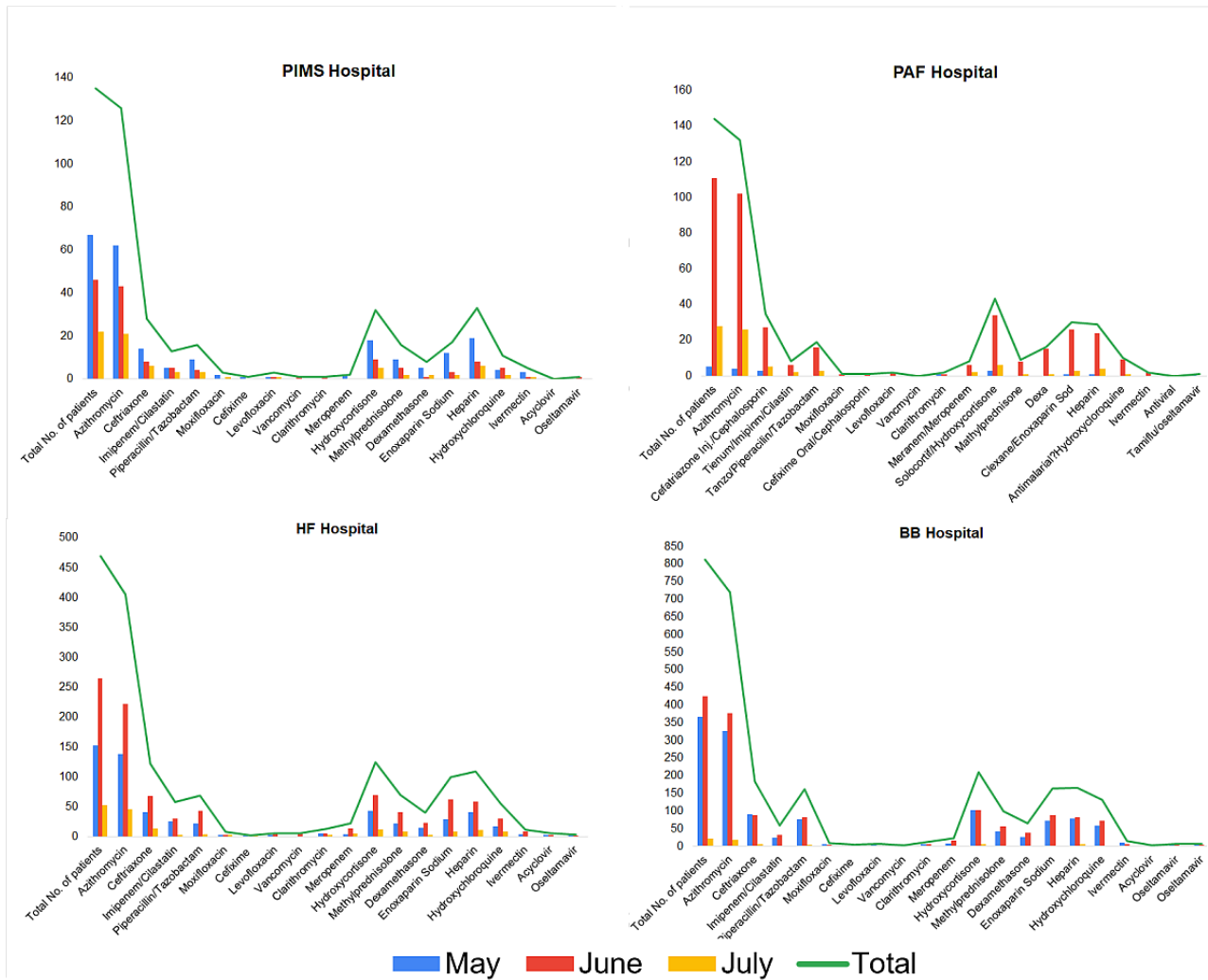
Characteristic	Value
Age (years), mean (SD)	47.35 (17.03)
<b>Gender</b>	
Male	1064 (68.1)
Female	498 (31.9)
<b>Admission frequency of patients across hospitals, n (%)</b>	
Benazir Bhutto Shaheed Hospital, Rawalpindi	813 (52.0)
Holy Family Hospital, Rawalpindi	470 (30.1)
Pakistan Institute of Medical Sciences Hospital, Islamabad	135 (8.3)
Pakistan Air Force Hospital, Islamabad	144 (9.2)
<b>Admission frequency of patients across the period of the study, n (%)</b>	
May 2020	592 (37.9)
June 2020	846 (54.2)
July 2020	124 (7.9)

Of the 19 drugs reportedly used for treatment of COVID-19 and management of COVID-19-related symptoms, the most frequently used antibiotic was azithromycin (1384/1562, 88.6%), followed by ceftriaxone (369/1562, 23.6%). Anticoagulants such as heparin (337/1562, 21.6%) and enoxaparin sodium (310/1562, 19.8%) and steroids such as hydrocortisone (409/1562, 25.7%) were also among the 5 most frequently used drugs. The relative distribution of administered drugs across hospitals during the first wave of COVID-19 is given in [Figure 1](#). The load of patients at each hospital was different; however,

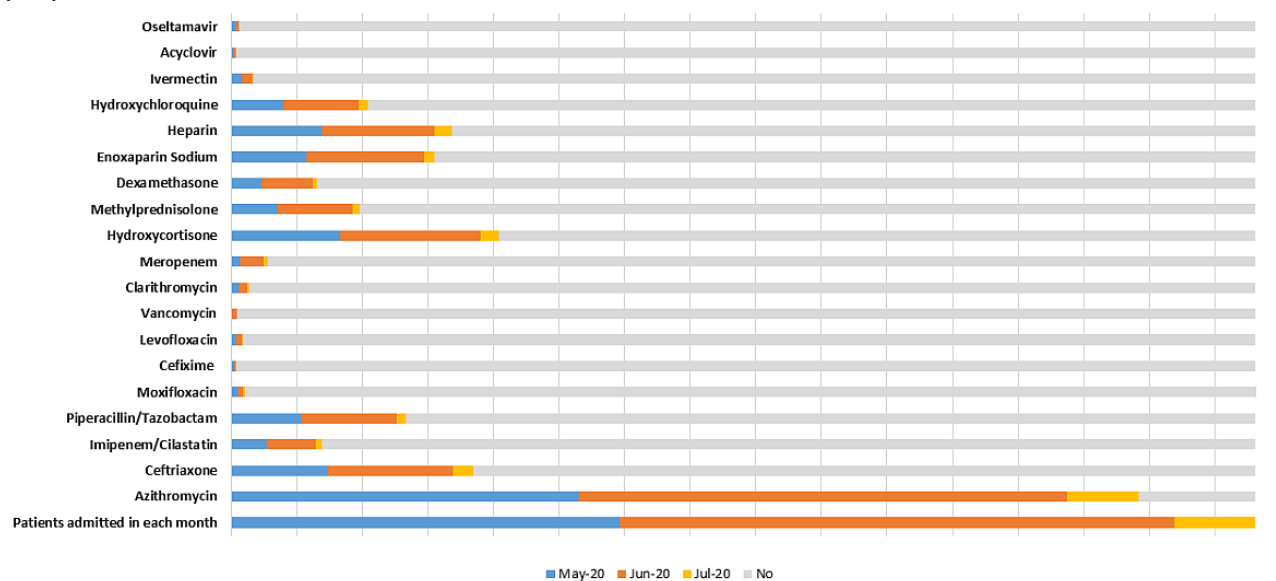
the trends of the regimens used were similar. The peak of the first wave of COVID-19 in Rawalpindi-Islamabad was observed during June 2020. The trends of drug use during the first wave of COVID-19 in Pakistan are shown in [Figure 2](#) and [Table 2](#).

Although the load over hospital varied during the 3 months, the choices of drugs used to treat COVID-19 remained the same. The frequencies and percentages of the prescription of these drugs are given in [Table 3](#). Different combinations were used, and these combinations included drugs from various categories, such as anticoagulants, corticosteroids, and antibiotics.

**Figure 1.** Hospital-wise relative distribution of different drugs administered to patients with COVID-19 during the first wave of the pandemic in Pakistan. BB: Benazir Bhutto; HF: Holy Family; PAF: Pakistan Air Force; PIMS: Pakistan Institute of Medical Sciences.



**Figure 2.** Relative distributions of different drugs administered to patients with COVID-19 in each month during the first wave of the pandemic (May-July 2020) in Pakistan.



**Table 2.** Distributions of different drugs administered to patients with COVID-19 (N=1562) in each month during the first wave of the pandemic (May-July 2020) in Pakistan.

