# JMIR Public Health and Surveillance

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

## Contents

### Original Papers

## Review

## Corrigenda and Addenda

Original Paper

# Mental Health Presentations Across Health Care Settings During the First 9 Months of the COVID-19 Pandemic in England: Retrospective Observational Study

Gillian E Smith[1,2], MBBS; Sally E Harcourt[1], MPH; Uy Hoang[3], MBBS; Agnieszka Lemanska[3], PhD; Alex J Elliot[1,2], PhD; Roger A Morbey[1,2], PhD; Helen E Hughes[1], PhD; Iain Lake[2,4], PhD; Obaghe Edeghere[1,2], MBBS; Isabel Oliver[5,6], MBBS; Julian Sherlock[3], BSc; Richard Amlôt[2,5,7], PhD; Simon de Lusignan[3,8,9], MBBS

[1]Real-time Syndromic Surveillance Team, Field Service, UK Health Security Agency, Birmingham, United Kingdom

[2]National Institute for Health and Care Research Health Protection Research Unit in Emergency Preparedness and Response, King's College London, London, United Kingdom

[3]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, United Kingdom

[4]School of Environmental Science, University of East Anglia, Norwich, United Kingdom

[5]National Institute for Health and Care Research Health Protection Research Unit in Behavioural Science and Evaluation, Population Health Sciences, University of Bristol, Bristol, United Kingdom

[6]Science Group, UK Health Security Agency, London, United Kingdom

[7]Behavioural Science and Insights Unit, UK Health Security Agency, London, United Kingdom

[8]Faculty of Health and Medical Sciences, University of Surrey, Surrey, United Kingdom

[9]Royal College of General Practitioners, London, United Kingdom

**Corresponding Author:**
Alex J Elliot, PhD
Real-time Syndromic Surveillance Team
Field Service
UK Health Security Agency
2nd Floor 23 Stephenson Street
Birmingham, B2 4BH
United Kingdom
Phone: 44 77407 40944
Email: alex.elliot@ukhsa.gov.uk

## Abstract

**Background:** The COVID-19 pandemic has resulted in an unprecedented impact on the day-to-day lives of people, with several features potentially adversely affecting mental health. There is growing evidence of the size of the impact of COVID-19 on mental health, but much of this is from ongoing population surveys using validated mental health scores.

**Objective:** This study investigated the impact of the pandemic and control measures on mental health conditions presenting to a spectrum of national health care services monitored using real-time syndromic surveillance in England.

**Methods:** We conducted a retrospective observational descriptive study of mental health presentations (those calling the national medical helpline, National Health Service [NHS] 111; consulting general practitioners [GPs] in and out-of-hours; calling ambulance services; and attending emergency departments) from January 1, 2019, to September 30, 2020. Estimates for the impact of lockdown measures were provided using an interrupted time series analysis.

**Results:** Mental health presentations showed a marked decrease during the early stages of the pandemic. Postlockdown, attendances for mental health conditions reached higher than prepandemic levels across most systems—a rise of 10% compared to that expected for NHS 111 and 21% for GP out-of-hours service—while the number of consultations to GP in-hours service was 13% lower compared to the same time previous year. Increases were observed in calls to NHS 111 for sleep problems.

**Conclusions:** These analyses showed marked changes in the health care attendances and prescribing for common mental health conditions across a spectrum of health care provision, with some of these changes persisting. The reasons for such changes are likely to be complex and multifactorial. The impact of the pandemic on mental health may not be fully understood for some time, and therefore, these syndromic indicators should continue to be monitored.

*(JMIR Public Health Surveill 2022;8(8):e32347)* doi:10.2196/32347

**KEYWORDS**

pandemic; public health; syndromic surveillance; mental health; anxiety; sleep problems; COVID-19; health care; health surveillance; health care service

## Introduction

Previous infectious disease outbreaks have been shown to worsen mental health [1]. For example, the severe acute respiratory syndrome (SARS) outbreak in 2003 resulted in increased incidence of posttraumatic stress disorder and depressive illness in health care workers [2]. The COVID-19 pandemic has resulted in an unprecedented impact on peoples' day-to-day lives, with several features potentially adversely affecting mental health. Features include the direct effects of the disease, impact on employment and income, and the prolonged time of restrictions on activities and normal life for the majority of the population.

There is growing research on the size of the impact of COVID-19 on mental health [3-8], much of this from ongoing population surveys using validated mental health scores demonstrating significant impact and that the effect varies across population groups. Young women have been particularly impacted, with higher levels of clinically significant distress [6]. The impacts of previous major coronavirus outbreaks, including the COVID-19 pandemic, on health and social care workers demonstrated a high risk of posttraumatic stress disorder among emergency health care workers [2]. A systematic review of available longitudinal cohort studies concluded a small rise in mental health symptoms immediately after the onset of the pandemic, which dropped to prepandemic levels by mid-2020. A further study examined the impact of the pandemic on primary care–recorded mental health disorders and described a drop in reported illness during March/April 2020. Selected mental health disorders had returned to similar levels by September 2020 in England [3].

However, there is little evidence about how the current pandemic has affected the presentation of mental health conditions to a spectrum of health care settings. We are not aware of work examining the impact of COVID-19 on mental health care usage across multiple health care settings and using routinely available health care data. We hypothesized that common mental health conditions, including depression, anxiety, and sleep disorders, would have been adversely impacted by the first 9 months of the COVID-19 pandemic, and investigated the impact on health care seeking behavior.

Here, we investigated the impact of the COVID-19 pandemic on mental health conditions presenting to a variety of health care services monitored using syndromic surveillance in England. The syndromic surveillance systems use a variety of categorizations to describe the reasons for people presenting, and we tried to identify those presentations that are relevant to mental health. Based on these findings, we proposed a surveillance package of indicators to monitor trends in mental health conditions in real time to provide timely information for action for future events.

## Methods

### Syndromic Surveillance Systems: Background

Syndromic surveillance systems aim to detect outbreaks, to provide situational awareness on the impact of events on the population, and to provide reassurance about the lack of impact of events such as mass gatherings. Real-time syndromic surveillance (using data on patients' symptoms) is a helpful adjunct to laboratory surveillance and is being used to monitor the impact of COVID-19 on health care–seeking behavior for respiratory illness [9]. The UK Health Security Agency (UKHSA) coordinates a suite of national syndromic surveillance systems that are able to monitor attendances to health care settings in England in near real time (Multimedia Appendix 1, Table S1) [10]. These syndromic surveillance systems are used mainly to monitor the impact of infections (eg, COVID-19 and seasonal influenza) [11,12] and the impact of environmental hazards (eg, heatwaves and flooding). However, the utility of syndromic surveillance systems to monitor changes in the presentation of other diseases or conditions (eg, mental health) in the event of a major incident is being explored.

The primary care database of the Oxford-Royal College of General Practitioners (RCGP) Clinical Informatics Digital Hub (ORCHID) is a database from one of the longest-established primary care sentinel networks worldwide [13,14]. The Oxford RCGP network is able to monitor a wide range of diagnoses, in addition to notifiable diseases and other infections. We used a subset of ORCHID, the Oxford-RCGP Research and Surveillance Centre (RSC) UKHSA COVID-19 Vaccine Effectiveness cohort with good data quality (which was developed to support COVID-19 surveillance [15,16]) to explore recent trends in general practitioner (GP) in-hours consultations for common mental health conditions (Multimedia Appendix 1, Table S1).

### Study Design and Period

We conducted a retrospective observational descriptive study using UKHSA real-time syndromic surveillance systems covering the population of England [12] and the ORCHID GP in-hours data set [16]. We estimated the impact of national lockdown measures using an interrupted time series approach and generalized linear modeling. We extracted data for the period of January 1, 2019, to September 30, 2020.

### Surveillance Data

National Health Service (NHS) 111 calls were extracted from the UKHSA Remote Health Advice syndromic surveillance system. NHS 111 uses "pathways" to triage calls [17]. The data extracted included the number of daily calls that were triaged by the NHS 111 call handlers for the "mental health problems" and "sleep difficulties" pathways and the total number of daily calls in the UKHSA data set. The pathways included in the data set for this study were the first pathway selected by the call handler during the triage process (Multimedia Appendix 1, Table S2).

GP in-hours consultations were based on a total of 504 practices, which included 7,057,447 registered patients during the period of this study. We extracted daily counts of consultations and prescriptions for commonly occurring mental health conditions, including depression and anxiety. Prescriptions included antidepressants, anxiolytics, and hypnotics extracted using lists generated based on the British National Formulary (BNF) [18]. We used a case definition of common mental health problems (CMHPs) developed for the evaluation of community psychology services [19,20], which we subsequently updated from a Read code to the Systematized Nomenclature of Medicine (SNOMED) Clinical Terms [21]. The SNOMED clinical terms are listed in Multimedia Appendix 1, Table S2.

Daily GP out-of-hours consultations were extracted from the UKHSA GP out-of-hours syndromic surveillance system [10,22] for the following: total consultations, all consultations with a clinical (Read) code, consultations with a mental health diagnosis (based on Read code chapter E, "Mental Disorders"; Multimedia Appendix 1, Table S2), consultations for anxiety, and consultations for depression.

The UKHSA National Ambulance Surveillance System (NASS) syndromic data set includes data on specified syndromes and does not represent all ambulance calls. There was no overarching mental health indicator for this system, and thus, we extracted the daily number of ambulance calls for overdoses/ingestion/poisoning based on the chief complaint codes used by the ambulance services (Multimedia Appendix 1, Table S2; we assumed that these were all deliberate overdoses/poisonings but acknowledge that some may have been accidental).

Emergency department (ED) attendances were extracted from the UKHSA Emergency Department Syndromic Surveillance System (EDSSS) for all mental health attendances (as identified in the Emergency Care Data Set diagnosis coding list) [23], acute alcohol intoxication, and drug overdoses (Multimedia Appendix 1, Table S2). In total, 94 type 1 EDs were eligible for inclusion as they had provided data to the UKHSA EDSSS every day for the period of the study.

The diagnosis/triage descriptors were not the same across the syndromic systems. For some of the syndromic surveillance systems (eg, the GP in-hours system), there are validated diagnostic codes describing mental health conditions, whereas for others (eg, NHS 111 and ambulance), calls are based on triage groupings. For each system, we tried to identify an overarching mental health categorization or a description for a condition relevant to mental health (eg, sleep disorders). For each surveillance system included in the study, counts of calls/consultations/attendances were extracted by day and by gender.

### Statistical Analysis

Data were visualized graphically as daily counts and 7-day moving averages (7dma, adjusted for public [bank] holidays) for each of the mental health conditions and surveillance systems from January 1 to September 30, 2019, compared to the equivalent dates in 2020. Data were presented graphically by International Organisation for Standardisation (ISO) week (ISO weeks 1-40).

Data were subdivided into 3 periods: prelockdown (before March 23, 2020), lockdown (March 23-May 31, 2020; ISO weeks 13-22), and postlockdown (June 1-September 30, 2020; ISO weeks 23-40). Generalized linear models (GLMs) were used to model the data, and an interrupted time series approach was used to estimate the impact of national lockdown measures and the changes in health care–seeking behavior since pre- and postlockdown compared to 2019. Count data were modeled using a negative binomial distribution to account for overdispersion, which is common in health data. Systematic differences in the daily data caused by weekends and public holidays were accounted for by including a binary variable for working days versus weekends and public holidays. Annual seasonality was modeled by including a harmonic term using Fourier transforms. For each of the 3 periods (pre-, during, and postlockdown), variables were included to model step changes and trends separately. The resulting models were compared with the actual data, and the residuals for signs of bias were checked.

To estimate the impact of lockdown and changes postlockdown, GLMs were used to create counterfactual models of what would have been expected if the pandemic and lockdown had not occurred. The lockdown period (March 23-May 31, 2020) was characterized by a sudden sharp decrease in health care–seeking activity, followed by an increasing trend; therefore, the estimate for the impact of lockdown was based on a single date (March 23, 2020) to show the full extent of the impact. Postlockdown (June 1-September 30, 2020), trends were more stable, so comparing average activity across the whole period provided an estimate for the longer-term impacts. First, the actual data on March 23, 2020, were compared with the counterfactual model for March 23, 2020, setting the variables for the step change and trend during lockdown, to lockdown not having occurred. Second, to estimate how activity has changed postlockdown compared to what we would expect at this time of year, actual activity postlockdown was compared with the counterfactual model.

The advantage of using an interrupted time series approach over simply comparing with the previous year's data is that we could account for any long-term trends and lessen the impact of any short fluctuations in data that would make 2019 incomparable with 2020, thus providing less biased estimates for the direct effects of lockdown. To provide 95% CIs around our estimates for the change in postlockdown activity, a bootstrap method was used to calculate the bias-corrected and accelerated bootstrap interval. The model and formulae used are included in Multimedia Appendix 1.

All statistical analyses were completed in R software (R Foundation for Statistical Computing) using the *Modern Applied Statistics with S* (*MASS*), *tsModel*, and *boot* packages [24-28].

### Ethical Considerations

All data used in this study were anonymized. The UKHSA has access to a range of data sources under Regulation 3 (Health

Protection) of the Health Service (Control of Patient Information) Regulations 2002. The use of ORCHID data was specifically approved by the UKHSA Caldicott Guardian as an addendum to the data sharing agreement with the University of Oxford. Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research.

## Results

### Calls/Consultations/Attendances

From January 1, 2019, to September 30, 2020, the syndromic data included 25,718,106 total calls to NHS 111 (an average of 40,247 daily calls); 1,427,507 GP in-hours mental health consultations (including telephone consultations) in the sentinel network (an average of 2199 daily consultations); 16,090,272 total GP out-of-hours consultations (an average of 25,180 daily consultations), of which 6,307,387 (39.2%) had a clinical code; 9,284,990 total ambulance calls (an average of 14,531 daily calls); and 13,821,306 total ED attendances (an average of 21,630 daily attendances). These figures represent the data routinely available through the syndromic surveillance systems, though coverage of England for each of the systems varies (Multimedia Appendix 1, Table S3).

### All Mental Health Presentations and GP Prescriptions for Mental Health Medications

Calls to NHS 111 triaged using the mental health problem pathways occurred at a slightly increased level at the beginning of 2020 compared to the same time in 2019 and showed an initial peak in mid-February 2020 (ISO week 8); see Figure 1A. Call numbers thereafter decreased to the lowest level on March 19, 2020 (ISO week 12), just before the lockdown commenced (on March 23, 2020; Table 1), and then increased throughout the lockdown and remained elevated throughout the postlockdown period (Figure 1A). Call levels, as estimated by the interrupted time series model, during the postlockdown period (June 1-September 30, 2020) were approximately 10% above expected levels of the counterfactual model (additional daily mean of 62 calls; 95% CI 51-73; Figure 2 and Table 2).

GP in-hours consultations for all mental health conditions began to drop sharply in the week commencing March 2, 2020 (ISO week 10), and continued to fall until the week commencing April 6, 2020 (ISO week 15), when consultations started to rise again, though they remained at reduced levels (Figure 1B). Mean daily levels of GP in-hours consultations for all mental health conditions reduced by 13% in the postlockdown period (June 1-September 30, 2020) compared to those modeled if the pandemic had not occurred (Table 2). Consultations during the whole period were higher in females compared to males (Figure 1B). GP in-hours prescriptions for mental health medications showed a sharp spike just prior to lockdown (Figure 1C), increasing by 27% on March 23, 2020, compared to those expected if the pandemic had not occurred (Table 1), and reduced by 13% compared to those expected for the postlockdown period (Table 2).

Mean daily GP out-of-hours consultations for all mental health conditions occurred at a slightly reduced level at the beginning of 2020 compared to 2019 and then started to decrease from late February 2020 (ISO week 9) to levels on March 23, 2020, approximately 12% below that expected from the model (Table 1). Levels subsequently started to increase, and postlockdown remained elevated until early June (ISO week 23), after which the levels were similar to 2019 (Figure 1D). Mean daily levels of GP out-of-hours consultations for all mental health conditions increased by 21% compared to those expected in the postlockdown period (June 1-September 30, 2020), with an additional daily mean of 23 consultations (95% CI 19-27; Table 2).

ED attendances for all mental health diagnoses occurred at slightly higher levels during the first part of 2020 compared to 2019 (Figure 1E) and, as for other systems, decreased during March and remained low for the first half of the lockdown period (Figure 1E). The number of attendances on March 23, 2020, was 38% below that expected from the counterfactual model (Table 1). Following the period of lockdown (March 23-May 31, 2020), levels returned to those similar to those expected (Figure 2 and Table 2), while total ED attendances reduced by 17%.

**Table 1.** Interrupted time series analysis illustrating a comparison of modeled versus measured call, consultation, attendance, and prescription counts presenting to a number of health care systems: NHS[a] 111, GP[b] in-hours and out-of-hours consultations, ambulance services, and EDs[c] on the first day of lockdown (March 23, 2020).

| System and syndrome | Modeled (ie, if pandemic had not happened) number on first day of lockdown | Actual number on first day of lockdown | Estimated change on first day of lockdown (actual number – modeled number) | Percentage change (%) |
|---|---|---|---|---|
| **NHS 111 calls** | | | | |
| Total calls | 33,104 | 37,572 | 4468 | 13 |
| Mental health problems | 550 | 214 | 336 | –61 |
| Sleep difficulties | 24 | 12 | 12 | –49 |
| **GP in-hours consultations or prescriptions** | | | | |
| Mental health problems | 3155 | 2859 | 296 | –9 |
| Mental health prescriptions | 20,639 | 26,137 | 5496 | 27 |
| Depression | 1560 | 1421 | 139 | –9 |
| Anxiety | 1428 | 1420 | –8 | –1 |
| **GP out-of-hours consultations** | | | | |
| Total consultations | 20,861 | 20,628 | –233 | –1 |
| Mental health | 87 | 76 | –11 | –12 |
| Depression | 18 | 7 | –11 | –60 |
| Anxiety | 49 | 51 | 2 | 4 |
| **Ambulance calls** | | | | |
| Total syndromic calls | 14,705 | 17,156 | 2451 | 17 |
| Overdose/ingestion/poisoning | 509 | 362 | –147 | –29 |
| **ED attendances** | | | | |
| Total attendances | 23,758 | 13,191 | –10,567 | –44 |
| Mental health | 434 | 269 | –165 | –38 |
| Overdose | 182 | 97 | –85 | –47 |
| Excess alcohol use | 162 | 86 | –76 | -47 |

[a] NHS: National Health Service.

[b] GP: general practitioner.

[c] ED: emergency department.

**Figure 1.** Calls, consultations, and attendances for mental health conditions presenting to NHS 111, GP in-hours and GP out-of-hours and EDs, and GP in-hours mental health medications in comparison to selected key dates in the pandemic. (A) NHS 111 calls for mental health problems, (B) GP in-hours consultations for mental health conditions, (C) GP in-hours prescriptions for mental health medications, (D) GP out-of-hours consultations for all mental health conditions, and (E) ED attendances for mental health conditions. Daily calls/consultations/attendances/prescriptions presented as 7dma adjusted for bank holidays (BH) and by gender. The start of lockdown (March 23, 2020) and the start of the postlockdown period (June 1, 2020) are indicated by vertical lines. 7dma: 7-day moving averages; ED: emergency department; GP: general practitioner; ISO: International Organisation for Standardisation; NHS: National Health Service.

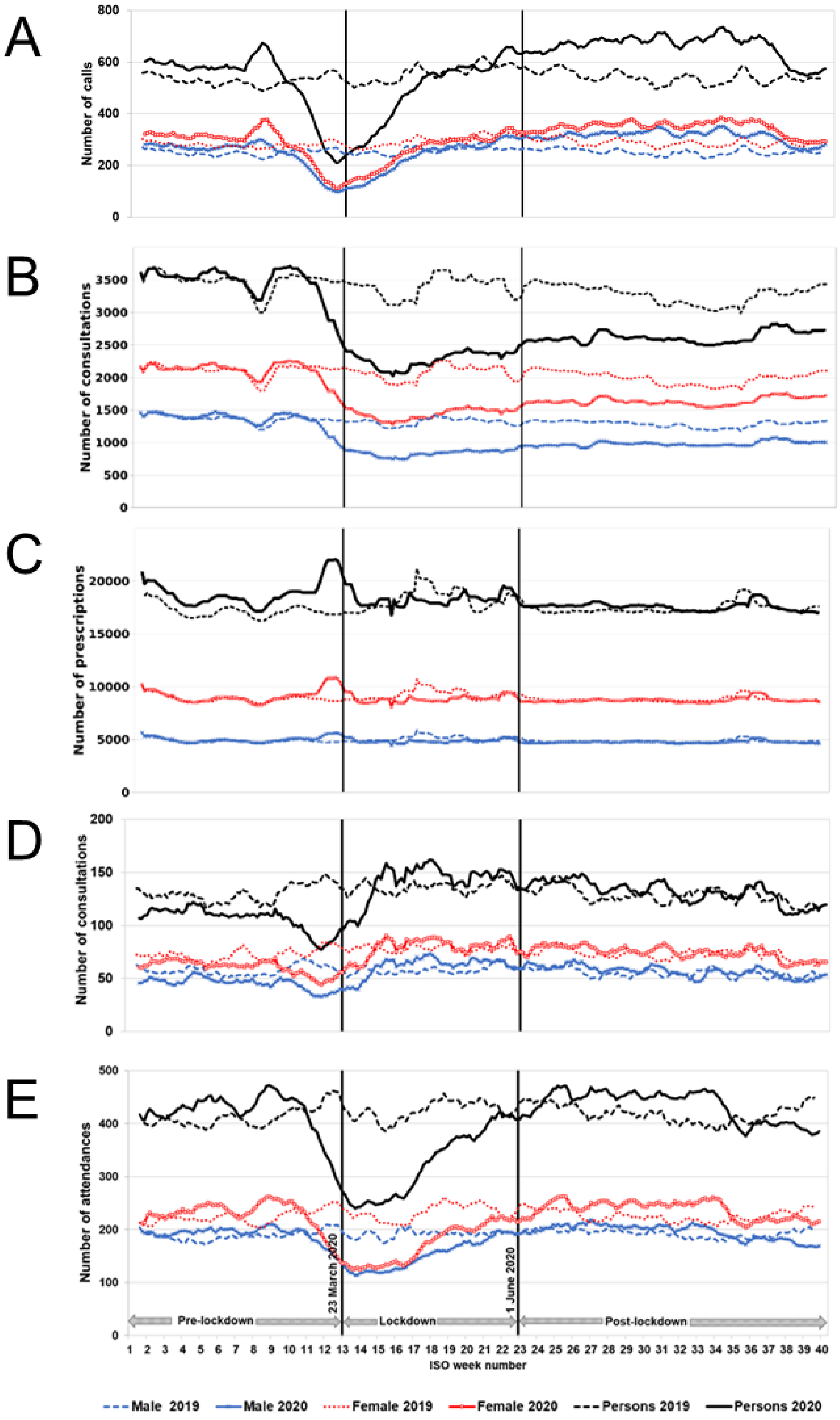


**Figure 2.** Summary of changes in syndromic indicators for the postlockdown period across systems compared to that expected. GP: general practitioner; NHS: National Health Service.

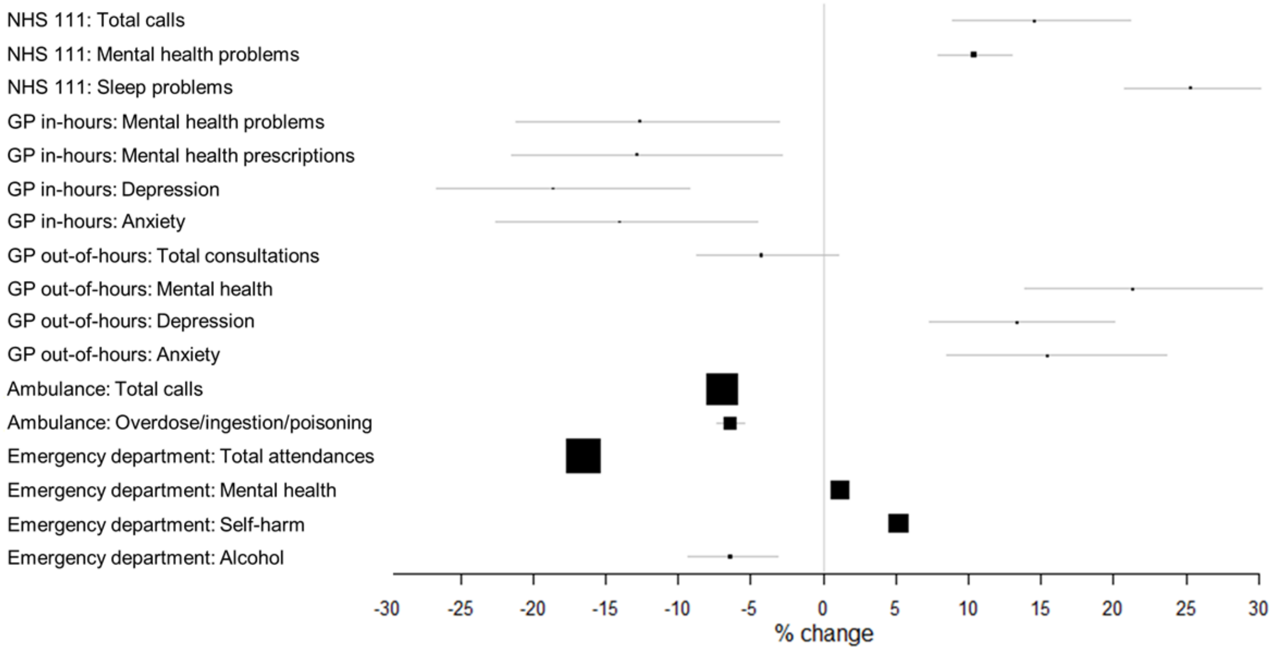


**Table 2.** Interrupted time series analysis illustrating a comparison of modeled versus measured call, consultation, attendance, and prescription counts presenting to a number of health care systems: NHS[a] 111, GP[b] in-hours and out-of-hours consultations, ambulance services, and EDs[c] during the postlockdown period (June 1-September 30, 2020).

| System and syndrome | Modeled (ie, if pandemic had not happened) daily mean number in postlockdown period, estimate (95% CI) | Actual daily mean number in postlockdown period | Estimated difference due to pandemic in daily mean postlockdown period, estimate (95% CI) | Percentage change (%) |
|---|---|---|---|---|
| **NHS 111 calls** | | | | |
| Total calls | 37,606 (35,553-39,532) | 43,071 | 5465 (4653-6295) | 15 |
| Mental health problems | 599 (585-613) | 661 | 62 (51-73) | 10 |
| Sleep difficulties | 27 (26-28) | 34 | 7 (5-8) | 25 |
| **GP in-hours consultations or prescriptions** | | | | |
| Mental health problems | 2178 (1963-2414) | 1903 | –275 (–317 to –232) | –13 |
| Mental health prescriptions | 14,592 (13,093-16,197) | 12722 | –1870 (–2342 to –1392) | –13 |
| Depression | 1090 (978-1210) | 887 | –202 (–229 to –176) | –19 |
| Anxiety | 1022 (920-1134) | 878 | –144 (–166 to –122) | –14 |
| **GP out-of-hours consultations** | | | | |
| Total consultations | 24,444 (23,149-25,634) | 23,391 | –1053 (–1562 to –512) | –4 |
| Mental health | 109 (101-116) | 132 | 23 (19-27) | 21 |
| Depression | 20 (18-21) | 22 | 3 (2-4) | 13 |
| Anxiety | 62 (58-66) | 71 | 10 (7-12) | 15 |
| **Ambulance calls** | | | | |
| Total syndromic calls | 14,883 (14,827-14,938) | 13,842 | –1041 (–1194 to –889) | –7 |
| Overdose/ ingestion/ poisoning | 571 (566-577) | 535 | –37 (–45 to –28) | –6 |
| **ED attendances** | | | | |
| Total attendances | 23,865 (23,776-23,959) | 19,925 | –3940 (–4201 to –3681) | –17 |
| Mental health | 428 (426-431) | 433 | 5 (–1 to 11) | 1 |
| Overdose | 179 (178-180) | 188 | 9 (6-12) | 5 |
| Excess alcohol use | 198 (192-205) | 186 | –13 (–17 to –8) | –6 |

[a] NHS: National Health Service.

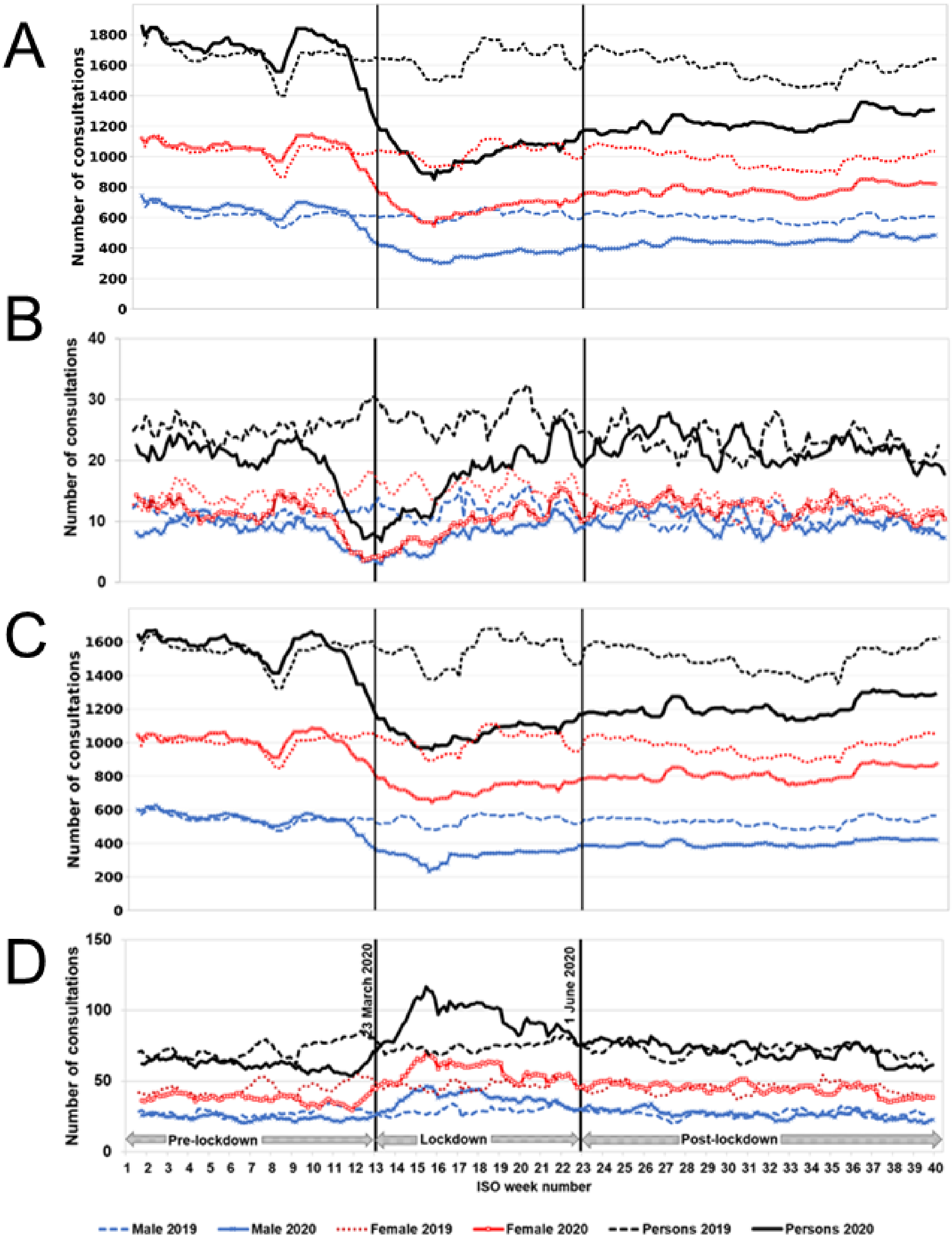
[b] GP: general practitioner.

[c] ED: emergency department.

## Depression

GP in-hours consultations for depression showed a similar pattern to all mental health conditions (Figure 3A). Mean daily levels of GP in-hours consultations for depression showed a decrease of 19% in the postlockdown period (June 1-September 30, 2020) compared to that expected had the pandemic not occurred (Table 2). GP out-of-hours consultations for depression showed a similar pattern to all mental health conditions (Figure 3B). Mean daily levels of GP out-of-hours consultations for depression showed an increase of 13% in the postlockdown period, although daily numbers were small (Figure 2 and Table 2).

**Figure 3.** Consultations for depression and anxiety presenting to GP in-hours and out-of-hours in comparison to selected key dates in the pandemic. (A) GP in-hours consultations for depression, (B) GP out-of-hours consultations for depression, (C) GP in-hours consultations for anxiety, and (D) GP out-of-hours consultations for anxiety. Daily consultations presented as 7dma adjusted for bank holidays (BH) and by gender. The start of the lockdown (March 23, 2020) and the start of the postlockdown period (June 1, 2020) are indicated by vertical lines. 7dma: 7-day moving averages; GP: general practitioner; ISO: International Organisation for Standardisation.



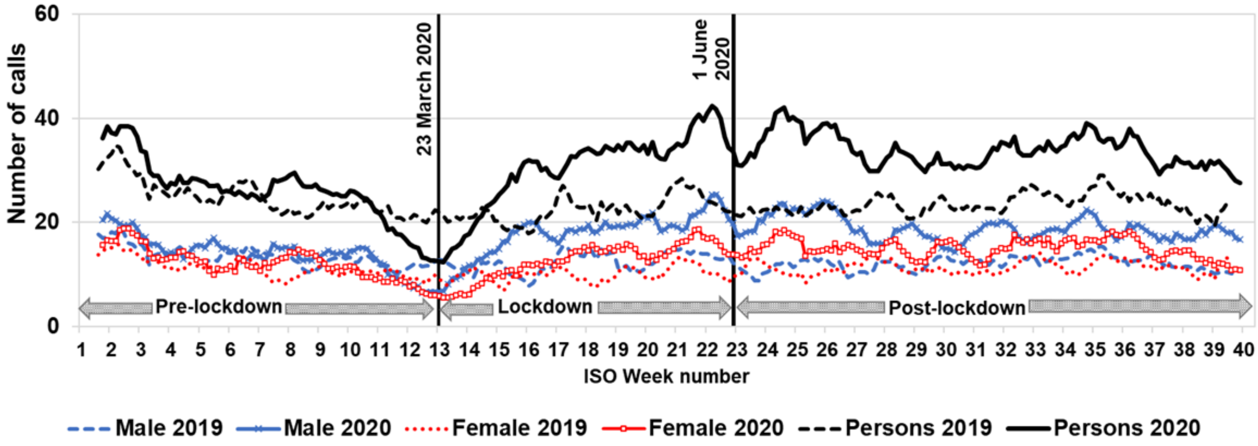
## Anxiety

GP in-hours consultations for anxiety reduced as the lockdown approached with the introduction of social distancing measures and remained below levels seen in 2019 for the remainder of the study period (Figure 3C). In the postlockdown period (June 1-September 30, 2020), total consultations for anxiety were 14% below modeled expected levels if the pandemic had not occurred (Figure 2 and Table 2). GP out-of-hours consultations for anxiety were below levels seen in 2019 but relatively stable until mid-March (ISO week 11), after which levels rose until a peak on April 9, 2020 (ISO week 15; Figure 3D). Overall anxiety consultations remained 15% above expected levels (had the pandemic not occurred) during the postlockdown period (Figure 2 and Table 2). GP consultations (in-hours/out-of-hours) for anxiety were higher in females than in males in both 2019 and 2020 (Figures 3C and 3D).

## Sleep Difficulties

Calls to NHS 111 triaged for sleep difficulties fell sharply in January 2020, a trend also seen in January 2019. Calls to NHS 111 for sleep difficulties rose slightly in mid-February 2020 (ISO week 8; Figure 4) and then reduced to a low of approximately 50% of expected levels at the start of lockdown on March 23, 2020 (Table 1). Thereafter, calls for sleep difficulties increased to 25% above modeled expected levels in the postlockdown period (June 1-September 30, 2020; Table 2). Calls for sleep difficulties for males were higher than those for females, but calls by both genders peaked just before lockdown easing commenced at the beginning of June 2020 (ISO week 23; Figure 4).

**Figure 4.** Calls to NHS 111 for sleep difficulties in comparison to selected key dates in the pandemic. Daily numbers of calls presented as bank holiday (BH)-adjusted 7dma and by gender. The start of the lockdown (March 23, 2020) and the start of the postlockdown period (June 1, 2020) are indicated by vertical lines. 7dma: 7-day moving averages; ISO: International Organisation for Standardisation; NHS: National Health Service.

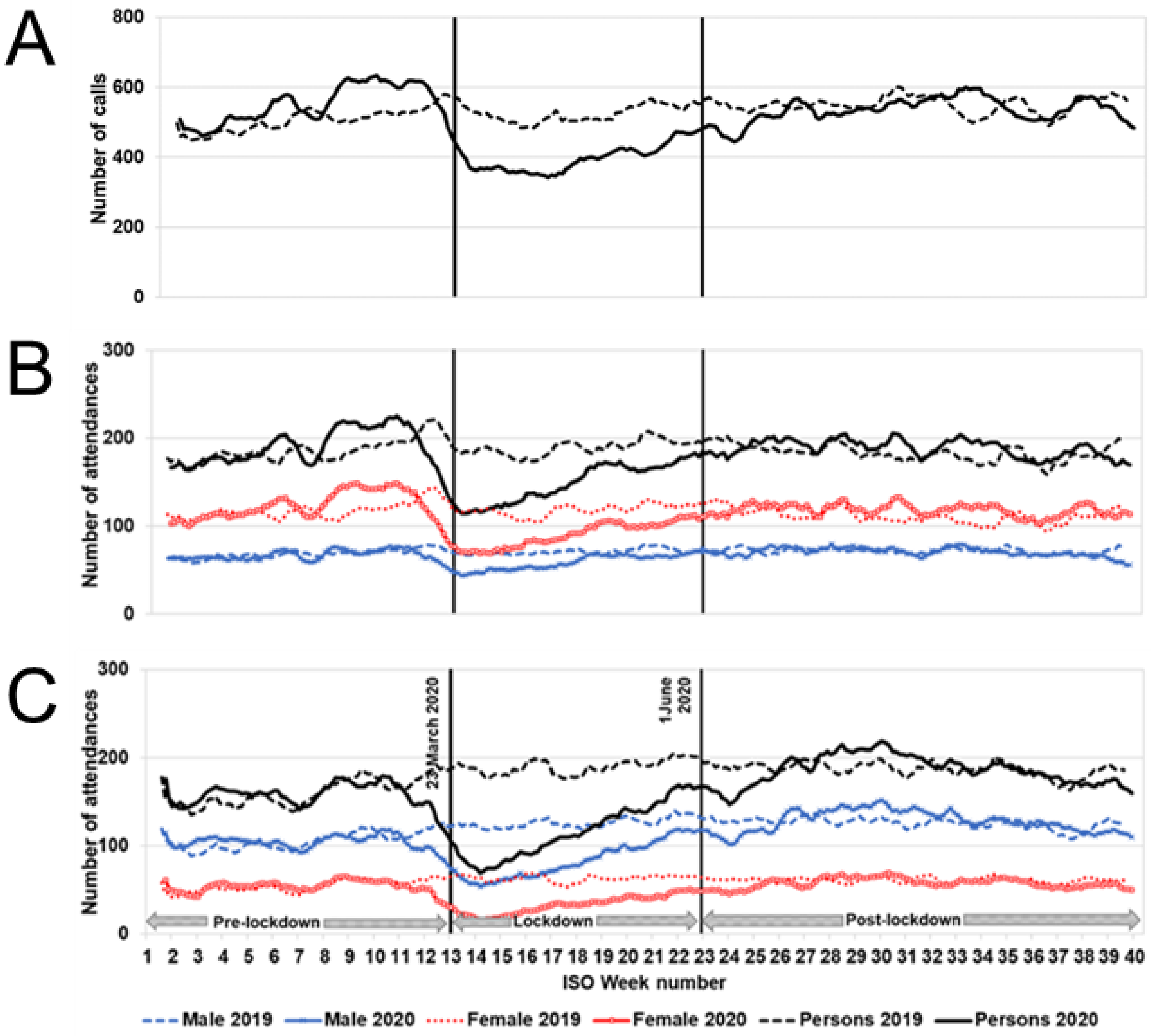


## Measures of Self-Harm

### *Overdose*

From January 2020 to the announcement of stay-at-home and social distancing advice on March 11, 2020 (ISO week 11), ambulance calls for overdose/ingestion/poisoning increased and then sharply decreased until the start of lockdown (March 23, 2020; Figure 5A), when calls reduced by 29% compared to those expected from the model (Table 1). From the start of lockdown, the number of calls gradually increased, and during the postlockdown period (June 1-September 30, 2020), calls were slightly reduced at 6% lower than estimated had the pandemic not occurred (37 fewer mean daily call-outs; 95% CI –45 to –28; Table 1).

**Figure 5.** Ambulance calls and ED attendances for indicators of self-harm (overdose and excess alcohol use) in comparison to selected key dates in the pandemic. (A) Ambulance calls for overdose, (B) ED attendances for overdose, and (C) ED attendances for excess alcohol use. Daily numbers of call-outs/attendances presented as bank holiday (BH)-adjusted 7dma and by gender (ED only). The start of lockdown (March 23, 2020) and the start of the postlockdown period (June 1, 2020) are indicated by vertical lines. 7dma: 7-day moving averages; ED: emergency department; ISO: International Organisation for Standardisation.



Attendances at EDs for overdoses markedly increased during January and February 2020 (particularly in females) compared to 2019 (Figure 5B). Attendances showed a sharp drop following the introduction of social distancing advice on March 11, 2020 (ISO week 11), and by the start of lockdown (March 23, 2020), levels reduced by 47% compared to those expected using the model (Table 1). This was followed by a gradual increase to levels similar to 2019 (and for both genders) during the postlockdown period (June 1-September 30, 2020; Figure 5B).

### *Excess Alcohol Use*

Attendances to EDs for excess alcohol use showed a drop following the introduction of social distancing advice in early March 2020 (ISO week 11) and continued to drop at the start of lockdown (March 23, 2020; Figure 5C). The interrupted time series model estimated that there were 47% fewer attendances than expected on March 23, 2020 (Table 1). During lockdown (March 23-May 31, 2020), there was a gradual increase, with levels postlockdown (June 1-September 30, 2020) only slightly reduced (6%) compared to those expected using the model (Table 2). Attendances were consistently higher in males than in females.

## Discussion

### Principal Findings

Looking across the health care systems, all showed an initial dip in attendance for mental health conditions after the introduction of social distancing advice in early March 2020 and the first lockdown and then increased. This pattern mirrored total (all cause) activity in each system and attendances for other non-COVID-19 conditions [10]. For NHS 111 and GP out-of-hours services, mental health activity levels postlockdown increased (by 10% for NHS 111 and 21% for GP out-of-hours services). The levels of GP in-hours consultations for mental health remained approximately 13% lower compared to modeled levels expected if the pandemic had not occurred. It is possible that there has been a shift in consulting on mental health conditions from GP in-hours services to other health services, such as NHS 111 and GP out-of-hours services.

GP in-hours health care contacts for depression mirrored those for all mental health attendances, showing a decrease during the prelockdown (before March 23, 2020) and lockdown periods and then returning to levels approximately a fifth lower than those expected. GP out-of-hours health care contacts for depression mirrored those for other attendances, showing a decrease during the prelockdown (before March 23, 2020) and lockdown periods and then returning to levels about 13% increased to those expected (although daily numbers were low).

The number of GP contacts for anxiety showed different patterns in-hours and out-of-hours. GP in-hours contacts decreased and remained 14% lower compared to those expected during the postlockdown period. GP out-of-hours health care contacts for anxiety increased during lockdown and remained at about 15% above expected levels during the postlockdown period.

Health care contacts to NHS 111 for sleep disorders increased during lockdown and then remained elevated until the end of the study period. Daily numbers of calls to NHS 111 about sleep difficulties increased by approximately a quarter in the postlockdown period to those expected; thus, there was a persisting and notable continuing impact.

## Surveillance of Mental Health During COVID-19

The COVID-19 pandemic has resulted in several surveillance initiatives to monitor the impact of the pandemic on mental health. The UKHSA publishes a regular overview of such impact (particularly using population surveys, longitudinal studies, and results from academic studies) [29]. Analysis using the Clinical Practice Research Datalink (CPRD) showed similar trends as our study, with a marked reduction in GP in-hours consultations for a variety of mental health conditions and a persisting impact with reduced levels of consultations lasting until July 2020 [5]. The authors used an interrupted time series approach using weekly data, taking the exposure as the introduction of lockdown and comparing back to 2017. The authors described the likely unmet need for mental health services and highlighted the need to prepare for increased demand. Reports from the Nuffield Trust and the NHS Confederation found evidence that fewer people were able to access mental health services during the first lockdown. New referrals for treatment and support for common mental health conditions, such as depression and anxiety, provided by the Improving Access to Psychological Therapies (IAPT) program fell by 61% over the first lockdown [30,31]. This was reflected in a survey of 130 countries by the World Health Organization (WHO) during June-August 2020, which reported widespread disruptions to many critical mental health services [32,33].

A further study used primary care electronic health records to examine the impact of the pandemic on mental health conditions presenting to GPs and showed a drop in reported illness during March/April 2020. Selected mental health disorders had returned to similar levels by September 2020 in England; however, the rates of incident depression and anxiety disorder remained a third lower in the rest of the United Kingdom (UK), consistent with the sustained reduction we noted in presentations to GP in-hours consultations [3].

Results from 2 longitudinal UK population cohorts showed that anxiety and lower well-being, but not depression, increased during the COVID-19 pandemic compared to prepandemic assessments. The percentage of individuals with probable anxiety disorder was almost double during the COVID-19 pandemic [4]. Our study, focusing on health care–seeking behavior, showed similar increases in anxiety presenting to GP out-of-hours service but, conversely, reductions in anxiety presenting to GP in-hours service (again likely reflecting the overall reduction in people presenting for all causes).

The marked and continuing impact of the pandemic on good sleep is described in other studies (our work suggesting a 25% increase in calls, as monitored by NHS 111); in the UK, those experiencing sleep problems increased from 16% to 25% in April 2020 [29]. In Italy, during the period of lockdown, 42% people reported sleep disturbances, with 17% [34] disturbances described as moderate or severe; and in a cross-sectional survey in France, 19% people were categorized as having insomnia [35]. A study in the United States using ED syndromic surveillance showed a similar reduction in consulting for a variety of mental health conditions in early March, but the median visit rates for suicide attempts and overdoses for the period of mid-March 2020 to October 2020 were higher than the rates for the same period in 2019 [36]. Finally, real-time surveillance used Google trend data to assess the impact of the pandemic on mental health in the United States, identifying pandemic-associated spikes in anxiety [37].

## Syndromic Surveillance of Mental Health Following Incidents

There are examples of syndromic surveillance systems being used to monitor the impact on mental health after public health incidents. Such systems have been predominantly using a single data source rather than across health care services and include the use of ED [38] and Twitter (social media) [39] analysis following terrorist attacks in France. ED surveillance for mental health in New York State was conducted post–Hurricane Sandy [40], and ED surveillance of attendances for mental health and substance use presenting to Californian EDs concluded that mental health data from syndromic systems are uniquely available in real time as an indicator of service utilization and thus particularly useful for emergency events [41].

Although not included in our study, the Improved Access to Psychological Therapies (IAPT) program in England also offers a service to people with CMHPs. IAPT principally offers cognitive behavioral therapies, and people can be referred or can self-refer. IAPT reports a reduction in referral (including self-referral), entering and completing therapy, postlockdown (Multimedia Appendix 1, Figure S1) [42].

## Strengths and Limitations

This work has several strengths. It describes impact on health care–seeking behavior for mental health conditions across a variety of health care provisions ranging from NHS telephone help lines to ED attendances. The surveillance systems used here are well established and cover England (although several are sentinel systems). Such diversity of surveillance systems enables us to triangulate and describe both consistent trends across systems and to look for changes in severity.

The multiple health care systems on which these surveillance systems are based use various coding systems/triage mechanisms, and thus, we have established different data sets but similar diagnostic/syndromic groupings to enable a multiple cross-condition "snapshot" for monitoring the impact of future major public health incidents. Although we analyzed these data retrospectively, we now have a "common mental health" presentation surveillance package, including an ontology of relevant codes across the multiple systems, which can be prospectively incorporated into routine monitoring, thus enabling the real-time use for mental health surveillance with validated baselines for future events. Such a suite of indicators will provide timely information for incident directors and those managing incidents as to where resources may be needed at the time of an incident and subsequently. Such analyses could additionally include assessing the impact by age, sex, severity, and geography. These data are available in near real time (daily except for the ORCHID system, which is twice weekly), and further work includes establishing which of the indicators are most useful in assessing the impact of differing types of incidents (eg, epidemics, deliberate incidents, and flooding) and exploring inequalities in access.

There are, however, several limitations to this work: The changes in health care provision and guidance issued to the public on which services to use during the pandemic will have impacted on established baselines, causing difficulties in interpretation of changes in consulting. For example, the observed change in consulting numbers may have been driven either by true changes in incidence or by the national advice not to consult in person with a GP. It is also possible that other changes in the scheduled GP service, such as greater use of text messaging or online consultations, may have meant that not all encounters were captured or be recorded as "clinical administration" within the GP computerized medical record. The move to 15-minute appointments may have also contributed to the fall in consultation numbers [43].

Using routinely available health care data, it is difficult to disentangle true changes in the incidence of mental health conditions from the effect of public health messaging, health care–seeking behavior, and changes in health care provision. These multiple and complex drivers of change have made interpretation of surveillance data difficult during the COVID-19 pandemic [11]. We focus here on the cross–health care usage for syndromes associated with mental health and describe trends, rather than directly inferring changes in community incidence.

The changing trends we have observed are likely to reflect the "tip of the iceberg" in terms of mental health impact on the community. It is known that most patients with mental health conditions or poor well-being are likely to self-care or not seek help from a health care provider [44-46]. Further work is needed to understand the impact of this pandemic on mental health and well-being. This work has established a surveillance package that can be applied to routine public health surveillance programs to undertake real-time surveillance of mental health presentations during future major health protection incidents.

## Conclusion

These analyses showed marked changes in the health care attendances and prescribing for common mental health conditions, across a spectrum of health care provision, with some of these changes persisting. The reasons for such changes are likely to be complex and multifactorial. The impact of the pandemic on mental health may not be fully understood for some time, and therefore, these syndromic indicators should continue to be monitored.

## Acknowledgments

The authors acknowledge the contribution and support from all syndromic data providers, including: National Health Service (NHS) 111, NHS England, Gareth Studdard, NHS Digital; Oxford-Royal College of General Practitioners Clinical Informatics Digital Hub (ORCHID) practices and patients; Advanced Health & Care, Alex Yates, and the participating general practitioner (GP) out-of-hours service providers; North East, North West, Yorkshire, East Midlands, West Midlands, East of England, London, South East Coast, South Central, and South Western NHS Ambulance Trusts and the Association of Ambulance Chief Executives; and emergency departments participating in the Emergency Department Syndromic Surveillance System (EDSSS) and the Royal College of Emergency Medicine, Tom Hughes, and Kirsty Challen. We also thank Paul Loveridge for data extraction.

GES, AJE, RAM, IL, and RA receive support from the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Emergency Preparedness and Response at King's College London in partnership with the UK Health Security Agency (UKHSA), in collaboration with the University of East Anglia. IO receives support from the NIHR HPRU in Behavioral Science and Evaluation at the University of Bristol. GES, AJE, HEH, IL, and OE receive support from the NIHR HPRU in Gastrointestinal Infections at the University of Liverpool. AL received support from the National Physical Laboratory (NPL), UK, through the cross-theme National Measurement Strategy under the Life Sciences & Health care theme (Digital Health [12247] Data Curation program), which was funded by the Department for Business, Energy and Industrial Strategy (BEIS). The views expressed are those of the authors and not necessarily those of the NIHR, the UKHSA, or the Department of Health and Social Care.

## Data Availability

The data sets used in this study are not publicly available. The aggregated data used for the time series analyses can be made available on request through the UK Health Security Agency (UKHSA) Office for Data Release. The Oxford-Royal College of General Practitioners Clinical Informatics Digital Hub (ORCHID) data can be accessed by researchers. Approval is on a project-by-project basis. Ethical approval by a UK National Health Service Research Ethics Committee is needed before any data release or other appropriate approval. Researchers wishing to directly analyze patient-level pseudonymized data will be required to complete information governance training and work on the data from the secure servers at the University of Oxford. Patient-level data cannot be taken out of the secure network. We encourage interested researchers to attend the short courses on how to analyze primary care or Royal College of General Practitioners (RCGP) Research and Surveillance Centre data, which are open to enrolment twice a year.

## Authors' Contributions

GES, SEH, SdeL, and AJE conceived the study; SEH, AL, HEH, and RAM extracted data and performed the data analysis; RAM provided statistical support for the analysis; and GES, SEH, AL, UH, and RAM wrote the first draft of the manuscript. All authors drafted the manuscript for important intellectual content, contributed to revision of the final version of the manuscript, and approved the final version submitted.

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

## Conflicts of Interest

SdeL has received funding through his university for vaccine-related research from AstraZeneca, GSK, Sanofi, Seqirus, and Takeda. He has also been a member of advisory boards for AstraZeneca, Sanofi, and Seqirus. All other authors have none to declare.

Multimedia Appendix 1
Supplementary file including tables, figures, and scripts.
[DOCX File , 242 KB - publichealth_v8i8e32347_app1.docx ]

## References

1. Scobie G, Whitehead E. What Are the Impacts of Past Infectious Disease Outbreaks on Non-communicable Health Outcomes?. URL: http://www.healthscotland.scot/media/3187/impacts-of-past-infectious-disease-outbreaks-on-non-communicable-health-outcomes-sep20-english.pdf [accessed 2022-01-09]
2. Carmassi C, Foghi C, Dell'Oste V, Cordone A, Bertelloni CA, Bui E, et al. PTSD symptoms in healthcare workers facing the three coronavirus outbreaks: what can we expect after the COVID-19 pandemic. Psychiatry Res 2020 Oct;292:113312 [FREE Full text] [doi: 10.1016/j.psychres.2020.113312] [Medline: 32717711]
3. Carr MJ, Steeg S, Webb RT, Kapur N, Chew-Graham CA, Abel KM, et al. Effects of the COVID-19 pandemic on primary care-recorded mental illness and self-harm episodes in the UK: a population-based cohort study. Lancet Public Health 2021 Feb;6(2):e124-e135. [doi: 10.1016/s2468-2667(20)30288-7]
4. Kwong ASF, Pearson RM, Adams MJ, Northstone K, Tilling K, Smith D, et al. Mental health before and during the COVID-19 pandemic in two longitudinal UK population cohorts. Br J Psychiatry 2021 Jun 24;218(6):334-343 [FREE Full text] [doi: 10.1192/bjp.2020.242] [Medline: 33228822]
5. Mansfield KE, Mathur R, Tazare J, Henderson AD, Mulick AR, Carreira H, et al. Indirect acute effects of the COVID-19 pandemic on physical and mental health in the UK: a population-based study. Lancet Digital Health 2021 Apr;3(4):e217-e230. [doi: 10.1016/s2589-7500(21)00017-0]
6. Pierce M, Hope H, Ford T, Hatch S, Hotopf M, John A, et al. Mental health before and during the COVID-19 pandemic: a longitudinal probability sample survey of the UK population. Lancet Psychiatry 2020 Oct;7(10):883-892. [doi: 10.1016/s2215-0366(20)30308-4]
7. University College London. COVID-19 Social Study. URL: https://www.covidsocialstudy.org/ [accessed 2021-06-17]
8. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. Brain Behav Immun 2020 Oct;89:531-542 [FREE Full text] [doi: 10.1016/j.bbi.2020.05.048] [Medline: 32485289]
9. UK Health Security Agency. National Flu and COVID-19 Surveillance Reports. URL: https://www.gov.uk/government/statistics/national-flu-and-covid-19-surveillance-reports [accessed 2021-06-17]
10. UK Health Security Agency. Syndromic Surveillance: Systems and Analyses. URL: https://www.gov.uk/government/collections/syndromic-surveillance-systems-and-analyses [accessed 2021-06-17]

11. Elliot AJ, Harcourt SE, Hughes HE, Loveridge P, Morbey RA, Smith S, et al. The COVID-19 pandemic: a new challenge for syndromic surveillance. Epidemiol Infect 2020 Jun 18;148:e122 [FREE Full text] [doi: 10.1017/S0950268820001314] [Medline: 32614283]
12. Elliot A, Morbey R, Hughes H, Harcourt S, Smith S, Loveridge P, et al. Syndromic surveillance: a public health legacy of the London 2012 Olympic and Paralympic Games. Public Health 2013 Aug;127(8):777-781. [doi: 10.1016/j.puhe.2013.05.007] [Medline: 23870845]
13. de Lusignan S, Correa A, Smith GE, Yonova I, Pebody R, Ferreira F, et al. RCGP Research and Surveillance Centre: 50 years' surveillance of influenza, infections, and respiratory conditions. Br J Gen Pract 2017 Sep 29;67(663):440-441. [doi: 10.3399/bjgp17x692645]
14. University of Oxford. Oxford-Royal College of General Practitioners Clinical Informatics Digital Hub. URL: https://orchid.phc.ox.ac.uk/ [accessed 2022-03-10]
15. Correa A, Hinton W, McGovern A, van Vlymen J, Yonova I, Jones S, et al. Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) sentinel network: a cohort profile. BMJ Open 2016 Apr 20;6(4):e011092 [FREE Full text] [doi: 10.1136/bmjopen-2016-011092] [Medline: 27098827]
16. de Lusignan S, Jones N, Dorward J, Byford R, Liyanage H, Briggs J, et al. The Oxford Royal College of General Practitioners Clinical Informatics Digital Hub: protocol to develop extended COVID-19 surveillance and trial platforms. JMIR Public Health Surveill 2020 Jul 02;6(3):e19773 [FREE Full text] [doi: 10.2196/19773] [Medline: 32484782]
17. NHS Digital. NHS Pathways. URL: https://digital.nhs.uk/services/nhs-pathways [accessed 2021-06-17]
18. BNF Publications. URL: https://www.bnf.org/ [accessed 2022-06-16]
19. Chan T, Cohen A, de Lusignan S. Using routine data to conduct small area health needs assessment through observing trends in demographics, recording of common mental health problems (CMHPs) and sickness certificates: longitudinal analysis of a northern and London locality. Inform Prim Care 2010 Dec 01;18(4):273-282 [FREE Full text] [doi: 10.14236/jhi.v18i4.782] [Medline: 22040854]
20. de Lusignan S, Chan T, Parry G, Dent-Brown K, Kendrick T. Referral to a new psychological therapy service is associated with reduced utilisation of healthcare and sickness absence by people with common mental health problems: a before and after comparison. J Epidemiol Community Health 2012 Jun 03;66(6):e10-e10. [doi: 10.1136/jech.2011.139873] [Medline: 21969520]
21. de Lusignan S. Codes, classifications, terminologies and nomenclatures: definition, development and application in practice. Inform Prim Care 2005 Mar 01;13(1):65-70 [FREE Full text] [doi: 10.14236/jhi.v13i1.580] [Medline: 15949178]
22. Harcourt SE, Fletcher J, Loveridge P, Bains A, Morbey R, Yeates A, et al. Developing a new syndromic surveillance system for the London 2012 Olympic and Paralympic Games. Epidemiol Infect 2012 Dec;140(12):2152-2156. [doi: 10.1017/S0950268812001781] [Medline: 22892324]
23. NHS Digital. ECDS Enhanced Technical Output Specification (ETOS) v3. URL: https://digital.nhs.uk/data-and-information/data-collections-and-data-sets/data-sets/emergency-care-data-set-ecds/ecds-latest-update [accessed 2021-05-19]
24. Venables W, Ripley B. Modern Applied Statistics with S. Fourth ed. New York: Springer; 2002:387.
25. Peng R, McDermott A. Package 'tsModel': Time Series Modeling for Air Pollution and Health. URL: https://cran.r-project.org/web/packages/tsModel/tsModel.pdf [accessed 2022-06-16]
26. Canty A, Ripley B. boot: Bootstrap R (S-Plus) functions. R package version 1 2017:3-20.
27. Davison A, Hinkley D. Bootstrap Methods and Their Applications. Cambridge: Cambridge University Press; 1997:521.
28. R Core Team, R Foundation for Statistical Computing. R: A Language and Environment for Statistical Computing. URL: https://www.R-project.org/ [accessed 2022-06-16]
29. Office for Health Improvement and Disparities. COVID-19: Mental Health and Wellbeing Surveillance Report. URL: https://www.gov.uk/government/publications/covid-19-mental-health-and-wellbeing-surveillance-report [accessed 2020-06-17]
30. NHS Confederation. Mental Health Services and COVID-19: Preparing for the Rising Tide. URL: https://www.nhsconfed.org/sites/default/files/media/Mental-health-services-COVID-19_4.pdf [accessed 2022-03-09]
31. Nuffield Trust. What Impact Has Covid-19 Had on Mental Health Services?. URL: https://www.nuffieldtrust.org.uk/news-item/what-impact-has-covid-19-had-on-mental-health-services [accessed 2022-03-09]
32. World Health Organization. COVID-19 Disrupting Mental Health Services in Most Countries, WHO Survey. URL: https://www.who.int/news/item/05-10-2020-covid-19-disrupting-mental-health-services-in-most-countries-who-survey [accessed 2022-03-09]
33. World Health Organization. The Impact of COVID-19 on Mental, Neurological and Substance Use Services. URL: https://www.who.int/publications/i/item/978924012455 [accessed 2022-03-09]
34. Gualano MR, Lo Moro G, Voglino G, Bert F, Siliquini R. Effects of Covid-19 lockdown on mental health and sleep disturbances in Italy. Int J Environ Res Public Health 2020 Jul 02;17(13):4779 [FREE Full text] [doi: 10.3390/ijerph17134779] [Medline: 32630821]
35. Kokou-Kpolou CK, Megalakaki O, Laimou D, Kousouri M. Insomnia during COVID-19 pandemic and lockdown: prevalence, severity, and associated risk factors in French population. Psychiatry Res 2020 Aug;290:113128 [FREE Full text] [doi: 10.1016/j.psychres.2020.113128] [Medline: 32563951]

36. Holland KM, Jones C, Vivolo-Kantor AM, Idaikkadar N, Zwald M, Hoots B, et al. Trends in US emergency department visits for mental health, overdose, and violence outcomes before and during the COVID-19 pandemic. JAMA Psychiatry 2021 Apr 01;78(4):372-379 [FREE Full text] [doi: 10.1001/jamapsychiatry.2020.4402] [Medline: 33533876]
37. Hoerger M, Alonzi S, Perry LM, Voss HM, Easwar S, Gerhart JI. Impact of the COVID-19 pandemic on mental health: real-time surveillance using Google Trends. Psychol Trauma 2020 Sep;12(6):567-568. [doi: 10.1037/tra0000872] [Medline: 32790441]
38. Vandentorren S, Paty A, Baffert E, Chansard P, Caserio-Schönemann C. Syndromic surveillance during the Paris terrorist attacks. Lancet 2016 Feb;387(10021):846-847. [doi: 10.1016/s0140-6736(16)00507-9]
39. Gruebner O, Sykora M, Lowe SR, Shankardass K, Trinquart L, Jackson T, et al. Mental health surveillance after the terrorist attacks in Paris. Lancet 2016 May;387(10034):2195-2196. [doi: 10.1016/s0140-6736(16)30602-x]
40. Lauper U, Chen J, Lin S. Window of opportunity for new disease surveillance: developing keyword lists for monitoring mental health and injury through syndromic surveillance. Disaster Med Public Health Prep 2017 Apr 23;11(2):173-178. [doi: 10.1017/dmp.2016.99] [Medline: 28430095]
41. Goldman-Mellor S, Jia Y, Kwan K, Rutledge J. Syndromic surveillance of mental and substance use disorders: a validation study using emergency department chief complaints. Psychiatr Serv 2018 Jan 01;69(1):55-60. [doi: 10.1176/appi.ps.201700028] [Medline: 28945179]
42. NHS Digital. Psychological Therapies: Reports on the Use of IAPT Services, England January 2021 Final Including a Report on the IAPT Employment Advisors Pilot. URL: https://digital.nhs.uk/data-and-information/publications/statistical/psychological-therapies-report-on-the-use-of-iapt-services/january-2021-final-including-a-report-on-the-iapt-employment-advisors-pilot [accessed 2021-04-22]
43. Royal College of General Practitioners. 15-Minute Minimum Consultations, Continuity of Care through 'Micro-teams', and an End to Isolated Working: This Is the Future of General Practice. URL: https://www.rcgp.org.uk/about-us/news/2019/may/15-minute-minimum-consultations-continuity-of-care.aspx [accessed 2021-04-26]
44. Bennett D. The patient iceberg: some characteristics and variations in consultation behaviour. Health Soc Serv J 1980;90(4681):C34-C40.
45. McAteer A, Elliott AM, Hannaford PC. Ascertaining the size of the symptom iceberg in a UK-wide community-based survey. Br J Gen Pract 2011 Jan 01;61(582):e1-e11. [doi: 10.3399/bjgp11x548910]
46. Elliott AM, McAteer A, Hannaford PC. Revisiting the symptom iceberg in today's primary care: results from a UK population survey. BMC Fam Pract 2011 Apr 07;12(1):16 [FREE Full text] [doi: 10.1186/1471-2296-12-16] [Medline: 21473756]

## Abbreviations

**7dma:** 7-day moving averages
**CMHP:** common mental health problem
**ED:** emergency department
**EDSSS:** Emergency Department Syndromic Surveillance System
**GLM:** generalized linear model
**GP:** general practitioner
**IAPT:** Improved Access to Psychological Therapies
**ISO:** International Organisation for Standardisation
**NHS:** National Health Service
**ORCHID:** Oxford-Royal College of General Practitioners Clinical Informatics Digital Hub
**RCGP:** Royal College of General Practitioners
**SNOMED:** Systematized Nomenclature of Medicine
**UKHSA:** UK Health Security Agency

---

*Edited by T Sanchez, A Mavragani; submitted 26.07.21; peer-reviewed by T Newlove-Delgado, M Schranz; comments to author 23.02.22; revised version received 15.03.22; accepted 26.04.22; published 03.08.22.*

*Please cite as:*
*Smith GE, Harcourt SE, Hoang U, Lemanska A, Elliot AJ, Morbey RA, Hughes HE, Lake I, Edeghere O, Oliver I, Sherlock J, Amlôt R, de Lusignan S*
*Mental Health Presentations Across Health Care Settings During the First 9 Months of the COVID-19 Pandemic in England: Retrospective Observational Study*
*JMIR Public Health Surveill 2022;8(8):e32347*
*URL: https://publichealth.jmir.org/2022/8/e32347*
*doi:10.2196/32347*
*PMID:35486809*

Original Paper

# Development and Validation of Indicators for Population Injury Surveillance in Hong Kong: Development and Usability Study

Keith T S Tung[1], PhD; Rosa S Wong[1], PhD; Frederick K Ho[2], PhD; Ko Ling Chan[3], PhD; Wilfred H S Wong[1], PhD; Hugo Leung[1], IB; Ming Leung[4], PhD; Gilberto K K Leung[5], PhD; Chun Bong Chow[1], MD; Patrick Ip[1], MPH

[1]Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Hong Kong, Hong Kong

[2]Institute of Health and Wellbeing, University of Glasgow, Glasgow, United Kingdom

[3]Department of Applied Social Sciences, The Hong Kong Polytechnic University, Hong Kong, Hong Kong

[4]Accident and Emergency Department, Princess Margaret Hospital, Hong Kong, Hong Kong

[5]Department of Surgery, The University of Hong Kong, Hong Kong, Hong Kong

**Corresponding Author:**
Patrick Ip, MPH
Department of Paediatrics and Adolescent Medicine
The University of Hong Kong
NCB 123, Queen Mary Hospital
Hong Kong
Hong Kong
Phone: 852 22554090
Fax: 852 22554089
Email: patricip@hku.hk

## Abstract

**Background:** Injury is an increasingly pressing global health issue. An effective surveillance system is required to monitor the trends and burden of injuries.

**Objective:** This study aimed to identify a set of valid and context-specific injury indicators to facilitate the establishment of an injury surveillance program in Hong Kong.

**Methods:** This development of indicators adopted a multiphased modified Delphi research design. A literature search was conducted on academic databases using injury-related search terms in various combinations. A list of potential indicators was sent to a panel of experts from various backgrounds to rate the validity and context-specificity of these indicators. Local hospital data on the selected core indicators were used to examine their applicability in the context of Hong Kong.

**Results:** We reviewed 142 articles and identified 55 indicators, which were classified into 4 domains. On the basis of the ratings by the expert panel, 13 indicators were selected as core indicators because of their good validity and high relevance to the local context. Among these indicators, 10 were from the construct of health care service use, and 3 were from the construct of postdischarge outcomes. Regression analyses of local hospitalization data showed that the Hong Kong Safe Community certification status had no association with 5 core indicators (admission to intensive care unit, mortality rate, length of intensive care unit stay, need for a rehabilitation facility, and long-term behavioral and emotional outcomes), negative associations with 4 core indicators (operative intervention, infection rate, length of hospitalization, and disability-adjusted life years), and positive associations with the remaining 4 core indicators (attendance to accident and emergency department, discharge rate, suicide rate, and hospitalization rate after attending the accident and emergency department). These results confirmed the validity of the selected core indicators for the quantification of injury burden and evaluation of injury-related services, although some indicators may better measure the consequences of severe injuries.

**Conclusions:** This study developed a set of injury outcome indicators that would be useful for monitoring injury trends and burdens in Hong Kong.

***(JMIR Public Health Surveill 2022;8(8):e36861)*** doi:10.2196/36861

**KEYWORDS**

injury; indicators; modified Delphi research design; surveillance

## Introduction

Injuries, including both unintentional injuries and violence, are serious public health threats that accounts for approximately 10% of the world's fatalities [1]. Similar to other countries, injuries are a significant public health problem in Hong Kong. Injuries have consistently been among the top 5 causes of mortality since 2001 and accounted for approximately 1850 registered deaths in 2019 [2]. In addition, at least 6.2% of the population has experienced functional impairment resulting from at least one episode of unintentional injury [3]. Injuries were also found to be the leading cause of death in the age group of 1 to 14 years over the past decades [2].

Thus, it is important to develop robust strategies to monitor and prevent injuries. However, quantification of the injury burden is a challenging process because of considerable variations in injury mechanisms, duration, and outcomes [4,5]. This process should be guided by a set of measurable injury indicators [6,7]. Broadly, indicators are defined as derivatives of primary data that provide information and describe the state of a phenomenon to a degree of significance beyond raw measurements [8]. Establishing a set of injury indicators would provide a standardized tool to estimate the local injury burden and increase the validity and comparability of these estimates between populations [9].

As the occurrence of injuries partly depends on environmental and social factors [4,5], injury patterns could vary substantially, even within the same population and across regions [10]. The use of local context-specific indicators is recommended to standardize the definitions of injuries and increase the reliability and representativeness of the results in reflecting the injury situation at the population level [11]. Country-specific sets of indicators have been established in Western countries, including Canada, the Netherlands, and the United Kingdom [6,12,13]. However, there has been no comprehensive review of the injury indicators specific to Hong Kong. Hong Kong has 18 districts, each with unique demographic, environmental, and socioeconomic characteristics. It is also known for extremely high–living density multistory apartments, and thus, its injury patterns could be different from those in other regions. Therefore, this study aimed to develop a valid set of Hong Kong–specific injury indicators through a multi-phased modified Delphi research design. The resulting insights would be beneficial for the planning, implementation, and evaluation of injury surveillance and prevention programs [14]. The surveillance system, in turn, can provide information for the early identification of warning signs of injuries and timely intervention for individuals who may be at risk of a physical or psychological injury, ultimately reducing health care use and spending at both individual and societal levels [6,7].

## Methods

### Ethics Approval

The study protocol was approved by the Institutional Review Board of the Hospital Authority, Hong Kong West Cluster (reference UW 15-549). Informed consent was not required from participants as all data provided by the Clinical Data Analysis and Reporting System (CDARS) were deidentified.

### Study Design

#### *Overview*

The development of injury indicators adopted a multiphase modified Delphi research design, as described in previous studies [6,7]. Individuals can first express their opinions impersonally, followed by a whole-group discussion to reach a consensus [15]. The Delphi process emphasizes collective expert opinions rather than precise analytical techniques [16], which makes it particularly suitable for studying population-level research questions or problems. Although the original Delphi process includes a series of iterative steps to collect aggregated expert opinions through multiple rounds of questionnaires, the modified version adopted in our study initiated the discussion with a list of carefully preselected items to facilitate the process of reaching consensus. Following the modified Delphi process protocol, 5 phases were involved: (1) searching and reviewing relevant studies from academic databases, (2) extracting potential indicators from identified studies, (3) achieving a consensus opinion among experts on locally relevant indicators, (4) specification of the selected indicators, and (5) applicability testing of the selected indicators using local health data.

#### *Phase 1: Searching and Reviewing Relevant Studies*

A scoping review was conducted to identify previously adopted valid injury indicators by summarizing the evidence from the included studies that met the prespecified inclusion criteria [17]. This is an evidence-based method to create a rich database as groundwork for further research or review and has been used in previous studies to investigate different research questions and topics [18,19]. Specifically, a literature search was conducted to identify existing outcome indicators for all types of injuries that require medical attention, both intentional and unintentional, from academic databases, including ProQuest, Web of Science, PubMed, Ovid, PsycINFO, and Google Scholar. Guided by the International Classification of Diseases-9), which focuses on the consequences of injuries, the following search terms were combined in various ways to perform the search: *burns*, *poisoning*, *dislocations*, *drowning*, *road traffic accident*, *facial trauma*, *head trauma*, *internal injury of thorax*, *abdomen and pelvis*, *fracture*, *internal injury*, *injury to nerves*, *injury to spinal cord*, *open wounds*, *falls*, *blunt injury*, *suicide*, *self-harm*, *self-inflicted injury*, *injury*, *outcome*, *consequence*, *intentional*, *unintentional*, *psychological*, *mental health*, *mental disorders*, *Abbreviated Injury Scale*, *Glasgow Coma Score*, *Injury Severity Scale*, and *disability*.

The articles included in this review met the following inclusion criteria: (1) having an injury case definition, (2) including at least one indicator of outcome after injury, (3) providing possible data source or sources for the indicator or indicators, (4) being published in an academic peer-reviewed journal, and (5) written in English.

### *Phase 2: Extracting Potential Indicators From Selected Studies*

The aim of this phase was to extract relevant information from the selected studies for subsequent expert reviews. The extracted information included the study year, type of injury, severity of the injury, study population, outcome indicators, and type of study. All the data were recorded and compiled in a spreadsheet for further analysis. Data extraction was conducted by trained research assistants under the supervision of experienced researchers from various fields, including social sciences, medicine, statistics, and biology. The purpose of including a cross-disciplinary and diverse research team was to ensure the accuracy of extracted information. On the basis of their characteristics and measurement purpose, the indicators identified from the literature were grouped into 4 constructs: health care service use, functional and psychological outcomes, biological and physiological outcomes, and postdischarge outcomes.

### *Phase 3: Achieving Consensus Opinion Among Experts on Locally Relevant Indicators*

The indicators identified in the literature were considered suitable for potential use in Hong Kong. The list of potential indicators identified by the research team was sent to a panel of 18 experts in the field of injury for evaluation. Experts from different sectors, including the government, academia, health care, and the community, are well recognized for their work and contributions to injury measures, data management, and community safety and prevention programs. A 22-item checklist adopted from Pike et al [6] and the Child Health Indicators of Life and Development project [20] was used to evaluate the validity, consistency, local relevance, and sensitivity of the potential indicators. The evaluation process involves 2 steps. The first step was a web-based survey inviting experts to view and rate the indicators according to checklist criteria. The second step was face-to-face discussion to resolve disagreements among experts [21]. For each indicator, the response of *YES* denotes satisfactory fulfillment of the specific criterion, whereas the response of *NO* denotes a failure to fulfill that criterion. Indicators receiving *YES* for ≥11 prespecified criteria from more than half of the panel members were deemed as the core locally relevant injury indicators. In addition, panel members were asked to propose other suitable indicators to be included in the list. The newly proposed indicators are then circulated among the panel members for a second round of review.

### *Phase 4: Specification of Selected Indicators*

In this phase, core indicators were clearly defined and specified by the research team according to the specification format adopted from previously published reports on injury indicators [22-24]. Each indicator has its own specification items, including the definition of the indicator and relevant terms, justification for its inclusion, operational definition of a case, method and tools for calculation, data sources and availability, units of measurement, and limitations.

### *Phase 5: Applicability Testing of Selected Indicators Using Local Health Data*

The applicability of these core indicators was evaluated through a series of regression analyses using local health data. Regression analyses were conducted to test the associations between core indicators and certification of the Hong Kong Safe Community in different districts in Hong Kong. The Safe Community model aims to promote safety through the prevention of accidents and injuries through cross-sectorial collaboration in the community [25]. To be certified as a Hong Kong Safe Community, the district must fulfill the following six criteria: (1) establishment of community safety policy, (2) establishment of Safe Community organization, (3) identification of community safety needs, (4) implementation of community safety programs, (5) evaluation of community safety programs, and (6) sharing of safety community experience [25]. Previous studies have demonstrated a reduction in injury incidence after the implementation of the Safe Community model [26,27]. To test the applicability of the core indicators for the quantification of injury burden, all data concerning accident and emergency department (AED) attendance (based on a trauma flag entered by nurses) and hospitalization (based on International Classification of Diseases-9 codes) attributable to injuries during the period from January 1, 2001, to December 31, 2016, were extracted from the CDARS. The CDARS is a territory-wide electronic health record database managed by the Hospital Authority, which is the official governing body of all public hospitals in Hong Kong. All AED attendance and inpatient records of the Hong Kong local public hospitals are housed in the CDARS. A difference-in-differences comparison was adopted in our multivariable regression models to examine the effects of the Hong Kong Safe Community model. The time-varying injury indicator variables were the outcomes. The rate indicators were modeled using a negative binomial model with the log-transformed population during that period to be the offsets. Continuous indicators were modeled using linear regression models. The primary independent variable of interest was a time-varying binary variable with *0* and *1* indicating pre and post–Safe Community implementation. The overall year trend was adjusted for in the model as a continuous variable. This approach can help minimize the temporal influences on injury incidence in Hong Kong.

## Results

### Phase 1 to Phase 2

The initial literature search in phase 1 identified 3525 records. Among these 3525 records, 142 (4.03%) met our prespecified inclusion criteria and were included in the review process (Figure 1). From the 142 reviewed articles, we identified 55 injury outcome indicators and categorized them into 4 constructs based on their characteristics: functional and psychological outcomes (19/55, 35% indicators), health care service use (17/55, 31% indicators), postdischarge outcomes (10/55, 18% indicators), and biological and physiological outcomes (9/55, 16% indicators). Owing to the high heterogeneity of information within the construct of functional and psychological outcomes, indicators in this construct were further divided into 5 subcategories: integrated outcomes (6/19, 32% indicators), lower limbs (5/19, 26% indicators), cognitive (3/19, 16% indicators), psychiatric (3/19, 16% indicators), and upper limbs (2/19, 11% indicators). In contrast, as most indicators in the construct of biological and physiological outcomes were injury specific, they were further regrouped into 9 broad categories based on their similarities to expedite the expert review process. Table 1 displays all indicators identified from the literature by the research team.

**Figure 1.** Flow diagram of the scoping review.

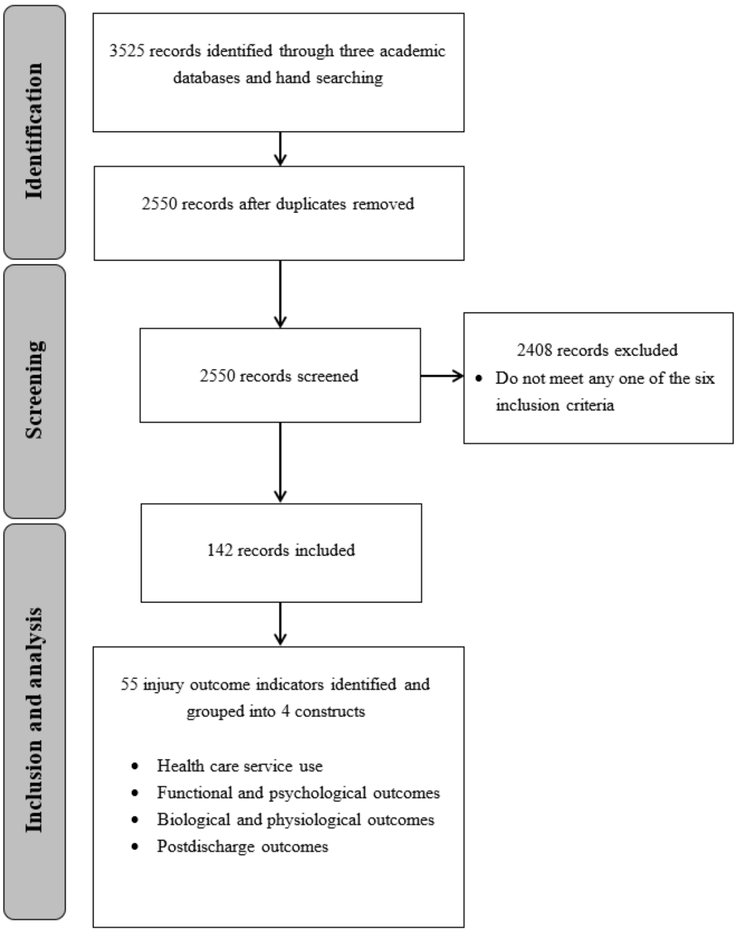


**Table 1.** Potential injury outcome indicators under the 4 constructs.

| Indicator | Definition |
|---|---|
| **Health care service use indicators** | |
| Operative intervention [28-44] | The percentage of cases that requires operative intervention within a particular year |
| Infection rates [28,45-53] | The percentage of cases that have any type of infection within a particular year |
| Admission rate to ICU[a] [30,32,33,35,38,44,54-67] | The percentage of cases admitted to the ICU within a particular year |
| Immediate mortality rate [32,33,35-41,44-46,50,54-60,62,64-66,68-105] | The cause-specific death rate per 100,000 population within a particular year |
| Length of ICU stay [40,44,61,62,64,67,90,98,103,106] | The average number of days spent in the ICU within a particular year |
| Length of hospitalization [30,31,33,34,36,40-42,44-48,50,52,54-56,61-64,68,71,72,75,76,78,87,90,98,99,103-117] | The average number of days spent in hospital for a particular year |
| Admission rate to AED[b] [43,66,69,100-102,117-121] | The cause-specific admission rate to the AED per 100,000 population for a particular year |
| Time for wound healing [50,109] | Average amount of time required for the healing of injury-induced open wounds within 1 particular year |
| Need for rehabilitation facility [30] | Total number of cases that need to be referred to an inpatient rehabilitation facility within a particular year |
| Hospitalization rate after leaving AED [30,35,38,53-55,58,60,61,66,69,77,83,100-102,105,107,108,111,117-120,122,123] | The percentage of cases that require inpatient hospital admissions after leaving AED per 100,000 population within a particular year |
| Intubation duration [30,52,62,64,80,90,103] | The average number of days that the cases require intubation, a process of inserting through the mouth into the airway to assist with their breathing, within a particular year |
| Need for secondary procedures [31-34,48,115] | The percentage of cases that need secondary surgical procedures within a particular year |
| Mean duration of operation [37] | The average amount of time needed for the operative intervention conducted within a particular year |
| Presence of complications [32,33,36,37,46,49,51,58,63,78,86,92,106,109,113-115,124,125] | The percentage of cases that have injury-induced complications within a particular year |
| Morbidity [46,60,83-85,88,95] | The frequency of having any injury-induced disease or medical condition within a particular year |
| Discharge rate [70,80,97-99,105,117,120,126] | The percentage of cases discharged from the hospital within a particular year |
| Need for nursing facility [89] | Total number of cases discharged to a nursing facility within a particular year |
| **Functional and psychological outcome indicators** | |
| **Cognitive outcomes** | |
| Gray Oral Reading Test [127] | An efficient and objective measure of growth in oral reading fluency and comprehension and an aid in the diagnosis of oral reading difficulties |
| Cognitive Performance Scale [89,106] | A scale used for accessing patients' loss in everyday cognitive performance from independent to full dependency based on 5 domains: daily decision-making, eating self-performance, ability to make self-understood, short-term memory, and being comatose |
| Stanford-Binet Intelligence Scale [127] | A cognitive ability and intelligence test used to diagnose developmental or intellectual deficiencies based on 5 factors: knowledge, quantitative reasoning, visual-spatial processing, working memory, and fluid reasoning |
| **Psychiatric outcomes** | |

| Indicator | Definition |
|---|---|
| Structured Clinical Interview for DSM-5[c] or other related mental health scales [112,117,121,128-131] | A semistructured interview guide for making DSM-5 diagnoses or other mental health scales not stated |
| General Health Questionnaire [132] | A screening device for identifying minor psychiatric disorders in the general population and within the community or nonpsychiatric clinical settings such as primary care or general medical outpatients |
| Health Status Questionnaire [29,109,133-135] | A scale for measuring health-related quality of life, including physical functioning, role limitations owing to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations because of emotional problems, and mental health |
| **Upper limb outcomes** | |
| American Shoulder and Elbow Surgeons Evaluation [136] | A standardized method for assessing patient-rated shoulder pain and function or disability |
| Disabilities of the Arm, Shoulder, and Hand Questionnaire [137] | A region-specific outcome instrument developed as a measure of physical function and symptoms in patients with any or several musculoskeletal disorders of the upper limb |
| **Lower limb outcomes** | |
| Walking Index for Spinal Cord Injury [138] | A research tool in clinical trials to measure improvements in walking in person with acute and chronic spinal cord injury |
| Lysholm score and Tegner Activity scale [139] | A scale used for measuring patients' everyday activity limitations and participation restrictions before and after arthroscopic knee surgery |
| American Knee Society score [140] | A scale used with patients with osteoarthritis or who have undergone total knee arthroplasty for measuring patients' functionality and their knee clinically through physical examination |
| Foot and Ankle Outcome score [28,141] | A scale used with patients with lateral ankle instability, Achilles tendinosis, and plantar fasciitis for assessing foot and ankle pain, symptoms, function in daily living, sport and recreation, and foot- and ankle-related quality of life |
| American Spinal Injury Association Impairment scale [28] | A scale used by the rehabilitation team to assess the sensory and motor levels that were affected by the spinal cord injury |
| **Integrated outcomes** | |
| Neurological impairment [59,60,83,142,143] | A broad group of disorders in which the central nervous system does not function properly and leads to some form of physical or mental problems |
| Musculoskeletal Function Assessment [29,124,137] | An instrument used with a range of patients with musculoskeletal disorders for measuring their health status, including lower and upper mobility, activity level and satisfaction, social support, pain, emotional status, and quality of life, in clinical practice |
| Functional Independence Measure [98,127,135,144] | A basic indicator of patient disability and the amount of assistance required for the patient to conduct activities of daily living in 18 categories, focusing on motor and cognitive function |
| Grading Medical Impairment [145] | Grading rules used for assessing the medical impairment and functional reduction originating from an injury using patients' medical records before and after the injury |
| Glasgow Outcome Scale [41,81,94,96,125-127,146-149] | A global scale used with patients with brain injuries for rating function outcomes into 5 ordered categories: dead, vegetative state, severe disability, moderate disability, or good recovery |
| Range of motion [89,98,114,137,139,141] | The measurement of movement around a specific joint or body part |
| **Biological and physiological outcome indicators** | |

| Indicator | Definition |
|---|---|
| Duration of antibiotic use [34] | The number of days in which individuals are prescribed to receive antibiotic treatment because of injury |
| Hematological findings [32,58,70,113] | Laboratory tests on examining the blood content such as hormones, ions, lactates, and inflammatory mediators in the blood |
| Cardiovascular findings [32,39,50,81,86,91,92,95,106,113] | Any measures or tests performed related to heart or blood vessels, such as arterial blood pressure, heart rate, and initial heart rhythm |
| Histological findings [45] | Results of examination of tissue specimens under a microscope to study the manifestations of a disease |
| Renal findings [45,58,150] | Laboratory tests on evaluating kidney function using blood or urine samples, mainly blood urea nitrogen and creatinine |
| Toxicological findings [52,116,125,150-152] | Laboratory tests on the type and quantity of substances present in an individual's body, such as urine toxicology screening |
| Metabolic measurements [32,45,70,116,125,152-154] | Measurements related to individuals' metabolism, such as resting energy expenditure and rewarming speed |
| Osteological signs [28,48,49,62,88,104,118,124,137,155,156] | Laboratory tests on the structure and function of bones, such as bone measurements and bone mineral density test |
| Neurological signs and findings [41,42,51,52,58,59,63,80,83,86,92,97,104,106,116,142-144,148,157] | A series of tests and measures in examining the function of the brain and the central and autonomic nervous systems, such as intracranial pressure, computed tomography scans, magnetic resonance imaging scans, and cerebral angiography |
| **Postdischarge outcomes** | |
| Long-term behavioral and emotional outcomes [67,135,147,155,158-162] | The long-term outcomes of emotions and behaviors characterized by alteration of feeling tone and by physiological behavioral changes |
| Social dependency [163,164] | Capacities necessary for the performance of everyday self-care competence, mobility competence, and social competence |
| Possibility of posttraumatic stress disorder or other mental disorders [55,67,97,131,132,135,148,151,159,162,164-166] | The possibility of having mental illnesses that affect one's mood, thinking, and behavior after experiencing a shocking, scary, or dangerous event |
| Presence or absence of disabilities [32,48-50,56,66,74,82,93,101,103,134,135,167] | The presence of disabilities, which refer to impairments, activity limitations, and participation restrictions |
| Suicide rate [43,121,159] | The number of people taking their own life after injury per 100,000 population in a period |
| Effect on employment or studies [79,106,134,135,140,147,159,161,168] | The consequences of the injury on one's work life and study life |
| Walking distance [28,138] | The distance a person is able to walk in a period, such as the 6-minute walk test |
| Quality of life [28,67,70,88,110,111,124,133-136,144,151,162,163,167,169] | The overall enjoyment of life, including aspects of an individual's sense of well-being, ability to perform various activities, and quality of life with domains of physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health |
| Disability-adjusted life year [67,135,162] | A measure expressed as the number of years lost because of ill health, disability, or early death used to reflect the overall disease burden |
| Quality-adjusted life year [67,135,162] | A measure used to reflect the overall disease burden by considering both the quality and quantity of the life lived |

[a] ICU: intensive care unit.