Drug	Prescriptions, n (%)			
	Patients admitted in May 2020 (n=592)	Patients admitted in June 2020 (n=846)	Patients admitted in July 2020 (n=124)	Patients not prescribed <sup>a</sup>
Azithromycin	531 (89.7)	743 (87.8)	110 (88.7)	178 (11.4)
Ceftriaxone	148 (25)	191 (22.6)	30 (24.2)	1193 (76.4)
Imipenem/cilastatin	55 (9.3)	74 (8.7)	10 (8.1)	1423 (91.1)
Piperacillin/tazobactam	107 (18.1)	145 (17.1)	14 (11.3)	1296 (83)
Moxifloxacin	11 (1.9)	7 (0.8)	3 (2.4)	1542 (98.7)
Cefixime	4 (0.7)	3 (0.4)	1 (0.8)	1554 (99.5)
Levofloxacin	8 (1.4)	9 (1.1)	1 (0.8)	1544 (98.8)
Vancomycin	1 (0.2)	8 (0.9)	0 (0)	1553 (99.4)
Clarithromycin	12 (2.0)	13 (1.5)	3 (2.4)	1534 (98.2)
Meropenem	14 (2.3)	35 (4.1)	7 (5.6)	1506 (96.4)
Hydrocortisone	166 (28)	214 (25.3)	29 (23.4)	1153 (73.8)
Methylprednisolone	72 (12.2)	113 (13.4)	12 (9.7)	1365 (87.4)
Dexamethasone	46 (7.8)	78 (9.2)	6 (4.8)	1432 (91.7)
Enoxaparin sodium	115 (19.4)	180 (21.3)	15 (12.1)	1252 (80.2)
Heparin	138 (23.3)	172 (20.3)	27 (21.8)	1225 (78.4)
Hydroxychloroquine	79 (13.3)	116 (13.7)	13 (10.5)	1354 (86.7)
Ivermectin	17 (2.9)	16 (1.9)	1 (0.8)	1528 (97.8)
Acyclovir	3 (0.5)	5 (0.6)	0 (0)	1554 (99.5)
Oseltamivir	7 (1.2)	5 (0.6)	0 (0)	1550 (99.2)

<sup>a</sup>Percentages calculated based on the total number of patients across 3 months (N=1562).

**Table 3.** Drugs used during the first wave of COVID-19 to treat patients (N=1562) in all four hospitals under study.

Drug	Value, n (%)
<b>Antibiotics</b>	
Azithromycin	1384 (88.6)
Ceftriaxone	369 (23.6)
Cefixime	8 (0.51)
Meropenem	56 (3.6)
Imipenem/cilastatin	139 (8.9)
Piperacillin/tazobactam	266 (17.0)
Vancomycin	9 (0.6)
Clarithromycin	28 (1.8)
Moxifloxacin	21 (1.3)
Levofloxacin	18 (1.1)
<b>Corticosteroids</b>	
Hydrocortisone	409 (26.2)
Methylprednisolone	197 (12.6)
Dexamethasone	130 (8.3)
<b>Anticoagulants</b>	
Enoxaparin sodium	310 (19.8)
Heparin	337 (21.6)
<b>Antimalarial</b>	
Hydroxychloroquine	208 (13.3)
<b>Antiparasitic</b>	
Ivermectin	34 (2.2)
<b>Antiviral</b>	
Acyclovir	8 (0.5)
Oseltamivir	12 (0.8)

## Discussion

### Principal Findings

Our results show that the highest proportion of admissions occurred in the month of June (846/1562, 54.2%), just after Eid-ul-Fitr (the Muslim festival, which was held on May 23 and 24 in 2020). It is worth noting that this was the time when the first wave of COVID-19 infections was at its peak in Pakistan; however, the trend of the treatment regimen remained the same during the period of the first wave [35-37]. However, after this period, a dramatic decrease in infections was observed due to effective precautions and regulations imposed by the government, including “smart lockdown” in potential hotspots, implementation of standard operating procedures, and closure of academic buildings [38].

Our study reports the use of up to 10 antibiotics of different classes. The effectiveness of the use of antibiotics for the treatment of COVID-19 is debatable, and evidence of their direct inhibitory effect on viral replication or pathogenesis remains to be proved. These antibiotics are generally used to treat upper respiratory tract infections, pneumonia, and other infections

caused by opportunistic bacteria due to low immunity during viral infection. Azithromycin was widely used because it is a broad-spectrum antibiotic and can treat chest infections, including pneumonia, which is also a manifestation of COVID-19 infection; infections of the nose and throat, such as sinus infections (sinusitis); skin infections; Lyme disease; and some sexually transmitted infections [39].

In addition to antibiotics, some other frequently used drugs were anticoagulants (heparin and enoxaparin sodium) and corticosteroids (hydrocortisone and methylprednisolone). Use of anticoagulants and steroids is indicated for reduction of the inflammatory effects of SARS-CoV-2, which helps control disease progression to a limited extent; however, no succinct combination was observed in terms of treating COVID-19 [40].

### Challenges and Shortcomings on the Therapeutic Front

Despite the fact that the antibiotics supported the combined therapies used against COVID-19, there is still no evidence that supports the use of these antibiotics to treat viral infection by health care professionals in Pakistan. Other drugs, such as anticoagulants and steroids, were also used as supportive

therapy; however, there is a need to establish standard guidelines to treat patients with COVID-19–related complications. The experimental hit-and-trial approach of various combinations of drugs and the alarming frequency with which antibiotics were used will eventually lead to antibiotic resistance in the human population. One of the major challenges faced by health care professionals globally was the reliability on available therapies against the newly introduced virus. Mutations in RNA viruses are more frequent compared to those in DNA species; COVID-19, being an RNA virus, is a great threat to humanity. Modern research is necessary to study mutable infectious agents to develop multifaceted therapies to target the pathways of infection.

## Conclusion

This study highlights the trend of drugs used to treat COVID-19 infections in early the months of the pandemic across Pakistan. The use of antibiotics by health care professionals to treat COVID-19 is questionable. It signifies the lack of specific guidelines that must be followed by all hospitals in terms of treatment regimens, and organizations such as the NIH and the Centers for Disease Control and Prevention must not only provide guidelines to address the pandemic but also ensure that those guidelines are strictly being followed throughout the country. This study reveals the weaknesses in the health care

infrastructure and the inadequacy of hospitals and staff in Pakistan. With the second wave emerging in various countries and a mutant strain of SARS-CoV-2 causing infections, it is important to ensure that the standard operating procedures are being strictly followed, a proper treatment guideline is provided, and drugs used for symptomatic treatment are monitored to avoid antibiotic resistance in the future.

## Limitations of the Study

The study was limited to the Rawalpindi and Islamabad regions of Pakistan, which are large cities with relatively good health care facilities and checks and balances on health care practitioners. Data from other cities, especially small towns and rural regions, can be helpful in analyzing the misuse of medicines prescribed for treatment of COVID-19–related symptoms and complications. The study was performed on patients admitted in mid-2020 during the peak of the first wave, and a better analysis could be performed if data were taken from the months of the second wave as well. Collecting data during the first wave was difficult due to limited access to COVID-19 wards and a shortage of personal protection equipment. The number of subjects included in the study was under 2000; comprehensive information could be gathered from a large population size.

## Acknowledgments

The authors would like to acknowledge Global Health Development/Eastern Mediterranean Public Health Network for their support. We would also like to acknowledge the support of NIH, Islamabad. We also wish to acknowledge our colleagues for their time and invaluable contributions to this ongoing study in the region.

## Conflicts of Interest

None declared.

## References

1. Zhu H, Wei L, Niu P. The novel coronavirus outbreak in Wuhan, China. *Glob Health Res Policy* 2020;5:6 [FREE Full text] [doi: [10.1186/s41256-020-00135-6](https://doi.org/10.1186/s41256-020-00135-6)] [Medline: [32226823](https://pubmed.ncbi.nlm.nih.gov/32226823/)]
2. Layne SP, Hyman JM, Morens DM, Taubenberger JK. New coronavirus outbreak: framing questions for pandemic prevention. *Sci Transl Med* 2020 Mar 11;12(534). [doi: [10.1126/scitranslmed.abb1469](https://doi.org/10.1126/scitranslmed.abb1469)] [Medline: [32161107](https://pubmed.ncbi.nlm.nih.gov/32161107/)]
3. Lai C, Shih T, Ko W, Tang H, Hsueh P. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): the epidemic and the challenges. *Int J Antimicrob Agents* 2020 Mar;55(3):105924 [FREE Full text] [doi: [10.1016/j.ijantimicag.2020.105924](https://doi.org/10.1016/j.ijantimicag.2020.105924)] [Medline: [32081636](https://pubmed.ncbi.nlm.nih.gov/32081636/)]
4. Tomo S, Karli S, Dharmalingam K, Yadav D, Sharma P. The clinical laboratory: a key player in diagnosis and management of COVID-19. *EJIFCC* 2020 Nov;31(4):326-346 [FREE Full text] [Medline: [33376473](https://pubmed.ncbi.nlm.nih.gov/33376473/)]
5. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020 Apr 30;382(18):1708-1720. [doi: [10.1056/nejmoa2002032](https://doi.org/10.1056/nejmoa2002032)]
6. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020 Mar 17;323(11):1061-1069 [FREE Full text] [doi: [10.1001/jama.2020.1585](https://doi.org/10.1001/jama.2020.1585)] [Medline: [32031570](https://pubmed.ncbi.nlm.nih.gov/32031570/)]
7. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, the Northwell COVID-19 Research Consortium, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020 May 26;323(20):2052-2059 [FREE Full text] [doi: [10.1001/jama.2020.6775](https://doi.org/10.1001/jama.2020.6775)] [Medline: [32320003](https://pubmed.ncbi.nlm.nih.gov/32320003/)]
8. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020 Apr 07;323(13):1239-1242. [doi: [10.1001/jama.2020.2648](https://doi.org/10.1001/jama.2020.2648)] [Medline: [32091533](https://pubmed.ncbi.nlm.nih.gov/32091533/)]
9. Coronavirus. Worldometer. URL: <https://www.worldometers.info/coronavirus/> [accessed 2021-02-24]



10. Subbaraman N. Why daily death tolls have become unusually important in understanding the coronavirus pandemic. *Nature* 2020 Apr 09. [doi: [10.1038/d41586-020-01008-1](https://doi.org/10.1038/d41586-020-01008-1)] [Medline: [32273624](https://pubmed.ncbi.nlm.nih.gov/32273624/)]
11. Reporter T. Covid infection in Punjab reaches June peak level. *Dawn News*. 2020 Dec 08. URL: <https://www.dawn.com/news/1594625> [accessed 2021-05-17]
12. Saeed U, Sherdil K, Ashraf U, Mohey-Ud-Din G, Younas I, Butt HJ, et al. Identification of potential lockdown areas during COVID-19 transmission in Punjab, Pakistan. *Public Health* 2021 Jan;190:42-51 [FREE Full text] [doi: [10.1016/j.puhe.2020.10.026](https://doi.org/10.1016/j.puhe.2020.10.026)] [Medline: [33338902](https://pubmed.ncbi.nlm.nih.gov/33338902/)]
13. Cacciapaglia G, Cot C, Sannino F. Second wave COVID-19 pandemics in Europe: a temporal playbook. *Sci Rep* 2020 Sep 23;10(1):15514 [FREE Full text] [doi: [10.1038/s41598-020-72611-5](https://doi.org/10.1038/s41598-020-72611-5)] [Medline: [32968181](https://pubmed.ncbi.nlm.nih.gov/32968181/)]
14. Gebhard C, Regitz-Zagrosek V, Neuhauser HK, Morgan R, Klein SL. Impact of sex and gender on COVID-19 outcomes in Europe. *Biol Sex Differ* 2020 May 25;11(1):29 [FREE Full text] [doi: [10.1186/s13293-020-00304-9](https://doi.org/10.1186/s13293-020-00304-9)] [Medline: [32450906](https://pubmed.ncbi.nlm.nih.gov/32450906/)]
15. Tadiri CP, Gisinger T, Kautzy-Willer A, Kublickiene K, Herrero MT, Raparelli V, GOING-FWD Consortium. The influence of sex and gender domains on COVID-19 cases and mortality. *CMAJ* 2020 Sep 08;192(36):E1041-E1045 [FREE Full text] [doi: [10.1503/cmaj.200971](https://doi.org/10.1503/cmaj.200971)] [Medline: [32900766](https://pubmed.ncbi.nlm.nih.gov/32900766/)]
16. Harrison SL, Fazio-Eynullayeva E, Lane DA, Underhill P, Lip GYH. Comorbidities associated with mortality in 31,461 adults with COVID-19 in the United States: a federated electronic medical record analysis. *PLoS Med* 2020 Sep 10;17(9):e1003321 [FREE Full text] [doi: [10.1371/journal.pmed.1003321](https://doi.org/10.1371/journal.pmed.1003321)] [Medline: [32911500](https://pubmed.ncbi.nlm.nih.gov/32911500/)]
17. Alaa A, Qian Z, Rashbass J, Bengler J, van der Schaar M. Retrospective cohort study of admission timing and mortality following COVID-19 infection in England. *BMJ Open* 2020 Nov 23;10(11):e042712 [FREE Full text] [doi: [10.1136/bmjopen-2020-042712](https://doi.org/10.1136/bmjopen-2020-042712)] [Medline: [33234660](https://pubmed.ncbi.nlm.nih.gov/33234660/)]
18. Bavel JJV, Baicker K, Boggio PS, Capraro V, Cichocka A, Cikara M, et al. Using social and behavioural science to support COVID-19 pandemic response. *Nat Hum Behav* 2020 May;4(5):460-471. [doi: [10.1038/s41562-020-0884-z](https://doi.org/10.1038/s41562-020-0884-z)] [Medline: [32355299](https://pubmed.ncbi.nlm.nih.gov/32355299/)]
19. Ahmed MS, Yunus FM. Trend of COVID-19 spreads and status of household handwashing practice and its determinants in Bangladesh - situation analysis using national representative data. *Int J Environ Health Res* 2020 Sep 13:1-9. [doi: [10.1080/09603123.2020.1817343](https://doi.org/10.1080/09603123.2020.1817343)] [Medline: [32924565](https://pubmed.ncbi.nlm.nih.gov/32924565/)]
20. Leung CC, Cheng KK, Lam TH, Migliori GB. Mask wearing to complement social distancing and save lives during COVID-19. *Int J Tuberc Lung Dis* 2020 Jun 01;24(6):556-558. [doi: [10.5588/ijtld.20.0244](https://doi.org/10.5588/ijtld.20.0244)] [Medline: [32553007](https://pubmed.ncbi.nlm.nih.gov/32553007/)]
21. Weinstein E, Ragazzoni L, Burkle F, Allen M, Hogan D, Della Corte F. Delayed primary and specialty care: the coronavirus disease-2019 pandemic second wave. *Disaster Med Public Health Prep* 2020 Jun;14(3):e19-e21 [FREE Full text] [doi: [10.1017/dmp.2020.148](https://doi.org/10.1017/dmp.2020.148)] [Medline: [32438940](https://pubmed.ncbi.nlm.nih.gov/32438940/)]
22. Callaway E. What Pfizer's landmark COVID vaccine results mean for the pandemic. *Nature* 2020 Nov 09. [doi: [10.1038/d41586-020-03166-8](https://doi.org/10.1038/d41586-020-03166-8)] [Medline: [33169027](https://pubmed.ncbi.nlm.nih.gov/33169027/)]
23. Callaway E. Coronavirus vaccine trials have delivered their first results—but their promise is still unclear. *Nature* 2020 May;581(7809):363-364. [doi: [10.1038/d41586-020-01092-3](https://doi.org/10.1038/d41586-020-01092-3)] [Medline: [32433634](https://pubmed.ncbi.nlm.nih.gov/32433634/)]
24. MacPherson Y. What is the world doing about COVID-19 vaccine acceptance? *J Health Commun* 2020 Oct 02;25(10):757-760. [doi: [10.1080/10810730.2020.1868628](https://doi.org/10.1080/10810730.2020.1868628)] [Medline: [33719875](https://pubmed.ncbi.nlm.nih.gov/33719875/)]
25. Khamsi R. If a coronavirus vaccine arrives, can the world make enough? *Nature* 2020 Apr 9;580(7805):578-580. [doi: [10.1038/d41586-020-01063-8](https://doi.org/10.1038/d41586-020-01063-8)] [Medline: [32273621](https://pubmed.ncbi.nlm.nih.gov/32273621/)]
26. Callaway E. Why Oxford's positive COVID vaccine results are puzzling scientists. *Nature* 2020 Dec 23;588(7836):16-18. [doi: [10.1038/d41586-020-03326-w](https://doi.org/10.1038/d41586-020-03326-w)] [Medline: [33230278](https://pubmed.ncbi.nlm.nih.gov/33230278/)]
27. Magagnoli J, Narendran S, Pereira F, Cummings TH, Hardin JW, Sutton SS, et al. Outcomes of hydroxychloroquine usage in United States veterans hospitalized with COVID-19. *Med (N Y)* 2020 Dec 18;1(1):114-127.e3 [FREE Full text] [doi: [10.1016/j.medj.2020.06.001](https://doi.org/10.1016/j.medj.2020.06.001)] [Medline: [32838355](https://pubmed.ncbi.nlm.nih.gov/32838355/)]
28. Molina J, Delaugerre C, Le Goff J, Mela-Lima B, Ponscarne D, Goldwirt L, et al. No evidence of rapid antiviral clearance or clinical benefit with the combination of hydroxychloroquine and azithromycin in patients with severe COVID-19 infection. *Med Mal Infect* 2020 Jun;50(4):384 [FREE Full text] [doi: [10.1016/j.medmal.2020.03.006](https://doi.org/10.1016/j.medmal.2020.03.006)] [Medline: [32240719](https://pubmed.ncbi.nlm.nih.gov/32240719/)]
29. Mahévas M, Tran V, Roumier M, Chabrol A, Paule R, Guillaud C, et al. Clinical efficacy of hydroxychloroquine in patients with covid-19 pneumonia who require oxygen: observational comparative study using routine care data. *BMJ* 2020 May 14;369:m1844 [FREE Full text] [doi: [10.1136/bmj.m1844](https://doi.org/10.1136/bmj.m1844)] [Medline: [32409486](https://pubmed.ncbi.nlm.nih.gov/32409486/)]
30. Park YJ, Farooq J, Cho J, Sadanandan N, Cozene B, Gonzales-Portillo B, et al. Fighting the war against COVID-19 via cell-based regenerative medicine: lessons learned from 1918 Spanish Flu and other previous pandemics. *Stem Cell Rev Rep* 2021 Feb 13;17(1):9-32 [FREE Full text] [doi: [10.1007/s12015-020-10026-5](https://doi.org/10.1007/s12015-020-10026-5)] [Medline: [32789802](https://pubmed.ncbi.nlm.nih.gov/32789802/)]
31. Borlongan MC, Borlongan MC, Sanberg PR. The disillusioned comfort with COVID-19 and the potential of convalescent plasma and cell therapy. *Cell Transplant* 2020;29:963689720940719 [FREE Full text] [doi: [10.1177/0963689720940719](https://doi.org/10.1177/0963689720940719)] [Medline: [32841042](https://pubmed.ncbi.nlm.nih.gov/32841042/)]
32. Siam MHB, Nishat NH, Ahmed A, Hossain MS. Stopping the COVID-19 pandemic: a review on the advances of diagnosis, treatment, and control measures. *J Pathog* 2020;2020:9121429 [FREE Full text] [doi: [10.1155/2020/9121429](https://doi.org/10.1155/2020/9121429)] [Medline: [33133697](https://pubmed.ncbi.nlm.nih.gov/33133697/)]