[b] AED: accident and emergency department.

[c] DSM-5: Diagnostic and Statistical Manual of Mental Disorders (fifth edition).

## Phase 3 to Phase 4

After review and discussion among the expert panel members, 13 core indicators were identified from the list. The core indicators included the need for operative intervention, infection rate, admission to the intensive care unit (ICU), mortality rate, length of ICU stay, length of hospitalization, AED attendance rate, need for a rehabilitation facility, hospitalization rate after AED, discharge rate, long-term behavioral and emotional outcomes, suicide rate, and disability-adjusted life years (DALYs) per 100,000. Among these 13 indicators, 10 (77%) were from the construct of health care service use and 3 (23%) were from the construct of postdischarge outcomes.

## Phase 5

Table 2 displays the results of the multivariable regression analyses of the associations between core indicators and certified Hong Kong Safe Community status. Applicability tests showed that the Hong Kong Safe Community certification status was not associated with 5 core indicators (admission to ICU, mortality rate, length of ICU stay, need for a rehabilitation facility, and long-term behavioral and emotional outcomes), negatively associated with 4 core indicators (operative intervention, infection rate, length of hospitalization, and DALYs), and positively associated with the remaining 4 core indicators (attendance to AED, discharge rate, suicide rate, and hospitalization rate after attending AED). For example, the Safe Community model implementation was found to reduce the risk of AED attendance (risk ratio=0.65; *P*<.001) and to lower the DALYs per 100,000 (β=−1.91; *P*=.046). These results confirmed the data availability, applicability, and local relevance of the selected core indicators.

**Table 2.** Applicability testing of injury outcome indicators (illustrated by multivariable regression analyses).

| Injury outcome indicators | Certified Hong Kong Safe Community | |
|---|---|---|
| | Effect (95% CI)[a] | *P* value |
| Operative intervention, β | −.23 (−0.40 to −0.07) | .007[b] |
| Infection rates, β (ICD-9CM[c] 680-686[d]) | −.18 (−0.33 to −0.02) | .03[e] |
| Admission to ICU[f], β | .04 (−0.02 to 0.11) | .21 |
| Mortality rate, risk ratio | 1.29 (0.98 to 1.69) | .07 |
| Length of stay in ICU, β | −0.02 (−0.08 to 0.04) | .54 |
| Length of hospitalization, β | −1.09 (−1.63 to −0.54) | <.001[g] |
| Attendance to AED[h], risk ratio | 0.65 (0.64 to 0.65) | <.001[g] |
| Need for a rehabilitation facility, β (based on discharge destination[i]) | .00 (0.00 to 0.00) | .38 |
| Hospitalization rate after attending AED, β | 1.34 (0.47 to 2.22) | .003[b] |
| Discharge rate, β | .09 (0.04 to 0.15) | .001[b] |
| Long-term behavioral and emotional outcomes, β (proxy measure: ICD-9CM 905-909[j]) | −0.03 (−0.17 to 0.10) | .64 |
| Suicide rate, risk ratio | 1.23 (1.00 to 1.50) | .045[e] |
| DALYs[k] per 100,000, β | −1.91 (−3.79 to −0.04) | .046[e] |

[a] Adjusted for sex and year of attendance as covariates and district and age groups as random intercepts.

[b] *P*<.01.

[c] ICD-9CM: International Classification of Diseases, Ninth Revision, Clinical Modification.

[d] Infections of skin and subcutaneous tissue.

[e] *P*<.05.

[f] ICU: intensive care unit.

[g] *P*<.001.

[h] AED: accident and emergency department.

[i] Destination to MacMehose Medical Rehabilitation Centre, Cheshire House (Sha Tin, Chun Hom Kok).

[j] Late effects of injuries, poisonings, toxic effects, and other external causes.

[k] DALY: disability-adjusted life year.

## Discussion

### Principal Findings

This study used a multiphased modified Delphi approach to develop a set of core injury outcome indicators specific to the Hong Kong population. These identified indicators have the potential to become standardized tools for the surveillance and evaluation of injury burden and management services in Hong Kong. Specifically, we identified 55 injury outcome indicators from the literature and categorized them into 4 domains: health care service use, functional and psychological outcomes, biological and physiological outcomes, and postdischarge outcomes. On the scoring and ranking by panel experts on data availability, applicability, and validity, 13 indicators were ranked as core indicators because of their high local relevance and reflectiveness of the injury burden in Hong Kong. In addition, we used local hospitalization data to perform applicability testing analyses. These findings support the applicability of these core indicators in local contexts. They would serve as the groundwork for the future establishment of a comprehensive injury surveillance system in Hong Kong, as well as an example of a systematic approach for developing and validating indicators for injury surveillance.

By reviewing the relevant literature, we found that the most common injury outcome construct was health care service use. Approximately 57.7% (82/142) of the reviewed articles used measures of health care service use as indicators of injury outcomes compared with 31.7% (45/142) for functional and psychological outcomes, 21.8% (31/142) for postdischarge outcomes, and 14.8% (21/142) for biological and physiological outcomes. This could be because most measures included in the health care service use construct, such as length of hospitalization, length of stay in ICU, and immediate death status, are frequently used as injury indicators in many countries [54,55,68,69].

It should be noted that other outcome indicator constructs also have their own characteristics. From a clinical perspective, functional and psychological and biological and physiological outcomes can provide information on the holistic impact of an injury on patients. Notably, many functional and psychological outcomes were measured using standardized and psychometrically validated scales or indexes such as the General Health Questionnaire and Glasgow Outcome Scale, which can increase the comparability of results between studies and across countries [170]. Conversely, the biological and physiological construct is difficult to compare, because of its injury-specific and heterogeneous nature. For example, Kraft et al [45] assessed the level of blood hormones in patients with burn injuries, whereas Alanazi et al [153] assessed the level of blood ions in poisoned patients. Owing to these between-study differences in biological outcome measures, we could not compare and determine which injury type may have caused a greater physiological burden on the patient. Thus, it is important to reach a consensus on the most appropriate and readily measurable injury indicators at the biological and physiological level. For instance, some evidence has suggested that injury-associated inflammation is a potentially universal phenomenon among injuries [171-173]. Future research should identify the injury type associated with severe biological and physiological damage and compare inflammatory marker levels (eg, interleukins) between injuries to characterize their respective inflammatory profiles and to examine whether postinjury functional and inflammatory changes would correlate with each other.

Moreover, injury outcome indicators can be time specific. For example, previous studies measured quality of life as an indicator of patients' perceived outcomes immediately after injury [28,70]. However, considering the fluctuation in the quality of life over time, local experts recommended DALYs and quality-adjusted life years as indicators of outcomes after discharge from the hospital. In addition, there could be overlaps between the domains of injury outcome indicators. More studies are needed to clarify the associations among functional and psychological outcomes, biological and physiological outcomes, and other long-term postinjury outcomes.

From the list of potential indicators, 13 indicators were rated by a panel of experts as suitable for local use. Surprisingly, certification of a Safe Community was associated with higher suicide rates, perhaps as the primary goal of the Safe Community program was to prevent unintentional injuries [25,174], and therefore might be less effective in reducing intentional injuries such as suicidal behaviors. The increase in suicide rate may affect the patterns of estimates of other indicators, as it is often related to more serious consequences and complications [175]. For example, the rate of hospitalization following AED attendance was higher in districts with a Safe Community certification, which could be because of the increased number of suicide cases. In addition, although the estimates of universal injury indicators (eg, length of hospitalization) were reduced in certified Hong Kong Safe Communities, severe injury indicators (eg, mortality rate and ICU admission) showed no differences between districts with and without Safe Community certification. These results suggest that the estimates of severe injury indicators could be influenced by other unmeasured factors than safety measures.

This study developed a set of injury indicators that can be used to evaluate and monitor injury trends and services in Hong Kong. It is evident that a well-established injury surveillance system integrating different data sources can be a valuable tool to assist health care professionals in making better decisions regarding injury trends and preventive services [174,176]. Having demonstrated their functionality and applicability to the context of Hong Kong, health care professionals can use these indicators to develop a better understanding of local injury trends and obtain a more accurate estimate of the impact of injuries on the local health care system. However, challenges exist because of the lack of reliable, sensitive, and standardized data sources for some indicators in Hong Kong [177]. Although the literature review identified indicators in 4 constructs (health care service use, functional and psychological outcomes, biological and physiological outcomes, and postdischarge outcomes), only health care service use and postdischarge outcome indicators were found to have limited applicability as severe injuries are relatively rare in Hong Kong. These findings indicate a lack of postinjury data in local surveillance systems.

Moreover, functional and psychological and biological and physiological measures should be integrated as part of routine clinical care for injured patients in Hong Kong. The inclusion of these indicators can help establish a more comprehensive surveillance system to evaluate and monitor injury trends and services more accurately in Hong Kong. Furthermore, assessment methods and tools should be standardized to enhance comparability with other regions.

This study had several limitations. First, gray literature such as government reports was not searched in the review process; hence, we may have missed some relevant indicators, although we consulted experts to confirm whether our list included all important indicators. Second, the Hong Kong Safe Community model was not the most appropriate model for testing the validity of the core injury outcome indicators, as the model cannot address issues related to intentional injuries such as suicide and abuse, which often result in severe consequences and complications. Third, owing to the lack of appropriate data sources in Hong Kong, we could not include all identified injury outcome indicator constructs in the final list of core indicators, which limits the generalizability of the results to other populations.

## Conclusions

This study used a multiphased modified Delphi method to develop a set of indicators to monitor injury trends and burdens in Hong Kong. A total of 55 injury outcome indicators were identified through a literature review and discussed among local experts from different sectors, including the government, health care, community, and academia. A total of 13 indicators were included in the final list of core indicators; however, biological and physiological and functional and psychological outcomes were not included because of the lack of data sources. Model testing results based on a set of core indicator data showed that these core indicators can be applied to Hong Kong settings. The approach used in this study will be a useful example for other cities and regions that aim to systematically tackle the injury burden.

## Acknowledgments

Funding for this study was provided by the Health and Medical Research Fund (reference 13142541). The Health and Medical Research Fund had no role in the study design, collection, analysis, or interpretation of the data, writing of the manuscript, or decision to submit the paper for publication.

The authors would like to thank all the professionals, academics, and experts in the field for their valuable feedback and contributions to this study.

## Conflicts of Interest

None declared.

## References

1. Injuries and violence: the facts. World Health Organization. 2010. URL: http://apps.who.int/iris/bitstream/handle/10665/44288/9789241599375_eng.pdf?sequence=1 [accessed 2021-07-10]
2. Action plan to strengthen prevention of unintentional injuries in Hong Kong. Department of Health, Hong Kong Special Administrative Region. 2014. URL: https://www.change4health.gov.hk/en/strategic_framework/structure/working_group_injuries/action_plan/ [accessed 2021-07-13]
3. Injury survey 2008. Surveillance and Epidemiology Branch Centre for Health Protection, Department of Health, Hong Kong Special Adminstrative Region. 2010 Sep. URL: https://www.chp.gov.hk/files/pdf/injury_survey_eng.pdf [accessed 2021-07-13]
4. Hotz G, Kennedy A, Lutfi K, Cohn S. Preventing pediatric pedestrian injuries. J Trauma 2009 May;66(5):1492-1499. [doi: 10.1097/TA.0b013e31819d9c9b] [Medline: 19430259]
5. Theurer WM, Bhavsar AK. Prevention of unintentional childhood injury. Am Fam Physician 2013 May 01;87(7):502-509 [FREE Full text] [Medline: 23547592]
6. Pike I, Piedt S, Warda L, Yanchar N, Macarthur C, Babul S, et al. Developing injury indicators for Canadian children and youth: a modified-Delphi approach. Inj Prev 2010 Jul 22;16(3):154-160. [doi: 10.1136/ip.2009.025007] [Medline: 20570983]
7. Cryer C, Langley J. Developing indicators of injury incidence that can be used to monitor global, regional and local trends. University of Otago. 2007. URL: https://www.researchgate.net/publication/283794181_Developing_indicators_of_injury_incidence_that_can_be_used_to_monitor_global_regional_and_local_trends [accessed 2021-07-13]
8. Cryer C. ICE Injury Indicators Group (ICEIInG) - progress Report, aspirations, goals and strategy development. In: Proceedings of the International Collaborative Effort on Injury Statistics Volume IV. 2003 Presented at: ICE '03; April 13-14, 2003; Paris, France. [doi: 10.1136/injuryprev-2011-040037]
9. Mathers C, Fat DM, Boerma J. The Global Burden of Disease: 2004 Update. Geneva, Switzerland: World Health Organization; 2008.

10. Hong Kong 2016 Population By-census - Summary Results. Census and Statistics Department, The Government of the Hong Kong Special Administrative Region. 2017. URL: https://www.censtatd.gov.hk/en/EIndexbySubject.html?scode=459&pcode=B1120094 [accessed 2021-07-13]
11. Von Schirnding Y. Health in Sustainable Development Planning: The Role of Indicators. Geneva, Switzerland: World Health Organization; 2002.
12. Pike I, McDonald R, Piedt S, Macpherson A. Developing injury indicators for First Nations and Inuit children and youth in Canada: a modified Delphi approach. Chronic Dis Inj Can 2014 Nov;34(4):203-209. [doi: 10.24095/hpcdp.34.4.03]
13. MacKay M, Vincenten J. Child Safety Report Card 2009: Europe Summary for 24 Countries. Amsterdam, The Netherlands: European Child Safety Alliance, Eurosafe; 2009.
14. Lyons RA, Brophy S, Pockett R, John G. Purpose, development and use of injury indicators. Int J Inj Contr Saf Promot 2005 Dec;12(4):207-211. [doi: 10.1080/17457300500172776] [Medline: 16471152]
15. Fink A, Kosecoff J, Chassin M, Brook RH. Consensus methods: characteristics and guidelines for use. Am J Public Health 1984 Oct;74(9):979-983. [doi: 10.2105/ajph.74.9.979] [Medline: 6380323]
16. Hsu C, Sandford B. The Delphi technique: making sense of consensus. Practical Assess Res Eval 2007;12:1-8. [doi: 10.4018/978-1-4666-0074-4.ch011]
17. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol 2005 Feb;8(1):19-32. [doi: 10.1080/1364557032000119616]
18. Howell D, Molloy S, Wilkinson K, Green E, Orchard K, Wang K, et al. Patient-reported outcomes in routine cancer clinical practice: a scoping review of use, impact on health outcomes, and implementation factors. Ann Oncol 2015 Oct;26(9):1846-1858 [FREE Full text] [doi: 10.1093/annonc/mdv181] [Medline: 25888610]
19. Archer N, Fevrier-Thomas U, Lokker C, McKibbon KA, Straus SE. Personal health records: a scoping review. J Am Med Inform Assoc 2011 Jul 01;18(4):515-522 [FREE Full text] [doi: 10.1136/amiajnl-2011-000105] [Medline: 21672914]
20. Rigby MJ, Kohler LI, Blair ME, Metchler R. Child Health Indicators for Europe: a priority for a caring society. Eur J Public Health 2003 Sep 01;13(suppl 3):38-46. [doi: 10.1093/eurpub/13.suppl_3.38]
21. LeMessurier J, O'Donnell S, Walsh P, McRae L, Bancej C. The development of national indicators for the surveillance of osteoporosis in Canada. Chronic Dis Inj Can 2012 Mar;32(2):101-107. [doi: 10.24095/hpcdp.32.2.06]
22. Cryer C, Langley J, Stephenson S. Developing Valid Injury Outcome Indicators: A Report for the New Zealand Injury Prevention Strategy / Colin Cryer, John Langley, Shaun Stephenson. Dunedin, New Zealand: Injury Prevention Research Unit, Department of Preventive and Social Medicine, University of Otago; 2004.
23. Canadian Institute for Health Information. Pan-Canadian Primary Health Care Indicators: Pan-Canadian Primary Health Care Indicator Development Project: Report 1, Volume 2. Ottawa, Ontario: Canadian Institute for Health Information; 2006.
24. Harrison JE, Steenkamp M. Technical Review and Documentation of Current NHPA Injury Indicators and Data Sources. Adelaide, Australia: Australian Institute of Health and Welfare; 2002.
25. Hong Kong Safe Community: together we build safe community. Occupational Safety and Health Council. 2017 Jul. URL: https://www.oshc.org.hk/oshc_data/files/ProfessionalServices/safecom/HK_safe_com_leaflet.pdf [accessed 2022-08-08]
26. Lindqvist K, Timpka T, Schelp L, Risto O. Evaluation of a child safety program based on the WHO safe community model. Inj Prev 2002 Mar;8(1):23-26 [FREE Full text] [doi: 10.1136/ip.8.1.23] [Medline: 11928968]
27. Rahimi-Movaghar V. Controlled evaluation of injury in an international safe community: Kashmar, Iran. Public Health 2010 May;124(4):190-197. [doi: 10.1016/j.puhe.2010.02.014] [Medline: 20417350]
28. White T, Guy P, Cooke C, Kennedy S, Droll K, Blachut P, et al. The results of early primary open reduction and internal fixation for treatment of OTA 43.C-type tibial pilon fractures: a cohort study. J Orthop Trauma 2010 Dec;24(12):757-763. [doi: 10.1097/BOT.0b013e3181d04bc0] [Medline: 21076248]
29. Eroglu O, Sari E, Vural S, Coskun F. Warning: this may be as dangerous as firearm injuries;"grease-gun injury": a case report. Pan Afr Med J 2015 Jan 14;20:40 [FREE Full text] [doi: 10.11604/pamj.2015.20.40.5892] [Medline: 26029329]
30. Almahmoud K, Namas R, Abdul-Malak O, Zaaqoq A, Zamora R, Zuckerbraun B, et al. Impact of injury severity on dynamic inflammation networks following blunt trauma. Shock 2015 Aug;44(2):101-109 [FREE Full text] [doi: 10.1097/SHK.0000000000000395] [Medline: 26009819]
31. Bagheri SC, Dierks EJ, Kademani D, Holmgren E, Bell RB, Hommer L, et al. Application of a facial injury severity scale in craniomaxillofacial trauma. J Oral Maxillofac Surg 2006 Mar;64(3):408-414. [doi: 10.1016/j.joms.2005.11.013] [Medline: 16487802]
32. Toon MH, Maybauer DM, Arceneaux LL, Fraser JF, Meyer W, Runge A, et al. Children with burn injuries--assessment of trauma, neglect, violence and abuse. J Inj Violence Res 2011 Jul;3(2):98-110 [FREE Full text] [doi: 10.5249/jivr.v3i2.91] [Medline: 21498973]
33. Haik J, Liran A, Tessone A, Givon A, Orenstein A, Peleg K, Israeli Trauma Group. Burns in Israel: demographic, etiologic and clinical trends, 1997-2003. Isr Med Assoc J 2007 Sep;9(9):659-662 [FREE Full text] [Medline: 17939628]
34. Tarim A, Nursal TZ, Basaran O, Yildirim S, Türk E, Moray G, et al. Scalding in Turkish children: comparison of burns caused by hot water and hot milk. Burns 2006 Jun;32(4):473-476. [doi: 10.1016/j.burns.2005.11.004] [Medline: 16621318]

35. Cameron PA, Mitra B, Fitzgerald M, Scheinkestel CD, Stripp A, Batey C, et al. Black Saturday: the immediate impact of the February 2009 bushfires in Victoria, Australia. Med J Aust 2009 Jul 06;191(1):11-16. [doi: 10.5694/j.1326-5377.2009.tb02666.x] [Medline: 19580529]
36. Akçay MN, Oztürk G, Aydinli B, Ozoğul B. Tandir burns: a severe cause of burns in rural Turkey. Burns 2008 Mar;34(2):268-270. [doi: 10.1016/j.burns.2007.03.007] [Medline: 17689872]
37. Salem K, Shannak O, Scammell B, Moran C. Predictors and outcomes of treatment in hip hemiarthroplasty dislocation. Ann R Coll Surg Engl 2014 Sep;96(6):446-451 [FREE Full text] [doi: 10.1308/003588414X13946184903045] [Medline: 25198977]
38. McClure RJ, Peel N, Kassulke D, Neale R. Appropriate indicators for injury control? Public Health 2002 Sep;116(5):252-256. [doi: 10.1038/sj.ph.1900859] [Medline: 12209399]
39. Meghoo CA, Dennis JW, Tuman C, Fang R. Diagnosis and management of evacuated casualties with cervical vascular injuries resulting from combat-related explosive blasts. J Vasc Surg 2012 May;55(5):1329-1367 [FREE Full text] [doi: 10.1016/j.jvs.2011.11.125] [Medline: 22325667]
40. Tinkoff G, Esposito T, Reed J, Kilgo P, Fildes J, Pasquale M, et al. American Association for the Surgery of Trauma Organ Injury Scale I: spleen, liver, and kidney, validation based on the National Trauma Data Bank. J Am Coll Surg 2008 Nov;207(5):646-655. [doi: 10.1016/j.jamcollsurg.2008.06.342] [Medline: 18954775]
41. Jagannathan J, Okonkwo DO, Dumont AS, Ahmed H, Bahari A, Prevedello DM, et al. Outcome following decompressive craniectomy in children with severe traumatic brain injury: a 10-year single-center experience with long-term follow up. J Neurosurg 2007 Apr;106(4 Suppl):268-275. [doi: 10.3171/ped.2007.106.4.268] [Medline: 17465359]
42. Polites S, Sebastian A, Habermann E, Iqbal C, Stuart M, Ishitani M. Youth ice hockey injuries over 16 years at a pediatric trauma center. Pediatrics 2014 Jun;133(6):e1601-e1607. [doi: 10.1542/peds.2013-3628] [Medline: 24864187]
43. Horrocks J, Price S, House A, Owens D. Self-injury attendances in the accident and emergency department: clinical database study. Br J Psychiatry 2003 Jul;183:34-39. [doi: 10.1192/bjp.183.1.34] [Medline: 12835241]
44. Roberts D, Ouellet J, Sutherland F, Kirkpatrick A, Lall R, Ball C. Severe street and mountain bicycling injuries in adults: a comparison of the incidence, risk factors and injury patterns over 14 years. Can J Surg 2013 Jun;56(3):E32-E38 [FREE Full text] [doi: 10.1503/cjs.027411] [Medline: 23706856]
45. Kraft R, Kulp GA, Herndon DN, Emdad F, Williams FN, Hawkins HK, et al. Is there a difference in clinical outcomes, inflammation, and hypermetabolism between scald and flame burn? Pediatr Crit Care Med 2011 Nov;12(6):e275-e281 [FREE Full text] [doi: 10.1097/PCC.0b013e31820ac2c5] [Medline: 21297515]
46. Ansari-Moghaddam A, Baghbanian A, Dogoonchi M, Chooban B, Mostaghim-Roudi M, Torkfar G. Epidemiology of burn injuries in south-eastern Iran: a retrospective study. J Pak Med Assoc 2013 Dec;63(12):1476-1481 [FREE Full text] [Medline: 24397088]
47. Rimmer RB, Weigand S, Foster KN, Wadsworth MM, Jacober K, Matthews MR, et al. Scald burns in young children--a review of Arizona burn center pediatric patients and a proposal for prevention in the Hispanic community. J Burn Care Res 2008;29(4):595-605. [doi: 10.1097/BCR.0b013e31817db8a4] [Medline: 18535476]
48. Chua W, De SD, Lin WK, Kagda F, Murphy D. Early versus late flap coverage for open tibial fractures. J Orthop Surg (Hong Kong) 2014 Dec;22(3):294-298 [FREE Full text] [doi: 10.1177/230949901402200305] [Medline: 25550005]
49. Stannard J, Volgas D, Stewart R, McGwin JG, Alonso J. Negative pressure wound therapy after severe open fractures: a prospective randomized study. J Orthop Trauma 2009 Sep;23(8):552-557. [doi: 10.1097/BOT.0b013e3181a2e2b6] [Medline: 19704269]
50. Yavuz C, Demirtas S, Caliskan A, Ertas F, Kaya H, Aydin M, et al. The predictors of poor outcomes in patients with femoral artery injuries. Eur Rev Med Pharmacol Sci 2013 Jul;17(14):1901-1908 [FREE Full text] [Medline: 23877855]
51. Chapman JR, Agel J, Jurkovich GJ, Bellabarba C. Thoracolumbar flexion-distraction injuries: associated morbidity and neurological outcomes. Spine (Phila Pa 1976) 2008 Mar 15;33(6):648-657. [doi: 10.1097/BRS.0b013e318166df7b] [Medline: 18344859]
52. Tsai JR, Sheu CC, Cheng MH, Hung JY, Wang CS, Chong IW, et al. Organophosphate poisoning: 10 years of experience in southern Taiwan. Kaohsiung J Med Sci 2007 Mar;23(3):112-119 [FREE Full text] [doi: 10.1016/S1607-551X(09)70385-7] [Medline: 17389175]
53. Thiels CA, Hernandez MC, Zielinski MD, Aho JM. Injury patterns and outcomes of ice-fishing in the United States. Am J Emerg Med 2016 Jul;34(7):1258-1261 [FREE Full text] [doi: 10.1016/j.ajem.2016.02.078] [Medline: 27117462]
54. Karaca MA, Kartal ND, Erbil B, Öztürk E, Kunt MM, Şahin TT, et al. Evaluation of gunshot wounds in the emergency department. Ulus Travma Acil Cerrahi Derg 2015 Jul;21(4):248-255 [FREE Full text] [doi: 10.5505/tjtes.2015.64495] [Medline: 26374410]
55. Pavoni V, Gianesello L, Paparella L, Buoninsegni LT, Barboni E. Outcome predictors and quality of life of severe burn patients admitted to intensive care unit. Scand J Trauma Resusc Emerg Med 2010 Apr 27;18(1):24 [FREE Full text] [doi: 10.1186/1757-7241-18-24] [Medline: 20420719]
56. Di Scala C, Gallagher S, Schneps S. Causes and outcomes of pediatric injuries occurring at school. J Sch Health 1997 Nov;67(9):384-389. [doi: 10.1111/j.1746-1561.1997.tb07182.x] [Medline: 9471091]

57. Brusselaers N, Hoste EA, Monstrey S, Colpaert KE, De Waele JJ, Vandewoude KH, et al. Outcome and changes over time in survival following severe burns from 1985 to 2004. Intensive Care Med 2005 Dec;31(12):1648-1653. [doi: 10.1007/s00134-005-2819-6] [Medline: 16220315]
58. Güzel A, Duran L, Paksu S, Akdemir H, Paksu M, Katı C, et al. Drowning and near-drowning: experience of a university hospital in the Black Sea region. Turk J Pediatr 2013;55(6):620-627. [Medline: 24577981]
59. Zuckerman GB, Gregory PM, Santos-Damiani SM. Predictors of death and neurologic impairment in pediatric submersion injuries. The Pediatric Risk of Mortality Score. Arch Pediatr Adolesc Med 1998 Feb;152(2):134-140. [doi: 10.1001/archpedi.152.2.134] [Medline: 9491038]
60. Biggart MJ, Bohn DJ. Effect of hypothermia and cardiac arrest on outcome of near-drowning accidents in children. J Pediatr 1990 Aug;117(2 Pt 1):179-183. [doi: 10.1016/s0022-3476(05)80526-8] [Medline: 2380813]
61. Con J, Friese RS, Long DM, Zangbar B, O'Keeffe T, Joseph B, et al. Falls from ladders: age matters more than height. J Surg Res 2014 Oct;191(2):262-267 [FREE Full text] [doi: 10.1016/j.jss.2014.05.072] [Medline: 25066188]
62. Backstrom I, MacLennan P, Sawyer J, Creek A, Rue IL, Gilbert S. Pediatric obesity and traumatic lower-extremity long-bone fracture outcomes. J Trauma Acute Care Surg 2012 Oct;73(4):966-971 [FREE Full text] [doi: 10.1097/TA.0b013e31825a78fa] [Medline: 22902734]
63. Hierholzer C, Bühren V, Woltmann A. Operative timing and management of spinal injuries in multiply injured patients. Eur J Trauma Emerg Surg 2007 Oct;33(5):488-500. [doi: 10.1007/s00068-007-7127-0] [Medline: 26814934]
64. Andruszkow H, Liodakis E, Lefering R, Krettek C, Hildebrand F, Haasper C. Knee injuries in severe trauma patients: a trauma registry study in 3.458 patients. J Trauma Manag Outcomes 2012 Aug 06;6(1):7 [FREE Full text] [doi: 10.1186/1752-2897-6-7] [Medline: 22866995]
65. Cardona Cano S, Tiemeier H, Van Hoeken D, Tharner A, Jaddoe VW, Hofman A, et al. Trajectories of picky eating during childhood: a general population study. Int J Eat Disord 2015 Sep;48(6):570-579. [doi: 10.1002/eat.22384] [Medline: 25644130]
66. Kraus JF, Fife D, Conroy C. Incidence, severity, and outcomes of brain injuries involving bicycles. Am J Public Health 1987 Jan;77(1):76-78. [doi: 10.2105/ajph.77.1.76] [Medline: 3789243]
67. Jenewein J, Moergeli H, Wittmann L, Büchi S, Kraemer B, Schnyder U. Development of chronic pain following severe accidental injury. Results of a 3-year follow-up study. J Psychosom Res 2009 Feb;66(2):119-126. [doi: 10.1016/j.jpsychores.2008.07.011] [Medline: 19154854]
68. Brusselaers N, Monstrey S, Vogelaers D, Hoste E, Blot S. Severe burn injury in Europe: a systematic review of the incidence, etiology, morbidity, and mortality. Crit Care 2010;14(5):R188 [FREE Full text] [doi: 10.1186/cc9300] [Medline: 20958968]
69. de Carvalho Ponce J, Muñoz DR, Andreuccetti G, de Carvalho DG, Leyton V. Alcohol-related traffic accidents with fatal outcomes in the city of Sao Paulo. Accid Anal Prev 2011 May;43(3):782-787. [doi: 10.1016/j.aap.2010.10.025] [Medline: 21376866]
70. Eich C, Bräuer A, Timmermann A, Schwarz SK, Russo SG, Neubert K, et al. Outcome of 12 drowned children with attempted resuscitation on cardiopulmonary bypass: an analysis of variables based on the "Utstein Style for Drowning". Resuscitation 2007 Oct;75(1):42-52. [doi: 10.1016/j.resuscitation.2007.03.013] [Medline: 17499417]
71. Schoeneberg C, Kauther M, Hussmann B, Keitel J, Schmitz D, Lendemans S. Gender-specific differences in severely injured patients between 2002 and 2011: data analysis with matched-pair analysis. Crit Care 2013 Nov 29;17(6):R277 [FREE Full text] [doi: 10.1186/cc13132] [Medline: 24289182]
72. Peng J, Wheeler K, Shi J, Groner JI, Haley KJ, Xiang H. Trauma with injury severity score of 75: are these unsurvivable injuries? PLoS One 2015 Jul 31;10(7):e0134821 [FREE Full text] [doi: 10.1371/journal.pone.0134821] [Medline: 26230931]
73. Shinsugi C, Stickley A, Konishi S, Ng CF, Watanabe C. Seasonality of child and adolescent injury mortality in Japan, 2000-2010. Environ Health Prev Med 2015 Jan 31;20(1):36-43 [FREE Full text] [doi: 10.1007/s12199-014-0421-7] [Medline: 25358906]
74. Kobusingye O, Guwatudde D, Lett R. Injury patterns in rural and urban Uganda. Inj Prev 2001 Mar;7(1):46-50 [FREE Full text] [doi: 10.1136/ip.7.1.46] [Medline: 11289535]
75. Hill A, Pinto R, Nathens A, Fowler R. Age-related trends in severe injury hospitalization in Canada. J Trauma Acute Care Surg 2014 Oct;77(4):608-613. [doi: 10.1097/TA.0000000000000412] [Medline: 25250602]
76. Monuteaux M, Lee L, Fleegler E. Children injured by violence in the United States: emergency department utilization, 2000-2008. Acad Emerg Med 2012 May;19(5):535-540 [FREE Full text] [doi: 10.1111/j.1553-2712.2012.01341.x] [Medline: 22594357]
77. Gofin R, Avitzour M, Haklai Z, Jellin N. Intentional injuries among the young: presentation to emergency rooms, hospitalization, and death in Israel. J Adolesc Health 2000 Dec;27(6):434-442. [doi: 10.1016/s1054-139x(00)00091-4] [Medline: 11090746]
78. Lam NN, Dung NT. First aid and initial management for childhood burns in Vietnam--an appeal for public and continuing medical education. Burns 2008 Feb;34(1):67-70. [doi: 10.1016/j.burns.2007.01.006] [Medline: 18054172]
79. Reeb-Whitaker CK, Eckert CM, Anderson NJ, Bonauto DK. Occupational hydrofluoric acid injury from car and truck washing--Washington State, 2001-2013. MMWR Morb Mortal Wkly Rep 2015 Aug 21;64(32):874-877 [FREE Full text] [doi: 10.15585/mmwr.mm6432a4] [Medline: 26292206]

80. Kim KI, Lee WY, Kim HS, Jeong JH, Ko HH. Extracorporeal membrane oxygenation in near-drowning patients with cardiac or pulmonary failure. Scand J Trauma Resusc Emerg Med 2014 Dec 12;22:77 [FREE Full text] [doi: 10.1186/s13049-014-0077-8] [Medline: 25496812]
81. Nitta M, Kitamura T, Iwami T, Nadkarni VM, Berg RA, Topjian AA, et al. Out-of-hospital cardiac arrest due to drowning among children and adults from the Utstein Osaka Project. Resuscitation 2013 Nov;84(11):1568-1573 [FREE Full text] [doi: 10.1016/j.resuscitation.2013.06.017] [Medline: 23831805]
82. Centers for Disease Control and Prevention (CDC). Fatal and nonfatal injuries involving fishing vessel winches--Southern shrimp fleet, United States, 2000-2011. MMWR Morb Mortal Wkly Rep 2013 Mar 08;62(9):157-160 [FREE Full text] [Medline: 23466433]
83. Allman FD, Nelson WB, Pacentine GA, McComb G. Outcome following cardiopulmonary resuscitation in severe pediatric near-drowning. Am J Dis Child 1986 Jun;140(6):571-575. [doi: 10.1001/archpedi.1986.02140200081033] [Medline: 3706238]
84. Cummings P, Quan L. Trends in unintentional drowning: the role of alcohol and medical care. JAMA 1999 Jun 16;281(23):2198-2202. [doi: 10.1001/jama.281.23.2198] [Medline: 10376572]
85. Bell N, Cai B. Reliability of the American Community Survey for unintentional drowning and submersion injury surveillance: a comprehensive assessment of 10 socioeconomic indicators derived from the 2006-2013 annual and multi-year data cycles. Inj Epidemiol 2015;2(1):33 [FREE Full text] [doi: 10.1186/s40621-015-0065-0] [Medline: 26753124]
86. Leroy P, Smismans A, Seute T. Invasive pulmonary and central nervous system aspergillosis after near-drowning of a child: case report and review of the literature. Pediatrics 2006 Aug;118(2):e509-e513. [doi: 10.1542/peds.2005-2901] [Medline: 16864641]
87. Demetriades D, Murray J, Brown C, Velmahos G, Salim A, Alo K, et al. High-level falls: type and severity of injuries and survival outcome according to age. J Trauma 2005 Feb;58(2):342-345. [doi: 10.1097/01.ta.0000135161.44100.d8] [Medline: 15706198]
88. Gill TM, Murphy TE, Gahbauer EA, Allore HG. The course of disability before and after a serious fall injury. JAMA Intern Med 2013 Oct 28;173(19):1780-1786 [FREE Full text] [doi: 10.1001/jamainternmed.2013.9063] [Medline: 23958741]
89. Neuman MD, Silber JH, Magaziner JS, Passarella MA, Mehta S, Werner RM. Survival and functional outcomes after hip fracture among nursing home residents. JAMA Intern Med 2014 Aug;174(8):1273-1280 [FREE Full text] [doi: 10.1001/jamainternmed.2014.2362] [Medline: 25055155]
90. Imahara S, Hopper R, Wang J, Rivara F, Klein M. Patterns and outcomes of pediatric facial fractures in the United States: a survey of the National Trauma Data Bank. J Am Coll Surg 2008 Nov;207(5):710-716 [FREE Full text] [doi: 10.1016/j.jamcollsurg.2008.06.333] [Medline: 18954784]
91. Kaye P, O'Sullivan I. Myocardial contusion: emergency investigation and diagnosis. Emerg Med J 2002 Jan;19(1):8-10 [FREE Full text] [doi: 10.1136/emj.19.1.8] [Medline: 11777862]
92. Gómez PA, de-la-Cruz J, Lora D, Jiménez-Roldán L, Rodríguez-Boto G, Sarabia R, et al. Validation of a prognostic score for early mortality in severe head injury cases. J Neurosurg 2014 Dec;121(6):1314-1322. [doi: 10.3171/2014.7.JNS131874] [Medline: 25237737]
93. MRC CRASH Trial Collaborators, Perel P, Arango M, Clayton T, Edwards P, Komolafe E, et al. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. BMJ 2008 Feb 23;336(7641):425-429 [FREE Full text] [doi: 10.1136/bmj.39461.643438.25] [Medline: 18270239]
94. Adelson PD, Wisniewski SR, Beca J, Brown SD, Bell M, Muizelaar JP, Paediatric Traumatic Brain Injury Consortium. Comparison of hypothermia and normothermia after severe traumatic brain injury in children (Cool Kids): a phase 3, randomised controlled trial. Lancet Neurol 2013 Jun;12(6):546-553 [FREE Full text] [doi: 10.1016/S1474-4422(13)70077-2] [Medline: 23664370]
95. Chesnut RM, Marshall LF, Klauber MR, Blunt BA, Baldwin N, Eisenberg HM, et al. The role of secondary brain injury in determining outcome from severe head injury. J Trauma 1993 Feb;34(2):216-222. [doi: 10.1097/00005373-199302000-00006] [Medline: 8459458]
96. Ducrocq SC, Meyer PG, Orliaguet GA, Blanot S, Laurent-Vannier A, Renier D, et al. Epidemiology and early predictive factors of mortality and outcome in children with traumatic severe brain injury: experience of a French pediatric trauma center. Pediatr Crit Care Med 2006 Sep;7(5):461-467. [doi: 10.1097/01.PCC.0000235245.49129.27] [Medline: 16885795]
97. Ling G, Bandak F, Armonda R, Grant G, Ecklund J. Explosive blast neurotrauma. J Neurotrauma 2009 Jun;26(6):815-825. [doi: 10.1089/neu.2007.0484] [Medline: 19397423]
98. Haider AH, Efron DT, Haut ER, DiRusso SM, Sullivan T, Cornwell 3rd EE. Black children experience worse clinical and functional outcomes after traumatic brain injury: an analysis of the National Pediatric Trauma Registry. J Trauma 2007 May;62(5):1259-1263. [doi: 10.1097/TA.0b013e31803c760e] [Medline: 17495733]
99. Beckman K, Mittendorfer-Rutz E, Lichtenstein P, Larsson H, Almqvist C, Runeson B, et al. Mental illness and suicide after self-harm among young adults: long-term follow-up of self-harm patients, admitted to hospital care, in a national cohort. Psychol Med 2016 Dec;46(16):3397-3405. [doi: 10.1017/S0033291716002282] [Medline: 27644850]
100. Cryer C, Langley JD, Jarvis SN, Mackenzie SG, Stephenson SR, Heywood P. Injury outcome indicators: the development of a validation tool. Inj Prev 2005 Feb;11(1):53-57 [FREE Full text] [doi: 10.1136/ip.2003.004143] [Medline: 15691991]

101. Gururaj G. Road traffic deaths, injuries and disabilities in India: current scenario. Natl Med J India 2008;21(1):14-20. [Medline: 18472698]
102. Smink B, Ruiter B, Lusthof K, de Gier JJ, Uges D, Egberts A. Drug use and the severity of a traffic accident. Accid Anal Prev 2005 May;37(3):427-433. [doi: 10.1016/j.aap.2004.12.003] [Medline: 15784196]
103. Murdock MA, Waxman K. Helmet use improves outcomes after motorcycle accidents. West J Med 1991 Oct;155(4):370-372 [FREE Full text] [Medline: 1771873]
104. Schiff MA, Holt VL. Pregnancy outcomes following hospitalization for motor vehicle crashes in Washington State from 1989 to 2001. Am J Epidemiol 2005 Mar 15;161(6):503-510. [doi: 10.1093/aje/kwi078] [Medline: 15746466]
105. Tefft BC. Impact speed and a pedestrian's risk of severe injury or death. Accid Anal Prev 2013 Jan;50:871-878. [doi: 10.1016/j.aap.2012.07.022] [Medline: 22935347]
106. Samuelson H, Nekludov M, Levander M. Neuropsychological outcome following near-drowning in ice water: two adult case studies. J Int Neuropsychol Soc 2008 Jul;14(4):660-666. [doi: 10.1017/S1355617708080855] [Medline: 18577297]
107. Finès P, Bougie E, Oliver N, Kohen D. Hospitalizations for unintentional injuries among Canadian adults in areas with a high percentage of Aboriginal-identity residents. Chronic Dis Inj Can 2013 Sep;33(4):204-217 [FREE Full text] [Medline: 23987217]
108. Randall SM, Fear MW, Wood FM, Rea S, Boyd JH, Duke JM. Long-term musculoskeletal morbidity after adult burn injury: a population-based cohort study. BMJ Open 2015 Sep 11;5(9):e009395 [FREE Full text] [doi: 10.1136/bmjopen-2015-009395] [Medline: 26362668]
109. Carayanni VJ, Tsati EG, Spyropoulou GC, Antonopoulou FN, Ioannovich JD. Comparing oil based ointment versus standard practice for the treatment of moderate burns in Greece: a trial based cost effectiveness evaluation. BMC Complement Altern Med 2011 Dec 01;11:122 [FREE Full text] [doi: 10.1186/1472-6882-11-122] [Medline: 22132709]
110. Druery M, Brown TL, La H Brown T, Muller M. Long term functional outcomes and quality of life following severe burn injury. Burns 2005 Sep;31(6):692-695. [doi: 10.1016/j.burns.2005.03.001] [Medline: 16129223]
111. Kimmo T, Jyrki V, Sirpa A. Health status after recovery from burn injury. Burns 1998 Jun;24(4):293-298. [doi: 10.1016/s0305-4179(98)00007-2] [Medline: 9688192]
112. Mahendraraj K, Durgan DM, Chamberlain RS. Acute mental disorders and short and long term morbidity in patients with third degree flame burn: a population-based outcome study of 96,451 patients from the Nationwide Inpatient Sample (NIS) database (2001-2011). Burns 2016 Dec;42(8):1766-1773. [doi: 10.1016/j.burns.2016.06.001] [Medline: 27576933]
113. Gregorakos L, Markou N, Psalida V, Kanakaki M, Alexopoulou A, Sotiriou E, et al. Near-drowning: clinical course of lung injury in adults. Lung 2009;187(2):93-97. [doi: 10.1007/s00408-008-9132-4] [Medline: 19132444]
114. Yaokreh J, Odehouri-Koudou T, Tembely S, Dieth A, Kouamé DB, Ouattara O, et al. Delayed treatment of supracondylar elbow fractures in children. Orthop Traumatol Surg Res 2012 Nov;98(7):808-812 [FREE Full text] [doi: 10.1016/j.otsr.2012.07.005] [Medline: 23064021]
115. Sekhon LH, Fehlings MG. Epidemiology, demographics, and pathophysiology of acute spinal cord injury. Spine (Phila Pa 1976) 2001 Dec 15;26(24 Suppl):S2-12. [doi: 10.1097/00007632-200112151-00002] [Medline: 11805601]
116. Wang G, Yin S, Shear B, Heard K. Severe poisoning after accidental pediatric ingestion of glycol ethers. Pediatrics 2012 Oct;130(4):e1026-e1029. [doi: 10.1542/peds.2011-3849] [Medline: 23008459]
117. Olfson M, Gameroff MJ, Marcus SC, Greenberg T, Shaffer D. National trends in hospitalization of youth with intentional self-inflicted injuries. Am J Psychiatry 2005 Jul;162(7):1328-1335. [doi: 10.1176/appi.ajp.162.7.1328] [Medline: 15994716]
118. El-Khoury F, Cassou B, Charles M, Dargent-Molina P. The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials. BMJ 2013 Oct 29;347:f6234 [FREE Full text] [doi: 10.1136/bmj.f6234] [Medline: 24169944]
119. Lee JC, Tung KT, Li TM, Ho FK, Ip P, Wong WH, et al. Fall-related attendance and associated hospitalisation of children and adolescents in Hong Kong: a 12-year retrospective study. BMJ Open 2017 Feb 07;7(2):e013724 [FREE Full text] [doi: 10.1136/bmjopen-2016-013724] [Medline: 28174223]
120. Sulyman N, Kim MK, Rampa S, Allareddy V, Nalliah RP, Allareddy V. Self Inflicted Injuries among Children in United States - estimates from a nationwide emergency department sample. PLoS One 2013 Jul 18;8(7):e69874 [FREE Full text] [doi: 10.1371/journal.pone.0069874] [Medline: 23875006]
121. Linehan MM, Comtois KA, Brown MZ, Heard HL, Wagner A. Suicide Attempt Self-Injury Interview (SASII): development, reliability, and validity of a scale to assess suicide attempts and intentional self-injury. Psychol Assess 2006 Sep;18(3):303-312. [doi: 10.1037/1040-3590.18.3.303] [Medline: 16953733]
122. Tan N, Ang A, Heng D, Chen J, Wong H. Evaluation of playground injuries based on ICD, E codes, international classification of external cause of injury codes (ICECI), and abbreviated injury scale coding systems. Asia Pac J Public Health 2007;19(1):18-27. [doi: 10.1177/10105395070190010501] [Medline: 17784655]
123. Oliver L, Finès P, Bougie E, Kohen D. Intentional injury hospitalizations in geographical areas with a high percentage of Aboriginal-identity residents, 2004/2005 to 2009/2010. Chronic Dis Inj Can 2014 Jul;34(2-3):82-93 [FREE Full text] [Medline: 24991771]

124. Kreder HJ, Rozen N, Borkhoff CM, Laflamme YG, McKee MD, Schemitsch EH, et al. Determinants of functional outcome after simple and complex acetabular fractures involving the posterior wall. J Bone Joint Surg Br 2006 Jun;88(6):776-782. [doi: 10.1302/0301-620X.88B6.17342] [Medline: 16720773]
125. Zakharov S, Navratil T, Salek T, Kurcova I, Pelclova D. Fluctuations in serum ethanol concentration in the treatment of acute methanol poisoning: a prospective study of 21 patients. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2015 Dec;159(4):666-676 [FREE Full text] [doi: 10.5507/bp.2015.008] [Medline: 25732977]
126. Leach P, Pathmanaban ON, Patel HC, Evans J, Sacho R, Protheroe R, et al. Outcome after severe head injury: focal surgical lesions do not imply a better Glasgow Outcome Score than diffuse injuries at 3 months. J Trauma Manag Outcomes 2009 Apr 03;3:5 [FREE Full text] [doi: 10.1186/1752-2897-3-5] [Medline: 19344513]
127. Ewing-Cobbs L, Prasad MR, Kramer L, Cox CS, Baumgartner J, Fletcher S, et al. Late intellectual and academic outcomes following traumatic brain injury sustained during early childhood. J Neurosurg 2006 Oct;105(4 Suppl):287-296 [FREE Full text] [doi: 10.3171/ped.2006.105.4.287] [Medline: 17328279]
128. Kenardy J, Spence S, Macleod A. Screening for posttraumatic stress disorder in children after accidental injury. Pediatrics 2006 Sep;118(3):1002-1009. [doi: 10.1542/peds.2006-0406] [Medline: 16950991]
129. He F, Zhou Q, Zhao Z, Zhang Y, Guan H. Effect of perceived social support and dispositional optimism on the depression of burn patients. J Health Psychol 2016 Jun;21(6):1119-1125. [doi: 10.1177/1359105314546776] [Medline: 25161173]
130. McGarry S, Burrows S, Ashoorian T, Pallathil T, Ong K, Edgar DW, et al. Mental health and itch in burns patients: potential associations. Burns 2016 Jun;42(4):763-768. [doi: 10.1016/j.burns.2016.01.010] [Medline: 26948956]
131. Schäfer I, Barkmann C, Riedesser P, Schulte-Markwort M. Posttraumatic syndromes in children and adolescents after road traffic accidents--a prospective cohort study. Psychopathology 2006;39(4):159-164. [doi: 10.1159/000092676] [Medline: 16612135]
132. Wu K, Chan S, Yiu VF. Psychometric properties and confirmatory factor analysis of the posttraumatic stress disorder checklist for Chinese survivors of road traffic accidents. Hong Kong J Psychiatry 2008;18(4):144-152.
133. Anzarut A, Chen M, Shankowsky H, Tredget EE. Quality-of-life and outcome predictors following massive burn injury. Plast Reconstr Surg 2005 Sep;116(3):791-797. [doi: 10.1097/01.prs.0000176257.22583.4b] [Medline: 16141817]
134. Girotto JA, MacKenzie E, Fowler C, Redett R, Robertson B, Manson PN. Long-term physical impairment and functional outcomes after complex facial fractures. Plast Reconstr Surg 2001 Aug;108(2):312-327. [doi: 10.1097/00006534-200108000-00005] [Medline: 11496168]
135. Hours M, Chossegros L, Charnay P, Tardy H, Nhac-Vu H, Boisson D, et al. Outcomes one year after a road accident: results from the ESPARR cohort. Accid Anal Prev 2013 Jan;50:92-102. [doi: 10.1016/j.aap.2012.03.037] [Medline: 23200444]
136. Whelan D, Litchfield R, Wambolt E, Dainty K, Joint Orthopaedic Initiative for National Trials of the Shoulder (JOINTS). External rotation immobilization for primary shoulder dislocation: a randomized controlled trial. Clin Orthop Relat Res 2014 Aug;472(8):2380-2386 [FREE Full text] [doi: 10.1007/s11999-013-3432-6] [Medline: 24385033]
137. Goldfarb CA, Ricci WM, Tull F, Ray D, Borrelli J. Functional outcome after fracture of both bones of the forearm. J Bone Joint Surg Br 2005 Mar;87(3):374-379. [doi: 10.1302/0301-620x.87b3.15509] [Medline: 15773649]
138. Musselman K, Fouad K, Misiaszek J, Yang J. Training of walking skills overground and on the treadmill: case series on individuals with incomplete spinal cord injury. Phys Ther 2009 Jun;89(6):601-611. [doi: 10.2522/ptj.20080257] [Medline: 19423643]
139. Angelini F, Helito C, Bonadio M, da Mota E Albuquerque RF, Pecora J, Camanho G. Surgical management of knee dislocations with ligament reconstruction associated with a hinged external fixator. Orthop Traumatol Surg Res 2015 Feb;101(1):77-81 [FREE Full text] [doi: 10.1016/j.otsr.2014.11.001] [Medline: 25530481]
140. Manidakis N, Dosani A, Dimitriou R, Stengel D, Matthews S, Giannoudis P. Tibial plateau fractures: functional outcome and incidence of osteoarthritis in 125 cases. Int Orthop 2010 Apr;34(4):565-570 [FREE Full text] [doi: 10.1007/s00264-009-0790-5] [Medline: 19440710]
141. de Haan J, Schep NW, Zengerink I, van Buijtenen J, Tuinebreijer WE, den Hartog D. Dislocation of the elbow: a retrospective multicentre study of 86 patients. Open Orthop J 2010 Feb 17;4:76-79 [FREE Full text] [doi: 10.2174/1874325001004020076] [Medline: 20352027]
142. Davey NJ, Smith HC, Wells E, Maskill DW, Savic G, Ellaway PH, et al. Responses of thenar muscles to transcranial magnetic stimulation of the motor cortex in patients with incomplete spinal cord injury. J Neurol Neurosurg Psychiatry 1998 Jul;65(1):80-87 [FREE Full text] [doi: 10.1136/jnnp.65.1.80] [Medline: 9667566]
143. Yoon S, Shim Y, Park Y, Chung J, Nam J, Kim M, et al. Complete spinal cord injury treatment using autologous bone marrow cell transplantation and bone marrow stimulation with granulocyte macrophage-colony stimulating factor: phase I/II clinical trial. Stem Cells 2007 Aug;25(8):2066-2073 [FREE Full text] [doi: 10.1634/stemcells.2006-0807] [Medline: 17464087]
144. Casha S, Zygun D, McGowan M, Bains I, Yong V, Hurlbert RJ. Results of a phase II placebo-controlled randomized trial of minocycline in acute spinal cord injury. Brain 2012 Apr;135(Pt 4):1224-1236. [doi: 10.1093/brain/aws072] [Medline: 22505632]
145. Malm S, Krafft M, Kullgren A, Ydenius A, Tingvall C. Risk of permanent medical impairment (RPMI) in road traffic accidents. Ann Adv Automot Med 2008 Oct;52:93-100 [FREE Full text] [Medline: 19026226]

146. Macpherson P, Teasdale E, Dhaker S, Allerdyce G, Galbraith S. The significance of traumatic haematoma in the region of the basal ganglia. J Neurol Neurosurg Psychiatry 1986 Jan;49(1):29-34 [FREE Full text] [doi: 10.1136/jnnp.49.1.29] [Medline: 3958729]
147. Olver JH, Ponsford JL, Curran CA. Outcome following traumatic brain injury: a comparison between 2 and 5 years after injury. Brain Inj 1996 Nov;10(11):841-848. [doi: 10.1080/026990596123945] [Medline: 8905161]
148. Kazim SF, Shamim MS, Tahir M, Enam SA, Waheed S. Management of penetrating brain injury. J Emerg Trauma Shock 2011 Jul;4(3):395-402 [FREE Full text] [doi: 10.4103/0974-2700.83871] [Medline: 21887033]
149. Berger RP, Beers SR, Richichi R, Wiesman D, Adelson PD. Serum biomarker concentrations and outcome after pediatric traumatic brain injury. J Neurotrauma 2007 Dec;24(12):1793-1801. [doi: 10.1089/neu.2007.0316] [Medline: 18159990]
150. Hedman H, Holmdahl J, Mölne J, Ebefors K, Haraldsson B, Nyström J. Long-term clinical outcome for patients poisoned by the fungal nephrotoxin orellanine. BMC Nephrol 2017 Apr 03;18(1):121 [FREE Full text] [doi: 10.1186/s12882-017-0533-6] [Medline: 28372584]
151. Zatzick DF, Jurkovich GJ, Gentilello L, Wisner D, Rivara FP. Posttraumatic stress, problem drinking, and functional outcomes after injury. Arch Surg 2002 Feb;137(2):200-205. [doi: 10.1001/archsurg.137.2.200] [Medline: 11822960]
152. Rentschler G, Broberg K, Lundh T, Skerfving S. Long-term lead elimination from plasma and whole blood after poisoning. Int Arch Occup Environ Health 2012 Apr;85(3):311-316 [FREE Full text] [doi: 10.1007/s00420-011-0673-0] [Medline: 21701834]
153. Alanazi MQ, Al-Jeraisy M, Salam M. Severity scores and their associated factors among orally poisoned toddlers: a cross sectional single poison center study. BMC Pharmacol Toxicol 2016 Jan 04;17(1):1 [FREE Full text] [doi: 10.1186/s40360-015-0044-7] [Medline: 26729401]
154. Peltz E, D'Alessandro A, Moore E, Chin T, Silliman C, Sauaia A, et al. Pathologic metabolism: an exploratory study of the plasma metabolome of critical injury. J Trauma Acute Care Surg 2015 Apr;78(4):742-751 [FREE Full text] [doi: 10.1097/TA.0000000000000589] [Medline: 25807403]
155. Su Y, Chen W, Zhang Q, Liu S, Zhang T, Zhang Y. Bony destructive injuries of the calcaneus: long-term results of a minimally invasive procedure followed by early functional exercise: a retrospective study. BMC Surg 2014 Apr 11;14:19 [FREE Full text] [doi: 10.1186/1471-2482-14-19] [Medline: 24725606]
156. Frey-Rindova P, de Bruin E, Stüssi E, Dambacher M, Dietz V. Bone mineral density in upper and lower extremities during 12 months after spinal cord injury measured by peripheral quantitative computed tomography. Spinal Cord 2000 Jan;38(1):26-32. [doi: 10.1038/sj.sc.3100905] [Medline: 10762194]
157. Miyanji F, Furlan JC, Aarabi B, Arnold PM, Fehlings MG. Acute cervical traumatic spinal cord injury: MR imaging findings correlated with neurologic outcome--prospective study with 100 consecutive patients. Radiology 2007 Jun;243(3):820-827. [doi: 10.1148/radiol.2433060583] [Medline: 17431129]
158. Hammig B, Jozkowski K, Jones C. Injury-related visits and comorbid conditions among homeless persons presenting to emergency departments. Acad Emerg Med 2014 Apr;21(4):449-455 [FREE Full text] [doi: 10.1111/acem.12343] [Medline: 24730408]
159. Sheridan RL, Hinson MI, Liang MH, Nackel AF, Schoenfeld DA, Ryan CM, et al. Long-term outcome of children surviving massive burns. JAMA 2000 Jan 05;283(1):69-73. [doi: 10.1001/jama.283.1.69] [Medline: 10632282]
160. Wong JS, Brooks D, Inness EL, Mansfield A. The impact of falls on motor and cognitive recovery after discharge from in-patient stroke rehabilitation. J Stroke Cerebrovasc Dis 2016 Jul;25(7):1613-1621 [FREE Full text] [doi: 10.1016/j.jstrokecerebrovasdis.2016.03.017] [Medline: 27062418]
161. Brzuzy S, Corrlgan JD. Predictors of living independently after moderate to severe traumatic brain injury: a comparison study. J Head Trauma Rehabil 1996;11(3):74-83. [doi: 10.1097/00001199-199606000-00011]
162. Mayou R, Bryant B. Outcome 3 years after a road traffic accident. Psychol Med 2002 May;32(4):671-675. [doi: 10.1017/s0033291702005470] [Medline: 12102381]
163. Peeters GM, Jones M, Byles J, Dobson AJ. Long-term consequences of noninjurious and injurious falls on well-being in older women. J Gerontol A Biol Sci Med Sci 2015 Dec;70(12):1519-1525. [doi: 10.1093/gerona/glv102] [Medline: 26273020]
164. Ruchholtz S, Pajonk FG, Waydhas C, Lewan U, Nast-Kolb D, Schweiberer L. Long-term results and quality of life after parasuicidal multiple blunt trauma. Crit Care Med 1999 Mar;27(3):522-530. [doi: 10.1097/00003246-199903000-00029] [Medline: 10199531]
165. Bui E, Brunet A, Allenou C, Camassel C, Raynaud J, Claudet I, et al. Peritraumatic reactions and posttraumatic stress symptoms in school-aged children victims of road traffic accident. Gen Hosp Psychiatry 2010;32(3):330-333. [doi: 10.1016/j.genhosppsych.2010.01.014] [Medline: 20430239]
166. Logsetty S, Shamlou A, Gawaziuk JP, March J, Doupe M, Chateau D, et al. Mental health outcomes of burn: a longitudinal population-based study of adults hospitalized for burns. Burns 2016 Jun;42(4):738-744. [doi: 10.1016/j.burns.2016.03.006] [Medline: 27049068]
167. Tang D, Li-Tsang CW, Au RK, Li K, Yi X, Liao L, et al. Functional outcomes of burn patients with or without rehabilitation in Mainland China. Hong Kong J Occup Ther 2015 Dec 01;26(1):15-23. [doi: 10.1016/j.hkjot.2015.08.003]
168. Brenneman FD, Redelmeier DA, Boulanger BR, McLellan BA, Culhane JP. Long-term outcomes in blunt trauma: who goes back to work? J Trauma 1997 May;42(5):778-781. [doi: 10.1097/00005373-199705000-00004] [Medline: 9191655]

169. Ly TV, Travison TG, Castillo RC, Bosse MJ, MacKenzie EJ, LEAP Study Group. Ability of lower-extremity injury severity scores to predict functional outcome after limb salvage. J Bone Joint Surg Am 2008 Aug;90(8):1738-1743 [FREE Full text] [doi: 10.2106/JBJS.G.00136] [Medline: 18676906]
170. De Silva MJ, Roberts I, Perel P, Edwards P, Kenward MG, Fernandes J, CRASH Trial Collaborators. Patient outcome after traumatic brain injury in high-, middle- and low-income countries: analysis of data on 8927 patients in 46 countries. Int J Epidemiol 2009 May 09;38(2):452-458. [doi: 10.1093/ije/dyn189] [Medline: 18782898]
171. Biffl WL, Moore EE, Moore FA, Peterson VM. Interleukin-6 in the injured patient. Marker of injury or mediator of inflammation? Ann Surg 1996 Nov;224(5):647-664. [doi: 10.1097/00000658-199611000-00009] [Medline: 8916880]
172. Hur J, Yang HT, Chun W, Kim J, Shin S, Kang HJ, et al. Inflammatory cytokines and their prognostic ability in cases of major burn injury. Ann Lab Med 2015 Jan;35(1):105-110 [FREE Full text] [doi: 10.3343/alm.2015.35.1.105] [Medline: 25553289]
173. Corps KN, Roth TL, McGavern DB. Inflammation and neuroprotection in traumatic brain injury. JAMA Neurol 2015 Mar;72(3):355-362 [FREE Full text] [doi: 10.1001/jamaneurol.2014.3558] [Medline: 25599342]
174. Spinks A, Turner C, Nixon J, McClure R. The 'WHO Safe Communities' model for the prevention of injury in whole populations. Cochrane Database Syst Rev 2009 Jul 08;2009(3):CD004445 [FREE Full text] [doi: 10.1002/14651858.CD004445.pub3] [Medline: 19588359]
175. Plemmons G, Hall M, Doupnik S, Gay J, Brown C, Browning W, et al. Hospitalization for suicide ideation or attempt: 2008-2015. Pediatrics 2018 Jun;141(6):e20172426. [doi: 10.1542/peds.2017-2426] [Medline: 29769243]
176. Chow C, Leung M, Lai A, Chow Y, Chung J, Tong K, et al. Development of an electronic emergency department-based geo-information injury surveillance system in Hong Kong. Injury 2012 Jun;43(6):739-748. [doi: 10.1016/j.injury.2011.08.008] [Medline: 21924722]
177. Shipton D, Stone DH. The Yorkhill CHIRPP story: a qualitative evaluation of 10 years of injury surveillance at a Scottish children's hospital. Inj Prev 2008 Aug;14(4):245-249. [doi: 10.1136/ip.2008.018358] [Medline: 18676783]

## Abbreviations

**AED:** accident and emergency department
**CDARS:** Clinical Data Analysis and Reporting System
**DALY:** disability-adjusted life year
**ICU:** intensive care unit

*Edited by Y Khader; submitted 28.01.22; peer-reviewed by E Kemler, J Trevino; comments to author 01.04.22; revised version received 26.05.22; accepted 09.06.22; published 18.08.22.*

*Please cite as:*
*Tung KTS, Wong RS, Ho FK, Chan KL, Wong WHS, Leung H, Leung M, Leung GKK, Chow CB, Ip P*
*Development and Validation of Indicators for Population Injury Surveillance in Hong Kong: Development and Usability Study*
*JMIR Public Health Surveill 2022;8(8):e36861*
*URL: https://publichealth.jmir.org/2022/8/e36861*
*doi:10.2196/36861*
*PMID:35980728*

Original Paper

# Differences in Clinical Presentation With Long COVID After Community and Hospital Infection and Associations With All-Cause Mortality: English Sentinel Network Database Study

Bernardo Meza-Torres[1], MBBS, MSc, MA, PhD; Gayathri Delanerolle[1], MBBS, BSc, MSc; Cecilia Okusi[1], BSc, MSc; Nikhil Mayor[2], MBBS; Sneha Anand[1], BSc, MSc, PhD; Jack Macartney[1], BSc; Piers Gatenby[2], MBBS, PhD; Ben Glampson[3], BSc; Martin Chapman[4], BSc, MSc, PhD; Vasa Curcin[4], BSc, PhD; Erik Mayer[3], MBBS, PhD; Mark Joy[1], BSc, PhD; Trisha Greenhalgh[1], MBBS, BSc, MSc, PhD; Brendan Delaney[5], MBBS, BSc, PhD; Simon de Lusignan[1], MBBS, MSc, MD

[1]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, United Kingdom
[2]Royal Surrey NHS Foundation Trust, Guildford, United Kingdom
[3]Imperial College Healthcare NHS Trust, Imperial Clinical Analytics, Research & Evaluation (iCARE), London, United Kingdom
[4]King's College London, Population Health Sciences, London, United Kingdom
[5]Department of Surgery & Cancer, Institute of Global Health Innovation, Imperial College London, London, United Kingdom

**Corresponding Author:**
Simon de Lusignan, MBBS, MSc, MD
Nuffield Department of Primary Care Health Sciences
University of Oxford
Eagle House
Walton Well Road
Oxford, OX2 6ED
United Kingdom
Phone: 44 01865 616600
Email: simon.delusignan@phc.ox.ac.uk

## Abstract

**Background:** Most studies of long COVID (symptoms of COVID-19 infection beyond 4 weeks) have focused on people hospitalized in their initial illness. Long COVID is thought to be underrecorded in UK primary care electronic records.

**Objective:** We sought to determine which symptoms people present to primary care after COVID-19 infection and whether presentation differs in people who were not hospitalized, as well as post–long COVID mortality rates.

**Methods:** We used routine data from the nationally representative primary care sentinel cohort of the Oxford–Royal College of General Practitioners Research and Surveillance Centre (N=7,396,702), applying a predefined long COVID phenotype and grouped by whether the index infection occurred in hospital or in the community. We included COVID-19 infection cases from March 1, 2020, to April 1, 2021. We conducted a before-and-after analysis of long COVID symptoms prespecified by the Office of National Statistics, comparing symptoms presented between 1 and 6 months after the index infection matched with the same months 1 year previously. We conducted logistic regression analysis, quoting odds ratios (ORs) with 95% CIs.

**Results:** In total, 5.63% (416,505/7,396,702) and 1.83% (7623/416,505) of the patients had received a coded diagnosis of COVID-19 infection and diagnosis of, or referral for, long COVID, respectively. People with diagnosis or referral of long COVID had higher odds of presenting the prespecified symptoms after versus before COVID-19 infection (OR 2.66, 95% CI 2.46-2.88, for those with index community infection and OR 2.42, 95% CI 2.03-2.89, for those hospitalized). After an index community infection, patients were more likely to present with nonspecific symptoms (OR 3.44, 95% CI 3.00-3.95; *P*<.001) compared with after a hospital admission (OR 2.09, 95% CI 1.56-2.80; *P*<.001). Mental health sequelae were more strongly associated with index hospital infections (OR 2.21, 95% CI 1.64-2.96) than with index community infections (OR 1.36, 95% CI 1.21-1.53; *P*<.001). People presenting to primary care after hospital infection were more likely to be men (OR 1.43, 95% CI 1.25-1.64; *P*<.001), more socioeconomically deprived (OR 1.42, 95% CI 1.24-1.63; *P*<.001), and with higher multimorbidity scores (OR 1.41, 95% CI 1.26-1.57; *P*<.001) than those presenting after an index community infection. All-cause mortality in people with long COVID was associated with increasing age, male sex (OR 3.32, 95% CI 1.34-9.24; *P*=.01), and higher multimorbidity score

(OR 2.11, 95% CI 1.34-3.29; *P*<.001). Vaccination was associated with reduced odds of mortality (OR 0.10, 95% CI 0.03-0.35; *P*<.001).

**Conclusions:** The low percentage of people recorded as having long COVID after COVID-19 infection reflects either low prevalence or underrecording. The characteristics and comorbidities of those presenting with long COVID after a community infection are different from those hospitalized. This study provides insights into the presentation of long COVID in primary care and implications for workload.

***(JMIR Public Health Surveill 2022;8(8):e37668)*** doi:10.2196/37668

**KEYWORDS**

medical record systems; computerized; Systematized Nomenclature of Medicine; post–acute COVID-19 syndrome; phenotype; COVID-19; post–COVID-19 syndrome; long COVID; ethnicity; social class; general practitioners; data accuracy; data extracts; biomedical ontologies; SARS-CoV-2; hospitalization

## Introduction

### Background

Long COVID (LC) is defined as fatigue, breathlessness, cognitive dysfunction, and a variety of other symptoms occurring after COVID-19 infection [1,2]. More than 1 million people in the United Kingdom are estimated to have prolonged symptoms after COVID-19 infection, with 60% of the patients with long COVID reporting extended symptoms lasting months and 240,000 people reporting symptoms that limit day-to-day activity [3,4]. The spectrum of symptoms implies widespread involvement of organs, and there is a recognizable pattern of long COVID disease resulting from autonomic dysfunction and mast cell disorder [5]. The Office for National Statistics (ONS) suggests that the prevalence of long COVID is greater in women, middle-aged people, those from the most deprived areas, and those with an activity-limiting health condition or disability [4]. Symptoms are wide ranging, but fatigue, shortness of breath, and cognitive difficulties (termed *brain fog* by patients) are most commonly reported [6-8]. In late 2020, there was a release of International Classification of Disease and Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) to support long COVID coding (termed post–COVID-19 condition) but recording in primary care electronic records varied [9,10]. However, primary care data remain the most useful source of epidemiological data outside hospital records and bespoke surveys to understand the symptoms that patients with long COVID present to primary care after documented COVID-19 infection [6]. There is a need to characterize the prevalence, risk factors, and symptom patterns in patients with long COVID using routine clinical data to understand the symptoms that people present with at primary care facilities after COVID-19 infection and whether presentation and postacute mortality differ in people who were not hospitalized.

### This Study

This study reports the symptoms, sociodemographic profile, and outcomes of people identified as having long COVID in English primary care. Our study has four components: (1) a comparison of clinical symptoms of people with long COVID before and after COVID-19 infection, (2) a description of the characteristics of people with long COVID compared with those without long COVID, (3) a comparison of those with long COVID who were hospitalized with COVID-19 infection versus those who were not, and (4) an analysis of all-cause mortality in people with long COVID.

## Methods

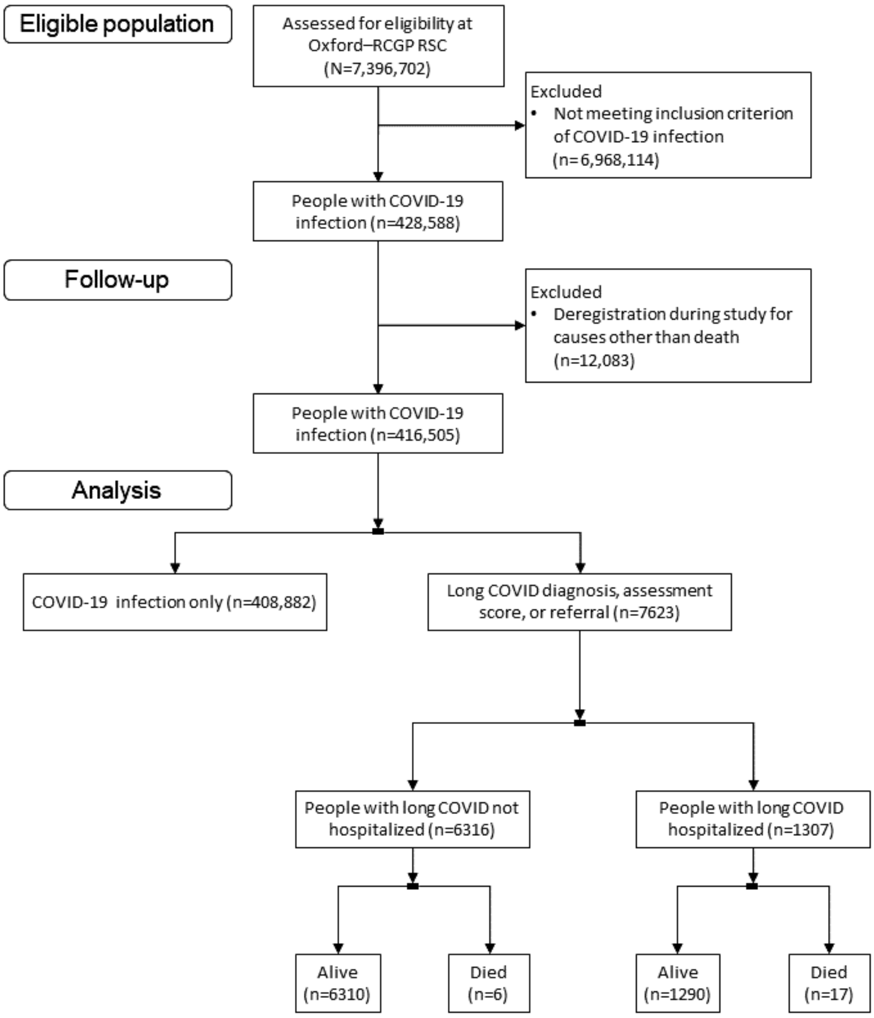
### Overview

This study was conducted as part of the Predicting Risk of Hospital Admission in Patients With Suspected COVID-19 in a Community Setting (Remote COVID-19 Assessment in Primary Care) project [11-13]. The project included creating a phenotype for LC through an observational study. The population characteristics, baseline data, and our LC phenotype were published in the study protocol [14]. The protocol also set out the details of the comparisons undertaken in this study. These were as follows: (1) undertaking a before-and-after comparison of the number of symptoms identified by the ONS as more common in LC; (2) comparing sociodemographic, comorbid, and exposure characteristics of people who had received a coded diagnosis of LC from their general practitioner (GP) with those of people who had not; (3) comparing characteristics of people with LC who had contracted their index infection in hospital with those of people who had contracted a community infection; and (4) an analysis of all-cause mortality in people with LC. The study period included COVID-19 infection cases between March 1, 2020, and April 1, 2021, with a follow-up period of a further 6 months, up to September 30, 2021.

### Study Population

We used pseudonymized data extracted from the primary care sentinel cohort (PCSC) of the Oxford–Royal College of General Practitioners Research and Surveillance Centre [15]. The PCSC includes 743 practices (N=7,396,702) that were recruited to be nationally representative of the English population, and it is one of Europe’s oldest sentinel systems [11]. PCSC data have been widely used in COVID-19 research [16]. Practices are encouraged to have high-quality records and to record cases of LC [10]. Key diagnoses in primary care in England are recorded in computerized medical records (CMRs) using SNOMED CT [17]. This includes COVID-19 test results and vaccination. Over the period of the study, all community COVID-19 test and vaccination data were posted electronically back into patients’ CMRs. We have previously found that 7.81% (58/743) of the practices did not have any LC cases recorded in their CMR systems, and these practices were excluded from the study. The registered population of the PCSC was 7,396,702 patients at the time of the study; after exclusions, approximately 6.9 million patients were included, and 6.15% (428,588/6,968,114) had COVID-19 infection recorded in their CMR (Figure 1).

**Figure 1.** CONSORT (Consolidated Standards of Reporting Trials) diagram of the English primary care sentinel cohort population, the people with COVID-19 infection, those with long COVID, and the numbers of people with index community infection and those hospitalized for treatment for their index infection. Oxford–RCGP RSC: Oxford–Royal College of General Practitioners Research and Surveillance Centre.



## Long COVID Cases

LC cases were defined using our phenotype, with LC cases being defined by a clinical term for a case, referral to an LC service, or a symptom score suggestive of LC based on the ONS set of possible LC symptoms. The phenotype also differentiated community cases from hospital cases. Using this phenotype, 1.83% (7623/416,505) of the population who had been exposed to COVID-19 infection were recorded in the GP CMR as having LC; 82.85% (6316/7623) were index community COVID-19 infection cases, and 17.15% (1307/7623) had been hospitalized for treatment for their primary COVID-19 infection; and 0.3% (23/7623) of the people with a prior record of LC diagnosis had died. Most (7347/7623, 96.38%) of our LC cases had not received a vaccination dose before their diagnosis, 3.49% (266/7623) had received a single vaccine dose, and 0.13% (10/7623) had received 2 doses. We have set out how the PCSC population was subdivided to identify people with LC in Figure 1. Sociodemographic details included age, sex, use of the Index of Multiple Deprivation as a measure of deprivation, ethnicity, population density, obesity, and smoking. The Index of Multiple Deprivation score was dichotomized into the top 3 (*least*) and bottom 2 (*most*) deprived quintiles. Ethnicity was also dichotomized into White and non-White. Population density categories were based on the ONS national figures and categorized into conurbation (highest density), town and city (medium density), and rural (lowest density). Obesity was reported based on BMI>30 kg/m$^2$ or a term for obesity from SNOMED CT. Symptoms associated with LC were those present >28 days after the index infection.

## Before-and-After Study

We compared the recording of symptoms associated with LC in the period between 1 and 6 months after the index COVID-19 infection. We made a historical comparison matched by month in the year before the index COVID-19 infection. We did this to make allowance for seasonality in symptom presentations in primary care.

Reporting frequencies and underreporting are likely to be similar to unrecorded cases of patients with LC. The comparisons between before-and-after symptoms reported among patients with LC before the pandemic were matched by month, provided that an acute COVID-19 infection code was present; for example, patients with a COVID-19 infection code entered on January 1, 2021, would have a follow-up period beginning from February 1, 2021, to July 31, 2021, with a historic comparator period from February 1, 2019, to July 31, 2019. This comparative method demonstrated the clinical phenotype variation.

### Comparing LC and Uncomplicated COVID-19 Infection

We compared people with LC with those with COVID-19 infection uncomplicated by subsequent LC. We made this comparison across all variables of interest, identified through a literature review reported in our protocol [14]. In addition, we included the Cambridge Multimorbidity Score (CMS) as an overall measure of comorbidity; although CMS was initially developed using the Read clinical terminology, we have subsequently validated it using SNOMED CT [17]. An increasing CMS is associated with greater levels of comorbidity and associated with increased risk of mortality [18]. We conducted a multivariate logistic regression analysis to characterize people with LC.

### Comparison of Hospitalized and Community Initial Infections

We used the same variables to make comparisons between patients who were hospitalized with their index COVID-19 infection and those who were not. We compared people with posthospitalization LC with those who had index community COVID-19 infection followed by LC.

### All-Cause Mortality as an Outcome for LC

We measured all-cause mortality as an outcome for all patients with LC drawn from the hospitalized and community groups. We conducted a multivariate analysis using age, sex, geographical location, CMS, and whether the patients had received their vaccination doses before or after their COVID-19 infection diagnosis.

### Statistical Methods

We conducted this secondary analysis of routine data from the PCSC, and full details are available in our protocol [18]. We reported descriptive statistics of mean, median, and proportion, with measures of dispersion such as SD and IQR for normally distributed data and nonparametric data, respectively. We conducted a univariate analysis reporting odds ratios (ORs) and 95% CIs. We used the Bonferroni correction to correct for multiple testing in our before-and-after study of symptoms associated with LC. The probability of an observed difference happening by chance (*P* values) were reported for categorical variables using chi-square tests. ANOVA was used for continuous variables.

Multivariate logistic regression modelling was used to identify comorbidities, demographics, and exposure covariates associated with (1) LC diagnosis, (2) hospitalization, and (3) all-cause mortality as binary outcomes in separate models. For each model, relevant risk factors identified in the literature underwent univariate analysis, and all covariates were then included in a 3-step backward elimination using thresholds of α levels of .20, .10, and .05 in each step respectively, where a 2-sided α value of .05 was considered statistically significant. Age and sex were forced into the model at each step. Results were presented through forest plots.

### Ethics Approval

Retrospective pseudonymized routine data were used for this study. These data are held at the Oxford–Royal College of General Practitioners Clinical Informatics Digital Hub, a trusted research environment [19] that meets the NHS Digital Data Security and Protection standards [20]. Ethics approval was granted by the North West–Greater Manchester East Research Ethics Committee and Health Research Authority on May 27, 2021 (Integrated Research Application System number: 283024; Research Ethics Committee reference number: 20/NW/0266).

## Results

### Cohort Summary

A total of 416,505 people had a record of acute COVID-19 infection between March 1, 2020, and April 1, 2021. Baseline characteristics of the population are reported in Table 1. The mean age of the patients was 44.5 (SD 21.7) years, with a majority being women (232,775/416,505, 55.89%). The most common comorbid conditions were obesity, anxiety, depression, eczema, hypertension, and asthma. The all-cause mortality rate within the study population was 4.08% (16,993/416,505). Only 1.81% (7531/416,505) of the deaths were attributable to complications related to COVID-19 infection.

**Table 1.** Frequencies of baseline characteristics and univariate odds ratios for people with COVID-19 infection stratified by long COVID status in the primary care sentinel cohort in England (March 1, 2020, to April 1, 2021; N=416,505).

| Variable and category | COVID-19 infection, n=408,882 | Long COVID, n=7623 | Unadjusted odds ratio (95% CI) | *P* value |
|---|---|---|---|---|
| **Sociodemographic characteristics** | | | | |
| **Age (years), mean (SD)** | | | | |
| Continuous | 44.5 (21.77) | 47.7 (14.82) | 1.01 (1.01-1.01) | <.001 |
| **Sex, n (%)** | | | | |
| Female (reference) | 227,849 (55.7) | 4926 (64.6) | 1.00 (N/A[a]) | N/A |
| Male | 181,033 (44.3) | 2697 (35.4) | 0.69 (0.66-0.72) | <.001 |
| **Deprivation, n (%)** | | | | |
| Least deprived (reference) | 164,001 (40.1) | 3048 (40) | 1.00 (N/A) | N/A |
| Most deprived | 244,881 (59.9) | 4575 (60) | 1.01 (0.96-1.05) | .83 |
| **Ethnicity, n (%)** | | | | |
| White (reference) | 268,624 (65.7) | 5529 (72.5) | 1.00 (N/A) | N/A |
| Non-White | 56,645 (13.9) | 1094 (14.4) | 0.94 (0.88-1.00) | .06 |
| Missing | 83,613 (20.4) | 1000 (13.1) | 0.58 (0.54-0.62) | <.001 |
| **Population density, n (%)** | | | | |
| City (reference) | 205,159 (50.2) | 3191 (41.9) | 1.00 (N/A) | N/A |
| Conurbation | 137,378 (33.6) | 3196 (41.9) | 1.50 (1.42-1.57) | <.001 |
| Rural | 66,345 (16.2) | 1236 (16.2) | 1.20 (1.12-1.28) | <.001 |
| **BMI, n (%)** | | | | |
| Nonobese (reference) | 252,114 (61.7) | 4522 (59.3) | 1.00 (N/A) | N/A |
| Obese | 101,386 (24.8) | 2575 (33.8) | 1.42 (1.35-1.49) | <.001 |
| Missing | 55,382 (13.5) | 526 (6.9) | 0.53 (0.48-0.58) | <.001 |
| **Smoker, n (%)** | | | | |
| Nonsmoker (reference) | 210,505 (51.5) | 4458 (58.5) | 1.00 (N/A) | N/A |
| Smoker or former smoker | 149,583 (36.6) | 2945 (38.6) | 0.93 (0.89-0.97) | <.001 |
| Missing | 48,794 (11.9) | 220 (2.9) | 0.21 (0.19-0.24) | <.001 |
| **Comorbidities** | | | | |
| **Depression, n (%)** | | | | |
| No (reference) | 315,510 (77.2) | 4862 (63.8) | 1.00 (N/A) | N/A |
| Yes | 93,372 (22.8) | 2761 (36.2) | 1.92 (1.83-2.01) | <.001 |
| **Anxiety, n (%)** | | | | |
| No (reference) | 313,782 (76.7) | 4969 (65.2) | 1.00 (N/A) | N/A |
| Yes | 95,100 (23.3) | 2654 (34.8) | 1.76 (1.68-1.85) | <.001 |
| **Asthma, n (%)** | | | | |
| No (reference) | 333,083 (81.5) | 5821 (76.4) | 1.00 (N/A) | N/A |
| Yes | 75,799 (18.5) | 1802 (23.6) | 1.36 (1.29-1.43) | <.001 |
| **Chronic lung disease, n (%)** | | | | |
| No (reference) | 394,414 (96.5) | 7429 (97.5) | 1.00 (N/A) | N/A |
| Yes | 14,468 (3.5) | 194 (2.5) | 0.71 (0.62-0.82) | <.001 |
| **COPD[b], n (%)** | | | | |
| No (reference) | 396,024 (96.9) | 7473 (98) | 1.00 (N/A) | N/A |

| Variable and category | COVID-19 infection, n=408,882 | Long COVID, n=7623 | Unadjusted odds ratio (95% CI) | *P* value |
|---|---|---|---|---|
| Yes | 12,858 (3.1) | 150 (2) | 0.62 (0.53-0.73) | <.001 |
| **Hypertension, n (%)** | | | | |
| No (reference) | 328,025 (80.2) | 6001 (78.7) | 1.00 (N/A) | N/A |
| Yes | 80,857 (19.8) | 1622 (21.3) | 1.10 (1.04-1.16) | <.001 |
| **Ischemic heart disease** | | | | |
| No (reference) | 387,015 (94.7) | 7283 (95.5) | 1.00 (N/A) | N/A |
| Yes | 21,867 (5.3) | 340 (4.5) | 0.83 (0.74-0.92) | <.001 |
| **Atrial fibrillation, n (%)** | | | | |
| No (reference) | 395,170 (96.6) | 7490 (98.3) | 1.00 (N/A) | N/A |
| Yes | 13,712 (3.4) | 133 (1.7) | 0.51 (0.43-0.61) | <.001 |
| **Congestive heart failure, n (%)** | | | | |
| No (reference) | 400,573 (98) | 7558 (99.1) | 1.00 (N/A) | N/A |
| Yes | 8309 (2) | 65 (0.9) | 0.41 (0.32-0.53) | <.001 |
| **CKD[c], n (%)** | | | | |
| No (reference) | 385,985 (94.4) | 7350 (96.4) | 1.00 (N/A) | N/A |
| Yes | 22,897 (5.6) | 273 (3.6) | 0.63 (0.55-0.71) | <.001 |
| **Type 2 diabetes, n (%)** | | | | |
| No (reference) | 378,258 (92.5) | 7042 (92.4) | 1.00 (N/A) | N/A |
| Yes | 30,624 (7.5) | 581 (7.6) | 1.02 (0.94-1.11) | .67 |
| **Type 1 diabetes, n (%)** | | | | |
| No (reference) | 406,311 (99.4) | 7581 (99.4) | 1.00 (N/A) | N/A |
| Yes | 2571 (0.6) | 42 (0.6) | 0.88 (0.64-1.19) | .38 |
| **Cirrhosis, n (%)** | | | | |
| No (reference) | 407,827 (99.7) | 7607 (99.8) | 1.00 (N/A) | N/A |
| Yes | 1055 (0.3) | 16 (0.2) | 0.81 (0.50-1.33) | .40 |
| **Eczema, n (%)** | | | | |
| No (reference) | 318,124 (77.8) | 5891 (77.3) | 1.00 (N/A) | N/A |
| Yes | 90,758 (22.2) | 1732 (22.7) | 1.03 (0.98-1.09) | .28 |
| **CMS[d], mean (SD)** | | | | |
| Continuous | 0.45 (1.59) | 0.29 (1.12) | 0.94 (0.92-0.95) | <.001 |
| **Exposures** | | | | |
| **ICU[e] admission, n (%)** | | | | |
| No (reference) | 406,302 (99.4) | 7351 (96.4) | 1.00 (N/A) | N/A |
| Yes | 2580 (0.6) | 272 (3.6) | 5.83 (5.13-6.62) | <.001 |
| **Vaccination at any time, n (%)** | | | | |
| No vaccine (reference) | 84,094 (20.6) | 872 (11.4) | 1.00 (N/A) | N/A |
| One dose | 25,571 (6.3) | 371 (4.9) | 1.40 (1.24-1.58) | <.001 |
| Two doses | 299,217 (73.2) | 6380 (83.7) | 2.06 (1.92-2.21) | <.001 |
| **Pre– long COVID vaccination, n (%)** | | | | |
| No vaccine (reference) | 392,324 (96) | 7347 (96.4) | 1.00 (N/A) | N/A |
| One dose | 15,832 (3.9) | 266 (3.5) | 0.90 (0.79-1.01) | .08 |

| Variable and category | COVID-19 infection, n=408,882 | Long COVID, n=7623 | Unadjusted odds ratio (95% CI) | *P* value |
|---|---|---|---|---|
| Two doses | 726 (0.2) | 10 (0.1) | 0.74 (0.39-1.37) | .31 |
| **Outcomes** | | | | |
| **All-cause mortality, n (%)** | | | | |
| No (reference) | 391,912 (95.8) | 7600 (99.7) | 1.00 (N/A) | N/A |
| Yes | 16,970 (4.2) | 23 (0.3) | 0.07 (0.05-0.11) | <.001 |

[a] N/A: not applicable.