33. Barkhordari M, Padyab M, Hadaegh F, Azizi F, Bozorgmanesh M. Stata modules for calculating novel predictive performance indices for logistic models. *Int J Endocrinol Metab* 2016 Jan;14(1):e26707 [FREE Full text] [doi: [10.5812/ijem.26707](https://doi.org/10.5812/ijem.26707)] [Medline: [27279830](https://pubmed.ncbi.nlm.nih.gov/27279830/)]
34. Burnard P. *Nice vital statistics SPSS/PC + and SPSS for Windows: A Beginner's Guide to Data Analysis*, 2nd edition. Foster JJ et al 1993 Price: Supplier: Computer Manuals , Birmingham. £14.95 021-706-6000. *Nurs Stand* 1994 Feb 02;8(19):53. [doi: [10.7748/ns.8.19.53.s61](https://doi.org/10.7748/ns.8.19.53.s61)] [Medline: [27657247](https://pubmed.ncbi.nlm.nih.gov/27657247/)]
35. Noreen K, Umar M, Sabir SA, Rehman R. Outbreak of coronavirus disease 2019 (COVID-19) in Pakistan: psychological impact and coping strategies of health care professionals. *Pak J Med Sci* 2020;36(7):1478-1483 [FREE Full text] [doi: [10.12669/pjms.36.7.2988](https://doi.org/10.12669/pjms.36.7.2988)] [Medline: [33235560](https://pubmed.ncbi.nlm.nih.gov/33235560/)]
36. Shah PT, Xing L. Puzzling increase and decrease in COVID-19 cases in Pakistan. *New Microbes New Infect* 2020 Nov;38:100791 [FREE Full text] [doi: [10.1016/j.nmni.2020.100791](https://doi.org/10.1016/j.nmni.2020.100791)] [Medline: [33101693](https://pubmed.ncbi.nlm.nih.gov/33101693/)]
37. Hussain I, Majeed A, Saeed H, Hashmi FK, Imran I, Akbar M, et al. A national study to assess pharmacists' preparedness against COVID-19 during its rapid rise period in Pakistan. *PLoS One* 2020;15(11):e0241467 [FREE Full text] [doi: [10.1371/journal.pone.0241467](https://doi.org/10.1371/journal.pone.0241467)] [Medline: [33151984](https://pubmed.ncbi.nlm.nih.gov/33151984/)]
38. Waris A, Atta UK, Ali M, Asmat A, Baset A. COVID-19 outbreak: current scenario of Pakistan. *New Microbes New Infect* 2020 May;35:100681 [FREE Full text] [doi: [10.1016/j.nmni.2020.100681](https://doi.org/10.1016/j.nmni.2020.100681)] [Medline: [32322403](https://pubmed.ncbi.nlm.nih.gov/32322403/)]
39. Bleyzac N, Goutelle S, Bourguignon L, Tod M. Azithromycin for COVID-19: more than just an antimicrobial? *Clin Drug Investig* 2020 Aug;40(8):683-686 [FREE Full text] [doi: [10.1007/s40261-020-00933-3](https://doi.org/10.1007/s40261-020-00933-3)] [Medline: [32533455](https://pubmed.ncbi.nlm.nih.gov/32533455/)]
40. Gavriatopoulou M, Ntanasis-Stathopoulos I, Korompoki E, Fotiou D, Migkou M, Tzanninis I, et al. Emerging treatment strategies for COVID-19 infection. *Clin Exp Med* 2021 May;21(2):167-179 [FREE Full text] [doi: [10.1007/s10238-020-00671-y](https://doi.org/10.1007/s10238-020-00671-y)] [Medline: [33128197](https://pubmed.ncbi.nlm.nih.gov/33128197/)]

## Abbreviations

**NIH:** National Institute of Health

*Edited by M Alyahya; submitted 08.03.21; peer-reviewed by DF Javed, M Asgari Mehrabadi; comments to author 18.03.21; revised version received 24.04.21; accepted 02.05.21; published 27.05.21.*

*Please cite as:*

Akhtar H, Akhtar S, Rahman FU, Afridi M, Khalid S, Ali S, Akhtar N, Khader YS, Ahmad H, Khan MM

*An Overview of the Treatment Options Used for the Management of COVID-19 in Pakistan: Retrospective Observational Study*

*JMIR Public Health Surveill* 2021;7(5):e28594

URL: <https://publichealth.jmir.org/2021/5/e28594>

doi: [10.2196/28594](https://doi.org/10.2196/28594)

PMID: [33945498](https://pubmed.ncbi.nlm.nih.gov/33945498/)

©Hashaam Akhtar, Samar Akhtar, Fazal-Ul Rahman, Maham Afridi, Sundas Khalid, Sabahat Ali, Nasim Akhtar, Yousef S Khader, Hamaad Ahmad, Muhammad Mujeeb Khan. Originally published in *JMIR Public Health and Surveillance* (<https://publichealth.jmir.org>), 27.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Public Health and Surveillance*, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

Original Paper

# YouTube Videos and Informed Decision-Making About COVID-19 Vaccination: Successive Sampling Study

Charles E Basch<sup>1</sup>, PhD; Corey H Basch<sup>2</sup>, EdD, MPH; Grace C Hillyer<sup>3</sup>, EdD, MPH; Zoe C Meleo-Erwin<sup>2</sup>, PhD, MA; Emily A Zagnit<sup>4</sup>, MS, MPH

<sup>1</sup>Teachers College, Columbia University, New York, NY, United States

<sup>2</sup>William Paterson University, Wayne, NJ, United States

<sup>3</sup>Mailman School of Public Health, Columbia University, New York, NY, United States

<sup>4</sup>Milken Institute School of Public Health, George Washington University, Washington, DC, United States

**Corresponding Author:**

Charles E Basch, PhD

Teachers College, Columbia University

525 W 120th St

New York, NY, 10027

United States

Phone: 1 212 678 3983

Email: [ceb35@columbia.edu](mailto:ceb35@columbia.edu)

## Abstract

**Background:** Social media platforms such as YouTube are used by many people to seek and share health-related information that may influence their decision-making about COVID-19 vaccination.

**Objective:** The purpose of this study was to improve the understanding about the sources and content of widely viewed YouTube videos on COVID-19 vaccination.

**Methods:** Using the keywords “coronavirus vaccination,” we searched for relevant YouTube videos, sorted them by view count, and selected two successive samples (with replacement) of the 100 most widely viewed videos in July and December 2020, respectively. Content related to COVID-19 vaccines were coded by two observers, and inter-rater reliability was demonstrated.

**Results:** The videos observed in this study were viewed over 55 million times cumulatively. The number of videos that addressed fear increased from 6 in July to 20 in December 2020, and the cumulative views correspondingly increased from 2.6% (1,449,915 views) to 16.6% (9,553,368 views). There was also a large increase in the number of videos and cumulative views with respect to concerns about vaccine effectiveness, from 6 videos with approximately 6 million views in July to 25 videos with over 12 million views in December 2020. The number of videos and total cumulative views covering adverse reactions almost tripled, from 11 videos with approximately 6.5 million (11.7% of cumulative views) in July to 31 videos with almost 15.7 million views (27.2% of cumulative views) in December 2020.

**Conclusions:** Our data show the potentially inaccurate and negative influence social media can have on population-wide vaccine uptake, which should be urgently addressed by agencies of the United States Public Health Service as well as its global counterparts.

(*JMIR Public Health Surveill* 2021;7(5):e28352) doi:[10.2196/28352](https://doi.org/10.2196/28352)

## KEYWORDS

YouTube; vaccination; COVID-19; social media; communication; misinformation; disinformation; adverse reactions

## Introduction

At the end of 2019, the World Health Organization (WHO) was informed by the Chinese health authorities about a cluster of pneumonia cases, which was shortly thereafter attributed to a novel coronavirus (SARS-CoV-2) [1]. By the end of January 2020, the WHO characterized these outbreaks as a public health emergency [2]. At the time of writing this manuscript,

approximately 1 year following this declaration, over 2 million deaths worldwide [3] had been directly attributed to COVID-19, the disease caused by SARS-CoV-2. At a similar time, the United States' Centers for Disease Control and Prevention (CDC) issued a warning that a variant of SARS-CoV-2, first identified in England in late 2020 and known as “B.1.1.7,” had been detected in at least 10 US states [4]. Research suggests that B.1.1.7, as with other identified variants circulating globally,

is more highly transmissible. The spread of the variant is of great public health concern in terms of repercussions on case counts and, consequently, hospital capacity and eventual mortality [4]. To say that the impacts of the COVID-19 global pandemic on morbidity, mortality, and global economies have been devastating would be a vast understatement. The degree to which the pandemic has exacerbated preexisting economic and health inequities has been staggering. Yet, the record speed with which multiple COVID-19 vaccinations were developed and received emergency use authorization in under a year's time not only provides hope but represents an astounding scientific accomplishment.

In early January 2020, scientists first made the genome sequence of SARS-CoV-2 available on the web [5], and by mid-March 2020, Moderna's experimental messenger RNA (mRNA)-based vaccine entered phase 1 of clinical trials [6]. By early December 2020, regulators in the United Kingdom approved the emergency authorization status for the Pfizer and BioNTech COVID-19 vaccines [7], and 6 days later, the United States Food and Drug Administration (FDA) followed suit [8]. By December 18, 2020, a second mRNA vaccine developed by Moderna was also granted emergency use authorization in the United States by the FDA [9]. Although the rollout of vaccines in many countries has been slower than anticipated [10], as of March 1, 2021, nearly 7.8 billion vaccinations have been administered globally [11]. It is well known that the pipeline from vaccine development to distribution is normally rather slow, in no small part due to the tremendous expense involved. However, the rapid sequencing of the virus (SARS-CoV-2), international scientific collaboration, and government financial support [6] have helped to dramatically speed up the pace in this case. The nature of the mRNA vaccines, which do not require culturing or fermentation but instead rely on synthetic RNA, has further facilitated more rapid development [6].

Despite the highly encouraging safety and efficacy profiles of COVID-19 vaccines that have been granted emergency use authorization, thus far, the very processes that allowed for rapid development have also been a source of public concern, with possible negative effects on the uptake of vaccination [12]. Vaccine hesitancy is multi-factorial phenomenon, often driven by a confluence of factors. Not the least of which is a mistrust of scientific experts and government officials [13], which, for some populations, is grounded in the trauma of racist exploitation, disregard, and injustice [14]. Although vaccine hesitancy has a long history [15,16], it is fair to say that today, the internet facilitates, if not drives, both vaccine misinformation and disinformation [17]. Vaccine misinformation pertains to erroneous conclusions based on incomplete or incorrect facts, whereas vaccine disinformation involves the purposeful spread of falsehoods related to both specific vaccines and vaccination, in general [17]. The spread of misinformation is likely facilitated by fear and misunderstanding of vaccine development and approval processes. In contrast, in the latter case, the intent is clearly nefarious in nature.

Social media platforms have become a dominant communication channel through which people seek and share health-related information [18,19]. Research suggests that this is no less the case for information on COVID-19 [20]. Although different

age cohorts tend to prefer different social media platforms, overall, YouTube is extremely popular, with nearly three-quarters of the US adult population known to have used the platform [21]. Founded in 2005, YouTube has over 2 billion users [22]. YouTube videos can be accessed in 80 different languages, and over a billion hours of video are streamed every day [22]. As with social media platforms in general, health-related content shared on YouTube is often not empirically grounded and yet can easily be accessed [23]. Research on coronavirus-related videos on YouTube is nascent but the results thus far are mixed, with some studies finding that the majority of video content is reliable [24,25], whereas other studies, including those previously undertaken by authors of this study group [26], demonstrating otherwise. At the time of this study, there is little published research on COVID-19 vaccination content on YouTube, with the exception of our previous study that revealed that the majority of videos were uploaded by news outlets and did not contain misinformation [27]. Our prior investigation was conducted relatively early in the pandemic (early-April 2020). Continued monitoring and analysis of social media coverage of COVID-19 vaccine messages is vital to improve its understanding among public health officials about responding to questions and concerns that may produce vaccine hesitance and impede community mitigation. The purpose of this study was, therefore, to build on and update the findings of our previous investigation and add to the repository of scientific knowledge on COVID-19 social media content.

## Methods

Using a cleared browsing history, and the keywords "coronavirus vaccination," we searched YouTube for relevant videos, sorted them by view count, and conducted a successive sampling study. Two successive samples (with replacement) were selected and each included the 100 most widely viewed videos in July and December 2020, respectively. Half of the videos in each sample were independently coded by one researcher (EZ or CHB), and a 10% random sample was coded by both researchers to demonstrate inter-rater reliability (using the Kappa coefficient), which was found to be high ( $\kappa=.969$  in Round 1 and  $\kappa=.963$  in Round 2). Metadata were gathered for each video, including date uploaded, source, length (in minutes), and number of views. A video content checklist developed for this and our prior study of vaccine use on YouTube was based on a CDC fact sheet [27]. Content coverage related to vaccine development, fast-tracking, emergency use authorization, manufacturing, dissemination, eligibility, dosing, herd immunity, concerns about adverse reactions, fear, effectiveness, and immunity duration were dichotomously coded as "present" or "absent." The analysis comprised frequency and percentage distributions for dichotomous content variables and the proportion of total cumulative views garnered by videos addressing each content category. For continuous variables (number of video views and length of video), mean and SD were computed. Analysis was conducted within each of the successive samples using SPSS software (version 25.0; IBM Corp.). At William Paterson University and Columbia University, studies that do not involve human subjects are not

subject to review; the Institutional Review Board at Teachers College of Columbia University reviewed the study protocol and deemed the research exempt from review.

## Results

The videos evaluated in this study were viewed over 55 million times. Twenty-nine of the videos from the July sample were retained in December. The mean length of the videos in the two samples was 7.5 minutes (see [Table 1](#)). Over 80% of the widely viewed videos in each sample originated from television or internet news, whereas fewer than 10% of the videos originated from consumers, professionals, or entertainment television. Between the two rounds, there were 14 professional videos, 7 in each round with 4 overlapping between the rounds. The professional videos in Round 1 comprised 4.4% of the total views (2,403,245/55,086,261) and those in Round 2 comprised 3.8% of the total views (2,157,142/57,506,506).