[b] COPD: chronic obstructive pulmonary disease.

[c] CKD: chronic kidney disease.

[d] CMS: Cambridge Multimorbidity Score.

[e] ICU: intensive care unit.

## Before-and-After Study

Overall, symptomatic presentations to primary care increased in people after their diagnosis compared with a matched historic period. The odds of presenting with these symptoms more than doubled. The increased ORs were 2.66 (95% CI 2.46-2.88) and 2.42 (95% CI 2.03-2.89) for community and hospitalized patients, respectively (Figure 2).

There were no differences between people who had been hospitalized with COVID-19 infection and those who had contracted community infections by category, other than the differences in general and mental health symptoms. Patients presented with more general symptoms after an index community infection (OR 3.44, 95% CI 3.00-3.95) than after an index hospital infection (OR 2.09, 95% CI 1.56-2.80; *P*<.001). Presentations with mental health sequelae were associated more with index hospital infections (OR 2.21, 95% CI 1.64-2.96) than with index community infections (OR 1.36, 95% CI 1.21-1.53).

There was an overall increase in reporting individual symptoms for 95% (20/21) of the symptoms monitored in both the index hospital and community infection groups. Among those hospitalized, shortness of breath (OR 15.8, 95% CI 9.5-26.4), loss of taste (OR 6.0, 95% CI 0.73-50.0), and memory loss and confusion (OR 5.0, 95% CI 0.58-43.32) were the symptoms that showed a higher increase after LC. For the community group, difficulty concentrating (OR 11.7, 95% CI 3.6-38.0), loss of taste (OR 8.7, 95% CI 3.4-21.7), and loss of smell (OR 7.5, 95% CI 4.2-13.2) showed a higher increase after LC. Only abdominal pain in the hospitalized group saw a decrease after LC versus before LC (Table 2).

**Figure 2.** Change in long COVID symptom presentation by symptom category for people who contracted a posthospitalization and index community COVID-19 infection. Univariate odds ratios (ORs) and 95% CIs are presented for COVID-19 infection cases in the primary care sentinel cohort in England between March 1, 2020, and April 1, 2021. ONS: Office for National Statistics.

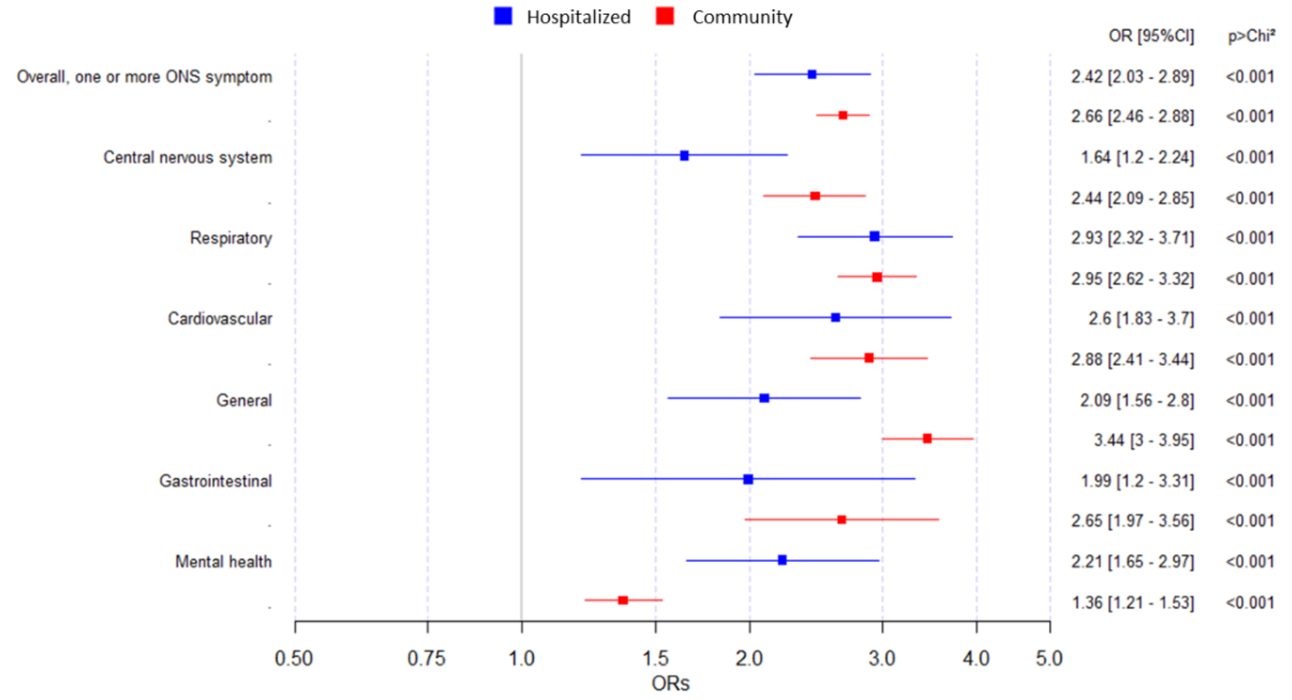


**Table 2.** Change in symptoms in the hospitalized and community groups before and after developing long COVID for people presenting with COVID-19 infection in the primary care sentinel cohort in England between March 1, 2020, and April 1, 2021 (N=7609).

| ONS[a] symptom variables | Long COVID: hospitalized (n=1294) | | | Unadjusted OR[b] (95% CI) | *P* value | Long COVID: community (n=6315) | | | Unadjusted OR (95% CI) | *P* value |
|---|---|---|---|---|---|---|---|---|---|---|
| | Before, n (%) | After, n (%) | Difference, % | | | Before, n (%) | After, n (%) | Difference, % | | |
| Overall, one or more ONS symptom[c] | 315 (24.34) | 567 (43.82) | 19.48 | 2.42 (2.03-2.89) | <.001 | 1326 (21) | 2616 (41.43) | 20.43 | 2.66 (2.46-2.88) | <.001 |
| **Central nervous system[c]** | 65 (5.02) | 103 (7.96) | 2.94 | 1.64 (1.2-2.24) | .004 | 250 (3.96) | 578 (9.15) | 5.19 | 2.44 (2.09-2.86) | <.001 |
| Memory loss and confusion | 1 (0.08) | 5 (0.39) | 0.31 | 5.02 (0.58-43.32) | .22 | 4 (0.06) | 14 (0.22) | 0.16 | 3.51 (1.15-10.71) | .03 |
| Difficulty concentrating | 0 | 6 (0.46) | 0.46 | Inf[d] | .04 | 3 (0.23) | 35 (0.55) | 0.32 | 11.73 (3.62-38.01) | <.001 |
| Loss of smell | 3 (0.23) | 6 (0.46) | 0.23 | 2 (0.5-8.06) | .50 | 14 (0.22) | 103 (1.63) | 1.41 | 7.46 (4.23-13.17) | <.001 |
| Trouble sleeping | 9 (0.7) | 21 (1.62) | 0.92 | 2.36 (1.08-5.16) | .05 | 19 (0.3) | 46 (0.73) | 0.43 | 2.43 (1.43-4.13) | <.001 |
| Headache | 37 (2.86) | 48 (3.71) | 0.85 | 1.31 (0.85-2.01) | .28 | 158 (2.5) | 306 (4.85) | 2.35 | 1.98 (1.63-2.41) | <.001 |
| Loss of taste | 1 (0.08) | 6 (0.46) | 0.38 | 6.02 (0.73-50.02) | .12 | 5 (0.08) | 43 (0.68) | 0.6 | 8.65 (3.44-21.74) | <.001 |
| Vertigo and dizziness | 16 (1.24) | 30 (2.32) | 1.08 | 1.9 (1.03-3.48) | .05 | 66 (1) | 137 (2.17) | 1.17 | 2.1 (1.56-2.82) | <.001 |
| **Respiratory[c]** | 118 (9.12) | 294 (22.72) | 13.6 | 2.93 (2.32-3.71) | <.001 | 416 (6.59) | 1088 (17.24) | 10.65 | 2.95 (2.62-3.32) | <.001 |
| Sore throat | 16 (1.24) | 18 (1.39) | 0.15 | 0.36 (0.21-0.62) | .86 | 83 (1.31) | 77 (1.22) | –0.09 | 0.93 (0.68-1.27) | .71 |
| Shortness of breath | 49 (3.79) | 214 (16.54) | 12.75 | 15.83 (9.51-26.35) | <.001 | 150 (2.38) | 714 (11.31) | 8.93 | 5.24 (4.39-6.25) | <.001 |
| Cough | 70 (5.41) | 114 (8.81) | 3.4 | 1.69 (1.23-2.31) | .002 | 250 (3.96) | 544 (8.61) | 4.65 | 2.29 (1.96-2.68) | <.001 |
| **Cardiovascular[c]** | 46 (3.55) | 113 (8.73) | 5.18 | 2.6 (1.82-3.69) | <.001 | 171 (2.71) | 468 (7.41) | 4.7 | 2.88 (2.41-3.43) | <.001 |
| Palpitations | 9 (0.7) | 26 (2) | 1.3 | 2.93 (1.36-6.29) | .007 | 38 (0.6) | 128 (2.01) | 1.41 | 3.42 (2.35-4.96) | <.001 |
| Chest pain | 38 (2.94) | 97 (7.5) | 4.6 | 2.68 (1.81-3.96) | .001 | 143 (2.26) | 371 (5.87) | 3.61 | 2.69 (2.21-3.28) | <.001 |
| **General[c]** | 78 (6.03) | 153 (11.82) | 5.79 | 2.09 (1.56-2.8) | <.001 | 341 (5.4) | 1037 (16.42) | 11.02 | 3.44 (3-3.95) | <.001 |
| Weakness and tiredness | 26 (2.01) | 95 (7.34) | 5.33 | 3.86 (2.51-5.95) | .001 | 123 (1.95) | 786 (12.45) | 10.5 | 7.16 (5.88-8.71) | <.001 |
| Fever | 11 (0.85) | 20 (1.55) | 0.7 | 1.83 (0.87-3.86) | .16 | 48 (0.76) | 105 (1.66) | 0.9 | 2.21 (1.55-3.14) | <.001 |
| Muscle aches | 8 (0.62) | 24 (1.85) | 1.23 | 3.04 (1.36-6.79) | .004 | 33 (0.52) | 121 (1.92) | 1.4 | 3.72 (2.51-5.5) | <.001 |
| Abdominal pain | 40 (3.09) | 37 (2.86) | –0.23 | 0.92 (0.59-1.45) | .83 | 158 (2.5) | 178 (2.82) | 0.32 | 1.13 (0.91-1.4) | .30 |
| **Gastrointestinal[c]** | 23 (1.78) | 45 (3.48) | 1.7 | 1.99 (1.2-3.31) | .01 | 64 (1.01) | 167 (2.64) | 1.63 | 2.65 (1.98-3.56) | <.001 |
| Nausea and vomiting | 7 (0.54) | 23 (1.78) | 1.24 | 3.33 (1.43-7.73) | .006 | 27 (0.43) | 72 (1.14) | 0.71 | 2.69 (1.71-4.22) | <.001 |

| ONS[a] symptom variables | Long COVID: hospitalized (n=1294) | | | Unadjusted OR[b] (95% CI) | *P* value | Long COVID: community (n=6315) | | | Unadjusted OR (95% CI) | *P* value |
|---|---|---|---|---|---|---|---|---|---|---|
| | Before, n (%) | After, n (%) | Difference, % | | | Before, n (%) | After, n (%) | Difference, % | | |
| Loss of appetite | 2 (0.15) | 6 (0.46) | 0.31 | 3.01 (0.6-15.01) | .29 | 9 (0.14) | 35 (0.55) | 0.41 | 3.9 (1.89-8.06) | <.001 |
| Diarrhea | 16 (1.24) | 25 (1.93) | 0.69 | 1.57 (0.84-2.95) | .21 | 34 (0.54) | 79 (1.25) | 0.71 | 2.34 (1.55-3.53) | <.001 |
| **Mental health[c]** | 70 (5.41) | 145 (11.21) | 5.8 | 2.21 (1.64-2.96) | <.001 | 457 (7.24) | 607 (9.61) | 2.37 | 1.36 (1.21-1.53) | <.001 |
| Worry and anxiety | 33 (2.55) | 82 (6.34) | 3.79 | 2.59 (1.71-3.9) | <.001 | 274 (4.34) | 407 (6.44) | 2.1 | 1.52 (1.3-1.78) | <.001 |
| Low mood and not enjoying anything | 57 (4.4) | 97 (7.5) | 3.1 | 1.76 (1.26-2.45) | .002 | 292 (4.62) | 389 (6.16) | 1.54 | 1.35 (1.16-1.58) | <.001 |

[a] ONS: Office for National Statistics.

[b] OR: odds ratio.

[c] The *P* values by category of symptoms have had the Bonferroni correction applied for multiple testing.

[d] Inf: infinite.

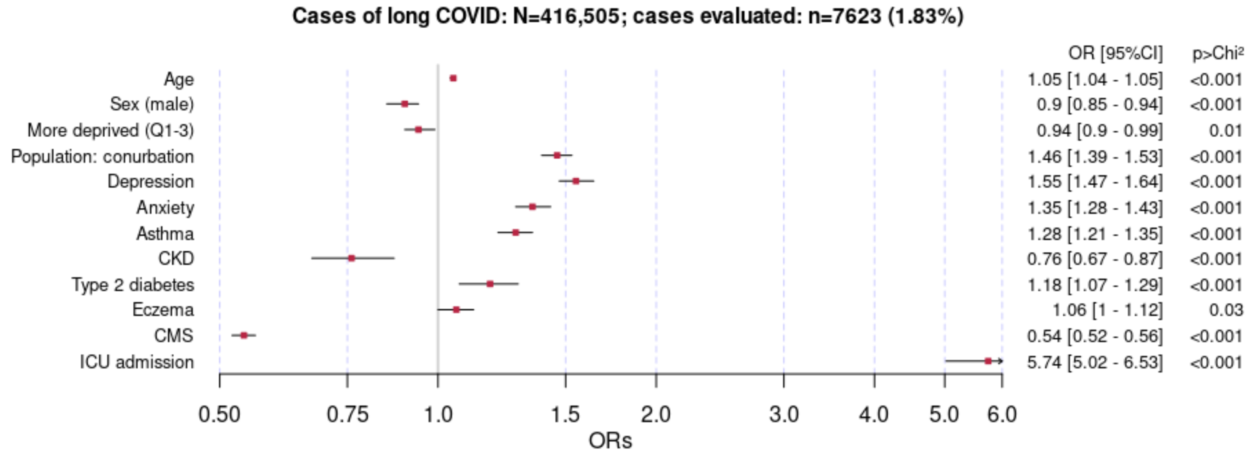
## Comparison of People With COVID-19 Infection Without LC and Those With LC

The frequencies of baseline characteristics and univariate ORs for people with COVID-19 infection stratified by LC status are shown in Table 1 (n=416,505). The mean age was 44.5 (SD 21.77) years for the COVID-19 infection group and 47.7 (SD 14.8) years for the LC group. A higher proportion of those with LC was found among women (4926/7623, 64.62%), and male sex was associated with a lower odds of an LC diagnosis (OR 0.69, 95% CI 0.66-0.72). The proportion of those with a record of intensive care unit (ICU) admission was 0.63% (2580/408,882) in people with COVID-19 infection and 3.57% (272/7623) in people with LC, and a record of ICU admission was associated with a higher odds of an LC diagnosis (OR 5.83, 95% CI 5.13-6.62). A moderate association with LC was found for history of depression, anxiety, living in a conurbation, and COVID-19 vaccination at any time. A lower association was found for people with obesity, asthma, and hypertension.

The multivariate logistic regression analysis using LC as an outcome (Figure 3) showed that a greater odds of having LC was associated with increasing age, higher population density (conurbation), mental health problems (anxiety and depression), and ICU admission. By contrast, male sex, being more deprived, chronic kidney disease (CKD), and a higher comorbidity score (measured using the CMS) were not.

An additional year of age was associated with a 5% increase in odds of an LC diagnosis (OR 1.05, 95% CI 1.04-1.05). After adjusting for confounders, the demographic factors associated with a decreased odds of an LC diagnosis among people with COVID-19 infection included male sex (OR 0.9, 95% CI 0.85-0.94) and higher deprivation (OR 0.94, 95% CI 0.9-0.99). However, residing in a conurbation was associated with increased odds of an LC diagnosis (OR 1.46, 95% CI 1.39-1.53). Among the history of comorbidities and exposures, depression (OR 1.55, 95% CI 1.47-1.64), anxiety (OR 1.35, 95% CI 1.28-1.35), asthma (OR 1.28, 95% CI 1.21-1.35), type 2 diabetes (OR 1.18, 95% CI 1.07-1.29), eczema (OR 1.06, 95% CI 1-1.12), and a record of ICU admission (OR 5.74, 95% CI 5.02-6.53) were associated with increased odds of an LC diagnosis. By contrast, history of CKD (OR 0.76, 95% CI 0.67-0.87) and a higher CMS (OR 0.54, 95% CI 0.52-0.56) were associated with lower odds of an LC diagnosis (Figure 3).

**Figure 3.** Multivariate logistic regression analysis showing associations with long COVID among people with COVID-19 infection diagnosed in the primary care sentinel cohort in England (March 1, 2020, to April 1, 2021). Results are shown as odds ratios (ORs) with 95% CIs. CKD: chronic kidney disease; CMS: Cambridge Multimorbidity Score; ICU: intensive care unit; Q: quintiles.



## Comparison of Posthospitalization- and Postcommunity Infection With LC

The frequencies of baseline characteristics and univariate ORs for people with LC stratified by community versus hospital index infection are shown in Table 3 (n=7623). Among baseline characteristics, the mean age was 54.8 (SD 14.3) years for the posthospitalization-infection LC group and 46.2 (SD 14.5) years for the postcommunity-infection LC group, whereas the proportion of female patients was 53.94% (705/1307) in the posthospitalization-infection LC group and 66.83% (4221/6316) in the postcommunity-infection LC group. Demographic factors associated with higher odds of hospitalization included male sex, higher deprivation, and non-White ethnicity. Among comorbidities, congestive heart failure, type 2 diabetes, CKD, ischemic heart disease, hypertension, chronic lung disease, obesity, and atrial fibrillation were all significantly associated with higher odds of a posthospitalization LC diagnosis.

The multivariate logistic regression analysis using posthospitalization LC as an outcome produced results (Figure 4) that contrasted with the previous analysis. Although increasing age, asthma, and type 2 diabetes remained associated with LC after both index community infection and hospitalization for the index COVID-19 infection, people who had received a diagnosis of LC after hospitalization were more likely to be men, more deprived, of non-White ethnicity, and have CKD and higher comorbidity scores (Figure 4).

An additional year of age was associated with a 1% increase in odds of having been hospitalized for COVID-19 infection (OR 1.01, 95% CI 1-1.02). After adjusting for confounders, the demographic factors associated with an increased odds of an LC diagnosis after hospitalization for COVID-19 infection included male sex (OR 1.43, 95% CI 1.25-1.64), higher deprivation (OR 1.42, 95% CI 1.24-1.63), non-White ethnicity (OR 1.78, 95% CI 1.5-2.12), and obesity (OR 2.18, 95% CI 1.9-2.5). Asthma (OR 1.27, 95% CI 1.1-1.47), CKD (OR 1.44, 95% CI 1.08-1.09), and type 2 diabetes (OR 1.66, 95% CI 1.35-2.02) were also associated with LC after hospitalization for COVID-19 infection. An increase in CMS was also associated with a 41% increase in odds of a posthospitalization LC diagnosis (OR 1.41, 95% CI 1.26-1.57). Only history of depression was associated with lower odds (OR 0.84, 95% CI 0.73-0.96).

**Table 3.** Frequencies of baseline characteristics and univariate odds ratios (ORs) for people with long COVID stratified by community versus hospital index infection in the primary care sentinel cohort in England (March 1, 2020, to April 1, 2021; N=7623).

| Variable and category | Community, n=6316 | Hospitalized, n=1307 | Unadjusted odds ratio (95% CI) | *P* value |
|---|---|---|---|---|
| **Sociodemographic characteristics** | | | | |
| **Age (years), mean (SD)** | | | | |
| Continuous | 46.2 (14.49) | 54.8 (14.3) | 1.04 (1.04-1.05) | <.001 |
| **Sex, n (%)** | | | | |
| Female (reference) | 4221 (66.83) | 705 (53.94) | 1.00 (N/A[a]) | N/A |
| Male | 2095 (33.17) | 602 (46.06) | 1.72 (1.52-1.94) | <.001 |
| **Deprivation, n (%)** | | | | |
| Least deprived (reference) | 2639 (41.78) | 409 (31.29) | 1.00 (N/A) | N/A |
| Most deprived | 3677 (58.22) | 898 (68.71) | 1.58 (1.39-1.79) | <.001 |
| **Ethnicity, n (%)** | | | | |
| White (reference) | 4619 (73.13) | 910 (69.63) | 1.00 (N/A) | N/A |
| Non-White | 844 (13.36) | 250 (19.13) | 1.50 (1.28-1.76) | <.001 |
| Missing | 853 (13.51) | 147 (11.25) | 0.87 (0.72-1.06) | .16 |
| **Population density, n (%)** | | | | |
| City (reference) | 2639 (41.78) | 552 (42.23) | 1.00 (N/A) | N/A |
| Conurbation | 2621 (41.5) | 575 (43.99) | 1.05 (0.92-1.19) | .47 |
| Rural | 1056 (16.72) | 180 (13.77) | 0.81 (0.68-0.98) | .03 |
| **BMI, n (%)** | | | | |
| Nonobese (reference) | 3957 (62.65) | 565 (43.23) | 1.00 (N/A) | N/A |
| Obese | 1882 (29.8) | 693 (53.02) | 2.58 (2.28-2.92) | <.001 |
| Missing | 477 (7.55) | 49 (3.75) | 0.72 (0.53-0.98) | .03 |
| **Smoker, n (%)** | | | | |
| Nonsmoker (reference) | 3696 (58.52) | 762 (58.3) | 1.00 (N/A) | N/A |
| Smoker or former smoker | 2411 (38.17) | 534 (40.86) | 1.07 (0.95-1.21) | .25 |
| Missing | 209 (3.31) | 11 (0.84) | 0.26 (0.14-0.47) | <.001 |
| **Comorbidities** | | | | |
| **Depression, n (%)** | | | | |
| No (reference) | 4029 (63.79) | 833 (63.73) | 1.00 (N/A) | N/A |
| Yes | 2287 (36.21) | 474 (36.27) | 1.00 (0.89-1.13) | .97 |
| **Anxiety, n (%)** | | | | |
| No (reference) | 4094 (64.82) | 875 (66.95) | 1.00 (N/A) | N/A |
| Yes | 2222 (35.18) | 432 (33.05) | 0.91 (0.80-1.03) | .14 |
| **Asthma, n (%)** | | | | |
| No (reference) | 4869 (77.09) | 952 (72.84) | 1.00 (N/A) | N/A |
| Yes | 1447 (22.91) | 355 (27.16) | 1.25 (1.10-1.44) | <.001 |
| **Chronic lung disease, n (%)** | | | | |
| No (reference) | 6185 (97.93) | 1244 (95.18) | 1.00 (N/A) | N/A |
| Yes | 131 (2.07) | 63 (4.82) | 2.39 (1.76-3.25) | <.001 |
| **COPD[b], n (%)** | | | | |
| No (reference) | 6218 (98.45) | 1255 (96.02) | 1.00 (N/A) | N/A |
| Yes | 98 (1.55) | 52 (3.98) | 2.63 (1.87-3.70) | <.001 |

| Variable and category | Community, n=6316 | Hospitalized, n=1307 | Unadjusted odds ratio (95% CI) | *P* value |
|---|---|---|---|---|
| **Hypertension, n (%)** | | | | |
| No (reference) | 5168 (81.82) | 833 (63.73) | 1.00 (N/A) | N/A |
| Yes | 1148 (18.18) | 474 (36.27) | 2.56 (2.25-2.92) | <.001 |
| **Ischemic heart disease, n (%)** | | | | |
| No (reference) | 6102 (96.61) | 1181 (90.36) | 1.00 (N/A) | N/A |
| Yes | 214 (3.39) | 126 (9.64) | 3.04 (2.42-3.82) | <.001 |
| **Atrial fibrillation, n (%)** | | | | |
| No (reference) | 6228 (98.61) | 1262 (96.56) | 1.00 (N/A) | N/A |
| Yes | 88 (1.39) | 45 (3.44) | 2.52 (1.75-3.63) | <.001 |
| **Congestive heart failure, n (%)** | | | | |
| No (reference) | 6283 (99.48) | 1275 (97.55) | 1.00 (N/A) | N/A |
| Yes | 33 (0.52) | 32 (2.45) | 4.78 (2.93-7.80) | <.001 |
| **CKD[c], n (%)** | | | | |
| No (reference) | 6155 (97.45) | 1195 (91.43) | 1.00 (N/A) | N/A |
| Yes | 161 (2.55) | 112 (8.57) | 3.58 (2.79-4.60) | <.001 |
| **Type 2 diabetes, n (%)** | | | | |
| No (reference) | 5982 (94.71) | 1060 (81.1) | 1.00 (N/A) | N/A |
| Yes | 334 (5.29) | 247 (18.9) | 4.17 (3.50-4.98) | <.001 |
| **Type 1 diabetes, n (%)** | | | | |
| No (reference) | 6282 (99.46) | 1299 (99.39) | 1.00 (N/A) | N/A |
| Yes | 34 (0.54) | 8 (0.61) | 1.14 (0.53-2.46) | .75 |
| **Cirrhosis, n (%)** | | | | |
| No (reference) | 6305 (99.83) | 1302 (99.62) | 1.00 (N/A) | N/A |
| Yes | 11 (0.17) | 5 (0.38) | 2.20 (0.76-6.35) | .17 |
| **Eczema, n (%)** | | | | |
| No (reference) | 4871 (77.12) | 1020 (78.04) | 1.00 (N/A) | N/A |
| Yes | 1445 (22.88) | 287 (21.96) | 0.95 (0.82-1.09) | .47 |
| **CMS[d], mean (SD)** | | | | |
| Continuous | 0.16 (1.03) | 0.95 (1.33) | 1.75 (1.66-1.84) | <.001 |
| **Exposures** | | | | |
| **ICU[e] admission, n (%)** | | | | |
| No (reference) | 6316 (100) | 1035 (79.19) | 1.00 (N/A) | N/A |
| Yes | 0 (0) | 272 (20.81) | Inf[f] | <.001 |
| **Vaccination at any time, n (%)** | | | | |
| No vaccine (reference) | 743 (11.76) | 129 (9.87) | 1.00 (N/A) | N/A |
| One dose | 326 (5.16) | 45 (3.44) | 0.80 (0.55-1.14) | .21 |
| Two doses | 5247 (83.07) | 1133 (86.69) | 1.24 (1.02-1.52) | .03 |
| **Pre–long COVID vaccination, n (%)** | | | | |
| No vaccine (reference) | 6108 (96.71) | 1239 (94.8) | 1.00 (N/A) | N/A |
| One dose | 199 (3.15) | 67 (5.13) | 1.66 (1.25-2.20) | <.001 |
| Two doses | 9 (0.14) | 1 (0.08) | 0.55 (0.07-4.33) | .54 |
| **Outcomes** | | | | |

| Variable and category | Community, n=6316 | Hospitalized, n=1307 | Unadjusted odds ratio (95% CI) | *P* value |
|---|---|---|---|---|
| **All-cause mortality, n (%)** | | | | |
| No (reference) | 6310 (99.91) | 1290 (98.7) | 1.00 (N/A) | N/A |
| Yes | 6 (0.09) | 17 (1.3) | 13.9 (5.5-35.2) | <.001 |

[a] N/A: not applicable.

[b] COPD: chronic obstructive pulmonary disease.

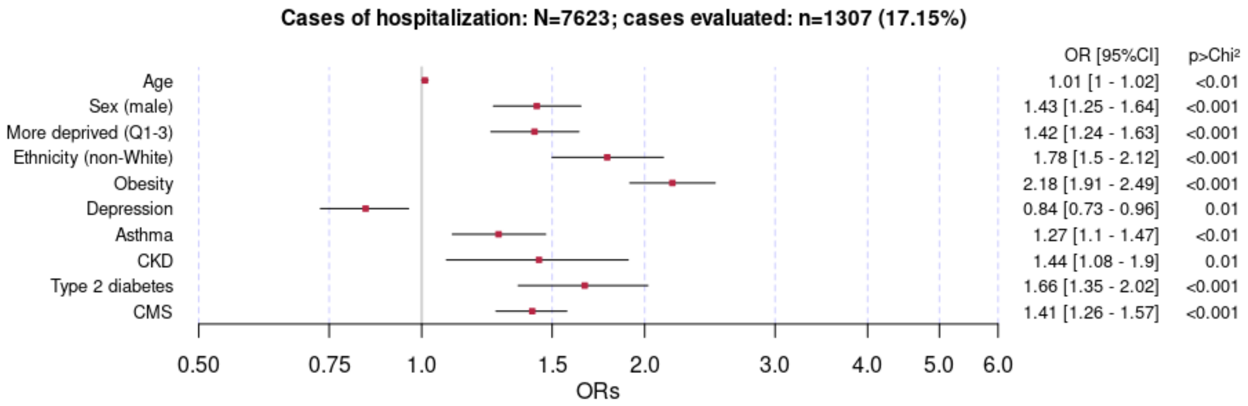
[c] CKD: chronic kidney disease.

[d] CMS: Cambridge Multimorbidity Score.

[e] ICU: intensive care unit.

[f] Inf: infinite.

**Figure 4.** Multivariate logistic regression analysis showing associations with long COVID acquired after hospitalization. Results are shown as odds ratios (ORs) with 95% CIs. CKD: chronic kidney disease; CMS: Cambridge Multimorbidity Score; Q: quintiles.



## LC and All-Cause Mortality

The frequencies of baseline characteristics and univariate ORs for people with LC stratified by vital status are shown in Table 4 (n=7623). We paired data for people with LC who died (23/7623, 0.3%) and those who remained alive within the study period (7600/7623, 99.7%). Demographic factors associated with a higher risk of mortality include male sex (OR 4.19, 95% CI 1.72-10.21) and age, where the mean age was 75.7 (SD 8.23) years in the mortality group and 47.6 (SD 14.75) years in the living group. Every additional year of age was associated with a 10% increased risk of death (OR 1.15, 95% CI 1.11-1.19). Among comorbidities, all cardiovascular comorbidities were associated with a higher risk of mortality, particularly congestive heart failure (OR 26, 95% CI 8.60-78.74) and atrial fibrillation (OR 20.8, 95% CI 8.06-53.54). Pulmonary conditions, including chronic obstructive pulmonary disease (OR 14.3, 95% CI 5.23-38.99) and chronic lung disease (OR 13.9, 95% CI 5.43-35.69) were also associated with higher mortality. Among metabolic and inflammatory conditions, cirrhosis, type 1 diabetes, type 2 diabetes, and eczema were associated with all-cause mortality. Finally, ICU admission (OR 7.63, 95% CI 2.81-20.70) was associated with a higher risk of death.

The results for the multivariate logistic regression analysis for people with LC using all-cause mortality as an outcome are presented in Figure 5. Age (OR 1.08, 95% CI 1.02-1.14), male sex, and a higher CMS were all associated with higher odds of mortality. By contrast, COVID-19 vaccination at any time and living in a conurbation were associated with lower odds of mortality (Figure 5).

**Table 4.** Frequencies of baseline characteristics and univariate odds ratios for people with LC stratified by vital status in the primary care sentinel cohort in England (March 1, 2020, to April 1, 2021; N=7623).

| Variable and category | Alive, n=7600 | All-cause mortality, n=23 | Unadjusted odds ratio (95% CI) | *P* value |
|---|---|---|---|---|
| **Sociodemographic characteristics** | | | | |
| **Age (years), mean (SD)** | | | | |
| Continuous | 47.6 (14.75) | 75.7 (8.23) | 1.15 (1.11-1.19) | <.001 |
| **Sex, n (%)** | | | | |
| Female (reference) | 4919 (64.72) | 7 (30.43) | 1.00 (N/A[a]) | N/A |
| Male | 2681 (35.28) | 16 (69.57) | 4.19 (1.72-10.21) | <.001 |
| **Deprivation, n (%)** | | | | |
| Least deprived (reference) | 3042 (40.01) | 6 (26.09) | 1.00 (N/A) | N/A |
| Most deprived | 4558 (59.97) | 17 (73.9) | 1.89 (0.74-4.80) | .16 |
| **Ethnicity, n (%)** | | | | |
| White (reference) | 5509 (72.49) | 20 (86.96) | 1.00 (N/A) | N/A |
| Non-White | 1092 (14.37) | 2 (8.7) | 0.50 (0.12-2.16) | .31 |
| Missing | 999 (13.14) | 1 (4.35) | 0.28 (0.04-2.06) | .12 |
| **Population density, n (%)** | | | | |
| City (reference) | 3179 (41.83) | 12 (52.17) | 1.00 (N/A) | N/A |
| Conurbation | 3191 (42) | 5 (21.74) | 0.42 (0.15-1.18) | .08 |
| Rural | 1230 (16.18) | 6 (26.09) | 1.29 (0.48-3.45) | .61 |
| **BMI, n (%)** | | | | |
| Nonobese (reference) | 4506 (59.29) | 16 (69.57) | 1.00 (N/A) | N/A |
| Obese | 2568 (33.79) | 7 (30.43) | 0.77 (0.32-1.87) | .55 |
| Missing | 526 (6.92) | 0 (0) | 0.26 (0.02-4.33) | .06 |
| **Smoker, n (%)** | | | | |
| Nonsmoker (reference) | 4447 (58.51) | 11 (47.82) | 1.00 (N/A) | N/A |
| Smoker or former smoker | 2933 (38.59) | 12 (52.17) | 1.65 (0.73- 3.75) | .23 |
| Missing | 220 (2.89) | 0 (0) | 0.88 (0.05-14.93) | .30 |
| **Comorbidities** | | | | |
| **Depression, n (%)** | | | | |
| No (reference) | 4843 (63.72) | 19 (82.61) | 1.00 (N/A) | N/A |
| Yes | 2757 (36.28) | 4 (17.39) | 0.37 (0.13-1.09) | .05 |
| **Anxiety, n (%)** | | | | |
| No (reference) | 4952 (65.16) | 17 (73.91) | 1.00 (N/A) | N/A |
| Yes | 2648 (34.84) | 6 (26.09) | 0.66 (0.26-1.68) | .37 |
| **Asthma, n (%)** | | | | |
| No (reference) | 5802 (76.34) | 19 (82.61) | 1.00 (N/A) | N/A |
| Yes | 1798 (23.66) | 4 (17.39) | 0.68 (0.23-2.00) | .47 |
| **Chronic lung disease, n (%)** | | | | |
| No (reference) | 7412 (97.53) | 17 (73.91) | 1.00 (N/A) | N/A |
| Yes | 188 (2.47) | 6 (26.09) | 13.91 (5.43-35.69) | <.001 |
| **COPD[b] , n (%)** | | | | |
| No (reference) | 7455 (98.09) | 18 (78.26) | 1.00 (N/A) | N/A |
| Yes | 145 (1.91) | 5 (21.74) | 14.28 (5.23-38.99) | <.001 |

| Variable and category | Alive, n=7600 | All-cause mortality, n=23 | Unadjusted odds ratio (95% CI) | *P* value |
|---|---|---|---|---|
| **Hypertension, n (%)** | | | | |
| No (reference) | 5993 (78.86) | 8 (34.78) | 1.00 (N/A) | N/A |
| Yes | 1607 (21.14) | 15 (65.22) | 6.99 (2.96-16.52) | <.001 |
| **Ischemic heart disease, n (%)** | | | | |
| No (reference) | 7265 (95.59) | 18 (78.26) | 1.00 (N/A) | N/A |
| Yes | 335 (4.41) | 5 (21.74) | 6.02 (2.22-16.32) | <.001 |
| **Atrial fibrillation, n (%)** | | | | |
| No (reference) | 7473 (98.33) | 17 (73.91) | 1.00 (N/A) | N/A |
| Yes | 127 (1.67) | 6 (26.09) | 20.77 (8.06-53.54) | <.001 |
| **Congestive heart failure, n (%)** | | | | |
| No (reference) | 7539 (99.2) | 19 (82.61) | 1.00 (N/A) | N/A |
| Yes | 61 (0.8) | 4 (17.39) | 26.02 (8.60-78.74) | <.001 |
| **CKD[c, n (%)]** | | | | |
| No (reference) | 7332 (96.47) | 18 (78.26) | 1.00 (N/A) | N/A |
| Yes | 268 (3.53) | 5 (21.74) | 7.60 (2.80-20.62) | <.001 |
| **Type 2 diabetes, n (%)** | | | | |
| No (reference) | 7028 (92.47) | 14 (60.87) | 1.00 (N/A) | N/A |
| Yes | 572 (7.53) | 9 (39.13) | 7.90 (3.40-18.33) | <.001 |
| **Type 1 diabetes, n (%)** | | | | |
| No (reference) | 7559 (99.46) | 22 (95.65) | 1.00 (N/A) | N/A |
| Yes | 41 (0.54) | 1 (4.35) | 8.38 (1.10-63.64) | .12 |
| **Cirrhosis, n (%)** | | | | |
| No (reference) | 7585 (99.8) | 22 (95.65) | 1.00 (N/A) | N/A |
| Yes | 15 (0.2) | 1 (4.35) | 22.98 (2.91-181.62) | .04 |
| **Eczema, n (%)** | | | | |
| No (reference) | 5878 (77.34) | 13 (56.52) | 1.00 (N/A) | N/A |
| Yes | 1722 (22.66) | 10 (43.48) | 2.63 (1.15-6.00) | .03 |
| **CMS[d], mean (SD)** | | | | |
| Continuous | 0.28 (1.11) | 3.37 (1.1) | 3.24 (2.55-4.11) | <.001 |
| **Exposures** | | | | |
| **ICU[e] admission, n (%)** | | | | |
| No (reference) | 7333 (96.49) | 18 (78.26) | 1.00 (N/A) | N/A |
| Yes | 267 (3.51) | 5 (21.74) | 7.63 (2.81-20.70) | <.001 |
| **Vaccination at any time, n (%)** | | | | |
| No vaccine (reference) | 867 (11.41) | 5 (21.74) | 1.00 (N/A) | N/A |
| One dose | 367 (4.83) | 4 (17.39) | 1.89 (0.50-7.08) | .35 |
| Two doses | 6366 (83.76) | 14 (60.87) | 0.38 (0.14-1.06) | .09 |
| **Pre– long COVID vaccination, n (%)** | | | | |
| No vaccine (reference) | 7326 (96.39) | 21 (91.3) | 1.00 (N/A) | N/A |
| One dose | 264 (3.47) | 2 (8.7) | 2.64 (0.62- 11.33) | .25 |

| Variable and category | Alive, n=7600 | All-cause mortality, n=23 | Unadjusted odds ratio (95% CI) | *P* value |
|---|---|---|---|---|
| Two doses | 10 (0.13) | 0 (0) | Inf[f] | N/A |

[a] N/A: not applicable.

[b] COPD: chronic obstructive pulmonary disease.

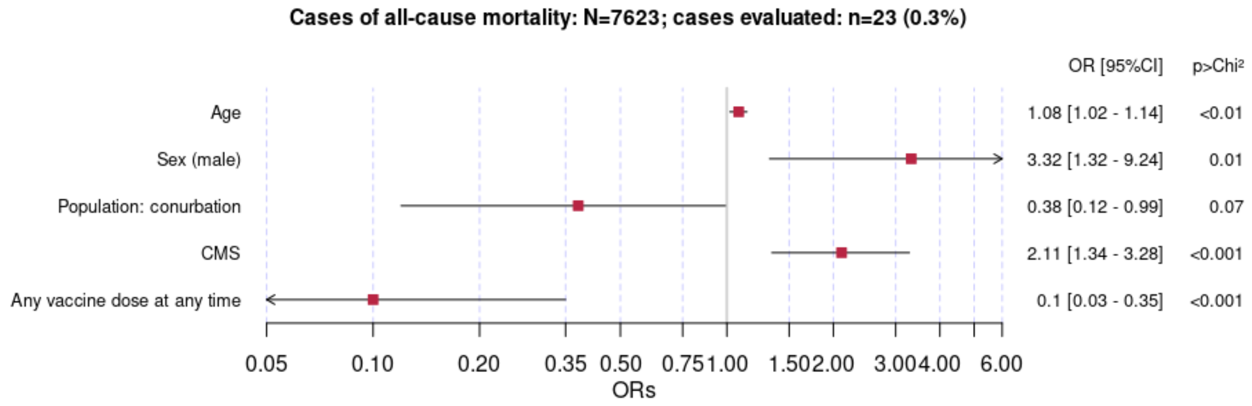
[c] CKD: chronic kidney disease.

[d] CMS: Cambridge Multimorbidity Score.

[e] ICU: intensive care unit.

[f] Inf: infinite.

**Figure 5.** Multivariate logistic regression analysis of risk factors for all-cause mortality in people with long COVID. Results are shown as odds ratios (ORs) with 95% CIs. CMS: Cambridge Multimorbidity Score.



## Discussion

### Principal Findings

Although rates of recording of LC are low, an LC diagnosis was associated with an odds of more than twice as many consultations with ONS-defined LC-related symptoms in the 6 months after contracting the index infection compared with a historical control period. The increase in symptoms did not differ between those who had their initial COVID-19 infection managed in the hospital and those who were a community case. However, people with LC after hospitalization had greater odds of presenting with mental health problems, and those with LC after community infection had greater odds of presenting with general symptoms (weakness and tiredness, fever, myalgia, and abdominal pain).

There were some similarities, but there were marked contrasts between the characteristics of people who had been diagnosed with LC after a hospital infection and those who had been diagnosed with LC after a community infection. The similarities were associations with increasing age, asthma, and type 2 diabetes. The differences in the posthospitalization LC group were male sex, more deprivation, history of CKD, and higher multimorbidity scores, whereas those in the postcommunity LC group were female sex, less deprived, and more likely to have depression and anxiety as well as lower levels of comorbidities.

All-cause mortality in people with LC was higher in older men and those with higher multimorbidity scores, associations that were similar to those with hospitalized patients. COVID-19 vaccination was associated with lower odds of all-cause mortality in patients with LC.

### Comparison With the Literature

Posthospitalization LC was associated with higher deprivation, non-White ethnicity, obesity, CKD, and type 2 diabetes compared with postcommunity LC. There are similarities between our study, Living Risk Prediction Algorithm (QCOVID) study [21], and other studies [6,7] that reported the same risk factors, although with different outcomes. Data from the UK Health Security Agency and ONS indicated economic disadvantage to the prevalence of sex, obesity, diabetes, hypertension, and cardiovascular disease. These disparities may have been exacerbated because of the COVID-19 pandemic, especially among ethnic groups. However, there remains uncertainty regarding the degree to which the risk of developing posthospitalization LC in more deprived segments is linked to the severity of the disease (COVID-19) and more comorbidities [22] or to the propensity to consult in primary care, as reported for other respiratory conditions [23]. Disentangling the relationship between LC and hospital versus community is confounded by the presence of post-ICU syndrome in patients admitted to the ICU, many of the features of which (anxiety, cognitive difficulties, and breathlessness) overlap with LC. It is possible that the differences in the 2 groups are due to this confounding.

There are similarities between our study, Living Risk Prediction Algorithm (QCOVID) study [21], and other reports [3,24] regarding sociodemographic and comorbidity variables associated with mortality. These include cardiometabolic conditions (eg, CKD, type 2 diabetes, ischemic heart disease, and atrial fibrillation), chronic obstructive pulmonary disease, and asthma. However, we additionally report on vaccination status and conurbation as associated with lower odds of death. A UK Health Security Agency report indicated twice the risk of death due to COVID-19 infection among people from Bangladesh in comparison with White British people. Caribbean, Indian, Pakistani, Chinese, and Black ethnic groups were identified to have a 10% to 50% higher risk of mortality in comparison with White British people. We do not report differences on mortality per ethnicity because the number of deaths in the LC group was too small to enable us to find differences across groups.

We identified a lower prevalence of LC compared with self-report population surveys (eg, ONS) [4], but the prevalence was higher than those reported by other studies using routine data [9]. The OpenSAFELY study found that 27% of practices had no LC recording compared with 7.8% in our sentinel cohort [9]. Low rates of clinical coding of LC and interpractice variation are a national problem. COVID-19 coding evolved over the course of the pandemic, and the United Kingdom also has a region-specific version of SNOMED CT, which further complicates the issue [19,25]. LC clinical codes were introduced to SNOMED CT in January 2021; therefore, primary care staff did not have access to these until February 2021 [9,10]. Levels recorded in GP CMRs are dependent both on patients consulting their GP (many do not) and the GP both recognizing LC and coding it; therefore, our estimate of 1.83% (7623/416,505) will be very conservative. In addition, vaccination has been shown to decrease the risk of developing LC by approximately half; therefore, risks will have fallen over time (ONS).

### Strengths and Limitations

The data were sourced from a representative network (PCSC) where practices have received feedback throughout the pandemic. Data on COVID-19 infection diagnoses and comorbidity are likely to be of good quality [17,26]. Linkage to hospital and mortality data adds reliability compared with only using coded data. Clinicians may well be underrecording LC, either by not recognizing it or by coding it with a *presenting symptom* code. The ONS symptoms are the most well-validated set of LC symptoms available at present; however, a validation study is pending. In addition, LC may be diagnosed as other conditions and coded as such; for example, a patient with pre-existing anxiety may well have their LC-related tachycardia and breathlessness diagnosed as worsening anxiety. It is known that GPs tend not to record symptoms reliably in the record and tend to only record symptoms that support their working diagnosis, introducing bias [27]. As a result, vital data may not be coded and included in this study because of these being available as free text within CMRs. Considerable care needs to be taken in interpreting these very granular data from the CMR.

### Implications of the Findings

It is very likely that LC was underrecorded, and clinicians should continue to be encouraged to record this condition in clinical records. LC is an important comorbidity that needs to be captured so that it can be taken into consideration in health service planning and assessment of vaccine benefit risk.

The differences between those presenting to community and hospital care may have represented the propensity of different groups to consult (eg, women more than men in primary care) and the possibility that some groups experienced more serious disease (eg, men and increasing age), as well as the potential for disparities in presentation.

As COVID-19 continues to circulate in the community, albeit with lower death and morbidity rates because of vaccines and a current less-virulent strain, learning to recognize groups of patients at greatest risk of acquiring LC and managing associated risk factors may affect presentations and disease impact. Comorbid conditions that increase the risk of acquiring LC, such as asthma, may shed light on possible etiological risk factors.

### Call for Further Research

LC case identification within primary care requires improved data recording. Better case identification will enable successful interventions to be implemented. A range of incentives to improve case ascertainment and data quality have been successfully implemented in primary care. This would further aid in understanding communicable disease risk and to develop better controls in the future.

### Conclusions

LC recording in primary care records was low, reflecting either low prevalence or underrecording. There are differences between the sociodemographic profiles and comorbidities of LC symptoms presented after an index community infection compared with those hospitalized with a COVID-19 infection. Factors associated with hospital presentation are also associated with higher all-cause mortality, although vaccination is protective. This suggests that the disparities flagged throughout the COVID-19 pandemic may also apply to LC, where better tools to identify and intervene are needed in those at greatest risk.

## Acknowledgments

This study shares funding sources through the Remote COVID-19 Assessment in Primary Care project. The sources of funding for the project include the Community Jameel, the Imperial College President’s Excellence Fund, the Economic and Social Research Council (ES/V010069/1), UK Research and Innovation, Health Data Research UK (HDRUK2020.139), the NIHR Imperial Biomedical Research Centre (IS-BRC-1215-20013), the NIHR Oxford Biomedical Research Centre (BRC-1215-20008 and 132807), and the NIHR Imperial Patient Safety Translational Research Centre (PSTRC-2016-004). The research was enabled by the iCARE environment and used the iCARE team and data resources. NM was also funded by a Health Education England Academic Foundation Programme. BMT was supported by the Marie Skłodowska-Curie Innovative Training Network for Healthcare Performance Intelligence Professionals, which is funded by the European Union Research Framework Programme

Horizon 2020 (765141). The authors wish to acknowledge the patients registered with practice members of the Oxford–Royal College of General Practitioners Research and Surveillance Centre (Oxford–RCGP RSC) who allowed their pseudonymized data to be shared for this research; EMIS, TPP, InPractice Systems, and Wellbeing for facilitating our pseudonymized data extraction. The Oxford–RCGP RSC is principally funded by the UK Health Security Agency; Dr Katie Marsden during her Academic Foundation Programme from the Royal Surrey Hospital and Dr Samantha Line while a member of the Clinical Informatics and Health Outcomes Research Group; and Mr Julian Sherlock for his role in data analysis at the Oxford–RCGP RSC.

## Conflicts of Interest

SdeL reports that through his university he has received grants from AstraZeneca, GSK, Sanofi, Seqirus, and Takeda for vaccine-related research, and he also reports membership of advisory boards of AstraZeneca, Sanofi, and Seqirus.

## References

1. Sivan M, Rayner C, Delaney B. Fresh evidence of the scale and scope of long covid. BMJ 2021 Apr 01;373:n853. [doi: 10.1136/bmj.n853] [Medline: 33795224]
2. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV. A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis 2022 Apr;22(4):e102-e107. [doi: 10.1016/s1473-3099(21)00703-9]
3. Ayoubkhani D, Khunti K, Nafilyan V, Maddox T, Humberstone B, Diamond I, et al. Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study. BMJ 2021 Mar 31;372:n693 [FREE Full text] [doi: 10.1136/bmj.n693] [Medline: 33789877]
4. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK : 3 February 2022. Office of National Statistics. URL: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/3february2022 [accessed 2022-07-28]
5. Davis HE, Assaf GS, McCorkell L, Wei H, Low RJ, Re'em Y, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. EClinicalMedicine 2021 Aug;38:101019 [FREE Full text] [doi: 10.1016/j.eclinm.2021.101019] [Medline: 34308300]
6. Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. Nat Med 2021 Apr 10;27(4):626-631 [FREE Full text] [doi: 10.1038/s41591-021-01292-y] [Medline: 33692530]
7. Aiyegbusi OL, Hughes SE, Turner G, Rivera SC, McMullan C, Chandan JS, et al. Symptoms, complications and management of long COVID: a review. J R Soc Med 2021 Sep 15;114(9):428-442 [FREE Full text] [doi: 10.1177/01410768211032850] [Medline: 34265229]
8. Deer RR, Rock MA, Vasilevsky N, Carmody L, Rando H, Anzalone AJ, et al. Characterizing long COVID: deep phenotype of a complex condition. EBioMedicine 2021 Dec;74:103722 [FREE Full text] [doi: 10.1016/j.ebiom.2021.103722] [Medline: 34839263]
9. Walker AJ, MacKenna B, Inglesby P, Tomlinson L, Rentsch CT, Curtis HJ, (The OpenSAFELY Collaborative). Clinical coding of long COVID in English primary care: a federated analysis of 58 million patient records using OpenSAFELY. Br J Gen Pract 2021 Nov;71(712):e806-e814 [FREE Full text] [doi: 10.3399/BJGP.2021.0301] [Medline: 34340970]
10. Mayor N, Tsang R, Joy M, Hobbs FR, de Lusignan S. Long covid: coding is caring. BMJ 2021 May 19;373:n1262. [doi: 10.1136/bmj.n1262] [Medline: 34011495]
11. de Lusignan S, Dorward J, Correa A, Jones N, Akinyemi O, Amirthalingam G, et al. Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study. Lancet Infect Dis 2020 Sep;20(9):1034-1042. [doi: 10.1016/s1473-3099(20)30371-6]
12. de Lusignan S, Joy M, Oke J, McGagh D, Nicholson B, Sheppard J, et al. Disparities in the excess risk of mortality in the first wave of COVID-19: cross sectional study of the English sentinel network. J Infect 2020 Nov;81(5):785-792 [FREE Full text] [doi: 10.1016/j.jinf.2020.08.037] [Medline: 32858068]
13. Espinosa-Gonzalez AB, Neves AL, Fiorentino F, Prociuk D, Husain L, Ramtale SC, et al. Predicting risk of hospital admission in patients with suspected COVID-19 in a community setting: protocol for development and validation of a multivariate risk prediction tool. JMIR Res Protoc 2021 May 25;10(5):e29072 [FREE Full text] [doi: 10.2196/29072] [Medline: 33939619]
14. Mayer N, Meza-torres B, Okusi C, Delanerolle G, Wang W, Anand S. Developing a long covid phenotype for post-acute COVID-19 in a national primary care sentinel cohort: an observational retrospective database analysis. JMIR Preprints 2022. [doi: 10.2196/preprints.36989]
15. Puntmann VO, Carerj ML, Wieters I, Fahim M, Arendt C, Hoffmann J, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020 Nov 01;5(11):1265-1273 [FREE Full text] [doi: 10.1001/jamacardio.2020.3557] [Medline: 32730619]
16. Joy M, Hobbs FR, Bernal JL, Sherlock J, Amirthalingam G, McGagh D, et al. Excess mortality in the first COVID pandemic peak: cross-sectional analyses of the impact of age, sex, ethnicity, household size, and long-term conditions in people of known SARS-CoV-2 status in England. Br J Gen Pract 2020 Oct 19;70(701):e890-e898. [doi: 10.3399/bjgp20x713393]

17. de Lusignan S. Codes, classifications, terminologies and nomenclatures: definition, development and application in practice. Inform Prim Care 2005 Mar 01;13(1):65-70 [FREE Full text] [doi: 10.14236/jhi.v13i1.580] [Medline: 15949178]
18. Payne RA, Mendonca SC, Elliott MN, Saunders CL, Edwards DA, Marshall M, et al. Development and validation of the Cambridge Multimorbidity Score. CMAJ 2020 Feb 03;192(5):E107-E114 [FREE Full text] [doi: 10.1503/cmaj.190757] [Medline: 32015079]
19. de Lusignan S, Liyanage H, McGagh D, Jani BD, Bauwens J, Byford R, et al. COVID-19 surveillance in a primary care sentinel network: in-pandemic development of an application ontology. JMIR Public Health Surveill 2020 Nov 17;6(4):e21434 [FREE Full text] [doi: 10.2196/21434] [Medline: 33112762]
20. Data Security and Protection Toolkit. NHS Digital. URL: https://www.dsptoolkit.nhs.uk/ [accessed 2022-07-28]
21. Clift AK, Coupland CA, Keogh RH, Diaz-Ordaz K, Williamson E, Harrison EM, et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. BMJ 2020 Oct 20;371:m3731 [FREE Full text] [doi: 10.1136/bmj.m3731] [Medline: 33082154]
22. de Lusignan S, McGee C, Webb R, Joy M, Byford R, Yonova I, et al. Conurbation, urban, and rural living as determinants of allergies and infectious diseases: royal college of general practitioners research and surveillance centre annual report 2016-2017. JMIR Public Health Surveill 2018 Nov 26;4(4):e11354 [FREE Full text] [doi: 10.2196/11354] [Medline: 30478022]
23. de Lusignan S, Correa A, Pathirannehelage S, Byford R, Yonova I, Elliot AJ, et al. RCGP Research and Surveillance Centre Annual Report 2014–2015: disparities in presentations to primary care. Br J Gen Pract 2016 Dec 19;67(654):e29-e40. [doi: 10.3399/bjgp16x688573]
24. Pérez-González A, Araújo-Ameijeiras A, Fernández-Villar A, Crespo M, Poveda E, Cabrera J. Long COVID in hospitalized and non-hospitalized patients in a large cohort in Northwest Spain, a prospective cohort study. Sci Rep 2022;12(1):8. [doi: 10.1101/2021.08.05.21261634]
25. de Lusignan S, Williams J. To monitor the COVID-19 pandemic we need better quality primary care data. BJGP Open 2020 Apr 15;4(2):bjgpopen20X101070. [doi: 10.3399/bjgpopen20x101070]
26. de Lusignan S, Correa A, Smith GE, Yonova I, Pebody R, Ferreira F, et al. RCGP Research and Surveillance Centre: 50 years' surveillance of influenza, infections, and respiratory conditions. Br J Gen Pract 2017 Sep 29;67(663):440-441. [doi: 10.3399/bjgp17x692645]
27. Kostopoulou O, Tracey C, Delaney B. Can decision support combat incompleteness and bias in routine primary care data? J Am Med Inform Assoc 2021 Jul 14;28(7):1461-1467 [FREE Full text] [doi: 10.1093/jamia/ocab025] [Medline: 33706367]

## Abbreviations

**CKD:** chronic kidney disease
**CMR:** computerized medical record
**CMS:** Cambridge Multimorbidity Score
**GP:** general practitioner
**ICU:** intensive care unit
**ONS:** Office for National Statistics
**OR:** odds ratio
**PCSC:** primary care sentinel cohort
**SNOMED CT:** Systematized Nomenclature of Medicine Clinical Terms

*Edited by T Sanchez, A Mavragani; submitted 02.03.22; peer-reviewed by O Tamburis, A Teixeira; comments to author 02.05.22; revised version received 06.05.22; accepted 17.05.22; published 16.08.22.*

*Please cite as:*
*Meza-Torres B, Delanerolle G, Okusi C, Mayor N, Anand S, Macartney J, Gatenby P, Glampson B, Chapman M, Curcin V, Mayer E, Joy M, Greenhalgh T, Delaney B, de Lusignan S*
*Differences in Clinical Presentation With Long COVID After Community and Hospital Infection and Associations With All-Cause Mortality: English Sentinel Network Database Study*
*JMIR Public Health Surveill 2022;8(8):e37668*
*URL: https://publichealth.jmir.org/2022/8/e37668*
*doi:10.2196/37668*
*PMID:35605170*

Original Paper

# Estimating the Health Effects of Adding Bicycle and Pedestrian Paths at the Census Tract Level: Multiple Model Comparison

Ross Gore[1], BSc, MSc, PhD; Christopher J Lynch[1], BSc, MSc, PhD; Craig A Jordan[1], BSc, MSc; Andrew Collins[2], BSc, MSc, PhD; R Michael Robinson[1], BSc, MSc, PhD; Gabrielle Fuller[3], BSc; Pearson Ames[4], BA; Prateek Keerthi[5], BTech, MSc; Yash Kandukuri[1], BTech, MSc

[1]Virginia Modeling Analysis and Simulation Center, Old Dominion University, Suffolk, VA, United States
[2]Engineering Management & Systems Engineering, Old Dominion University, Norfolk, VA, United States
[3]Department of Biomedical Engineering, University of Virginia, Charlottesville, VA, United States
[4]Department of Economics, Chapman University, Orange, CA, United States
[5]Hampton Roads Biomedical Research Consortium, Norfolk, VA, United States

**Corresponding Author:**
Ross Gore, BSc, MSc, PhD
Virginia Modeling Analysis and Simulation Center
Old Dominion University
1030 University Dr
Suffolk, VA, 23435
United States
Phone: 1 757 686 6200
Fax: 1 757 686 6214
Email: ross.gore@gmail.com

## Abstract

**Background:** Adding additional bicycle and pedestrian paths to an area can lead to improved health outcomes for residents over time. However, quantitatively determining which areas benefit more from bicycle and pedestrian paths, how many miles of bicycle and pedestrian paths are needed, and the health outcomes that may be most improved remain open questions.

**Objective:** Our work provides and evaluates a methodology that offers actionable insight for city-level planners, public health officials, and decision makers tasked with the question “To what extent will adding specified bicycle and pedestrian path mileage to a census tract improve residents’ health outcomes over time?”

**Methods:** We conducted a factor analysis of data from the American Community Survey, Center for Disease Control 500 Cities project, Strava, and bicycle and pedestrian path location and use data from two different cities (Norfolk, Virginia, and San Francisco, California). We constructed 2 city-specific factor models and used an algorithm to predict the expected mean improvement that a specified number of bicycle and pedestrian path miles contributes to the identified health outcomes.

**Results:** We show that given a factor model constructed from data from 2011 to 2015, the number of additional bicycle and pedestrian path miles in 2016, and a specific census tract, our models forecast health outcome improvements in 2020 more accurately than 2 alternative approaches for both Norfolk, Virginia, and San Francisco, California. Furthermore, for each city, we show that the additional accuracy is a statistically significant improvement ($P$<.001 in every case) when compared with the alternate approaches. For Norfolk, Virginia (n=31 census tracts), our approach estimated, on average, the percentage of individuals with high blood pressure in the census tract within 1.49% (SD 0.85%), the percentage of individuals with diabetes in the census tract within 1.63% (SD 0.59%), and the percentage of individuals who had >2 weeks of poor physical health days in the census tract within 1.83% (SD 0.57%). For San Francisco (n=49 census tracts), our approach estimates, on average, that the percentage of individuals who had a stroke in the census tract is within 1.81% (SD 0.52%), and the percentage of individuals with diabetes in the census tract is within 1.26% (SD 0.91%).

**Conclusions:** We propose and evaluate a methodology to enable decision makers to weigh the extent to which 2 bicycle and pedestrian paths of equal cost, which were proposed in different census tracts, improve residents’ health outcomes; identify areas where bicycle and pedestrian paths are unlikely to be effective interventions and other strategies should be used; and quantify the minimum amount of additional bicycle path miles needed to maximize health outcome improvements. Our methodology shows statistically significant improvements, compared with alternative approaches, in historical accuracy for 2 large cities (for 2016) within different geographic areas and with different demographics.

***(JMIR Public Health Surveill 2022;8(8):e37379)*** doi:10.2196/37379

**KEYWORDS**

bicycle paths; pedestrian paths; bicycling; walking; diabetes; high blood pressure; physical health; factor analysis; digital neighborhoods; data analysis

## Introduction

The addition of bicycle and pedestrian paths to an area is a theoretically valuable resource for city-level planners, public health officials, and decision makers to increase physical activity and improve health outcomes. Most existing research has found a negative association between the prevalence of bicycle and pedestrian paths and poor health outcomes (ie, diabetes, stroke, obesity, heart disease, high blood pressure, and ailments to physical and mental health) [1-10].

### Objectives

Our objective is to provide and evaluate a methodology for officials addressing the question "To what extent will adding specified bicycle and pedestrian path mileage to a census tract improve residents' health outcomes over time?" The methodology we propose uses factor analysis to filter and organize variables from publicly available data sets at the census tract level within a given city. The data sets included (1) the US Census [11], (2) the American Communities Survey (ACS) [12], (3) Centers for Disease Control and Prevention (CDC) 500 Cities project data [13], (4) municipality data [14,15], and (5) the GPS walking, running, and cycling tracking social network app, Strava [16,17].

The result of this analysis is a city-specific factor model describing the relationship among variables related to individuals, bicycling and walking behaviors, and health outcomes. Then, the factor model, built using past data, is used in an algorithm to predict the extent to which adding a future specified number of bicycle and pedestrian path miles to a certain location in the city quantitatively impacts certain health outcomes.

### Background

We are not aware of any other applications of factor analysis to develop predictive algorithms related to the placement and efficacy of bicycle and pedestrian paths with respect to health outcomes. However, there are researchers who approach bicycle and pedestrian path planning from a similar perspective. Smith and Haghani [18] proposed an approach that adds bicycle and pedestrian paths within a city such that the length of the average trip within the bicycle and pedestrian path network is minimized, and the level of service of the bicycle and pedestrian paths is maximized. Mesbah et al [19] explored the addition of bicycle and pedestrian paths within a city by identifying locations that minimized the total travel time of automobiles within the city. Researchers assume that bicycle and pedestrian paths take road space from cars. Although this assumption may occasionally be true, in most instances, bicycle and pedestrian paths narrow car lanes but do not reduce the total number available. Duthie and Unnikrishnan [20] identified instances within a city where the addition of bicycle and pedestrian paths maximized the connectivity of the existing bicycle and pedestrian path network. This approach ignores the use of the current bicycle and pedestrian path network and aims to "open up" as many new routes as possible regardless of current demand [21].

Although they are not prevalent in identifying bicycle and pedestrian path placement, optimization techniques have also been explored for choosing existing routes rather than developing new ones. Allen-Munley et al [22] developed a model that rates bicycle routes based on predictions of injury severity [18]. Other researchers have proposed allowing users to select multiple criteria and then eliminate certain routes (ie, steep slopes and heavy traffic) before providing a set of suggestions [23,24]. More recently, researchers have explored the use of multiobjective optimization as a means of retrofitting the existing cycling infrastructure for commuter cyclists. The objective of the formulation is to maximize the network for a number of different criteria, including accessibility, minimization of the number of intersections, maximization of bicycle level of service, and minimization of total construction cost subject to space-time constraints and monetary budget [25-27].

Ospina et al [28] addressed a similar problem but framed it as a maximal covering bicycle network design problem. The maximal covering bicycle network design problem involves making investment decisions to build a cycling network aimed at maximizing the coverage of cyclists while maintaining a minimum total network cost. The derived network is subject to budget and accounts for the entire connectivity and directness as fundamental bicycle network design criteria. This approach focuses only on the network and not on the health outcomes. There is no consideration of the extent to which each path in the network improves any health outcome within an area.

It is important to note that there are arguments against defining the placement of bicycle and pedestrian paths as a systems engineering problem. Szimba and Rothengatter [29] demonstrated that interdependencies between infrastructure projects can create cost incentives to place bicycle and pedestrian paths in certain areas, even if the payoff of the addition is not optimal with respect to the use, connectivity, or health benefits of the bicycle and pedestrian path. In addition, in areas where congestion and the propagation of congestion along bicycle and pedestrian paths occur, researchers have demonstrated that optimizing the use and distance of bicycle and pedestrian paths would only exacerbate traffic within the network and not produce effective results [30-32].

Furthermore, significant work has been conducted to estimate demand [33,34] and understand why people choose to use bicycle and pedestrian paths [35-40]. Our work also considers motivation related to bicycle and pedestrian path use but does not directly attempt to optimize bicycle and pedestrian path use. We made this design choice because adding bicycle and pedestrian paths based only on the existing demand can lead to a chicken-and-egg problem. Here, areas with advanced bicycle and pedestrian path infrastructure improve, and areas without bicycle and pedestrian path infrastructure are neglected. These dynamics can create inequitable living conditions and produce enormous health and environmental disparities within a city [41].

In summary, the algorithm used in this study is unique from previous approaches used for estimating demand, evaluating network efficacy, and optimizing the placement of bicycle and pedestrian paths. The problem examined here focuses on understanding what health outcomes can be improved by adding bicycle and pedestrian paths, in which census tracts will adding bicycle and pedestrian paths improve health outcomes the most, and finally, how many miles of bicycle and pedestrian paths within a given census tract need to be added to have an impact on the residents' health outcomes.

The remainder of this paper is organized as follows. First, we review the data and methods used in our approach to construct city-specific models. Next, we apply the approach to two different cities: Norfolk, Virginia, and San Francisco, California. We then evaluate our approach for the 2 different cities. In the evaluation, our approach was tested against 2 alternate approaches for predicting improvements in health outcomes by adding bicycle and pedestrian paths. The evaluation shows that our approach offers more accurate predictions than both alternatives and that the superior difference in accuracy is statistically significant ($P<.001$ in all cases). Finally, we identify several limitations to our work and threats to its validity and review other avenues of related research.

# Methods

## Ethical Considerations

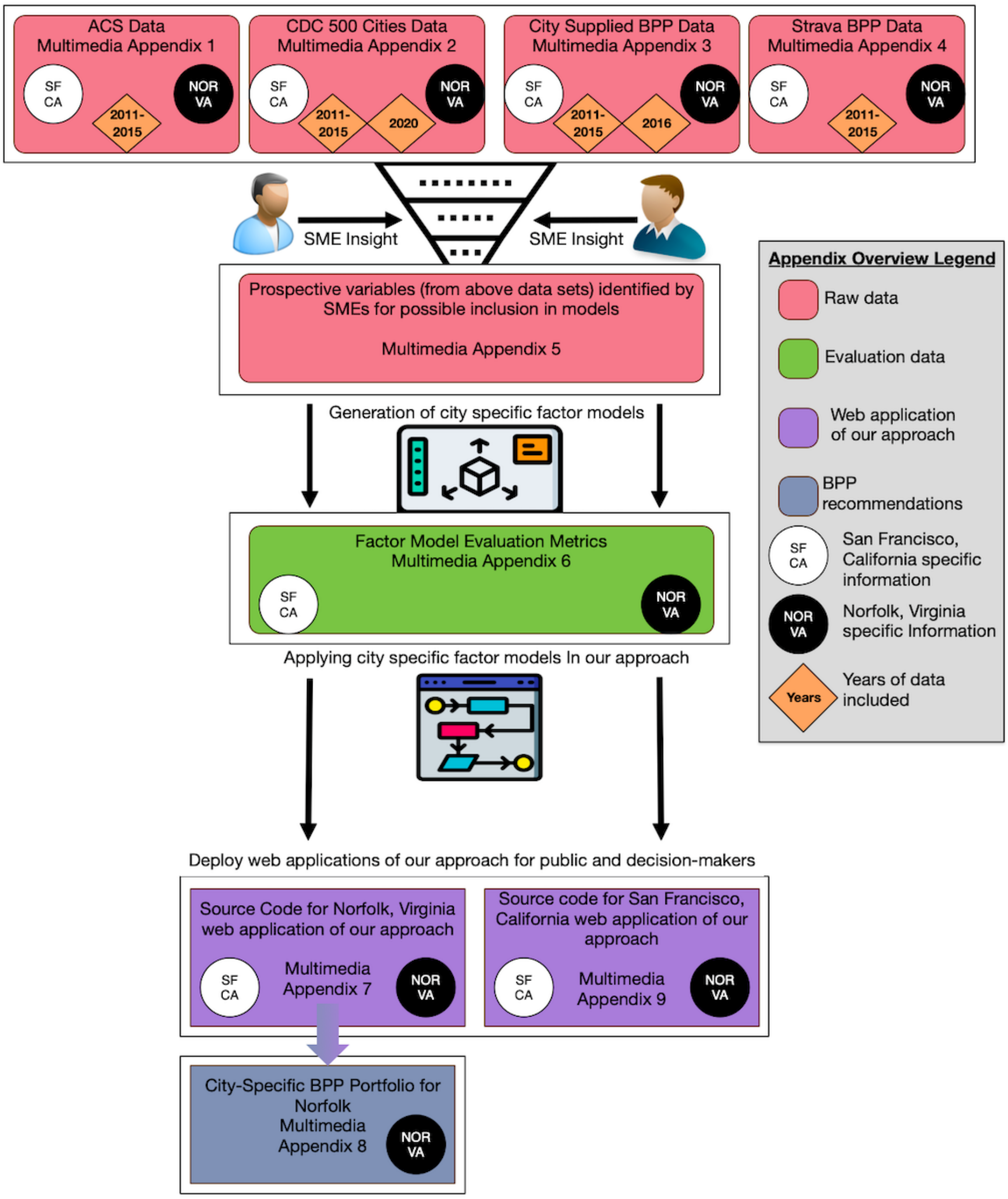
Our work uses publicly-available data related to urban infrastructure and resident demographics and health outcomes. The data sets reflect aggregate variables measured at the census tract level of a city and do not contain any personally identifiable information. Therefore, they do not involve human subjects as defined by federal regulations and their use does not require ethics board review or approval [42].

## Data Sets

### *Overview*

Our approach to modeling the health effects of adding bicycle and pedestrian paths at the census tract level uses data from (1) census tract boundaries used in the US Census [11]; (2) demographic variables from the ACS [12]; (3) census tract–level estimates for health outcomes, health statuses, healthy behaviors, and disease prevention from the CDC [13]; (4) bicycle and pedestrian path location and use data from Norfolk, Virginia, and San Francisco, California [14,15]; and (5) bicycle and pedestrian path use data from the GPS walking, running, and cycling tracking social network app, Strava. Combining these data sets resulted in >400 variables for each census tract in Norfolk, Virginia, and San Francisco, California [16,17]. An overview of all the data sets and other supplementary materials supplied in the multimedia appendices of this paper is shown in Figure 1.

**Figure 1.** An overview of the data sets and other supplementary materials supplied in the multimedia appendices. ACS: American Communities Survey; BPP: bicycle and pedestrian path; CDC: Centers for Disease Control and Prevention; NOR: Norfolk; SF: San Francisco; SME: subject matter expert.



### US Census and ACS

Census tracts are small, contiguous, and relatively permanent statistical subdivisions of a county or an equivalent entity. The populations in census tracts vary from 1200 to 8000. Census tracts provide a stable geographic unit for statistical analysis in the US Census and ACS [43].

The ACS is an ongoing national survey that samples a subset of individuals within the same geographic areas in the US Census. Using the same questions, data were collected each month throughout the year. In contrast, the US Census provides a more comprehensive sample of individuals in the United States, collecting data from more individuals during a particular period (March to August) but administered only once every 10 years. A metaphor helps elucidate the differences between the 2 surveys. The US Census serves as a high-resolution photograph of the US population once every 10 years, whereas the ACS serves as many low-resolution continually updated videos over the same period [43]. Multimedia Appendix 1 provides the data included in the ACS for this study.

### CDC 500 Cities Project

The census tract–level estimates and methodology for estimating health outcomes, health statuses, healthy behaviors, and disease prevention are provided by the CDC 500 Cities project. The 500 Cities project is a collaboration between the CDC and the Robert Wood Johnson Foundation. The small area estimates provided by the project allow policymakers and local health departments to better understand the burden and geographic distribution of health-related variables in their jurisdictions and assist them in planning public health interventions [13]. The data included in the CDC 500 Cities project for this study are provided in Multimedia Appendix 2.

### City-Supplied Bicycle and Pedestrian Path Data

The bicycle and pedestrian path data for Norfolk, Virginia, and San Francisco, California include the latitude and longitude location of bicycle lanes, routes, and paths built and maintained in each city. Bicycle use data were taken from bicycle counters used in each city [14,15]. The data included from Norfolk, Virginia, and San Francisco, California, for this study are provided in Multimedia Appendix 3.

### Strava Data

We used the Strava Metro rollup data set for Norfolk, Virginia, and San Francisco, California. This data set contains walking, running, and bicycling activity counts per road segment for a given year. These counts can then be aggregated at the census tract level. The road count segment is referred to as edge within Strava. Each edge is associated with a latitude and longitude bounding box using the Strava application programming interface [16,17]. The Strava data for Norfolk, Virginia, and San Francisco, California for this study are provided in Multimedia Appendix 4. There are limitations to using the Strava data, which we describe in the *Discussion* section.

## Data Selection

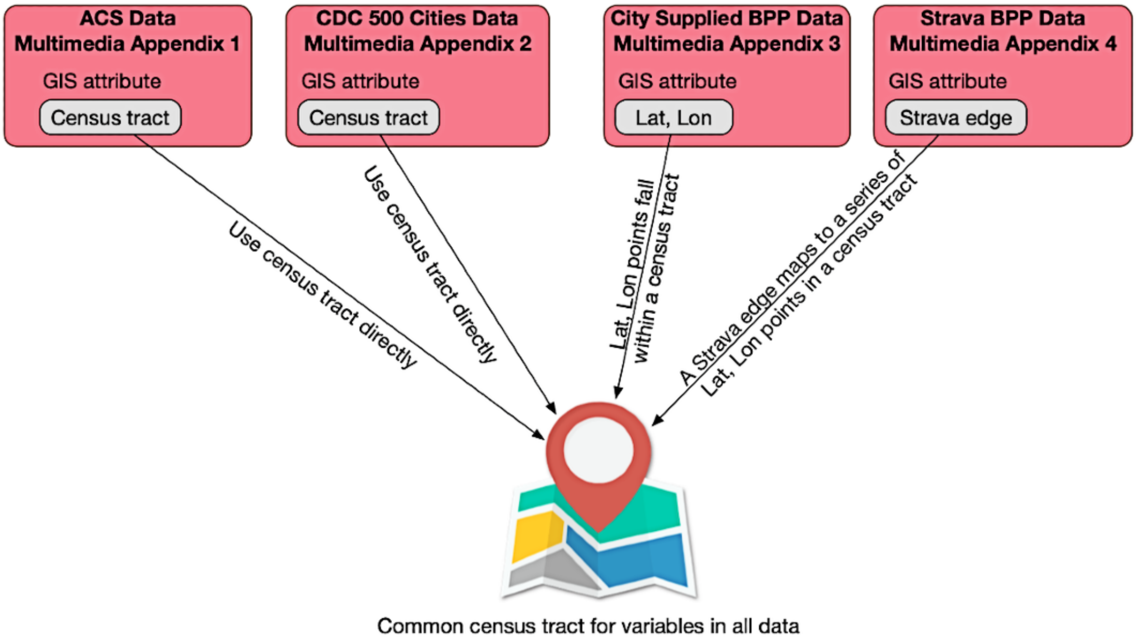
Our data set included a wide range of variables collected from multiple sources. From this data set, we selected a subset of the variables that individuals with domain expertise identified as possibly contributing to the use of bicycle and pedestrian paths and the impact of bicycle and pedestrian paths on health outcomes when additional mileage was added to a geographic area (ie, census tract). The expertise of these individuals spanned social work, health science and nutrition, community health, public health, and transportation. Textbox 1 shows the categories of variables identified by domain experts for each census tract in Norfolk, Virginia, and San Francisco, California. Multimedia Appendix 5 provides the list of observed variables for each category. These variables can be combined using common Geographical Information System attributes to align data at the census tract level. The approach for joining these data together at the census travel level is shown in Figure 2.

**Textbox 1.** The categories of variables from our data sets that are included in our factor analysis for Norfolk, Virginia, and San Francisco, California.

**Data set and variable category**

- American Communities Survey
  - Race
  - Educational attainment
  - Employment status
  - Income and benefits
  - Marital status
  - Sex and age
  - Commuting to work
  - Citizenship
  - Health insurance
  - Occupation
  - Household by type
  - Relationship
- Centers for Disease Control and Prevention 500 Cities project
  - Health outcomes
  - Health risk behaviors
  - Prevention
  - Health status
- City Bicycle and Pedestrian Path data
  - Bicycle and Pedestrian Path use data
  - Bicycle and Pedestrian Path mileage data
- Strava Bicycle and Pedestrian Path data
  - Bicycle and Pedestrian Path use data

**Figure 2.** The approach to joining together the data sets at the census tract level. ACS: American Communities Survey; BPP: bicycle and pedestrian path; CDC: Centers for Disease Control and Prevention; GIS: Geographical Information System.



## Factor Analysis

### Overview

Next, we applied factor analysis to reduce these observed variables into latent variables (ie, factors). Factor analysis generates a model that measures how changes in one factor predict changes in another by reducing a large number of observed variables to a handful of comprehensible underlying factors. The result is an interpretable and actionable model of concepts that are otherwise difficult to measure [44].

The Honesty-Humility (H), Emotionality (E), Extraversion (X), Agreeableness (A), Conscientiousness (C), and Openness to Experience (O) 6D model of the human personality structure is a widely known result of the application of factor analysis. The ability of factor analysis to reduce the many observed variables related to personality into 6 distinct factors has pushed the state of the art in psychological research [45]. Our goal of applying factor analysis was similar.

We applied exploratory factor analysis (EFA) to filter the observed variables from the data described in Textbox 1 and reduced them into a model composed of factors that include residents' (1) demographics and background characteristics (DBC), (2) health, and (3) bicycling and pedestrian habits (BPH). Using this model, we can understand how changes in one factor predict changes in others.

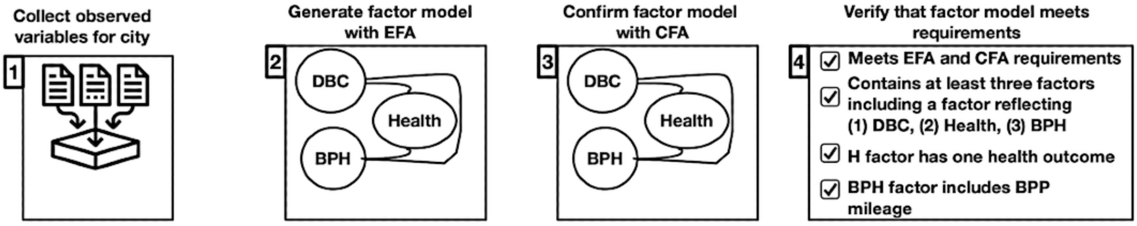
### EFA Summary

In our approach, EFA was used to fit a factor model. Before the EFA began, data corresponding to half of a given city's census tracts were selected at random. In the application of our approach, data from 2011 to 2015 were used. Then, using these data, an EFA model was fitted.

Figure 3 shows the fitting of the model using EFA. The process is iterative, and each iteration comprises 3 stages. Figure 3A shows the observed variables that underwent analysis for a given iteration. These observed variables are organized into a number of factors that optimize the fit of the model in Figure 3B. The optimization constructs a model with the minimum number of factors such that the observed variables associated with each factor have maximum commonality with one another and minimal commonality with the observed variables in all other factors. Commonality reflects the amount of variance an observed variable shares with other variables in a factor [44,46].

Finally, the model was assessed. The assessment tests if all factors are composed of variables with high communality (>0.5) with respect to the factor they are associated with and low communality (<0.5) with all other factors. If this is true, the process terminates. Otherwise, variables that do not meet the communality requirement are discarded and the process is repeated for another iteration. Figure 3C shows the assessment stage of the iteration. The requirements imposed in this stage are consistent with the established factor analysis guidelines [46].

**Figure 3.** The process of generating a factor model for a city and verifying that it meets our defined restrictions. BPH: bicycling and pedestrian habits; BPP: bicycle and pedestrian path; CFA: confirmatory factor analysis; DBC: demographics and background characteristics; EFA: exploratory factor analysis.



### Confirmatory Factor Analysis Summary

Next, the fit of the hypothesized model was confirmed or rejected by applying confirmatory factor analysis (CFA) using the other half of the data from 2011 to 2015. The goal of CFA is to confirm or reject the hypothesized model. As a result, (1) only observed variables were included, (2) the variables were loaded onto the same factors as in the CFA, and (3) the communality of the variables in the model was assessed. The model was confirmed if it satisfied the same requirements as specified for EFA [46].

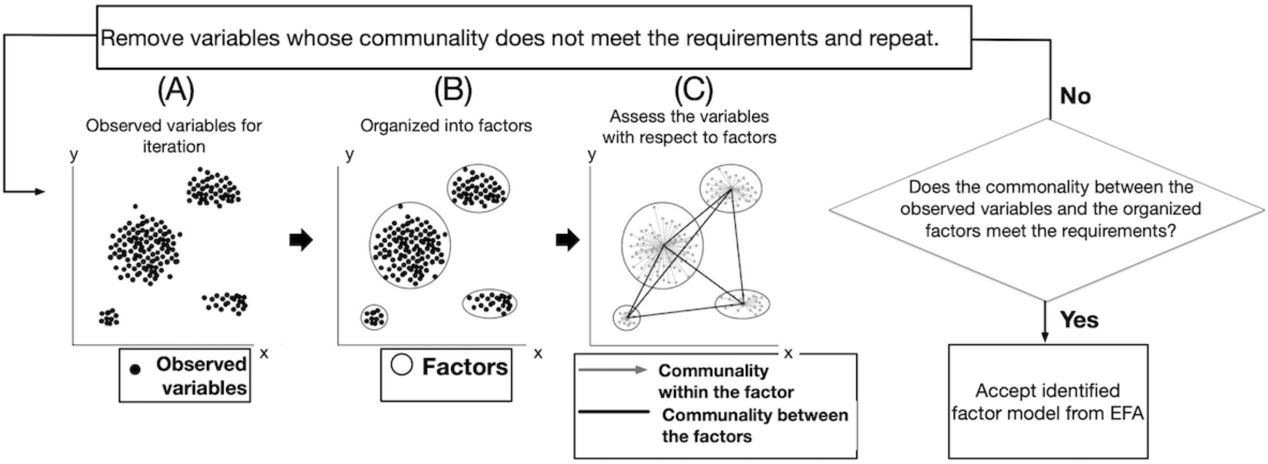
### Factor Restrictions and Limitations

The application of factor analysis imposes several limitations on our approach for estimating the health effects of adding bicycle and pedestrian paths to the city-specific factor model. First, a model that meets our requirements must be generated using EFA and confirmed using CFA. Furthermore, to apply our algorithm, the model must consist of at least three factors reflecting residents' (1) DBC, (2) health, and (3) BPH. Finally, the health factor must include at least one observed variable related to a health outcome, and the BPH must include an observed variable related to the amount of bicycle and pedestrian path mileage in the census tract. The process of generating a factor model and determining whether it meets these restrictions is illustrated in Figure 4.

We imposed these restrictions because our health outcome prediction algorithm computes the factor scores for each census tract in a city based on these factors. Factor scores are continuous numbers reflecting the extent to which each census tract manifests each factor. For each factor, the scores were distributed normally, with a mean of 0 and an SD of 1. Large positive values reflect census tracts where the factor is heavily present, and large negative values reflect census tracts where the factor is not present at all [47].

Without these factors, the proposed algorithm could not be applied. It does not have sufficient data or structure to produce estimates of the health effects of adding bicycle and pedestrian paths. This is a limitation of the proposed approach. This limitation is discussed in more detail in the *Discussion* section.

**Figure 4.** The three stages of an EFA iteration—(A) observed variable identification, (B) organization of variables into factors, and (C) assessment of the communality of variables within and between each of the identified factors. EFA: exploratory factor analysis.



## Estimating the Health Effects of Adding Bicycle Paths at the Census Tract Level

### Overview

Given a factor model hypothesized by EFA and confirmed by CFA, we proposed an algorithm to predict the health effects of adding bicycle and pedestrian paths at the census tract level. For this purpose, we defined the input as an observed variable identified from the factor model. The variable then progressed through a sequence of steps that were applied to each census track and resulted in a predicted health outcome change for each identified health factor. The steps of this algorithm are enumerated in the following sections. Finally, the output from the algorithm was a list of hypothesized health improvement outcomes.

### Input

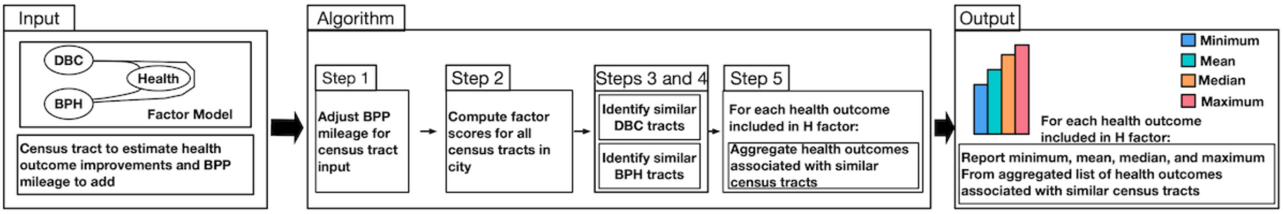
In our problem statement, there was only one observed variable in the model that could be changed directly by a city-level planner, public health official, or decision maker. This variable represented the additional bicycle and pedestrian path mileage for a census tract within a city. This was the input to our algorithm, along with the factor model generated for the city.