The vaccine development process was the most covered topic, followed by fast-tracking of the vaccine (see [Table 2](#)). The

vaccine manufacturing process was covered in 31 videos in July 2020 and 36 videos in December 2020, garnering almost one-third of the cumulative views in each sample. There was a 44% increase in the share of cumulative views of videos addressing vaccine dissemination from July (10,197,203/55,086,261, 18.5%) to December 2020 (14,732,085/57,506,506, 25.6%). This is attributable to the approximately 60% increase in videos covering this topic, from 17 in July 2020 to 27 in December 2020. From July to December, videos covering vaccine eligibility more than doubled (from 12 to 25), with the cumulative views increasing from <5.5 million to >9.5 million; however, even in December 2020, videos covering this topic accounted for only 16.8% (9,652,883/57,506,506) of the cumulative views. The number of videos addressing vaccine dosing increased from 4 to 26, and cumulative views of videos addressing dosing increased from 4% (2,217,251 views) to 15.7% (9,017,039 views). There was relatively little change in the percentage of cumulative views garnered by videos addressing herd immunity or the duration of immunity derived from COVID-19 vaccines.

**Table 1.** Characteristics of successive samples of YouTube videos about COVID-19 vaccination, July through December 2020.

Characteristic	Value, n (%)	
	July 2020 (n=100)	December 2020 (n=100)
<b>Video views</b>		
Total views	55,086,261	57,506,506
Mean views (SD)	550,863 (620,691)	575,065 (604,247)
Range	135,729-4,016,406	196,294-4,038,435
<b>Video length (minutes)</b>		
Mean length (SD)	8.2 (9.4)	7.2 (6.3)
Range	0.4-51.4	0.5-35.4
<b>Source</b>		
Consumer	5 (5)	8 (8)
Professional	7 (7)	7 (7)
Television or internet news	84 (84)	81 (81)
Entertainment television	4 (4)	4 (4)

**Table 2.** Content of successive samples of YouTube videos about COVID-19 vaccination, July through December 2020.

Content covered	July 2020			December 2020		
	Number of videos (n)	Number of views (n)	Percentage of cumulative views (%)	Number of videos (n)	Number of views (n)	Percentage of cumulative views (%)
Vaccine development	77	47,745,687	86.7	93	52,907,010	92.0
Fast-tracking	57	31,891,480	57.9	70	40,140,849	69.8
Emergency use authorization	3	593,609	1.1	22	10,132,084	17.6
Vaccine manufacturing	31	17,498,885	31.8	36	18,817,111	32.7
Vaccine dissemination	17	10,197,203	18.5	27	14,732,085	25.6
Vaccine eligibility	12	5,410,203	9.8	25	9,652,883	16.8
Vaccine dosing	4	2,217,251	4.0	26	9,017,039	15.7
Herd immunity	5	2,286,901	4.2	6	3,173,062	5.5
Adverse reactions to the vaccine	11	6,456,465	11.7	31	15,686,832	27.3
Fear	6	1,449,915	2.6	20	9,553,368	16.6
Concerns about effectiveness	6	5,966,961	10.8	25	12,317,526	21.4
Concerns about immunity duration	5	2,415,092	4.4	10	3,953,045	6.9

In contrast, the number of videos that addressed fear increased from 6 (July 2020) to 20 (December 2020), and the corresponding percentage of cumulative views increased from 2.6% (1,449,915 views) to 16.6% (9,553,368 views). There was also a large increase in the number of videos and cumulative views between the two samples with respect to concerns about vaccine effectiveness, from 6 videos with approximately 6 million views to 25 videos with over 12 million views, and a commensurate increase in the proportion of cumulative views (from 10.8% to 21.4%). The number of videos and total cumulative views covering adverse reactions almost tripled from 11 videos with approximately 6.5 million views (11.7% of cumulative views) in July to 31 videos with almost 15.7 million views (27.2% of cumulative views) in December 2020.

## Discussion

Vaccinations have resulted in the eradication of small pox and considerable reductions in measles, mumps, rubella, polio, varicella, and many other infectious diseases [28]. Studying vaccinations historically shows the large time gaps that occur between scientific conceptualization, development, manufacturing, approval, and population-wide uptake. The current pandemic provides a remarkable example of unprecedented speed in developing, testing, and emergency use authorization of multiple vaccines [6,29,30], and bodes well for primary prevention of COVID-19.

The only two ways to achieve primary prevention of COVID-19 is by decreasing exposure to SARS-CoV-2 and evolving variants and reducing susceptibility through active infection or vaccination (although the efficacy of vaccines is less than 100% and the duration of immunity conferred through active infection or vaccination is equivocal). As long as COVID-19 is spreading through communities, social distancing, mask use, and hand hygiene are the best ways for reducing exposure among susceptible people [31-33]. Manufacturing and distributing

vaccines in ways that result in widespread uptake is the key public health strategy for reducing population-wide susceptibility to COVID-19 [34].

Behaviors for reducing exposure and susceptibility both require voluntary decision-making by individuals. Reducing exposure through social distancing, mask use, avoiding crowded or poorly ventilated spaces, and practicing hand hygiene is challenging for many reasons. Not only are there economic pressures for frontline workers to be around others, but because people are inherently social and have been isolated to a greater or lesser degree since the pandemic was declared a global public health emergency by the WHO in January 2020, it is also inevitable that COVID-19 will continue to be transmitted within and among communities. Hence, reducing susceptibility through vaccination provides the greatest long-term hope for primary prevention of COVID-19.

The main public health challenge now is the population-wide vaccine uptake and concomitant herd immunity. Observations in fields ranging from agriculture to technology indicate that something new—in this case, the uptake of a new vaccine—follows predictable patterns of adoption, with some population segments likely to adopt an innovation, and successive population segments adopting at slower rates over time until the last segment—laggards, who are most resistant and may never adopt the innovation [35]. A substantial proportion of the United States [36] and the global [37] population is reportedly hesitant to receive a COVID-19 vaccination. In the United States, population segments that appear most hesitant vary by demographic and social characteristics; for example, those who appear to be more hesitant are women, younger and middle-aged adults, non-Hispanic Black people, adults with lower income and educational attainment and no health insurance, and adults residing in nonmetropolitan areas [36,38]. Various reasons for vaccine hesitancy have been identified, including concerns about

side effects, safety, effectiveness, lack of trust in the government, and how politics has influenced vaccine development [35].

The main implication for public health education is that different messages are more or less relevant to assist different population segments to make informed decisions about vaccination, and the nature of messaging is dynamic and influenced by rapidly changing social context. Communication strategies have been proposed based on the level of vaccine hesitancy [39]. The current challenge is different than those of the past, not only because the speed with which new information about COVID-19 and vaccination effectiveness and availability is being generated but also because of the speed with which information is disseminated throughout the population via social media. Although a very small proportion of serious adverse reactions have occurred following the 76+ million doses of COVID-19 vaccinations administered between December 14, 2020, and March 1, 2021 [40], our results show that the number of widely viewed YouTube videos covering the topic of adverse reactions to COVID-19 vaccine almost tripled from 11 in July to 31 in December 2020, with a commensurate increase in the proportion of cumulative views (from 11.7%, representing 6.4 million views, to 27.2%, representing 15.6 million views). The coverage of concerns about effectiveness more than quadrupled with regard to the number of videos (6 videos in July to 25 videos in December 2020), and almost doubled with regard to the proportion of cumulative views (from 10.8%, representing approximately 6 million views, to 21.4%, representing >12 million views). The extent to which messages are widely viewed can affect consumers' beliefs and decision-making regarding the uptake of COVID-19 vaccination. Public health agencies responsible for helping people make informed decisions about vaccination must, therefore, monitor widely viewed social media on a daily basis to identify and address sources of misinformation and disinformation. In the context of this global public health emergency, we believe social media companies also share this responsibility [41].

A comprehensive national prevention strategy is needed to mitigate further morbidity and mortality caused by COVID-19, and an essential element of this strategy is to discover ways to assist the public in making informed decisions about vaccination [42,43]. Disseminating up-to-date and accurate information through social media is one of the most effective ways to reach a large proportion of the population. To date, public health agencies have had limited effectiveness in achieving this goal. Equally, if not more concerning, is that the efforts by individuals and groups to discourage vaccination are effectively reaching people who are uncertain or ambivalent about being vaccinated

[44]. It is also essential for an effective national prevention strategy to recognize and address other barriers that preclude individuals' ability to make informed decisions about vaccination, such as limited access to the internet necessary to schedule an appointment, loss of income from taking time off from work, and lack of transportation.

This study is delimited in scope in several ways. First, only the time period between July and December 2020 was sampled. The choice of these two points in time was somewhat arbitrary, but represents different pivotal points in the vaccine development process. Second, only 100 videos were included in each sample. Third, only certain content was coded. Fourth, attributes of videos were only examined in relation to the number of views, and we cannot distinguish between the number of views and the number of viewers. We did not have data on the characteristics of viewers such as geography or demographics, nor did we know the extent to which, if any, these videos impacted behavior. Finally, we relied on the keywords "coronavirus vaccine" to search for and sort the videos; thus, we relied on YouTube search algorithms. The main outcome for this study—the number of views—relied on YouTube numbers and sorting algorithms. Despite these delimitations, with the exception of our pilot study [27], we did not identify any published studies examining YouTube videos related to COVID-19 vaccine messages. Although the sample size was small, the videos examined were widely viewed. This study was intended as a stepping-stone to improve understanding about videos that reach a large number of people. This is not only important for reaching the general population with accurate information about vaccinations but also for being aware and responding to disinformation and misinformation that may be disseminated through widely viewed content on social media, and influence the hesitancy of people who are uncertain about receiving a vaccine.