### *Algorithm*

The algorithm proceeded as follows, as conveyed visually in Figure 5.

1. The algorithm adds the bicycle and pedestrian path mileage to the specified census tract in the data set for the city.
2. Factor scores are computed for the following three factors: DBC, health, and BPH.
3. Given the DBC factor score for the input census tract, the algorithm identifies all other census tracts in the city with a DBC factor score within the threshold value—x. This list of census tracts reflects those that are similar to the input census tract with respect to the DBC factor. Recall that the factor scores are normally distributed, with an SD of 1. Thus, a census tract within a factor score x of the tract being analyzed reflects a census tract within SDs of the input tract [47].
4. Given the BPH factor score for the input census tract (which includes the newly added bicycle and pedestrian path mileage), the algorithm identifies all other census tracts in the city with BPH factor scores within x. This list of census tracts reflects those that are similar to the input census tract with respect to the BPH factor.
5. For each observed health outcome within the health factor, the algorithm creates a list that stores the difference between the value of the health outcome for each census tract identified in steps 3 and 4 and the value of the health outcome for the input census tract. This list of differences is a distribution of hypothesized improvements in a health outcome by adding a specified amount of bicycle and pedestrian path mileage to a census tract. Any differences that are <0 are discarded because these differences indicate that adding bicycle and pedestrian path mileage to the census tract will degrade health outcomes.

**Figure 5.** Instantiation of the algorithm for predicting how much additional BPP mileage in a census tract will improve health outcomes. BPH: bicycling and pedestrian habits; BPP: bicycle and pedestrian path; DBC: demographics and background characteristics.



### *Output*

For each list of hypothesized improvements for health outcomes generated in step 5, the algorithm output the minimum, mean, median, and maximum values of the improvements to the user. The algorithm could also report the entire distribution of possible improvements and SD of the distribution for each health outcome.

# Results

## Overview

The accuracy of our algorithm was elucidated through an empirical evaluation of alternative approaches for two different cities (Norfolk, Virginia, and San Francisco, California). In our evaluation, we computed how accurately each approach predicted the health outcome improvements of the bicycle and pedestrian paths added in each city in 2016. Specifically, for a given census tract, in each city that added bicycle and pedestrian paths miles in 2016, we evaluated how accurately our algorithm estimated an improvement in health outcomes in 2020. We chose to use a 5-year time-lapse period for our evaluation because research has shown that is the expected amount of time for a fully realized change in health outcomes given outdoor exercise infrastructure interventions [48,49].

## Factor Analyses

Applying the process described in the *Methods* section and shown in Figures 3 and 4 with the data from half the census tracts in each city for each year from 2011 to 2015 yields the EFA models shown in Figure 6A (n=195) and Figure 7A (n=490). Confirmation of these models using the remaining half of the census in each city for each year from 2011 to 2015 is shown in Figure 6B (n=190) and Figure 7B (n=485). Within the figures, the numbers labeled with single-headed arrows reflect the commonality of an observed variable with the associated factor. The double-headed arrows reflect the shared variance between factors [44,46]. The goodness-of-fit statistics corresponding to the CFA for each model are provided in Multimedia Appendix 6 (Norfolk, Virginia) and Multimedia Appendix 6 (San Francisco, California) along with guidelines on how to interpret the goodness-of-fit statistics.

Figures 6 and 7 show that the factor models for each city met our requirements. These models served as inputs for our estimation algorithm in the evaluation. It is important to note that although each model had the three required factors (DBC, health, and BPH), there were differences in the observed variables that form the factors. The factor analysis showed that changes in high blood pressure, diabetes, and poor physical health were predicted by changes in DBC and BPH in Norfolk, Virginia, whereas changes in stroke and diabetes were predicted by changes in DBC and BPH in San Francisco, California. This was not unexpected or a violation of the requirements of our approach. Although we required the 3 factors to be present, we anticipated that different observed variables would form these 3 factors for different cities.

**Figure 6.** Exploratory factor analysis and confirmation factor analysis models for Norfolk, Virginia, using data sets from 2011 to 2015. Single-headed arrows reflect the commonality of an observed variable with a factor. Double-headed arrows reflect the value of the shared variance between factors. BPH: bicycling/pedestrian habits; BPP: bicycle and pedestrian path; DBC: demographics and background characteristics.

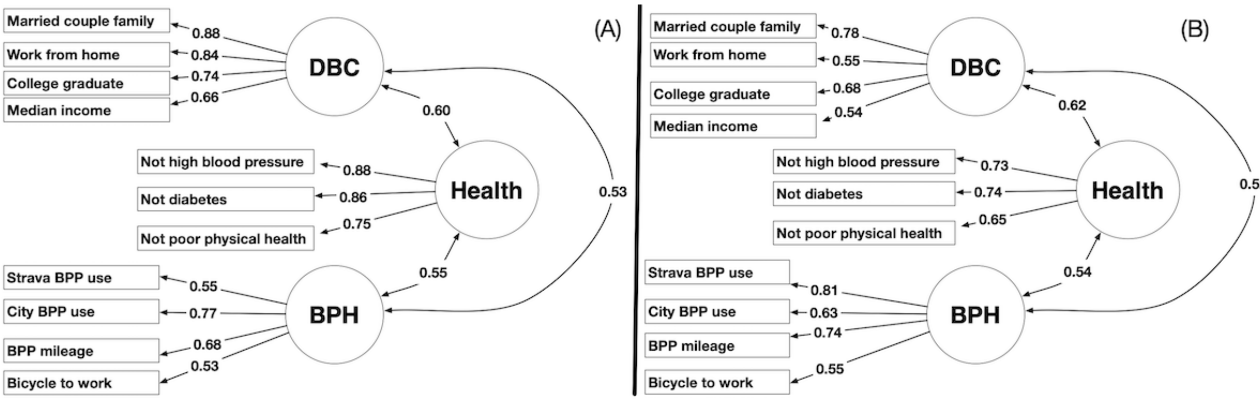
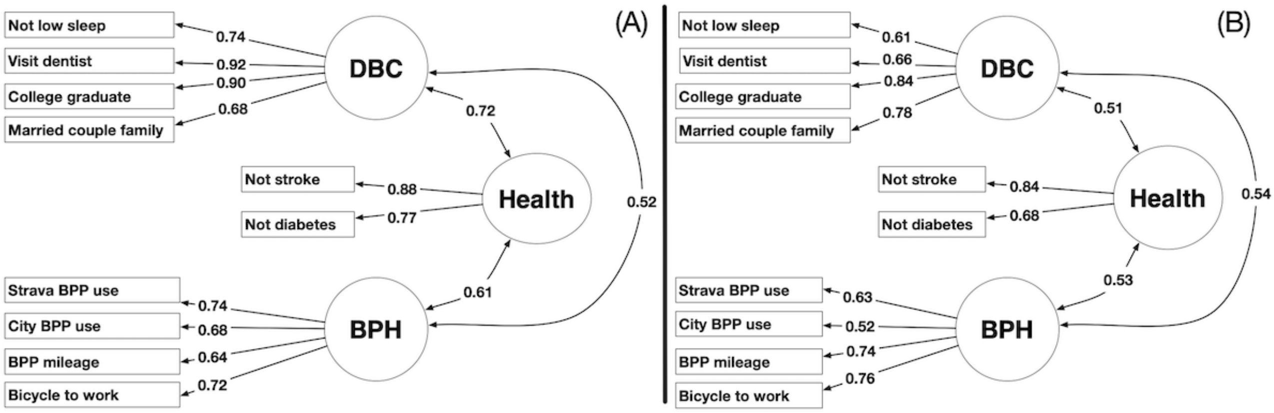


**Figure 7.** Exploratory factor analysis and confirmation factor analysis models for San Francisco, CA, using data sets from 2011 to 2015. Single-headed arrows reflect the commonality of an observed variable with a factor. Double-headed arrows reflect the value of the shared variance between factors. BPH: bicycling and pedestrian habits; BPP: bicycle and pedestrian path; DBC: demographics and background characteristics.



## Evaluation

Recall that our algorithm took an input: (1) the factor model for a given city and (2) the census tract and amount of bicycle and pedestrian path mileage to be added. It then output the minimum, mean, median, and maximum estimated improvements by adding the bicycle and pedestrian path mileage to the input census tract. In the evaluation, we only used the median improvement estimate from the algorithm.

In our evaluation, we used our factor model constructed using data from 2011 to 2015 to estimate the accuracy of our approach and 2 alternative approaches with respect to the improvements in health outcomes provided by bicycle and pedestrian paths installed in 2016. The evaluation included 31.58 miles (50.81 km) of bicycle and pedestrian paths added in Norfolk, Virginia, across 31 census tracts and 52.36 miles (84.25 km) of bicycle and pedestrian paths added tracts in San Francisco, California, across 49 census tracts. Table 1 provides additional details regarding the setup of the evaluation.

**Table 1.** Evaluation setup metadata for Norfolk, Virginia, and San Francisco, California, in 2016.

| | Norfolk, Virginia | San Francisco, California |
|---|---|---|
| BPP[a] miles (km) added | 31.58 (50.81) | 52.36 (84.25) |
| Census tracts with paths added, n | 31 | 49 |
| Census tracts in city, n | 77 | 195 |
| Health outcomes evaluated | Diabetes %; poor physical health %; high blood pressure % | Diabetes %; stroke % |

[a] BPP: bicycle and pedestrian path.

## Alternative Approaches

We evaluated our algorithm using 2 alternative approaches. The first alternative assumed that each health outcome within a census tract in the future would be same as the average value for that health outcome for the census tract from 2011 to 2015. This approach mirrored the prediction that the temperature tomorrow would be the same as the average temperature of the previous 5 days.

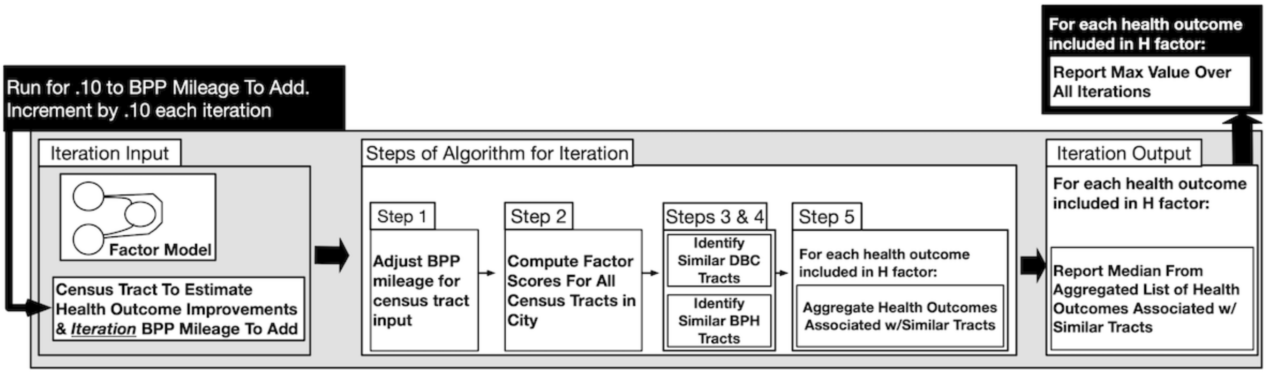
The second alternative used linear regression modeling [50]. This approach used regression to predict future changes in each health outcome using a weighted linear combination of the (1) DBC factor and (2) BPH factor scores of the census tract based on the constructed factor model using data from 2011 to 2015, after the specified increase in mileage.

## Approach

We evaluated our approach by using x=0.50. Recall that x is the threshold used to identify similar census tracts in terms of the (1) DBC factor and (2) BPH factor scores. In addition, our evaluation approach is an extension of the algorithm described in the *Methods* section. For our evaluation, given a specified number of bicycle and pedestrian path miles to be added and a census tract, we ran the algorithm for every 0.10-mile increment of bicycle and pedestrian paths up to the specified number of miles.

Each time the algorithm was executed, the median improvement from the algorithm was collected. The largest improvement over all the runs was reported. A version of our approach is shown in Figure 8. It implemented the assumption that adding more bicycle and pedestrian path mileage (ie, 1.0 miles as opposed to 0.5 miles) to a given census tract would not be detrimental to the expected improvement in a health outcome.

**Figure 8.** The specific version of our algorithm included in the applied evaluation. BPP: bicycle and pedestrian path; BPH: bicycling and pedestrian habits; DBC: demographics and background characteristics.



## Measures of Effectiveness

For a given city and a given approach to estimating the improvement in a health outcome for bicycle and pedestrian paths added in 2016, we computed the following two measures of effectiveness (MOEs): (1) the root mean squared error (RMSE) and (2) the mean absolute error (MAE). These are 2 established metrics used to measure the accuracy of continuous variables. MAE measures the average magnitude of the errors in a set of predictions without considering their direction. It reflects the average over the evaluation of the absolute differences between the prediction and actual observation where all individual differences have equal weight. RMSE also measures the average magnitude of the error. However, it reflects the square root of the average squared differences between the predicted and actual observations. Within the RMSE, the errors were squared before they were averaged. As a result, the RMSE gives a relatively high weight to large errors [51]. By using both metrics as MOEs, we could capture the accuracy of each approach for decision makers who (1) view all errors equally (MAE) and (2) view large errors as particularly undesirable (RMSE).

## Measures of Success

We deem our approach successful if, for each city included in our evaluation, our approach is more accurate across every MOE than the best alternative approach, and these differences are all statistically significant at $P<.01$, when a 1-tailed paired sample $t$ test is applied. We used a 1-tailed paired sample $t$ test to determine whether the mean paired difference between the MOEs of our approach and an alternate approach was <0 (ie, our approach was more accurate). In this procedure, paired observations reflected the MOEs for a given census tract. Within the pair, one observation corresponded to our approach, and the other corresponded to an alternative approach [52].

# Discussion

## Principal Findings

In our evaluation, we compare the accuracy of our factor model approach, a linear regression approach, and predict no change approach. Each approach estimates the improvements in health outcomes provided by bicycle and pedestrian paths installed in 2016 in 31 census tracts in Norfolk, Virginia and 49 census tracts in San Francisco, California. The results of the evaluation are shown in Table 2.

Table 3 shows that our approach is more accurate than the alternatives, and Table 4 shows that those improvements in accuracy over the best alternative are statistically significant because $P<.001$ for every health outcome in each city when the 1-tailed paired $t$ test is applied.

We expected our approach to outperform the “predict no change approach” because the CDC 500 Cities project and bicycle and pedestrian path data for both cities show that most of the time when a bicycle path of any length is added, the health outcomes identified by the factor analysis improve within 5 years. However, we did not know whether our approach outperformed the linear regression approach.

The results of the evaluation showed that our approach outperformed the linear regression models because it assumed that critical thresholds within the DBC and BPH factors existed (parameter x in steps 3 and 4 of the algorithm). The linear regression approach did not make this assumption [50]. By accounting for this threshold, our approach ensured that it did not overpredict the improvement offered by additional bicycle path miles when the DBC or BPH factor for the census tract indicated that the additional path miles would be ineffective.

By not accounting for this threshold, the linear regression approach could overpredict the expected improvement in health outcomes within a census tract. This was because the linear regression approach assumed that some amount of bicycle and pedestrian paths in each census tract would yield a population without any negative health outcomes. This is unrealistic. Our evaluation results in Tables 3 and 4 demonstrate that linear regression yields statistically significant inferior accuracy, as measured by our 1-tailed paired *t* test.

**Table 2.** Evaluation of approaches for bicycle and pedestrian paths added in Norfolk, Virginia, in 2016.

| Health outcome and MOE[a] (% of individuals who experience a negative health outcome) | Predict no change (census tract: n=31), mean (SD) | Linear regression (census tract: n=31), mean (SD) | Our approach (census tract: n=31), mean (SD) |
|---|---|---|---|
| **Diabetes** | | | |
| MAE[b] | 2.33 (0.66) | 2.14 (0.67) | 1.63 (0.59) |
| RMSE[c] | 2.41 (0.62) | 2.29 (0.61) | 1.67 (0.55) |
| **Poor physical health** | | | |
| MAE | 2.69 (0.72) | 2.21 (0.69) | 1.83 (0.57) |
| RMSE | 2.64 (0.69) | 2.27 (0.66) | 1.94 (0.56) |
| **High blood pressure** | | | |
| MAE | 2.95 (1.17) | 2.27 (1.07) | 1.49 (0.85) |
| RMSE | 3.18 (1.13) | 2.38 (0.92) | 1.55 (0.82) |

[a] MOE: measure of effectiveness.

[b] MAE: mean absolute error.

[c] RMSE: root mean squared error.

**Table 3.** Evaluation of approaches for bicycle and pedestrian paths added in San Francisco, California, in 2016.

| Health outcome and MOE[a] (% of individuals who experience a negative health outcome) | Predict no change (census tract: n=49), mean (SD) | Linear regression (census tract: n=49), mean (SD) | Our approach (census tract: n=49), mean (SD) |
|---|---|---|---|
| **Diabetes** | | | |
| MAE[b] | 2.32 (1.19) | 2.18 (1.18) | 1.24 (0.91) |
| RMSE[c] | 2.44 (1.11) | 2.41 (1.11) | 1.35 (0.90) |
| **Stroke** | | | |
| MAE | 2.68 (0.58) | 2.78 (0.68) | 1.81 (0.52) |
| RMSE | 3.19 (0.52) | 2.97 (0.64) | 1.88 (0.49) |

[a] MOE: measure of effectiveness.

[b] MAE: mean absolute error.

[c] RMSE: root mean squared error.

**Table 4.** Assessment of whether the improved accuracy of bicycle and pedestrian paths added in 2016 is statistically significant.

| City, health outcome, and MOE[a] | Statistical significance of our approach MOE versus best alternative MOE, *P* value |
|---|---|
| **Norfolk, Virginia (census tract: n=31)** | |
| **Diabetes** | |
| MAE[b] | <.001 |
| RMSE[c] | <.001 |
| **Poor physical health** | |
| MAE | <.001 |
| RMSE | <.001 |
| **High blood pressure** | |
| MAE | <.001 |
| RMSE | <.001 |
| **San Francisco, California (census tract: n=49)** | |
| **Diabetes** | |
| MAE | <.001 |
| RMSE | <.001 |
| **Stroke** | |
| MAE | <.001 |
| RMSE | <.001 |

[a] MOE: measure of effectiveness.

[b] MAE: mean absolute error.

[c] RMSE: root mean squared error.

## Comparison With Prior Work

Our study builds on a significant amount of previous research. Numerous researchers have used statistical analyses to (1) explore the health effects of commuting via bicycle or by foot [4,53-62] and (2) assess the health benefits of bicycling and bicycle and pedestrian paths versus the risk of injury or death [63-67]. This study captured data related to walking and bicycling using telephone and web-based surveys [53,54,68], GPS, accelerometers, heart rate monitors [6,58,69-77], bicycling shares [78-80], and social media [17,81].

Predicting which bicycle and pedestrian paths residents will choose is also related to our work. Within this arena, researchers have found different results with respect to the extent to which bicycle and pedestrian path users prefer to take paths that minimize the total travel distance. For example, Broach et al [71,82] used data from Portland, Oregon, to formulate a model that estimated that preferred routes were <10% longer than the shortest path distance. Similarly, Winters et al [39] found that 75% of trips in Vancouver, British Columbia, Canada, were within 10% of the shortest path distance. However, Aultman-Hall et al [83] found no clear relationship between the shortest path distance and percent route deviation in Ontario, Canada, and Krizek et al [84] looked at data in Minneapolis, Minnesota, and found that the average path traveled was roughly twice as long as the shortest path available.

There is also significant research focused on understanding the rate at which future use of bicycle and pedestrian paths will change, as commuters who currently do not use bicycle and pedestrian paths start to transition into commuting by foot or bicycle. Waldykowski et al [85] developed a simulation that explored the conditions under which motor vehicle commuters switch over to commute by bicycle and pedestrian path [85]. Similarly, Mahfouz et al [86] combined distance decay, route calculation, and network analysis methods to examine (1) where future bicycle and pedestrian path commuter demand is within a city, (2) if it is likely to rise, and (3) how such demand could be accommodated within existing bicycle and pedestrian path networks. Finally, Liu et al [87] proposed a connectivity measure that captures the importance of a link in connecting the origins of cyclists and nearby subway stations and incorporated it into a statistical model.

In addition, researchers have attempted to better understand the impact of bicycle and pedestrian paths on health outcomes. This work includes (1) cost-benefit analysis of bicycle and pedestrian paths with respect to health improvements [10,88]; (2) lessons learned from cities with especially enthusiastic cycling culture such as Amsterdam, the Netherlands; Barcelona, Spain; and Chicago, Illinois [49,89,90]; and (3) understanding what type of bicycle and pedestrian paths cyclists and pedestrians prefer [69].

These studies demonstrate the need for granular analysis with actionable outcomes with respect to bicycle and pedestrian paths. Furthermore, although the studies have had a significant impact on the research community, none of them constructed a city-specific model to advise decision makers about the extent to which adding bicycle and pedestrian paths to a census tract would improve residents' health outcomes. Our study addresses this problem within a larger bicycle and pedestrian path research area.

## Limitations

### *Data Limitations*

Strava has emerged as a tool of interest for collecting data on bicycling, running, and walking, understanding the effects of new interventions for users, and promoting safety among riders. However, this crowdsourced data are biased toward recreational riders, who are frequent users of GPS-enabled fitness apps. Thus, there is a need to quantify and correct the inherent bias in crowdsourced data to better represent all residents across various demographics. Strava users tend to be more frequently identified as male, be older, and have more income than the general population [17]. In addition, there are limitations to how well the data counted by municipalities reflect the actual volume of bicycle and pedestrian traffic on bicycle and pedestrian paths [91,92]. Research has shown that accounting for biases in placement, time, and day of the week needs to be performed to address these issues [93,94].

Controlling for these biases in the Strava and municipal count data is beyond the scope of our work. However, it is important to note that there were biases in the data. Ultimately, these limitations mean that the Strava data sets that informed our study are nonuniform subsamples of the traffic of cyclists, walkers, and runners in Norfolk, Virginia, and San Francisco, California.

It is also important to note that the use of e-bikes has changed significantly during the period of our study [6]. e-Bikes present a potential opportunity to encourage active transportation while reducing personal barriers to active transportation [95,96]. Survey results suggest that e-bikes may reduce some personal barriers to traditional cycling and allow riders to travel greater distances [97,98]. In addition, e-bikes may have the added benefit of promoting health among individuals who are otherwise reluctant to engage in physical activity [99] and improve metabolic fitness [100] and enjoyment [101]. Exploring how the increased use of e-bikes affects our approach is an opportunity for future work.

### *Approach Limitations*

Recall that our approach uses 5 years of past data to fit a factor model and requires the factor model to consist of at least three factors where unique factors reflect residents' (1) DBC, (2) health, and (3) BPH. In addition, the health factor must include at least one observed variable related to a health outcome, and the BPH factor must include an observed variable related to the amount of bicycle and pedestrian path mileage in the census tract. For cities in which these requirements cannot be met, our approach cannot be applied. This limits its utility and geographic area of applicability. However, related research has shown that these factors are important to account for and often present when understanding who chooses to use bicycle and pedestrian path and how effective bicycle and pedestrian paths are in improving health outcomes [2,56,78,102-104]. Furthermore, these factors provide a structure that enables our approach to predict improvements in health outcomes more accurately than the alternative approaches.

## Validity Threats

Threats to internal and external validity affected our study. Threats to internal validity arose when factors affected the dependent variables without evaluators' knowledge. It is possible that some flaws in the implementation of our model could have affected the evaluation results. However, our approach used established libraries to conduct factor analysis, and the source code passed internal reviews [105,106].

Threats to external validity occur when evaluation results cannot be generalized. Although the evaluation was performed using more than 83 miles of added bicycle paths in 80 census tracts across the 2 cities, the factor models and accuracy results cannot necessarily be generalized to other areas. In addition, the factor analysis that generates our models assumes that each pair of variables follows a bivariate normal distribution. Although we verified that this assumption was true in our data, it may not be generalizable to other data sets and other cities where the approach is applied. However, it is very important to note that our approach, which yielded models producing these results, can be applied to other cities assuming that factor models that meet our requirements exist [105,106].

## Conclusions

Our work is directly actionable for policy makers, public health professionals, and urban planners in Norfolk, Virginia, and San Francisco, California, by providing concrete insight into the question "To what extent will adding specified bicycle and pedestrian path mileage to a census tract improve residents' health outcomes over time?" Specifically, it enables them to (1) weigh the extent to which 2 bicycle and pedestrian paths of equal cost proposed in 2 different census tracts improve the health outcomes of the residents, (2) identify areas where bicycle and pedestrian paths are unlikely to be effective public health interventions and other strategies should be used to help residents, and (3) quantify the minimum amount of bicycle path miles that need to be added in a given census tract to maximize the improvement in health outcomes for residents. Our results demonstrate that for 2 different cities, our approach estimates improvements in health outcomes more accurately than alternate approaches, and these improvements are statistically significant.

A web application that implements our algorithm and summarizes its findings in an actionable manner is available [107]. Multimedia Appendix 7 provides the source code for the web application. This application was used to identify a recommended set of bicycle and pedestrian paths across census tracts in Norfolk, Virginia. A time series forecast of the expected improvements in health outcomes for these recommendations was also conducted. These artifacts, which are examples of the types of analyses enabled by our approach, are available in Multimedia Appendix 8. A similar web application that implements our algorithm for San Francisco, California, is available [108]. The source code for it is provided in Multimedia Appendix 9.

## Acknowledgments

This study was funded by the Hampton Roads Biomedical Research Consortium (300675-010 IRAD). The Hampton Roads Biomedical Research Consortium reviewed and approved the submission of the manuscript.

## Data Availability

The contents of the multimedia appendices are specified below and are supplied in the paper. They are also available on the web as Mendeley Data [109].

## Authors' Contributions

RG, CAJ, RMR, AC, and CJL conceived and designed the experiments. RG performed the experiments. RG, GF, YK, and PK analyzed the data. RG, PA, PK, and YK contributed the reagents, materials, and analysis tools. RG, CJL, CAJ, GF, AC, and RMR wrote the paper.

## Conflicts of Interest

None declared.

Multimedia Appendix 1
American Community Survey data used for factor analysis.
[ZIP File (Zip Archive), 4528 KB - publichealth_v8i8e37379_app1.zip ]

Multimedia Appendix 2
The Centers for Disease Control and Prevention 500 Cities project data were used for factor analysis and evaluation.
[ZIP File (Zip Archive), 2144 KB - publichealth_v8i8e37379_app2.zip ]

Multimedia Appendix 3
City-supplied bicycle and pedestrian count and path length data used for factor analysis.
[ZIP File (Zip Archive), 488 KB - publichealth_v8i8e37379_app3.zip ]

Multimedia Appendix 4
Strava-supplied bicycle and pedestrian trip count data used for factor analysis.
[ZIP File (Zip Archive), 49327 KB - publichealth_v8i8e37379_app4.zip ]

Multimedia Appendix 5
Prospective variables identified by subject matter experts for factor analysis.
[ZIP File (Zip Archive), 10 KB - publichealth_v8i8e37379_app5.zip ]

Multimedia Appendix 6
Goodness-of-fit measure descriptions and statistics for generated factor models.
[ZIP File (Zip Archive), 5 KB - publichealth_v8i8e37379_app6.zip ]

Multimedia Appendix 7
Data and source code for web application deployment of model for Norfolk, Virginia.
[ZIP File (Zip Archive), 23680 KB - publichealth_v8i8e37379_app7.zip ]

Multimedia Appendix 8
Data and source code for research artifacts produced from the model for Norfolk, Virginia, including recommended portfolios of bicycle and pedestrian paths and time series of expected health outcome improvements.
[ZIP File (Zip Archive), 381 KB - publichealth_v8i8e37379_app8.zip ]

Multimedia Appendix 9
Data and source code for web application deployment of the model for San Francisco, California.
[ZIP File (Zip Archive), 20857 KB - publichealth_v8i8e37379_app9.zip ]

## References

1. Calise TV, Dumith SC, Dejong W, Kohl 3rd HW. The effect of a neighborhood built environment on physical activity behaviors. J Phys Act Health 2012 Nov;9(8):1089-1097. [doi: 10.1123/jpah.9.8.1089] [Medline: 22207103]
2. Cohen JM, Boniface S, Watkins S. Health implications of transport planning, development and operations. J Transport Health 2014 Mar;1(1):63-72. [doi: 10.1016/j.jth.2013.12.004]
3. Dill J. Bicycling for transportation and health: the role of infrastructure. J Public Health Policy 2009;30 Suppl 1:S95-110. [doi: 10.1057/jphp.2008.56] [Medline: 19190585]
4. Ding D, Gebel K. Built environment, physical activity, and obesity: what have we learned from reviewing the literature? Health Place 2012 Jan;18(1):100-105 [FREE Full text] [doi: 10.1016/j.healthplace.2011.08.021] [Medline: 21983062]
5. Garrard J. Health benefits of cycling. In: Pucher J, Buehler R, editors. City Cycling. Cambridge, MA, USA: MIT Press; 2012:11.
6. Hoj TH, Bramwell JJ, Lister C, Grant E, Crookston BT, Hall C, et al. Increasing active transportation through e-bike use: pilot study comparing the health benefits, attitudes, and beliefs surrounding e-bikes and conventional bikes. JMIR Public Health Surveill 2018 Nov 29;4(4):e10461 [FREE Full text] [doi: 10.2196/10461] [Medline: 30497998]
7. Khreis H, May AD, Nieuwenhuijsen MJ. Health impacts of urban transport policy measures: a guidance note for practice. J Transport Health 2017 Sep;6(C):209-227. [doi: 10.1016/j.jth.2017.06.003]
8. 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]
9. Oja P, Titze S, Bauman A, de Geus B, Krenn P, Reger-Nash B, et al. Health benefits of cycling: a systematic review. Scand J Med Sci Sports 2011 Aug;21(4):496-509. [doi: 10.1111/j.1600-0838.2011.01299.x] [Medline: 21496106]
10. Wang G, Macera CA, Scudder-Soucie B, Schmid T, Pratt M, Buchner D. Cost effectiveness of a bicycle/pedestrian trail development in health promotion. Prev Med 2004 Feb;38(2):237-242. [doi: 10.1016/j.ypmed.2003.10.002] [Medline: 14715217]
11. Smith J. Non-Premium Medical Expenditures for Families and Children: 2010 and 2011. United States Census Bureau. 2014 Mar. URL: https://citeseerx.ist.psu.edu/viewdoc/download;jsessionid=393640797E042C0AFA92FA26C6D21B45?doi=10.1.1.639.5426&rep=rep1&type=pdf [accessed 202-08-17]
12. National Research Council. Using the American Community Survey: Benefits and Challenges. Washington, DC, USA: The National Academies Press; 2007.
13. National Center for Chronic Disease Prevention and Health Promotion (U.S.), Division of Population Health, Epidemiology and Surveillance Branch, Centers for Disease Control and Prevention (U.S.), Robert Wood Johnson Foundation, CDC Foundation. 500 Cities Project : local data for better health, 2016 : Allen, TX. Centers for Disease Control and Prevention. 2018 Sep. URL: https://stacks.cdc.gov/view/cdc/61637 [accessed 2022-08-17]
14. San Francisco Open Data Portal. DataSF. 2021. URL: https://datasf.org/opendata/ [accessed 2022-02-03]
15. Norfolk Open Data Portal. City of Norfolk. 2022. URL: https://data.norfolk.gov/ [accessed 2022-02-03]
16. Albergotti R. Strava, popular with cyclists and runners, wants to sell its data to urban planners. The Wall Street Journal Blog. 2014. URL: https://www.wsj.com/digital-print-edition?mod=wsjheader [accessed 2022-02-03]
17. Lee K, Sener IN. Strava Metro data for bicycle monitoring: a literature review. Transport Rev 2020 Jul 30;41(1):27-47. [doi: 10.1080/01441647.2020.1798558]
18. Smith H, Haghani L. A mathematical optimization model for a bicycle network design considering bicycle level of service. In: Transportation Research Board 91st Annual Meeting. 2012 Presented at: TRID '12; January 22-26, 2012; Washington, DC, USA.
19. Mesbah M, Thompson R, Moridpour S. Bilevel optimization approach to design of network of bike lanes. Transport Res Record 2012 Jan 01;2284(1):21-28. [doi: 10.3141/2284-03]
20. Duthie J, Unnikrishnan A. Optimization framework for bicycle network design. J Transp Eng 2014 Jul;140(7):04014028. [doi: 10.1061/(ASCE)TE.1943-5436.0000690]
21. Larsen J, El-Geneidy A, Yasmin F. Beyond the quarter mile: re-examining travel distances by active transportation. Can J Urban Res 2010;19(1):70-88.
22. Allen-Munley C, Daniel J, Dhar S. Logistic model for rating urban bicycle route safety. Transp Res Record 2004 Jan 01;1878(1):107-115. [doi: 10.3141/1878-13]
23. Hochmair H. Towards a classification of route selection criteria for route planning tools. In: Proceedings of the 11th International Symposium on Developments in Spatial Data Handling. 2004 Presented at: SDH '04; August 23-25, 2004; Leicester, UK. [doi: 10.1007/3-540-26772-7_37]
24. Su JG, Winters M, Nunes M, Brauer M. Designing a route planner to facilitate and promote cycling in Metro Vancouver, Canada. Transp Res Part A Policy Pract 2010 Aug;44(7):495-505. [doi: 10.1016/j.tra.2010.03.015]
25. Zhu S, Zhu F. Multi-objective bike-way network design problem with space–time accessibility constraint. Transportation 2019 Jun 19;47(5):2479-2503. [doi: 10.1007/s11116-019-10025-7]

26. Zuo T, Wei H. Bikeway prioritization to increase bicycle network connectivity and bicycle-transit connection: a multi-criteria decision analysis approach. Transp Res Part A Policy Pract 2019 Nov;129:52-71. [doi: 10.1016/j.tra.2019.08.003]
27. Buehler R, Dill J. Bikeway networks: a review of effects on cycling. Transp Rev 2016;36(1):9-27. [doi: 10.1080/01441647.2015.1069908]
28. Ospina JP, Duque JC, Botero-Fernández V, Montoya A. The maximal covering bicycle network design problem. Transp Res Part A Policy Pract 2022 May;159(C):222-236. [doi: 10.1016/j.tra.2022.02.004]
29. Szimba E, Rothengatter W. Spending scarce funds more efficiently - including the pattern of interdependence in cost-benefit analysis. J Infrastruct Syst 2012 Dec;18(4):242-251. [doi: 10.1061/(asce)is.1943-555x.0000102]
30. Yang H, Bell MG. Models and algorithms for road network design: a review and some new developments. Transp Rev 1998 Jul;18(3):257-278. [doi: 10.1080/01441649808717016]
31. Farahani RZ, Miandoabchi E, Szeto WY, Rashidi H. A review of urban transportation network design problems. Eur J Oper Res 2013 Sep;229(2):281-302. [doi: 10.1016/j.ejor.2013.01.001]
32. Kepaptsoglou K, Karlaftis M. Transit route network design problem: review. J Transp Eng 2009 Aug;135(8):491-505.
33. An M, Chen M. Estimating nonmotorized travel demand. Transp Res Record 2007 Jan 01;2002(1):18-25. [doi: 10.3141/2002-03]
34. Turner S, Shunk G, Hottenstein A. Development of a methodology to estimate bicycle and pedestrian travel demand. Federal Highway Administration. 1998 Sep. URL: https://static.tti.tamu.edu/tti.tamu.edu/documents/1723-S.pdf [accessed 2022-02-03]
35. Handy SL, Xing Y, Buehler TJ. Factors associated with bicycle ownership and use: a study of six small U.S. cities. Transportation 2010 Apr 21;37(6):967-985. [doi: 10.1007/s11116-010-9269-x]
36. Park H, Lee YJ, Shin HC, Sohn K. Analyzing the time frame for the transition from leisure-cyclist to commuter-cyclist. Transportation 2011;38(2):305-319. [doi: 10.1007/s11116-010-9299-4]
37. Parkin J, Wardman M, Page M. Estimation of the determinants of bicycle mode share for the journey to work using census data. Transportation 2007 Aug 3;35(1):93-109. [doi: 10.1007/s11116-007-9137-5]
38. Pucher J, Dill J, Handy S. Infrastructure, programs, and policies to increase bicycling: an international review. Prev Med 2010 Jan;50 Suppl 1:S106-S125. [doi: 10.1016/j.ypmed.2009.07.028] [Medline: 19765610]
39. Winters M, Brauer M, Setton EM, Teschke K. Built environment influences on healthy transportation choices: bicycling versus driving. J Urban Health 2010 Dec;87(6):969-993 [FREE Full text] [doi: 10.1007/s11524-010-9509-6] [Medline: 21174189]
40. Winters M, Davidson G, Kao D, Teschke K. Motivators and deterrents of bicycling: comparing influences on decisions to ride. Transportation 2010 Jun 13;38(1):153-168. [doi: 10.1007/s11116-010-9284-y]
41. Zuniga-Teran AA, Gerlak AK, Elder AD, Tam A. The unjust distribution of urban green infrastructure is just the tip of the iceberg: a systematic review of place-based studies. Environ Sci Policy 2021 Dec;126:234-245. [doi: 10.1016/j.envsci.2021.10.001]
42. 45 CFR 46. Code of Federal Regulations. Title 45. Public Welfare. Department of Health and Human Services. Part 46. Office for Human Research Protections, US Department of Health and Human Services. 2017 Jan 19. URL: https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html [accessed 2022-08-17]
43. Berkley J. Using American community survey estimates and margins of error. United States Census Bureau. 2017. URL: https://www.census.gov/content/dam/Census/programs-surveys/acs/guidance/training-presentations/20170419_MOE_Transcript.pdf [accessed 2022-02-03]
44. Rummel RJ. Applied Factor Analysis. Evanston, IL, USA: Northwestern University Press; 1988.
45. Lee K, Ashton MC. Psychometric properties of the HEXACO personality inventory. Multivariate Behav Res 2004 Apr 01;39(2):329-358. [doi: 10.1207/s15327906mbr3902_8] [Medline: 26804579]
46. Thompson B. Exploratory and Confirmatory Factor Analysis: Understanding Concepts and Applications. Washington, DC, USA: American Psychological Association; 2004.
47. DiStefano C, Zhu M, Mindrila D. Understanding and using factor scores: considerations for the applied researcher. Pract Assess Res Eval 2009;14(1):20. [doi: 10.7275/da8t-4g52]
48. Sallis JF, Bauman A, Pratt M. Environmental and policy interventions to promote physical activity. Am J Prev Med 1998 Nov;15(4):379-397. [doi: 10.1016/s0749-3797(98)00076-2] [Medline: 9838979]
49. van Goeverden K, Nielsen TS, Harder H, van Nes R. Interventions in bicycle infrastructure, lessons from Dutch and Danish cases. Transp Res Procedia 2015;10:403-412. [doi: 10.1016/j.trpro.2015.09.090]
50. Kutner MH, Nachtsheim CJ, Neter J, Li W. Applied Linear Statistical Models. 5th edition. Boston, MA, USA: McGraw-Hill Irwin; 2005.
51. Chai T, Draxler RR. Root mean square error (RMSE) or mean absolute error (MAE)? – arguments against avoiding RMSE in the literature. Geosci Model Dev 2014 Jun 30;7(3):1247-1250. [doi: 10.5194/gmd-7-1247-2014]
52. Lowry R. Concepts and Applications of Inferential Statistics. Poughkeepsie, NY, USA: Richard Lowry; 2014.
53. Moritz WE. Survey of North American bicycle commuters: design and aggregate results. Transp Res Record 1997 Jan 01;1578(1):91-101. [doi: 10.3141/1578-12]

54. McKenzie B. Modes Less Traveled—Bicycling and Walking to Work in the United States: 2008–2012. United States Census Bureau. 2014 May 8. URL: https://www2.census.gov/library/publications/2014/acs/acs-25.pdf [accessed 2022-02-03]
55. Buehler R, Pucher J. Cycling to work in 90 large American cities: new evidence on the role of bike paths and lanes. Transportation 2011 Jul 6;39(2):409-432. [doi: 10.1007/s11116-011-9355-8]
56. Avila-Palencia I, de Nazelle A, Cole-Hunter T, Donaire-Gonzalez D, Jerrett M, Rodriguez DA, et al. The relationship between bicycle commuting and perceived stress: a cross-sectional study. BMJ Open 2017 Jun 23;7(6):e013542 [FREE Full text] [doi: 10.1136/bmjopen-2016-013542] [Medline: 28645948]
57. Pucher J, Dijkstra L. Promoting safe walking and cycling to improve public health: lessons from The Netherlands and Germany. Am J Public Health 2003 Sep;93(9):1509-1516. [doi: 10.2105/ajph.93.9.1509] [Medline: 12948971]
58. Ek A, Alexandrou C, Söderström E, Bergman P, Delisle Nyström C, Direito A, et al. Effectiveness of a 3-month mobile phone-based behavior change program on active transportation and physical activity in adults: randomized controlled trial. JMIR Mhealth Uhealth 2020 Jun 08;8(6):e18531 [FREE Full text] [doi: 10.2196/18531] [Medline: 32510462]
59. Chatterjee K, Sherwin H, Jain J, Christensen J, Marsh S. Conceptual model to explain turning points in travel behavior: application to bicycle use. Transp Res Record 2012 Jan 01;2322(1):82-90. [doi: 10.3141/2322-09]
60. Lindqvist AK, Rutberg S. One step forward: development of a program promoting active school transportation. JMIR Res Protoc 2018 May 08;7(5):e123 [FREE Full text] [doi: 10.2196/resprot.9505] [Medline: 29739733]
61. Robroek SJ, Brouwer W, Lindeboom D, Oenema A, Burdorf A. Demographic, behavioral, and psychosocial correlates of using the website component of a worksite physical activity and healthy nutrition promotion program: a longitudinal study. J Med Internet Res 2010 Sep 30;12(3):e44 [FREE Full text] [doi: 10.2196/jmir.1402] [Medline: 20921001]
62. van den Berg MH, Schoones JW, Vliet Vlieland TP. Internet-based physical activity interventions: a systematic review of the literature. J Med Internet Res 2007 Sep 30;9(3):e26 [FREE Full text] [doi: 10.2196/jmir.9.3.e26] [Medline: 17942388]
63. Schepers P, Fishman E, Beelen R, Heinen E, Wijnen W, Parkin J. The mortality impact of bicycle paths and lanes related to physical activity, air pollution exposure and road safety. J Transp Health 2015 Dec;2(4):460-473. [doi: 10.1016/j.jth.2015.09.004]
64. Teschke K, Reynolds CC, Ries FJ, Gouge B, Winters M. Bicycling: health risk or benefit? UBC Med J 2012;3(2):6-11 [FREE Full text]
65. Johan de Hartog J, Boogaard H, Nijland H, Hoek G. Do the health benefits of cycling outweigh the risks? Environ Health Perspect 2010 Aug;118(8):1109-1116 [FREE Full text] [doi: 10.1289/ehp.0901747] [Medline: 20587380]
66. Rojas-Rueda D, de Nazelle A, Tainio M, Nieuwenhuijsen MJ. The health risks and benefits of cycling in urban environments compared with car use: health impact assessment study. BMJ 2011 Aug 04;343:d4521 [FREE Full text] [doi: 10.1136/bmj.d4521] [Medline: 21816732]
67. Zhang C, Soliman-Hamad M, Robijns R, Verberkmoes N, Verstappen F, IJsselsteijn WA. Promoting physical activity with self-tracking and mobile-based coaching for cardiac surgery patients during the discharge-rehabilitation gap: protocol for a randomized controlled trial. JMIR Res Protoc 2020 Aug 19;9(8):e16737 [FREE Full text] [doi: 10.2196/16737] [Medline: 32812886]
68. Krykewycz GR, Pollard C, Canzoneri N, He E. Web-based “crowdsourcing” approach to improve areawide “bikeability” scoring. Transp Res Record 2011 Jan 01;2245(1):1-7. [doi: 10.3141/2245-01]
69. Hood J, Sall E, Charlton B. A GPS-based bicycle route choice model for San Francisco, California. Transp Lett 2011;3(1):63-75. [doi: 10.3328/tl.2011.03.01.63-75]
70. Casello JM, Usyukov V. Modeling cyclists’ route choice based on GPS data. Transp Res Record 2014 Jan 01;2430(1):155-161. [doi: 10.3141/2430-16]
71. Broach J, Dill J, Gliebe J. Where do cyclists ride? A route choice model developed with revealed preference GPS data. Transp Res Part A Policy Pract 2012 Dec;46(10):1730-1740. [doi: 10.1016/j.tra.2012.07.005]
72. Bricka S, Zmud J, Wolf J, Freedman J. Household travel surveys with GPS: an experiment. Transp Res Record 2009 Jan 01;2105(1):51-56. [doi: 10.3141/2105-07]
73. Elwood S, Goodchild MF, Sui DZ. Researching volunteered geographic information: spatial data, geographic research, and new social practice. Ann Assoc Am Geograph 2012 May;102(3):571-590. [doi: 10.1080/00045608.2011.595657]
74. Dorn D, Gorzelitz J, Gangnon R, Bell D, Koltyn K, Cadmus-Bertram L. Automatic identification of physical activity type and duration by wearable activity trackers: a validation study. JMIR Mhealth Uhealth 2019 May 23;7(5):e13547 [FREE Full text] [doi: 10.2196/13547] [Medline: 31124470]
75. Muggeridge DJ, Hickson K, Davies AV, Giggins OM, Megson IL, Gorely T, et al. Measurement of heart rate using the polar OH1 and Fitbit charge 3 wearable devices in healthy adults during light, moderate, vigorous, and sprint-based exercise: validation study. JMIR Mhealth Uhealth 2021 Mar 25;9(3):e25313 [FREE Full text] [doi: 10.2196/25313] [Medline: 33764310]
76. Lindqvist A, Rutberg S, Söderström E, Ek A, Alexandrou C, Maddison R, et al. User perception of a smartphone app to promote physical activity through active transportation: inductive qualitative content analysis within the smart city active mobile phone intervention (SCAMPI) study. JMIR Mhealth Uhealth 2020 Aug 05;8(8):e19380 [FREE Full text] [doi: 10.2196/19380] [Medline: 32755889]

77. Suminski Jr RR, Dominick G, Saponaro P. Assessing physical activities occurring on sidewalks and streets: protocol for a cross-sectional study. JMIR Res Protoc 2019 Jul 30;8(7):e12976 [FREE Full text] [doi: 10.2196/12976] [Medline: 31364605]
78. Bachand-Marleau J, Lee BH, El-Geneidy AM. Better understanding of factors influencing likelihood of using shared bicycle systems and frequency of use. Transp Res Record 2012 Jan 01;2314(1):66-71. [doi: 10.3141/2314-09]
79. Goodman A, Green J, Woodcock J. The role of bicycle sharing systems in normalising the image of cycling: an observational study of London cyclists. J Transp Health 2014 Mar;1(1):5-8 [FREE Full text] [doi: 10.1016/j.jth.2013.07.001] [Medline: 25568838]
80. DeMaio P. Bike-sharing: history, impacts, models of provision, and future. J Public Transp 2009 Dec;12(4):41-56. [doi: 10.5038/2375-0901.12.4.3]
81. Evans-Cowley JS, Griffin G. Microparticipation with social media for community engagement in transportation planning. Transp Res Record 2012 Jan 01;2307(1):90-98. [doi: 10.3141/2307-10]
82. Broach J, Gliebe J, Dill J. Bicycle route choice model developed using revealed preference GPS data. In: Proceedings of the 90th Annual Meeting of the Transportation Research Board. 2011 Presented at: TRB '11; January 23-27, 2011; Washington, DC, USA.
83. Aultman-Hall L, Hall FL, Baetz BB. Analysis of bicycle commuter routes using geographic information systems: implications for bicycle planning. Transp Res Record 1997 Jan 01;1578(1):102-110. [doi: 10.3141/1578-13]
84. Krizek KJ, El-Geneidy A, Thompson K. A detailed analysis of how an urban trail system affects cyclists' travel. Transportation 2007 Jul 18;34(5):611-624. [doi: 10.1007/s11116-007-9130-z]
85. Wałdykowski P, Adamczyk J, Dorotkiewicz M. Sustainable urban transport—why a fast investment in a complete cycling network is most profitable for a city. Sustainability 2021 Dec 23;14(1):119. [doi: 10.3390/su14010119]
86. Mahfouz H, Arcaute E, Lovelace R. A road segment prioritization approach for cycling infrastructure. arXiv 2021 May 8.
87. Liu B, Bade D, Chow JY. Bike count forecast model with multimodal network connectivity measures. Transp Res Record 2021 Jul 16;2675(7):320-334. [doi: 10.1177/03611981211021849]
88. Edwards RD, Mason CN. Spinning the wheels and rolling the dice: life-cycle risks and benefits of bicycle commuting in the U.S. Prev Med 2014 Jul;64:8-13. [doi: 10.1016/j.ypmed.2014.03.015] [Medline: 24657549]
89. Collins AJ, Jordan CA, Robinson RM, Cornelius C, Gore R. Exploring good cycling cities using multivariate statistics. Environ Syst Decis 2020;40(4):526-543. [doi: 10.1007/s10669-019-09753-z]
90. Harkey DL, Reinfurt DW, Knuiman M. Development of the bicycle compatibility index. Transp Res Record 1998 Jan 01;1636(1):13-20. [doi: 10.3141/1636-03]
91. Hyde-Wright A, Graham B, Nordnack K. Counting bicyclists with pneumatic tube counters on shared roadways. ITE J 2014 Feb;84(2):32-37.
92. Griffin G. The National Academies of Sciences, Engineering, and Medicine. 2011 Sep 6. URL: https://trid.trb.org/view/1141140 [accessed 2022-02-03]
93. Figliozzi M, Johnson P, Monsere C, Nordback K. Methodology to characterize ideal short-term counting conditions and improve AADT estimation accuracy using a regression-based correcting function. J Transp Eng 2014 May 1;140(5):404-414. [doi: 10.1061/(asce)te.1943-5436.0000663]
94. Nordback K, Marshall WE, Janson BN. Development of estimation methodology for bicycle and pedestrian volumes based on existing counts. Colorado Department of Transportation. 2013 Oct. URL: https://rosap.ntl.bts.gov/view/dot/26644 [accessed 2022-02-03]
95. Berntsen S, Malnes L, Langåker A, Bere E. Physical activity when riding an electric assisted bicycle. Int J Behav Nutr Phys Act 2017 Apr 26;14(1):55 [FREE Full text] [doi: 10.1186/s12966-017-0513-z] [Medline: 28446180]
96. Louis J, Brisswalter J, Morio C, Barla C, Temprado JJ. The electrically assisted bicycle: an alternative way to promote physical activity. Am J Phys Med Rehabil 2012 Nov;91(11):931-940. [doi: 10.1097/PHM.0b013e318269d9bb] [Medline: 23085705]
97. MacArthur J, Dill J, Person M. Electric bikes in North America: results of an online survey. Transp Res Record 2014 Jan 01;2468(1):123-130. [doi: 10.3141/2468-14]
98. Haustein S, Møller M. Age and attitude: changes in cycling patterns of different e-bike user segments. Int J Sustain Transp 2016 Mar 23;10(9):836-846. [doi: 10.1080/15568318.2016.1162881]
99. Gloekler S, Wenaweser P, Lanz J, Stoller M. How e-biking can boost cardiovascular health. Eur Heart J 2015 Aug 14;36(31):2033. [doi: 10.1093/eurheartj/ehv154] [Medline: 25935878]
100. Peterman JE, Morris KL, Kram R, Byrnes WC. Pedelecs as a physically active transportation mode. Eur J Appl Physiol 2016 Aug;116(8):1565-1573. [doi: 10.1007/s00421-016-3408-9] [Medline: 27299435]
101. Sperlich B, Zinner C, Hébert-Losier K, Born DP, Holmberg HC. Biomechanical, cardiorespiratory, metabolic and perceived responses to electrically assisted cycling. Eur J Appl Physiol 2012 Dec;112(12):4015-4025. [doi: 10.1007/s00421-012-2382-0] [Medline: 22446956]
102. Brown BB, Smith KR. Complex active travel bout motivations: gender, place, and social context associations. J Transp Health 2017 Sep;6:335-346 [FREE Full text] [doi: 10.1016/j.jth.2017.01.014] [Medline: 29104857]

103. Pinjari AR, Eluru N, Bhat CR, Pendyala RM, Spissu E. Joint model of choice of residential neighborhood and bicycle ownership: accounting for self-selection and unobserved heterogeneity. Transp Res Record 2008 Jan 01;2082(1):17-26. [doi: 10.3141/2082-03]
104. Griffin G, Nordback K, Götschi T, Stolz E, Kothuri S. Monitoring bicyclist and pedestrian travel and behavior: current research and practice. Transportation Research Circular(E-C183). 2014 Mar. URL: https://onlinepubs.trb.org/onlinepubs/circulars/ec183.pdf [accessed 2022-02-03]
105. Spencer CD. Two types of role playing: threats to internal and external validity. Am Psychol 1978 Mar;33(3):265-268. [doi: 10.1037/0003-066x.33.3.265]
106. Yu CH. Threats to validity of research design. Creative Wisdom!. 2010. URL: http://www.creative-wisdom.com/teaching/WBI/threat.shtml [accessed 2022-02-03]
107. Modeling Bike and Pedestrian Paths at the Census Tract Level In Norfolk, VA. Modeling The Health Effects Of Adding Bicycle Paths At The Census Tract-Level. 2022. URL: https://rgore-vmasc.shinyapps.io/norfolk-bike-ped/ [accessed 2022-02-03]
108. San Francisco Census Tract Stroke and Diabetes Rate Improvement Estimation Based On Adding Bicycle and Pedestrian Paths. Modeling The Health Effects Of Adding Bicycle Paths At The Census Tract-Level. 2022. URL: https://rgore-vmasc.shinyapps.io/sf-bike-ped/ [accessed 2022-02-03]
109. Gore R. Modeling The Health Effects of Adding Bicycle and Pedestrian Paths At The Census Tract-Level Supplementary Information. Mendeley Data. 2022. URL: https://www.narcis.nl/dataset/RecordID/oai%3Aeasy.dans.knaw.nl%3Aeasy-dataset%3A242304 [accessed 2022-07-21]

## Abbreviations

**ACS:** American Communities Survey
**BPH:** bicycling and pedestrian habits
**CDC:** Centers for Disease Control and Prevention
**CFA:** confirmatory factor analysis
**DBC:** demographics and background characteristics
**EFA:** exploratory factor analysis
**MAE:** mean absolute error
**MOE:** measure of effectiveness
**RMSE:** root mean squared error

---

*Edited by A Mavragani, Y Khader; submitted 11.04.22; peer-reviewed by J Delgado-Ron, C Jeong; comments to author 14.05.22; revised version received 13.07.22; accepted 29.07.22; published 24.08.22.*

*Please cite as:*
*Gore R, Lynch CJ, Jordan CA, Collins A, Robinson RM, Fuller G, Ames P, Keerthi P, Kandukuri Y*
*Estimating the Health Effects of Adding Bicycle and Pedestrian Paths at the Census Tract Level: Multiple Model Comparison*
*JMIR Public Health Surveill 2022;8(8):e37379*
*URL: https://publichealth.jmir.org/2022/8/e37379*
*doi:10.2196/37379*
*PMID:36001362*

Original Paper

# Google Trends on Human Papillomavirus Vaccine Searches in the United States From 2010 to 2021: Infodemiology Study

Akshaya Srikanth Bhagavathula[1*], PharmD, PhD; Philip M Massey[1*], MPH, PhD

[1] Center for Public Health and Technology, Department of Health, Human Performance, and Recreation, College of Education and Health Professions, University of Arkansas, Fayetteville, AR, United States

[*] all authors contributed equally

**Corresponding Author:**
Philip M Massey, MPH, PhD
Center for Public Health and Technology
Department of Health, Human Performance, and Recreation, College of Education and Health Professions
University of Arkansas
346 West Ave.
West Avenue Annex Building, Suite 317
Fayetteville, AR, 72701
United States
Phone: 1 479 575 8491
Email: masseyp@uark.edu

**Related Article:**

This is a corrected version. See correction statement: https://publichealth.jmir.org/2022/10/e42812

## Abstract

**Background:** The human papillomavirus (HPV) vaccine is recommended for adolescents and young adults to prevent HPV-related cancers and genital warts. However, HPV vaccine uptake among the target age groups is suboptimal.

**Objective:** The aim of this infodemiology study was to examine public online searches in the United States related to the HPV vaccine from January 2010 to December 2021.

**Methods:** Google Trends (GT) was used to explore online searches related to the HPV vaccine from January 1, 2010, to December 31, 2021. Online searches and queries on the HPV vaccine were investigated using relative search volumes (RSVs). Analysis of variance was performed to investigate quarterly differences in HPV vaccine searches in each year from 2010 to 2021. A joinpoint regression was used to identify statistically significant changes over time; the $\alpha$ level was set to .05.

**Results:** The year-wise online search volume related to the HPV vaccine increased from 2010 to 2021, often following federal changes related to vaccine administration. Joinpoint regression analysis showed that HPV vaccine searches significantly increased on average by 8.6% (95% CI 5.9%-11.4%) across each year from 2010 to 2021. Moreover, HPV vaccine searches demonstrated a similar pattern across years, with search interest increasing through August nearly every year. At the state level, the highest 12-year mean RSV was observed in California (59.9, SD 14.3) and the lowest was observed in Wyoming (17.4, SD 8.5) during the period of 2010-2021.

**Conclusions:** Online searches related to the HPV vaccine increased by an average of 8.6% across each year from 2010 to 2021, with noticeable spikes corresponding to key changes in vaccine recommendations. We identified patterns across years and differences at the state level in the online search interest related to the HPV vaccine. Public health organizations can use GT as a tool to characterize the public interest in and promote the HPV vaccine in the United States.

***(JMIR Public Health Surveill 2022;8(8):e37656)*** doi:10.2196/37656

**KEYWORDS**

Google Trends; HPV vaccine; Google search; attitude; infodemiology; searches; United States of America

## Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States, and certain strains are associated with the majority of cancers of the cervix (90%), anus (90%), vagina and vulva (70%), penis (60%), and oropharynx (71%) [1]. In the United States, with nearly 80 million people currently infected with HPV and an estimated 14 million new cases each year, there is a significant burden of HPV-associated cancers [2]. Vaccination against HPV is highly effective at preventing HPV-related cancers, and the US Advisory Committee on Immunization Practices (ACIP) recommends two doses of the HPV vaccine for males and females aged 9-14 years, with catch-up doses recommended up to age 26 [3]. The US Department of Health and Human Services has set a goal to increase the proportion of adolescents who receive the recommended doses of the HPV vaccine to 80% by 2030 [4]. In 2020, up-to-date HPV vaccine coverage among adolescents remained below this mark at 58.6%; however, coverage was up from 54.2% in 2019 [5]. Although the HPV vaccine is safe, effective, and widely available, rates of HPV vaccine coverage in the United States remain suboptimal.

In the internet age, Google searches represent a common approach for discovering information online [6] and the HPV vaccine is one of the most widely discussed vaccinations on the internet [7]. Existing research on the HPV vaccine and social media using various platforms such as YouTube [7,8], Facebook [9], Instagram [10], and Twitter [11,12] have shown that a sizable proportion of HPV vaccine–related misinformation has created a negative perception of the HPV vaccine by the public [13]. During the first decade of HPV vaccine availability, research suggests that its representation on the internet is both positive and negative, with a growing number of false conspiracies and myths circulating [14].

Google Trends (GT) is a popular tool used to analyze online search behavior and search queries in the field of big data analytics in health care and public health research [15]. GT can show changes in online interest for any selected term in any country or region over a selected time period, and can also compare different regions simultaneously [16]. Data from GT have proven to be valuable to monitor health information–seeking behavior trends, often contributing to predictions or detection of outbreaks [17-21]. The emerging discipline of “infodemiology” focuses on these online behaviors, examining data from the internet, including GT, and is defined as “the science of distribution and determinants of information in an electronic medium, specifically the Internet, or in a population, with the ultimate aim to inform public health and public policy” [22].

To date, several studies have examined HPV vaccine–related misinformation [6-11], vaccine hesitancy [23], and arguments circulating on the internet [10,12]. However, there has been little to no research that has used the data of GT to look exclusively at online interest in the HPV vaccine based on search behavior. The purpose of this study was to characterize US public online searches and queries related to the HPV vaccine from 2010 to 2021, and determine the year-over-year changes in searches as well as differences across US states.

## Methods

### Data Collection

We collected monthly search volumes and search queries for the term “HPV vaccine” from GT between January 1, 2010, and December 31, 2021; the GT data retrieval period was from November 1, 2021, to January 31, 2022. GT provides a public database of the proportion of searches of a selected query performed on Google Search, and presents the data as a relative search volume (RSV) in a normalized format. The data can be delineated by specific topics and search terms, time and year, and location. Specific to each search term, the RSV value ranges from 0 (minimal to no interest) to 100 (high popularity) based on the term’s search volume. An RSV value of 100 indicates the maximum search interest for the time and location selected relative to that specific term.

GT enables exploring online searches at different time intervals and retrieval queries for any keywords entered in the Google search engine. Using this technique, we retrieved monthly online search queries and normalized RSVs related to the HPV vaccine across states in the United States. GT allows for queries of both “search terms” and “search topics.” The “search terms” query provides the results for all keywords that fall within the category and the “search topic” query renders the results of a group of terms that share the same concept in any language [16]. We used both search terms and search topics to query results for “HPV vaccine.”

We used the framework described by Mavragani and Ochoa [24] for the region selection and time period selection to retrieve query data from GT. Briefly, we searched for the keyword “HPV vaccine” at the country level (ie, the entire United States) to understand the overall RSVs in each year. Subsequently, using this information, we retrieved RSVs at the state level. All queries were searched between January 1, 2010, and December 31, 2021. The time periods demonstrating high-value RSVs were further investigated by checking with news bulletins or the scientific literature to identify any events associated with these same time periods.

### Statistical Analysis

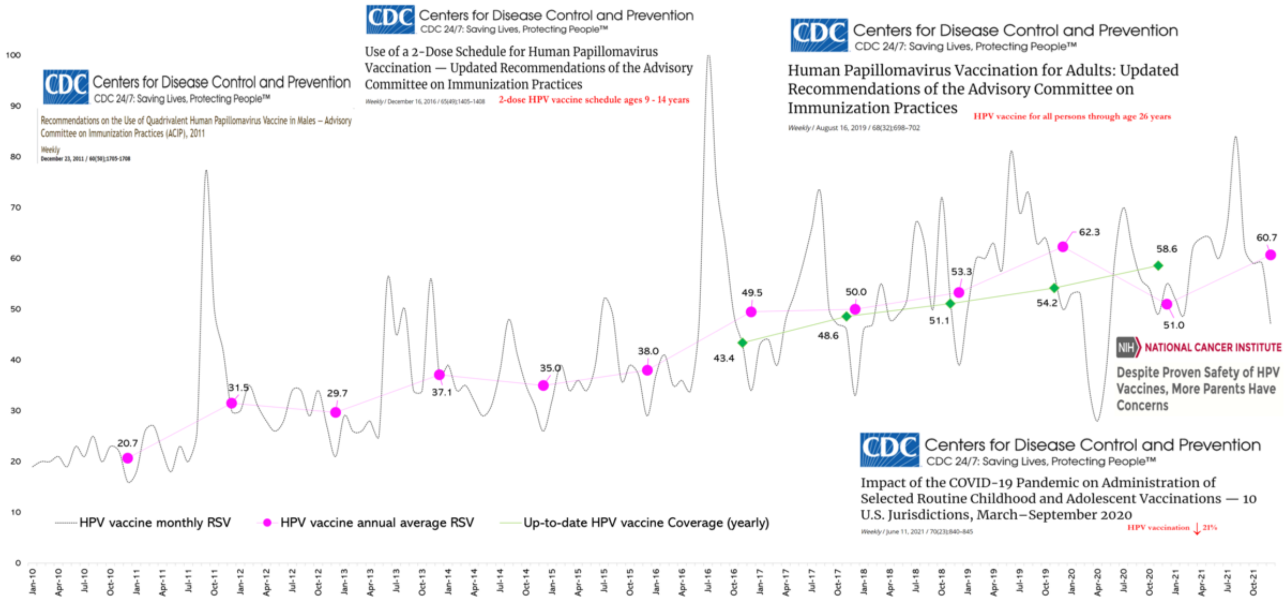
We plotted a line chart to describe “HPV vaccine” search trends from January 1, 2010, to December 31, 2021. The annual mean (SD) is used to summarize the online searches for each year between 2010 and 2021. One-way analysis of variance followed by the Tukey posthoc test was performed to identify overall and quarterly differences in HPV vaccine searches in each year between 2010 and 2021. A joinpoint regression analysis was performed for each year to analyze the time trend in the GT data using the Joinpoint Regression program (version 4.9.1.0) developed by the National Cancer Institute [25]. This software analyzes trends by regression modeling while searching for temporal trend changes at time points called “joinpoints,” and estimates the regression function from previous joinpoints [26]. The number of joinpoints is obtained using a permutation test via Monte Carlo resampling [26] and the analysis criteria were set to find up to three joinpoints. The monthly percentage changes (MPCs) or annual percentage changes (APCs) between trend-change points were determined with their 95% CIs.

## Results

### Trends in RSVs Related to HPV Vaccine

Figure 1 shows the trends in HPV vaccine online searches from 2010 to 2021, including both the monthly and annual mean RSVs, as well as the up-to-date HPV vaccine rates among 13-17 year-olds in the United States from 2016 to 2020. An increase in searches was observed in October 2011, when the ACIP recommended routine use of the quadrivalent HPV vaccine for boys aged 11-12 years [27]. Between January 2012 and June 2016, there were minimal increases in HPV vaccine searches. The RSV for HPV vaccine reached the highest peak value of 100% (ie, the most popular time the search term was used in our data set from 2010 and 2021) in late 2016, when the ACIP updated the HPV vaccination recommendation to use a 2-dose schedule for boys and girls who initiate the vaccination series at ages 9-14 years [28]. In June 2019, the ACIP recommended a catch-up HPV vaccination for all individuals aged up to 26 years, and the RSV on HPV vaccine reached 81% at this time [3]. Further, in 2020, there was a dramatic decrease in the RSV (28%) during the early COVID-19 pandemic and a comparable situation was observed in the latter half of 2021. The highest annual mean RSVs were recorded in 2018 (62.3%) and 2021 (60.7%), and the lowest annual mean RSVs were recorded in 2010 (20.7%).

**Figure 1.** Human papillomavirus (HPV) vaccine–related relative search volumes (RSVs) on Google Trends from 2010 to 2021 in the United States with the corresponding timeline of Centers for Disease Control and Prevention (CDC) guidelines for HPV vaccine administration.



### Quarterly HPV Searches From 2010 to 2021

Table 1 demonstrates the quarterly RSVs of HPV vaccine searches in each year from 2010 to 2021. Online search interest differed significantly across quarters in the years 2014, 2016, and 2017. In 2014, the search interest in the third quarter (July 1-September 30) was significantly higher than that in the second quarter (April 1-June 30) and fourth quarter (October 1-December 31). In 2016, search interest in the third quarter was significantly higher than that in the first, second, and fourth quarters. In 2017, third-quarter search interest was significantly higher than that in the first and fourth quarters.

**Table 1.** Quarterly differences in relative search volumes on Google Trends for the term "HPV vaccine" from 2010 to 2021 in the United States.

| Year | Relative search volume point estimate, mean (SD) | | | | $F^a$ (*df*=3) | *P* value |
|---|---|---|---|---|---|---|
| | January 1-March 31 (group 1) | April 1-June 30 (group 2) | July 1-September 30 (group 3) | October 1-December 31 (group 4) | | |
| 2010 | 19.6 (0.5) | 21.0 (2.0) | 22.0 (2.6) | 20.3 (3.7) | 0.463 | .72 |
| 2011 | 23.6 (4.9) | 21.0 (2.6) | 41.0 (31.3) | 40.6 (10.0) | 1.242 | .36 |
| 2012 | 32.0 (2.6) | 27.3 (1.1) | 32.3 (2.1) | 27.3 (6.5) | 1.588 | .27 |
| 2013 | 27.0 (1.7) | 36.3 (17.1 | 43.0 (8.1) | 42.3 (11.9) | 1.306 | .34 |
| 2014 | 36.0 (2.6) | 30.6 (1.5) | 42.3 (5.2) | 30.6 (4.5) | 6.593 | .02[b, c] |
| 2015 | 35.0 (3.6) | 36.3 (2.5) | 45.6 (8.5) | 35.0 (5.2) | 2.659 | .12 |
| 2016 | 37.6 (3.0) | 39.3 (7.5) | 79.3 (18.8) | 42.0 (7.5) | 9.014 | .005[b, c, d] |
| 2017 | 42.0 (2.6) | 53.3 (5.5) | 63.0 (11.8) | 42.0 (7.8) | 5.192 | .03[c, d] |
| 2018 | 49.3 (4.9) | 49.6 (2.0) | 60.0 (8.8) | 54.3 (16.6) | 0.780 | .54 |
| 2019 | 56.6 (5.7) | 67.3 (12.0) | 68.3 (5.0) | 57.0 (7.0) | 1.914 | .21 |
| 2020 | 47.0 (10.4) | 42.0 (16.3) | 62.6 (7.0) | 52.6 (3.2) | 2.166 | .17 |
| 2021 | 54.3 (6.8) | 62.6 (2.3) | 71.0 (11.5) | 55.0 (6.9) | 3.146 | .09 |

[a] One-way analysis of variance followed by Tukey posthoc test for multiple comparisons.

[b] Significant ($P<.05$) difference between group 2 and group 3.

[c] Significant ($P<.05$) difference between group 2 and group 4.

[d] Significant ($P<.05$) difference between group 3 and group 1.

### State-Level HPV Vaccine Searches and Changes in HPV Vaccine Searches

Table 2 describes the average RSV of HPV vaccine searches at the state level for each year from 2010 to 2021 as well as the average across all 12 years. The highest 12-year mean RSVs were observed in California, New York, Texas, Florida, and Massachusetts, whereas Delaware, North Dakota, South Dakota, Vermont, and Wyoming recorded the lowest HPV vaccine searches.

**Table 2.** “HPV vaccine” relative search volume on Google Trends by US states for each year from 2010 to 2021.

| State | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | Mean (SD) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Alabama | 18.5 | 17.9 | 25.5 | 29.4 | 35.3 | 42 | 35.2 | 32 | 58.6 | 53.9 | 43.3 | 40.1 | 36.0 (12.6) |
| Alaska | 11 | 16.9 | 18.2 | 28.9 | 22.2 | 19.2 | 36.7 | 23.8 | 34.9 | 23.9 | 26.8 | 28.8 | 24.3 (7.5) |
| Arizona | 22.8 | 19.7 | 45 | 45.3 | 36.4 | 41.7 | 40.7 | 35 | 42.8 | 48.8 | 45.2 | 55.1 | 39.9 (10.2) |
| Arkansas | 15.5 | 27.2 | 31.7 | 30.9 | 23 | 35 | 32.1 | 35.7 | 30.2 | 37.7 | 39.9 | 41.2 | 31.7 (7.3) |
| California | 57.8 | 26.2 | 70 | 42.8 | 61.3 | 67.8 | 53.4 | 61.8 | 60.3 | 64.5 | 74 | 79.4 | 59.9 (14.3) |
| Colorado | 24.7 | 22 | 36.4 | 27.3 | 48.2 | 48.9 | 40.6 | 53.8 | 51.2 | 56.3 | 51.9 | 53 | 42.9 (12.3) |
| Connecticut | 25.6 | 23.1 | 36.2 | 32.7 | 31.7 | 50 | 40.6 | 47 | 57.7 | 54.3 | 40 | 45 | 40.3 (11.0) |
| Delaware | 8.2 | 20.8 | 15.5 | 20.2 | 19.4 | 24.3 | 19.9 | 28.8 | 25 | 29.7 | 33.3 | 32.6 | 23.1 (7.3) |
| District of Columbia | 34.2 | 18.5 | 41.5 | 23.9 | 34.5 | 56.6 | 44.1 | 42.2 | 26.1 | 31.7 | 24.9 | 31.5 | 34.1 (10.6) |
| Florida | 57.6 | 26.5 | 60.1 | 49.3 | 67 | 57 | 47 | 49.1 | 38.5 | 60.1 | 63.4 | 53.9 | 52.5 (11.3) |
| Georgia | 42.5 | 27.3 | 54.3 | 48.1 | 48 | 41.8 | 50.8 | 52.7 | 52 | 57 | 57.8 | 50.6 | 48.6 (8.3) |
| Hawaii | 21.9 | 37.5 | 29.1 | 27.2 | 43 | 32.3 | 32.2 | 34.7 | 39.4 | 33.3 | 40.5 | 34.5 | 33.8 (5.9) |
| Idaho | 9.7 | 18.1 | 25.1 | 23.6 | 37.1 | 26.2 | 32.6 | 24.8 | 35.8 | 36.8 | 31.9 | 28.8 | 27.5 (8.1) |
| Illinois | 41 | 26.1 | 56 | 41.6 | 39.7 | 56.6 | 48.3 | 50.8 | 51.9 | 59.4 | 33.9 | 60.7 | 47.2 (10.8) |
| Indiana | 36.1 | 29.8 | 37.7 | 52.8 | 39.2 | 42.6 | 41 | 43.6 | 43 | 52.5 | 58.5 | 50 | 43.9 (8.2) |
| Iowa | 8.4 | 26.3 | 28.1 | 29 | 42.8 | 35 | 44 | 35.9 | 36.1 | 40.1 | 42 | 38.3 | 33.8 (9.9) |
| Kansas | 27.1 | 18 | 33.6 | 44.7 | 18.3 | 30.7 | 32.7 | 29 | 49.2 | 41 | 44.7 | 38.3 | 33.9 (10.1) |
| Kentucky | 32.2 | 29.3 | 39.5 | 35.8 | 37.3 | 42 | 26.1 | 39.8 | 33.9 | 48.1 | 47 | 38.4 | 37.5 (6.6) |
| Louisiana | 28.5 | 18.7 | 40.3 | 38.8 | 41.4 | 36.3 | 38.8 | 33.8 | 57.7 | 50.2 | 47.5 | 53.8 | 40.5 (10.9) |
| Maine | 8.6 | 30.1 | 27.2 | 22.2 | 12.4 | 25 | 34.6 | 24.6 | 34.9 | 32.5 | 15.1 | 33.1 | 25.0 (8.9) |
| Maryland | 39.1 | 25 | 48.4 | 46.5 | 45.9 | 39.9 | 43 | 35.6 | 43 | 56.7 | 51.6 | 64.5 | 44.9 (10.1) |
| Massachusetts | 43.8 | 27.3 | 54.1 | 46.5 | 56.7 | 52.4 | 45.8 | 50.1 | 58.3 | 64.7 | 51.4 | 65.4 | 51.4 (10.2) |
| Michigan | 34.4 | 24.3 | 41.2 | 32.8 | 35.9 | 57.5 | 46.7 | 53.5 | 58.2 | 58 | 62.3 | 64.8 | 47.5 (13.4) |
| Minnesota | 40.8 | 18.5 | 40.5 | 53 | 50.9 | 38 | 36.5 | 45.7 | 43.3 | 57.6 | 50.6 | 53.7 | 44.1 (10.5) |
| Mississippi | 18.2 | 18.5 | 28.7 | 32.5 | 21.1 | 22.4 | 34.7 | 31.1 | 38.6 | 39.4 | 34.1 | 49.3 | 30.7 (9.5) |
| Missouri | 40 | 25.3 | 49.4 | 37.9 | 48.2 | 52.7 | 34.4 | 31.7 | 47.6 | 50.9 | 38.1 | 47 | 41.9 (8.6) |
| Montana | 11.2 | 17.7 | 24.3 | 20.4 | 20.6 | 20 | 26 | 25.2 | 24.5 | 34.7 | 32.8 | 30.6 | 24.0 (6.6) |
| Nebraska | 21.3 | 18.3 | 32 | 39.3 | 33.2 | 26 | 20.3 | 35.4 | 41.4 | 44.5 | 42.1 | 43.7 | 33.1 (9.6) |
| Nevada | 21.8 | 14.7 | 29.2 | 35.2 | 38.4 | 39.7 | 38.1 | 39 | 42.3 | 41.5 | 38 | 59.7 | 36.5 (11.2) |
| New Hampshire | 19.2 | 15.8 | 31 | 29.4 | 25.4 | 30 | 28 | 28.5 | 35 | 40 | 28 | 31.5 | 28.5 (6.4) |
| New Jersey | 43.3 | 29.7 | 39.5 | 44.2 | 39 | 58.3 | 47.1 | 48.5 | 46.6 | 51.8 | 44.9 | 59.7 | 46.1 (8.3) |
| New Mexico | 24 | 20.7 | 21.6 | 29.9 | 26 | 27.1 | 35.1 | 41.1 | 40.5 | 30.7 | 20.1 | 33.8 | 29.2 (7.3) |
| New York | 51.2 | 25.3 | 47.3 | 58.7 | 51.4 | 66.6 | 55.6 | 62.1 | 62.6 | 56.4 | 60.6 | 72.4 | 55.9 (11.9) |
| North Carolina | 34.7 | 17.6 | 51.4 | 51.4 | 48.7 | 61.4 | 44.4 | 54.3 | 56.7 | 54 | 53.8 | 61.6 | 49.2 (12.3) |
| North Dakota | 9.5 | 22.7 | 25.1 | 18.4 | 17 | 26.7 | 25.3 | 24.6 | 30.2 | 29.1 | 21.2 | 23.9 | 22.8 (5.7) |
| Ohio | 43.5 | 24.4 | 52.4 | 33 | 41.2 | 38.6 | 40.7 | 44.2 | 58.4 | 57.6 | 54.6 | 55.5 | 45.3 (10.6) |
| Oklahoma | 23.2 | 14.6 | 37.5 | 39.5 | 39.7 | 46.6 | 43 | 34.2 | 50.5 | 41.1 | 38.9 | 43 | 37.7 (9.9) |
| Oregon | 21.6 | 31.7 | 38.5 | 31.2 | 48.4 | 38.2 | 33.5 | 54.9 | 29.7 | 50.8 | 43.6 | 40.5 | 38.6 (9.7) |
| Pennsylvania | 50.1 | 35 | 53.4 | 24.9 | 43.2 | 52.9 | 46.1 | 55.2 | 51.1 | 69.3 | 61.4 | 69.8 | 51.0 (13.0) |
| Rhode Island | 21 | 18 | 28.7 | 22 | 21 | 10.8 | 37.9 | 27.3 | 30.3 | 39.5 | 37.4 | 32 | 27.2 (8.9) |
| South Carolina | 19.9 | 32.3 | 39.3 | 47 | 39.3 | 37.7 | 31.4 | 43.7 | 43.2 | 45.3 | 50.6 | 53 | 40.2 (9.2) |
| South Dakota | 12 | 16.7 | 23.6 | 14.7 | 20.5 | 16.4 | 25.8 | 28.1 | 31.4 | 26.1 | 27.5 | 26 | 22.4 (6.2) |

| State | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | Mean (SD) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Tennessee | 27.6 | 26.3 | 35.2 | 41.4 | 46.9 | 33.4 | 42.8 | 39.2 | 50.5 | 52.2 | 49.7 | 58 | 41.9 (10.0) |
| Texas | 55 | 22.1 | 52.7 | 55.2 | 51.2 | 63.8 | 50 | 52.5 | 65 | 53.6 | 60.5 | 61.5 | 53.6 (11.1) |
| Utah | 31.4 | 25.2 | 36.3 | 28.8 | 31 | 33 | 32.8 | 41 | 21 | 46.1 | 49.3 | 48.3 | 35.4 (9.1) |
| Vermont | 12.6 | 15.6 | 15.1 | 23.3 | 22.1 | 25.3 | 21.3 | 27.8 | 24.9 | 16.6 | 16.7 | 33.8 | 21.3 (6.2) |
| Virginia | 59.1 | 25.8 | 61.5 | 43.4 | 30 | 38.2 | 44.8 | 55.1 | 58.8 | 59.3 | 58.9 | 62.8 | 49.8 (12.9) |
| Washington | 40 | 16.7 | 53.3 | 41.3 | 47.6 | 51.1 | 37.7 | 54.7 | 56 | 64 | 51.4 | 57.9 | 47.6 (12.5) |
| West Virginia | 12.8 | 26.1 | 16.8 | 29.8 | 33.9 | 23.1 | 29 | 29.3 | 43.8 | 41.5 | 33.7 | 39.4 | 29.9 (9.4) |
| Wisconsin | 31.4 | 28.7 | 44.7 | 47 | 20.8 | 45.1 | 42.4 | 39.8 | 55.3 | 44.3 | 44.2 | 62.2 | 42.2 (11.2) |
| Wyoming | 9.5 | 7.9 | 3.5 | 17.3 | 14 | 22.2 | 13.5 | 13.9 | 25.4 | 31.5 | 26.7 | 23.5 | 17.4 (8.5) |

### Trends in HPV Vaccine Searches 2010-2021

The joinpoint regression plots are provided in Figure 2 and Table 3 gives the corresponding MPCs in the HPV vaccine searches in each full year from 2010 to 2021. Four out of the 12 years examined had no joinpoints (2010, 2011, 2012, 2013), suggesting no changes in search trends across the year. Five of the 12 years (2015, 2017, 2018, 2019, and 2021) had one joinpoint, suggesting two distinct time trends (one increasing and one decreasing) in searches during that year period. Three of the 12 years (2014, 2016, and 2020) had two joinpoints, suggesting three distinct trends, or changes, in searches. With respect to HPV vaccine searches, a common increasing trend across years in search volume (ie, search interest) was observed leading up to August.

Two joinpoints were noted in 2014, 2016, and 2020, all demonstrating similar patterns: a decrease in search interest early in the year, followed by an increase from April/May to August, and finishing with a decrease through December. Specifically, in 2014, there was a significant increase in the RSVs by 17.8% (*P*<.001) from May to August, followed by a significant decrease in the RSVs by 13.1% (*P*<.001) from August until December. The RSV search interest in 2016 demonstrated a very similar pattern. The beginning of 2020 demonstrated the largest significant downward trend of all time periods in the joinpoint regression, decreasing by 20% (*P*<.001) from January to April (ie, corresponding to the early COVID-19 pandemic time period). This sharp decrease was followed by an increase from April to July, although it was not significant.

To explore annual temporal changes in trends in HPV vaccine RSVs in the United States from 2010 to 2021, we estimated the APCs using joinpoint regression analysis and fit three models, allowing for no joinpoints, one joinpoint, and two joinpoints, respectively (Table 4). Model 1 showed that from 2010 to 2021, there was a significant annual average increase of 8.6% in RSVs. In Model 2, the joinpoint regression identified two trends: from 2010 to 2018 there was a significant annual average increase of 11.6% in RSVs, with an annual average decrease of –2.2% in RSVs from 2018 to 2021, although the decrease was not significant. In Model 3, the joinpoint regression analysis identified three separate trends, with only the period from 2012 to 2018 demonstrating a significant annual change in RSVs. Model 1 was the best-fitting model based on the permutation method [29].

**Figure 2.** Joinpoint regression analysis indicating trends in "HPV vaccine" relative search volume (RSV) on Google Trends from 2010 to 2021 in the United States. Monthly percentage changes (MPCs) in the HPV vaccine RSVs are described in Table 2. The number of slopes is determined by the number of joinpoints identified by the analysis. Joinpoints are the time points when statistically significant changes in the linear slopes are noted.

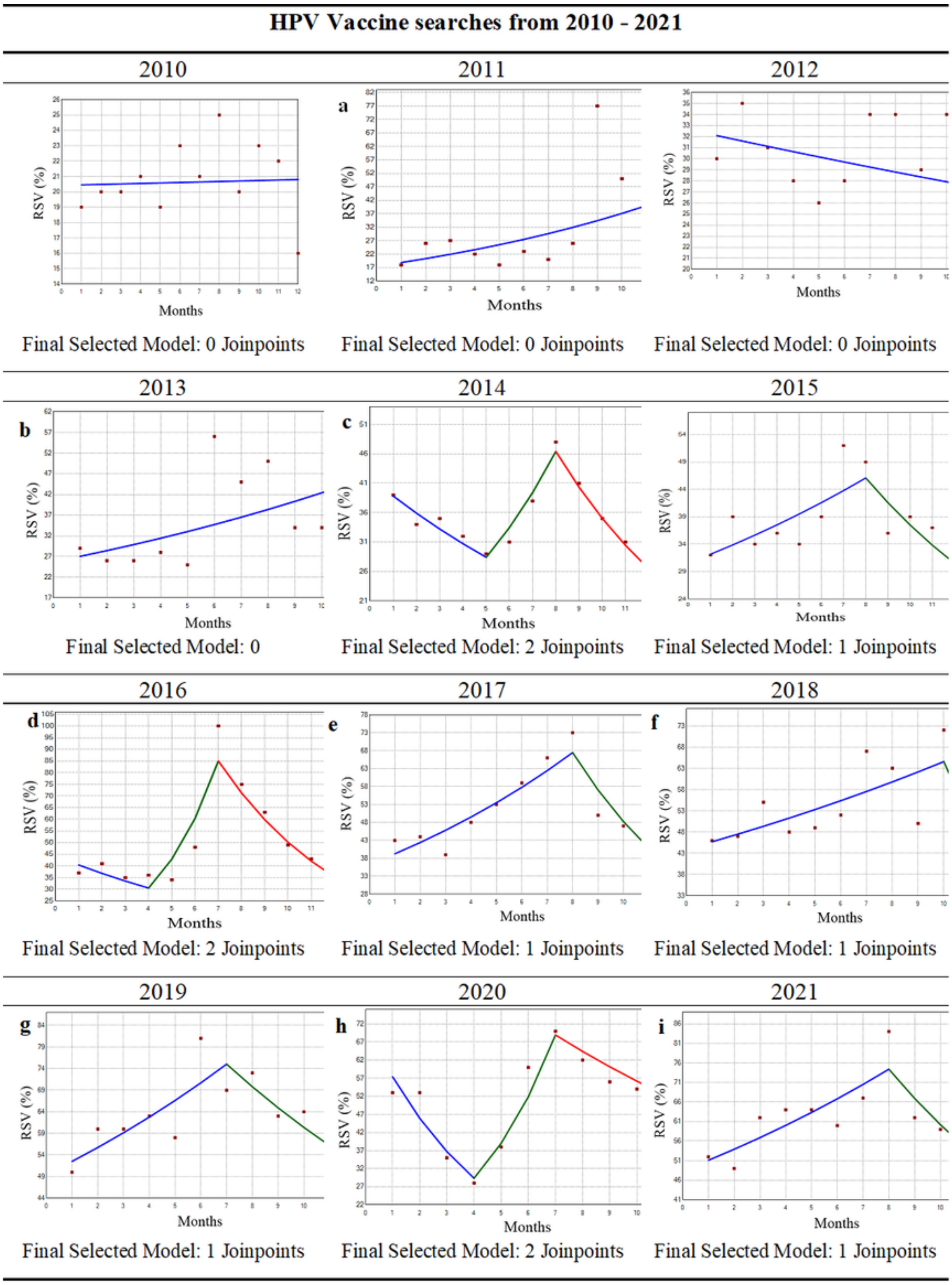


**Table 3.** Monthly percentage changes (MPCs) in the “HPV vaccine” relative search volumes (RSVs) corresponding to the regression graphs (a–i) in Figure 2.

| Regression graph in Figure 2 | Year | Specified monthly period[a] | MPC in RSVs[b] |
|---|---|---|---|
| a | 2011 | 1-12 | 7.80 |
| b | 2013 | 1-12 | 5.13 |
| c | 2014 | 1-5 | 7.50 |
| c | 2014 | 5-8 | 17.77 |
| c | 2014 | 8-12 | –13.12 |
| d | 2016 | 4-7 | 40.73 |
| d | 2016 | 7-12 | –16.14 |
| e | 2017 | 1-8 | 8.05 |
| e | 2017 | 8-12 | –15.44 |
| f | 2018 | 1-10 | 3.91 |
| f | 2018 | 10-12 | –21.73 |
| g | 2019 | 1-7 | 6.13 |
| g | 2019 | 7-12 | –6.99 |
| h | 2020 | 1-4 | –20.04 |
| i | 2021 | 1-8 | 5.51 |
| i | 2021 | 8-12 | –10.05 |

[a] Nonsignificant monthly periods are not displayed.

[b] The MPC is significantly different from 0 at α=.05 in all periods.