In conclusion, our data show the potentially inaccurate and negative influence social media can have on population-wide vaccine uptake that should be urgently addressed by agencies of the United States Public Health Service as well as its global counterparts. At the time of this study (the second half of 2020), videos uploaded by public health agencies or professionals have had limited presence among the widely viewed YouTube videos that have reached millions of people. Different approaches are needed to understand and address the concerns subgroups of people have about COVID-19 vaccination. Improving the extent to which social media reaches the public with comprehensible, up-to-date, and scientifically accurate information must be a part of a comprehensive national strategy to help people make informed decisions about vaccination.

---

## Conflicts of Interest

None declared.

---

## References

1. Neilson S, Woodward A. A comprehensive timeline of the coronavirus pandemic at 1 year, from China's first case to the present. Insider. 2020 Dec 24. URL: <https://www.businessinsider.com/coronavirus-pandemic-timeline-history-major-events-2020-3> [accessed 2020-03-01]

2. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). World Health Organization. 2020 Jan 30. URL: <https://tinyurl.com/26txmcpr> [accessed 2021-03-01]
3. Ahluwalia S. Global COVID-19 death toll tops 2 million. Thomson Reuters. 2021 Jan 15. URL: <https://www.reuters.com/article/us-health-coronavirus-global-casualties/global-covid-19-death-toll-tops-2-million-idUSKBN29K2EW> [accessed 2021-03-01]
4. Galloway SE, Paul P, MacCannell DR, Johansson MA, Brooks JT, MacNeil A, et al. Emergence of SARS-CoV-2 B.1.1.7 lineage - United States, December 29, 2020-January 12, 2021. *MMWR Morb Mortal Wkly Rep* 2021 Jan 22;70(3):95-99 [FREE Full text] [doi: [10.15585/mmwr.mm7003e2](https://doi.org/10.15585/mmwr.mm7003e2)] [Medline: [33476315](https://pubmed.ncbi.nlm.nih.gov/33476315/)]
5. Paden CR, Tao Y, Queen K, Zhang J, Li Y, Uehara A, et al. Rapid, sensitive, full-genome sequencing of Severe Acute Respiratory Syndrome Coronavirus 2. *Emerg Infect Dis* 2020 Oct;26(10):2401-2405 [FREE Full text] [doi: [10.3201/eid2610.201800](https://doi.org/10.3201/eid2610.201800)] [Medline: [32610037](https://pubmed.ncbi.nlm.nih.gov/32610037/)]
6. Lurie N, Saville M, Hatchett R, Halton J. Developing Covid-19 vaccines at pandemic speed. *N Engl J Med* 2020 May 21;382(21):1969-1973. [doi: [10.1056/nejmp2005630](https://doi.org/10.1056/nejmp2005630)]
7. Ledford H, Cyranoski D, Van Noorden R. The UK has approved a COVID vaccine - here's what scientists now want to know. *Nature* 2020 Dec;588(7837):205-206. [doi: [10.1038/d41586-020-03441-8](https://doi.org/10.1038/d41586-020-03441-8)] [Medline: [33288887](https://pubmed.ncbi.nlm.nih.gov/33288887/)]
8. FDA Takes Key Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for First COVID-19 Vaccine. U.S. Food & Drug Administration. 2020 Dec 11. URL: <https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19#:~:text=Today%2C%20the%20U.S.%20Food%20and,years%20of%20age%20and%20older> [accessed 2021-03-01]
9. Moderna COVID-19 vaccine. U.S. Food & Drug Administration. URL: <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccine> [accessed 2021-03-01]
10. Beaumont P. Covid vaccinations: slow start around world brings dose of reality. *The Guardian*. 2021 Jan 5. URL: <https://www.theguardian.com/world/2021/jan/05/covid-vaccinations-slow-start-around-world-dose-reality> [accessed 2021-03-01]
11. Ritchie H, Ortiz-Ospina E, Beltekian D, Mathieu E, Hasell J, Macdonald B. Coronavirus (COVID-19) vaccinations. Our World in Data. URL: <https://ourworldindata.org/covid-vaccinations> [accessed 2021-03-01]
12. Kekatos M. Nearly 80% of Americans think that the speedy approval process of a coronavirus vaccine is driven by politics—NOT by proof that shots work. *The Harris Poll*. URL: <https://theharrispoll.com/nearly-80-of-americans-think-that-the-speedy-approval-process-of-a-coronavirus-vaccine-is-driven-by-politics-not-by-proof-that-shots-work/> [accessed 2021-03-01]
13. Verger P, Dubé E. Restoring confidence in vaccines in the COVID-19 era. *Expert Rev Vaccines* 2020 Nov;19(11):991-993. [doi: [10.1080/14760584.2020.1825945](https://doi.org/10.1080/14760584.2020.1825945)] [Medline: [32940574](https://pubmed.ncbi.nlm.nih.gov/32940574/)]
14. Warren RC, Forrow L, Hodge DA, Truog RD. Trustworthiness before Trust — Covid-19 Vaccine Trials and the Black Community. *N Engl J Med* 2020 Nov 26;383(22):e121. [doi: [10.1056/nejmp2030033](https://doi.org/10.1056/nejmp2030033)]
15. Harrison EA, Wu JW. Vaccine confidence in the time of COVID-19. *Eur J Epidemiol* 2020 Apr;35(4):325-330 [FREE Full text] [doi: [10.1007/s10654-020-00634-3](https://doi.org/10.1007/s10654-020-00634-3)] [Medline: [32318915](https://pubmed.ncbi.nlm.nih.gov/32318915/)]
16. McAteer J, Yildirim I, Chahroudi A. The VACCINES Act: Deciphering vaccine hesitancy in the time of COVID-19. *Clin Infect Dis* 2020 Jul 28;71(15):703-705 [FREE Full text] [doi: [10.1093/cid/ciaa433](https://doi.org/10.1093/cid/ciaa433)] [Medline: [32282038](https://pubmed.ncbi.nlm.nih.gov/32282038/)]
17. Igoe K. Establishing the truth: Vaccines, social media, and the spread of misinformation. Harvard T.H. Chan School of Public Health. 2019 Jul 10. URL: <https://www.hsph.harvard.edu/ecpe/vaccines-social-media-spread-misinformation/> [accessed 2021-03-01]
18. Fox S. The social life of health information. Pew Research Center. 2014 Jan 15. URL: <https://www.pewresearch.org/fact-tank/2014/01/15/the-social-life-of-health-information/> [accessed 2021-03-01]
19. The Internet and Health. Pew Research Center. 2013 Feb 12. URL: <https://www.pewresearch.org/internet/2013/02/12/the-internet-and-health/>. [accessed 2021-03-01]
20. Larson HJ. A call to arms: helping family, friends and communities navigate the COVID-19 infodemic. *Nat Rev Immunol* 2020 Aug;20(8):449-450 [FREE Full text] [doi: [10.1038/s41577-020-0380-8](https://doi.org/10.1038/s41577-020-0380-8)] [Medline: [32616908](https://pubmed.ncbi.nlm.nih.gov/32616908/)]
21. Perrin A, Anderson M. Share of U.S. adults using social media, including Facebook, is mostly unchanged since 2018. Pew Research Center. 2019 Apr 10. URL: <https://www.pewresearch.org/fact-tank/2019/04/10/share-of-u-s-adults-using-social-media-including-facebook-is-mostly-unchanged-since-2018/> [accessed 2021-03-01]
22. YouTube for Press. URL: <https://www.youtube.com/about/press/> [accessed 2021-03-01]
23. Madathil KC, Rivera-Rodriguez AJ, Greenstein JS, Gramopadhye AK. Healthcare information on YouTube: A systematic review. *Health Informatics J* 2015 Sep;21(3):173-194 [FREE Full text] [doi: [10.1177/1460458213512220](https://doi.org/10.1177/1460458213512220)] [Medline: [24670899](https://pubmed.ncbi.nlm.nih.gov/24670899/)]
24. D'Souza RS, D'Souza S, Strand N, Anderson A, Vogt MNP, Olatoye O. YouTube as a source of medical information on the novel coronavirus 2019 disease (COVID-19) pandemic. *Glob Public Health* 2020 Jul;15(7):935-942. [doi: [10.1080/17441692.2020.1761426](https://doi.org/10.1080/17441692.2020.1761426)] [Medline: [32397870](https://pubmed.ncbi.nlm.nih.gov/32397870/)]