**Table 4.** Joinpoint regression analysis showing changes in “HPV vaccine” relative search volume on Google Trends over time in the United States.

| Segment | Period | Change year | Annual percentage change (95% CI) | *t* value | *P* value[b] |
|---|---|---|---|---|---|
| Model 1[a] | 2010-2021 | None | 8.6 (5.9 to 11.4) | 7.2 | <.001 |
| Model 2 | 2010-2018 | 2018 | 11.6 (7.3 to 16.1) | 6.6 | <.001 |
| Model 2 | 2018-2021 | 2021 | –2.2 (–18.4 to 17.2) | –0.3 | .78 |
| Model 3 | 2010-2012 | 2012 | 17.9 (–16.8 to 67.0) | 1.3 | .26 |
| Model 3 | 2012-2018 | 2018 | 10.3 (2.0 to 19.3) | 3.5 | .03 |
| Model 3 | 2018-2021 | 2021 | –1.3 (–17.1 to 17.5) | –0.2 | .85 |

[a] Final selected model, best fitting based on the permutation method.

[b] *P*<.05 indicates that the annual percentage change is significantly different from zero.

# Discussion

## Main Findings

To our knowledge, this is one of the first studies to examine US public online searches regarding the HPV vaccine using GT data. In analyzing the data on HPV vaccine–related online searches in the period from January 2010 to December 2021, we identified important trends, including an overall increase in online searches with noticeable spikes corresponding to key changes in vaccine recommendations. Overall, the joinpoint regression showed a significant average annual percentage increase of 8.6% in HPV vaccine search interest from 2012 to 2021, along with various time trends in HPV vaccine searches across years as well as within years. At the state level, the 12-year average annual HPV vaccine search interest in the United States was the greatest in California (59.9, SD 14.3), New York (55.9, SD 11.9), and Texas (53.6, SD 11.1), while Wyoming (17.4, SD 8.5) recorded the lowest interest in HPV vaccine searches.

## Comparison With Prior Studies

Although previous studies in the United States have explored the influence of social media on HPV vaccine communication [30-34], misinformation [10-14], social interactions, and HPV vaccination behavior [35-37], they also highlighted the need for specific strategies to counter misinformation spreading on the HPV vaccine. In our study, we documented an upward trend in HPV vaccine–related searches following federal changes related to vaccine administration. Despite the consistent evidence that the HPV vaccine is safe and effective, the up-to-date HPV vaccination coverage in 13-17–year-old adolescents was only 59% in 2020 [4]. Moreover, the percentage of parents who refused the HPV vaccine due to safety concerns nearly doubled [38]. Results from a recent study by Sonawane et al [39] showed that HPV vaccine safety concerns are increasing in 30 states. However, much of the information available on social media is not peer-reviewed or evidence-based, and researchers indicated that the information warning about the HPV vaccine is often comprised of innuendos, half-truths, or baseless propaganda [40]. Therefore, continuous monitoring of the trends specific to HPV vaccination across the national and regional landscape is essential to document online health information–seeking behaviors and potential safety concerns.

By using joinpoint regression, we found significant variation in the HPV vaccine RSVs trend by month and year. In nearly every year (8 out of 12), we saw a similar pattern with a significant rise in searches (ie, RSVs) leading up to July and August, followed by a drop in searches, suggesting that HPV vaccine interest was short-lived. This pattern of RSV peaks in July/August syncs with the annual school calendar and the back-to-school period. This is worth noting, as many states and school districts continue to weigh the benefits and costs of vaccine mandates, and whether the HPV vaccine will be required for school attendance [41]. Moreover, public health campaigns can partner with schools during this period to raise public awareness, strengthen parental knowledge, and offer HPV vaccination to all eligible students. This also has important implications, as public health authorities can use this period to promote public health campaigns through internet-based media. There was a considerable decrease in RSVs at the beginning of 2020, corresponding to the start of the COVID-19 pandemic, which could have diverted public interest away from the HPV vaccine onto COVID-19. Nevertheless, our findings showed a positive trend in the online interest of HPV vaccine health–seeking behavior from 2010 to 2021.

HPV vaccine searches differed by US states and demonstrated wide variations in year-over-year searches. All of the US states showed a positive trend in annual HPV vaccine searches from 2010 to 2021; however, some states such as Delaware (mean 23.1, SD 7.3), North Dakota (mean 22.8, SD 6.2), South Dakota (mean 22.4, SD 6.2), Vermont (mean 21.3, SD 6.2), and Wyoming (mean 17.4, SD 8.5) recorded lower RSVs. Although the underlying reasons for these differences are not clear, the changing trend in HPV vaccine searches indicates a positive impact on health-seeking behavior. In this regard, information technology interventions may consider targeting states with lower search volumes to raise awareness, or, alternatively, targeting states with higher search volumes to provide resources for action. Overall, targeted health education materials are needed to ensure that accurate, reliable, and updated information on the HPV vaccine is available online for parents, caregivers, adolescents, and young adults.

Our study identified variations in HPV vaccine search volume by time and geography. These findings could be used to inform targeted search engine advertisements that describe the benefits of the HPV vaccine and how it can prevent cancers, tailoring to different times, geographies, and topics. This approach builds upon prior work using Google Ads to deliver health education materials based on keyword searches [42,43] and geography [44]. For example, our findings demonstrate sharp increases in search volume after changes to HPV vaccine administration, such as making the vaccine available to boys or altering to a 2-dose series. When future changes or announcements arise, we may anticipate a large increase in online searches and create targeted and tailored messaging, utilizing Google Ads, to provide health education materials in the same space people are using to seek information. This approach can be tailored by geography (ie, targeting ads to searches from specific states) or even by topic (ie, tailoring ads to address vaccine safety, age eligibility, or misinformation, to name a few). Targeted online ads may also be utilized to link online searches to community resources or health care providers in local areas.

## Limitations

This study has several limitations. First, GT data are observational data; therefore, making causal inferences (eg, more HPV vaccine searching leads to greater HPV vaccine coverage) is not possible. However, we can use these infodemiology data, demonstrating variation in online searches by time and topic, to tailor health education and promotion materials related to HPV vaccination. These materials may be made available online and even targeted as search engine advertisements during periods of high search volume. Second, our study's units of analysis were at the national and state levels. While these data provide overall indicators for online searches and vaccine coverage, they do not capture the relationship that may be present at other levels of analysis, such as at the community or county level. Third, we are unable to determine the true causes behind changes in search volume; that is, we do not know exactly what prompted increases or declines in searches, but we are able to surmise potential associations based on known federal guideline changes and other information. Fourth, our findings are biased in that they only represent individuals who have internet access and who use Google as their search engine. While most internet users use Google as their search engine (90%) [45], this does not represent the entire US population and may overrepresent certain types of individuals. Finally, variability in the data in specific years may have resulted in the statistical software incorrectly identifying joinpoints.

## Conclusions

This study supports the growing body of work examining online and other digital data, and their application to health care and public health research. Specific to the HPV vaccine, we examined GT data to document online search trends from 2010 to 2021. Our observational findings can be used to inform online intervention points such as event-based opportunities (ie, back-to-school night) and state-specific programs. Notably, we observed a marked decline in online searches during the start of the 2020 COVID-19 pandemic. Further investigation is needed to understand whether the significant factors and variations observed in our study hold to HPV vaccination trends outside of the United States.

## Authors' Contributions

Conceptualization, ASB and PM; methodology, ASB and PM; software, ASB; validation, ASB and PM; formal analysis, ASB; writing—original draft preparation, ASB; writing—review and editing, PM; visualization, ASB; supervision, PM. All authors have read and agreed to the published version of the manuscript.

## Conflicts of Interest

None declared.

## References

1. Cancers caused by HPV. Centers for Disease Control and Prevention. 2019. URL: https://www.cdc.gov/hpv/parents/cancer.html [accessed 2021-11-27]
2. Van Dyne EA, Henley SJ, Saraiya M, Thomas CC, Markowitz LE, Benard VB. Trends in human papillomavirus-associated cancers - United States, 1999-2015. MMWR Morb Mortal Wkly Rep 2018 Aug 24;67(33):918-924. [doi: 10.15585/mmwr.mm6733a2] [Medline: 30138307]
3. Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human papillomavirus vaccination for adults: updated recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2019 Aug 16;68(32):698-702. [doi: 10.15585/mmwr.mm6832a3] [Medline: 31415491]
4. Increase the proportion of adolescents who get recommended doses of the HPV vaccine - IID-08. Healthy People 2030 US Department of Health and Human Services. URL: https://health.gov/healthypeople/objectives-and-data/browse-objectives/vaccination/increase-proportion-adolescents-who-get-recommended-doses-hpv-vaccine-iid-08 [accessed 2022-04-14]
5. Pingali C, Yankey D, Elam-Evans LD, Markowitz LE, Williams CL, Fredua B, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13-17 years - United States, 2020. MMWR Morb Mortal Wkly Rep 2021 Sep 03;70(35):1183-1190. [doi: 10.15585/mmwr.mm7035a1] [Medline: 34473682]
6. Brin S, Page L. Reprint of: The anatomy of a large-scale hypertextual web search engine. Comput Netw 2012 Dec;56(18):3825-3833. [doi: 10.1016/j.comnet.2012.10.007]
7. Keelan J, Pavri-Garcia V, Tomlinson G, Wilson K. YouTube as a source of information on immunization: a content analysis. JAMA 2007 Dec 05;298(21):2482-2484. [doi: 10.1001/jama.298.21.2482] [Medline: 18056901]
8. Ekram S, Debiec KE, Pumper MA, Moreno MA. Content and commentary: HPV vaccine and YouTube. J Pediatr Adolesc Gynecol 2019 Apr;32(2):153-157. [doi: 10.1016/j.jpag.2018.11.001] [Medline: 30445163]
9. Mohanty S, Leader AE, Gibeau E, Johnson C. Using Facebook to reach adolescents for human papillomavirus (HPV) vaccination. Vaccine 2018 Sep 25;36(40):5955-5961. [doi: 10.1016/j.vaccine.2018.08.060] [Medline: 30172634]
10. Massey PM, Kearney MD, Hauer MK, Selvan P, Koku E, Leader AE. Dimensions of misinformation about the HPV vaccine on Instagram: content and network analysis of social media characteristics. J Med Internet Res 2020 Dec 03;22(12):e21451 [FREE Full text] [doi: 10.2196/21451] [Medline: 33270038]
11. Dunn AG, Leask J, Zhou X, Mandl KD, Coiera E. Associations between exposure to and expression of negative opinions about human papillomavirus vaccines on social media: an observational study. J Med Internet Res 2015 Jun 10;17(6):e144 [FREE Full text] [doi: 10.2196/jmir.4343] [Medline: 26063290]
12. Surian D, Nguyen DQ, Kennedy G, Johnson M, Coiera E, Dunn AG. Characterizing Twitter discussions about HPV vaccines using topic modeling and community detection. J Med Internet Res 2016 Aug 29;18(8):e232 [FREE Full text] [doi: 10.2196/jmir.6045] [Medline: 27573910]
13. Dunn AG, Surian D, Leask J, Dey A, Mandl KD, Coiera E. Mapping information exposure on social media to explain differences in HPV vaccine coverage in the United States. Vaccine 2017 May 25;35(23):3033-3040 [FREE Full text] [doi: 10.1016/j.vaccine.2017.04.060] [Medline: 28461067]
14. Sonawane K, Zhu Y, Montealegre JR, Lairson DR, Bauer C, McGee LU, et al. Parental intent to initiate and complete the human papillomavirus vaccine series in the USA: a nationwide, cross-sectional survey. Lancet Public Health 2020 Sep;5(9):e484-e492 [FREE Full text] [doi: 10.1016/S2468-2667(20)30139-0] [Medline: 32707126]
15. Nuti SV, Wayda B, Ranasinghe I, Wang S, Dreyer RP, Chen SI, et al. The use of google trends in health care research: a systematic review. PLoS One 2014 Oct 22;9(10):e109583 [FREE Full text] [doi: 10.1371/journal.pone.0109583] [Medline: 25337815]
16. Google Trends. Google. URL: https://trends.google.com/trends/ [accessed 2022-01-10]
17. Bragazzi NL, Barberis I, Rosselli R, Gianfredi V, Nucci D, Moretti M, et al. How often people google for vaccination: qualitative and quantitative insights from a systematic search of the web-based activities using Google Trends. Hum Vaccin Immunother 2017 Feb 16;13(2):464-469 [FREE Full text] [doi: 10.1080/21645515.2017.1264742] [Medline: 27983896]
18. Cervellin G, Comelli I, Lippi G. Is Google Trends a reliable tool for digital epidemiology? Insights from different clinical settings. J Epidemiol Glob Health 2017 Sep;7(3):185-189 [FREE Full text] [doi: 10.1016/j.jegh.2017.06.001] [Medline: 28756828]

19. Sycinska-Dziarnowska M, Paradowska-Stankiewicz I, Woźniak K. The global interest in vaccines and its prediction and perspectives in the era of COVID-19. Real-time surveillance using Google Trends. Int J Environ Res Public Health 2021 Jul 24;18(15):7841 [FREE Full text] [doi: 10.3390/ijerph18157841] [Medline: 34360134]
20. Lu Y, Wang S, Wang J, Zhou G, Zhang Q, Zhou X, et al. An epidemic avian influenza prediction model based on Google Trends. Lett Org Chem 2019 Mar 20;16(4):303-310. [doi: 10.2174/1570178615666180724103325]
21. Yousefinaghani S, Dara R, Mubareka S, Sharif S. Prediction of COVID-19 waves using social media and Google search: a case study of the US and Canada. Front Public Health 2021 Apr 16;9:656635. [doi: 10.3389/fpubh.2021.656635] [Medline: 33937179]
22. Eysenbach G. Infodemiology: The epidemiology of (mis)information. Am J Med 2002 Dec 15;113(9):763-765. [doi: 10.1016/s0002-9343(02)01473-0] [Medline: 12517369]
23. Nan X, Madden K. HPV vaccine information in the blogosphere: how positive and negative blogs influence vaccine-related risk perceptions, attitudes, and behavioral intentions. Health Commun 2012 Nov;27(8):829-836. [doi: 10.1080/10410236.2012.661348] [Medline: 22452582]
24. Mavragani A, Ochoa G. Google Trends in infodemiology and infoveillance: methodology framework. JMIR Public Health Surveill 2019 May 29;5(2):e13439 [FREE Full text] [doi: 10.2196/13439] [Medline: 31144671]
25. Joinpoint RP, Version 4. Joinpoint Trend Analysis Software. National Institute of Health National Cancer Institute Division of Cancer Control & Population Sciences. URL: https://surveillance.cancer.gov/joinpoint/ [accessed 2022-04-13]
26. Kim H, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000 Feb 15;19(3):335-351. [doi: 10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z] [Medline: 10649300]
27. Robinson CL, Advisory Committee on Immunization Practices (ACIP), ACIP Child/Adolescent Immunization Work Group. Advisory Committee on Immunization Practices recommended immunization schedules for persons aged 0 through 18 Years--United States, 2016. MMWR Morb Mortal Wkly Rep 2016 Feb 05;65(4):86-87. [doi: 10.15585/mmwr.mm6504a4] [Medline: 26845283]
28. Meites E, Kempe A, Markowitz LE. Use of a 2-dose schedule for human papillomavirus vaccination - updated recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2016 Dec 16;65(49):1405-1408. [doi: 10.15585/mmwr.mm6549a5] [Medline: 27977643]
29. How Joinpoint Selects the Final Model. National Institute of Health National Cancer Institute Division of Cancer Control & Population Sciences. URL: https://surveillance.cancer.gov/help/joinpoint/setting-parameters/method-and-parameters-tab/model-selection-method [accessed 2022-04-13]
30. Thompson EL, Galvin AM, Garg A, Moore JD, Litt DM. Exploring novel strategies for social media HPV vaccine information. Hum Vaccin Immunother 2021 Dec 02;17(12):5397-5401. [doi: 10.1080/21645515.2021.1993040] [Medline: 34736366]
31. Tung W, Lin Y, Chao HW, Chen Y. HPV vaccination, information sources, and acculturation among Chinese college students aged 18-26 in the United States. Res Nurs Health 2022 Apr;45(2):194-204. [doi: 10.1002/nur.22185] [Medline: 34549448]
32. Pho A, Bakken S, Lunn M, Lubensky M, Flentje A, Dastur Z, et al. Online health information seeking, health literacy, and human papillomavirus vaccination among transgender and gender-diverse people. J Am Med Inform Assoc 2022 Jan 12;29(2):285-295 [FREE Full text] [doi: 10.1093/jamia/ocab150] [Medline: 34383916]
33. Argyris YA, Kim Y, Roscizewski A, Song W. The mediating role of vaccine hesitancy between maternal engagement with anti- and pro-vaccine social media posts and adolescent HPV-vaccine uptake rates in the US: The perspective of loss aversion in emotion-laden decision circumstances. Soc Sci Med 2021 Aug;282:114043. [doi: 10.1016/j.socscimed.2021.114043] [Medline: 34147269]
34. Galvin AM, Garg A, Moore JD, Litt DM, Thompson EL. Quality over quantity: human papillomavirus vaccine information on social media and associations with adult and child vaccination. Hum Vaccin Immunother 2021 Oct 03;17(10):3587-3594 [FREE Full text] [doi: 10.1080/21645515.2021.1932219] [Medline: 34086517]
35. Margolis MA, Brewer NT, Shah PD, Calo WA, Gilkey MB. Stories about HPV vaccine in social media, traditional media, and conversations. Prev Med 2019 Jan;118:251-256. [doi: 10.1016/j.ypmed.2018.11.005] [Medline: 30414396]
36. Gilkey MB, Calo WA, Marciniak MW, Brewer NT. Parents who refuse or delay HPV vaccine: differences in vaccination behavior, beliefs, and clinical communication preferences. Hum Vaccin Immunother 2017 Mar 04;13(3):680-686 [FREE Full text] [doi: 10.1080/21645515.2016.1247134] [Medline: 27763818]
37. Buller DB, Pagoto S, Henry K, Berteletti J, Walkosz BJ, Bibeau J, et al. Human papillomavirus vaccination and social media: results in a trial with mothers of daughters aged 14-17. Front Digit Health 2021;3:683034 [FREE Full text] [doi: 10.3389/fdgth.2021.683034] [Medline: 34713152]
38. Despite proven safety of HPV vaccines, more parents have concerns. National Cancer Institute. URL: https://www.cancer.gov/news-events/cancer-currents-blog/2021/hpv-vaccine-parents-safety-concerns [accessed 2022-01-01]
39. Sonawane K, Lin Y, Damgacioglu H, Zhu Y, Fernandez ME, Montealegre JR, et al. Trends in human papillomavirus vaccine safety concerns and adverse event reporting in the United States. JAMA Netw Open 2021 Sep 01;4(9):e2124502. [doi: 10.1001/jamanetworkopen.2021.24502] [Medline: 34533574]

40. Osazuwa-Peters N, Rohde RL, Boakye EA. HPV vaccination is safe-you don't have to whisper it. JAMA Netw Open 2021 Sep 01;4(9):e2125124 [FREE Full text] [doi: 10.1001/jamanetworkopen.2021.25124] [Medline: 34533578]
41. HPV vaccine mandates for elementary and secondary schools. Immunize.org. 2022. URL: https://www.immunize.org/laws/hpv.asp [accessed 2022-01-02]
42. Cidre Serrano W, Chren M, Resneck JS, Aji NN, Pagoto S, Linos E. Online advertising for cancer prevention: Google Ads and tanning beds. JAMA Dermatol 2016 Jan 01;152(1):101-102. [doi: 10.1001/jamadermatol.2015.3998] [Medline: 26444220]
43. Upadhyay UD, Jovel IJ, McCuaig KD, Cartwright AF. Using Google Ads to recruit and retain a cohort considering abortion in the United States. Contraception: X 2020;2:100017. [doi: 10.1016/j.conx.2019.100017]
44. Murphy AL, Peltekian S, Gardner DM. Website analytics of a Google Ads campaign for a men's mental health website: comparative analysis. JMIR Ment Health 2018 Dec 13;5(4):e12428 [FREE Full text] [doi: 10.2196/12428] [Medline: 30545812]
45. Worldwide desktop market share of leading search engines from January 2010 to September. Statista. 2021. URL: https://www.statista.com/statistics/216573/worldwide-market-share-of-search-engines/.htm [accessed 2022-01-17]

## Abbreviations

**ACIP:** Advisory Committee on Immunization Practices
**APC:** annual percentage change
**GT:** Google Trends
**HPV:** human papillomavirus
**MPC:** monthly percentage change
**RSV:** relative search volume

*Edited by A Mavragani; submitted 01.03.22; peer-reviewed by M Lotto, K Taira, I Mircheva; comments to author 27.03.22; revised version received 20.05.22; accepted 18.07.22; published 29.08.22.*

*Please cite as:*
*Bhagavathula AS, Massey PM*
*Google Trends on Human Papillomavirus Vaccine Searches in the United States From 2010 to 2021: Infodemiology Study*
*JMIR Public Health Surveill 2022;8(8):e37656*
*URL: https://publichealth.jmir.org/2022/8/e37656*
*doi:10.2196/37656*
*PMID:36036972*

Original Paper

# Trends and Characteristics of #HIVPrevention Tweets Posted Between 2014 and 2019: Retrospective Infodemiology Study

Raquel Burgess[1], MSc; Josemari T Feliciano[2], MPH; Leonardo Lizbinski[1,3], MPH, MSc; Yusuf Ransome[1], MPH, DrPH

[1]Department of Social and Behavioral Sciences, Yale School of Public Health, Yale University, New Haven, CT, United States
[2]Department of Biostatistics, Yale School of Public Health, Yale University, New Haven, CT, United States
[3]The Warren Alpert Medical School, Brown University, Providence, RI, United States

**Corresponding Author:**
Raquel Burgess, MSc
Department of Social and Behavioral Sciences
Yale School of Public Health
Yale University
60 College Street
New Haven, CT, 06510
United States
Phone: 1 203 785 2867
Email: raquel.burgess@yale.edu

## Abstract

**Background:** Twitter is becoming an increasingly important avenue for people to seek information about HIV prevention. Tweets about HIV prevention may reflect or influence current norms about the acceptability of different HIV prevention methods. Therefore, it may be useful to empirically investigate trends in the level of attention paid to different HIV prevention topics on Twitter over time.

**Objective:** The primary objective of this study was to investigate temporal trends in the frequency of tweets about different HIV prevention topics on Twitter between 2014 and 2019.

**Methods:** We used the Twitter application programming interface to obtain English-language tweets employing #HIVPrevention between January 1, 2014, and December 31, 2019 (n=69,197, globally). Using iterative qualitative content analysis on samples of tweets, we developed a keyword list to categorize the tweets into 10 prevention topics (eg, condom use, preexposure prophylaxis [PrEP]) and compared the frequency of tweets mentioning each topic over time. We assessed the overall change in the proportions of #HIVPrevention tweets mentioning each prevention topic in 2019 as compared with 2014 using chi-square and Fisher exact tests. We also conducted descriptive analyses to identify the accounts posting the most original tweets, the accounts retweeted most frequently, the most frequently used word pairings, and the spatial distribution of tweets in the United States compared with the number of state-level HIV cases.

**Results:** PrEP (13,895 tweets; 20.08% of all included tweets) and HIV testing (7688, 11.11%) were the most frequently mentioned topics, whereas condom use (2941, 4.25%) and postexposure prophylaxis (PEP; 823, 1.19%) were mentioned relatively less frequently. The proportions of tweets mentioning PrEP (327/2251, 14.53%, in 2014, 5067/12,971, 39.1%, in 2019; *P*≤.001), HIV testing (208/2251, 9.24%, in 2014, 2193/12,971, 16.91% in 2019; *P*≤.001), and PEP (25/2251, 1.11%, in 2014, 342/12,971, 2.64%, in 2019; *P*≤.001) were higher in 2019 compared with 2014, whereas the proportions of tweets mentioning abstinence, condom use, circumcision, harm reduction, and gender inequity were lower in 2019 compared with 2014. The top retweeted accounts were mostly UN-affiliated entities; celebrities and HIV advocates were also represented. Geotagged #HIVPrevention tweets in the United States between 2014 and 2019 (n=514) were positively correlated with the number of state-level HIV cases in 2019 (r=0.81, *P*≤.01).

**Conclusions:** Twitter may be a useful source for identifying HIV prevention trends. During our evaluation period (2014-2019), the most frequently mentioned prevention topics were PrEP and HIV testing in tweets using #HIVPrevention. Strategic responses to these tweets that provide information about where to get tested or how to obtain PrEP may be potential approaches to reduce HIV incidence.

***(JMIR Public Health Surveill 2022;8(8):e35937)*** doi:10.2196/35937

**KEYWORDS**

HIV; social media; Twitter; prevention; infodemiology

## Introduction

Globally, 1.5 million (1.1-2.0 million) people became infected with HIV in 2021 [1]. In the United States, an estimated 34,800 new HIV infections occurred in 2019, representing an 8% decline from 2015 [2]. An estimated 13% of HIV-infected individuals in the United States in 2019 did not know they were infected [3,4]. Levels of awareness of prevention methods such as preexposure prophylaxis (PrEP) are low among some high risk populations and there is substantial room for improvement in knowledge of HIV prevention across many states [5,6].

Social media sites are becoming increasingly important avenues for people of all age groups to seek information about health issues, including HIV [7]. Social media may be a particularly important avenue for promoting HIV prevention among younger people, given that younger people have a higher likelihood of using social media for health communication and they represent the highest burden of new HIV infections [2,8].

Previous research on social media and HIV information suggests that social media may be an effective avenue for spreading and consuming HIV information because it allows for anonymity and reduces stigma-related barriers to information seeking [7,9]. This may occur in part because discussing sexual health on social media mitigates the feelings of discomfort that can occur when discussing sexual health topics in-person among some population groups [7]. Yet, other research describes how a lack of privacy and the potential for bullying may deter individuals from sharing or interacting with sexual health content on social media [10,11].

Some research suggests that social media may have a beneficial effect on the adoption of HIV prevention behaviors. For example, social support provided by social media engagement prevention-specific messages have been associated with improved access to and uptake of HIV prevention and testing [7,12-15]. Moreover, interventions deployed via social media have been shown to increase HIV testing among men who have sex with men (MSM) [16] and to promote knowledge of sexually transmitted infections among young adults [17]. Support for the beneficial effect of HIV prevention communication on social media on HIV prevention behaviors is enhanced by evidence suggesting that higher rates of HIV-specific tweet activity per capita have been associated with lower HIV incidence in the following year [18].

Despite these positive findings, it has also been shown that Twitter can be used to propagate messages that perpetuate HIV-related stigma and endorse risky sexual behaviors [19]. These types of messages may also influence HIV incidence: in one study, the authors used an index of the proportion of Twitter users who posted risk behavior tweets (eg, “alcohol”, “without condom”) among all Twitter users to operationalize behavioral risk. They found that higher scores on the index were positively correlated with a higher rate of new HIV diagnoses across US counties [20]. Overall, this body of research suggests that social media messages about HIV can play an important role in HIV prevention and risk behavior.

Taggart and colleagues [21] further advance the view that “messaging matters” by providing a historical analysis of the evolution of public health messaging about HIV/AIDS. They provide evidence to suggest that initial public health communication about HIV was fear based, which transitioned to a focus on individual risk behaviors, and later, to empowerment and structural factors [21]. They also described the evolution of messaging about specific prevention methods. In the 1980s, HIV prevention messaging focused on harm reduction, such as safe sex and HIV testing. In response to innovations in HIV testing and treatment, messaging in the 2000s maintained focus on HIV testing while also promoting early detection and initiation of antiretroviral treatment. By the 2010s, PrEP was being promoted for high-risk individuals and later expanded to more general populations [21].

Importantly, Taggart and colleagues [21] described how messaging about prevention methods shifted social norms about the acceptability of HIV prevention methods over time. For example, PrEP was initially promoted only for individuals at a high risk of HIV, which may have contributed to PrEP-related stigma and slower-than-expected uptake of the drug [21]. Further research across other health issues corroborates the idea that social media can influence social norms about healthy behaviors, including with respect to sexual health [22-26].

This study was designed based on the same reasoning employed by Taggart and colleagues [21]: that is, there is utility in examining trends in how people talk about HIV prevention over time, as these trends may both reflect and influence changes in the acceptability and uptake of these prevention methods [13,16,27]. Trends in how individuals use social media to search for and provide health information can be studied using infodemiological approaches, which involve using information available on the internet to inform efforts to improve public health [28]. In this study, we used an infodemiological approach to examine temporal trends in the relative attention paid to different HIV prevention methods on Twitter. To the best of our knowledge, this is the first study to compare tweet activity about different HIV prevention topics and to investigate how tweet activity about HIV prevention topics has changed over time. Describing trends in the relative attention paid to different HIV prevention topics may provide public health professionals valuable insights about the acceptability and popularity of different HIV prevention methods; these insights could be used to inform strategic health communication efforts about HIV prevention.

We employed a passive, retrospective infodemiology approach in which we collected tweets that included #HIVPrevention (n=69,197) during a 6-year timeframe (2014-2019) corresponding to a critical period related to the uptake of PrEP in the United States and globally. We examined trends in the frequency of mentions of 10 different HIV prevention topics and assessed changes in the proportion of tweets mentioning each topic in 2019 as compared with 2014. We also report descriptive information on the spatial distribution of geotagged #HIVPrevention tweets in relation to the number of state-level HIV cases in the United States, the most frequently used word pairings in the tweets, the accounts posting the most original tweets, and the accounts retweeted most frequently. We conclude by discussing the implications of our findings and suggesting the opportunities for leveraging HIV prevention communication on Twitter to reduce HIV incidence.

# Methods

## Study Design

We conducted a retrospective infodemiology study using publicly available tweets employing #HIVPrevention between 2014 and 2019.

## Data

We utilized the Twitter application programming interface to collect all tweets (including original tweets, retweets, quote tweets, and replies) written in the English language that employed #HIVPrevention between January 1, 2014, and December 31, 2019 (n=69,197). We selected the timeframe 2014-2019 because it corresponds to a period following Food and Drug Administration (FDA) approval of PrEP for HIV prevention in the United States (occurring in 2012) [29]. Moreover, during this period, the World Health Organization (WHO) issued several expansions to its recommendations of population groups that should consider using PrEP [30]. Therefore, this is an interesting period to examine not only to understand changes in the attention paid to PrEP on Twitter, but also to understand how attention to other prevention methods may have changed during this time. We did not apply any geographical constraints to our sample as most tweets are not geotagged and individuals can be easily exposed to tweets generated in various regions of the world. We selected the hashtag #HIVPrevention as a proxy for HIV prevention-related tweets because it was the hashtag used by the Joint United Nations Programme on HIV/AIDS (UNAIDS) in 2016 to promote World AIDS Day (WAD) [31], and was used throughout the entire study period within tweets that discussed HIV prevention topics. WAD is an international day organized by UNAIDS to raise awareness about HIV [31]. In 2016, UNAIDS used #HIVPrevention to promote awareness of 9 different HIV prevention topics in the 9 weeks leading up to WAD; the topics were condoms, harm reduction, voluntary medical male circumcision (VMMC), elimination of mother-to-child transmission of HIV (EMTCT), PrEP, empowerment of young girls/women, testing viral suppression, targeting key populations, and investing in HIV prevention [31].

## Descriptive Analyses

We performed several descriptive analyses (eg, tabulation, Pearson correlation) to investigate the characteristics of the data. All analyses were conducted in R statistical software (version 4.0.3; R Foundation for Statistical Computing).

To investigate the change in activity related to tweets using #HIVPrevention over the study period, we tabulated original tweets (including replies and relevant quote tweets) and retweets (including relevant quote tweets) by month and year to identify trends.

To determine the Twitter accounts that generated the highest proportion of original #HIVPrevention tweets during the study period, we tabulated the number of original tweets as a function of unique account usernames.

To determine which Twitter accounts’ #HIVPrevention tweets were retweeted at the highest frequencies, we tabulated the number of retweets associated with #HIVPrevention tweets that each unique account username received.

To identify the most frequently used word pairings, also known as bigrams, we used the tidytext package (version 0.3.1) in R. This method allows for an indication of the context in which words are used. For example, a tweet containing the text “PrEP is an effective tool” will correspond to the following 2 bigrams: (1) PrEP and effective, and (2) effective and tool. Using *Gephi* (version 0.9.2), we created a visual word network of the top 50 bigrams found in our sample.

To understand the relationship between geotagged tweets and the number of HIV cases, we performed a Pearson correlation to assess the relationship between the number of geotagged tweets at the state level between 2014 and 2019 and the number of HIV cases in 2019 at the state level [32]. We mapped the geotagged tweets in the United States (n=514) and 2019 HIV cases at the state level using the leaflet package (version 2.0.4.1) in R.

## Analysis of the HIV Prevention Topics Referenced Most Often in #HIVPrevention Tweets

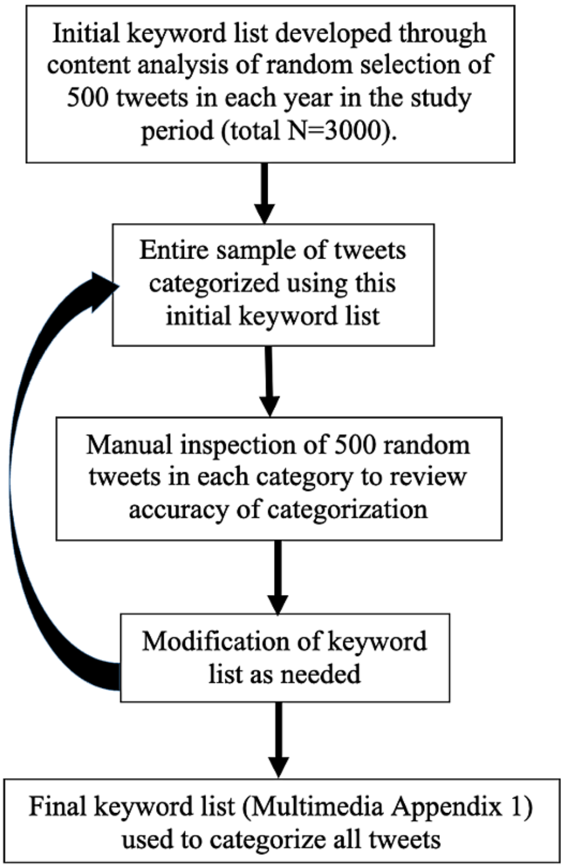
To determine the frequency at which various HIV prevention topics were mentioned in #HIVPrevention tweets and retweets and whether this changed over the study period, we first developed a list of 10 prevention topics and relevant keywords. We selected prevention topics based on the topics identified by the UNAIDS 2016 WAD campaign and our review of the literature. The 10 selected prevention topics were PrEP, postexposure prophylaxis (PEP), condom use, abstinence, VMMC, EMTCT, HIV testing, harm reduction, gender inequity and violence against women, and sex work.

We developed a keyword list for these 10 prevention topics by drawing on the initial stages of summative qualitative content analysis [33], in which text is explored to identify how words are used in context. For example, we were able to identify that the term “daily blue” was used to refer to PrEP without naming PrEP explicitly. We believe this process helped us to identify keywords that would have been otherwise overlooked and improved the accuracy of our tweet categorization.

Following initial development of our keyword list, we iteratively refined it using a manual inspection process to ensure that our keyword list had a high level of sensitivity and an acceptable level of specificity. That is, we sought to identify all tweets mentioning a particular prevention method (true positives) while minimizing any miscategorization (false positives). An example of a false positive would be a tweet referring to the US President’s Emergency Plan for AIDS Relief (PEPFAR) that was categorized under PEP. As some miscategorization was inevitable, we accepted an error level that was ≤5% (ie, in our manual inspection, ≤25 of the 500 inspected tweets were not related to the respective prevention method). If greater than 5% error was detected, we made appropriate modifications to our keyword list to fix the inaccuracies. We similarly inspected samples of the tweets which were uncategorized to determine if we missed any keywords that were relevant to a particular category (ie, to minimize false negatives). When these were discovered, we refined our keyword list to include the relevant keyword. If a tweet mentioned keywords related to more than 1 prevention topic (eg, “PrEP”, “condom”), then that tweet was categorized in each respective category. If a tweet mentioned multiple keywords related to the same prevention category, that tweet was counted in the respective category only once. The manual inspection process was conducted by the first author (RB) and the final list of keywords (Multimedia Appendix 1) was further verified by the senior author (YR), a content expert in HIV. A depiction of our iterative manual inspection process for refining our keyword list is presented in Figure 1.

To evaluate how attention to each topic changed over the study period, we compared the proportion of tweets related to each respective topic in 2019 with the proportion of tweets related to each respective topic in 2014 using chi-square and Fisher exact tests.

**Figure 1.** Manual inspection process for refining the keyword list.



### Ethical Considerations

The study was granted an Ethics Exemption by the Yale University Institutional Review Board (#2000028381).

## Results

### Descriptive Analyses

Our sample consisted of 25,031 original tweets and 44,166 retweets, totaling 69,197 tweets. Geotagged tweets represented 1.81% (n=1253) of the sample and were tweeted from 76 countries.

Figure 2 presents the number of tweets (including retweets) and unique accounts employing #HIVPrevention between 2014 and 2019 as a function of the year. The number of tweets and accounts using #HIVPrevention is lowest in 2014, at 2251/69,197 tweets (3.25% of the total sample) generated by 1097 accounts. A substantial increase in tweet activity is observed in 2016 as compared with 2014 and 2015, with 28,254/69,197 tweets (40.83%) posted in 2016 from 13,109 accounts. A closer inspection of the data confirmed that the 2016 tweets were primarily related to WAD. This substantial increase in activity was not sustained in 2017 (10,811/69,197 tweets, 15.62%; 5188 accounts), although the number of #HIVPrevention tweets posted in 2017 was higher than the number posted in 2015 (3209/69,197 tweets, 4.64%; 1215 accounts). This likely reflects higher usage of the term #HIVPrevention following the 2016 campaign rather than an actual increase in the number of tweets addressing HIV prevention, although it could reflect both factors. The number of users utilizing #HIVPrevention follows a similar pattern to the number of total tweets over the study period.

The 10 accounts that generated the most original #HIVPrevention tweets between 2014 and 2019 are presented in Table 1. The individual who is responsible for the account @HIV_Insight also reports being responsible for @Sex_Worker_Hlth and @Hlth_Literacy, suggesting that they are responsible for 66.37% (4072/6135) of the original content provided by the top 10 content contributing accounts. @DrMbere, @Health_HIV2030, and @himmoderator also identify as individual-run accounts in their Twitter account descriptions, whereas the remaining accounts were identified as run by institutions. In total, individuals are responsible for 80.84% (4960/6135) of the original content provided by the top 10 content contributing accounts.

**Figure 2.** Annual frequency of #HIVPrevention tweets between 2014 and 2019.

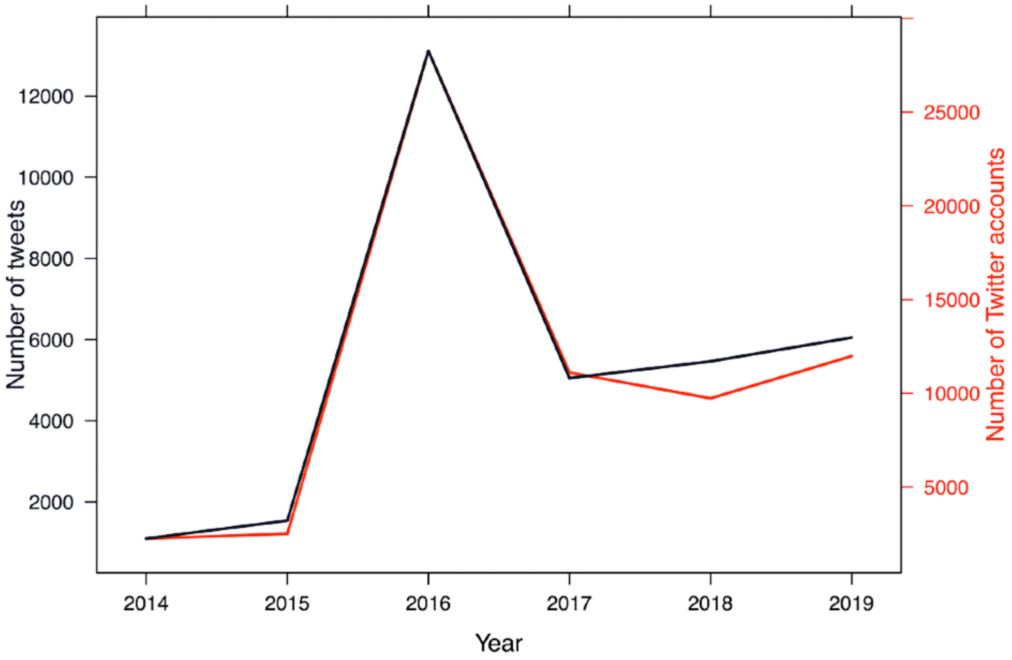


**Table 1.** Accounts with the most original and retweeted #HIVPrevention tweets between 2014 and 2019.

| Accounts with the most original #HIVPrevention tweets | Number of original tweets per account | Accounts whose #HIVPrevention tweets were retweeted at the highest frequencies | Number of retweets per account |
|---|---|---|---|
| @HIV_Insight | 3144 | @UNAIDS | 11,239 |
| @Sex_Worker_Hlth | 484 | @HIV_Insight | 1880 |
| @DrMbere | 465 | @MichelSidibe | 1551 |
| @Hlth_Literacy | 444 | @UN | 908 |
| @HIVIreland | 396 | @MissUniverse | 705 |
| @UNAIDS | 296 | @UNAIDS_AP | 687 |
| @EPICBrowardOrg | 262 | @HIVpxresearch | 499 |
| @Health_HIV2030 | 240 | @accphivprn | 493 |
| @HopeandHelpInc | 221 | @AniShakari | 470 |
| @himmoderator | 183 | @HIVIreland | 468 |

The 10 accounts whose #HIVPrevention tweets were retweeted at the highest frequencies between 2014 and 2019 are presented in Table 1. The United Nations is responsible for 3 of these accounts (@UN, @UNAIDS, and @UNAIDS_AP [UNAIDS Asia-Pacific]) and the accounts @MichelSidebe and @AniShakari publicly identify themselves as current or former employees of UNAIDS. The remaining accounts are also run by institutions that work on the HIV/AIDS epidemic, with the notable exceptions of @HIV_Insight and @MissUniverse; the latter ran a campaign on HIV prevention in 2016 for WAD, which involved promotion of various HIV prevention methods by Miss Universe contestants. The accounts @UN (12,047,848 followers), @MissUniverse (1,022,563), and @UNAIDS (258,322) corresponded to the largest numbers of followers at the time of data collection (March 2020).

Figure 3 presents a word network depicting the 50 most frequently used bigrams seen in #HIVPrevention tweets between 2014 and 2019. The most frequently used words (not listed in the order of frequency) were PrEP, testing, treatment, prevent, access, strategy, transmission, HIV, health, and free.

Figures 4 and 5 display the geographic distribution of geotagged #HIVPrevention tweets between 2014 and 2019 and the number of state-level HIV cases in 2019, respectively. The data set presented in Figure 5 is publicly available from the Centers of Disease Control and Prevention [32]. The number of #HIVPrevention tweets per state was positively correlated with the number of state-level HIV cases in 2019 (*r*=0.81, *P*<.01; Figure 6).

**Figure 3.** A visual word network of the 50 most frequently used bigrams (word-pairings) in #HIVPrevention tweets between 2014 and 2019.

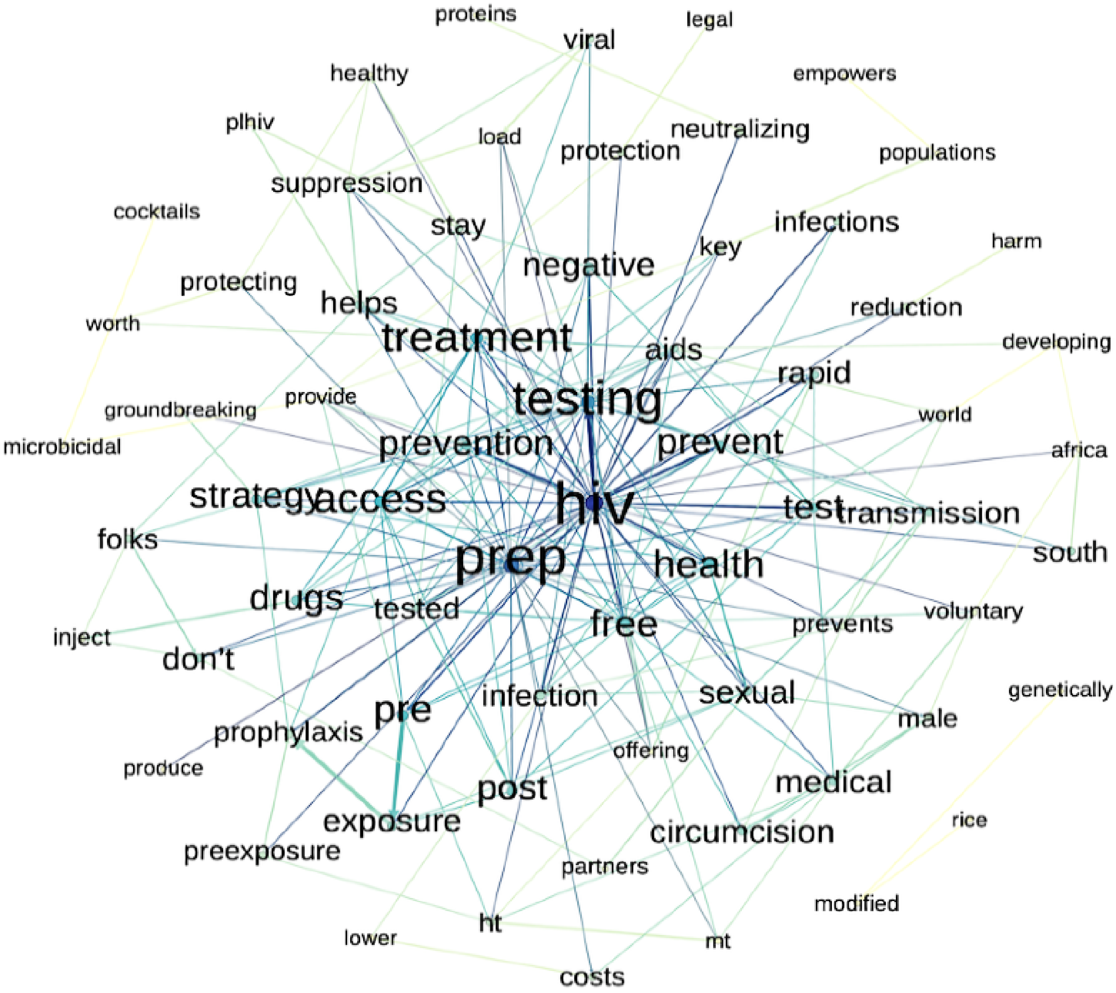


**Figure 4.** Geographic distribution of geotagged English #HIVPrevention tweets (n=514) in the United States between 2014 and 2019. The numbers in the figure correspond to the number of tweets geotagged to the respective locations indicated on the map. The mapping data presented here is available under the Open Database (CC-BY-SA) License [34].

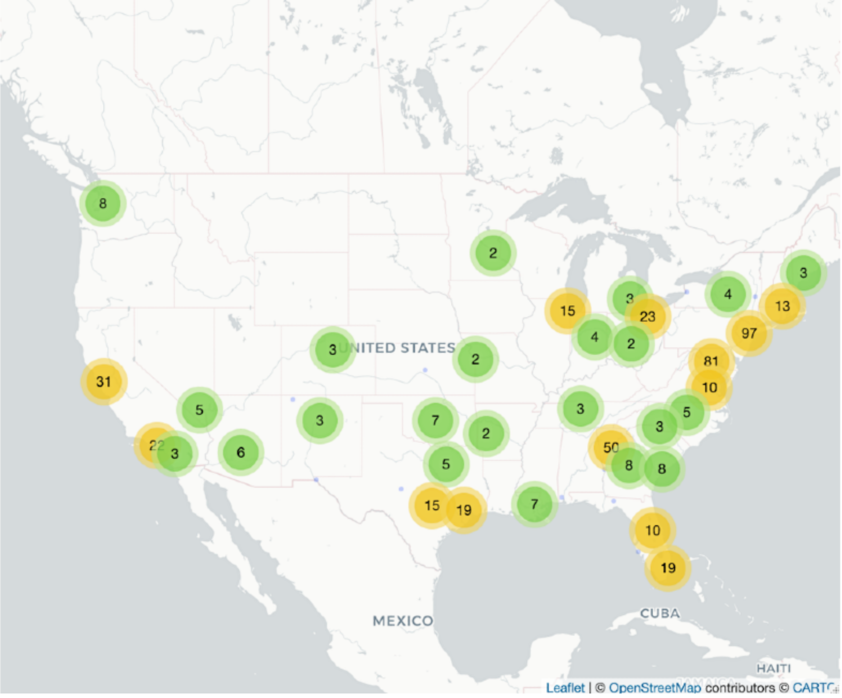


**Figure 5.** Geographic distribution of the number of HIV cases in the United States in 2019, displayed at the state level. The mapping data presented here is available under the Open Database (CC-BY-SA) License [34].

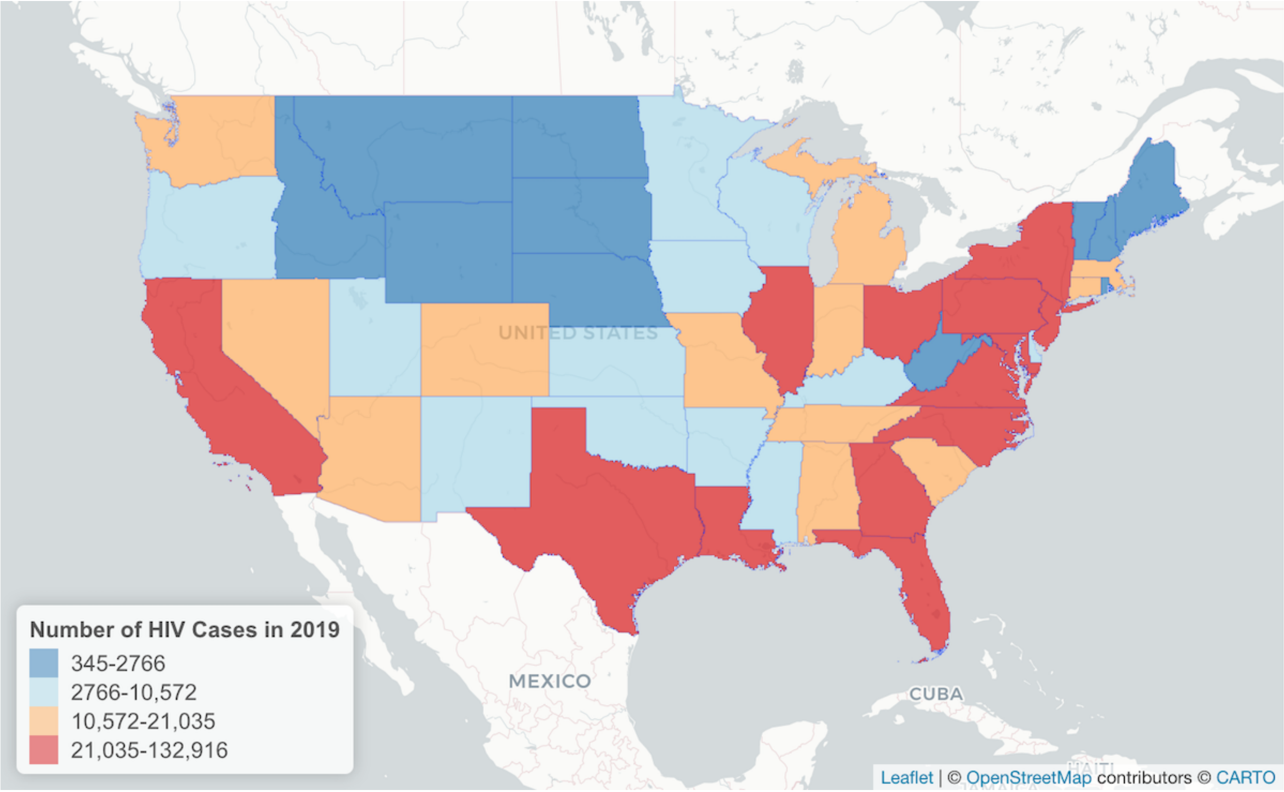
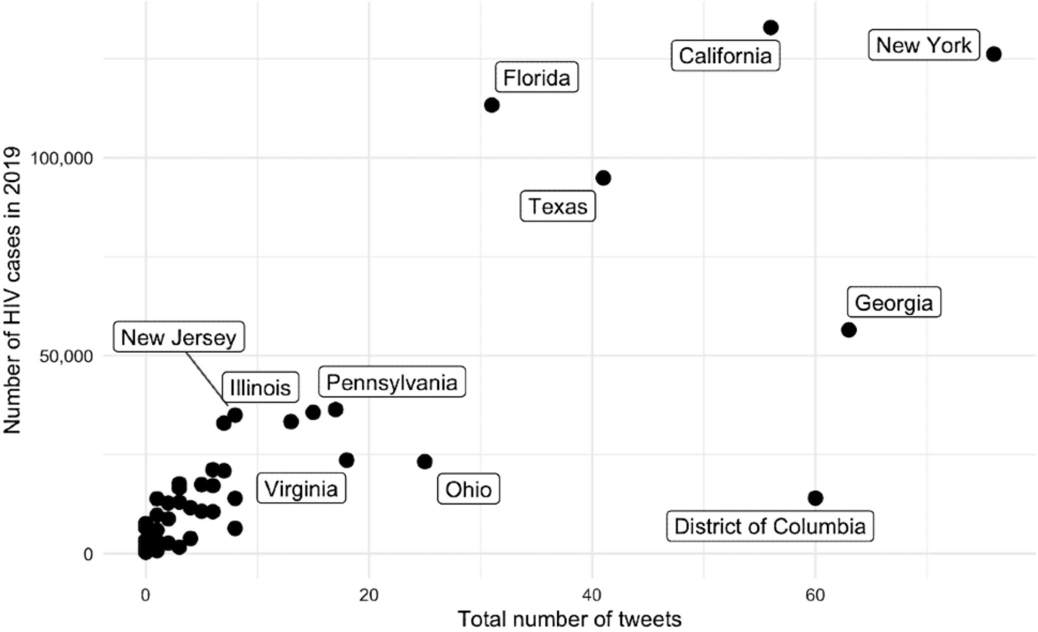


**Figure 6.** Relationship between the total number of geotagged #HIVPrevention tweets at the state level between 2014-2019 and the number of 2019 HIV cases by state.



## Analysis of the HIV Prevention Topics Being Referenced Most Often in #HIVPrevention Tweets

Of the total 69,197 #HIVPrevention tweets in the sample, 28,135 tweets (40.66%) were categorized into 1 or more of the 10 identified prevention topics. The highest proportion of mentions were seen for PrEP (13,895/69,197 tweets, 20.08% of all tweets). This was followed by the proportion of mentions related to HIV testing (7688/69,197, 11.11%), condoms (2941/69,197, 4.25%), harm reduction (2173/69,197, 3.14%), gender equity and violence against women (1695/69,197, 2.45%), VMMC (969/69,197, 1.40%), sex work (872/69,197, 1.26%), PEP (823/69,197, 1.19%), EMTCT (277/69,197, 0.40%), and abstinence (180/69,197, 0.26%). Categorized tweet totals do not add to 28,135, given that some tweets were categorized in more than 1 category.

Figure 7 illustrates the proportion of annual topic-specific tweets (original and retweets) as a function of total annual tweets for the following direct prevention topics: abstinence, condoms, PEP, testing, VMMC, EMTCT, and PrEP. The bottom panel of Figure 7 is presented on a smaller scale so the reader can better see the trends in the frequency of mentions of condom use, VMMC, PEP, EMTCT, and abstinence.

Table 2 displays the results of our chi-square and Fisher exact tests. The proportion of tweets mentioning PrEP, HIV testing, and PEP significantly increased between 2014 and 2019 (*P*≤.01 for all cases), whereas the proportion of tweets mentioning abstinence, condom use, VMMC, harm reduction, and gender equity significantly decreased in this period (*P*≤.01 for all cases).

**Figure 7.** Annual frequency of mentions of keywords related to abstinence, condom use, elimination of mother-to-child transmission, HIV testing, post-exposure prophylaxis, pre-exposure prophylaxis, and voluntary medical male circumcision as a proportion of total annual #HIVPrevention tweets between 2014 and 2019.

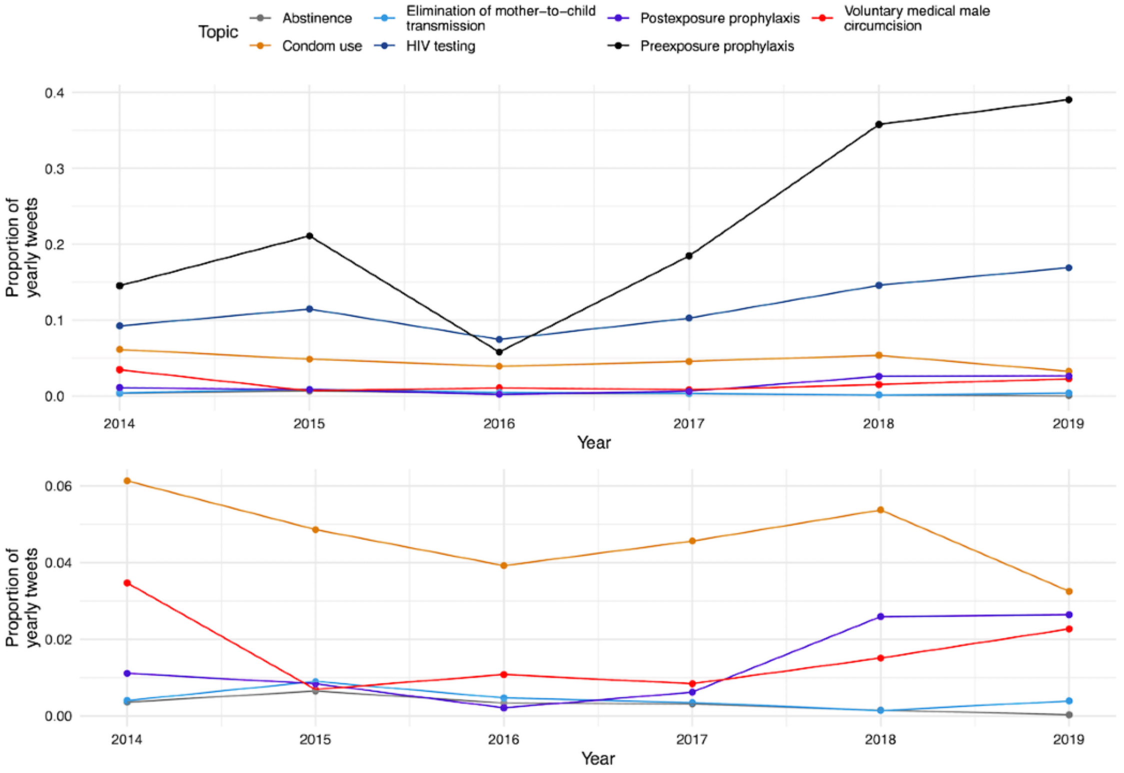


**Table 2.** Results of the chi-square and Fisher exact tests[a] evaluating the overall change in the proportion of tweets related to each topic area in 2014 versus 2019.

| Prevention topic | 2014 tweets (n=2251), n (%) | 2019 tweets (n=12,971), n (%) | *P* value | Direction of change |
|---|---|---|---|---|
| Abstinence | 8 (0.36) | 4 (0.03) | *≤.01*[b] | Lower |
| Condom use | 138 (6.13) | 421 (3.25) | *≤.01*[b] | Lower |
| Preexposure prophylaxis | 327 (14.53) | 5067 (39.06) | *≤.01*[b] | Higher |
| Voluntary medical male circumcision | 78 (3.47) | 295 (2.27) | *≤.01*[b] | Lower |
| Postexposure prophylaxis | 25 (1.11) | 342 (2.64) | *≤.01*[b] | Higher |
| Harm reduction | 93 (4.13) | 336 (2.59) | *≤.01*[b] | Lower |
| Gender inequity and violence against women | 74 (3.29) | 251 (1.94) | *≤.01*[b] | Lower |
| Elimination of mother-to-child transmission | 9 (0.40) | 51 (0.39) | .96 | N/A[c] |
| Sex work | 39 (1.73) | 198 (1.53) | .47 | N/A |
| HIV testing | 208 (9.24) | 2193 (16.91) | *≤.01* | Higher |

[a] Fisher exact test used when expected frequencies are less than 5.

[b] Italicized values are statistically significant.

[c] N/A: not applicable.

## Discussion

### Principal Findings

In this study, we investigated temporal trends in the frequency of mentions of 10 different HIV prevention topics in #HIVPrevention tweets between 2014 and 2019. Our findings describe how attention to different HIV prevention methods on Twitter has changed over time, which may provide insight into changes in the acceptability and uptake of these prevention methods. We also report useful descriptive information about our sample, such as the characteristics of accounts receiving the most retweets of #HIVPrevention tweets. These findings may assist public health professionals in identifying strategic approaches to improving the dissemination of HIV prevention information on Twitter.

Key findings from our analysis include the following: both PrEP and HIV testing were discussed at relatively high frequencies during the study period as compared with other HIV prevention methods such as condom use, VMMC, EMTCT, and PEP. Moreover, there were significantly higher proportions of #HIVPrevention tweets mentioning PrEP, HIV testing, and PEP in 2019 as compared with 2014, although the largest changes are seen for PrEP and testing. There were significantly lower proportions of #HIVPrevention tweets mentioning abstinence, VMMC, condom use, harm reduction, and gender inequity and violence against women in 2019 as compared with 2014. The increases in the proportion of tweets related to PrEP in 2017, 2018, and 2019 likely reflect approvals of PrEP for use in countries around the world between 2016 and 2018, including South Africa, South Korea, and the European Union [35], and updates to the WHO recommendations on which populations should use PrEP [30]. The relatively lower proportion of PrEP-related tweets in 2016 may reflect a larger representation of other prevention methods in comparison to PrEP during the WAD campaign. The significant decrease in the proportion of tweets mentioning condom use in 2019 as compared with 2014 might reflect the decrease in condom use which has been associated with uptake of PrEP in some populations [36,37]. The decline in abstinence-related tweets likely reflects the shift away from limited efficacy abstinence-based approaches to HIV prevention [38].

The high proportion of #HIVPrevention tweets related to PrEP and HIV testing is promising given that PrEP is highly effective at preventing HIV transmission [39] and research suggests that social media messages about PrEP directly or indirectly (through communication about PrEP use) correlate with HIV testing and PrEP use in regions with higher populations of MSM [12]. Moreover, a recent modeling study found that a scale-up of targeted PrEP and HIV testing in 6 US cities is expected to yield the largest reduction in new HIV infections as compared with other strategies such as harm reduction and initiation and retention of individuals diagnosed with HIV in antiretroviral therapy [40].

However, optimal adherence to PrEP can be a challenge for at-risk individuals; barriers include stigma, health system inaccessibility, and competing life stressors [41]. The efficacy of PrEP decreases as adherence decreases and with 2 doses per week, PrEP efficacy is similar to that of consistent condom use [39,42]. Moreover, the cost of PrEP (estimated at around US $24,000 a year) may pose a barrier to uptake by populations who do not have health insurance; even with insurance, out-of-pocket costs can be substantial [43]. For some populations, strong advocacy surrounding PrEP use for HIV prevention may deflect attention from more economically feasible or individually preferred prevention methods such as condoms [40,44]. It may also divert attention from the underlying social determinants of health relevant to HIV such as addiction, sex work, poverty, racial inequities, and gender inequity [13]; both gender equity and harm reduction represented proportionally less #HIVPrevention tweets (although higher absolute numbers) in 2019 compared with 2014. Scholars suggest that a combination of prevention options is required to effectively combat the HIV epidemic [22], as any one prevention method is unlikely to be a panacea. Our analysis suggests that condom use and especially PEP, EMTCT, and VMMC have received relatively little attention compared with PrEP on this platform; it may prove advantageous to ensure that information about these prevention topics is disseminated widely on Twitter to increase uptake and acceptability [5,40].

## Secondary Findings

Although our analysis reveals that individuals are responsible for the majority of accounts that correspond to the highest number of original #HIVPrevention tweets, UN-affiliated institutions and individuals appear to be reaching the most people as indicated by their retweet and follower counts, an unsurprising finding given the 2016 WAD campaign. However, the analysis of content generating and retweeted accounts also reveals the importance of informal advocates (eg, @HIV_Insight) and celebrity endorsements (eg, @MissUniverse); the latter may be particularly effective given the sheer number of users following celebrity accounts and the influence celebrities can have on health promotion [45].

Finally, our analysis of geotagged tweets suggests that #HIVPrevention tweets at a state level between 2014 and 2019 are positively correlated with the number of state-level HIV cases in the United States in 2019. This finding should be interpreted with caution given the small number of tweets in our sample that were geotagged. However, this finding is aligned with other research that suggests that tweet content such as discussing HIV risk-related behavior (eg, drug use) is associated with the geographic distribution of HIV [18,20].

## Study Strengths and Implications

To the best of our knowledge, this study is the first to investigate temporal trends in the relative attention received by different HIV prevention methods on Twitter. We are hopeful that the findings provide useful insight into how attention to HIV prevention methods on Twitter has changed over time, which may reflect or influence changes in the acceptability of these methods.

Some of the findings may be useful in informing strategic approaches to the dissemination of HIV prevention information on Twitter. For example, the findings indicate that a large portion of #HIVPrevention tweets mention PrEP and HIV testing. These tweets could be responded to by providing specific information about where to obtain an HIV test or how to access PrEP, which may empower individuals to engage in these behaviors. Furthermore, public health entities could consider leveraging celebrities as HIV advocates on Twitter given their wide reach and popularity, especially with young people. Finally, public health institutions may consider increasing communication about certain HIV prevention methods on Twitter such as condom use to ensure that populations with diverse needs and resources are aware of the HIV prevention options available to them.

## Study Limitations

There are some limitations of our study. First, we were limited to results procured from a single Twitter hashtag. Although this was a necessary methodological decision to define a sample of tweets focused on HIV prevention, it omits tweets that discuss HIV prevention but do not employ #HIVPrevention and it is possible that these tweets differ importantly from those that do employ the hashtag. Although we examined tweets corresponding to a critical period in the evolution of the acceptability of PrEP, resource and feasibility constraints limited us from investigating tweets posted immediately after PrEP was approved in the United States in 2012. We point the reader to previous research that yields insights into earlier periods [46-48] and encourage other researchers to investigate HIV prevention discussion on Twitter during the COVID-19 pandemic. Some prevention topics, such as gender inequity and harm reduction, are relatively more abstract and difficult to capture than others (eg, PrEP). Moreover, our analysis was restricted to tweets that are written in English, which obscures insights about HIV prevention discussions in other languages. This limits the validity of our map of geotagged #HIVPrevention tweets as a marker of overall discussion about HIV prevention on Twitter in the United States, as does the relatively small proportion of #HIVPrevention tweets that were geotagged. Moreover, disparities in access to internet services across the United States [49] may have influenced the characteristics of individuals who were tweeting about HIV prevention in our sample and the regions the tweets originated from. We were unable to ascertain the age or other demographic characteristics of the users in our data as a variable in our analysis.

## Conclusions

Twitter is an important avenue for information seeking about HIV prevention and may be a particularly important platform for disseminating information to young adults who represent a large burden of new infections [2,50]. Previous evidence suggests that public health messaging shapes the ways in which we conceptualize and respond to the HIV epidemic and thus examining trends in communication about HIV prevention over time is an important step for better understanding the course of the epidemic and planning effective strategies for the future [21]. The findings of our study indicate that PrEP and HIV testing have received the most attention in #HIVPrevention tweets between 2014 and 2019 as compared with other HIV prevention topics and that attention to PrEP and HIV testing in #HIVPrevention tweets increased over that period. Public health professionals may wish to leverage the findings to inform multifaceted efforts toward reducing HIV incidence.

## Acknowledgments

The authors thank all in the scholarly community who provided insight or asked critical questions about the study, such as when the findings were presented at the American Public Health Association Annual Meeting in October 2021. Funding to present this work at the American Public Health Association Conference in October 2021 was provided by the Yale School of Public Health and the Yale Graduate Student Assembly. RB’s PhD stipend is funded in part by a Doctoral Foreign Study Award from the Canadian Institutes of Health Research. The article processing fee (APF) for this article was paid by YR’s K01 grant (#K01MH111374).

## Data Availability

Data from this study are available upon request. Please email requests to josemari.feliciano@yale.edu. Proof of ethics approval/exemption for proposed use may be required.

## Authors' Contributions

RB led the study conceptualization, literature search, the qualitative component of the data analysis, data interpretation, and original draft writing. JTF led the data collection, quantitative data analysis, figure creation, and contributed to data interpretation and original draft writing. LL contributed to the study conceptualization, literature search, data interpretation, and manuscript editing. YR contributed to the study design, data interpretation, manuscript revision, and supervised the project. RB and JTF have directly accessed and verified the underlying data reported in the manuscript.

## Conflicts of Interest

None declared.

Multimedia Appendix 1
Identified prevention methods, associated keywords and examples of tweets related to each topic.
[DOCX File , 24 KB - publichealth_v8i8e35937_app1.docx ]

## References

1. UNAIDS. URL: https://www.unaids.org/en/resources/fact-sheet [accessed 2022-06-22]
2. Estimated HIV incidence and prevalence in the United States 2015-2019: HIV Surveillance Supplemental Report. CDC. 2021. URL: https://stacks.cdc.gov/view/cdc/112160 [accessed 2022-07-24]
3. Basic Statistics. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/hiv/basics/statistics.html [accessed 2022-07-24]

4. HIV Surveillance Report. Centers for Disease Control and Prevention. 2019. URL: http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html [accessed 2022-07-24]
5. Koblin BA, Usher D, Nandi V, Tieu H, Bravo E, Lucy D, et al. Post-exposure Prophylaxis Awareness, Knowledge, Access and Use Among Three Populations in New York City, 2016-17. AIDS Behav 2018 Aug;22(8):2718-2732. [doi: 10.1007/s10461-018-2175-5] [Medline: 29858737]
6. Eaton LA, Matthews DD, Driffin DD, Bukowski L, Wilson PA, Stall RD, POWER Study Team. A Multi-US City Assessment of Awareness and Uptake of Pre-exposure Prophylaxis (PrEP) for HIV Prevention Among Black Men and Transgender Women Who Have Sex with Men. Prev Sci 2017 Jul 18;18(5):505-516 [FREE Full text] [doi: 10.1007/s11121-017-0756-6] [Medline: 28101813]
7. Taggart T, Grewe M, Conserve D, Gliwa C, Roman Isler M. Social Media and HIV: A Systematic Review of Uses of Social Media in HIV Communication. J Med Internet Res 2015 Nov 02;17(11):e248 [FREE Full text] [doi: 10.2196/jmir.4387] [Medline: 26525289]
8. Huo J, Desai R, Hong Y, Turner K, Mainous A, Bian J. Use of Social Media in Health Communication: Findings From the Health Information National Trends Survey 2013, 2014, and 2017. Cancer Control 2019;26(1):1073274819841442 [FREE Full text] [doi: 10.1177/1073274819841442] [Medline: 30995864]
9. Ko N, Hsieh C, Wang M, Lee C, Chen C, Chung A, et al. Effects of Internet popular opinion leaders (iPOL) among Internet-using men who have sex with men. J Med Internet Res 2013 Feb 25;15(2):e40 [FREE Full text] [doi: 10.2196/jmir.2264] [Medline: 23439583]
10. Byron P, Albury K, Evers C. “It would be weird to have that on Facebook”: young people's use of social media and the risk of sharing sexual health information. Reproductive Health Matters 2013 May 14;21(41):35-44. [doi: 10.1016/s0968-8080(13)41686-5]
11. Kesten J, Dias K, Burns F, Crook P, Howarth A, Mercer C, et al. Acceptability and potential impact of delivering sexual health promotion information through social media and dating apps to MSM in England: a qualitative study. BMC Public Health 2019 Sep 06;19(1):1236 [FREE Full text] [doi: 10.1186/s12889-019-7558-7] [Medline: 31492120]
12. Chan M, Morales A, Zlotorzynska M, Sullivan P, Sanchez T, Zhai C, et al. Estimating the influence of Twitter on pre-exposure prophylaxis use and HIV testing as a function of rates of men who have sex with men in the United States. AIDS 2021 May 01;35(Suppl 1):S101-S109. [doi: 10.1097/QAD.0000000000002838] [Medline: 33867493]
13. León A, Cáceres C, Fernández E, Chausa P, Martin M, Codina C, et al. A new multidisciplinary home care telemedicine system to monitor stable chronic human immunodeficiency virus-infected patients: a randomized study. PLoS One 2011 Jan 21;6(1):e14515 [FREE Full text] [doi: 10.1371/journal.pone.0014515] [Medline: 21283736]
14. Hailey J, Arscott J. Using technology to effectively engage adolescents and young adults into care: STAR TRACK Adherence Program. J Assoc Nurses AIDS Care 2013;24(6):582-586. [doi: 10.1016/j.jana.2013.03.001] [Medline: 23809658]
15. Mo PKH, Coulson NS. Exploring the communication of social support within virtual communities: a content analysis of messages posted to an online HIV/AIDS support group. Cyberpsychol Behav 2008 Jun;11(3):371-374. [doi: 10.1089/cpb.2007.0118] [Medline: 18537512]
16. Cao B, Gupta S, Wang J, Hightow-Weidman L, Muessig K, Tang W, et al. Social Media Interventions to Promote HIV Testing, Linkage, Adherence, and Retention: Systematic Review and Meta-Analysis. J Med Internet Res 2017 Nov 24;19(11):e394 [FREE Full text] [doi: 10.2196/jmir.7997] [Medline: 29175811]
17. Jones K, Eathington P, Baldwin K, Sipsma H. The impact of health education transmitted via social media or text messaging on adolescent and young adult risky sexual behavior: a systematic review of the literature. Sex Transm Dis 2014 Jul;41(7):413-419. [doi: 10.1097/OLQ.0000000000000146] [Medline: 24922099]
18. Stevens R, Bonett S, Bannon J, Chittamuru D, Slaff B, Browne SK, et al. Association Between HIV-Related Tweets and HIV Incidence in the United States: Infodemiology Study. J Med Internet Res 2020 Jun 24;22(6):e17196 [FREE Full text] [doi: 10.2196/17196] [Medline: 32579119]
19. Roszkowska N, Lazarus E, Bannon J, Dowshen N, Stevens R. 2. From Bots to Jokes: Is There a Place For HIV Prevention on Twitter? Journal of Adolescent Health 2020 Feb;66(2):S1-S2. [doi: 10.1016/j.jadohealth.2019.11.005]
20. Li Z, Qiao S, Jiang Y, Li X. Building a social media-based HIV risk behavior index to inform the prediction of HIV new diagnosis: a feasibility study. AIDS 2021 May 01;35(Suppl 1):S91-S99 [FREE Full text] [doi: 10.1097/QAD.0000000000002787] [Medline: 33867492]
21. Taggart T, Ritchwood TD, Nyhan K, Ransome Y. Messaging matters: achieving equity in the HIV response through public health communication. The Lancet HIV 2021 Jun;8(6):e376-e386. [doi: 10.1016/s2352-3018(21)00078-3]
22. Litt D, Rodriguez L, Stewart S. Examining Associations Between Social Networking Site Alcohol-Specific Social Norms, Posting Behavior, and Drinking to Cope During the COVID-19 Pandemic. Cyberpsychol Behav Soc Netw 2021 Nov;24(11):715-721. [doi: 10.1089/cyber.2020.0568] [Medline: 33733832]
23. Young S, Jordan A. The influence of social networking photos on social norms and sexual health behaviors. Cyberpsychol Behav Soc Netw 2013 Apr;16(4):243-247 [FREE Full text] [doi: 10.1089/cyber.2012.0080] [Medline: 23438268]
24. Cerezo A, Ramirez A, O'Shaughnessy T, Sanchez A, Mattis S, Ross A. Understanding the Power of Social Media during COVID-19: Forming Social Norms for Drinking among Sexual Minority Gender Expansive College Women. J Homosex 2021 Mar 21;68(4):560-576. [doi: 10.1080/00918369.2020.1868183] [Medline: 33428564]

25. Lee T, Su L. When a Personal HPV Story on a Blog Influences Perceived Social Norms: The Roles of Personal Experience, Framing, Perceived Similarity, and Social Media Metrics. Health Commun 2020 Apr;35(4):438-446. [doi: 10.1080/10410236.2019.1567440] [Medline: 30719938]
26. Wombacher K, Reno J, Veil S. NekNominate: Social Norms, Social Media, and Binge Drinking. Health Commun 2017 May;32(5):596-602. [doi: 10.1080/10410236.2016.1146567] [Medline: 27331576]
27. Storey D, Seifert-Ahanda K, Andaluz A, Tsoi B, Matsuki J, Cutler B. What is health communication and how does it affect the HIV/AIDS continuum of care? A brief primer and case study from New York City. J Acquir Immune Defic Syndr 2014 Aug 15;66 Suppl 3:S241-S249. [doi: 10.1097/QAI.0000000000000243] [Medline: 25007193]
28. Eysenbach G. Infodemiology and infoveillance: framework for an emerging set of public health informatics methods to analyze search, communication and publication behavior on the Internet. J Med Internet Res 2009 Mar 27;11(1):e11 [FREE Full text] [doi: 10.2196/jmir.1157] [Medline: 19329408]
29. In Brief: FDA continues to encourage ongoing education about the benefits and risks associated with PrEP, including additional steps to help reduce the risk of getting HIV. Food and Drug Administration (FDA). 2019. URL: https://www.fda.gov/news-events/fda-brief/fda-brief-fda-continues-encourage-ongoing-education-about-benefits-and-risks-associated-prep [accessed 2022-07-24]
30. WHO Expands Recommendation on Oral Pre-Exposure Prophylaxis of HIV Infection (PrEP). World Health Organization (WHO). 2015. URL: https://www.who.int/hiv [accessed 2022-07-25]
31. World AIDS Day 2016. UNAIDS. 2016. URL: https://www.unaids.org/en/resources/campaigns/WAD2016 [accessed 2022-06-22]
32. NCHHSTP Atlas Plus. Centers for Disease Control and Prevention (CDC). URL: https://www.cdc.gov/nchhstp/atlas/index.htm [accessed 2022-07-25]
33. Hsieh H, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res 2005 Nov;15(9):1277-1288. [doi: 10.1177/1049732305276687] [Medline: 16204405]
34. OpenStreetMap. URL: https://www.openstreetmap.org/#map=0/-32/21 [accessed 2022-03-01]
35. National Policies and Guidelines for PrEP. PrEPWatch. 2021. URL: https://www.prepwatch.org/prep-planning/national-policies-guidelines/ [accessed 2022-07-25]
36. Holt M, Lea T, Mao L, Kolstee J, Zablotska I, Duck T, et al. Community-level changes in condom use and uptake of HIV pre-exposure prophylaxis by gay and bisexual men in Melbourne and Sydney, Australia: results of repeated behavioural surveillance in 2013-17. Lancet HIV 2018 Aug;5(8):e448-e456. [doi: 10.1016/S2352-3018(18)30072-9] [Medline: 29885813]
37. Montaño MA, Dombrowski JC, Dasgupta S, Golden MR, Duerr A, Manhart LE, et al. Changes in Sexual Behavior and STI Diagnoses Among MSM Initiating PrEP in a Clinic Setting. AIDS Behav 2019 Feb 16;23(2):548-555 [FREE Full text] [doi: 10.1007/s10461-018-2252-9] [Medline: 30117076]
38. Santelli J, Speizer I, Edelstein Z. Abstinence promotion under PEPFAR: the shifting focus of HIV prevention for youth. Glob Public Health 2013;8(1):1-12 [FREE Full text] [doi: 10.1080/17441692.2012.759609] [Medline: 23327516]
39. Anderson PL, Glidden DV, Liu A, Buchbinder S, Lama JR, Guanira JV, iPrEx Study Team. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. Sci Transl Med 2012 Sep 12;4(151):151ra125 [FREE Full text] [doi: 10.1126/scitranslmed.3004006] [Medline: 22972843]
40. Krebs E, Dale L. The impact of localized implementation: determining the cost-effectiveness of HIV prevention and care interventions across six United States cities. HIV Spec 2020 Mar;12(1):20-27. [Medline: 32368759]
41. Wood S, Gross R, Shea JA, Bauermeister JA, Franklin J, Petsis D, et al. Barriers and Facilitators of PrEP Adherence for Young Men and Transgender Women of Color. AIDS Behav 2019 Oct 16;23(10):2719-2729 [FREE Full text] [doi: 10.1007/s10461-019-02502-y] [Medline: 30993479]
42. Weller S, Davis-Beaty K. Using condoms consistently reduces sexual transmission of HIV infection. Cochrane. 2002 Jan 21. URL: https://tinyurl.com/3yh794yj [accessed 2022-07-25]
43. Furukawa NW, Zhu W, Huang YA, Shrestha RK, Hoover KW. National Trends in Drug Payments for HIV Preexposure Prophylaxis in the United States, 2014 to 2018. Ann Intern Med 2020 Nov 17;173(10):799-805. [doi: 10.7326/m20-0786]
44. Greene GJ, Swann G, Fought AJ, Carballo-Diéguez A, Hope TJ, Kiser PF, et al. Preferences for Long-Acting Pre-exposure Prophylaxis (PrEP), Daily Oral PrEP, or Condoms for HIV Prevention Among U.S. Men Who Have Sex with Men. AIDS Behav 2017 May 21;21(5):1336-1349 [FREE Full text] [doi: 10.1007/s10461-016-1565-9] [Medline: 27770215]
45. Francis DB, Stevens EM, Noar SM, Widman L. Public Reactions to and Impact of Celebrity Health Announcements: Understanding the Charlie Sheen Effect. Howard Journal of Communications 2018 Dec 24;30(5):479-494. [doi: 10.1080/10646175.2018.1532852]
46. Odlum M, Yoon S, Broadwell P, Brewer R, Kuang D. How Twitter Can Support the HIV/AIDS Response to Achieve the 2030 Eradication Goal: In-Depth Thematic Analysis of World AIDS Day Tweets. JMIR Public Health Surveill 2018 Nov 22;4(4):e10262 [FREE Full text] [doi: 10.2196/10262] [Medline: 30467102]
47. McLaughlin ML, Hou J, Meng J, Hu C, An Z, Park M, et al. Propagation of Information About Preexposure Prophylaxis (PrEP) for HIV Prevention Through Twitter. Health Commun 2016 Aug;31(8):998-1007. [doi: 10.1080/10410236.2015.1027033] [Medline: 26756069]

48. Schwartz J, Grimm J. PrEP on Twitter: Information, Barriers, and Stigma. Health Commun 2017 Apr;32(4):509-516. [doi: 10.1080/10410236.2016.1140271] [Medline: 27295507]
49. Yu RP, Ellison NB, McCammon RJ, Langa KM. Mapping the two levels of digital divide: Internet access and social network site adoption among older adults in the USA. Information, Communication & Society 2015 Nov 19;19(10):1445-1464. [doi: 10.1080/1369118x.2015.1109695]
50. Lim MS, Vella A, Sacks-Davis R, Hellard ME. Young people's comfort receiving sexual health information via social media and other sources. Int J STD AIDS 2014 Dec;25(14):1003-1008. [doi: 10.1177/0956462414527264] [Medline: 24616114]

## Abbreviations

**EHE:** ending the HIV epidemic in the United States
**EMTCT:** elimination of mother-to-child transmission
**FDA:** Food and Drug Administration
**MSM:** men who have sex with men
**PEP:** postexposure prophylaxis
**PEPFAR:** US President’s Emergency Plan for AIDS Relief
**PrEP:** preexposure prophylaxis
**UNAIDS:** Joint United Nations Programme on HIV/AIDS
**VMMC:** voluntary medical male circumcision
**WAD:** World AIDS Day
**WHO:** World Health Organization

*Edited by A Mavragani; submitted 23.12.21; peer-reviewed by A Wilson, R Shimkhada; comments to author 14.02.22; revised version received 24.06.22; accepted 11.07.22; published 11.08.22.*

*Please cite as:*
*Burgess R, Feliciano JT, Lizbinski L, Ransome Y*
*Trends and Characteristics of #HIVPrevention Tweets Posted Between 2014 and 2019: Retrospective Infodemiology Study*
*JMIR Public Health Surveill 2022;8(8):e35937*
*URL: https://publichealth.jmir.org/2022/8/e35937*
*doi:10.2196/35937*
*PMID:35969453*

Original Paper

# Estimating Changes in Population Size and Behavioral Characteristics in Men Who Have Sex With Men Between 2014 and 2019: Longitudinal Study

Zijie Yang[1,2,3], MPH; Lan Wei[1], PhD; Wei Xie[1], BM; Lin Chen[1], BM; Zhengrong Yang[1], MD; Yan Zhang[1], BM; Shaochu Liu[1], MPH; Wei Tan[1], MPH; Chenli Zheng[1], BM; Yongxia Gan[1], BM; Dongmin Li[4], MD; Huachun Zou[5], PhD; Wanying Chen[4], MPH; Ling Ma[6], MPH; Niu Ju[5], MPH; Yinghui Sun[5], MD; Fan Lv[4*], MD; Jin Zhao[1,3*], PhD

[1]Shenzhen Center for Disease Control and Prevention, Shenzhen, China
[2]School of Public Health, Peking Unversity, Beijing, China
[3]School of Public Health, Shantou Unversity, Shantou, China
[4]National Center for AIDS/Sexually Transmitted Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China
[5]School of Public Health, Sun Yat-sen University, Shenzhen, China
[6]Binhu District Centers for Disease Control and Prevention, Wuxi, China
[*]these authors contributed equally

**Corresponding Author:**
Jin Zhao, PhD
Shenzhen Center for Disease Control and Prevention
No. 8 Longyuan, Nanshan
Shenzhen, 518000
China
Phone: 86 75525632404
Email: szhaojin@gmail.com

## Abstract

**Background:** Men who have sex with men (MSM) are at high risk for HIV infection. Accurate estimation of the population size and monitoring the risk sexual behavioral change of MSM is of great importance to develop targeted HIV prevention and interventions.

**Objective:** The goal of the research was accurate estimation of the population size and monitoring the risk sexual behavioral change of MSM.

**Methods:** Street interception investigation methods were conducted among males aged 16 years and older in selected sites in Shenzhen in 2014 and 2019. A population survey was used to estimate the population size of MSM. Logistic regression analysis was applied to evaluate the difference in behavioral characteristics in MSM from 2014 to 2019.

**Results:** In this study, we surveyed 10,170 participants in 2014, of whom 448 (4.41%, 95% CI 4.01%-4.80%) participants were men who have ever had sex with another man (MSMe) and 229 (2.25%, 95% CI 1.96%-2.54%) were men who had sex with another man in the previous 6 months (MSMa). A total of 10,226 participants were surveyed in 2019, of which 500 (4.90%, 95% CI 4.47%-5.31%) and 208 (2.03%, 95% CI 1.76%-2.31%) participants were MSMe and MSMa, respectively. The results showed that the population size of MSM who are active (MSMa) in Shenzhen was 155,469 (2.29%, 95% CI 2.28%-2.30%) in 2014 and 167,337 (2.05%, 95% CI 2.04%-2.06%) in 2019. It was estimated that there were about 12,005,445 (2.04%, 95% CI 2.04%-2.04%) MSMa in China in 2019. Compared with 2014, the MSMa in 2019 were more likely to seek sex partners through mobile phone apps and less likely to have male and female sex partners in addition to having inconsistent condom use and more than 6 sex partners in the previous 6 months.

**Conclusions:** In Shenzhen, the proportion of MSMa among the general male population was lower in 2019 than in 2014, and the prevalence of HIV risk behavior was reduced in 2019. Although the preferred platform to find male sex partners among MSM has changed, intervention with high–HIV risk MSM could still help to reduce HIV risk behaviors among the whole MSM group. Because MSM prefer to seek sex partners through mobile phone apps, further study is needed to strengthen internet interventions with high–HIV risk MSM to curb the spread of HIV.

***(JMIR Public Health Surveill 2022;8(8):e34150)*** doi:10.2196/34150

**KEYWORDS**

men who have sex with men; population size; HIV/AIDS; behavioral characteristics

## Introduction

Men who have sex with men (MSM) are at high risk of HIV infection [1]. Previous studies suggested that the prevalence rate of HIV among MSM increased from 0.9% in 2003 to 6.3% in 2019 in China [2,3], and the proportion of MSM among newly diagnosed HIV/AIDS cases increased from 13.7% in 2011 to 23.3% in 2019 [4,5]. In Shenzhen, of the 99.6% of newly diagnosed HIV/AIDS cases in 2020 infected through sexual transmission, 62.6%were infected through male-to-male sexual transmission [6]. Accurate estimation of the prevalence of HIV among MSM depends on the precise population size of MSM, which remains underinvestigated in China. Accurate estimation of the precise population size of MSM could help us assess our progress toward the World Health Organization HIV testing and condom use targets of 95% coverage by 2030 [7].

Guidelines released by the Joint United Nations Programme on HIV and AIDS and the World Health Organization on estimating the size of populations most at risk of HIV infection recommend several methods (census and enumeration, capture-recapture, and multiplier) for estimating the MSM population size using data collected from the population at risk in addition to methods based on the general population (eg, population survey, network scale-up) [8]. In China, previous studies have mostly used the capture-recapture [9], multiplier [10], and network scale-up methods [11] to estimate the size of the MSM population; population survey has never been reported. The capture-recapture and multiplier methods mostly collect data from MSM venues, MSM websites, and social media, which may introduce sample selection bias by ignoring MSM who seek sex partners through other ways. MSM completing online surveys are more likely to be socially and sexually active [12]. Using the network scale-up method to estimate the size of the MSM population may introduce transmission error [8], meaning participants may be unaware that some of their network members are MSM because most MSM tend to conceal their homosexual status from family, relatives, and friends due to the stigma against homosexuality [13,14]. All methods mentioned above may contribute to underestimation of the size of the MSM population.

In recent years, social media has changed the way of social networking among MSM [15], especially for their homosexual partners [16]. Data on sentinel surveillance showed that HIV prevalence of MSM in some Chinese metropolises has been stable or slightly declining in the past several years [17], which might be attributed to the persistent and intensive HIV intervention and education focusing on MSM [18]. However, previous surveillance and intervention were implemented in MSM venues or their social network. The same sampling sources might lead to poor representativeness and exaggerate the effects of intervention. Whether similar change in behavioral patterns could be observed in all MSM needs further investigation. In this study, we used population survey with a quantifiable sampling frame to screen MSM samples from the general population, which is more representative and reliable for estimating MSM population size than other methods [19].

Shenzhen, the first city of reform and opening up in China, has shown high acceptance of homosexual culture and diverse MSM social venues [20]. A previous study suggested that Shenzhen is one of the most popular gathering places for MSM in China, with about 90% of MSM in Shenzhen being a floating population from all over the country [21]. Accurate estimation of the population size of MSM and evaluation of their behavioral changes are imperative for effective decision-making on public health resources allocation and planning and management of HIV prevention programmed to MSM. Therefore, we conducted a population survey among MSM in Shenzhen with aims to estimate the population size of MSM in Shenzhen and examine the changes of HIV risk behavioral characteristics of MSM in 2014 and 2019.

## Methods

### Data Collection

We selected investigation sites in Shenzhen in 2014 and 2019 according to the population, business district distribution, and the personnel migration (Figure 1, Table 1). Sites in the vicinity of MSM social venues were excluded. A street interception investigation method was conducted among males aged 16 years and older in selected sites. We adjusted the age and spatial distribution of the sample according to the age and spatial distribution of the total male population.

Each participant was required to complete a self-administered questionnaire on the tablet computer or paper questionnaire in 2014 and in 2019 by tablet computer or online questionnaire by scanning a QR code at designated sites. Duplicate participation was rejected after automated phone number check. Participants were reimbursed with a random amount ranging from 5 to 100 RMB (US $0.80-$16.00) by scanning one-time QR code in WeChat Pay after completing the questionnaire. The questionnaire consists of 2 sections: sociodemographic characteristics and HIV risk behaviors. Sociodemographic characteristics include age, educational level, household registration, length of time staying in Shenzhen, marital status, sexual orientation, and gender of sex partners. Participants who answered the gender of sex partners question male or male and female were asked to complete the section about HIV risk behaviors, which included preference for ways of social networking, number of male sex partners in the previous 6 months, frequency of sex with men in the previous 6 months, frequency of condom use during sex with regular/nonregular male sex partners in the previous 6 months, history of sexually transmitted infections (STIs), and HIV testing in the previous year.

**Figure 1.** Distribution of investigation sites in Shenzhen.

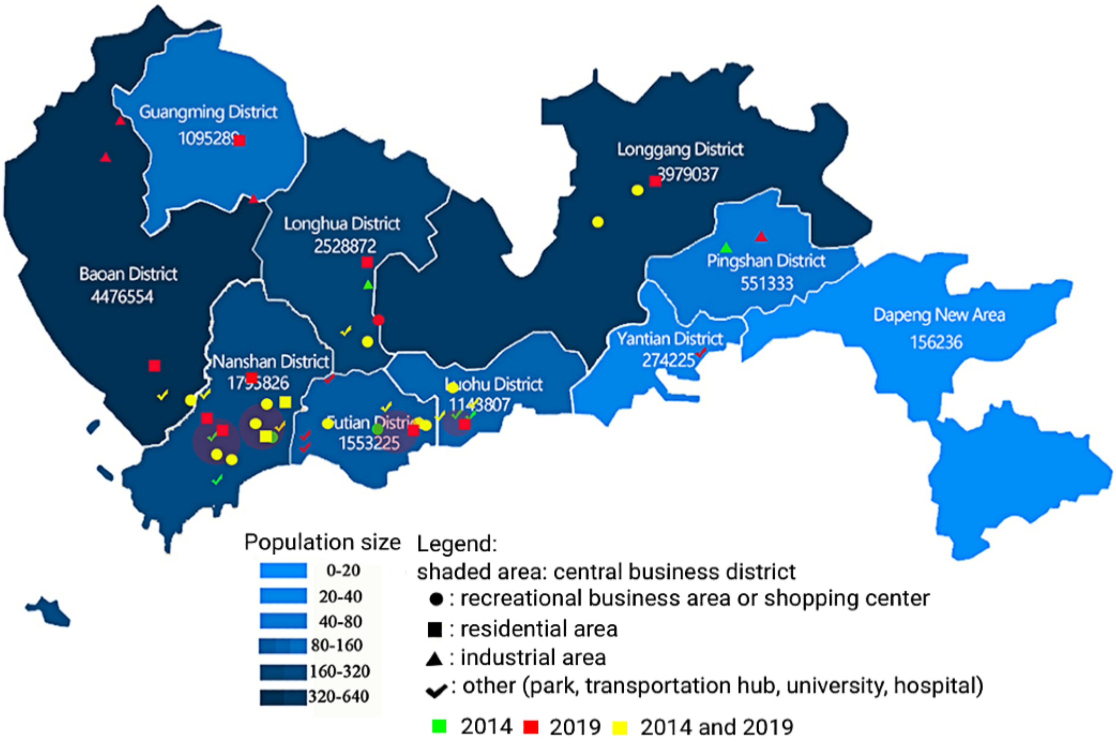


**Table 1.** Types of investigation sites in Shenzhen in 2014 and 2019.

| Sites | 2014, n | 2019, n |
|---|---|---|
| Recreational business area or shopping center | 22 | 16 |
| Residential area | 5 | 11 |
| Park | 10 | 7 |
| Transportation hub | 1 | 1 |
| University | 3 | 2 |
| Hospital | 3 | 3 |
| Industrial area | 4 | 5 |
| Total | 48 | 45 |

## Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval (SZCDC2019-010A) was granted by the ethics committee of the Shenzhen Center for Disease Control and Prevention.

## Calculation of Sample Size

The formula for calculating the sample size was computed as

$\alpha$ is type I error, $\alpha$=.05, then $U_\alpha$=1.96. $P_1$ is the proportion of MSM in the sample, estimated to be 4% according to experts from the Chinese Center for Disease Control and Prevention and the Shenzhen Center for Disease Control and Prevention. $\delta$ is the tolerance error, take $\delta=0.1P_1$. The sample size was 9220. Assuming the refusal rate is 10%, sample size was 10,245 participants in 2014. After the presurvey, we found that the actual refusal rate was less than 10%, so in 2019, we reduced the sample size to 10,000.

## Definition and Measure

Participants who had lived in Shenzhen longer than 6 months were considered local residents, while those who had been in Shenzhen for less than 6 months were considered part of the floating population. Men who had ever had sex with another man in their lifetime were designated *MSM ever* (MSMe), and men who had sex with another man in the previous 6 months were designated *MSM active* (MSMa). Participants were asked to estimate the frequency of condom use in sex with regular male sex partners in the previous 6 months and the frequency of condom use in sex with nonregular male sex partners in the previous 6 months, with these values totaling 100%.

## Population Size of MSM Estimation Methods

The formula for estimating the population size of MSM was computed as

$P_N$ is the proportion of MSM in the census population of males aged 16 years and older, $p$ is the proportion of MSM in participants, $n$ is the population of the different age groups in the census population, $N$ is the census population of males aged 16 years and older in Shenzhen, $i$ is the population category (1=local, 2=floating), and $j$ is the age group.

### Weighting

Considering the deviation of distribution in age and residence category (eg, local residents and floating population) between the sampled male participants and the census population of males aged 16 years and older in Shenzhen, weight adjustment was applied to control the confounding effect. The formula for calculating weight was computed as

$n_s$ is the population of different age groups in the sample, $N_s$ is the population of different residence categories in the sample, $n$ is the census population of different age group, $N$ is the census population of male aged 16 years and older of different residence categories in Shenzhen, $i$ is the residence category (1=local, 2=floating), and $j$ is the age group. The distribution of MSMe and MSMa in different age groups and population categories and the final weights are shown in Multimedia Appendix 1, Table S1.

### Statistical Analysis

The raw dataset was used to estimate the population size of MSM using equation 2, and other statistical analyses were conducted with the weighted data. A chi-square test was performed to examine the difference in frequency distribution. Logistic regression analysis was used to evaluate the difference in characteristics of MSM in 2019 versus 2014. Univariate analyses were further included in the multivariate analyses with forward stepwise selection ($P≤.05$ to enter, $P>.10$ to remove). All statistical analyses were performed in SPSS (version 20, IBM Corp). Odds ratio, adjusted odds ratio, and 95% confidence intervals were presented in the results. The significance level was .05.

## Results

### Descriptive Analysis

Of the men recruited in 2014, 41.3% (4200/10,170) were aged 21 to 30 years, 48.5% (4936/10,170) were married, and 82.9% (8438/10,170) were heterosexual. A total of 49.1% (4996/10,170) of participants had a household registration in other domestic provinces or regions, 79.9% (8128/10,170) were local residents, and 45.0% (4571/10,170) had attained an educational level of college or above. Of the men recruited in 2019, 36.9% (3775/10,226) were aged between 21 and 30 years, 48.6% (4970/10,226) were married, and 86.3% (8826/10,226) were heterosexual. A total of 46.5% (4751/10,226) of participants had a household registration in other provinces or regions, 77.9% (7966/10,226) were local residents, and 52.9% (5414/10,226) had an educational level of college or above (Multimedia Appendix 2).

In general, the proportion of MSMe and MSMa varied significantly ($P<.001$) by population categories, educational levels, marital status, and sexual orientation in 2014. The proportion of MSMe varied significantly by age ($P<.001$), and the proportion of MSMa varied significantly by household registration ($P=.02$, Multimedia Appendix 2). Of the MSMe in 2014 (Table 2), 58.0% (260/448) had both male and female sex partners, 17.6% (79/448) had been diagnosed with an STI, 23.9% (107/448) had HIV test in the previous year, and 33.9% (152/448) preferred to seek sex partners in MSM venues. Among the MSMa (Table 2), 55.9% (128/229) had both male and female sex partners, 27.1% (62/229) had been diagnosed with an STI in the previous year, 37.1% (85/229) had had an HIV test in the previous year, 42.4% (97/229) reported a preference for seeking sex partner in MSM venues, 80.8% (185/229) were non-100% condom use during the previous 6 months, 70.6% (161/229) reported 2 or more sex partners, and 72.9% (167/229) reported a frequency of sex with men 2 to 4 times per month in the previous 6 months. Multivariate logistic regression analysis showed that compared to the general male population, MSMe were less educated, more likely to be floating population, have unmarried status (divorced, widowed, separation, etc), and self-identify as homosexual or bisexual. The MSMa were more likely to be floating population, have other marital status, and self-identify as homosexual or bisexual compared to the general male population (Multimedia Appendix 1, Table S2).

As shown in Multimedia Appendix 2, the proportion of MSMe in 2019 varied significantly ($P<.05$) by age, population category, educational level, household registration status, marital status, and sexual orientation. The proportion of MSMa varied significantly ($P<.001$) by population category, marital status, and sexual orientation. Among the MSMe in 2019 (Table 2), 42.4% (212/500) had both male and female sex partners, 10.2% (51/500) had been diagnosed with an STI in the previous year, and 24.6% (123/500) had an HIV test in the previous year. Among the MSMa (Table 2), 31.7% (66/208) reported that they had both male and female sex partners, 16.8% (35/208) had been diagnosed with an STI in the previous year, 40.2% (84/208) had an HIV test in the previous year, 28.4% (59/208) reported preference to seek sex partner through mobile phone apps, 57.7% (120/208) were non-100% condom use, 56.7% (118/208) reported 2 or more sex partners, and 44.2% (92/208) reported sex with men 2 to 4 times every month in the previous 6 months. The result of multivariate logistic regression analysis showed that compared to the general male population, MSMe were less likely to be unmarried, aged 16 to 20 years, and more likely to be floating population and self-identify as homosexual or bisexual. The MSMa were more likely to be floating population, in unmarried status, and self-identify as homosexual or bisexual (Multimedia Appendix 1, Table S3).

**Table 2.** Prevalence of risk behaviors among men who have ever had sex with another man (MSMe) and men who had sex with another man in the previous 6 months (MSMa) in 2014 and 2019.

| | 2014 | | 2019 | |
|---|---|---|---|---|
| | MSMe (n=448), n (%) | MSMa (n=229), n (%) | MSMe, (n=500), n (%) | MSMa (n=208), n (%) |
| **Gender of sex partner** | | | | |
| Male only | 188 (41.96) | 101 (44.10) | 288 (57.60) | 142 (68.27) |
| Male and female | 260 (58.04) | 128 (55.90) | 212 (42.40) | 66 (31.73) |
| **STI[a] history** | | | | |
| Yes | 79 (17.63) | 62 (27.07) | 51 (10.20) | 35 (16.75) |
| No | 369 (82.37) | 167 (72.93) | 449 (89.80) | 174 (83.25) |
| **HIV testing history** | | | | |
| Yes | 107 (23.88) | 85 (37.12) | 123 (24.60) | 84 (40.19) |
| No | 341 (76.12) | 144 (62.88) | 377 (75.40) | 125 (59.81) |
| **Preferred platform to find male sex partners** | | | | |
| Venue frequented by MSM[b] | 152 (33.93) | 97 (42.36) | 90 (18.00) | 55 (26.44) |
| Internet | 127 (28.35) | 68 (29.69) | 87 (17.40) | 39 (18.75) |
| Mobile phone app | 71 (15.85) | 39 (17.03) | 119 (23.80) | 59 (28.37) |
| Other | 98 (21.88) | 25 (10.92) | 197 (39.40) | 55 (26.44) |
| **100% condom use when having sex with men** | | | | |
| No | —[c] | 185 (80.79) | — | 120 (57.69) |
| Yes | — | 44 (19.21) | — | 88 (42.31) |
| **Number of male sex partners** | | | | |
| 1 | — | 67 (29.4) | — | 90 (43.1) |
| 2 | — | 68 (29.7) | — | 40 (19.4) |
| 3-5 | — | 32 (14.1) | — | 43 (20.5) |
| ≥6 | — | 61 (26.8) | — | 35 (17.0) |
| **Frequency of sex with men** | | | | |
| ≤1 time a month | — | 62 (27.07) | — | 74 (35.58) |
| 2-4 times a month | — | 122 (53.28) | — | 92 (44.23) |
| ≥2 times a week | — | 45 (19.65) | — | 42 (20.19) |

[a] STI: sexually transmitted infections.

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

[c] Not applicable.

## Estimating the Population Size of MSM

In 2014, 448 (4.41%, 95% CI 4.01%-4.80%) participants were MSMe, and 229 (2.25%, 95% CI 1.96%-2.54%) were MSMa. In 2019, 500 (4.90%, 95% CI 4.47%-5.31%) were MSMe, and 208 (2.03%, 95% CI 1.76%-2.31%) participants were MSMa. Proportions of MSMe (*P*=.10) and MSMa (*P*=.28) were not significantly different between 2014 and 2019.

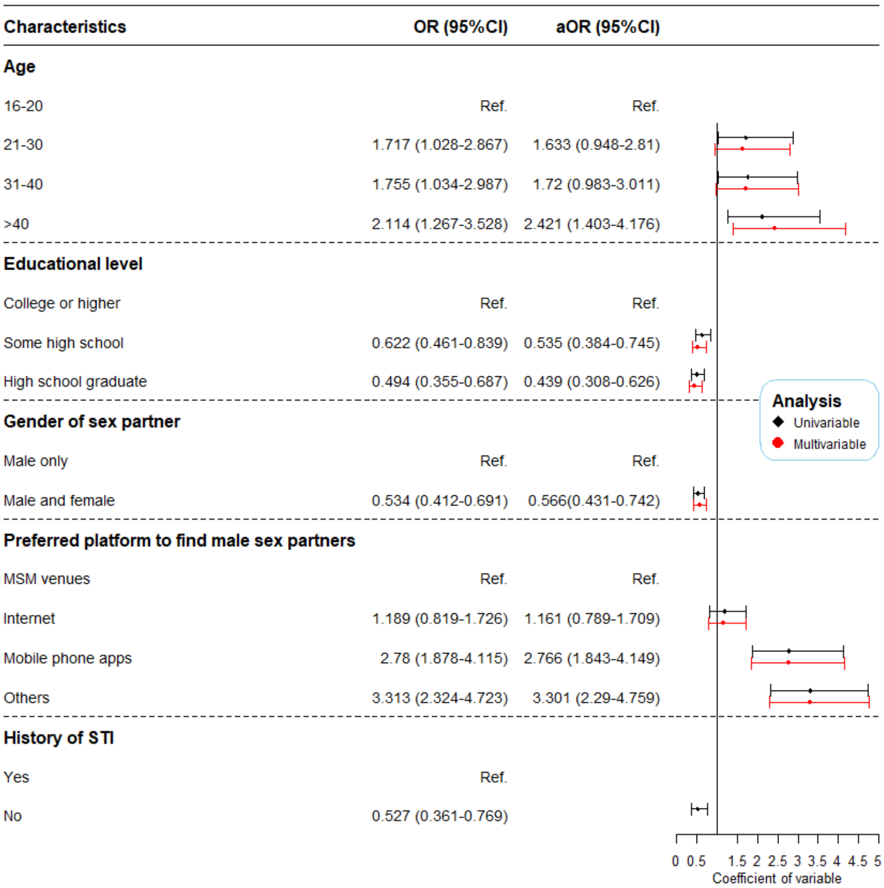
The proportion of MSMe in the male population aged 16 years and older was 4.51% (305,984/6,782,813, 95% CI 4.50%-4.53%) and 4.91% (400,689/8,158,157, 95% CI 4.90%-4.93%) in Shenzhen in 2014 and 2019, respectively. The proportion of MSMa in the male population aged 16 years and older was 2.29% (155,469/6,782,813, 95% CI 2.28%-2.30%) and 2.05% (167,337/8,158,157, 95% CI 2.04%-2.06%) in Shenzhen in 2014 and 2019, respectively.

In 2019, there were about 587.8 million males aged 16 years and older in China. Based on the proportion of MSM in Shenzhen in 2019, we estimated that the MSMe and MSMa population sizes in China were 30,434,062 (5.72%, 95% CI 5.72%-5.72%) and 12,005,445 (2.04%, 95% CI 2.04%-2.04%), respectively.

## Change in Characteristics of MSMe

Figure 2 summarized the difference in the characteristics of MSMe in 2014 and 2019. Based on the results of univariate logistic regression analysis, the variables age, length of stay in Shenzhen, educational level, gender of sex partner, preferred ways of seeking sex partners, and having been diagnosed with an STI in the previous year (*P*<.05) were included in multivariate logistic regression analysis. Compared to MSMe in 2014, MSMe in 2019 were more likely to be aged 41 years and older (aOR 2.42, 95% CI 1.40-4.18), preferred to seek sex partners through mobile phone apps (aOR 2.77, 95% CI 1.84-4.15) or other ways (aOR 3.30, 95% CI 2.29-4.76),were less likely to have an educational level of high school (aOR 0.44, 95% CI 0.31-0.63) or junior middle school or below (aOR 0.54, 95% CI 0.38-0.76), and reported having both male and female sex partners (aOR 0.57, 95% CI 0.43-0.74).

**Figure 2.** Changes in characteristics among men who have ever had sex with another man—2019 versus 2014. OR: odds ratio; ref: reference; MSM: men who have sex with men; STI: sexually transmitted disease.

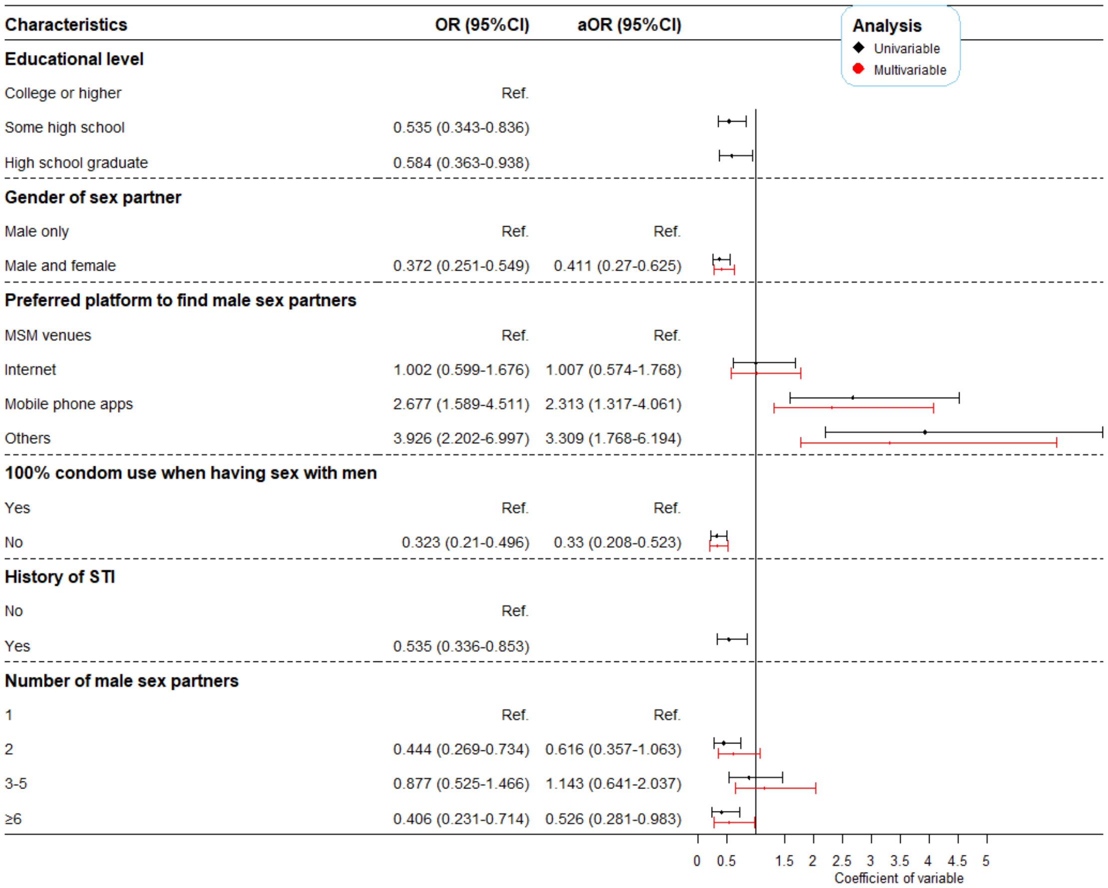


| Characteristics | OR (95%CI) | aOR (95%CI) |
|---|---|---|
| **Age** | | |
| 16-20 | Ref. | Ref. |
| 21-30 | 1.717 (1.028-2.867) | 1.633 (0.948-2.81) |
| 31-40 | 1.755 (1.034-2.987) | 1.72 (0.983-3.011) |
| >40 | 2.114 (1.267-3.528) | 2.421 (1.403-4.176) |
| **Educational level** | | |
| College or higher | Ref. | Ref. |
| Some high school | 0.622 (0.461-0.839) | 0.535 (0.384-0.745) |
| High school graduate | 0.494 (0.355-0.687) | 0.439 (0.308-0.626) |
| **Gender of sex partner** | | |
| Male only | Ref. | Ref. |
| Male and female | 0.534 (0.412-0.691) | 0.566(0.431-0.742) |
| **Preferred platform to find male sex partners** | | |
| MSM venues | Ref. | Ref. |
| Internet | 1.189 (0.819-1.726) | 1.161 (0.789-1.709) |
| Mobile phone apps | 2.78 (1.878-4.115) | 2.766 (1.843-4.149) |
| Others | 3.313 (2.324-4.723) | 3.301 (2.29-4.759) |
| **History of STI** | | |
| Yes | Ref. | |
| No | 0.527 (0.361-0.769) | |

## Change in Characteristics of MSMa

Figure 3 summarized the difference in characteristics of MSMa in 2014 and 2019. Variables including educational levels, gender of sex partner, non-100% condom use in the previous 6 months, being diagnosed with an STI in the previous year, preferred ways of social networking, and number of sex partners in the previous 6 months (*P*<.05) were added in the multivariate logistic regression model based on the results of univariate logistic regression analysis. The result showed that in 2019, MSMa were more likely to seek sex partner through mobile phone apps (aOR 2.31, 95% CI 1.32-4.06) and were less likely to have male and female sex partners (aOR 0.41, 95% CI 0.27-0.63), non-100% condom use (aOR 0.33, 95% CI 0.21-0.52), and more than 6 sex partners reported in the previous 6 months (aOR 0.53, 95% CI 0.28-0.98) compared to MSMa in 2014.

**Figure 3.** Changes in characteristics among men who had sex with another man in the previous 6 months—2019 versus 2014. OR: odds ratio; ref: reference; MSM: men who have sex with men; STI: sexually transmitted disease.



| Characteristics | OR (95%CI) | aOR (95%CI) |
|---|---|---|
| **Educational level** | | |
| College or higher | Ref. | |
| Some high school | 0.535 (0.343-0.836) | |
| High school graduate | 0.584 (0.363-0.938) | |
| **Gender of sex partner** | | |
| Male only | Ref. | Ref. |
| Male and female | 0.372 (0.251-0.549) | 0.411 (0.27-0.625) |
| **Preferred platform to find male sex partners** | | |
| MSM venues | Ref. | Ref. |
| Internet | 1.002 (0.599-1.676) | 1.007 (0.574-1.768) |
| Mobile phone apps | 2.677 (1.589-4.511) | 2.313 (1.317-4.061) |
| Others | 3.926 (2.202-6.997) | 3.309 (1.768-6.194) |
| **100% condom use when having sex with men** | | |
| Yes | Ref. | Ref. |
| No | 0.323 (0.21-0.496) | 0.33 (0.208-0.523) |
| **History of STI** | | |
| No | Ref. | |
| Yes | 0.535 (0.336-0.853) | |
| **Number of male sex partners** | | |
| 1 | Ref. | Ref. |
| 2 | 0.444 (0.269-0.734) | 0.616 (0.357-1.063) |
| 3-5 | 0.877 (0.525-1.466) | 1.143 (0.641-2.037) |
| ≥6 | 0.406 (0.231-0.714) | 0.526 (0.281-0.983) |

## Discussion

### Principal Findings

Accurate estimation of the population size of MSM is of great importance to develop HIV prevention and intervention and the strategy to achieve the 90-90-90 goals. As far as we know, this is the first study to estimate the MSM population size by population survey with random sampling in China. Based on this study, the population size of MSMa was estimated to be 154,059 in 2014 and 166,464 in 2019 in Shenzhen, higher than the 70,000 MSM estimated to be in Shenzhen in 2014 [20]; the population of MSMa in China was 12,005,445 in 2019, and the population of MSM in China was 8,288,536 in 2018 [9]. However, previous studies estimating the population size of MSM were based on the MSM venues [20] or social media [9] by capture-recapture, which recruited the sample from a specific group of MSM and might not fully represent the whole MSM population. In addition, the estimation of MSM population size based on social media may result in a high risk of bias because of duplicate registration in the app. For example, in Blued, the largest homosexual social media in China, the actual population size of MSM could be lower than the number of monthly active user (12 million in 2016) due to duplicate registration [22]. Furthermore, a previous study based on this social media only recruited Blued users as MSM, which might ignore the MSM who did not use this app and underestimate the population size of MSM in China [9]. In this study, we used a population survey with a large sample size of the general population to recruit MSM. It represented the whole MSM population and reduced the bias of estimation. Therefore, the results of this study could be reliable to reflect the actual population size of MSM.

The higher proportion of MSMe in 2019 compared to that in 2014 could mainly be attributed to the cumulative effect of time. Unlike MSMe, MSMa were sexually active and the main risky population in HIV prevention and control [23]. Since the reform and opening-up policy completed in the 1980s in China, the concept of sex among Chinese people has changed [24]. Casual sexual behavior has become more acceptable [25]. However, due to the lack of sex education, some teenagers learn about sexual orientation on their own, which may lead them to be induced to be homosexual [26,27]. The Chinese government has paid more attention to sex education since 2015 [28]. Teenagers can acquire sexual knowledge from school since 2015, and the whole society has become tolerant of homosexual behavior [29]. Consequently, teenagers can through the correct channels to learn sexual knowledge, including sexual orientation, which led to the proportion of MSMa being lower in 2019 than it was in 2014. Additionally, the prevalence of bisexual behaviors among MSMa was lower in 2019 than it was in 2014. With increasing tolerance of homosexuals in society [30], MSM would no longer have to get married to avoid stigma and social pressure. Therefore, the proportion of bisexual behavior was decreased accordingly, which helps reduce the risk of HIV transmission from MSM to women.

The epidemic of HIV/AIDS has been getting worse in China in the past decade [31] but declined in Shenzhen since 2017. This might be attributed to China's HIV treatment strategies and the reduced prevalence of HIV risk behavior among MSM in Shenzhen. China's HIV treatment strategy includes universal access to HIV Voluntary Counseling and Testing Clinics and free HIV treatment, which allows for greater access to testing and higher treatment adherence for people living with HIV in China than in other countries, thus facilitating our ability to reach the Undetectable=Untransmittable goal and even the 2030 goal of ending AIDS [32,33]. Shenzhen Center for Disease Control and Prevention has applied cross-sectional surveys on MSM annually by collecting samples in MSM venues or through social networks of these venue-based MSM since 2008 [34] and has implemented venue-specific interventions covering all the MSM venues in Shenzhen since 2015 [35]. The results of surveillance on MSM suggested that the prevalence of HIV risk behavior among the MSM who prefer to seek sex partners in specific venues was reduced after implementation of the venue-specific intervention [36]. However, because the series of cross-sectional studies only covered venue-based MSM and other MSM within their social network, the results cannot be extrapolated to the whole MSM group in Shenzhen. In this study, we found that prevalence of non-100% condom use, bisexual behavior, and more than 5 sex partners in the previous 6 months among MSMa in 2019 were much lower than that in 2014 and lower than in other countries [37]. In addition, the prevalence of HIV risk behavior was significantly lower in 2019 than it was in 2014 for MSM who preferred to seek sex partners in venues and other MSM subgroups. This finding indicates that the venue-specific interventions can not only directly influence MSM who preferred to seek sex partners in venues but also indirectly influence the whole population of MSM. The results of continuous surveillance based on MSM venues could help to deduce HIV risk behavior changes in the whole MSM population.

Data from annual MSM surveillance and this study suggested that the preferred way of seeking sex partners among MSMa changed from MSM venue to mobile phone apps from 2014 to 2019. A study in the United States suggested that gay app users had a higher risk of HIV infection and reported more sex partners and non-100% condom use than nonusers [38]. However, our study found that the prevalence of multiple sex partners among MSM who preferred to seek sex partners in venues was higher than other MSM, consistent with a series of cross-sectional studies [36] indicating that in Shenzhen, MSM who preferred to seek sex partners in venues have a higher risk than others of HIV infection. Furthermore, this study showed that 26.4% of MSMa sought sex partners in other ways (other-than-MSM venues, internet, and mobile phone apps) in 2019, increased by 3.3 times compared to that in 2014. That means MSM social networking preferences have become more diverse and private, leading to the increase of hidden MSM. This finding further verified that samples only from MSM venues, MSM websites, or social media might have selection bias and limit the representativeness of the whole MSM population.

In this study, we also found weak positive correlation between the prevalence of diagnosed STIs in the previous year and the prevalence of non-100% condom use among MSMa. The prevalence of diagnosed STIs in the previous year among MSMa was significantly decreased in univariate analysis from 2014 to 2019. However, the difference was not significant in the multivariate analysis; this may be attributed to the collinearity between the prevalence of diagnosed STIs in the previous year and the prevalence of non-100% condom use. Nevertheless, the causal relationships need to be validated in future studies.

## Limitations

Our study had several limitations. First, the result only reflected the population of Shenzhen, which might not be generalizable to the whole country. However, we have controlled the confounders and made a weight adjustment according to the census population, so the results of this study could offer a reference for other cities or areas in China. Second, MSM might conceal having sex with men because of the stigma and therefore induce reporting bias. We did our best to allow for this possibility by using self-administered questionnaires to elicit self-reported behavior and beliefs, which may have reduced the underreporting of sensitive behavior. All participants were informed that their contents were not visible to the field investigators and the questionnaire would not collect any personal identifiable information, which could prompt respondents to complete the questionnaire truthfully. Third, because of the sensitivity of the survey content, this study had a certain rate of rejection. Still, we calculated the population size by weighting on age and residence status. We also roughly assessed the age distribution of respondents and nonrespondents and found that they are similar.

## Conclusions

In Shenzhen, the proportion of MSMa among the general male population in 2019 was lower than in 2014, and the prevalence of HIV risk behavior was reduced in 2019. Although the preferred platform to find male sex partners among MSM has changed, the intervention on high HIV risk MSM could still help to reduce HIV risk behaviors among the whole MSM group. And because the MSM preferred to seek sex partners through mobile phone apps, further study is needed to strengthen internet intervention on high HIV risk MSM to curb the spread of HIV.

## Acknowledgments

This work was funded by grant 2019B1515120003 from the Guangdong Basic and Applied Basic Research Foundation, grant 81573211 from the National Natural Science Foundation of China, grant SZSM201811071 from the San-Ming Project of Medicine in Shenzhen, and grant SZXK064 from the Shenzhen Key Medical Discipline Construction Fund.

## Authors' Contributions

JZ, FL, and DL were responsible for conceptualization of the study and formulate the research goals and aims. ZJY, WX, SL, YZ, WT, CZ, YG, and JZ contributed to data collection. ZJY, JZ, LC, and ZRY contributed to data analysis and writing, and LW contributed to writing. ZJY, LW, DL, HZ, WC, LM, NJ, YS, JZ, and FL contributed to critical revision. Authors FL and JZ contributed equally as corresponding authors. All authors have approved the final version of this article and agree to be accountable for all aspects of the work.

## Conflicts of Interest

None declared.

Multimedia Appendix 1
Supplementary tables.
[DOCX File , 24 KB - publichealth_v8i8e34150_app1.docx ]

Multimedia Appendix 2
Proportion of men who have ever had sex with another man and men who had sex with another man in the previous 6 months among men in Shenzhen in 2014 and 2019 stratified by sociodemographic characteristics.
[DOCX File , 20 KB - publichealth_v8i8e34150_app2.docx ]

## References

1. Beyrer C, Baral SD, Collins C, Richardson ET, Sullivan PS, Sanchez J, et al. The global response to HIV in men who have sex with men. Lancet 2016 Jul;388(10040):198-206. [doi: 10.1016/s0140-6736(16)30781-4]
2. Tao J, Vermund SH, Lu H, Ruan Y, Shepherd BE, Kipp AM, et al. Impact of depression and anxiety on initiation of antiretroviral therapy among men who have sex with men with newly diagnosed HIV infections in China. AIDS Patient Care STDS 2017 Mar;31(2):96-104 [FREE Full text] [doi: 10.1089/apc.2016.0214] [Medline: 28170305]
3. The Joint United Nations Programme on HIV/AIDS. National HIV sentinel surveillance. URL: https://www.unaids.org/en/regionscountries/countries/china [accessed 2021-11-03]
4. STD and AIDS Prevention and Control Center. The epidemic situation of AIDS and STD in China and the progress of major prevention and treatment work in 2011. Chinese J AIDS STD 2012 Feb 26:64. [doi: 10.13419/j.cnki.aids.2012.02.007]
5. National Health Commission of the People's Republic of China. New progress in AIDS prevention and control in China in 2019. Chinese J AIDS STD 2019 Dec 26;25(12):1205. [doi: 10.13419/j.cnki.aids.2019.12.01]
6. The proportion of menstrual transmission among new AIDS cases in Shenzhen is 97%. URL: http://www.sznews.com/news/content/2019-12/01/content_22671756.htm [accessed 2022-07-27]
7. Nguyen P, Gilmour S, Le P, Onishi K, Kato K. Progress toward HIV elimination goals: trends in and projections of annual HIV testing and condom use in Africa. AIDS 2021;35(8):1253-1262. [doi: 10.1097/qad.0000000000002870]
8. UNAIDS: guidelines on estimating the size of populations most at risk to HIV. Geneva: World Health Organization; 2013. URL: http://data.unaids.org/pub/manual/2010/guidelines_popnestimationsize_en.pdf [accessed 2022-07-29]
9. Hu M, Xu C, Wang J. Spatiotemporal analysis of men who have sex with men in mainland china: social app capture-recapture method. JMIR Mhealth Uhealth 2020 Jan 24;8(1):e14800 [FREE Full text] [doi: 10.2196/14800] [Medline: 32012086]
10. Jing L, Cui Y, Lu Q, Yu H. Multiplier method estimates of the population of men who have sex with men: the effect of privacy protection. J Public Health (Oxf) 2020 May 26;42(2):429-434. [doi: 10.1093/pubmed/fdz019] [Medline: 30806667]
11. Guo W, Bao S, Lin W, Wu G, Zhang W, Hladik W, et al. Estimating the size of HIV key affected populations in Chongqing, China, using the network scale-up method. PLoS One 2013 Aug 13;8(8):e71796 [FREE Full text] [doi: 10.1371/journal.pone.0071796] [Medline: 23967246]
12. Marcus U, Hickson F, Weatherburn P, Schmidt AJ, EMIS Network. Estimating the size of the MSM populations for 38 European countries by calculating the survey-surveillance discrepancies (SSD) between self-reported new HIV diagnoses from the European MSM internet survey (EMIS) and surveillance-reported HIV diagnoses among MSM in 2009. BMC Public Health 2013 Oct 03;13(1):919 [FREE Full text] [doi: 10.1186/1471-2458-13-919] [Medline: 24088198]
13. Wang Y, Hu Z, Peng K, Xin Y, Yang Y, Drescher J, et al. Discrimination against LGBT populations in China. Lancet Public Health 2019 Sep;4(9):e440-e441. [doi: 10.1016/s2468-2667(19)30153-7]
14. Ding C, Chen X, Wang W, Yu B, Yang H, Li X, et al. Sexual minority stigma, sexual orientation concealment, social support and depressive symptoms among men who have sex with men in China: a moderated mediation modeling analysis. AIDS Behav 2020 Jan 29;24(1):8-17. [doi: 10.1007/s10461-019-02713-3] [Medline: 31664571]
15. Zou H, Fan S. Characteristics of men who have sex with men who use smartphone geosocial networking applications and implications for HIV interventions: a systematic review and meta-analysis. Arch Sex Behav 2017 May 4;46(4):885-894. [doi: 10.1007/s10508-016-0709-3] [Medline: 27043837]

16. Wang Z, Yang X, Mo PKH, Fang Y, Ip TKM, Lau JTF. Influence of social media on sexualized drug use and chemsex among Chinese men who have sex with men: observational prospective cohort study. J Med Internet Res 2020 Jul 24;22(7):e17894 [FREE Full text] [doi: 10.2196/17894] [Medline: 32706705]
17. Zhu Z, Yan H, Wu S, Xu Y, Xu W, Liu L, et al. Trends in HIV prevalence and risk behaviours among men who have sex with men from 2013 to 2017 in Nanjing, China: a consecutive cross-sectional survey. BMJ Open 2019 Jan 30;9(1):e021955 [FREE Full text] [doi: 10.1136/bmjopen-2018-021955] [Medline: 30705234]
18. Dong M, Peng B, Liu Z, Ye Q, Liu H, Lu X, et al. The prevalence of HIV among MSM in China: a large-scale systematic analysis. BMC Infect Dis 2019 Nov 27;19(1):1000 [FREE Full text] [doi: 10.1186/s12879-019-4559-1] [Medline: 31775654]
19. Mercer C, Fenton K, Copas A, Wellings K, Erens B, McManus S, et al. Increasing prevalence of male homosexual partnerships and practices in Britain 1990-2000: evidence from national probability surveys. AIDS 2004 Jul 02;18(10):1453-1458. [doi: 10.1097/01.aids.0000131331.36386.de] [Medline: 15199322]
20. Zhao J, Chen L, Cai W, Tan J, Tan W, Zheng C, et al. HIV infection and sexual behaviors among non-commercial men who have sex with men at different venues. Arch Sex Behav 2014 May 27;43(4):801-809. [doi: 10.1007/s10508-013-0167-0] [Medline: 23982566]
21. Zhao J, Cai W, Zheng C, Yang Z, Xin R, Li G, et al. Origin and outbreak of HIV-1 CRF55_01B among MSM in Shenzhen, China. J Acquir Immune Defic Syndr 2014 Jul 01;66(3):e65-e67. [doi: 10.1097/QAI.0000000000000144] [Medline: 24662297]
22. Wang L, Podson D, Chen Z, Lu H, Wang V, Shepard C, et al. Using social media to increase HIV testing among men who have sex with men—Beijing, China, 2013-2017. MMWR Morb Mortal Wkly Rep 2019 May 31;68(21):478-482 [FREE Full text] [doi: 10.15585/mmwr.mm6821a3] [Medline: 31145721]
23. Prestage GP, Hudson J, Down I, Bradley J, Corrigan N, Hurley M, et al. Gay men who engage in group sex are at increased risk of HIV infection and onward transmission. AIDS Behav 2009 Aug 26;13(4):724-730. [doi: 10.1007/s10461-008-9460-7] [Medline: 18818998]
24. Yu J. Teenage sexual attitudes and behaviour in China: a literature review. Health Soc Care Community 2012 Nov;20(6):561-582. [doi: 10.1111/j.1365-2524.2011.01054.x] [Medline: 22404303]
25. Li G, Jiang Y, Zhang L. HIV upsurge in China's students. Science 2019 May 24;364(6442):711. [doi: 10.1126/science.aay0799] [Medline: 31123112]
26. Hébert M, Cénat JM, Blais M, Lavoie F, Guerrier M. Child sexual abuse, bullying, cyberbullying, and mental health problems among high schools students: a moderated mediated model. Depress Anxiety 2016 Jul 01;33(7):623-629 [FREE Full text] [doi: 10.1002/da.22504] [Medline: 27037519]
27. Young JC, Widom CS. Long-term effects of child abuse and neglect on emotion processing in adulthood. Child Abuse Negl 2014 Aug;38(8):1369-1381 [FREE Full text] [doi: 10.1016/j.chiabu.2014.03.008] [Medline: 24747007]
28. Burki T. Sex education in China leaves young vulnerable to infection. Lancet Infect Dis 2016 Jan;16(1):26. [doi: 10.1016/s1473-3099(15)00494-6]
29. Tao J, Ruan Y, Yin L, Vermund SH, Shepherd BE, Shao Y, et al. Sex with women among men who have sex with men in China: prevalence and sexual practices. AIDS Patient Care STDS 2013 Sep;27(9):524-528 [FREE Full text] [doi: 10.1089/apc.2013.0161] [Medline: 23931683]
30. Chua RYJ, Huang KG, Jin M. Mapping cultural tightness and its links to innovation, urbanization, and happiness across 31 provinces in China. Proc Natl Acad Sci U S A 2019 Apr 02;116(14):6720-6725 [FREE Full text] [doi: 10.1073/pnas.1815723116] [Medline: 30833399]
31. National Health Commission of the People's Republic of China. Strategy and analysis of AIDS prevention and control in China. In: the 6th national academic conference on HIV/AIDS; Hangzhou, China; 2019 Presented at: 6th Natl Acad Conf HIV/AIDS; 2019; Hangzhou.
32. Le PM, Nguyen PT, Nguyen HV, Bui DH, Vo SH, Nguyen NV, et al. Adherence to highly active antiretroviral therapy among people living with HIV and associated high-risk behaviours and clinical characteristics: a cross-sectional survey in Vietnam. Int J STD AIDS 2021 Sep 16;32(10):911-918. [doi: 10.1177/09564624211002405] [Medline: 33861666]
33. Nguyen PT, Rahman MS, Le PM, Nguyen HV, Vu KD, Nguyen HL, et al. Trends in, projections of, and inequalities in reproductive, maternal, newborn and child health service coverage in Vietnam 2000-2030: a Bayesian analysis at national and sub-national levels. Lancet Reg Health West Pac 2021 Oct;15:100230 [FREE Full text] [doi: 10.1016/j.lanwpc.2021.100230] [Medline: 34528011]
34. Huang Y, Zhang Y, Li K, Zhao J. Changes in prevalence of HIV or syphilis among male sex workers and non-commercial men who have sex with men in Shenzhen, China: results of a second survey. PLoS One 2016;11(12):e0167619 [FREE Full text] [doi: 10.1371/journal.pone.0167619] [Medline: 27935980]
35. Tan JG, Cheng JQ, Lu ZX. [Evaluation of effects of combination intervention model to men who have sex with men]. Chin J Prev Med 2012 Aug;46(8):732-735. [Medline: 23157869]
36. Wei L, Chen L, Zhang H, Yang Z, Zou H, Yuan T, et al. Use of gay app and the associated HIV/syphilis risk among non-commercial men who have sex with men in Shenzhen, China: a serial cross-sectional study. Sex Transm Infect 2019 Nov 27;95(7):496-504. [doi: 10.1136/sextrans-2018-053902] [Medline: 30918120]

37. Nguyen PT, Gilmour S, Le PM, Nguyen TT, Tanuma J, Nguyen HV. Factors associated with high-risk behaviors of people newly diagnosed with HIV/AIDS: results from a cross-sectional study in Vietnam. AIDS Care 2021 May 13;33(5):607-615. [doi: 10.1080/09540121.2020.1761519] [Medline: 32397740]
38. Abuelezam NN, Reshef YA, Novak D, Grad YH, Seage Iii GR, Mayer K, et al. Interaction patterns of men who have sex with men on a geosocial networking mobile app in seven United States metropolitan areas: observational study. J Med Internet Res 2019 Sep 12;21(9):e13766 [FREE Full text] [doi: 10.2196/13766] [Medline: 31516124]

## Abbreviations

**aOR:** adjusted odds ratio
**MSM:** men who have sex with men
**MSMa:** men who had sex with another man in the previous 6 months
**MSMe:** men who have ever had sex with another man
**OR:** odds ratio
**STI:** sexually transmitted infection

---

*Edited by H Bradley; submitted 08.10.21; peer-reviewed by J Opoku, A Lansky, P Nguyen; comments to author 21.02.22; revised version received 18.05.22; accepted 26.06.22; published 16.08.22.*

*Please cite as:*
*Yang Z, Wei L, Xie W, Chen L, Yang Z, Zhang Y, Liu S, Tan W, Zheng C, Gan Y, Li D, Zou H, Chen W, Ma L, Ju N, Sun Y, Lv F, Zhao J*
*Estimating Changes in Population Size and Behavioral Characteristics in Men Who Have Sex With Men Between 2014 and 2019: Longitudinal Study*
*JMIR Public Health Surveill 2022;8(8):e34150*
*URL: https://publichealth.jmir.org/2022/8/e34150*
*doi:10.2196/34150*
*PMID:35972779*

Original Paper

# The Role of Depressive Symptoms and Physical Activity Levels in Mediating the Association Between HIV Status and Neurocognitive Functions Among Individuals Aged at Least 50 Years in China: Cross-sectional Study

Pei Qin[1,2], PhD; Jianmei He[3], MD; Xue Yang[2], PhD; Siyu Chen[2], MSc; Xi Chen[3], MD; Hui Jiang[2], PhD; Ada Wai Tung Fung[4], PhD; Zixin Wang[2*], PhD; Joseph Tak Fai Lau[2,5,6,7*], PhD

[1]Shenzhen Qianhai Shekou Free Zone Hospital, Shenzhen, China
[2]Jockey Club School of Public Health and Primary Care, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, Hong Kong
[3]Hunan Provincial Center for Disease Control and Prevention, Changsha, China
[4]Department of Applied Social Sciences, The Hong Kong Polytechnic University, Hong Kong, Hong Kong
[5]Affilliated Kangning Hospital of Wenzhou Medical University, Wenzhou Medical University, Wenzhou, China
[6]School of Mental Health, Wenzhou Medical University, Wen Zhou, China
[7]School of Public Health, Zhejiang University, Zhejiang, China
[*]these authors contributed equally

**Corresponding Author:**
Joseph Tak Fai Lau, PhD
Affilliated Kangning Hospital of Wenzhou Medical University
Wenzhou Medical University
No. 1 Shengjin Road, Huanglong Residential Area
Wenzhou, 325000
China
Phone: 86 400 000 2120
Email: jlau@cuhk.edu.hk

## Abstract

**Background:** Neurocognitive impairments are prevalent among older people in China. It is more problematic among older people living with HIV.

**Objective:** This study aims to compare neurocognitive performance between older people living with HIV and HIV-negative controls, and to explore whether the association between HIV status and neurocognitive performance was mediated by depressive symptoms and level of physical activity.

**Methods:** A cross-sectional study was conducted in Yongzhou, China. All people living with HIV aged ≥50 years listed in the registry were invited. Frequency matching was used to sample HIV-negative controls from the general population according to the distribution of age, sex, and years of formal education of older people living with HIV. A total of 315 older people living with HIV and 350 HIV-negative controls completed the face-to-face interview and comprehensive neuropsychological assessment of seven domains (learning, memory, working memory, verbal fluency, processing speed, executive function, and motor skills).

**Results:** As compared to HIV-negative controls, older people living with HIV performed worse in global score and all seven domains ($P<.05$). HIV infection was associated with higher depressive symptoms ($P<.001$) and lower level of physical activity ($P<.001$). Depressive symptoms and physical activity were negatively correlated ($P<.001$). Depressive symptoms and level of physical activity mediated the association between HIV status and global *z*-score and four domain *z*-scores of neurocognitive performance (learning, memory, verbal fluency, and processing speed).

**Conclusions:** Change in mental health and physical activity after HIV infection may partially explain why older people living with HIV are more susceptible to neurocognitive impairment. Promoting mental health and physical activity are potential entry points to slow down the progress of neurocognitive impairment among older people living with HIV.

***(JMIR Public Health Surveill 2022;8(8):e32968)*** doi:10.2196/32968

**KEYWORDS**

neurocognitive performance; HIV sero-status; depressive symptoms; level of physical activity; mediation effects; HIV; depression; physical activity; neurocognitive; mental health; public health

## Introduction

The Centres for Disease Control and Prevention specify the age of older people living with HIV as 50 and above [1,2]. Globally, the size of older people living with HIV has been increasing rapidly due to the advancement in the efficacy and coverage of antiretroviral therapy (ART) [3-5]. Take the United States as an example; the proportion of people living with HIV aged 50 years or above was about 45% in 2014 and was projected to exceed 75% in 2030 [6]. In China, such proportion has increased by 20% from 2001 (1.94%) to 2011 (21.1%) [7]. Older people living with HIV are more likely to have aging-related conditions due to HIV infection [8,9].

HIV infection is a risk factor of neurocognitive impairment. Studies showed older people living with HIV had poorer neurocognitive function as compared to HIV-negative individuals [10-12]. Neurocognitive impairment is prevalent and consequential among older people living with HIV [13]. The Central Nervous System HIV Antiretroviral Therapy Effects Research study reported that nearly half of people living with HIV suffered from neurocognitive impairment [13]. Other studies showed that 37.0%-69.9% of older people living with HIV in some western countries had such condition [14,15]. Neurocognitive impairment results in poorer adherence to ART, faster disease progression, poorer quality of life, and higher all-cause mortality among people living with HIV [16-20].

Mental health problems (eg, depression) are the most commonly reported comorbid conditions of people living with HIV [21]. Studies consistently showed that mental health problems are more common among older people living with HIV as compared to their younger counterparts [22]. Across countries, the prevalence of depression among older people living with HIV ranged from 39.1% to 60.5% [23-26]. There are potential reasons that may contribute to the elevated risk of mental health problems among older people living with HIV. Studies showed that age-related reduction in immune responses, impaired physical function, greater difficulties to cope with HIV-related stress, and reduced social support might contribute to or exacerbate existing mental health problems among older people living with HIV [22,25]. Studies suggest that depression is associated with brain vascular disease, which damages critical cortico-striatal circuits and results in neurocognitive impairment [27]. Depression is a strong risk factor of neurocognitive impairment among both general populations [28] and people living with HIV [11,29,30].

Physical activities are beneficial and recommended for older people living with HIV [31]. Studies showed that higher level of physical activity was associated with lower odds of neurocognitive impairment among older people living with HIV [32,33]. However, older people living with HIV encountered more barriers to perform physical activities as compared to their HIV-negative counterparts. Many barriers are related to their HIV-positive status. First, older people living with HIV are more likely to develop age-related chronic conditions, including cardiovascular diseases, lung diseases, and cancer, which have been shown to negatively affect physical function and the ability to perform physical activities [34]. Second, side effects of ART, reduced social support due to HIV infection, and social stigma or discrimination also hinder older people living with HIV to do physical activities [35,36]. Therefore, there is a large body of literatures showing that older people living with HIV, even when virally suppressed by ART, exhibit much lower level of physical activity when compared to age-matched HIV-negative controls [37-39]. A recent study showed that 86% of older people living with HIV did not achieve the recommended physical activity level, as measured by accelerometer [40].

Given depressive symptoms and physical activities were associated with both HIV infection and neurocognitive function among older people living with HIV, it is possible that depressive symptoms and level of physical activity would mediate the association between HIV infection and neurocognitive function. Identifying mediators is important to explain the difference in neurocognitive function between older people living with HIV and their HIV-negative counterparts. The path analysis has significant implications for interventions, and health workers can alleviate the adverse effect of HIV infection on neurocognitive function among older people. To our knowledge, no study has tested such a mediation hypothesis.

In this study, we compared neurocognitive performance (global score and seven domains), depressive symptoms, and level of physical activity between older people living with HIV and HIV-negative controls matched by age, gender, and education in China. We further test the hypothesis that depressive symptoms and level of physical activity would mediate the association between HIV infection and neurocognitive performance.

## Methods

### Study Design

A cross-sectional study was conducted in Yongzhou city in southern China from March to December 2017. The city has a population size of 6.3 million and a disposable income per capita of 15,292 RMB (US $2438) in 2015 (median in China was 22,408 RMB [US $3573]). The city consists of 2 districts and 9 counties. One district (Lingling) and 4 counties (Ningyuan, Lanshan, Qiyang, and Dao) were conveniently selected as the study sites.

### Participants

Participants were older people aged ≥50 who received confirmatory HIV diagnosis. Exclusion criteria included the following: (1) severe hearing loss or impaired vision observed by the interviewers, (2) history of brain injury with or without loss of consciousness (>30 minutes), brain tumor, stroke, or brain opportunistic infection; and (3) major psychiatric illnesses (schizophrenia and bipolar disorder). The second and third exclusion criteria were self-reported information or based on clinicians' assessments according to their medical records.

## Data Collection

Provincial or local Centres for Disease Control and Prevention and HIV clinics of local hospitals facilitated the recruitment of older people living with HIV. These institutions serve all people living with HIV in the selected district and counties and are responsible for HIV testing and diagnosis, CD4 (cluster of differentiation 4) testing, and management of the ART. The staff of these institutions contacted all older people living with HIV listed in the registries of the selected district and counties. With verbal consent, they screened prospective participants' eligibilities to join the study, briefed them about the purpose and logistics of the study, and invited them to be interviewed at the HIV clinics. The participants were assured that their information would be kept confidential, and refusal to participate would not affect their right to use future services. Written informed consent was obtained before conducting the face-to-face interviews and the neurocognitive assessments. The whole process took 1.5-2 hours to complete, with breaks in between. Upon completion, a monetary incentive of 50 RMB (US $7.96) was given to the participants for their time.

HIV-negative controls were recruited from general population in the corresponding study sites. In these study sites, health service centers provide comprehensive health-related services to local residents. These centers keep contact information of all residents living in the area. In this study, these health service centers facilitated the recruitment of HIV-negative controls. We used frequency matching to sample HIV-negative controls according to the distribution of age (SD 3 years), sex, and years of formal education of older people living with HIV. Staff of the health service centers approached households in person or via telephone, screened eligibility, and invited eligible residents to participate. The procedures for obtaining written informed consent and conducting face-to-face interview and neurocognitive assessment were the same as those for older people living with HIV. These participants were then invited to take a finger-prick HIV rapid test (Alere Determine HIV-1/2 rapid HIV screening test, Alere Inc, Watham, MA, United States; sensitivity: 99.75%, specificity: 100%).

## Ethics Approval

Ethics approval was obtained from the Survey and Behavioral Research Ethics Committees of the Chinese University of Hong Kong and the joint Chinese University of Hong Kong—New Territories East Cluster Clinical Research Ethics Committee (Ref# 2017.550).

## Neurocognitive Assessments

The comprehensive neuropsychological test battery was used in this study. It comprised of neuropsychological tests of seven domains. Learning and memory were assessed by the Chinese Auditory Verbal Learning Test [41]. Attention or working memory was measured by the digit span (forward and backward) and visual span (forward and backward) methods [42]. Information processing speed was assessed by the performance on the Chinese Trail Making Test Part A [43]. Executive function was assessed by the Chinese Trail Making Test Part B [44]. Verbal fluency was assessed by the category verbal fluency tests (animal, fruit, and vegetable) [45]. Motor skills were evaluated by the grooved pegboard for both dominant hand and nondominant hand [46]. These tests were commonly used in studies targeting people living with HIV [47] and were validated in the Chinese population [48].

PQ received intensive training on neurocognitive assessment from an experienced and practicing neuropsychologist. She completed neurocognitive assessments for ten older people living with HIV in the study sites. All practice assessments were audiotaped and sent to the neuropsychologist for review and competence assessment, which were found to be satisfactory. The first author then conducted a 2-week training workshop including guided practice and competence assessment for 4 other interviewers. They were deployed in fieldwork after they achieved satisfactory level of competence. During the first 2 weeks of fieldwork, PQ supervised neurocognitive assessments conducted by these 4 interviewers and provided individual feedback.

Raw scores of the aforementioned seven domains were transformed into standardized *z*-score, based on the mean and SD of the HIV-negative controls using the following formula: z-score = (raw test score – mean test score among HIV-negative controls) / SD of the test score among HIV-negative controls. Domain *z*-score was calculated by averaging the *z*-scores of tests in each domain, while global *z*-score was calculated by averaging the seven-domain *z*-scores. The same approach to calculate the domain and global score for neurocognitive performance has been used in published studies [49-51].

## Measurements

### Depressive Symptoms

Depressive symptoms were assessed by the 20-item validated Chinese version of the Center for Epidemiological Studies-Depression scale (CES-D-20) [52,53]. This scale has been used among people living with HIV in China [54]. Scores of CES-D-20 range from 0 to 60, with higher scores indicating more severe depressive symptoms. In this study, Cronbach alpha of the CES-D-20 was .93.

### Physical Activities

The 7-item International Physical Activity Questionnaire was used to measure walking as well as moderate- and vigorous-intensity activities in the past week [55]. Physical activity metabolic-equivalent tasks (METs) per week were computed [55]. High physical activity level was defined as (1) vigorous-intensity activity on at least 3 days and accumulating at least 1500 MET minutes per week, or (2) at least 5 days of any combination of walking and moderate-intensity or vigorous-intensity activities, achieving a minimum total physical activity of at least 3000 MET minutes per week. Moderate level was defined as meeting any one of the following criteria: (1) at least 3 days of vigorous activity of at least 20 minutes per day, (2) at least 5 days of moderate-intensity activity or walking of at least 30 minutes per day, or (3) at least 5 days of any combination of walking and moderate-intensity or vigorous-intensity activities, achieving a minimum total physical activity of at least 600 MET minutes per week. Individuals who did not meet the criteria for moderate or high levels of physical activity were considered as those with low physical activity or inactive.

### *Potential Confounders*

Sociodemographic characteristics of age, sex, years of formal education, marital status, personal annual income, and living arrangement (whether living alone or not) were obtained.

Blood pressure was measured twice at 5-minute intervals in the right arm and in the sitting position by some nurses or doctors with a mercury sphygmomanometer. Systolic and diastolic blood pressure were calculated by averaging the 2 measurements. The use of antihypertensive drugs was asked in the questionnaire. Hypertension was defined as systolic blood pressure of ≥140 mmHg or diastolic blood pressure of ≥90 mmHg or self-reported antihypertensive drugs use. Self-reported diabetes was determined by a positive response to the question "Have you ever been told by a health professional that you have diabetes?". Similar questions were used to measure the presence of hyperlipidemia, myocardial infarction, coronary heart disease, cerebrovascular disease, hepatitis B virus infection, hepatitis C virus infection, chronic bronchitis, chronic obstructive pulmonary disease, chronic liver disease, chronic kidney disease, peptic ulcer, stroke, cancer, peripheral vascular diseases, and connective tissue disease.

The participants were asked whether they are taking other medications, including diabetes medication, lipid-lowering drugs, aspirin, warfarin, drugs for heart disease, antidepressants, antidementia drugs, and nonsteroidal anti-inflammatory drugs. Two composite variables were constructed in this study by counting the number of affirmative item responses reflecting the number of chronic conditions and number of medications.

## Statistical Analysis

Descriptive statistics were presented. Between-group comparisons (depressive symptoms, physical activity level, and potential) were performed using the chi-square test or independent samples 2-tailed *t* test as appropriate. Potential confounders were controlled when comparing the differences in raw scores of neurocogitive tests and global- or domain-specific *z*-scores between older people living with HIV and HIV-negative controls using multivariable linear regression. Crude *P* values and adjusted *P* values were presented.

Path analysis was conducted to test the mediation model (Figure 1). HIV status was used as independent variable, while raw score of a neurocognitive test, or global or a domain *z*-score was included as a dependent variable in each mediation model. Standardized path coefficients (β) and unstandardized path coefficients (B) were reported. Bootstrapping analyses tested the mediation hypotheses. The 95% CIs of the indirect effects would be obtained from 5000 bootstrap samples. A statistically significant mediation effect would be observed when the CI did not include zero. SPSS 21.0 for Windows and AMOS 17.0 (IBM Corp) were used for data analysis; the level of significance was set to $P<.05$.

**Figure 1.** Mediation effects of physical activity and depressive symptoms in the association between HIV status and cognitive function (*z*-score); *: *P*<.05; **: *P*<.01; ***: *P*<.001. The path analysis presented the standardized regression weights and *P* value of each path.

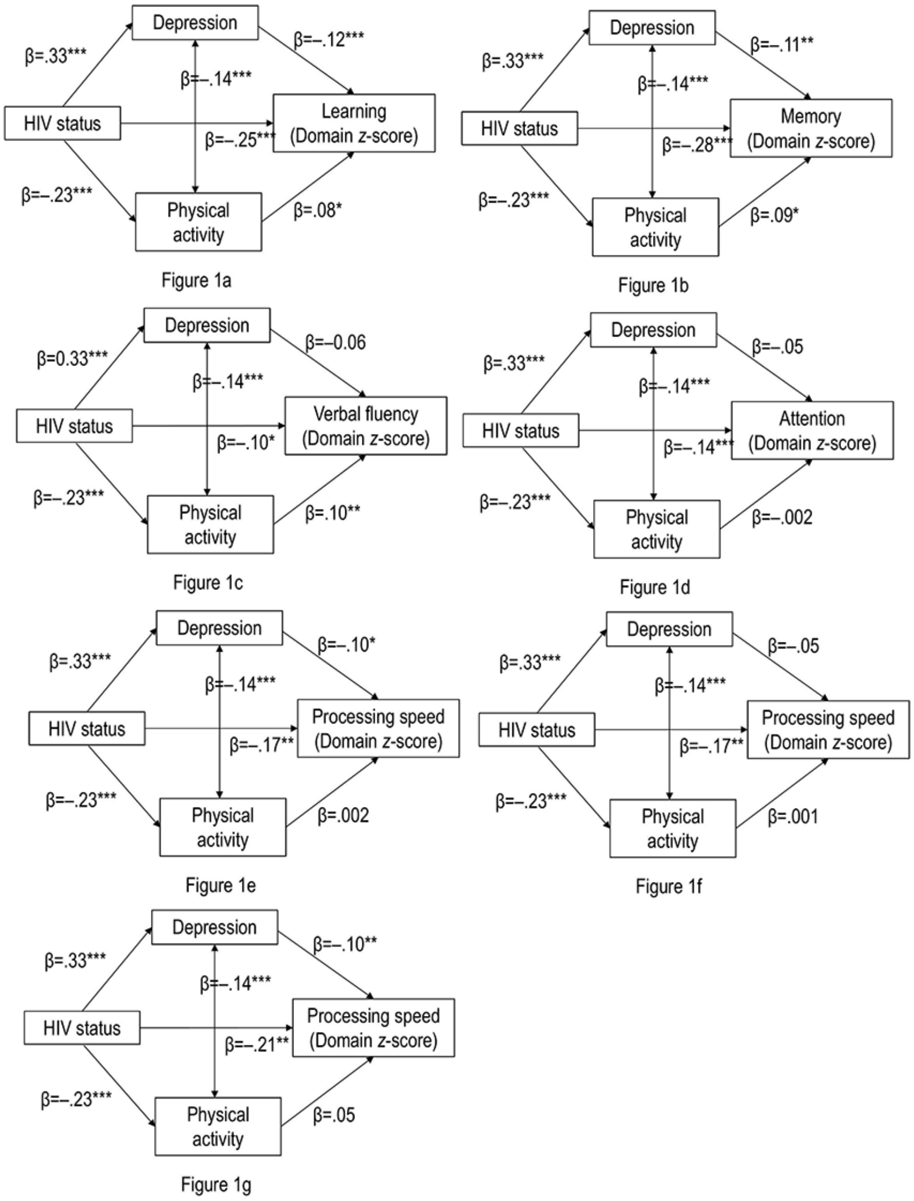


Figure 1a

Figure 1b

Figure 1c

Figure 1d

Figure 1e

Figure 1f

Figure 1g

# Results

## Descriptive Statistics

Of the 433 eligible older people living with HIV invited, 83 (19.2%) refused to join the study due to lack of time or interest. The response rate was 80.8% (350/433). Among the 350 participants consented to join the study, 14 (4%) and 21 (6%) did not complete the face-to-face interview and neurocognitive assessments, respectively; 315 (90%) completed both parts. Out of 434 controls being invited, 350 (80.6%) completed the face-to-face interview and neurocognitive assessments. None of the controls were screened to be HIV positive.

The mean age of the older people living with HIV was 61.3 (SD 6.8) years; 73.0% (230/315) were male; 52.1% (164/315) had an education level of primary school or below. Most of them were of Han ethnicity (307/315, 97.5%), were married (215/315, 68.3%), had an annual personal income of no more than 10,000 RMB (US $1507; 163/315, 52.1%), and were living with someone else (224/315, 71.1%). The number of chronic conditions and mediation use was 1.3 (SD 1.2) and 0.3 (SD 0.6), respectively. 79.4% (250/315) had received HIV diagnosis within 4 years, 56.4% (177/315) had a current CD4 level of <350 cells/μL, and 59.0% (186/315) had a CD4 nadir lower than 350 cells/μL. Of the 308 participants who were on ART, 21.9% (67/308) reported any missing dose in the last month, and 60.7% (187/308) were taking efavirenz.

Distributions of age (*P*=.62), sex (*P*=.53), and years of formal education (*P*=.48) did not differ between older people living with HIV and HIV-negative controls, reflecting successful matching. However, HIV-negative controls were less likely to be widowed (*P*<.001) and living alone. The between-group difference in mean number of chronic conditions was of marginal statistical significance (*P*=.07; Table 1).

**Table 1.** Characteristics of older people living with HIV and HIV-negative controls.

| Characteristics | Older people living with HIV (n=315), mean (SD) | HIV-negative controls (n=350) | *P* values |
|---|---|---|---|
| **Sociodemographics** | | | |
| Age (years), mean (SD) | 61.3 (6.8) | 61.1 (6.4) | .62 |
| **Sex, n (%)** | | | .53 |
| Male | 230 (73.0) | 257 (73.4) | |
| Female | 85 (27.0) | 83 (23.6) | |
| Years of education, mean (SD) | 5.7 (3.6) | 5.5 (3.4) | .48 |
| **Ethnicity, n (%)** | | | .09 |
| Han | 307 (97.5) | 347 (99.1) | |
| Others | 8 (2.5) | 3 (0.9) | |
| **Marital status, n (%)** | | | <.001 |
| Married | 215 (68.3) | 303 (86.8) | |
| Widowed | 72 (22.9) | 29 (8.3) | |
| Divorced or single | 28 (8.9) | 17 (4.9) | |
| **Annual personal income (RMB), n (%)** | | | .59 |
| ≤10,000[a] | 163 (52.1) | 187 (54.2) | |
| >10,000 | 150 (47.9) | 158 (45.8) | |
| **Living alone, n (%)** | | | <.001 |
| No | 224 (71.1) | 310 (88.8) | |
| Yes | 91 (28.9) | 39 (11.2) | |
| **Depressive symptoms** | | | |
| Score of CES-D-20[b], mean (SD) | 17.4 (13.0) | 9.4 (9.4) | <.001 |
| **Level of physical activity, n (%)** | | | <.001 |
| Low | 61 (19.4) | 32 (9.2) | |
| Moderate | 140 (44.4) | 115 (32.9) | |
| High | 114 (36.2) | 202 (57.7) | |
| **Presence of chronic conditions, n (%)** | | | |
| Hypertension | 162 (51.4) | 196 (56.0) | .24 |
| Diabetes | 23 (7.3) | 24 (6.9) | .81 |
| Hyperlipidemia | 12 (3.8) | 12 (3.4) | .84 |
| Chronic bronchitis | 26 (8.3) | 21 (6.0) | .29 |
| Chronic obstructive pulmonary disease | 7 (2.2) | 4 (1.1) | .27 |
| Cerebrovascular disease | 22 (7.0) | 24 (6.9) | .94 |
| Coronary heart disease | 15 (4.8) | 21 (6.0) | .48 |
| Myocardial infarction | 1 (0.3) | 3 (0.9) | .63 |
| Hepatitis B | 23 (7.3) | 2 (0.6) | <.001 |
| Hepatitis C | 1 (0.3) | 0 (0.0) | .47 |
| Liver dysfunction | 15 (4.8) | 3 (0.9) | .002 |
| Liver cirrhosis | 5 (1.6) | 0 (0.0) | .02 |
| Chronic kidney disease | 12 (3.8) | 6 (1.7) | .09 |
| Peptic ulcer disease | 31 (9.9) | 27 (7.7) | .33 |
| Cancer | 15 (4.8) | 6 (1.7) | .02 |

| Characteristics | Older people living with HIV (n=315), mean (SD) | HIV-negative controls (n=350) | *P* values |
|---|---|---|---|
| Peripheral vascular disease | 13 (4.1) | 5 (1.4) | .03 |
| Connective tissue disease | 26 (8.3) | 23 (6.6) | .39 |
| Number of chronic conditions, mean (SD) | 1.3 (1.2) | 1.1 (1.2) | .07 |
| **Use of medication** | | | |
| Number of medication use[c], mean (SD) | 0.3 (0.6) | 0.3 (0.7) | .12 |
| **HIV-related disease characteristics** | | | |
| **Duration since HIV diagnosis, n (%)** | | | |
| <1 year | 100 (31.7) | N/A[d] | N/A |
| 1-3 years | 150 (47.6) | N/A | |
| ≥4 years | 65 (20.6) | N/A | N/A |
| **Most recent CD4[e] count (cells/uL)** | | | |
| <350 | 177 (56.4) | N/A | N/A |
| 350-500 | 70 (22.3) | N/A | N/A |
| >500 | 67 (21.3) | N/A | N/A |
| **CD4 nadir, cells/μL** | | | |
| <200 | 109 (34.6) | N/A | N/A |
| 200-350 | 77 (24.4) | N/A | N/A |
| 350-500 | 20 (6.4) | N/A | N/A |
| >500 | 8 (2.5) | N/A | N/A |
| Missing | 101 (32.1) | N/A | N/A |
| **On ART[f], n (%)** | | | |
| Yes | 298 (97.8) | N/A | N/A |
| No | 7 (2.2) | N/A | N/A |
| **Missing of any ART doses in the last month (among those who were on ART; n=308), n (%)** | | | |
| Yes | 67 (21.9) | N/A | N/A |
| No | 241 (78.1) | N/A | N/A |

[a] 10,000 RMB= US $1507.

[b] CES-D-20: 20-item Center for Epidemiological Studies-Depression.

[c] The number of medications were constructed by counting the number of affirmative item responses on whether they are taking other medications, including diabetes medication, lipid-lowering drugs, aspirin, warfarin, drugs for heart disease, antidepressants, antidementia drugs, and nonsteroidal anti-inflammatory drugs.

[d] N/A: not applicable.

[e] CD4: cluster of differentiation 4.

[f] ART: antiretroviral therapy.

### Between-Group Differences in Neurocognitive Performance, Depressive Symptoms, and Physical Activities

After being controlled for age, sex, years of formal education, marital status, personal annual income, living arrangement (whether living alone or not), and number of chronic conditions and mediation use, older people living with HIV had poorer performance in all neurocognitive tests, with the exception of visual span—backward (*P*=.08). Older people living with HIV had poorer performance in all seven domains (*P*<.001 to *P*=.01) and global neurocognitive function (*P*<.001) compared with HIV-negative controls (Table 2).

As compared to HIV-negative controls, older people living with HIV had more severe depressive symptoms (CDS-D-20 score 17.4, SD 13.0 versus 9.4, SD 9.4; *P*<.001) and lower physical activity level (high physical activity level 36.2% versus 57.7%; *P*<.001; Table 1).

**Table 2.** Difference in raw scores of neurocognitive tests and z-scores of global or domain of neurocognitive performance between older people living with HIV and HIV-negative controls.

| Neurocognitive domains | Older people living with HIV (n=315), mean (SD) | HIV-negative controls (n=350), mean (SD) | Crude *P* values[a] | Adjusted *P* values[b] |
|---|---|---|---|---|
| **Learning** | | | | |
| CAVLT[c]–total learning (raw score) | 30.41 (10.54) | 36.65 (9.38) | <.001 | <.001 |
| Domain *z*-score[d] | –0.66 (1.12) | 0 (1) | <.001 | <.001 |
| **Memory** | | | | |
| CAVLT–delayed recall (raw score) | 5.64 (3.06) | 7.59 (2.85) | <.001 | <.001 |
| Domain *z*-score[d] | –0.68 (1.08) | 0 (1) | <.001 | <.001 |
| **Verbal fluency** | | | | |
| Animal (raw score) | 12.97 (3.51) | 13.45 (3.07) | .06 | .02 |
| Fruits (raw score) | 8.98 (2.77) | 9.65 (2.63) | .003 | <.001 |
| Vegetable (raw score) | 10.60 (3.17) | 11.34 (3.16) | .002 | .001 |
| Domain *z*-score[d] | –0.21 (0.85) | 0 (0.77) | .001 | <.001 |
| **Attention or working memory** | | | | |
| Digit span—forward (raw score) | 7.87 (2.61) | 8.64 (2.60) | <.001 | <.001 |
| Digit span—backward (raw score) | 3.71 (1.83) | 4.13 (2.75) | .02 | .01 |
| Visual span—forward (raw score) | 6.69 (1.67) | 7.07 (1.59) | .003 | .004 |
| Visual span—backward (raw score) | 4.63 (2.03) | 4.89 (1.78) | .08 | .08 |
| Domain *z*-score[d] | –0.21 (0.70) | 0 (0.69) | <.001 | .002 |
| **Processing speed** | | | | |
| CTMT-A[e] (raw score) | 22.82 (20.27) | 16.40 (10.99) | <.001 | <.001 |
| Domain *z*-score[d] | –0.58 (1.84) | 0 (1) | <.001 | <.001 |
| **Executive function** | | | | |
| CTMT-B[f] (raw score) | 140.70 (123.69) | 110.01 (94.46) | .001 | .001 |
| Domain *z*-score[d] | –0.32 (1.31) | 0 (1) | .001 | .001 |
| **Motor skills** | | | | |
| Dominant hand (raw score) | 113.99 (48.68) | 104.36 (43.55) | .02 | .02 |
| Non-dominant hand (raw score) | 123.04 (101.07) | 108.57 (38.65) | .01 | .01 |
| Domain *z*-score[d] | –0.30 (1.62) | 0 (0.96) | .01 | .01 |
| Global cognitive *z*-score[g] | –0.36 (0.73) | 0 (0.58) | <.001 | <.001 |

[a] *P* values obtained by univariate linear regression models.

[b] Adjusted for confounders—age, sex, years of formal education, marital status, personal annual income, living arrangement (whether living alone or not), number of chronic conditions, and mediation use.

[c] CAVLT: Chinese Auditory Verbal Learning Test.

[d] *z*-scores of individual tests were calculated by using the following formula: (raw test score – mean test score among HIV-negative control) / SD of test score among HIV-negative controls. Domain *z*-scores were calculated by averaging *z*-scores of the tests within the respective domain.

[e] CTMT-A: Chinese Trail Making Test Part A.

[f] CTMT-B: Chinese Trail Making Test Part B.

[g] Global *z*-scores were calculated by averaging *z*-scores in all tests used in this study.

## Testing the Mediation Hypotheses

The models fitted the data well (chi-square=136.33; degree of freedom=54; comparative fit index: 0.90 to 0.92; root mean square error of approximation=0.05; Table 3). After being controlled for potential confounders (age, sex, years of formal education, marital status, personal annual income, whether living alone or not, number of chronic conditions, and mediation use), path analyses showed that positive HIV status was associated with higher depressive symptoms (β=.33, P<.001) and lower level of physical activity (β=–.23, P<.001). Depressive symptoms and physical activity were negatively correlated (β=–.14, P<.001). Depressive symptoms were negatively associated with the global z-score (β=–.10, P=.002) and three domain z-scores, which were learning (β=–.12, P<.001), memory (β=–.11, P=.001), and processing speed (β=–.10, P=.02). The level of physical activity was positively associated with three domain z-scores, including learning (β=.08, P=.03), memory (β=.09, P=.01), and verbal fluency (β=.10, P=.01; Table 3 and Figure 1).

Significant indirect effects of HIV status were found on global z-score (β=–.06, 95% CI –0.10 to –0.03, P<.001) and four domain z-scores of learning (β=–.13, 95% CI –0.20 to –0.07, P=.001), memory (β=–.12, 95% CI –0.18 to –0.06, P=.001), verbal fluency (β=–.07, 95% CI –0.13 to –0.02, P=.002), and processing speed (β=–.10, 95% CI –0.22 to –0.02, P=.05; Table 3 and Figure 1).

Path analysis using raw scores of neurocognitive test as dependent variable and HIV status as independent variables were presented in Multimedia Appendix 1.

**Table 3.** Model fit and indirect effects of the proposed mediation model

| Dependent variable | CFI[a] | Total effect, β (95% CI)[b] | Indirect effect, β (95% CI) | Indirect effect (physical activity), β (95% CI) | Indirect effect (depression), β (95% CI) | PM[c] |
|---|---|---|---|---|---|---|
| Learning (domain z-score) | 0.93 | –.68 (–.83, –.55) | –.13 (–.20, –.07) | –.04 (–.09, –.01) | –.09 (–.15, –.04) | 19% |
| Memory (domain z-score) | 0.92 | –.70 (–.84, –.56) | –.12 (–.18, –.06) | –.04 (–.08, –.01) | –.08 (–.13, –.03) | 17% |
| Verbal fluency (domain z-score) | 0.91 | –.23 (–.35, –.11) | –.07 (–.13, –.02) | –.04 (–.08, –.01) | –.03 (–.08, .01) | 31% |
| Attention or working memory (domain z-score) | 0.93 | –.22 (–.31, –.13) | –.02 (–.06, .01) | .001 (–.02, .02) | –.02 (–.06, .006) | 11% |
| Processing speed (domain z-score) | 0.92 | –.61 (–.84, –.41) | –.10 (–.22, –.02) | –.001 (–.05, .05) | –.10 (–.22, –.02) | 17% |
| Executive function (domain z-score) | 0.91 | –.35 (–.53, –.17) | –.03 (–.13, .04) | .01 (–.03, .04) | –.04 (–.13, .03) | 9% |
| Motor skills (domain z-score) | 0.91 | –.29 (–.55, –.13) | –.05 (–.13, .07) | –.01 (–.06, .04) | –.04 (–.10, .03) | 18% |
| Global z-score | 0.93 | –.35 (–.44, –.26) | –.06 (–.10, –.03) | –.02 (–.04, .002) | –.04 (–.08, .02) | 17% |

[a] CFI: Comparative Fit Index.

[b] 95% bias-corrected confidence intervals were presented (bootstrap sample size=2000), which did not include 0, showing the mediation effect was statistically significant (P<.05). The results were reported after controlling for significant background variables (P<.10) and other potential confounders.

[c] PM: percent mediated.

# Discussion

## Principal Results

Our results confirmed that older people living with HIV performed more poorly in global and all domains of neruocognitive performance compared to HIV-negative controls. The prevalence of neurocognitive impairment may be high among older people living with HIV in China [56]. Integrating prevention, screening, and management of neurocognitive impairment with existing HIV services is hence important for older people living with HIV in China.

Older people living with HIV had more severe depressive symptoms compared with their HIV-negative counterparts. Such finding was consistent with those from previous studies [57-59]. As compared to HIV-negative controls, a higher proportion of older people living with HIV were unmarried or living alone. Such between-group differences might contribute to higher depression among older people living with HIV. Previous studies suggested that older adults who lived alone were more likely to report feeling of depression compared with those who live with a spouse or other family member [60]. Since the implementation of the *treat-all* policy, the overall ART coverage in China has increased sharply [61]. The target to have 90% of people living with HIV on ART to achieve viral suppression has been already achieved in China [61]. The life expectancy of people living with HIV in China will largely increase. It is time to pay more attention to improve the mental health well-being of people living with HIV. The Joint United Nations Program on HIV and AIDS proposes adding a 4th “90” to the HIV testing and treatment target, which is to have 90% of people living with HIV with viral load suppression to have good health-related quality of life [62]. However, there is a dearth of mental health services targeting older people living with HIV in China. Improvements are greatly needed.

Consistent with previous studies among people infected with HIV [11,29,30] and HIV-negative populations [28], more severe depressive symptoms were negatively associated with neurocognitive function. Our findings suggested that, among older people aged ≥50, deficits in learning, memory, and processing speed were sensitive to depressive symptoms. Since depression is modifiable through interventions, mental health promotion will contribute to preventing or slowing down the progression of neurocognitive impairment among older individuals. Given that pharmacological treatment (antidepressant medication) may negatively affect neurocognitive function [63], psychological interventions may have a priority. Positive psychological interventions are recommended because they have some advantages compared to traditional psychological interventions, such as being less dependent on psychologists or psychiatrists and having longer effects [64,65]. They are potentially suitable in resource-limiting regions such as China.

Older people living with HIV have lower levels of physical activity compared with HIV-negative controls, as they may have more barriers to perform physical activities, probably due to HIV-positive status. Consistent with the findings of previous studies [33,66], higher levels of physical activity were associated with better neurocognitive performance among older individuals, especially in domains such as learning as well as memory and verbal fluency. Previous studies have shown that Tai chi resulted in greater improvements in neurocognitive function compared to the attention-control groups, and Western exercises including aerobics incorporated endurance, resistance or strength, and flexibility exercises [67]. Since Tai chi is slow and gentle, it is suitable for older individuals. It is also highly acceptable by the Chinese population. Health workers should consider promoting Tai chi to prevent or slow down neurocognitive impairment among both HIV-positive and HIV-negative older individuals.

Depressive symptoms and level of physical activity partially mediated the associations between HIV status and global and four domains of neurocognitive function. It suggested that change in mental health and physical activity after HIV infection may partially explain why older people living with HIV are more susceptible to neurocognitive impairment. Therefore, promoting mental health well-being and physical activity are potential entry points to slow down the progress of neurocognitive impairment among older people living with HIV and should be incorporated into routine care for this group. Future studies should explore factors associated with depressive symptoms and physical activities among older people living with HIV in China to develop culturally appropriate interventions.

## Limitations

The strengths of this study included the use of comprehensive neurocognitive tests and well-matched HIV-negative controls. However, it also had some limitations. First, the cross-sectional study design limited the ability to establish the causality of depressive symptoms or physical activities on neurocognitive functions. Second, we did not obtain sociodemographic characteristics of individuals who refused to participate in the study, and hence were not able to compare the difference in these characteristics between participants and nonparticipants. A selection bias thus might exist. Third, since the participants all came from 1 Chinese city, caution should be taken when generalizing the results to older people living with HIV in China. Fourth, we did not measure high-risk behaviors among the study participants. Fifth, we did not measure survey satisfaction in this study. Moreover, we did not measure anxiety, another important psychological well-being indicator, in this study. Furthermore, because some exclusion criteria and disease conditions were based on self-reported data, reporting bias might exist. Finally, this study only used 1 test to measure the information processing speed (Chinese Trail Making Test Part A) and executive function (Chinese Trail Making Test Part B).

## Conclusions

Older people living with HIV performed more poorly in global and all specific domains of neruocognitive performance compared with the HIV-negative controls. They also reported more severe depressive symptoms and lower levels of physical activity compared with their HIV-negative counterparts. Depressive symptoms and level of physical activity partially mediated the associations between HIV status and neurocognitive function. Change in mental health and physical activity after HIV infection may partially explain why older people living with HIV are more susceptible to neurocognitive impairment. Promoting mental health well-being and physical activity are potential entry points to slow down the progress of neurocognitive impairment among older people living with HIV.

## Acknowledgments

This study was supported by the Health and Family Planning Commission in the Hunan Province, China (C2016031). The funder had no role in the study design, data collection, analysis and interpretation, or manuscript preparation.

## Authors' Contributions

JTFL and ZW contributed equally as corresponding authors.

## Conflicts of Interest

None declared.

Multimedia Appendix 1

Path analysis based on raw scores of neurocognitive test.