25. Marchal N, Au H, Howard P. Coronavirus News and Information on YouTube: A Content Analysis of Popular Search Terms. COMPROP Data Memo 2020. 2020 Apr 17. URL: <https://comprop.oii.ox.ac.uk/wp-content/uploads/sites/93/2020/04/YouTube-Memo-COVID-19-FINAL.pdf> [accessed 2021-03-01]
26. Basch C, Hillyer G, Meleo-Erwin Z, Jaime C, Mohlman J, Basch C. Preventive behaviors conveyed on YouTube to mitigate transmission of COVID-19: Cross-sectional study. *JMIR Public Health Surveill* 2020 Apr 2;6(2):e18807. [doi: [10.2196/18807](https://doi.org/10.2196/18807)]
27. Basch CH, Hillyer GC, Zagnit EA, Basch CE. YouTube coverage of COVID-19 vaccine development: implications for awareness and uptake. *Hum Vaccin Immunother* 2020 Nov 01;16(11):2582-2585. [doi: [10.1080/21645515.2020.1790280](https://doi.org/10.1080/21645515.2020.1790280)] [Medline: [32701403](https://pubmed.ncbi.nlm.nih.gov/32701403/)]
28. Greenwood B. The contribution of vaccination to global health: past, present and future. *Philos Trans R Soc Lond B Biol Sci* 2014;369(1645):20130433 [FREE Full text] [doi: [10.1098/rstb.2013.0433](https://doi.org/10.1098/rstb.2013.0433)] [Medline: [24821919](https://pubmed.ncbi.nlm.nih.gov/24821919/)]
29. Bloom DE, Cadarette D, Ferranna M, Hyer RN, Tortorice DL. How new models of vaccine development For COVID-19 have helped address an epic public health crisis. *Health Aff (Millwood)* 2021 Mar;40(3):410-418. [doi: [10.1377/hlthaff.2020.02012](https://doi.org/10.1377/hlthaff.2020.02012)] [Medline: [33539191](https://pubmed.ncbi.nlm.nih.gov/33539191/)]
30. Mukherjee S, Barouch D, Hamburg M, Weiss S, Yancopoulos G. Can a vaccine for Covid-19 be developed in record time? *The New York Times Magazine*. 2020 Jun 9. URL: <https://www.nytimes.com/interactive/2020/06/09/magazine/covid-vaccine.html> [accessed 2021-03-01]
31. Social Distancing - Keep a Safe Distance to Slow the Spread. Centers for Disease Control and Prevention. 2020. URL: <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/social-distancing.html> [accessed 2021-03-01]
32. Science Brief: Community Use of Cloth Masks to Control the Spread of SARS-CoV-2. Centers for Disease Control and Prevention. 2020 Nov. URL: <https://www.cdc.gov/coronavirus/2019-ncov/more/masking-science-sars-cov2.html#:~:text=SARS%2DCoV%2D2%20infection%20is,of%20SARS%2DCoV%2D2> [accessed 2021-03-01]
33. Handwashing: Clean Hands Save Lives. Centers for Disease Control and Prevention. URL: <https://www.cdc.gov/handwashing/index.html> [accessed 2021-03-01]
34. Slaoui M, Hepburn M. Developing safe and effective Covid vaccines - Operation Warp Speed's strategy and approach. *N Engl J Med* 2020 Oct 29;383(18):1701-1703. [doi: [10.1056/nejmp2027405](https://doi.org/10.1056/nejmp2027405)]
35. McKee C, Bohannon K. Exploring the reasons behind parental refusal of vaccines. *J Pediatr Pharmacol Ther* 2016;21(2):104-109 [FREE Full text] [doi: [10.5863/1551-6776-21.2.104](https://doi.org/10.5863/1551-6776-21.2.104)] [Medline: [27199617](https://pubmed.ncbi.nlm.nih.gov/27199617/)]
36. Nguyen KH, Srivastav A, Razzaghi H, Williams W, Lindley MC, Jorgensen C, et al. COVID-19 vaccination intent, perceptions, and reasons for not vaccinating among groups prioritized for early vaccination - United States, September and December 2020. *MMWR Morb Mortal Wkly Rep* 2021 Mar 12;70(6):217-222 [FREE Full text] [doi: [10.15585/mmwr.mm7006e3](https://doi.org/10.15585/mmwr.mm7006e3)] [Medline: [33571174](https://pubmed.ncbi.nlm.nih.gov/33571174/)]
37. Lin C, Tu P, Beitsch LM. Confidence and receptivity for COVID-19 vaccines: A rapid systematic review. *Vaccines (Basel)* 2020 Dec 30;9(1):16 [FREE Full text] [doi: [10.3390/vaccines9010016](https://doi.org/10.3390/vaccines9010016)] [Medline: [33396832](https://pubmed.ncbi.nlm.nih.gov/33396832/)]
38. Hamel L, Kirzinger A, Munana C, Brodie M. KFF COVID-19 Vaccine Monitor: December 2020. KFF (Kaiser Family Foundation). 2020 Dec 15. URL: <https://www.kff.org/coronavirus-covid-19/report/kff-covid-19-vaccine-monitor-december-2020/> [accessed 2021-03-01]
39. Wood S, Schulman K. Beyond politics - Promoting Covid-19 vaccination in the United States. *N Engl J Med* 2021 Feb 18;384(7):e23. [doi: [10.1056/nejmms2033790](https://doi.org/10.1056/nejmms2033790)]
40. Selected adverse events reported after COVID-19 vaccination. Centers for Disease Control and Prevention. URL: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html> [accessed 2021-03-01]
41. Donovan J. Social-media companies must flatten the curve of misinformation. *Nature* 2020 Apr 14. [doi: [10.1038/d41586-020-01107-z](https://doi.org/10.1038/d41586-020-01107-z)] [Medline: [32291410](https://pubmed.ncbi.nlm.nih.gov/32291410/)]
42. Lee TH, Chen AH. Last-mile logistics of Covid vaccination - The role of health care organizations. *N Engl J Med* 2021 Feb 25;384(8):685-687. [doi: [10.1056/nejmp2100574](https://doi.org/10.1056/nejmp2100574)]
43. Volpp KG, Loewenstein G, Buttenheim AM. Behaviorally informed strategies for a national COVID-19 vaccine promotion program. *JAMA* 2021 Jan 12;325(2):125-126. [doi: [10.1001/jama.2020.24036](https://doi.org/10.1001/jama.2020.24036)] [Medline: [33315079](https://pubmed.ncbi.nlm.nih.gov/33315079/)]
44. Johnson NF, Velásquez N, Restrepo NJ, Leahy R, Gabriel N, El Oud S, et al. The online competition between pro- and anti-vaccination views. *Nature* 2020 Jun;582(7811):230-233. [doi: [10.1038/s41586-020-2281-1](https://doi.org/10.1038/s41586-020-2281-1)] [Medline: [32499650](https://pubmed.ncbi.nlm.nih.gov/32499650/)]

## Abbreviations

**CDC:** Centers for Disease Control and Prevention  
**FDA:** Food and Drug Administration  
**mRNA:** messenger RNA  
**WHO:** World Health Organization

*Edited by T Sanchez; submitted 02.03.21; peer-reviewed by G Wilmlink, J Lee, N Noreen; comments to author 09.04.21; revised version received 16.04.21; accepted 19.04.21; published 06.05.21.*

*Please cite as:*

*Basch CE, Basch CH, Hillyer GC, Meleo-Erwin ZC, Zagnit EA*

*YouTube Videos and Informed Decision-Making About COVID-19 Vaccination: Successive Sampling Study*

*JMIR Public Health Surveill 2021;7(5):e28352*

*URL: <https://publichealth.jmir.org/2021/5/e28352>*

*doi: [10.2196/28352](https://doi.org/10.2196/28352)*

*PMID: [33886487](https://pubmed.ncbi.nlm.nih.gov/33886487/)*

©Charles E Basch, Corey H Basch, Grace C Hillyer, Zoe C Meleo-Erwin, Emily A Zagnit. Originally published in JMIR Public Health and Surveillance (<https://publichealth.jmir.org>), 06.05.2021. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on <https://publichealth.jmir.org>, as well as this copyright and license information must be included.

---

Publisher:  
JMIR Publications  
130 Queens Quay East.  
Toronto, ON, M5A 3Y5  
Phone: (+1) 416-583-2040  
Email: [support@jmir.org](mailto:support@jmir.org)

---

<https://www.jmirpublications.com/>