[PDF File (Adobe PDF File), 231 KB - publichealth_v8i8e32968_app1.pdf ]

## References

1. Fang X, Vincent W, Calabrese SK, Heckman TG, Sikkema KJ, Humphries DL, et al. Resilience, stress, and life quality in older adults living with HIV/AIDS. Aging Ment Health 2015 Jan 30;19(11):1015-1021 [FREE Full text] [doi: 10.1080/13607863.2014.1003287] [Medline: 25633086]
2. High K, Brennan-Ing M, Clifford D, Cohen M, Currier J, Deeks S, OAR Working Group on HIVAging. HIV and aging: state of knowledge and areas of critical need for research. A report to the NIH Office of AIDS Research by the HIV and Aging Working Group. J Acquir Immune Defic Syndr 2012 Jul 01;60 Suppl 1:S1-18 [FREE Full text] [doi: 10.1097/QAI.0b013e31825a3668] [Medline: 22688010]
3. The GAP report. Geneva: Joint United Nations Programme on HIV/AIDS. 2014. URL: http://www.unaids.org/en/resources/documents/2014 [accessed 2022-08-08]
4. Monteiro F, Canavarro MC, Pereira M. Factors associated with quality of life in middle-aged and older patients living with HIV. AIDS Care 2016 Feb 16;28 Suppl 1(sup1):92-98 [FREE Full text] [doi: 10.1080/09540121.2016.1146209] [Medline: 26881294]
5. Nguyen P, Gilmour S, Le P, Onishi K, Kato K, Nguyen H. Progress toward HIV elimination goals: trends in and projections of annual HIV testing and condom use in Africa. AIDS 2021 Jul 01;35(8):1253-1262. [doi: 10.1097/QAD.0000000000002870] [Medline: 33730746]
6. Siegler E, Brennan-Ing M. Adapting Systems of Care for People Aging With HIV. J Assoc Nurses AIDS Care 2017;28(5):698-707. [doi: 10.1016/j.jana.2017.05.006] [Medline: 28602461]
7. Xing J, Li Y, Tang W, Guo W, Ding Z, Ding G, et al. HIV/AIDS epidemic among older adults in China during 2005-2012: results from trend and spatial analysis. Clin Infect Dis 2014 Jul 15;59(2):e53-e60 [FREE Full text] [doi: 10.1093/cid/ciu214] [Medline: 24700658]
8. Freiberg MS, Chang CH, Kuller LH, Skanderson M, Lowy E, Kraemer KL, et al. HIV infection and the risk of acute myocardial infarction. JAMA Intern Med 2013 Apr 22;173(8):614-622 [FREE Full text] [doi: 10.1001/jamainternmed.2013.3728] [Medline: 23459863]
9. Scott JC, Woods SP, Carey CL, Weber E, Bondi MW, Grant I, HIV Neurobehavioral Research Center (HNRC) Group. Neurocognitive consequences of HIV infection in older adults: an evaluation of the "cortical" hypothesis. AIDS Behav 2011 Aug 24;15(6):1187-1196 [FREE Full text] [doi: 10.1007/s10461-010-9815-8] [Medline: 20865313]
10. Heaton RK, Cysique LA, Jin H, Shi C, Yu X, Letendre S, San Diego HIV Neurobehavioral Research Center Group. Neurobehavioral effects of human immunodeficiency virus infection among former plasma donors in rural China. J Neurovirol 2008 Nov;14(6):536-549 [FREE Full text] [doi: 10.1080/13550280802378880] [Medline: 18991068]
11. Giesbrecht CJ, Thornton AE, Hall-Patch C, Maan EJ, Côté HCF, Money DM, et al. Select neurocognitive impairment in HIV-infected women: associations with HIV viral load, hepatitis C virus, and depression, but not leukocyte telomere length. PLoS One 2014 Mar 4;9(3):e89556 [FREE Full text] [doi: 10.1371/journal.pone.0089556] [Medline: 24595021]
12. Becker JT, Lopez OL, Dew MA, Aizenstein HJ. Prevalence of cognitive disorders differs as a function of age in HIV virus infection. AIDS 2004 Jan 01;18 Suppl 1:S11-S18. [Medline: 15075493]
13. Heaton RK, Clifford DB, Franklin DR, Woods SP, Ake C, Vaida F, et al. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER Study. Neurology 2010 Dec 06;75(23):2087-2096. [doi: 10.1212/wnl.0b013e318200d727]
14. Filho SMMF, de Melo HRL. Frequency and risk factors for HIV-associated neurocognitive disorder and depression in older individuals with HIV in northeastern Brazil. Int. Psychogeriatr 2012 May 22;24(10):1648-1655. [doi: 10.1017/s1041610212000944]
15. Valcour V, Shikuma C, Shiramizu B, Watters M, Poff P, Selnes O, et al. Higher frequency of dementia in older HIV-1 individuals: the Hawaii Aging with HIV-1 Cohort. Neurology 2004 Sep 14;63(5):822-827 [FREE Full text] [doi: 10.1212/01.wnl.0000134665.58343.8d] [Medline: 15365130]
16. Heaton RK, Marcotte TD, Mindt MR, Sadek J, Moore DJ, Bentley H, et al. The impact of HIV-associated neuropsychological impairment on everyday functioning. J. Inter. Neuropsych. Soc 2004 May 1;10(03):317-331. [doi: 10.1017/s1355617704102130]
17. Shrestha R, Weikum D, Copenhaver M, Altice FL. The Influence of Neurocognitive Impairment, Depression, and Alcohol Use Disorders on Health-Related Quality of Life among Incarcerated, HIV-Infected, Opioid Dependent Malaysian Men: A Moderated Mediation Analysis. AIDS Behav 2017 Apr 20;21(4):1070-1081 [FREE Full text] [doi: 10.1007/s10461-016-1526-3] [Medline: 27544515]
18. Georgakis MK, Papadopoulos FC, Protogerou AD, Pagonari I, Sarigianni F, Biniaris-Georgallis S, Kalogirou, et al. Comorbidity of Cognitive Impairment and Late-Life Depression Increase Mortality: Results From a Cohort of Community-Dwelling Elderly Individuals in Rural Greece. J Geriatr Psychiatry Neurol 2016 Jul 25;29(4):195-204. [doi: 10.1177/0891988716632913] [Medline: 26917554]
19. de Galan BE, Zoungas S, Chalmers J, Anderson C, Dufouil C, Pillai A, ADVANCE Collaborative group. Cognitive function and risks of cardiovascular disease and hypoglycaemia in patients with type 2 diabetes: the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial. Diabetologia 2009 Nov 18;52(11):2328-2336. [doi: 10.1007/s00125-009-1484-7] [Medline: 19688336]

20. Le PM, Nguyen PT, Nguyen HV, Bui DH, Vo SH, Nguyen NV, et al. Adherence to highly active antiretroviral therapy among people living with HIV and associated high-risk behaviours and clinical characteristics: A cross-sectional survey in Vietnam. Int J STD AIDS 2021 Sep 16;32(10):911-918. [doi: 10.1177/09564624211002405] [Medline: 33861666]
21. Orza L, Bewley S, Logie CH, Crone ET, Moroz S, Strachan S, et al. How does living with HIV impact on women's mental health? Voices from a global survey. Journal of the International AIDS Society 2015 Dec 01;18:20289. [doi: 10.7448/ias.18.6.20289]
22. Liu H, He X, Levy JA, Xu Y, Zang C, Lin X. Psychological Impacts among Older and Younger People Living with HIV/AIDS in Nanning, China. J Aging Res 2014;2014:576592-576596. [doi: 10.1155/2014/576592] [Medline: 25132993]
23. Carmo Filho AD, Fakoury MK, Eyer-Silva WDA, Neves-Motta R, Kalil RS, Ferry FRDA. Factors associated with a diagnosis of major depression among HIV-infected elderly patients. Rev Soc Bras Med Trop 2013 Jun;46(3):352-354 [FREE Full text] [doi: 10.1590/0037-8682-1228-2013] [Medline: 23856860]
24. Greene M, Covinsky K, Valcour V, Miao Y, Madamba J, Lampiris H, et al. Geriatric Syndromes in Older HIV-Infected Adults. J Acquir Immune Defic Syndr 2015 Jun 01;69(2):161-167 [FREE Full text] [doi: 10.1097/QAI.0000000000000556] [Medline: 26009828]
25. Brown MJ, Cohen SA, DeShazo JP. Psychopathology and HIV diagnosis among older adults in the United States: disparities by age, sex, and race/ethnicity. Aging Ment Health 2020 Oct 05;24(10):1746-1753 [FREE Full text] [doi: 10.1080/13607863.2019.1636201] [Medline: 31274001]
26. Storholm ED, Halkitis PN, Kupprat SA, Hampton MC, Palamar JJ, Brennan-Ing M, et al. HIV-Related Stigma as a Mediator of the Relation Between Multiple-Minority Status and Mental Health Burden in an Aging HIV-Positive Population. Journal of HIV/AIDS & Social Services 2013 Jan;12(1):9-25. [doi: 10.1080/15381501.2013.767557]
27. Pellegrino LD, Peters ME, Lyketsos CG, Marano CM. Depression in cognitive impairment. Curr Psychiatry Rep 2013 Sep 11;15(9):384 [FREE Full text] [doi: 10.1007/s11920-013-0384-1] [Medline: 23933974]
28. Roca M, Vives M, López-Navarro E, García-Campayo J, Gili M. Cognitive impairments and depression: a critical review. Actas Esp Psiquiatr 2015 Sep;43(5):187-193 [FREE Full text] [Medline: 26320897]
29. Pinheiro C, Souza L, Motta J, Kelbert E, Souza M, Martins C, et al. Depression and diagnosis of neurocognitive impairment in HIV-positive patients. Braz J Med Biol Res 2016;49(10):1-7. [doi: 10.1590/1414-431X20165344]
30. Shimizu SM, Chow DC, Valcour V, Masaki K, Nakamoto B, Kallianpur KJ, et al. The Impact of Depressive Symptoms on Neuropsychological Performance Tests in HIV-Infected Individuals: A Study of the Hawaii Aging with HIV Cohort. World J AIDS 2011 Dec 01;1(4):139-145 [FREE Full text] [doi: 10.4236/wja.2011.14020] [Medline: 23061029]
31. O'Brien KK, Solomon P, Trentham B, MacLachlan D, MacDermid J, Tynan A, et al. Evidence-informed recommendations for rehabilitation with older adults living with HIV: a knowledge synthesis. BMJ Open 2014 May 14;4(5):e004692 [FREE Full text] [doi: 10.1136/bmjopen-2013-004692] [Medline: 24833687]
32. Chow F, Makanjuola A, Wu K, Berzins B, Kim K, Ogunniyi A, et al. Physical Activity Is Associated With Lower Odds of Cognitive Impairment in Women but Not Men Living With Human Immunodeficiency Virus Infection. J Infect Dis 2019 Jan 07;219(2):264-274 [FREE Full text] [doi: 10.1093/infdis/jiy503] [Medline: 30137500]
33. Fazeli PL, Marquine MJ, Dufour C, Henry BL, Montoya J, Gouaux B, HNRP Group. Physical Activity is Associated with Better Neurocognitive and Everyday Functioning Among Older Adults with HIV Disease. AIDS Behav 2015 Aug 3;19(8):1470-1477 [FREE Full text] [doi: 10.1007/s10461-015-1024-z] [Medline: 25731660]
34. Vancampfort D, Mugisha J, Richards J, De Hert M, Probst M, Stubbs B. Physical activity correlates in people living with HIV/AIDS: a systematic review of 45 studies. Disabil Rehabil 2018 Jul 22;40(14):1618-1629. [doi: 10.1080/09638288.2017.1306587] [Medline: 28325087]
35. Johs NA, Kellar-Guenther Y, Jankowski CM, Neff H, Erlandson KM. A qualitative focus group study of perceived barriers and benefits to exercise by self-described exercise status among older adults living with HIV. BMJ Open 2019 Mar 07;9(3):e026294 [FREE Full text] [doi: 10.1136/bmjopen-2018-026294] [Medline: 30850416]
36. Quigley A, Baxter L, Keeler L, MacKay-Lyons M. Using the Theoretical Domains Framework to identify barriers and facilitators to exercise among older adults living with HIV. AIDS Care 2019 Feb 18;31(2):163-168. [doi: 10.1080/09540121.2018.1499860] [Medline: 30021454]
37. Khoury AL, Morey MC, Wong TC, McNeil DL, Humphries B, Frankey K, et al. Diminished physical function in older HIV-infected adults in the Southeastern U.S. despite successful antiretroviral therapy. PLoS One 2017 Jun 29;12(6):e0179874 [FREE Full text] [doi: 10.1371/journal.pone.0179874] [Medline: 28662079]
38. Brothers TD, Kirkland S, Guaraldi G, Falutz J, Theou O, Johnston BL, et al. Frailty in people aging with human immunodeficiency virus (HIV) infection. J Infect Dis 2014 Oct 15;210(8):1170-1179. [doi: 10.1093/infdis/jiu258] [Medline: 24903667]
39. Oursler KK, Goulet JL, Crystal S, Justice AC, Crothers K, Butt AA, et al. Association of age and comorbidity with physical function in HIV-infected and uninfected patients: results from the Veterans Aging Cohort Study. AIDS Patient Care STDS 2011 Jan;25(1):13-20. [doi: 10.1089/apc.2010.0242] [Medline: 21214375]
40. Safeek RH, Hall KS, Lobelo F, del Rio C, Khoury AL, Wong T, et al. Low Levels of Physical Activity Among Older Persons Living with HIV/AIDS Are Associated with Poor Physical Function. AIDS Research and Human Retroviruses 2018 Nov;34(11):929-935. [doi: 10.1089/aid.2017.0309]

41. Lee TM, Yuen KS, Chan CC. Normative data for neuropsychological measures of fluency, attention, and memory measures for Hong Kong Chinese. J Clin Exp Neuropsychol 2002 Aug 09;24(5):615-632. [doi: 10.1076/jcen.24.5.615.1001] [Medline: 12187445]
42. Wechsler D. Wechsler Adult Intelligence Scale--Third Edition. San Antonio, TX, US: Psychological Corporation; 1997.
43. Lezak M, Howieson DB, Bigler ED, Tranel D. Neuropsychological Assessment, 5th Edition. New York, US: Oxford University Press; 2004.
44. Lu L, Bigler ED. Performance on Original and a Chinese Version of Trail Making Test Part B: A Normative Bilingual Sample. Applied Neuropsychology 2000 Dec;7(4):243-246. [doi: 10.1207/s15324826an0704_6]
45. Mok EHL, Lam LCW, Chiu HFK. Category verbal fluency test performance in chinese elderly with Alzheimer's disease. Dement Geriatr Cogn Disord 2004 Aug 13;18(2):120-124. [doi: 10.1159/000079190] [Medline: 15211065]
46. Ruff RM, Parker SB. Gender- and age-specific changes in motor speed and eye-hand coordination in adults: normative values for the Finger Tapping and Grooved Pegboard Tests. Percept Mot Skills 1993 Jun 21;76(3 Pt 2):1219-1230. [doi: 10.2466/pms.1993.76.3c.1219] [Medline: 8337069]
47. Kamminga J, Cysique LA, Lu G, Batchelor J, Brew BJ. Validity of cognitive screens for HIV-associated neurocognitive disorder: a systematic review and an informed screen selection guide. Curr HIV/AIDS Rep 2013 Dec 27;10(4):342-355 [FREE Full text] [doi: 10.1007/s11904-013-0176-6] [Medline: 24072534]
48. Lam LCW, Chau RCM, Wong BML, Fung AWT, Lui VWC, Tam CCW, et al. Interim follow-up of a randomized controlled trial comparing Chinese style mind body (Tai Chi) and stretching exercises on cognitive function in subjects at risk of progressive cognitive decline. Int J Geriatr Psychiatry 2011 Jul 09;26(7):733-740. [doi: 10.1002/gps.2602] [Medline: 21495078]
49. Shikuma CM, Kohorn L, Paul R, Chow DC, Kallianpur KJ, Walker M, et al. Sleep and neuropsychological performance in HIV+ subjects on efavirenz-based therapy and response to switch in therapy. HIV Clin Trials 2018 Aug 19;19(4):139-147 [FREE Full text] [doi: 10.1080/15284336.2018.1511348] [Medline: 30451595]
50. Ballegaard V, Pedersen K, Pedersen M, Brændstrup P, Kirkby N, Buus A, et al. Cytomegalovirus-Specific CD4+ T-cell Responses and CMV-IgG Levels Are Associated With Neurocognitive Impairment in People Living With HIV. J Acquir Immune Defic Syndr 2018 Sep 01;79(1):117-125. [doi: 10.1097/QAI.0000000000001753] [Medline: 29781883]
51. Mielke MM, Hagen CE, Wennberg AMV, Airey DC, Savica R, Knopman DS, et al. Association of Plasma Total Tau Level With Cognitive Decline and Risk of Mild Cognitive Impairment or Dementia in the Mayo Clinic Study on Aging. JAMA Neurol 2017 Sep 01;74(9):1073-1080 [FREE Full text] [doi: 10.1001/jamaneurol.2017.1359] [Medline: 28692710]
52. Radloff LS. The CES-D Scale. Applied Psychological Measurement 2016 Jul 26;1(3):385-401. [doi: 10.1177/014662167700100306]
53. Wong J, Ho S, Lam T. Central and Western District Adolescent Health Survey: Report of the Cross-sectional Survey. Hong Kong: Department of Community Medicine, University of Hong Kong; 2004.
54. Zhang J, Zhen-Yun WU, Fang G, Juan LI, Han BX. Development of the Chinese age norms of CES-D in urban area. Chinese Mental Health Journal 2010:139-143.
55. Sjostrom M, Ainsworth B, Bauman A, Bull F, Hamilton-Craig C, Sallis J. Guidelines for data processing analysis of the International Physical Activity Questionnaire (IPAQ) - short and long forms. Academia.edu. URL: http://www.academia.edu/5346814/Guidelines_for_Data_Processing_and_Analysis_of_the_International_Physical_Activity_Questionnaire_IPAQ_Short_and_Long_Forms_Contents [accessed 2022-08-08]
56. Xiao X, Zeng H, Feng C, Tan H, Wu L, Zhang H, et al. Cognitive Impairment Among Aging People Living With HIV on Antiretroviral Therapy: A Cross-Sectional Study in Hunan, China. J Assoc Nurses AIDS Care 2020;31(3):301-311. [doi: 10.1097/jnc.0000000000000122]
57. Ciesla JA, Roberts JE. Meta-analysis of the relationship between HIV infection and risk for depressive disorders. Am J Psychiatry 2001 May;158(5):725-730. [doi: 10.1176/appi.ajp.158.5.725] [Medline: 11329393]
58. Sueoka K, Goulet JL, Fiellin DA, Rimland D, Butt AA, Gibert C, et al. Depression symptoms and treatment among HIV infected and uninfected veterans. AIDS Behav 2010 Apr 22;14(2):272-279. [doi: 10.1007/s10461-008-9428-7] [Medline: 18648927]
59. Langebeek N, Kooij K, Wit F, Stolte I, Sprangers M, Reiss P, AGEhIV Cohort Study Group. Impact of comorbidity and ageing on health-related quality of life in HIV-positive and HIV-negative individuals. AIDS 2017 Jun 19;31(10):1471-1481. [doi: 10.1097/QAD.0000000000001511] [Medline: 28574965]
60. Stahl ST, Beach SR, Musa D, Schulz R. Living alone and depression: the modifying role of the perceived neighborhood environment. Aging Ment Health 2017 Oct 07;21(10):1065-1071 [FREE Full text] [doi: 10.1080/13607863.2016.1191060] [Medline: 27267633]
61. Country progress report - China. Global AIDS Monitoring 2018. 2018. URL: https://www.unaids.org/sites/default/files/country/documents/CHN_2018_countryreport.pdf [accessed 2022-08-08]
62. Webster P. UNAIDS survey aligns with so-called fourth 90 for HIV/AIDS. The Lancet 2019 Jun;393(10187):2188. [doi: 10.1016/s0140-6736(19)31231-0]

63. Moraros J, Nwankwo C, Patten SB, Mousseau DD. The association of antidepressant drug usage with cognitive impairment or dementia, including Alzheimer disease: A systematic review and meta-analysis. Depress Anxiety 2017 Mar 28;34(3):217-226 [FREE Full text] [doi: 10.1002/da.22584] [Medline: 28029715]
64. Sin NL, Lyubomirsky S. Enhancing well-being and alleviating depressive symptoms with positive psychology interventions: a practice-friendly meta-analysis. J Clin Psychol 2009 May;65(5):467-487. [doi: 10.1002/jclp.20593] [Medline: 19301241]
65. Proyer RT, Gander F, Wellenzohn S, Ruch W. Positive psychology interventions in people aged 50-79 years: long-term effects of placebo-controlled online interventions on well-being and depression. Aging Ment Health 2014 Apr 08;18(8):997-1005. [doi: 10.1080/13607863.2014.899978] [Medline: 24712501]
66. Gajewski PD, Falkenstein M. Physical activity and neurocognitive functioning in aging - a condensed updated review. Eur Rev Aging Phys Act 2016 Jan 21;13(1):1 [FREE Full text] [doi: 10.1186/s11556-016-0161-3] [Medline: 26865880]
67. Taylor-Piliae R, Newell K, Cherin R, Lee M, King A, Haskell W. Effects of Tai Chi and Western exercise on physical and cognitive functioning in healthy community-dwelling older adults. J Aging Phys Act 2010 Jul;18(3):261-279. [doi: 10.1123/japa.18.3.261] [Medline: 20651414]

## Abbreviations

**ART:** antiretroviral therapy
**CD4:** cluster of differentiation 4
**CES-D-20:** 20-item Center for Epidemiological Studies-Depression
**MET:** metabolic-equivalent task

*Edited by H Bradley; submitted 17.08.21; peer-reviewed by S Gunther, P Nguyen, ASW Chan ; comments to author 10.05.22; revised version received 13.06.22; accepted 26.06.22; published 19.08.22.*

*Please cite as:*
*Qin P, He J, Yang X, Chen S, Chen X, Jiang H, Fung AWT, Wang Z, Lau JTF*
*The Role of Depressive Symptoms and Physical Activity Levels in Mediating the Association Between HIV Status and Neurocognitive Functions Among Individuals Aged at Least 50 Years in China: Cross-sectional Study*
*JMIR Public Health Surveill 2022;8(8):e32968*
*URL: https://publichealth.jmir.org/2022/8/e32968*
*doi:10.2196/32968*
*PMID:35984684*

Original Paper

# Developing a Long COVID Phenotype for Postacute COVID-19 in a National Primary Care Sentinel Cohort: Observational Retrospective Database Analysis

Nikhil Mayor[1*], MBBS; Bernardo Meza-Torres[2,3*], MBBS, MSc, MPhil; Cecilia Okusi[4], BSc, MSc; Gayathri Delanerolle[4], MBChB, BSc, MSc, MBA; Martin Chapman[5], BSc, MSc, PhD; Wenjuan Wang[5], BSc, PhD; Sneha Anand[4], BSc, MSc, PhD; Michael Feher[2], MD; Jack Macartney[2], BSc; Rachel Byford[2], BA; Mark Joy[2], BSc, PhD; Piers Gatenby[1], MBBS, PhD; Vasa Curcin[5], BSc, PhD; Trisha Greenhalgh[2], MBBS, BSc, MSc, PhD; Brendan Delaney[4], MBBS, BSc, FRCGP, PhD; Simon de Lusignan[2,6], MBBS, MSc, MD, FRCGP

[1]Royal Surrey NHS Foundation Trust, Guildford, United Kingdom
[2]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, United Kingdom
[3]Department of Clinical and Experimental Medicine, University of Surrey, Guildford, United Kingdom
[4]Department of Surgery & Cancer, Institute of Global Health Innovation, Imperial College London, London, United Kingdom
[5]Population Health Sciences, Kings College London, London, United Kingdom
[6]Royal College of General Practitioners Research and Surveillance Centre, London, United Kingdom
[*]these authors contributed equally

**Corresponding Author:**
Simon de Lusignan, MBBS, MSc, MD, FRCGP
Nuffield Department of Primary Care Health Sciences
University of Oxford
Eagle House
7 Walton Well Road
Oxford, OX2 6ED
United Kingdom
Phone: 44 01865 616600
Email: simon.delusignan@phc.ox.ac.uk

## Abstract

**Background:** Following COVID-19, up to 40% of people have ongoing health problems, referred to as postacute COVID-19 or long COVID (LC). LC varies from a single persisting symptom to a complex multisystem disease. Research has flagged that this condition is underrecorded in primary care records, and seeks to better define its clinical characteristics and management. Phenotypes provide a standard method for case definition and identification from routine data and are usually machine-processable. An LC phenotype can underpin research into this condition.

**Objective:** This study aims to develop a phenotype for LC to inform the epidemiology and future research into this condition. We compared clinical symptoms in people with LC before and after their index infection, recorded from March 1, 2020, to April 1, 2021. We also compared people recorded as having acute infection with those with LC who were hospitalized and those who were not.

**Methods:** We used data from the Primary Care Sentinel Cohort (PCSC) of the Oxford Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC) database. This network was recruited to be nationally representative of the English population. We developed an LC phenotype using our established 3-step ontological method: (1) ontological step (defining the reasoning process underpinning the phenotype, (2) coding step (exploring what clinical terms are available, and (3) logical extract model (testing performance). We created a version of this phenotype using Protégé in the ontology web language for BioPortal and using PhenoFlow. Next, we used the phenotype to compare people with LC (1) with regard to their symptoms in the year prior to acquiring COVID-19 and (2) with people with acute COVID-19. We also compared hospitalized people with LC with those not hospitalized. We compared sociodemographic details, comorbidities, and Office of National Statistics–defined LC symptoms between groups. We used descriptive statistics and logistic regression.

**Results:** The long-COVID phenotype differentiated people hospitalized with LC from people who were not and where no index infection was identified. The PCSC (N=7.4 million) includes 428,479 patients with acute COVID-19 diagnosis confirmed by a laboratory test and 10,772 patients with clinically diagnosed COVID-19. A total of 7471 (1.74%, 95% CI 1.70-1.78) people were coded as having LC, 1009 (13.5%, 95% CI 12.7-14.3) had a hospital admission related to acute COVID-19, and 6462 (86.5%, 95% CI 85.7-87.3) were not hospitalized, of whom 2728 (42.2%) had no COVID-19 index date recorded. In addition, 1009 (13.5%, 95% CI 12.73-14.28) people with LC were hospitalized compared to 17,993 (4.5%, 95% CI 4.48-4.61; *P*<.001) with uncomplicated COVID-19.

**Conclusions:** Our LC phenotype enables the identification of individuals with the condition in routine data sets, facilitating their comparison with unaffected people through retrospective research. This phenotype and study protocol to explore its face validity contributes to a better understanding of LC.

***(JMIR Public Health Surveill 2022;8(8):e36989)*** doi:10.2196/36989

**KEYWORDS**

medical record systems; computerized; Systematized Nomenclature of Medicine; postacute COVID-19 syndrome; phenotype; COVID-19; long COVID; ethnicity; social class; general practitioners; data accuracy; data extracts; biomedical ontologies; SARS-CoV-2; hospitalization; epidemiology; surveillance; public health; BioPortal; electronic health record; disease management; digital tool

## Introduction

### Background

Postacute COVID-19 syndrome, otherwise known as long COVID (LC), is a complex, multisystem disease that follows SARS-CoV-2 infection and often follows a relapsing and remitting course [1]. The postacute sequelae of LC could manifest with mild symptoms or asymptomatically. Although a distinct clinical phenotype remains to be defined, current evidence suggests that fatigue with postexertional symptom exacerbation is the most prominent, followed by shortness of breath, muscle aches, and cognitive impairment (brain fog) [2-4]. Risk factors are not well understood, and it appears that the characteristics that increase the risk of developing a severe COVID-19 infection (older age, male sex, non-White ethnicity, and certain pre-existing comorbidities) do not translate into an increased risk of developing LC [5]. Current research indicates that the prevalence of LC is greater amongst females, those aged 20-70 years, and those with prepandemic mental health conditions and asthma [6]. As the symptom pattern varies widely between individuals and risk factors have not been defined [7], it is difficult to establish an evidence-based framework for the recognition, assessment, and management of this condition.

In the United Kingdom, the Office for National Statistics (ONS) has estimated that 1.3 million people continue to have ongoing health issues after COVID-19 infection, with over 800,000 people reporting at least some limitation to their daily lives [2], although cases remain underrecorded in primary care electronic health records (EHRs) [8]. In December 2020 (updated in December 2021), the United Kingdom's National Institute for Health and Care Excellence (NICE) recognized the lack of a clinical definition and released a rapid guideline [9]. NICE defines acute COVID-19 (symptoms lasting <4 weeks), ongoing symptomatic COVID-19 (symptoms lasting 4-12 weeks), and postacute COVID-19 syndrome (symptoms lasting >12 weeks), with the latter 2 considered as LC [3]. However, there remain limited treatment options or evidence-based rehabilitation guidance available for this condition, although research projects, such as the Long Covid Multidisciplinary Consortium: Optimising Treatments and Services across the National Health Service (NHS; LOCOMOTION), have been set up to address this [10].

Research on LC is confusing due to heterogenous study methods with minimal phenotypic information, and patient-reported symptoms often remain uncaptured [7]. Phenotypes are a standardized method for case definition and identification from routine data and are usually machine-processable. Computable phenotypes have become increasingly important in EHRs as they allow identification of patient characteristics using data that are generated during routine patient interactions [11]. An EHR-based phenotype definition is constructed by characterizing the disease in terms of its demographic profile, symptomatology, laboratory tests, and other clinically relevant data, such as referrals to specialist services [12]. This information can be displayed in the form of clinical codes or abstractly represented in the form of a logical data flow diagram [13]. In the United Kingdom, we use a national information standard, the Systematized Nomenclature of Medicine Clinical Terms (SNOMED-CT) and Read version 2 codes. It can then be written into a computational algorithm, which can be applied to EHRs to identify a specific cohort of patients. However, such a phenotype has to work within the constraints of data quality and clinical terminology used.

### Aims

The aim of this study is to develop a phenotype for LC using pseudonymized individual-level EHR data from English general practice that will enable the monitoring and evaluation of interventions for this condition. The specific objectives are:

- To develop a phenotype for LC
- To make this phenotype available in standard online formats in BioPortal and the PhenoFlow library
- To compare the symptoms reported by people with LC identified by the phenotype in the year prior to the pandemic with those they experienced during the pandemic
- To compare the symptoms of people with LC identified by the phenotype to those with acute COVID-19

- To compare people with LC identified by the phenotype who were hospitalized with those who were managed in the community

## Methods

### Data Source

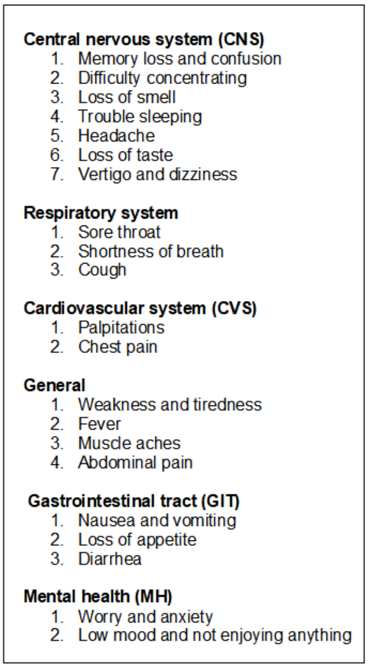
The LC phenotype was piloted in an observational retrospective database analysis of the English Primary Care Sentinel Cohort (PCSC), which used data from the Oxford Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC) sentinel network. This database is derived from pseudonymized patient data from EHRs and is recruited to be representative of the English population in terms of both demographic and clinical factors [14].

### Comparisons

This protocol piloted an LC phenotype in the PCSC and described the baseline characteristics and outcomes of those with LC. All people registered within the PCSC were eligible for inclusion in the study. The developed phenotype was used as a detailed reference for the inclusion and exclusion criteria. The study described further aspects of the epidemiology through 3 comparisons:

- Before-and-after symptom comparison in people with LC: We compared the presence of symptoms listed by the ONS between 1 and 6 months after index infection. We matched the period with the equivalent months for the previous year. The list of 21 symptoms developed by the ONS is broad and includes central nervous system symptoms, such as fatigue; respiratory symptoms; cardiovascular symptoms; general symptoms; gastrointestinal symptoms; and mental health symptoms (Figure 1). We defined an index date of COVID-19 hierarchically using our application ontology, which prioritized virologically proven cases (definite COVID-19) over clinical terms for a COVID-19–specific disease (probable COVID-19) over less definite clinical diagnoses (possible COVID-19) [15].
- Comparison of people with LC with those with acute COVID-19 uncomplicated by LC: We compared sociodemographic features, a range of comorbidities, vaccination status, and mortality between those who had LC and those who had a COVID-19 infection. Sociodemographic features included age; gender; ethnicity using 5 categories (Asian, Black, White, mixed, and others) [16]; socioeconomic status (SES), measured using the Index of Multiple Deprivation (IMD) [17]; population density divided into rural, town, city, and conurbation; the English Health Region; obesity, categorized by the BMI or the diagnostic clinical term into underweight, normal weight, overweight, obese, or severely obese; and, finally, smoking status, categorized into current smoker, ex-smoker, and nonsmoker. We conducted a literature review and identified a range of chronic diseases associated with the risk of COVID-19 complications (Figure 2) and an extended list differentiating long COVID and COVID-19 [1,5,8,18,19]. We reported the vaccination status stratified by the Cambridge Multimorbidity Score (CMMS) as an overall measure of multimorbidity [20]. The CMMS uses 37 conditions to predict primary care consultations, unplanned hospital admissions, and death as primary outcomes; it is useful to identify people who are at higher risk of specific outcomes based on their comorbidity profiles, as recorded in primary care EHR data.
- Comparison of those with LC who were hospitalized with those who were not: We used the same variables to compare people who were hospitalized and subsequently had LC with those who were not hospitalized but had LC diagnosed in the community. We conducted a sensitivity analysis where we subdivided the community cases into 2 groups: people who had an index COVID-19 infection either virologically confirmed or sometimes clinically diagnosed and those who have an LC diagnosis, a referral to an LC service, or a LC disability rating score compatible with an LC diagnosis (eg, Yorkshire LC score) [21].

**Figure 1.** Symptoms identified by the UK Office for National Statistics (ONS) that are associated with long COVID (LC).



**Central nervous system (CNS)**
1. Memory loss and confusion
2. Difficulty concentrating
3. Loss of smell
4. Trouble sleeping
5. Headache
6. Loss of taste
7. Vertigo and dizziness

**Respiratory system**
1. Sore throat
2. Shortness of breath
3. Cough

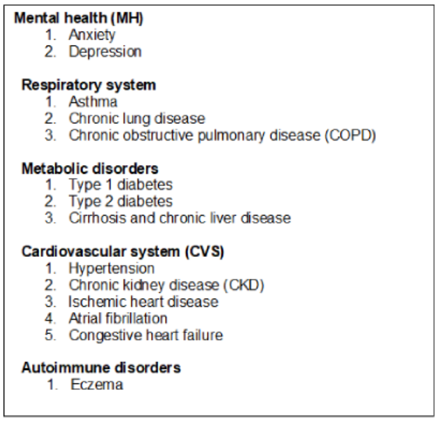
**Cardiovascular system (CVS)**
1. Palpitations
2. Chest pain

**General**
1. Weakness and tiredness
2. Fever
3. Muscle aches
4. Abdominal pain

**Gastrointestinal tract (GIT)**
1. Nausea and vomiting
2. Loss of appetite
3. Diarrhea

**Mental health (MH)**
1. Worry and anxiety
2. Low mood and not enjoying anything

**Figure 2.** Summary of comorbidities included in our analyses.



**Mental health (MH)**
1. Anxiety
2. Depression

**Respiratory system**
1. Asthma
2. Chronic lung disease
3. Chronic obstructive pulmonary disease (COPD)

**Metabolic disorders**
1. Type 1 diabetes
2. Type 2 diabetes
3. Cirrhosis and chronic liver disease

**Cardiovascular system (CVS)**
1. Hypertension
2. Chronic kidney disease (CKD)
3. Ischemic heart disease
4. Atrial fibrillation
5. Congestive heart failure

**Autoimmune disorders**
1. Eczema

## Phenotype Development

We used a 3-step ontological approach to create our phenotype [12], considering ontological, coding, and logical layers.

### *Ontological Layer*

The key concept identified in our ontological layer was an index date for COVID-19, noting that not all cases had virological confirmation (especially in the early part of the pandemic up to July 2020). Hence, some LC cases might only have been flagged on referral or later presentation. We wanted to also include whether cases were hospitalized, as hospitalization can be associated with poor outcomes [22]. Additionally, we included vaccination status to explore if protective.

### *Coding Layer*

We applied our existing ontology to identify COVID-19 cases. We included key outcomes related to hospital admissions. These were any hospitalization, admission to intensive care, or death in the hospital. To be a case of LC, we included disease codes, primarily recorded with SNOMED-CT or the World Health Organization's (WHO) *International Classification of Diseases* (ICD). The clinical term could be a diagnosis, a referral (eg, referral to post–COVID-19 assessment clinic), or completion of a rating scale that implied LC (eg, the Yorkshire Rehabilitation Scale, which records symptom severity, functional disability, and health status) [23].

### *Logical Data Extraction Model*

We planned our data extraction using pseudonymized primary care data. We supplemented these data with national data sets. The national data sets used were the Second Generation Surveillance System (SGSS) to capture any missing test data, the National Immunisation Management System (NIMS) to capture any missing vaccine recording, and Hospital Episode Statistics (HES) to add hospital outcome data. The ONS also provided death data. We pseudonymized all data as close to the source as possible using an NHS Digital–approved method. We used the same pseudonymization method to link primary care data to other data sources.

Our phenotype definition is presented as a structured multistep model (Figure 3) and as a logic model (Figure 4). This omitted the reporting of vaccine exposure by group.

**Figure 3.** PhenoFlow multilayer model describes each step within the multistep phenotype definition contained within the phenotype.

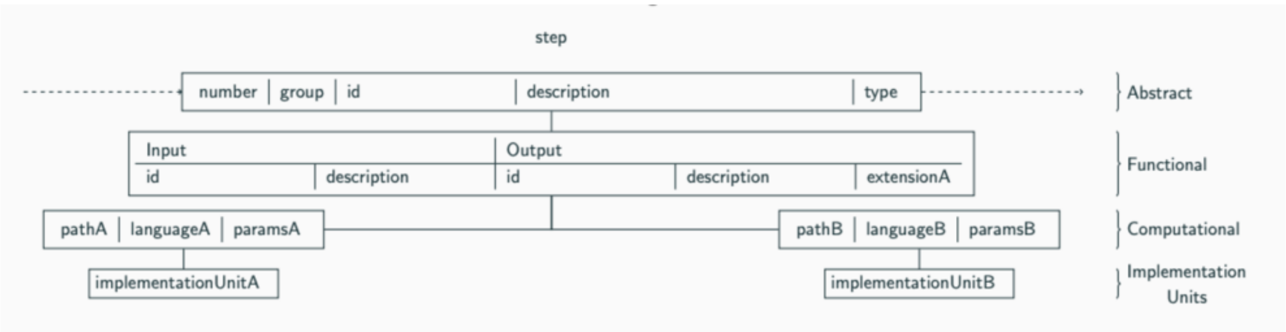
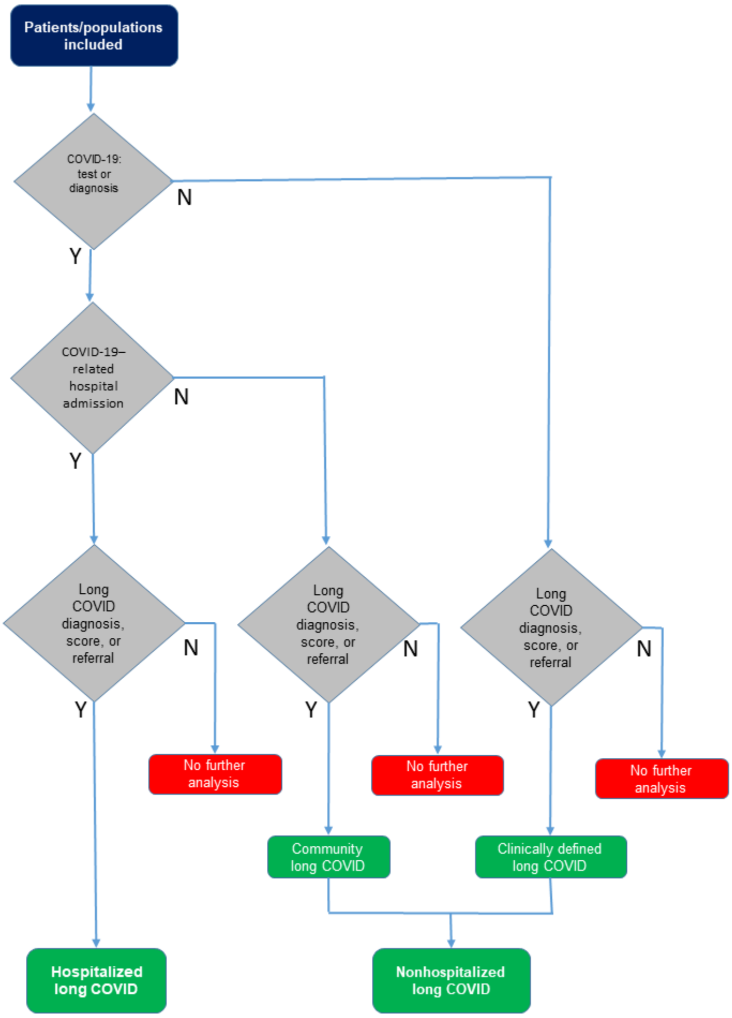


**Figure 4.** Logic model for the LC phenotype. LC: long COVID.



### *Formal Ontologies: BioPortal and PhenoFlow*

From the logic model, we created 2 formal ontologies. We used Protégé, an open source ontology editor, to construct a domain ontology, which we placed online via BioPortal. Protégé supports Ontology Web Language (OWL) version 2 and Resource Description Frameworks (RDFs) from the World Wide Web Consortium (W3C) [24]. BioPortal is part of the National Center for Biomedical Ontology (in the United States) that supports the creation of interoperable ontologies.

We also created a version within the PhenoFlow library [13]. The PhenoFlow library imports and standardizes abstract definitions under a workflow-based multilayer model, which is later used as the basis for autonomously generating a computable form of the definition. This can then be downloaded and executed locally to identify a patient cohort. Standardizing a definition under the PhenoFlow model also assists with manual phenotype translation as it supplements the use of clinical terminology and simplifies the representation of logical structures, thus increasing intelligibility (Figure 3). The model allows greater flexibility in updating phenotypes and also increases portability.

The model consisted of 3 layers and included the type or classification of the step's logic, with detailed information regarding inputs and outputs at each relevant step. This information was combined with 1 or more implemented units (eg, a piece of Python code) in order to realize a computable phenotype.

### Statistical Analysis

This study is a secondary analysis of existing pseudonymized data within the PCSC of the RSC. Although we noted that 58 (7.8%) of 743 practices had not recorded any LC cases in their EHR system, they were included in the analysis as it is likely that recording would improve during the course of the study, with increased interest in this condition [25].

The distribution of baseline characteristics among the study groups was summarized through descriptive statistics (eg, mean, median, and proportion) with measures of dispersion (eg, SD and IQRs). Univariate analyses included the calculation of odds ratios (ORs) for categorical risk factors versus outcome levels with 95% CIs by using the log(p/1 – p) link function. Logarithmic transformation of the outcome variable allowed a nonlinear association in a linear manner. *P* values were obtained from a chi-square test for categorical variables and one-way ANOVA for continuous variables. Data that were not documented in our database were reported as missing.

The primary outcome measure was the association with LC using our phenotype. Multivariate logistic regression modeling was used to identify factors associated with LC as a binary outcome within the study population. Relevant risk factors identified in the literature underwent univariate analysis and were included in multivariate logistic regression using a 3-step backward elimination procedure with of α threshold levels of 0.20, 0.10, and 0.05. A 2-sided α value of 0.05 was considered statistically significant. Missing data were presented as a separate category in univariate statistics and compared to the reference category. Missing data categories were imputed to the reference category if no significant differences were found in the reference category. Missing data categories were otherwise included in multivariate regression as a separate category, under the assumption that they may not be missing at random.

The following 3 comparisons were made, reporting frequencies between groups with *P* values obtained from the chi-square test:

- Symptoms reported by people with LC in the year prior to the pandemic versus those they experienced during the pandemic. The study period included COVID-19 cases from March 1, 2020, to April 1, 2021, with a follow-up period of a further 6 months up to, latest, September 30, 2021. This historical comparator period was month-matched; for example, if a patient had an acute COVID-19 code entered on February 1, 2021, their follow-up period was March 1-July 31, 2021, and the historic comparator period was March 1-July 31, 2019. This allowed the comparison of rates of relevant symptoms prior to having acute COVID-19 with after having acute COVID-19. The in-pandemic period was between 1 and 6 months after their index COVID-19 date. For those without a COVID-19 index date, we compared the 5 months prior to their LC recording with a matched period in the previous year.
- Symptoms of people with LC versus those with acute COVID-19. Although we accepted that LC is underrecorded, we considered this analysis of importance as the phenotype of those recorded was likely to be similar to those unrecorded, although potentially with more prominent or debilitating symptomatology.
- Those hospitalized with LC versus those managed in the community. A final comparison was then made between people requiring hospital admission for acute COVID-19 and those who were managed in the community and people who had no documented evidence of acute COVID-19. We also included a comparison between community cases with and without an index infection.

These comparisons enabled us to explore how the clinical phenotype varies. We also reported the vaccination uptake between people with and without LC diagnosis.

### Ethical Considerations

This study used existing data, and no subjects were recruited. RSC data used to create this phenotype were pseudonymized as close to the source as possible and sent in an encrypted format to the Oxford Royal College of General Practitioners Clinical Informatics Digital Hub (ORCHID) [15], which is recognized as a trusted research environment.

This study was part of the RECAP (Predicting Risk of Hospital Admission in Patients with Suspected COVID-19 in a Community Setting) study sponsored by the Imperial College London [26]. Although primarily a study to develop a risk prediction tool, it also included the creation of an LC phenotype. Ethical approval was granted by the North West–Greater Manchester East Research Ethics Committee and Health Research Authority on May 27, 2021 (Integrated Research Application System #283024, Research Ethics Committee reference #20/NW/0266).

## Results

### Phenotype: Logic Model

The logic model for the phenotype is shown in Figure 4. It depicts the hierarchical structure for identifying LC cases from the ontological layer of EHR data. The ontology logic runs hierarchically, first screening the population for COVID-19 cases (ie, firm diagnosis of acute COVID-19). Those with an index COVID-19 case were then screened for COVID-19–related hospital admissions. When no index COVID-19 cases were documented, the model still allowed for LC cases to be included as long as they had an entry within their EHRs, implying they had LC (ie, clinically defined LC).

### Phenotype: BioPortal and PhenoFlow

The LC phenotype definition was built in Protégé, which is an open source ontology editor that supports the latest OWL. This phenotype was then uploaded to BioPortal. The LC phenotype definition (Figure 5) can be accessed online [27] and provides a framework for researchers wanting to develop their own executable script to apply to databases.

Within BioPortal, the ontological layer of the structured phenotype is described within a class and subclass structure, while the coding layer is represented by individuals within each class and subclass. BioPortal ontologies can be readily updated.

The PhenoFlow library was used to transform the LC phenotype into a computable form (Figure 6). The LC phenotype can be accessed online with authorization [28], it can be downloaded, and, unlike BioPortal, it is ready for researchers to apply to EHR databases.

**Figure 5.** Individual steps of the LC phenotype definition logic. LC: long COVID.

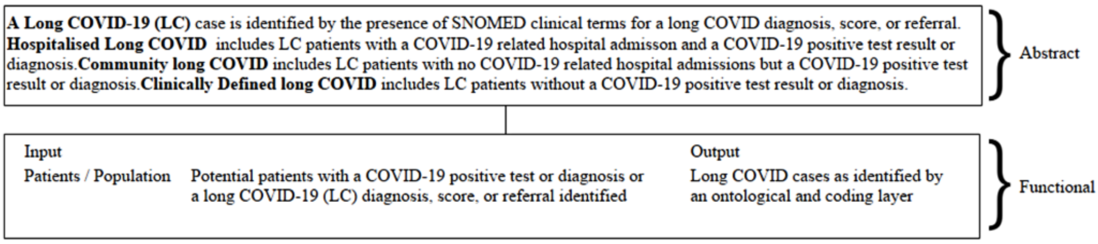
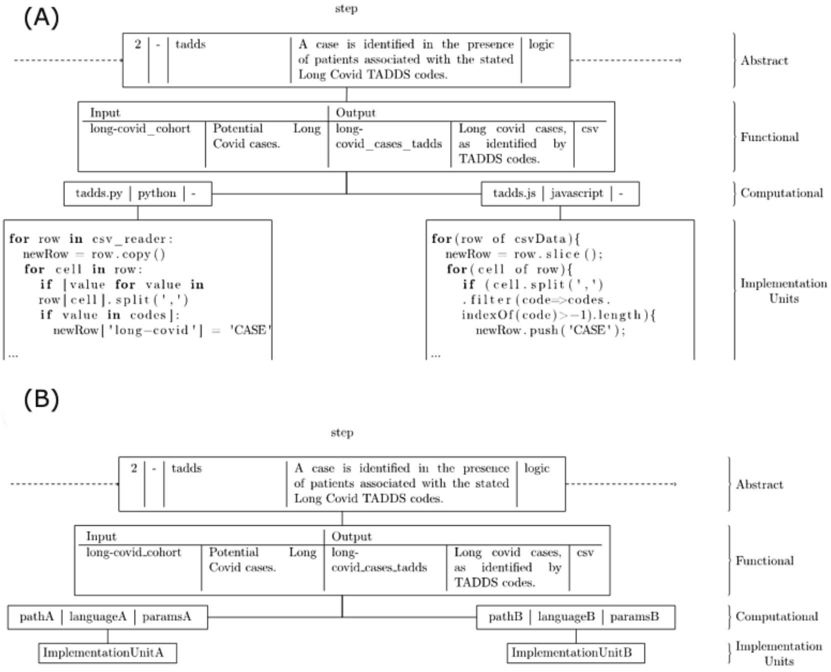


**Figure 6.** LC PhenoFlow model. (A) Individual steps of LC structured phenotype definition with and without implementation units and (B) individual steps of a structured phenotype using ORCHID-themed variable (TADDS) codes and implementation units. LC: long COVID; ORCHID: Oxford Royal College of General Practitioners Clinical Informatics Digital Hub.



```
for row in csv_reader:
  newRow = row.copy()
  for cell in row:
    if |value for value in
    row|cell|.split(',')
    if value in codes|:
      newRow|'long−covid'| = 'CASE'
...
```

```
for(row of csvData){
  newRow = row.slice();
  for(cell of row){
    if (cell.split(',')
    .filter(code=>codes.
    indexOf(code)>−1).length){
      newRow.push('CASE');
...
```

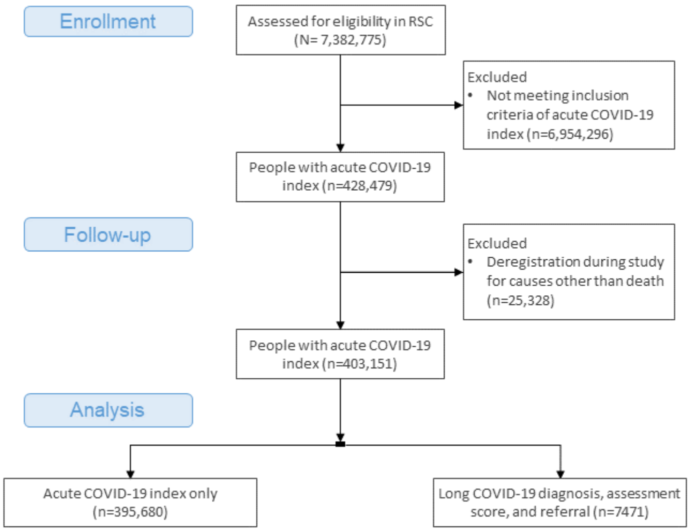
## Primary Care Sentinel Cohort

The PCSC of the RSC has a registered population of over 7 million (N=7,382,775). At the time of our data extraction, 428,479 (5.8%) of this population had an acute episode of COVID-19 recorded. Of this group, 42,321 (9.9%) were lost to follow-up; 40% (n=16,993) of this loss to follow-up was due to deaths, with just under half of these deaths (7531/16,993, 44.3%) being COVID-19 related. A total of 403,151 (94.1%) cases were included in the analysis, of whom 19,002 (4.7%) were hospitalized and 384,149 (95.3%) were not.

## People With LC

We identified 7471 (1.8%) of 428,479 people recorded as having LC within this included group (Figure 7). A greater proportion were hospitalized in the LC group compared to the overall hospitalization rate (1009/7471, 13.5%, *P*<.001). Within this group, there were a small number of deaths (23/7471, 0.3%, *P*<.001).

**Figure 7.** Consolidated Standards of Reporting Trials (CONSORT) diagram for the study population.



## Comparison of People With Acute COVID-19 and LC

We paired data for people with COVID-19 (n=395,680, 98.1%) and LC (n=7471, 1.9%), expecting to perform comparisons of baseline characteristics between both groups. Among the main preliminary findings, the mean age was 44.6 (SD 21.75) years for the COVID-19 group and 47.7 (SD 14.8) years for the LC group. A significantly higher proportion of those with LC were found among females (4836/7471, 64.7%), where the male gender was associated with lower odds for LC (OR 0.68, 95% CI 0.65-0.72). The proportion of those with a record of intensive care unit (ICU) admission was 0.6% (2523/395,680) in people with COVID-19 and 3.5% (261/7471) in people with LC, where a record of ICU admission was associated with higher odds of LC (OR 5.64, 95% CI 4.96-6.42). Sociodemographic characteristics reporting higher odds for LC in the univariate analysis included living in a conurbation (OR 1.49, 95% CI 1.42-1.57) and obesity (OR 1.40, 95% CI 1.34-1.48). Comorbidities associated with higher odds of LC included depression, anxiety, asthma, and hypertension. In contrast, chronic lung disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), ischemic heart disease, atrial fibrillation, and congestive heart failure were associated with lower odds of LC.

The baseline characteristics of the population are shown in Tables 1-4.

**Table 1.** Frequencies of baseline characteristics and univariate ORs[a] (sociodemographics) for people with COVID-19 stratified by long COVID (LC) status in the PCSC[b] in England (March 1, 2020-April 1, 2021).

| Variable and category | Overall (N=403,151) | COVID-19 (n=395,680) | LC (n=7471) | OR (95% CI) | *P* value |
|---|---|---|---|---|---|
| Age (years; continuous), mean (SD) | 44.62 (21.65) | 44.56 (21.75) | 47.74 (14.81) | 1.01 (1.01-1.01) | <.001 |
| **Gender, n (%)** | | | | | |
| Female (Ref.[c]) | 224,934 (55.8) | 220,098 (55.6) | 4836 (64.7) | 1.00 (N/A[d]) | N/A |
| Male | 178,217 (44.2) | 175,582 (44.4) | 2635 (35.3) | 0.68 (0.65-0.72) | <.001 |
| **Deprivation, n (%)** | | | | | |
| Least deprived (Ref.) | 156,115 (38.7) | 153,198 (38.7) | 2917 (39.0) | 1.00 (N/A) | N/A |
| Most deprived | 229,986 (57.0) | 225,608 (57.0) | 4378 (58.6) | 1.02 (0.97-1.07) | .43 |
| Missing | 17,050 (4.2) | 16,874 (4.3) | 176 (2.4) | 0.55 (0.47-0.64) | <.001 |
| **Ethnicity, n (%)** | | | | | |
| White (Ref.) | 262,878 (65.2) | 257,507 (65.1) | 5371 (71.9) | 1.00 (N/A) | N/A |
| Non-White | 55,609 (13.8) | 54,549 (13.8) | 1060 (14.2) | 0.93 (0.87-1.00) | .04 |
| Missing | 84,664 (21.0) | 83,624 (21.1) | 1040 (13.9) | 0.60 (0.56-0.64) | <.001 |
| **Ethnicity point, n (%)** | | | | | |
| Asian | 35,214 (8.7) | 34,587 (8.7) | 627 (8.4) | N/A | <.001 |
| Black | 11,286 (2.8) | 11,022 (2.8) | 264 (3.5) | N/A | N/A |
| Other | 9109 (2.3) | 8940 (2.3) | 169 (2.3) | N/A | N/A |
| Unknown | 84,664 (21.0) | 83,624 (21.1) | 1040 (13.9) | N/A | N/A |
| White | 262,878 (65.2) | 257,507 (65.1) | 5371 (71.9) | N/A | N/A |
| **Population density, n (%)** | | | | | |
| City (Ref.) | 201,839 (50.1) | 198,709 (50.2) | 3130 (41.9) | 1.00 (N/A) | N/A |
| Conurbation | 136,068 (33.8) | 132,942 (33.6) | 3126 (41.8) | 1.49 (1.42-1.57) | <.001 |
| Rural | 65,244 (16.2) | 64,029 (16.2) | 1215 (16.3) | 1.20 (1.13-1.29) | <.001 |
| **NHS[e] region, n (%)** | | | | | |
| London | 55,191 (13.7) | 53,721 (13.6) | 1470 (19.7) | N/A | <.001 |
| Midlands | 67,375 (16.7) | 66,405 (16.8) | 970 (13.0) | N/A | N/A |
| North and east | 95,209 (23.6) | 93,995 (23.8) | 1214 (16.2) | N/A | N/A |
| Northwest | 67,211 (16.7) | 65,768 (16.6) | 1443 (19.3) | N/A | N/A |
| South | 118,165 (29.3) | 115,791 (29.3) | 2374 (31.8) | N/A | N/A |
| **BMI, n (%)** | | | | | |
| Nonobese (Ref.) | 247,957 (61.5) | 243,520 (61.5) | 4437 (59.4) | 1.00 (N/A) | N/A |
| Obese | 101,194 (25.1) | 98,669 (24.9) | 2525 (33.8) | 1.40 (1.34-1.48) | <.001 |
| Missing | 54,000 (13.4) | 53,491 (13.5) | 509 (6.8) | 0.52 (0.48-0.57) | <.001 |
| **Smoker, n (%)** | | | | | |
| Nonsmoker (Ref.) | 207,788 (51.5) | 203,422 (51.4) | 4366 (58.4) | 1.00 (N/A) | N/A |
| Smoker/ex-smoker | 147,819 (36.7) | 144,930 (36.6) | 2889 (38.7) | 0.93 (0.89-0.97) | <.001 |
| Missing | 47,544 (11.8) | 47,328 (12.0) | 216 (2.9) | 0.21 (0.19-0.24) | <.001 |

[a] OR: odds ratio.

[b] PCSC: Primary Care Sentinel Cohort.

[c] Ref.: reference category.

[d] N/A: not applicable.

[e] NHS: National Health Service.

**Table 2.** Frequencies of baseline characteristics and univariate ORs[a] (comorbidities) for people with COVID-19 stratified by LC[b] status in the PCSC[c] in England (March 1, 2020-April 1, 2021).

| Variable and category | Overall (N=403,151) | COVID-19 (n=395,680) | LC (n=7471) | OR (95% CI) | *P* value |
|---|---|---|---|---|---|
| **Depression, n (%)** | | | | | |
| No (Ref.[d]) | 310,251 (77.0) | 305,486 (77.2) | 4765 (63.8) | 1.00 (N/A[e]) | N/A |
| Yes | 92,900 (23.0) | 90,194 (22.8) | 2706 (36.2) | 1.92 (1.83-2.02) | <.001 |
| **Anxiety, n (%)** | | | | | |
| No (Ref.) | 308,752 (76.6) | 303,878 (76.8) | 4874 (65.2) | 1.00 (N/A) | N/A |
| Yes | 94,399 (23.4) | 91,802 (23.2) | 2597 (34.8) | 1.76 (1.68-1.85) | <.001 |
| **Asthma, n (%)** | | | | | |
| No (Ref.) | 328,133 (81.4) | 322,434 (81.5) | 5699 (76.3) | 1.00 (N/A) | N/A |
| Yes | 75,018 (18.6) | 73,246 (18.5) | 1772 (23.7) | 1.37 (1.30-1.44) | <.001 |
| **Chronic lung disease, n (%)** | | | | | |
| No (Ref.) | 388,932 (96.5) | 381,651 (96.5) | 7281 (97.5) | 1.00 (N/A) | N/A |
| Yes | 14,219 (3.5) | 14,029 (3.5) | 190 (2.5) | 0.71 (0.61-0.82) | <.001 |
| **COPD[f], n (%)** | | | | | |
| No (Ref.) | 390,544 (96.9) | 383,219 (96.9) | 7325 (98.0) | 1.00 (N/A) | N/A |
| Yes | 12,607 (3.1) | 12,461 (3.1) | 146 (2.0) | 0.61 (0.52-0.72) | <.001 |
| **Hypertension, n (%)** | | | | | |
| No (Ref.) | 322,978 (80.1) | 317,094 (80.1) | 5884 (78.8) | 1.00 (N/A) | N/A |
| Yes | 80,173 (19.9) | 78,586 (19.9) | 1587 (21.2) | 1.09 (1.03-1.15) | <.003 |
| **CKD[g], n (%)** | | | | | |
| No (Ref.) | 380,699 (94.4) | 373,496 (94.4) | 7203 (96.4) | 1.00 (N/A) | N/A |
| Yes | 22,452 (5.6) | 22,184 (5.6) | 268 (3.6) | 0.63 (0.55-0.71) | <.001 |
| **Ischemic heart disease, n (%)** | | | | | |
| No (Ref.) | 381,585 (94.7) | 374,450 (94.6) | 7135 (95.5) | 1.00 (N/A) | N/A |
| Yes | 21,566 (5.3) | 21,230 (5.4) | 336 (4.5) | 0.83 (0.74-0.93) | <.001 |
| **Atrial fibrillation, n (%)** | | | | | |
| No (Ref.) | 389,749 (96.7) | 382,408 (96.6) | 7341 (98.3) | 1.00 (N/A) | N/A |
| Yes | 13,402 (3.3) | 13,272 (3.4) | 130 (1.7) | 0.51 (0.43-0.61) | <.001 |
| **Congestive heart failure, n (%)** | | | | | |
| No (Ref.) | 395,034 (98.0) | 387,625 (98.0) | 7409 (99.2) | 1.00 (N/A) | N/A |
| Yes | 8117 (2.0) | 8055 (2.0) | 62 (0.8) | 0.40 (0.31-0.52) | <.001 |
| **Type 2 diabetes, n (%)** | | | | | |
| No (Ref.) | 372,818 (92.5) | 365,912 (92.5) | 6906 (92.4) | 1.00 (N/A) | N/A |
| Yes | 30,333 (7.5) | 29,768 (7.5) | 565 (7.6) | 1.01 (0.92-1.10) | .90 |
| Yes | 13,402 (3.3) | 13,272 (3.4) | 130 (1.7) | 0.51 (0.43-0.61) | <.001 |
| **Type 1 diabetes, n (%)** | | | | | |
| No (Ref.) | 400,625 (99.4) | 393,196 (99.4) | 7429 (99.4) | 1.00 (N/A) | N/A |
| Yes | 2526 (0.6) | 2484 (0.6) | 42 (0.6) | 0.89 (0.66-1.22) | .47 |
| **Cirrhosis, n (%)** | | | | | |
| No (Ref.) | 402,118 (99.7) | 394,663 (99.7) | 7455 (99.8) | 1.00 (N/A) | N/A |
| Yes | 1033 (0.3) | 1017 (0.3) | 16 (0.2) | 0.83 (0.51-1.37) | .46 |

| Variable and category | Overall (N=403,151) | COVID-19 (n=395,680) | LC (n=7471) | OR (95% CI) | *P* value |
|---|---|---|---|---|---|
| **Eczema, n (%)** | | | | | |
| No (Ref.) | 313,703 (77.8) | 307,931 (77.8) | 5772 (77.3) | 1.00 (N/A) | N/A |
| Yes | 89,448 (22.2) | 87,749 (22.2) | 1699 (22.7) | 1.03 (0.98-1.09) | .25 |

[a] OR: odds ratio.

[b] LC: long COVID.

[c] PCSC: Primary Care Sentinel Cohort.

[d] Ref.: reference category.

[e] N/A: not applicable.

[f] COPD: chronic obstructive pulmonary disease.

[g] CKD: chronic kidney disease.

**Table 3.** Frequencies of baseline characteristics and univariate ORs[a] (exposures) for people with COVID-19 stratified by LC[b] status in the PCSC[c] in England (March 1, 2020-April 1, 2021).

| Variable and category | Overall (N=403,151) | COVID-19 (n=395,680) | LC (n=7471) | OR (95% CI) | *P* value |
|---|---|---|---|---|---|
| **Hospitalized, n (%)** | | | | | |
| No (Ref.[d]) | 384,149 (95.3) | 377,687 (95.5) | 6462 (86.5) | 1.00 (N/A[e]) | N/A |
| Yes | 19,002 (4.7) | 17,993 (4.5) | 1009 (13.5) | 3.28 (2.95-3.38) | <.001 |
| **ICU[f] admission, n (%)** | | | | | |
| No (Ref.) | 400,367 (99.3) | 393,157 (99.4) | 7210 (96.5) | 1.00 (N/A) | N/A |
| Yes | 2784 (0.7) | 2523 (0.6) | 261 (3.5) | 5.64 (4.96-6.42) | <.001 |
| **COVID-19 vaccination at any point, n (%)** | | | | | |
| No vaccine (Ref.) | 81,081 (20.1) | 80,229 (20.3) | 852 (11.4) | 1.00 (N/A) | N/A |
| One dose | 25,018 (6.2) | 24,655 (6.2) | 363 (4.9) | 1.39 (1.23-1.57) | <.001 |
| Two doses | 297,052 (73.7) | 290,796 (73.5) | 6256 (83.7) | 2.03 (1.89-2.18) | <.001 |
| **First vaccination brand, n (%)** | | | | | |
| AstraZeneca | 168,444 (41.8) | 164,652 (41.6) | 3792 (50.8) | N/A | <.001 |
| Pfizer-BioNTech | 146,328 (36.3) | 143,647 (36.3) | 2681 (35.9) | N/A | N/A |
| Other | 6986 (1.7) | 6843 (1.7) | 143 (1.9) | N/A | N/A |
| None | 81,393 (20.2) | 80,538 (20.4) | 855 (11.4) | N/A | N/A |
| **Second vaccination brand, n (%)** | | | | | |
| AstraZeneca | 163,206 (40.5) | 159,541 (40.3) | 3,665 (49.1) | N/A | <.001 |
| Pfizer-BioNTech | 127,048 (31.5) | 124,604 (31.5) | 2444 (32.7) | N/A | N/A |
| Other | 6279 (1.6) | 6150 (1.6) | 129 (1.7) | N/A | N/A |
| None | 106,605 (26.4) | 105,372 (26.6) | 1233 (16.5) | N/A | N/A |
| N/A | 13 (0) | 13 (0) | 0 | N/A | N/A |

[a] OR: odds ratio.

[b] LC: long COVID.

[c] PCSC: Primary Care Sentinel Cohort.

[d] Ref.: reference category.

[e] N/A: not applicable.

[f] ICU: intensive care unit.

**Table 4.** Frequencies of baseline characteristics and univariate ORs[a] (mortality) for people with COVID-19 stratified by LC[b] status in the PCSC[c] in England (March 1, 2020-April 1, 2021).

| Variable and category | Overall (N=403,151) | COVID-19 (n=395,680) | LC (n=7471) | OR (95% CI) | *P* value |
|---|---|---|---|---|---|
| **All-cause mortality, n (%)** | | | | | |
| No (Ref.[d]) | 386,158 (95.8) | 378,710 (95.7) | 7448 (99.7) | 1.00 (N/A[e]) | N/A |
| Yes | 16,993 (4.2) | 16,970 (4.3) | 23 (0.3) | 0.07 (0.05-0.10) | <.001 |

[a] OR: odds ratio.

[b] LC: long COVID.

[c] PCSC: Primary Care Sentinel Cohort.

[d] Ref.: reference category.

[e] N/A: not applicable.

### Comparison of Those Hospitalized and Those Not Hospitalized

For the group of people with LC, we paired data for people with a record of hospitalization (n=1009, 13.5%) and without hospitalization (n=6462, 86.5%). The mean age was 54.6 (SD 13.69) years for the hospitalized group and 46.7 (SD 14.7) years for the nonhospitalized group, while the proportion of females was 66.5% (4297/6462) in the nonhospitalized group and 53.4% (539/1009) in the hospitalized group. Factors associated with greater odds of hospitalization were the male gender (OR 1.73, 95% CI 1.51-1.98) and type 2 diabetes (OR 3.8, 95% CI 3.15-4.59).

## Discussion

### Principal Findings

We created a phenotype for LC and made it publicly available with the aim of facilitating research in this area. Our phenotype is straightforward but based on the presence of a postacute COVID-19 syndrome code being present in the EHR. The definition allows comparison of hospitalized and nonhospitalized groups and the inclusion of people with no baseline COVID-19 test data. Our phenotype's logical model can also allow vaccine exposure to be compared between groups.

Based on our network data, LC recording within primary care appears to be low and we noted interpractice variability, with some practices (8%) having no recorded cases. It was not possible to generate a symptom-related definition that might help close the gap between the level of recording in primary care and that identified through the ONS surveys [2].

Many different conditions have been associated with LC, and we made pragmatic, literature-based choices regarding which groups we should contrast where we make LC comparisons. We consider that before-and-after, acute COVID-19 compared with LC and hospitalized compared with nonhospitalized LC analyses will provide an assessment of our phenotype's performance and face validity.

Digitization of health systems worldwide has led to the emergence of EHR repositories for the study of both established and emerging diseases and trends. Phenotyping algorithms allow identification of patients within EHRs who share characteristics, and therefore play an important role in medical cohort studies. High-quality phenotypes must be portable, accessible, and reproducible. A number of phenotype libraries have been developed or are undergoing development [29] in order to collect and store validated phenotype definitions. Our LC phenotype is available to download from BioPortal, where researchers can use it to produce their own executable script. By additionally applying the phenotype using the PhenoFlow model with "functional" and "computational" layers, our phenotype goes 1 step further with the capability for immediate execution in EHRs. As the characteristics of LC change with more data, vaccines, and treatments becoming available, the flexibility of the PhenoFlow model allows the phenotype to be readily updated and reapplied.

### Comparison With Prior Work

Applying the phenotype within the RSC, we identified 7471 patients with LC. The LC group was older overall, more likely to be female, obese, and suffering from anxiety, depression, or asthma. These findings are in keeping with studies using patient-reported data and EHRs [5,6]. In the acute COVID-19 group, 17,993 (4.5%) of 395,680 patients were hospitalized. The number of patients hospitalized with COVID-19 in the LC group was much higher (1009/7471, 13.5%). Furthermore, patients with LC were more likely to have had an ICU admission: 261/7471 (3.5%) versus 2523/395,680 (0.6%). Similar findings were reported by O'Connor et al [23] in an observational study of 187 patients with 15% hospitalized and 5.4% admitted to the ICU. The Zoe Symptom Study app [5] reports even higher rates of patients attending the hospital (up to 44% of those experiencing symptoms for more than 56 days) but does not clarify whether these patients were admitted to the hospital. Survey studies such as these may also suffer from selection bias and are not necessarily representative of the wider population. Nevertheless, hospital attendance during the acute infection appears to be a risk factor for LC, and further work is required to address this.

### Strengths and Limitations

Our study used the PCSC of the RSC, 1 of Europe's oldest sentinel systems and one widely involved in pandemic research [14,15,30]. Data quality is good, and linkage to national registries ensured reliable data, including mortality [31]. Additionally, UK primary care is universal and a registration-based system. Nearly all emergency care is provided by the NHS, and national systems enable capture of COVID-19 tests and vaccination data.

The complexity of LC and its multiple symptoms and associations made this analysis challenging. We were selective based on the literature available on the conditions we compared. The statistical analysis was limited to establishing associations between known covariates and outcomes, testing the face validity our LC phenotype against other reports in the United Kingdom. Further research should explore causality of the reported findings under appropriate study designs.

We likely underestimated the frequency of ongoing symptoms following acute infection, because many people do not seek medical care for these. There were also, like all studies using routine data, some issues with data quality. For example, clinicians may have “coded” (used clinical terms) based on symptoms (eg, fatigue) rather than using a “long COVID-19” clinical term to “code” this illness. It is also possible that key data were not coded at all but were included in the free-text narrative within EHRs. Our study aimed to compare LC in the hospitalized and nonhospitalized groups. It is possible that these represent 2 separate populations with different symptom clusters. Those hospitalized with acute COVID-19 are more likely to suffer from respiratory and other organ damage, whereas those managed in the community may suffer from a potentially different range of LC symptoms with a lower risk of end-organ damage and mortality. The lack of fine-detailed symptom categorization in EHRs may have limited this comparison. Symptom coding was also impacted by clinicians’ cognitive biases, a known limitation of epidemiological research using routinely recorded data [32].

Finally, LC clinical terms were only added to SNOMED in January 2021 and thus would not have become available in EHRs until around February 2021, almost a year after the onset of the pandemic. The United Kingdom also has its own version of SNOMED-CT, and there are a range of different clinical terms available internationally.

Further research is required to explore symptom clusters and assess key differences in those hospitalized compared to those managed in the community.

## Conclusion

Developing and validating an LC phenotype will enable the identification of individuals with the condition and facilitate comparison between affected and unaffected people. However, LC is a complex condition with a wide variety of symptoms that will require further research to understand. This phenotype and study protocol to explore its face validity should contribute to a better understanding of LC.

## Acknowledgments

We thank patients registered with practice members of the Oxford Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC) who allowed their pseudonymized data to be shared for this research. We also thank EMIS, TPP, InPractice Systems, and Wellbeing for cooperation to facilitate data extraction. The RSC is principally funded by the UK Health Security Agency.

We are grateful to Dr Katie Marsden for her help during her Academic Foundation Programme from the Royal Surrey Hospital, Dr Samantha Line for her help while being a member of the Clinical Informatics and Health Outcomes Research Group, and Julian Sherlock for his role in data analysis at the Oxford RCGP RSC.

This study shares funding sources through Predicting Risk of Hospital Admission in Patients with Suspected COVID-19 in a Community Setting (RECAP). The sources of funding for RECAP include the Community Jameel and the Imperial College President’s Excellence Fund, the Economic and Social Research Council (ES/V010069/1), the UK Research and Innovation, Health Data Research UK (HDRUK2020.139), the National Institute for Health and Care Research (NIHR) Imperial Biomedical Research Centre, the NIHR Oxford Biomedical Research Centre (BRC-1215-20008 and 132807), and the NIHR Imperial Patient Safety Translational Research Centre.

NM was funded by a Health Education England Academic Foundation Programme. BM-T was supported by the Marie Skłodowska–Curie Innovative Training Network (HealthPros – Healthcare Performance Intelligence Professionals) funded by the European Union Research Framework Programme Horizon 2020 (Grant agreement 765141).

The study was funded by Health Data Research UK, Urgent Public Health Funding.

## Conflicts of Interest

SdL reports that through his university, he had grants from AstraZeneca, GlaxoSmithKlein (GSK), Sanofi, Seqirus, and Takeda for vaccine-related research and membership of advisory boards for AstraZeneca, Sanofi, and Seqirus. TG is a member of Independent SAGE. All other authors declare no conflicts of interest.

## References

1. Nurek M, Rayner C, Freyer A, Taylor S, Järte L, MacDermott N, et al. Recommendations for the recognition, diagnosis, and management of long COVID: a Delphi study. Br J Gen Pract 2021 Aug 02;71(712):e815-e825. [doi: 10.3399/bjgp.2021.0265]

2. Ayoubkhani D, King S, Bosworth M. Prevalence of Ongoing Symptoms Following Coronavirus (COVID-19) Infection in the UK: 2 December 2021. URL: https://tinyurl.com/4wbnxtrn [accessed 2022-08-06]
3. Deer RR, Rock MA, Vasilevsky N, Carmody L, Rando H, Anzalone AJ, et al. Characterizing long COVID: deep phenotype of a complex condition. EBioMedicine 2021 Dec;74:103722 [FREE Full text] [doi: 10.1016/j.ebiom.2021.103722] [Medline: 34839263]
4. Aiyegbusi OL, Hughes SE, Turner G, Rivera SC, McMullan C, Chandan JS, et al. Symptoms, complications and management of long COVID: a review. J R Soc Med 2021 Sep 15;114(9):428-442 [FREE Full text] [doi: 10.1177/01410768211032850] [Medline: 34265229]
5. Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. Nat Med 2021 Apr;27(4):626-631 [FREE Full text] [doi: 10.1038/s41591-021-01292-y] [Medline: 33692530]
6. Thompson E, Williams D, Walker A, Mitchell R, Niedzwiedz C, Yang T, OpenSAFELY Collaborative, et al. Risk factors for long COVID: analyses of 10 longitudinal studies and electronic health records in the UK. medRxiv 2021. [doi: 10.1101/2021.06.24.21259277]
7. Brat GA, Weber GM, Gehlenborg N, Avillach P, Palmer NP, Chiovato L, et al. International electronic health record-derived COVID-19 clinical course profiles: the 4CE consortium. NPJ Digit Med 2020;3:109 [FREE Full text] [doi: 10.1038/s41746-020-00308-0] [Medline: 32864472]
8. Walker AJ, MacKenna B, Inglesby P, Tomlinson L, Rentsch CT, Curtis HJ, OpenSAFELY Collaborative. Clinical coding of long COVID in English primary care: a federated analysis of 58 million patient records using OpenSAFELY. Br J Gen Pract 2021 Nov 28;71(712):e806-e814 [FREE Full text] [doi: 10.3399/BJGP.2021.0301] [Medline: 34340970]
9. National Institute for Health and Care Excellence (NICE). COVID-19 Rapid Guideline: Managing the Long-Term Effects of COVID-19. London, UK: NICE; 2020.
10. Sivan M. LOng COvid Multidisciplinary Consortium: Optimising Treatments and servIces Across the NHS (LOCOMOTION). URL: https://clinicaltrials.gov/ct2/show/NCT05057260 [accessed 2022-08-06]
11. Papež V, Denaxas S, Hemingway H. Evaluation of semantic web technologies for storing computable definitions of electronic health records phenotyping algorithms. AMIA Annu Symp Proc 2018;2017:1352-1361.
12. de Lusignan S. In this issue: ontologies a key concept in informatics and key for open definitions of cases, exposures, and outcome measures. J Innov Health Inform 2015 Jul 10;22(2):170 [FREE Full text] [doi: 10.14236/jhi.v22i2.170] [Medline: 26245238]
13. phenoflow: 'Long-covid' phenotype. URL: https://kclhi.org/phenoflow/phenotype/download/1392 [accessed 2022-08-06]
14. de Lusignan S, Correa A, Smith GE, Yonova I, Pebody R, Ferreira F, et al. RCGP Research and Surveillance Centre: 50 years' surveillance of influenza, infections, and respiratory conditions. Br J Gen Pract 2017 Sep 29;67(663):440-441. [doi: 10.3399/bjgp17x692645]
15. de Lusignan S, Liyanage H, McGagh D, Jani BD, Bauwens J, Byford R, et al. COVID-19 surveillance in a Primary Care Sentinel Network: in-pandemic development of an application ontology. JMIR Public Health Surveill 2020 Nov 17;6(4):e21434 [FREE Full text] [doi: 10.2196/21434] [Medline: 33112762]
16. Tippu Z, Correa A, Liyanage H, Burleigh D, McGovern A, Van Vlymen J, et al. Ethnicity recording in primary care computerised medical record systems: an ontological approach. J Innov Health Inform 2017 Mar 14;23(4):920 [FREE Full text] [doi: 10.14236/jhi.v23i4.920] [Medline: 28346128]
17. English Indices of Deprivation. URL: https://www.gov.uk/government/collections/english-indices-of-deprivation [accessed 2022-08-06]
18. Michelen M, Manoharan L, Elkheir N, Cheng V, Dagens A, Hastie C, et al. Characterising long COVID: a living systematic review. BMJ Glob Health 2021 Sep 27;6(9):e005427 [FREE Full text] [doi: 10.1136/bmjgh-2021-005427] [Medline: 34580069]
19. National Institute for Health and Care Research (NIHR). Living with Covid19 - Second Review. URL: https://evidence.nihr.ac.uk/themedreview/living-with-covid19-second-review/ [accessed 2022-08-06]
20. Payne RA, Mendonca SC, Elliott MN, Saunders CL, Edwards DA, Marshall M, et al. Development and validation of the Cambridge Multimorbidity Score. CMAJ 2020 Feb 03;192(5):E107-E114 [FREE Full text] [doi: 10.1503/cmaj.190757] [Medline: 32015079]
21. Sivan M, Parkin A, Makower S, Greenwood DC. Post-COVID syndrome symptoms, functional disability, and clinical severity phenotypes in hospitalized and nonhospitalized individuals: a cross-sectional evaluation from a community COVID rehabilitation service. J Med Virol 2022 Apr 23;94(4):1419-1427 [FREE Full text] [doi: 10.1002/jmv.27456] [Medline: 34783052]
22. Evans RA, McAuley H, Harrison EM, Shikotra A, Singapuri A, Sereno M, et al. . [doi: 10.1016/S2213-2600(21)00383-0]
23. O'Connor RJ, Preston N, Parkin A, Makower S, Ross D, Gee J, et al. The COVID-19 Yorkshire Rehabilitation Scale (C19-YRS): application and psychometric analysis in a post-COVID-19 syndrome cohort. J Med Virol 2022 Mar;94(3):1027-1034 [FREE Full text] [doi: 10.1002/jmv.27415] [Medline: 34676578]
24. Musen MA, Protégé Team. The Protégé Project: a look back and a look forward. AI Matters 2015 Jun;1(4):4-12 [FREE Full text] [doi: 10.1145/2757001.2757003] [Medline: 27239556]

25. Mayor N, Tsang R, Joy M, Hobbs FR, de Lusignan S. Long covid: coding is caring. BMJ 2021 May 19;373:n1262. [doi: 10.1136/bmj.n1262] [Medline: 34011495]
26. Espinosa-Gonzalez AB, Neves AL, Fiorentino F, Prociuk D, Husain L, Ramtale SC, et al. Predicting risk of hospital admission in patients with suspected COVID-19 in a community setting: protocol for development and validation of a multivariate risk prediction tool. JMIR Res Protoc 2021 May 25;10(5):e29072 [FREE Full text] [doi: 10.2196/29072] [Medline: 33939619]
27. BioPortal. Long Covid Phenotype Ontology. URL: https://bioportal.bioontology.org/ontologies/LONGCOVID [accessed 2022-08-06]
28. Clinical informatics and Health Outcomes Research Group, University of Oxford. Long Covid Phenoflow Phenotype. URL: https://kclhi.org/phenoflow/phenotype/download/1392 [accessed 2022-08-06]
29. Chapman M, Mumtaz S, Rasmussen LV, Karwath A, Gkoutos GV, Gao C, et al. Desiderata for the development of next-generation electronic health record phenotype libraries. Gigascience 2021 Sep 11;10(9):giab059 [FREE Full text] [doi: 10.1093/gigascience/giab059] [Medline: 34508578]
30. de Lusignan S, Dorward J, Correa A, Jones N, Akinyemi O, Amirthalingam G, et al. Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study. Lancet Infect Dis 2020 Sep;20(9):1034-1042 [FREE Full text] [doi: 10.1016/S1473-3099(20)30371-6] [Medline: 32422204]
31. Joy M, Hobbs FDR, McGagh D, Akinyemi O, de Lusignan S. Excess mortality from COVID-19 in an English sentinel network population. Lancet Infect Dis 2021 Apr;21(4):e74. [doi: 10.1016/s1473-3099(20)30632-0]
32. Kostopoulou O, Tracey C, Delaney BC. Can decision support combat incompleteness and bias in routine primary care data? J Am Med Inform Assoc 2021 Jul 14;28(7):1461-1467 [FREE Full text] [doi: 10.1093/jamia/ocab025] [Medline: 33706367]

## Abbreviations

**CMMS:** Cambridge Multimorbidity Score
**EHR:** electronic health record
**ICU:** intensive care unit
**LC:** long COVID
**NHS:** National Health Service
**NICE:** National Institute for Health and Care Excellence
**ONS:** Office for National Statistics
**OR:** odds ratio
**ORCHID:** Oxford Royal College of General Practitioners Clinical Informatics Digital Hub
**OWL:** Ontology Web Language
**PCSC:** Primary Care Sentinel Cohort
**RSC:** Research and Surveillance Centre
**RCGP:** Royal College of General Practitioners
**SNOMED-CT:** Systematized Nomenclature of Medicine Clinical Terms

*Edited by T Sanchez, A Mavragani; submitted 03.02.22; peer-reviewed by Z Zhou, H Schwermer; comments to author 02.05.22; revised version received 16.05.22; accepted 19.07.22; published 11.08.22.*

*Please cite as:*
*Mayor N, Meza-Torres B, Okusi C, Delanerolle G, Chapman M, Wang W, Anand S, Feher M, Macartney J, Byford R, Joy M, Gatenby P, Curcin V, Greenhalgh T, Delaney B, de Lusignan S*
*Developing a Long COVID Phenotype for Postacute COVID-19 in a National Primary Care Sentinel Cohort: Observational Retrospective Database Analysis*
*JMIR Public Health Surveill 2022;8(8):e36989*
*URL: https://publichealth.jmir.org/2022/8/e36989*
*doi:10.2196/36989*
*PMID:35861678*

Original Paper

# Association Between Neighborhood Factors and Adult Obesity in Shelby County, Tennessee: Geospatial Machine Learning Approach

Whitney S Brakefield[1,2], PhD; Olufunto A Olusanya[2], MPH, MD, PhD; Arash Shaban-Nejad[2], MPH, PhD

[1]Bredesen Center for Data Science and Engineering, University of Tennessee, Knoxville, TN, United States

[2]Center for Biomedical Informatics, Department of Pediatrics, College of Medicine, University of Tennessee Health Science Center, Memphis, TN, United States

**Corresponding Author:**
Arash Shaban-Nejad, MPH, PhD
Center for Biomedical Informatics
Department of Pediatrics
College of Medicine, University of Tennessee Health Science Center
50 N Dunlap Street, 491R
Memphis, TN, 38103
United States
Phone: 1 901 287 5836
Email: ashabann@uthsc.edu

## Abstract

**Background:** Obesity is a global epidemic causing at least 2.8 million deaths per year. This complex disease is associated with significant socioeconomic burden, reduced work productivity, unemployment, and other social determinants of health (SDOH) disparities.

**Objective:** The objective of this study was to investigate the effects of SDOH on obesity prevalence among adults in Shelby County, Tennessee, the United States, using a geospatial machine learning approach.

**Methods:** Obesity prevalence was obtained from the publicly available 500 Cities database of Centers for Disease Control and Prevention, and SDOH indicators were extracted from the US census and the US Department of Agriculture. We examined the geographic distributions of obesity prevalence patterns, using Getis-Ord Gi* statistics and calibrated multiple models to study the association between SDOH and adult obesity. Unsupervised machine learning was used to conduct grouping analysis to investigate the distribution of obesity prevalence and associated SDOH indicators.

**Results:** Results depicted a high percentage of neighborhoods experiencing high adult obesity prevalence within Shelby County. In the census tract, the median household income, as well as the percentage of individuals who were Black, home renters, living below the poverty level, 55 years or older, unmarried, and uninsured, had a significant association with adult obesity prevalence. The grouping analysis revealed disparities in obesity prevalence among disadvantaged neighborhoods.

**Conclusions:** More research is needed to examine links between geographical location, SDOH, and chronic diseases. The findings of this study, which depict a significantly higher prevalence of obesity within disadvantaged neighborhoods, and other geospatial information can be leveraged to offer valuable insights, informing health decision-making and interventions that mitigate risk factors of increasing obesity prevalence.

***(JMIR Public Health Surveill 2022;8(8):e37039)*** doi:10.2196/37039

**KEYWORDS**

obesity; obesity surveillance; disease surveillance; machine learning; geographic information systems; social determinants of health; SDOH; disparities

## Introduction

Obesity is a global epidemic with increasing prevalence from 3% to 11% among men and 6% to 15% among women within the past 40 years [1]. Obesity is responsible for at least 2.8 million deaths per year [2] and is defined by the Centers for Disease Control and Prevention (CDC) as "weight that is higher than what is considered healthy for a given height" with a BMI of 30 kg/m$^2$ or higher [3]. It is a noncommunicable disease (NCD) that could have a profound, lifelong adverse impact on individuals' overall life expectancy, quality of life, and other clinical outcomes. Moreover, obesity increases susceptibility to developing other NCDs such as diabetes mellitus, hypertension, heart disease, myocardial infarction, stroke, fatty liver disease, and cancers. According to the CDC, obesity is associated with the top leading causes of death in the United States. With over 42% of individuals living with obesity, there is a significant US $147 billion financial burden placed on the United States [4].

Although genetic and behavioral factors increase susceptibility, studies have shown that social determinants of health (SDOH) risk factors adversely affect health outcomes and are major contributing factors to the increasing occurrence of obesity and other NCDs [5-9]. Evidence suggests that the pattern of distribution for societal resources and socioeconomic status are correlated with the quality-of-life attributes as well as physical and psychosocial characteristics [10]. SDOH indicators including education attainment, financial security, health literacy, access to healthy food, poverty level, employment conditions, and health care access are determined to be the most significant predictors of an individual's health status. Moreover, SDOH indicators are perceived to be among major driving forces behind systematic social inequalities [11]. As a result, certain susceptible populations are more likely to be affected by obesity-associated SDOH stressors than other groups and populations [12]. The ongoing global pandemic caused by COVID-19 has further worsened SDOH burdens, since individuals diagnosed with preexisting conditions such as obesity have been disproportionately affected by COVID-19 morbidity and mortality [13]. Tailored and effective obesity prevention interventions should be implemented within the context of sociocultural, socioeconomical, environmental, psychosocial, and demographic indicators that influence population health.

There is a dearth of studies that have leveraged geospatial intelligence to examine SDOH indicators associated with obesity. In this study, we examined the geographical variations and prevalence patterns of obesity in Shelby County in the United States, using Getis-Ord Gi* statistics and calibrated multiple models to study the association between SDOH and adult obesity. We also adopted unsupervised machine learning to conduct grouping analysis and investigate the distribution of obesity prevalence and the associated SDOH indicators. In addition to facilitating the surveillance of obesity and other NCDs within Shelby County, our findings could inform innovative health strategies to tackle SDOH disparities and other adverse influences on health outcomes.

## Methods

### Data Source

In this study, data from well-known, publicly available multidimensional sources were merged at the census tract level. We used CDC 500 Cities data (2019) [14], which represents city-level data originating from 500 largest US cities, to determine obesity prevalence. The CDC 500 Cities data were merged with SDOH data extracted from the American Community Survey and the US Department of Agriculture (2018-2020) estimates [15,16]. Table 1 shows the summary statistics for variables included in the study.

**Table 1.** Summary statistics for obesity and related risk factors in census tracts of Shelby County, Tennessee.

| Variables | Operationalization | Source | Values, mean (SD) |
|---|---|---|---|
| Obesity | Model-based estimate for the crude prevalence of obesity among adults aged ≥18 years, 2018 | CDC[a] | 35.77 (7.84) |
| Low access to supermarket | Count of housing units without a vehicle and greater than half a mile from supermarket in the census tract | USDA[b] | 102.54 (108.37) |
| Black population | Percentage of the Black or African American population living in the census tract | US census | 58.02 (17.31) |
| Poverty | Percentage of the population living below the federal poverty line in the census tract | USDA | 24.89 (17.35) |
| Unemployment | Percentage of the unemployed population living in the census tract | US census | 4.32 (3.04) |
| High school diploma | Percentage of the population aged ≥25 years without a high school diploma in the census tract | US census | 9.33 (6.59) |
| Renters | Percentage of the population renting their homes | US census | 18.87 (11.85) |
| Average household size | Average household size in a census tract | US census | 2.57 (0.52) |
| Median household income | Median household income in a census tract (US $) | US census | 53,746 (29,335) |
| Female head of the household | Percentage of the households with a female head in a census tract | US census | 7.75 (4.23) |
| Uninsured | Model-based estimate for the crude prevalence of uninsured adults aged ≥18 years, 2018 | CDC | 18.84 (7.16) |
| Lack of physical activity | Model-based estimate for the crude prevalence of lack of physical activity among adults aged ≥18 years, 2018 | CDC | 32.88 (10.52) |
| Aged 55 years and older | Percentage of the population aged ≥55 years in a census tract | US census | 21.89 (7.81) |
| Single | Percentage of the population who are single in a census tract | US census | 13.70 (8.62) |

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

[b] USDA: The United States Department of Agriculture.

## Obesity Clusters

We explored the geospatial clustering and hot spots of adult obesity prevalence in Shelby County. We conducted this analysis by using Getis-Ord Gi* statistics with first order queen contiguity and applied the false discovery rate correction parameter to account for multiple testing and spatial dependence.

## Regression Modeling

### *Data Wrangling*

To prepare the data set for predictive modeling, we scaled our features such that columns had a mean of 0 and a SD of 1 [17]. Relative scales have been shown to reduce heterogeneity and allow for variable comparison [18].

### *Model Selection*

The predictor variables that were considered were the 13-census, tract-level risk factor variables, and the outcome variable was the adult obesity prevalence in the census tract (Table 1). We used the “forward and backward” stepwise regression to depict a subset of the variables and Akaike’s information criterion (AIC) as the metric [19,20]. Variance inflation factor (VIF) was applied to assess redundancy between predictor variables to prevent multicollinearity. VIF factors that exceeded 10 were removed [21]. Predictor variable values that were not significant ($P<.05$) were removed.

### *Models*

In this study, we applied multiple modeling techniques. Ordinary least squares (OLS) regression modeling was amongst these techniques, represented by the following equation:

$$Y = X\beta + \varepsilon \quad \textbf{(1)}$$

Equation 1 shows the regression model in matrix notation, where Y is an n×1 vector of n observations on the dependent variable; X is an n×q design matrix of n observations on q explanatory variables (first column in X matrix will consist of a vector of n ones for the intercept); β is a q×1 vector of regression coefficients; and ε represents an n×1 vector of random error terms (independently and identically distributed). To assess and compare the performance of the models, we used adjusted $R^2$ and AIC. To assess the heteroskedasticity of random error terms, we used the Koenker-Bassett test. To assess the normality of error distribution, the Jarque-Bera test was applied. We assessed the multicollinearity of the entire model using the condition number. To examine the independence of the terms Robust Lagrange Multiplier (error) and Robust Lagrange Multiplier (lag) methods were applied. First, order queen contiguity weights were constructed for spatial testing. Queen contiguity was chosen because areas sharing all boundaries and vertices are considered as neighbors, which yields more neighbors per area than the rook contiguity. If dependence was found among the terms, we incorporated the terms that accounted for autocorrelation in the model. Thus, we applied spatial autoregressive models: spatial lag or spatial error model (SEM)

[22]. The spatial lag model includes a spatially lagged dependent variable and is represented by equation 2:

$$Y = X\beta + \rho WY + \varepsilon \quad \textbf{(2)}$$

In equation 2, Y is an n×1 vector of n observations on the dependent variable; ρ is a scalar spatial lag parameter; WY is the spatially lagged dependent variable for an n×n weights matrix W; X is an n×q design matrix of n observations on q explanatory variables; β is an q×1 vector of regression coefficients; and ε represents an n×1 vector of error terms.

The spatial error model includes a spatial autoregressive error term and is represented by equation 3:

$$Y = X\beta + u,\ u = \lambda Wu + \varepsilon \quad \textbf{(3)}$$

In equation 3, Y is an n×1 vector of n observations on the dependent variable; X is an n×q design matrix of n observations on q explanatory variables; β is an q×1 vector of regression coefficients; λ is a scalar spatial error parameter; W represents the n×n spatial weights matrix; u represents an n×1 vector of error terms; Wu denotes a spatially lagged error term; and the represents an n×1 vector of error terms. OLS regression and spatial autoregressive models will be assessed and compared to depict the optimal performance.

### Grouping Analysis

In order to understand the dependent variable and significantly associated SDOH across the region, we used the hierarchical clustering unsupervised machine learning algorithm [23-25] in the "stats" package embedded in R software (version 4.0.3; RStudio, PBC) [25] to conduct an exploratory grouping analysis. Ward's Method was used to minimize the increase in the error sum of squares [26].

### Lack of Physical Activity, Obesity, and SDOH

We explored the geographical distribution of lack of physical activity, obesity, and the top four features significantly associated with obesity in Shelby County.

### Visualization and Tools

ArcGIS Pro software (version 2.9.0; Esri) was used to produce spatial distributions to investigate patterns (ie, spatial clustering). R Studio (version 4.0.3; RStudio, PBC) and GeoDa software (version 1.16.0.12; Luc Anselin) were used for statistical analyses.

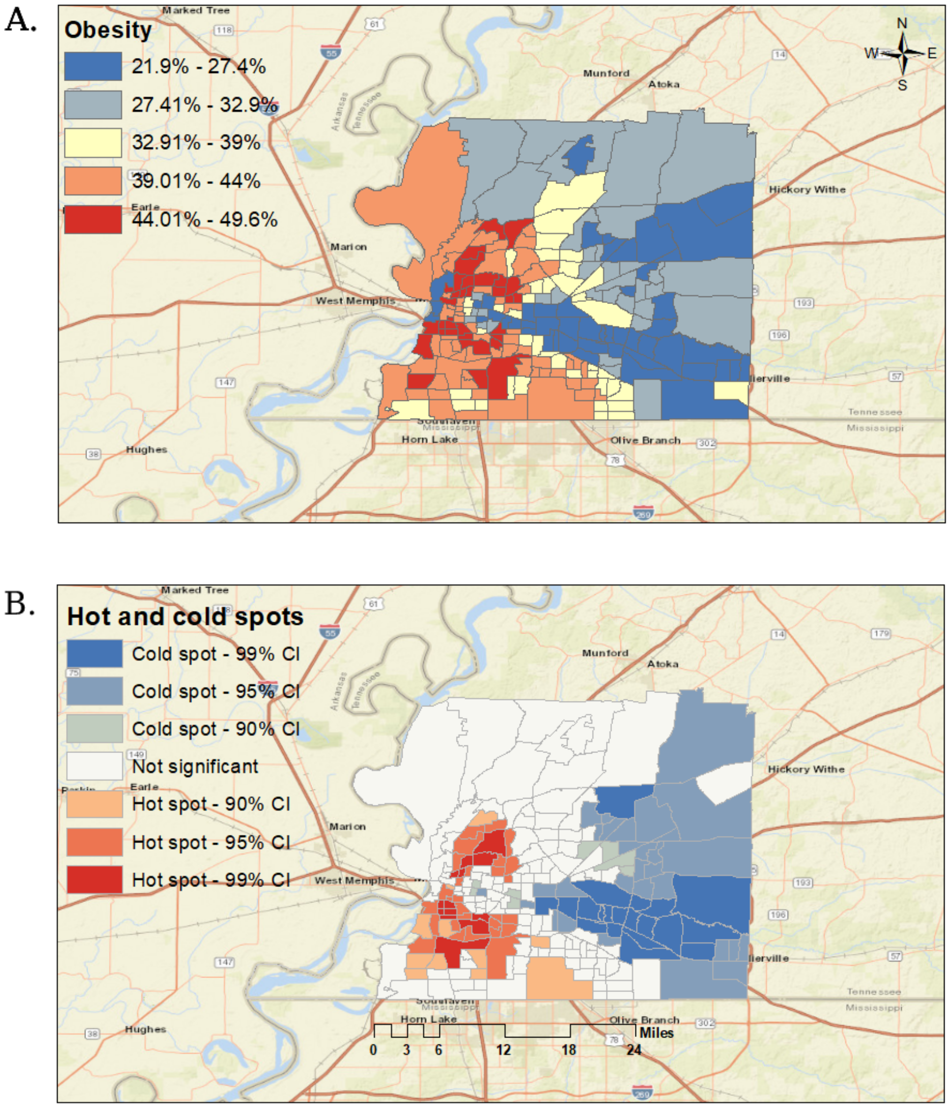
## Results

### Obesity Clusters

Figure 1 reflects adult obesity prevalence geospatial distribution and adult obesity prevalence significant clusters in the study region.

Figure 1A shows a high percentage of the population in the central and southwestern regions diagnosed with adult obesity, and Figure 1B shows that the central western region is also a significant hot spot for adult obesity. Conversely, significant cold spots are clustered along the eastern region of the Shelby County.

**Figure 1.** (A) represents geospatial distribution of adult obesity prevalence in Shelby County; (B) represents significant hot and cold spots of adult obesity prevalence in Shelby County.



## Model Selection

After conducting the analytical modeling techniques in the “Regression Modeling“ section, the percentage of population that lacks physical activity was removed during the VIF assessment (VIF=46.7), and the percentage of population with a female head of the household and the percentage of the population aged 25 years and older without high school education were removed during the AIC process (they were also found to be nonsignificant after conducting further experimental analysis). In addition, the average household size and households with low access to supermarkets were not significantly associated with obesity. However, there were 8 variables from Table 1 that were significantly associated with obesity prevalence: median household income, percentage of the Black population, poverty level, percentage of the uninsured population, percentage of the population aged 55 years or older, percentage of the population who are single, percentage of the unemployed population, and percentage of home renters. The significant variables each had a VIF ≤10.0.

## The Final OLS Model Results

The final OLS regression model results are shown in Table 2, which displays the predictor variables that best describe the model. The adjusted $R^2$ was 0.963, indicating that 96% of the variation in the outcome variable was explained by the predictors with an AIC of –88.34. There was a multicollinearity condition number of 6.99, which is less than 20, thus not suspected of multicollinearity. The Jarque-Bera test had a $P$ value <.001. Koenker-Bassett test had a $P$ value of .17, indicating the presence of constant variance in error terms. The $P$ value ($F$ statistics) less than .05 was deemed as significant or meaningful.

**Table 2.** Ordinary least squares regression results.

| Variable | Coefficient |
|---|---|
| Constant | –0.000 |
| Median household income | –0.046[a] |
| Poverty | 0.184[b] |
| Renters | –0.134[b] |
| Aged 55 years and older | 0.043[a] |
| Single | 0.091[c] |
| Uninsured | 0.445[b] |
| Unemployment | 0.042[a] |
| Black population | 0.438[b] |

[a] *P*<.05.

[b] *P*<.001.

[c] *P*<.01.

However, Robust Lagrange Multiplier (error) had a test value of 10.72 (*P*=.001), which was significantly higher than Robust Lagrange Multiplier (lag) with a test value of 8.449 (*P*=.003). OLS model results are not reliable due to significant spatial dependency. A spatial error term will be incorporated into the model.

## Spatial Error Model

Table 3 shows the SEM results. In the model, the percentage of the Black population, the percentage of the population below poverty rate, the percentage of the population who are single, the percentage of uninsured population, and the percentage of the population aged 55 years or older are positively associated with obesity, showing an increase in obesity. On the other hand, the median household income and the percentage of home renters are negatively associated with obesity, showing a decrease in obesity.

Since our variables are measured on the same scale, we were able to compare the strength of the effect of each predictor variable on obesity prevalence. We found that the percentage of uninsured population, the percentage of the Black population, the percentage of the population below poverty level, and the percentage of home renters were the most important variables when predicting obesity prevalence in Shelby County.

**Table 3.** Spatial Error Model results.

| Variable | Coefficient |
|---|---|
| Constant | –0.001 |
| Lambda | 0.488[a] |
| Median household income | –0.056[a] |
| Renters | –0.106[a] |
| Poverty | 0.146[a] |
| Aged 55 years or older | 0.051[b] |
| Single | 0.066[c] |
| Uninsured | 0.466[a] |
| Unemployment | 0.027 |
| Black population | 0.423[a] |

[a] *P*<.001.

[b] *P*<.01.

[c] *P*<.05.

## Overall Model Performance Comparison

After calibrating both models, we found that SEM outperformed the OLS model. Table 4 shows that the $R^2$ value improved to 0.968 after incorporating the error term in the model, and the AIC improved to –108.09, indicating a better model fit.

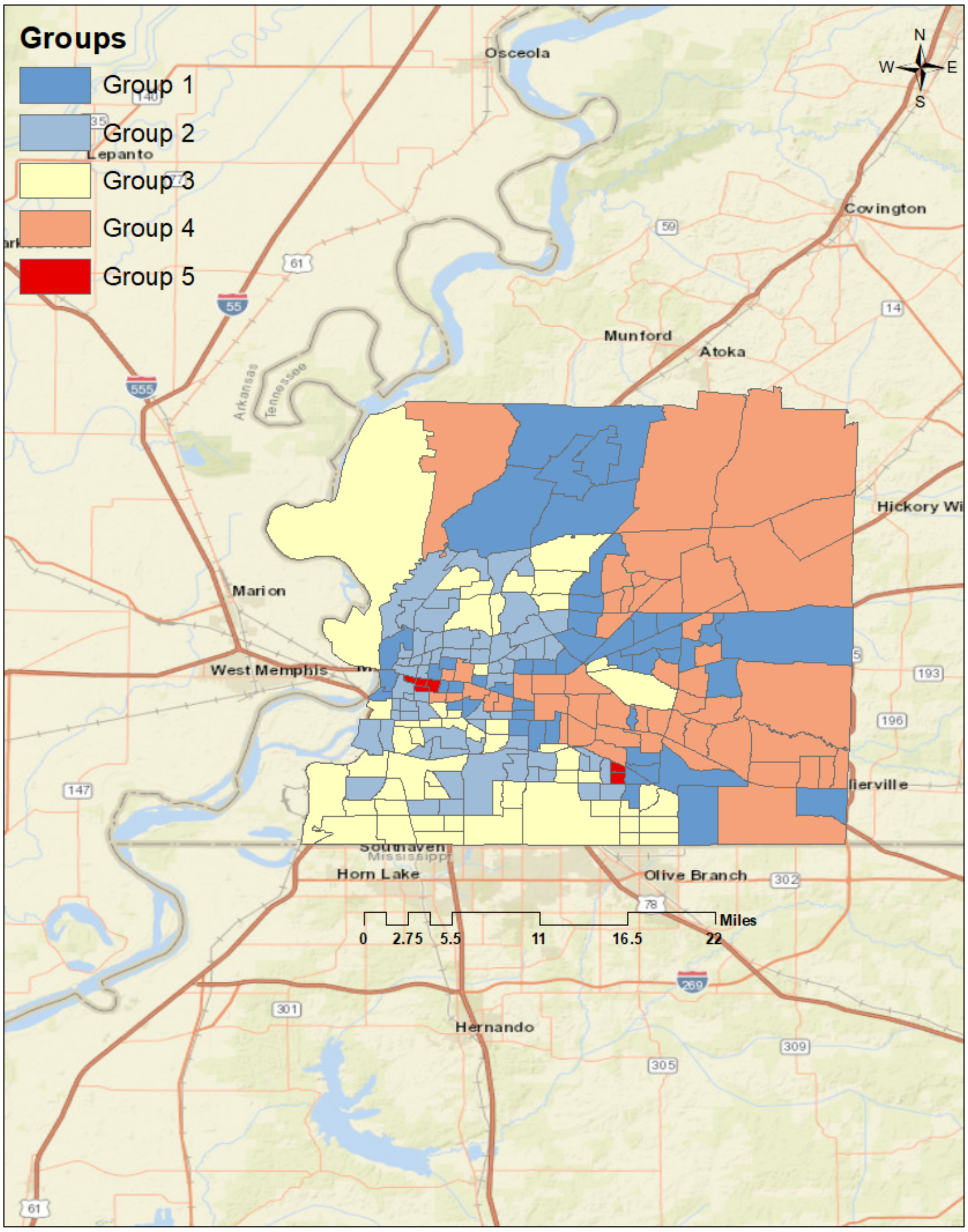
**Table 4.** Model performance.

| Model | Adjusted $R^2$ | Akaike’s information criterion |
|---|---|---|
| Ordinary least squares | 0.963 | –88.34 |
| Spatial error model | 0.968 | –108.09 |

## Grouping Analysis

Our grouping analysis divided the study area into 5 distinct groups across the Shelby region, based on the top four features that were significantly associated with obesity (Figure 2).

**Figure 2.** Grouping analyses results.



Group 1 spans the fourth largest area of the region (47 census tracts) and was quantified as being below average in obesity prevalence, percentage of the Black population, percentage of the population with an income below the poverty level, and percentage of the uninsured population; however, this group is around average in the percentage of renters.

Group 2 is the largest area in the region, comprising of 62 census tracts. This region is far above average in obesity prevalence, percentage of renters, percentage of the Black population, percentage of the population with an income below the poverty level, and percentage of the uninsured population.

Group 3 comprises of 52 census tracts. This region is above average in obesity prevalence, percentage of renters and percentage of the uninsured population, and it is far above average in percentage of the Black population; however, this group is around average in percentage of the population with an income below the poverty level and below average in percentage of renters.

Group 4 comprises of 52 census tracts and is quantified as being far below average in obesity prevalence, percentage of the Black population, percentage of the population with an income below the poverty level, percentage of renters, and percentage of the uninsured population.

Group 5 spans the smallest area of the region (6 census tracts) and is characterized as being average in obesity prevalence and percentage of the uninsured population; however, this group is far above average in percentage of the Black population, percentage of the population with an income below the poverty level, and percentage of renters.

## Lack of Physical Activity, Obesity, and SDOH

Even though lack of physical activity was removed during the “model selection” process due to multicollinearity, we examined the Spearman rank correlation coefficient (Table 5), the geospatial distribution of obesity (Figure 1A), and lack of physical activity (Figure 3), as well as the geospatial patterns among the top four obesity-associated features and lack of physical activity (Figure 3). The Spearman rank coefficient shows a strong positive relationship between lack of physical activity and obesity. Figure 1A shows a high prevalence of obesity clusters in the central and southwestern regions of Shelby County, consistent with the top four obesity-associated features and the lack of physical activity geospatial pattern.

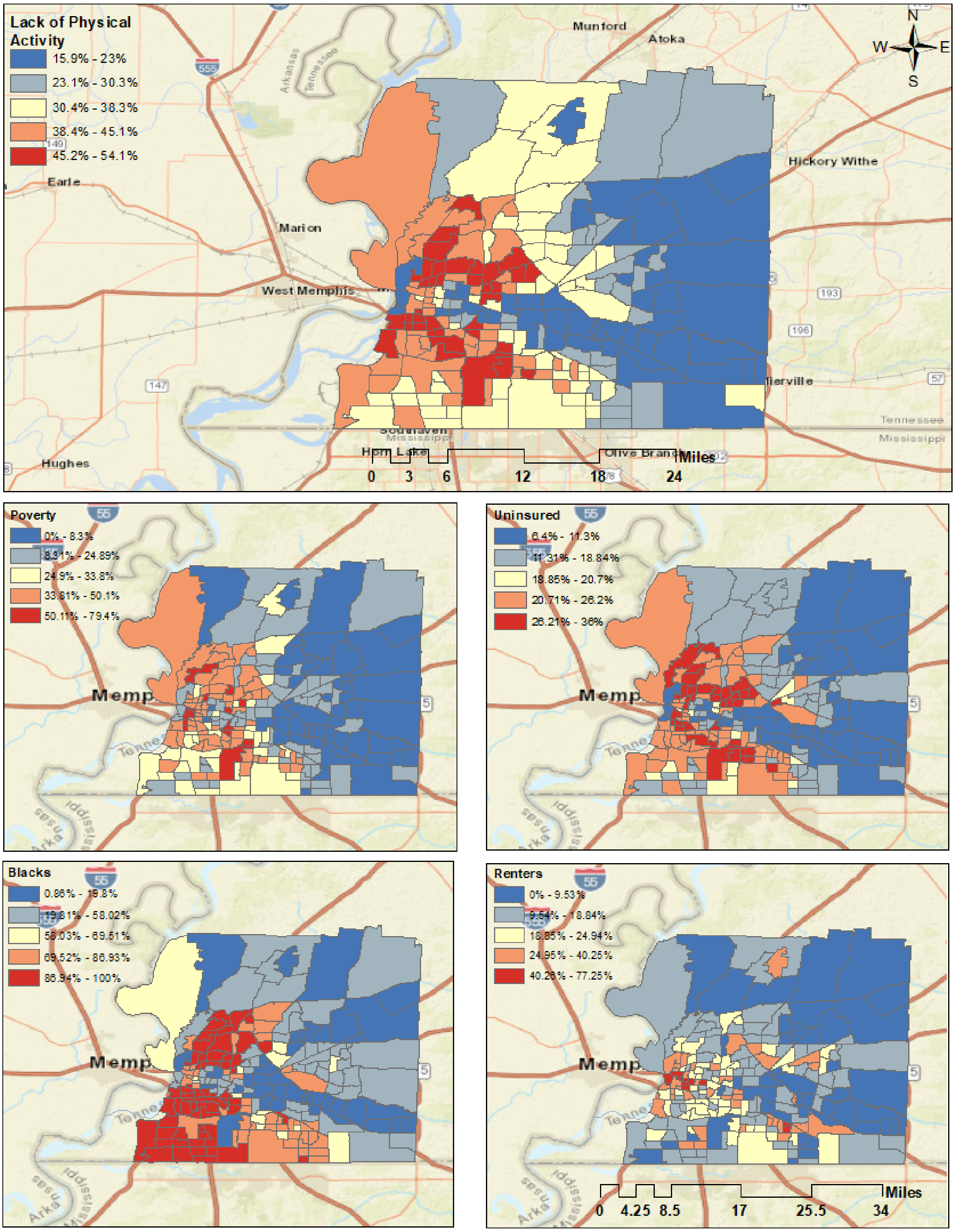
In addition, Table 5 shows a strong positive relationship between lack of physical activity and the top four features associated with obesity. Geographically, we found that the central and southwestern regions of Shelby County consisted of a high percentage of population who are below the poverty rate, Black, and uninsured, and the percentage of the population who lack physical activity was consistent with these geospatial patterns. On the other hand, the eastern region of Shelby County showed a consistent pattern among the low percentage of the population below poverty rate, percentage of the Black population, percentage of renters, and percentage of the uninsured population, and consisted of clustered census tracts that contained a low percentage of the population who lack physical activity.

**Table 5.** Spearman rank coefficients to assess the relationship between lack of physical activity and obesity and the top four obesity-associated features in Shelby County census tracts.

| Variables | Spearman rank coefficient |
|---|---|
| Obesity | 0.96[a] |
| Uninsured population | 0.95[a] |
| Black population | 0.76[a] |
| Renters | 0.43[a] |
| Poverty | 0.86[a] |

[a] $P$<.001.

**Figure 3.** Assessment of lack of physical activity and the top four features associated with obesity.



## Discussion

Obesity is a serious health condition that is associated with several comorbidities (eg, heart diseases, cancers, and diabetes) that are leading causes of death in the United States. SDOH factors such as the community, home, school, and workplace setting can impact physical activity and access to affordable healthy food. Some communities are more impacted, as evidenced by the disproportionality of adult obesity rates, compared to other populations [27,28]. Although a few studies have leveraged geospatial analysis in the United States to explore the relationship between neighborhood factors and obesity, this study was a critical step in understanding and effectively addressing chronic diseases. Using Getis-Ord Gi* statistics and unsupervised machine learning, this study examined how SDOH characteristics influenced obesity prevalence among adults 18 years or older in Shelby County. In a study by Cohen et al [29] in 2017, obesity rates were modeled against urban-rural geographic status, using the Behavioral Risk Factor Surveillance System. Moreover, our findings, showing associations between SDOH indicators (eg, race, income level, and poverty rate) and obesity, are consistent with the findings of other studies [29-31]. Our study also found that in the eastern region of Shelby County, where the percentage of home renters was low (Figure 3), the obesity rate was also low (Figure 1A). Thus, a population's rental status could play a role in the obesity prevalence. However, contrary to other studies [32-34], our study found that lack of educational attainment was not significantly associated with an increase in obesity prevalence. Given some of the SDOH risk factors that have been identified (eg, percentage of the population below poverty rate, low median household income, percentage of renters, Black population, and the uninsured population), as well as the high obesity prevalence depicted among socially disadvantaged groups within Shelby County, our study proposes that the effective planning and implementation of intervention strategies to address obesity are informed by SDOH surveillance. Notably, our model calibration results indicate that SEM outperformed the OLS model.

Unlike multiple studies [5-12,27-34] that have examined obesity and SDOH, we provided an analysis to assess adult obesity and SDOH at the census tract level in Shelby County, Tennessee. Admittedly, some limitations should be considered with our findings. First, cross-sectional studies such as ours are unable to detect causal relations between predictor and outcome variables nor are they able to qualitatively examine sociocontextual influences. Another limitation is that when aggregating data such as SDOH and analyzing at a specific level of granularity, a change in units could alter the findings (modifiable areal unit problem). In addition, our study may not be generalizable to the whole Tennessee state and the United States. In the future, we will conduct comparative studies to assess the generalizability of our results and include additional SDOH indicators (eg, proximity to green spaces, crime, and transportation) and social and community contexts (eg, social cohesion) to expand our study. In addition, 500 Cities only provide data for 219 of 221 census tracts in Shelby County, which could pose a problem during the integration process; we removed the missing census tracts (ie, 980200 and 980300) from other integrated data sets for parallelism. Another limitation is that CDC 500 Cities data relies on self-reported surveys that have not been continuously scrutinized for potential social desirability bias and measurement bias. However, this data set offers access to validated, regionally representative data. Despite these limitations, our study depicts that SDOH and environmental characteristics at a granular level are major risk factors for obesity in Shelby County.

Finally, results from this study will be incorporated into the analytics layer of our Urban Public Health Observatory knowledge-based surveillance platform [35,36] and Personal Health Libraries [37]. These platforms could facilitate the collection of public health evidence as well as surveillance data that will facilitate precision population health [38] to provide immediate insights to inform decision-making at multiple levels of authority, including among health officials, patients, physicians, and caregivers.

## Conclusion

Previous studies have found associations between sociogeographical determinants and health outcomes [39-42]. Likewise, our study found that a high percentage of disadvantaged neighborhoods within the Shelby region had significantly higher obesity prevalence and SDOH risk factors. Accordingly, policies should be implemented that are socioculturally adaptable and tailored toward vulnerable communities and can address SDOH disparities and are geared to tackle underlying determinants of the obesity epidemic.

## Conflicts of Interest

None declared.

## References

1. Jaacks LM, Vandevijvere S, Pan A, McGowan CJ, Wallace C, Imamura F, et al. The obesity transition: stages of the global epidemic. Lancet Diabetes Endocrinol 2019 Mar;7(3):231-240. [doi: 10.1016/s2213-8587(19)30026-9]
2. Obesity. World Health Organization. URL: https://www.who.int/health-topics/obesity#tab=tab_1 [accessed 2021-08-28]
3. Defining adult overweight and obesity. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/obesity/basics/adult-defining.html [accessed 2021-08-28]
4. Adult obesity facts. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/obesity/data/adult.html [accessed 2022-07-22]
5. Lee A, Cardel M, Donahoo W. Social and Environmental Factors Influencing Obesity. Feingold KR, Anawalt B, Boyce A. editors.EndotextInternet. South Dartmouth (MA): MDText.com, Inc; 2000. URL: https://www.ncbi.nlm.nih.gov/books/NBK278977/ [accessed 2022-07-27]
6. Suglia SF, Shelton RC, Hsiao A, Wang YC, Rundle A, Link BG. Why the neighborhood social environment is critical in obesity prevention. J Urban Health 2016 Feb 15;93(1):206-212 [FREE Full text] [doi: 10.1007/s11524-015-0017-6] [Medline: 26780582]
7. Suglia SF, Shelton RC, Hsiao A, Wang YC, Rundle A, Link BG. Why the neighborhood social environment is critical in obesity prevention. J Urban Health 2016 Feb 15;93(1):206-212 [FREE Full text] [doi: 10.1007/s11524-015-0017-6] [Medline: 26780582]

8. Reidpath DD, Burns C, Garrard J, Mahoney M, Townsend M. An ecological study of the relationship between social and environmental determinants of obesity. Health Place 2002 Jun;8(2):141-145. [doi: 10.1016/s1353-8292(01)00028-4]
9. Yang Y, Jiang Y, Xu Y, Mzayek F, Levy M. A cross-sectional study of the influence of neighborhood environment on childhood overweight and obesity: Variation by age, gender, and environment characteristics. Prev Med 2018 Mar;108:23-28. [doi: 10.1016/j.ypmed.2017.12.021] [Medline: 29289640]
10. McGill R, Anwar E, Orton L, Bromley H, Lloyd-Williams F, O'Flaherty M, et al. Are interventions to promote healthy eating equally effective for all? Systematic review of socioeconomic inequalities in impact. BMC Public Health 2015 May 02;15(1):457 [FREE Full text] [doi: 10.1186/s12889-015-1781-7] [Medline: 25934496]
11. Social determinants of health. World Health Organization. URL: https://www.who.int/social_determinants/sdh_definition/en/ [accessed 2022-07-22]
12. Javed Z, Valero-Elizondo J, Maqsood MH, Mahajan S, Taha MB, Patel KV, et al. Social determinants of health and obesity: Findings from a national study of US adults. Obesity (Silver Spring) 2022 Feb 27;30(2):491-502. [doi: 10.1002/oby.23336] [Medline: 35088551]
13. Singu S, Acharya A, Challagundla K, Byrareddy SN. Impact of social determinants of health on the emerging COVID-19 pandemic in the United States. Front Public Health 2020 Jul 21;8:406 [FREE Full text] [doi: 10.3389/fpubh.2020.00406] [Medline: 32793544]
14. 500 Cities project: 2016 to 2019. Centers for Disease Control Prevention. URL: https://www.cdc.gov/places/about/500-cities-2016-2019/index.html [accessed 2022-07-22]
15. The United States Census Bureau. About the American community survey. 2021. URL: https://www.census.gov/programs-surveys/acs/about.html [accessed 2021-08-28]
16. United SDOA. Data sources. USDA economic research service. 2021. URL: https://www.ers.usda.gov/topics/farm-economy/farm-sector-income-finances/data-sources [accessed 2022-07-27]
17. Gelman A. Scaling regression inputs by dividing by two standard deviations. Stat Med 2008 Jul 10;27(15):2865-2873. [doi: 10.1002/sim.3107] [Medline: 17960576]
18. Hemilä H, Friedrich JO. Many continuous variables should be analyzed using the relative scale: a case study of β-agonists for preventing exercise-induced bronchoconstriction. Syst Rev 2019 Nov 19;8(1):282 [FREE Full text] [doi: 10.1186/s13643-019-1183-5] [Medline: 31744533]
19. Bozdogan H. Model selection and Akaike's information criterion (AIC): the general theory and its analytical extensions. Psychometrika 1987 Sep;52(3):345-370. [doi: 10.1007/BF02294361]
20. Venables WN, Ripley BD. N. In: Modern Applied Statistics with S, Fourth Edition. New York: Springer; 2002.
21. Franke GR. Multicollinearity. Wiley Online Library 2010 Dec 15 [FREE Full text] [doi: 10.1002/9781444316568.wiem02066]
22. Anselin L. Spatial externalities, spatial multipliers, and spatial econometrics. IRSR 2016 Jul 26;26(2):153-166. [doi: 10.1177/0160017602250972]
23. Nielsen F. Hierarchical clustering. In: Introduction to HPC with MPI for Data Science. New York: Springer; 2016:195-211.
24. Gentleman R, Carey VJ. Unsupervised machine learning. In: Bioconductor Case Studies. New York: Springer; 2008:137-157.
25. Antoch J. Environment for statistical computing. Computer Science Review 2008 Aug;2(2):113-122 [FREE Full text] [doi: 10.1016/j.cosrev.2008.05.002]
26. Murtagh F, Legendre P. Ward's hierarchical agglomerative clustering method: which algorithms implement ward's criterion? J Classif 2014 Oct 18;31(3):274-295. [doi: 10.1007/s00357-014-9161-z]
27. Kirby JB, Liang L, Chen H, Wang Y. Race, place, and obesity: the complex relationships among community racial/ethnic composition, individual race/ethnicity, and obesity in the United States. Am J Public Health 2012 Aug;102(8):1572-1578. [doi: 10.2105/ajph.2011.300452]
28. de Oliveira AC, Leonard TC, Shuval K, Skinner CS, Eckel C, Murdoch JC. Economic preferences and obesity among a low-income African American community. J Econ Behav Organ 2016 Nov;131(B):196-208 [FREE Full text] [doi: 10.1016/j.jebo.2015.11.002] [Medline: 28133400]
29. Cohen SA, Cook SK, Kelley L, Foutz JD, Sando TA. A closer look at rural-urban health disparities: associations between obesity and rurality vary by geospatial and sociodemographic factors. J Rural Health 2017 Apr 24;33(2):167-179. [doi: 10.1111/jrh.12207] [Medline: 27557442]
30. Akil L, Ahmad HA. Effects of socioeconomic factors on obesity rates in four southern states and Colorado. Ethn Dis 2011;21(1):58-62 [FREE Full text] [Medline: 21462731]
31. Ameye H, Swinnen J. Obesity, income and gender: the changing global relationship. Glob Food Sec 2019 Dec;23:267-281. [doi: 10.1016/j.gfs.2019.09.003]
32. Kim Y. The long-run effect of education on obesity in the US. Econ Hum Biol 2016 May;21:100-109. [doi: 10.1016/j.ehb.2015.12.003] [Medline: 26828291]
33. Befort C, Nazir N, Perri MG. Prevalence of obesity among adults from rural and urban areas of the United States: findings from NHANES (2005-2008). J Rural Health 2012;28(4):392-397 [FREE Full text] [doi: 10.1111/j.1748-0361.2012.00411.x] [Medline: 23083085]
34. Devaux M, Sassi F, Church J, Cecchini M, Borgonovi F. Exploring the relationship between education and obesity. OECD: J Econ Stud 2011 Sep 15:1-40. [doi: 10.1787/eco_studies-2011-5kg5825v1k23]

35. Brakefield WS, Ammar N, Olusanya OA, Shaban-Nejad A. An urban population health observatory system to support COVID-19 pandemic preparedness, response, and management: design and development study. JMIR Public Health Surveill 2021 Jun 16;7(6):e28269 [FREE Full text] [doi: 10.2196/28269] [Medline: 34081605]
36. Brakefield WS, Ammar N, Shaban-Nejad A. An urban population health observatory for disease causal pathway analysis and decision support: underlying explainable artificial intelligence model. JMIR Form Res 2022 Jul 20;6(7):e36055. [doi: 10.2196/36055]
37. Ammar N, Bailey JE, Davis RL, Shaban-Nejad A. Using a personal health library-enabled mHealth recommender system for self-management of diabetes among underserved populations: use case for knowledge graphs and linked data. JMIR Form Res 2021 Mar 16;5(3):e24738 [FREE Full text] [doi: 10.2196/24738] [Medline: 33724197]
38. Shaban-Nejad A, Michalowski M, Peek N, Brownstein JS, Buckeridge DL. Seven pillars of precision digital health and medicine. Artif Intell Med 2020 Mar;103:101793. [doi: 10.1016/j.artmed.2020.101793] [Medline: 32143798]
39. Lawson JA, Janssen I, Bruner MW, Madani K, Pickett W. Urban-rural differences in asthma prevalence among young people in Canada: the roles of health behaviors and obesity. Ann Allergy Asthma Immunol 2011 Sep;107(3):220-228. [doi: 10.1016/j.anai.2011.06.014] [Medline: 21875540]
40. Betteridge JD, Armbruster SP, Maydonovitch C, Veerappan GR. Inflammatory bowel disease prevalence by age, gender, race, and geographic location in the U.S. military health care population. IBD 2013;19(7):1421-1427. [doi: 10.1097/mib.0b013e318281334d]
41. Thornton LE, Pearce JR, Kavanagh AM. Using Geographic Information Systems (GIS) to assess the role of the built environment in influencing obesity: a glossary. Int J Behav Nutr Phys Act 2011 Jul 01;8(1):71 [FREE Full text] [doi: 10.1186/1479-5868-8-71] [Medline: 21722367]
42. Congdon P. Obesity and urban environments. Int J Environ Res Public Health 2019 Feb 05;16(3):464 [FREE Full text] [doi: 10.3390/ijerph16030464] [Medline: 30764541]

## Abbreviations

**AIC:** Akaike’s information criterion
**CDC:** Centers for Disease Control and Prevention
**NCD:** noncommunicable disease
**OLS:** ordinary least squares
**SDOH:** social determinants of health
**SEM:** spatial error model
**VIF:** variance inflation factor

*Edited by Y Khader; submitted 04.02.22; peer-reviewed by N Maglaveras, C Zhao, C El Morr, D Carvalho; comments to author 11.04.22; revised version received 21.06.22; accepted 06.07.22; published 09.08.22.*

*Please cite as:*
*Brakefield WS, Olusanya OA, Shaban-Nejad A*
*Association Between Neighborhood Factors and Adult Obesity in Shelby County, Tennessee: Geospatial Machine Learning Approach*
*JMIR Public Health Surveill 2022;8(8):e37039*
*URL: https://publichealth.jmir.org/2022/8/e37039*
*doi:10.2196/37039*
*PMID:35943795*

Review

# The Landscape of Participatory Surveillance Systems Across the One Health Spectrum: Systematic Review

Carrie McNeil[1], DVM, MPH; Sarah Verlander[1], MSPH; Nomita Divi[1], MSPH; Mark Smolinski[1], MD, MPH

Ending Pandemics, San Francisco, CA, United States

**Corresponding Author:**
Carrie McNeil, DVM, MPH
Ending Pandemics
870 Market Street, Suite 528
San Francisco, CA, 94102
United States
Phone: 1 415 571 2175
Email: carrie@endingpandemics.org

## Abstract

**Background:** Participatory surveillance systems augment traditional surveillance systems through bidirectional community engagement. The digital platform evolution has enabled the expansion of participatory surveillance systems, globally, for the detection of health events impacting people, animals, plants, and the environment, in other words, across the entire One Health spectrum.

**Objective:** The aim of this landscape was to identify and provide descriptive information regarding system focus, geography, users, technology, information shared, and perceived impact of ongoing participatory surveillance systems across the One Health spectrum.

**Methods:** This landscape began with a systematic literature review to identify potential ongoing participatory surveillance systems. A survey was sent to collect standardized data from the contacts of systems identified in the literature review and through direct outreach to stakeholders, experts, and professional organizations. Descriptive analyses of survey and literature review results were conducted across the programs.

**Results:** The landscape identified 60 ongoing single-sector and multisector participatory surveillance systems spanning five continents. Of these, 29 (48%) include data on human health, 26 (43%) include data on environmental health, and 24 (40%) include data on animal health. In total, 16 (27%) systems are multisectoral; of these, 9 (56%) collect animal and environmental health data; 3 (19%) collect human, animal, and environmental health data; 2 (13%) collect human and environmental health data; and 2 (13%) collect human and animal health data. Out of 60 systems, 31 (52%) are designed to cover a national scale, compared to those with a subnational (n=19, 32%) or multinational (n=10, 17%) focus. All systems use some form of digital technology. Email communication or websites (n=40, 67%) and smartphones (n=29, 48%) are the most common technologies used, with some using both. Systems have capabilities to download geolocation data (n=31, 52%), photographs (n=29, 48%), and videos (n=6, 10%), and can incorporate lab data or sample collection (n=15, 25%). In sharing information back with users, most use visualization, such as maps (n=43, 72%); training and educational materials (n=37, 62%); newsletters, blogs, and emails (n=34, 57%); and disease prevention information (n=32, 53%). Out of the 46 systems responding to the survey regarding perceived impacts of their systems, 36 (78%) noted “improved community knowledge and understanding” and 31 (67%) noted “earlier detection.”

**Conclusions:** The landscape demonstrated the breadth of applicability of participatory surveillance around the world to collect data from community members and trained volunteers in order to inform the detection of events, from invasive plant pests to weekly influenza symptoms. Acknowledging the importance of bidirectionality of information, these systems simultaneously share findings back with the users. Such directly engaged community detection systems capture events early and provide opportunities to stop outbreaks quickly.

***(JMIR Public Health Surveill 2022;8(8):e38551)*** doi:10.2196/38551

**KEYWORDS**

participatory surveillance; One Health; citizen science; community-based surveillance; infectious disease; digital disease detection; community participation; mobile phone

## Introduction

The prevention and control of emerging pathogens relies on local-level surveillance for early detection of health events impacting people, animals, plants, and the environment. Many traditional animal and human health surveillance systems rely on data from astute clinicians, health center records, and laboratory testing to identify anomalies indicating potential outbreaks and emerging pathogens [1]. Plant surveillance systems also rely on laboratories, governmental systems, and border surveillance [2]. Unfortunately, access to health centers, laboratories, and veterinary services are not universally available to match the risk from emerging infections [3-5].

Exponential growth in accessibility to mobile technologies and web-based platforms across the globe has created unique opportunities for health surveillance systems to directly engage the public and key community stakeholders to rapidly collect data at the local level [1]. Direct engagement strategies have been employed across a spectrum of diseases to enhance disease surveillance [6]. The emergence of COVID-19 has led to a rapid increase in digital technology to directly engage the public in early detection and rapid response through apps for workplace health, contact tracing, and health information [7,8].

Participatory surveillance is defined as the bidirectional process of receiving and transmitting data for action through direct engagement of the target population. This approach can complement traditional surveillance systems by expanding engagement to larger segments of communities [1]. Participatory surveillance does not include data collected in a community for research or monitoring purposes when such data do not contribute to ongoing disease surveillance and do not provide information back to the community being monitored.

The evolution of participatory surveillance has been attributed to the use of participatory epidemiology in animal health, which recognized how local herdsmen and livestock owners have a deep knowledge of disease patterns and impacts among their livestock. Participatory epidemiology in animal health provides a co-learning opportunity between the animal health practitioner and the livestock owner that is built on trust and respect, in which practitioners interview livestock owners directly to understand disease burden among their herds. As such, this locally based surveillance data complements traditional animal health surveillance [3].

From animal health to human health, participatory surveillance integrates the locally based surveillance data to detect the emergence of an outbreak early, to expand surveillance capacity, and to inform control during outbreak response [3,9]. The earliest documented use of participatory surveillance in humans may have started with the “De Grote Griepmeting” in the Netherlands and Belgium in 2003 to monitor influenza-like illness [10]. Similar influenza-focused participatory surveillance systems now span several continents. Three International Workshops on Participatory Surveillance (IWOPS) have been held since 2013 to share best practices and explore innovative applications of this growing methodology [6]. COVID-19, Ebola virus disease, SARS, Middle East respiratory syndrome, and avian influenza outbreaks have highlighted the value of One Health in disease surveillance. One Health is a multisector approach that recognizes how the health of people, animals, plants, and the environment are inextricably connected [11,12]. For example, tracking changes in ecosystems helps identify potential areas for viral spillover [13]. With an estimated 60% of emerging infectious diseases being zoonotic in origin and 23% being vector-borne diseases, early detection among animal or vector hosts may limit or prevent outbreaks among people [12]. In addition to being vital components to health ecosystems, plants provide an estimated 70% of food sources to people and animals, thus ensuring that early detection of plant pathogens is critical for healthy environments, livestock, wildlife, and people [14].

Participatory surveillance systems vary in design and implementation. For human health, domesticated animal health, and crop health, participatory surveillance data are collected directly from the impacted individual, farmer, or rancher, or by a community or animal health worker on their behalf [15]. Wildlife and ecosystems provide a unique challenge as they do not have an “owner” to report, as would be expected for domesticated plants and animals. In these cases, the general public, trained volunteers, or land stewards, such as rangers, are typically called upon to assist in detecting morbidities and mortalities [16,17].

This landscape has been conducted to identify ongoing participatory surveillance systems across the One Health spectrum and to describe their geography, system logistics, and data and technology. Both single-sector and multisector systems are included in this landscape, as they both contribute to detection and response across the One Health spectrum.

## Methods

### Overview

Participatory surveillance systems for this landscape analysis were identified through existing partnerships, a systematic literature review, and surveys. Contacts of the systems identified through the literature review or ones known to the authors were sent a survey in order to collect the most up-to-date information where available. The survey link was also sent out through health organizations and to contacts of systems identified through stakeholder interviews in order to ensure that those systems not present in the peer-reviewed literature could be identified. Survey data and data abstracted from the literature were included in the analysis.

### Literature Review

In June 2021, a systematic literature review of English-language, peer-reviewed articles published after 1990 was performed using CAB Direct, PubMed, and the PubMed Veterinary Science search strategy. Preliminary search terms were developed based on input from the authors and were identified in an exploratory soft audit of phrases and words in an existing database of participatory surveillance articles using the text analysis tool Zotero 5.0 (Corporation for Digital Scholarship; Textbox 1).

**Textbox 1.** Search terms used in CAB Direct, PubMed, and the PubMed Veterinary Science search strategy for the literature review.

**Search terms**

- "participatory epidemiology"
- "participatory surveillance"
- "participatory disease surveillance"
- "'community-based surveillance' or 'community based surveillance'"
- "community event-based surveillance"
- "participatory" AND ("surveillance" OR "disease surveillance" OR "surveillance system" OR "disease detection")
- ("crowdsourcing" OR "crowdsourced" OR "crowd-sourced" OR "crowd-sourcing") AND ("surveillance" OR "disease surveillance" OR "surveillance system" OR "disease detection")
- ("internet-based" OR "internet based") AND ("surveillance" OR "disease surveillance" OR "surveillance system" OR "disease detection")
- ("citizen science" OR "citizen-science") AND ("surveillance" OR "disease surveillance" OR "surveillance system" OR "disease detection")

Inclusion criteria for articles required them to describe participatory systems as (1) ongoing, (2) disease related, and (3) consistent with the definition of participatory surveillance [1]. A secondary reviewer conducted a review of all identified systems, potential systems, and a selection of the articles not meeting the inclusion criteria.

At the time of this landscape, COVID-19 surveillance systems were just beginning. While systems solely focusing on COVID-19 are not included in this paper, a future landscape could include those that have remained as ongoing surveillance systems and not as short-term response tools. Pilot systems were excluded unless it was clear that they were now ongoing systems.

To minimize inclusion of articles not relevant to ongoing, disease-related participatory surveillance, articles about COVID-19, maternal health, injuries, chronic conditions, drugs and smoking, and natural disasters were flagged. A character-by-character search of titles in R (version 4.1.1; R Foundation for Statistical Computing) flagged articles using the following terms: "covid|sars-cov-2|sarscov2," "chronic|diabet|crohn," "maternal|fetal|natal|neonatal|pregnan|birth defect," "injur|collision|bike|car," "overdose|tobacco|smok|vape," and "natural disaster|storm|flood|drought." Final exclusion or inclusion of the flagged articles was determined by manual review of the title and abstract.

Using RStudio (version 1.4.1717; RStudio, PBC) and R, resulting articles were concatenated into a single collection and dereplicated by title. A manual review of abstracts retrieved from PubMed through the Rentrez program in R showed additional noninfectious disease–related articles [18]. Thus, the following additional terms were used to remove nondisease-related articles: "cancer|oncolog|birth|obstretics|violen|concussion." As the survey was to be sent to any programs already identified by the authors, articles describing those systems were also removed from abstraction.

A total of 1584 articles were retrieved from PubMed and the PubMed Veterinary Science search strategy, and 851 articles were retrieved from CAB Direct. After deduplication, 276 articles were removed based on the exclusion criteria. During article abstraction, an additional 166 were categorized as not disease related, another 195 were not about participatory surveillance, and another 3 were related to COVID-19 and, hence, removed.

For each system meeting the inclusion criteria, reviewers collected the name, location, stated purpose, geographic scale, year the system began, number of users, technology used, types of data used, and how often users enter data. Abstraction also captured logistical information, such as identifying who enters the data, who analyzes and interprets the data, who maintains and operates the system, who responds to the data, and how the system is funded. Reviewers also captured whether data are specifically being used in forecasting or modeling, any challenges in implementation, and how challenges were addressed. Systems were categorized as human health, animal health, or environmental health. Human health systems were described by their target population. Animal health included the subcategories of livestock, equine, or poultry; wildlife other than birds; wildlife birds; fisheries; dogs or cats; or other animal species. Environmental health was subcategorized by the following focus areas: vector, waterborne, land use, food safety or food quality, crop, wild plant, or other. Multisector programs were identified as a combination of human health, animal health, or environmental health, as appropriate.

## Survey

Using Alchemer (version 5; Alchemer LLC), an online survey was conducted to capture data that were not identified through the peer-reviewed literature and to verify the data captured from the literature review. The survey collected the same data as those that were abstracted during the literature review, with additional questions related to syndromic and exposure data elements and whether a system had data freely available for public use. Staff piloted the survey to review clarity, usability, and time for completion. The Alchemer internal survey analysis tools noted high accessibility and low fatigue level for the survey tool.

In July 2021, the survey was sent using Mailchimp (Intuit) to the primary contact authors identified in the literature review, to contacts of systems that the authors had previously identified, and to those recommended by key contacts across the One Health spectrum. The survey was also sent out through the networks of the following: TEPHINET (Training Programs in Epidemiology and Public Health Interventions Network), EpiCore, the Wildlife Disease Association, Emory University's Rollins School of Public Health and Environmental Health alumni, Johns Hopkins School of Public Health alumni, the National Plant Diagnostic Network, CORDS (Connecting Organizations for Regional Disease Surveillance), and the South Asia One Health Disease Surveillance Network.

### Ethical Considerations

The survey was not considered to be human subjects research, as data collected were limited to the organizational level for this landscape, which was designed to inform meeting planning for the fourth IWOPS; therefore, no ethics approval was applied for. This rationale is consistent with the Harvard University policies on human subjects research [19].

### Beta Review

Following survey data collection, reviewers reassessed which systems met the criteria to be considered as participatory surveillance systems. It was determined that bidirectional engagement requires feedback to be sent directly to the data-entering participants in order to inform them about the incidence of the event or any prevention or mitigation measures. Official government surveillance systems that were not bidirectional, including community health workers entering data into traditional surveillance systems, were excluded. Through this process, determinations were made to exclude those systems sharing data among veterinary professionals, as opposed to systems that collected data from paraprofessionals or volunteers from the general public. Those systems included the Small Animal Veterinary Surveillance Network, the Caribbean Animal Health Network, and Equinella, and they were excluded because such systems represented more of a traditional disease reporting system among health professionals.

### Data Analysis

To ensure the review contained the most up-to-date data available in this analysis, survey data were used where available; when they were not available, websites and literature review abstraction data were used. Descriptive data analyses were conducted in R and Microsoft Excel 2019 (version 2204).

## Results

### Overview

In total, 60 systems met the criteria for participatory surveillance (Multimedia Appendix 1) [15-17,20-57]. Systems were identified through the literature review (n=18, 30%) and from prior work by Ending Pandemics (n=21, 35%); the remainder were discovered through the survey outreach. The majority (n=43, 72%) of the programs discovered had a representative of the organization participate in the survey; information on the remaining programs (n=17, 28%) was gathered from available literature.

A total of 29 (48%) systems include data collected on human health, 26 (43%) include data collected on environmental health, and 24 (40%) include data collected on animal health. Of the 60 systems, 44 (73%) have a single-sector focus and 16 (27%) have a multisector focus (Table 1). Less than half of all systems self-identify as featuring a One Health focus (n=22, 37%).

Of the 44 single-sector programs, 22 (50%) only collect data on human health, 10 (23%) only collect data on animal health, and 12 (27%) only collect data on environmental health (Table 1) [16,17,20-23,25-31,35-39,45-52,56,57].

Among all 24 single-sector and multisector systems collecting data on animals, 16 (67%) only collect animal health data on wildlife, such as wild birds, mammals, reptiles, amphibians, and aquatics or fish [15-17,32-44,55-57]. In total, 8 (33%) systems collect data on domesticated animals, such as poultry, livestock, and companion animals. Only 1 (4%) system collects data on both wildlife and livestock animal populations [35].

Across the 26 systems that include data on environmental health, 16 (62%) collect data on vectors, 5 (19%) collect data on water quality, 3 (12%) collect data on food safety, 8 (31%) collect data on invasive species, 3 (12%) collect data on air quality, and 3 (12%) collect data on crops [15,32-34,40-54].

Most of the 29 systems collecting any data on human health look at multiple syndromes or diseases [26,27,29]. A total of 16 (55%) focus on influenza-like illness, with 12 (75%) of the influenza-focused systems expanded to incorporate COVID-19 surveillance. In total, 2 (7%) human health systems focus only on dengue.

Of the 16 multisector programs, the landscape found 2 (13%) systems focused on the combination of human and animal health, 9 (56%) focus on animal and environmental health, 2 (13%) focus on human and environmental health, and 3 (19%) focus on human, animal, and environmental health [15,32-34,40-44,53-55].

**Table 1.** Years in operation, geographic scale, and location of the participatory surveillance systems across the One Health spectrum.

| Program[a] focus | Programs (N=60), n (%) | Years in operation,[b] mean (SD, range) | Geographic scale, n (%) | | | Continent, n (%) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Multinational or regional (n=10) | National (n=31) | Subnational (n=20) | Africa (n=4) | North America (n=16) | Asia (n=13) | Europe (n=18) | Australia (n=7) | South America (n=2) |
| Animal only | 10 (17) | 16.4 (11.8, 3-34) | 2 (20) | 5 (16) | 3 (15) | 0 (0) | 5 (31) | 1 (8) | 2 (11) | 2 (29) | 0 (0) |
| Human only | 22 (37) | 7.5 (4.9, 1-17) | 5 (50) | 13 (42) | 4 (20) | 1 (25) | 3 (19) | 4 (31) | 12 (67) | 1 (14) | 1 (50) |
| Environment only | 12 (20) | 8.4 (4.9, 3-20) | 1 (10) | 6 (19) | 6 (30) | 0 (0) | 4 (25) | 2 (15) | 3 (17) | 2 (29) | 1 (50) |
| Human and animal | 2 (3) | 6.0 (0, 6-6) | 0 (0) | 2 (6) | 0 (0) | 1 (25) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) |
| Animal and environment | 9 (15) | 9.9 (4.7, 2-16) | 2 (20) | 4 (13) | 3 (15) | 1 (25) | 3 (19) | 2 (15) | 1 (6) | 2 (29) | 0 (0) |
| Human and environment | 2 (3) | 7.5 (2.12, 6-9) | 0 (0) | 0 (0) | 2 (10) | 0 (0) | 1 (6) | 1 (8) | 0 (0) | 0 (0) | 0 (0) |
| Human, animal, and environment | 3 (5) | 6.3 (1.5, 5-8) | 0 (0) | 1 (3) | 2 (10) | 1 (25) | 0 (0) | 2 (15) | 0 (0) | 0 (0) | 0 (0) |

[a] Data were from 60 participatory surveillance systems identified through the systematic literature review and surveys.

[b] The mean years in operation for all programs combined was 9.3 (SD 6.8, range 1-34).

## Geography of the Systems

Out of the 60 identified systems, approximately half (n=31, 52%) are designed to be used at a national scale, whereas one-third (n=20, 33%) have a subnational focus and one-sixth (n=10, 17%) have a multinational focus [17,26,27,29,35,36,45,46,49-53,56,57]. Among the 44 single-sector systems, 24 (55%) have a national focus. Out of the 16 multisector systems, 7 (44%) have a subnational geographic focus.

Only 4 systems out of 60 (7%) were identified from Africa. The remaining systems came from the Americas (n=18, 30%), Asia (n=13, 22%), Australia (n=7, 12%), and Europe (n=18, 30%; Table 1) [17,26,27,29,35,36,45,46,49-53,56,57]. Many of the multinational systems span the United States, Canada, Mexico, the United Kingdom, or Europe. Another multinational system is AVADAR (Audio-Visual Acute Flaccid Paralysis Detection and Reporting), which covers Nigeria, Sierra Leone, Liberia, the Democratic Republic of the Congo, Chad, Niger, South Sudan, and Cameroon [20]. WildHealthNet and SMART (Spatial Monitoring and Reporting Tool) for Health are used to provide actionable data on a national and subnational basis across Cambodia, Laos, and Vietnam.

## System Logistics

When asked to describe who enters the data, who responds to the data, how often those data are entered, and what feedback is provided back to the end user, systems reported a range of user types. For the 22 systems that only focus on human health, almost all (n=18, 82%) list the general public as the user; the remaining users are trained volunteers and health care workers [26,27,29]. Of the 10 systems that only focus on animal health, 5 (50%) rely only on the general public, 2 (20%) use trained volunteers and the general public, 1 (10%) uses trained volunteers, 1 (10%) uses wildlife rehabilitators, and 1 (10%) uses farmers and rangers [17,35,36,56,57].

When asked to categorize the number of users by range (from <500 to >50,000), 16 out of 60 (27%) systems reported having under 500 users, 14 (23%) reported having 500 to 5000 users, and 12 (20%) reported having 5000 to 15,000 users [26,27,29,35,36,45,46,50-52]. A total of 3 systems out of 60 (5%) reported having more than 50,000 users: FluTracking from Australia, California's West Nile Virus surveillance system, and Cambodia 115 Hotline [17].

Across the 60 identified systems, the user determines when to report in over half of the systems (n=34, 57%), including in 7 out of the 10 (70%) systems focused on only animal health, 10 of the 12 (83%) systems focused on environmental health, 14 of the 16 (88%) multisector systems, and only 3 of the 22 (14%) human health systems [17,26,27,29,35,36,45,46,49-53,56,57]. Out of the 23 programs using weekly reporting, 19 (83%) were systems that collect data only on human health [26,27,29,53]. The weekly reporting systems included the influenza surveillance systems, DoctorMe, Participatory One Health Digital Disease Detection, Kidenga, Egypt's Community-Based Animal Health Outreach (CAHO) surveillance system, and AVADAR [26,27,29,53]. DoctorMe, iMammalia, and Brazil's Guardians of Health reported that data are collected daily. FeederWatch reports are limited to November to April, when the greatest amount of bird feeder activity occurs [36]. Similarly, Mozzie Monitors, a mosquito surveillance system, focuses its reporting during peak mosquito season for the presence of vectors [46]. Outbreaks Near Me noted that they prompt users every 3 days by SMS.

A total of 42 systems stated that once data are reported, response is led by government or academic institutions [17,26,27,29,35,36,45,46,49-53,56,57]. Nonprofits are primary responders for 11 of these systems (26%), 6 of which (55%)

are systems that collect both animal and environmental data. Private sector partners are responders for 5 (13%) systems [35]. Government response agencies usually include health, environment, or agriculture agencies. iMammalia shares data with the Food and Agriculture Organization of the United Nations (FAO) as appropriate, and Outbreaks Near Me shares trends with government agencies. Guardians of Health specified that schools and universities are involved in the response.

### Data and Technology

All the systems in this analysis use some form of digital technology, with the exception of Egypt's CAHO, though 6 out of 60 (10%) still incorporate paper-based data collection. Email communication or websites (n=40, 67%) and smartphones (n=29, 48%) are the most common technologies used [17,26,27,29,36,45,46,49,51-53,56,57], with several systems using both. Smartphones are often used for collecting environmental health data only [45,46,49,51,53]. All systems that collect data only on human health use email or web-based systems [26,27,29]. The Ukraine Infectious Diseases of Animals system was the only program stating that they incorporate remote sensing. Cambodia 115 Hotline is the only system that reported using voice recording, also known as interactive voice response.

Many of the 60 systems have the capability to upload geolocation (n=31, 52%) and photographs (n=29, 48%); a few are able to upload videos (n=6, 10%) [17,35,36,45,46,49,51,52,56,57]. A total of 12 out of the 15 (80%) systems incorporating lab testing or diagnostics focus on animal health or environmental health; many collect carcass or vector samples [35,46,50,51]. The Cervid Disease Network often anonymizes location to protect the end user and their farms [35]. A total of 20 systems (33%) use data in forecasting or modeling [17].

Out of 43 systems that answered, a total of 11 (26%) survey respondents answered that their data are publicly available. In total, 21 (49%) systems reported that their data are not openly available. In addition to those 21 systems, 3 (7%) stated that data are held by government agencies and not available to the public; 8 (19%) systems specified that data are sometimes available in summary format or at the request of the researchers, but with redaction of any protected information.

Bidirectionality (ie, providing information back to the users) is essential for meeting the criteria for participatory surveillance. Systems (N=60) share information back to users in a variety of ways, including visualization, such as maps (n=43, 72%); training and educational materials (n=37, 62%); newsletters, blogs, and emails (n=34, 57%); and disease prevention information (n=32, 53%; Table 2) [17,26,27,29,36,45,46,49,51-53]. Vaccine information is shared back by 8 (13%) systems, and 5 (63%) of these have a human health focus. Treatment and medical advice (n=16, 27%) is also provided [45,46,51,53]. Users are provided with disease data by 16 (27%) systems [17]. FishWatch and PestWatch systems provide information back through the media and trained volunteers [56,57]. The California Wildlife Morbidity and Mortality Event Alert System noted that staffing constraints limit when they are able to respond directly back to a report. The Arizona Game and Fish Department specified that they report findings and results back to the users.

Survey respondents were asked to note all of the impacts their systems have had to date (Table 3). Out of the 46 systems that reported through the survey, 36 (78%) noted that "improved community knowledge and understanding" was an impact of their system and 31 (67%) stated that "earlier detection" was an impact of their system. In the text field, 1 (2%) system wrote "improved active surveillance" and another (n=1, 2%) wrote "slowly improving stakeholder and partner understanding." Survey respondents were not asked to justify or provide examples of these impacts.

**Table 2.** Information about participatory systems that reported providing information back to users.

| System[a] focus | Information provided by systems,[b] n (%) | | | | | | |
|---|---|---|---|---|---|---|---|
| | Visualization of the situation[c] (n=45 ) | Disease data from other sources (n=16) | Vaccine information (n=8) | Disease prevention information (n=34) | Treatment or medical advice (n=16) | Newsletters, blogs, or email updates (n=35) | Training or educational materials (n=40) |
| Animal only | 5 (11) | 4 (25) | 0 (0) | 4 (12) | 1 (6) | 6 (17) | 8 (20) |
| Human only | 18 (40) | 5 (31) | 5 (63) | 9 (26) | 3 (19) | 17 (49) | 8 (20) |
| Environment only | 10 (22) | 1 (6) | 0 (0) | 9 (26) | 3 (19) | 6 (17) | 12 (30) |
| Human and animal | 1 (2) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) |
| Animal and environment | 6 (13) | 4 (25) | 1 (13) | 6 (18) | 5 (31) | 5 (14) | 8 (20) |
| Human and environment | 2 (4) | 0 (0) | 0 (0) | 2 (6) | 2 (13) | 0 (0) | 2 (5) |
| Human, animal, and environment | 3 (7) | 2 (13) | 2 (25) | 3 (9) | 2 (13) | 1 (3) | 2 (5) |

[a] Data were from 60 participatory surveillance systems identified through the systematic literature review and surveys.

[b] Links to public health resources were not provided by any of the systems.

[c] Visualization included maps of cases.

**Table 3.** Self-reported impacts of participatory surveillance systems.

| System[a] focus | Impacts of systems, n (%) | | | | | |
|---|---|---|---|---|---|---|
| | Earlier detection (n=31) | Improved community knowledge and understanding (n=36) | Quicker response (n=26) | Better cross-sector coordination (n=25) | Policy or funding impacts (n=19) | Have not measured impacts (n=6) |
| Animal only | 5 (16) | 5 (14) | 5 (19) | 4 (16) | 3 (16) | 0 (0) |
| Human only | 11 (35) | 16 (44) | 7 (27) | 11 (44) | 5 (26) | 2 (33) |
| Environment only | 3 (10) | 4 (11) | 2 (8) | 1 (4) | 1 (5) | 1 (17) |
| Human and animal | 2 (6) | 1 (3) | 2 (8) | 1 (4) | 1 (5) | 0 (0) |
| Animal and environment | 7 (23) | 7 (19) | 7 (27) | 5 (20) | 6 (32) | 2 (33) |
| Human and environment | 1 (3) | 1 (3) | 1 (4) | 1 (4) | 1 (5) | 0 (0) |
| Human, animal, and environment | 2 (6) | 2 (6) | 2 (8) | 2 (8) | 2 (11) | 1 (17) |

[a] Data were provided by 46 of the programs through the survey.

## Discussion

### Principal Findings

Across the One Health spectrum, participatory surveillance is being used around the globe to improve animal, human, and environmental health. The majority of the systems in this paper were identified through the survey outreach, suggesting that many systems have not yet been described in the peer-reviewed, English-language literature. As such, numerous additional systems may exist that have not been captured within this assessment. As a complement to this manuscript, an updateable digital map will be made available to the public to provide a repository of the systems identified in this landscape and to provide a platform to add in new systems as they are identified.

Many systems reported impacts of improved early detection and quicker response. Trained volunteers and members of the public augment current disease surveillance activities of health department staff to engage larger populations and expand geographic coverage. Thus, such systems may identify events when traditional systems would not have the personnel or other resources to detect early. For example, faced with the challenge of identifying invasive species of plant pathogens and insect pests across the 244 million acres of cultivated crops and 640 million acres of federally managed public lands in the United States, the University of Georgia's participatory surveillance system captures data from over 30,000 professionals and trained volunteers, through the EDDMapS (Early Detection and Distribution Mapping System) [41], and from the public, through Wild Spotter. Data collected are able to inform official systems, such as the National Plant Diagnostic Network, so they may follow up with an appropriate response [58].

Nonprofits were noted to play a larger role in response regarding animal health and environmental health systems compared to human health; further assessment would be required to understand if this is due to their role in funding of the initial systems or due to limited government response capabilities in these fields.

Confirming bidirectionality was a challenge for wildlife and wildland surveillance, where there is not necessarily a direct ongoing link between the user and the impacted plant or animal. Numerous systems were identified that collect data from persons witnessing a change in a landscape, a dead animal, or a vector, but they did not specify whether information was reported back to the individuals; hence, they were not included in this analysis. In contrast, other wildland networks have incorporated repeated reporting of site locations to gather both negative report data and recurring records. One such case is the inclusion of a sentinel tree program by the United Kingdom group Observatree, where users selected a single tree or group of trees to report on their health and any changes in conditions several times a year [52]. While systems that rely solely on single event–based reporting with no additional follow-up were excluded from this landscape, they demonstrate distinct differences in how data are collected in wild versus domesticated situations, and the need to consider how to encapsulate such systems in the broader participatory surveillance landscape.

Often, systems with more users were those that collected data from the general public. Human health systems, many of which were based on a similar framework for influenza surveillance, were most likely to require regular reporting intervals. It will be interesting to see if changes in seasonal practices of reporting for birdfeeder and vector systems will be needed as climate change impacts migratory and weather patterns. This effort did not collect data on recruitment and sustainability; these would be worth exploring in future studies as well.

Impact data suggest that systems perceive they are meeting their stated goals for early detection, response, and outreach. Many animal and human health systems reported early detection and rapid response as outcomes from their systems. Further data collection through interviews and review of monitoring and evaluation systems would be required to assess and quantify impacts and to understand why fewer environmental systems had seen these impacts.

Multisector data collection and integration provide both challenges and opportunities to enabling a One Health approach to detection and response. Siloed government systems, data sharing challenges, different professional terminologies, and priorities create obstacles to developing multisector systems that capture human, animal, and environmental health data.

However, 14 multisector systems identified across 4 of the 5 OIE (World Organisation for Animal Health; formerly, Office International des Epizooties) regions have been active anywhere from 2 to 16 years. Conceivably, it may be easier to integrate data collection at the local level through participatory systems simply because the animals, people, and plants are geographically colocated. A next step in reviewing this dynamic should include assessing processes for data integration and interoperability among multisector participatory surveillance and discerning how those data can be used to inform potentially separate formal systems.

Innovations in technology are enhancing capabilities in capturing data from the public, from geolocation, to video, to sample collection. Pairing of laboratory data and point-of-care diagnostics with participatory surveillance systems may add to the specificity of this approach.

Emerging wearable technologies are creating new diagnostic capabilities for plants, animals, and people; these may continue to enhance the specificity of data collected from participatory surveillance [59-61]. In terms of geolocation data collection, the anonymization approach of the Cervid Disease Network may be worth considering for other livestock or crop surveillance systems for which concerns about farm identification may deter participation [35].

### Limitations

Selection bias may have skewed results based on outreach conducted through networks that may not encompass all systems. The survey identified numerous programs that were not identified in the literature review, indicating that not all systems are discoverable in the English-language peer-reviewed literature. Systems developed for limited duration focusing on a single outbreak response were not included. It is possible that such systems, like COVID-19 monitoring or new pilot efforts, will become long-term systems and may need to be included in the future. The literature review and survey were conducted exclusively in English, which also likely undercounted the number of systems that are currently active. In fact, one survey was not complete enough to include, and the limited answers that were provided were not in English. The authors will continue their discovery of systems; in addition, any new systems uncovered by the authors can be included in the interactive map that is under development and that will be made publicly available online at the Ending Pandemics website [62].

Incomplete data from respondents limited this study’s abilities to interpret findings across all systems. In addition, the fact that literature data were used when survey data were not available may have prevented inclusion of the most up-to-date information for those systems. Systems that began after July 2021 were not included in this analysis.

In 2017, Ending Pandemics published a landscape of participatory surveillance systems based on partnerships it had with other system developers through its convenings at the IWOPS. A loose collaboration of participatory surveillance system creators and stewards, IWOPS partners met for the first time in 2012 in San Francisco, United States; again in 2013 in Amsterdam, the Netherlands; and most recently in 2016 in Newcastle, Australia. IWOPS serves as an informal network to share best practices, consult on analytic methods, and catalyze innovations to advance the direct engagement of populations in voluntary reporting. The 2017 review was limited to IWOPS partner systems and revealed 23 distinct participatory surveillance tools or programs in 18 countries that encompassed human and animal health [6]. This study summarized results from the systematic review of the literature combined with a detailed survey of all identified systems in human, animal, and environmental health. While prior work focused on a convenience sample, this landscape incorporated literature review and survey methodology. This landscape also incorporated systems that only focus on plant health and environmental health.

### Conclusions

This landscape demonstrated the breadth of applicability of participatory surveillance, from tick identification in photographs, to One Health apps used by community members, to trained volunteers reporting invasive plant pests, to people tracking their own weekly influenza symptoms around the world. With globalization, trade, and travel, rapid disease spread across country borders creates a need for on-the-ground detection systems that can capture cases early and provide opportunities to stop outbreaks quickly. Developing mechanisms for information sharing among participatory surveillance systems may improve opportunities for systems to alert others as to what may be on the horizon. These actions may require revisiting ways to allow for public data access and sharing in formats that protect sensitive data.

In this review, some systems demonstrated the importance of being in place in advance of a pandemic, as they were able to be easily adapted for information collection and communication with the public specific to COVID-19. As the World Health Organization—in conjunction with the FAO, the OIE, and the United Nations Environment Programme—develops the Epidemic Intelligence from Open Sources platform, finding timely ways to integrate participatory surveillance data will be critical. For the hundreds of thousands of participatory surveillance users, seeing a global, as well as a local, impact of their efforts may help inspire them to continue in these voluntary roles.

---

## Acknowledgments

We would like to acknowledge Adam Crawley and Phoebe Lu for the early review and audit, which informed search term development. We would also like to thank Elizabeth Aaron, who coordinated survey correspondence and provided feedback for the survey design. We would like to thank Marlo Libel, Louise Gresham, Jay Atanda, and Jessica Shao, who provided feedback and outreach assistance throughout the design and execution of this effort. We would also like to recognize Onicio Leal Neto for his assistance in identifying systems and map development. We appreciate the assistance of the Emory University librarians in article retrieval. This project was funded by Ending Pandemics, a project of the Tides Foundation.

## Conflicts of Interest

None declared.

Multimedia Appendix 1

Supplementary table of data from participatory surveillance systems.

[XLSX File (Microsoft Excel File), 178 KB - publichealth_v8i8e38551_app1.xlsx ]

## References

1. Smolinski M. Innovations in participatory disease surveillance. Int J Infect Dis 2016 Dec;53:10. [doi: 10.1016/j.ijid.2016.11.030]
2. Brown N, Pérez-Sierra A, Crow P, Parnell S. The role of passive surveillance and citizen science in plant health. CABI Agric Biosci 2020;1(1):17 [FREE Full text] [doi: 10.1186/s43170-020-00016-5] [Medline: 33748770]
3. Mariner JC, Jones BA, Hendrickx S, El Masry I, Jobre Y, Jost CC. Experiences in participatory surveillance and community-based reporting systems for H5N1 highly pathogenic avian influenza: A case study approach. Ecohealth 2014;11(1):22-35 [FREE Full text] [doi: 10.1007/s10393-014-0916-0] [Medline: 24643858]
4. Nikolay B, Salje H, Sturm-Ramirez K, Azziz-Baumgartner E, Homaira N, Ahmed M, et al. Evaluating hospital-based surveillance for outbreak detection in Bangladesh: Analysis of healthcare utilization data. PLoS Med 2017 Jan;14(1):e1002218 [FREE Full text] [doi: 10.1371/journal.pmed.1002218] [Medline: 28095468]
5. Quinn SC, Kumar S. Health inequalities and infectious disease epidemics: A challenge for global health security. Biosecur Bioterror 2014;12(5):263-273 [FREE Full text] [doi: 10.1089/bsp.2014.0032] [Medline: 25254915]
6. 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] [Medline: 29021131]
7. Whitelaw S, Mamas MA, Topol E, Van Spall HGC. Applications of digital technology in COVID-19 pandemic planning and response. Lancet Digit Health 2020 Aug;2(8):e435-e440 [FREE Full text] [doi: 10.1016/S2589-7500(20)30142-4] [Medline: 32835201]
8. Ming LC, Untong N, Aliudin NA, Osili N, Kifli N, Tan CS, et al. Mobile health apps on COVID-19 launched in the early days of the pandemic: Content analysis and review. JMIR Mhealth Uhealth 2020 Sep 16;8(9):e19796 [FREE Full text] [doi: 10.2196/19796] [Medline: 32609622]
9. Jost CC, Mariner JC, Roeder PL, Sawitri E, Macgregor-Skinner GJ. Participatory epidemiology in disease surveillance and research. Rev Sci Tech 2007 Dec;26(3):537-549 [FREE Full text] [Medline: 18293603]
10. Marquet RL, Bartelds AI, van Noort SP, Koppeschaar CE, Paget J, Schellevis FG, et al. Internet-based monitoring of influenza-like illness (ILI) in the general population of the Netherlands during the 2003-2004 influenza season. BMC Public Health 2006 Oct 04;6:242 [FREE Full text] [doi: 10.1186/1471-2458-6-242] [Medline: 17018161]
11. Daszak P, Keusch GT, Phelan AL, Johnson CK, Osterholm MT. Infectious disease threats: A rebound to resilience. Health Aff (Millwood) 2021 Feb;40(2):204-211. [doi: 10.1377/hlthaff.2020.01544] [Medline: 33476187]
12. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, et al. Global trends in emerging infectious diseases. Nature 2008 Feb 21;451(7181):990-993 [FREE Full text] [doi: 10.1038/nature06536] [Medline: 18288193]
13. Becker DJ, Washburne AD, Faust CL, Pulliam JRC, Mordecai EA, Lloyd-Smith JO, et al. Dynamic and integrative approaches to understanding pathogen spillover. Philos Trans R Soc Lond B Biol Sci 2019 Sep 30;374(1782):20190014 [FREE Full text] [doi: 10.1098/rstb.2019.0014] [Medline: 31401959]
14. Rizzo DM, Lichtveld M, Mazet JAK, Togami E, Miller SA. Plant health and its effects on food safety and security in a One Health framework: Four case studies. One Health Outlook 2021;3:6 [FREE Full text] [doi: 10.1186/s42522-021-00038-7] [Medline: 33829143]
15. Verdugo C, El Masry I, Makonnen Y, Hannah H, Unger F, Soliman M, et al. Sensitivity and specificity estimation for the clinical diagnosis of highly pathogenic avian influenza in the Egyptian participatory disease surveillance program. Avian Dis 2016 Dec 1;60(4):805. [doi: 10.1637/11442-060316-reg]
16. Kelly TR, Pandit PS, Carion N, Dombrowski DF, Rogers KH, McMillin SC, et al. Early detection of wildlife morbidity and mortality through an event-based surveillance system. Proc Biol Sci 2021 Jul 14;288(1954):20210974 [FREE Full text] [doi: 10.1098/rspb.2021.0974] [Medline: 34256001]
17. Snyder RE, Feiszli T, Foss L, Messenger S, Fang Y, Barker CM, et al. West Nile virus in California, 2003-2018: A persistent threat. PLoS Negl Trop Dis 2020 Nov;14(11):e0008841 [FREE Full text] [doi: 10.1371/journal.pntd.0008841] [Medline: 33206634]
18. Winter DJ. rentrez: An R package for the NCBI eUtils API. R J 2017;9(2):520-526 [FREE Full text]

19. How do the federal regulations define human subject? Committee on the Use of Human Subjects, Harvard University. URL: https://tinyurl.com/yc7fbcap [accessed 2022-07-12]
20. Shuaib FMB, Musa PF, Gashu ST, Onoka C, Ahmed SA, Bagana M, et al. AVADAR (Auto-Visual AFP Detection and Reporting): Demonstration of a novel SMS-based smartphone application to improve acute flaccid paralysis (AFP) surveillance in Nigeria. BMC Public Health 2018 Dec 13;18(Suppl 4):1305 [FREE Full text] [doi: 10.1186/s12889-018-6187-x] [Medline: 30541508]
21. Case Study: Cambodia's 115 Hotline. Expanding Access to the Reporting and Detecting of Disease Outbreaks.: Principles for Digital Development URL: https://digitalprinciples.org/wp-content/uploads/Principles-Case-Study-Cambodia-115-Hotline-FINAL_-2.pdf [accessed 2022-07-14]
22. Lwin MO, Lu J, Sheldenkar A, Panchapakesan C, Tan Y, Yap P, et al. Effectiveness of a mobile-based influenza-like illness surveillance system (FluMob) among health care workers: Longitudinal study. JMIR Mhealth Uhealth 2020 Dec 07;8(12):e19712 [FREE Full text] [doi: 10.2196/19712] [Medline: 33284126]
23. Smolinski MS, Crawley AW, Baltrusaitis K, Chunara R, Olsen JM, Wójcik O, et al. Flu near you: Crowdsourced symptom reporting spanning 2 influenza seasons. Am J Public Health 2015 Oct;105(10):2124-2130. [doi: 10.2105/AJPH.2015.302696] [Medline: 26270299]
24. Chunara R, Aman S, Smolinski M, Brownstein JS. Flu Near You: An online self-reported influenza surveillance system in the USA. In: Proceedings of the 11th International Society for Disease Surveillance Conference. 2013 Presented at: The 11th International Society for Disease Surveillance Conference; December 4-5, 2012; San Diego, CA p. e133 URL: https://journals.uic.edu/ojs/index.php/ojphi/article/view/4456/3500 [doi: 10.5210/ojphi.v5i1.4456]
25. Carlson SJ, Dalton CB, Tuyl FA, Durrheim DN, Fejsa J, Muscatello DJ, et al. Flutracking surveillance: Comparing 2007 New South Wales results with laboratory confirmed influenza notifications. Commun Dis Intell Q Rep 2009 Sep;33(3):323-327 [FREE Full text] [Medline: 20043603]
26. Lee L, Saboui M, Mukhai S. FluWatchers: The Public Health Agency of Canada’s online community-based influenza-like illness surveillance system. In: Proceedings of the 6th International Conference on Digital Health. 2016 Presented at: The 6th International Conference on Digital Health; April 11-13, 2016; Montreal, QC URL: https://www.flickr.com/photos/131376234@N05/26257860181/
27. Adler AJ, Eames KTD, Funk S, Edmunds WJ. Incidence and risk factors for influenza-like-illness in the UK: Online surveillance using Flusurvey. BMC Infect Dis 2014 May 01;14:232 [FREE Full text] [doi: 10.1186/1471-2334-14-232] [Medline: 24885043]
28. Kjelsø C, Galle M, Bang H, Ethelberg S, Krause TG. Influmeter - An online tool for self-reporting of influenza-like illness in Denmark. Infect Dis (Lond) 2016 Apr;48(4):322-327. [doi: 10.3109/23744235.2015.1122224] [Medline: 26654752]
29. Bayer C, Remschmidt C, an der Heiden M, Tolksdorf K, Herzhoff M, Kaersten S, et al. Internet-based syndromic monitoring of acute respiratory illness in the general population of Germany, weeks 35/2011 to 34/2012. Euro Surveill 2014 Jan 30;19(4):20684 [FREE Full text] [doi: 10.2807/1560-7917.es2014.19.4.20684] [Medline: 24507468]
30. Freifeld CC, Chunara R, Mekaru SR, Chan EH, Kass-Hout T, Ayala Iacucci A, et al. Participatory epidemiology: Use of mobile phones for community-based health reporting. PLoS Med 2010 Dec 07;7(12):e1000376 [FREE Full text] [doi: 10.1371/journal.pmed.1000376] [Medline: 21151888]
31. Paolotti D, Carnahan A, Colizza V, Eames K, Edmunds J, Gomes G, et al. Web-based participatory surveillance of infectious diseases: The Influenzanet participatory surveillance experience. Clin Microbiol Infect 2014 Jan;20(1):17-21 [FREE Full text] [doi: 10.1111/1469-0691.12477] [Medline: 24350723]
32. Karimuribo ED, Mutagahywa E, Sindato C, Mboera L, Mwabukusi M, Kariuki Njenga M, et al. A smartphone app (AfyaData) for innovative one health disease surveillance from community to national levels in Africa: Intervention in disease surveillance. JMIR Public Health Surveill 2017 Dec 18;3(4):e94 [FREE Full text] [doi: 10.2196/publichealth.7373] [Medline: 29254916]
33. Susampao P, Chanachai K, Petra P, Yano T, Pattamakaew S, Laiya E, et al. Digital functions in a participatory One Health surveillance initiative aiming for pandemic averting. Int J Infect Dis 2016 Dec;53:32. [doi: 10.1016/j.ijid.2016.11.088]
34. Wilkes M, Papageorgiou S, Kim T, Baldrias L, Aguilar E, Kelly T, et al. One Health workers: Innovations in early detection of human, animal, and plant disease outbreaks. J Glob Health Rep 2019 Dec 26:3. [doi: 10.29392/joghr.3.e2019093]
35. Cohnstaedt LW, Snyder D, Maki E, Schafer S. Crowdsourcing methodology: Establishing the Cervid Disease Network and the North American Mosquito Project. Vet Ital 2016 Jun 30;52(3-4):195-200. [doi: 10.12834/VetIt.577.2765.2] [Medline: 27723027]
36. Bonter DN, Cooper CB. Data validation in citizen science: A case study from Project FeederWatch. Front Ecol Environ 2012 Aug;10(6):305-307. [doi: 10.1890/110273]
37. Lawson B. Ten years of garden wildlife surveillance: What lessons have we learned? In: Proceedings of the British Veterinary Zoological Society Spring Meeting. 2016 Presented at: The British Veterinary Zoological Society Spring Meeting; March 11-13, 2016; Chester, UK p. 12-15.
38. Stephen C. The Canadian Wildlife Health Cooperative: Addressing wildlife health challenges in the 21st century. Can Vet J 2015 Sep;56(9):925-927 [FREE Full text] [Medline: 26346834]

39. Blanco‐Aguiar J, Smith G, Vicente J. Update on the development of an app (adaptation of iMammalia) for early reporting of wild boar carcasses by a warning system. EFSA J 2022 Feb;19(2):EN-7192. [doi: 10.2903/sp.efsa.2022.en-7192]
40. Fasanmi OG, Ahmed SSU, Oladele-Bukola MO, El-Tahawy AS, Elbestawy AR, Fasina FO. An evaluation of biosecurity compliance levels and assessment of associated risk factors for highly pathogenic avian influenza H5N1 infection of live-bird-markets, Nigeria and Egypt. Acta Trop 2016 Dec;164:321-328. [doi: 10.1016/j.actatropica.2016.08.030] [Medline: 27603430]
41. Bargeron CT, Swearingen J, Douce GK, Moorhead DJ, Rawlins KA. EDDMapS: A collaborative, easy-to-use, early detection and distribution mapping system. In: Proceedings of the 21st US Department of Agriculture Interagency Research Forum on Invasive Species. 2011 Presented at: The 21st US Department of Agriculture Interagency Research Forum on Invasive Species; January 12-15, 2010; Annapolis, MD p. 68 URL: https://www.nrs.fs.fed.us/pubs/gtr/gtr-nrs-p-75papers/33bargeron-p-75.pdf
42. Nevolko O. Monitoring of brucellosis in agricultural animals in Ukraine during 2013-2015. In: Proceedings of the 15th International Society for Disease Surveillance Conference. 2017 Presented at: The 15th International Society for Disease Surveillance Conference; December 6-8, 2016; Atlanta, GA p. e156 URL: https://journals.uic.edu/ojs/index.php/ojphi/article/view/7750/6261
43. Kavhu B, Mpakairi KS. Spatial Monitoring and Reporting Tool (SMART) in Mid‐Zambezi Valley, Zimbabwe: Implementation challenges and practices. Conserv Sci Pract 2021 Jul;3(9):e492. [doi: 10.1111/csp2.492]
44. East I, Wicks R, Martin P, Sergeant E, Randall L, Garner M. Use of a multi-criteria analysis framework to inform the design of risk based general surveillance systems for animal disease in Australia. Prev Vet Med 2013 Nov 01;112(3-4):230-247. [doi: 10.1016/j.prevetmed.2013.09.012] [Medline: 24125696]
45. César de Sá N, Marchante H, Marchante E, Cabral JA, Honrado JP, Vicente JR. Can citizen science data guide the surveillance of invasive plants? A model-based test with Acacia trees in Portugal. Biol Invasions 2019 Mar 20;21(6):2127-2141. [doi: 10.1007/s10530-019-01962-6]
46. Braz Sousa L, Fricker SR, Doherty SS, Webb CE, Baldock KL, Williams CR. Citizen science and smartphone e-entomology enables low-cost upscaling of mosquito surveillance. Sci Total Environ 2020 Feb 20;704:135349. [doi: 10.1016/j.scitotenv.2019.135349] [Medline: 31837870]
47. Lyons L, Brand M, Gronemeyer P, Mateus-Pinilla N, Ruiz M, Stone C, et al. Comparing contributions of passive and active tick collection methods to determine establishment of ticks of public health concern within Illinois. J Med Entomol 2021 Jul 16;58(4):1849-1864 [FREE Full text] [doi: 10.1093/jme/tjab031] [Medline: 33855433]
48. Grez AA, Zaviezo T, Roy HE, Brown PMJ, Bizama G. Rapid spread of in Chile and its effects on local coccinellid biodiversity. Divers Distrib 2016 Jun 23;22(9):982-994. [doi: 10.1111/ddi.12455]
49. Babu AN, Niehaus E, Shah S, Unnithan C, Ramkumar PS, Shah J, et al. Smartphone geospatial apps for dengue control, prevention, prediction, and education: MOSapp, DISapp, and the mosquito perception index (MPI). Environ Monit Assess 2019 Jun 28;191(Suppl 2):393. [doi: 10.1007/s10661-019-7425-0] [Medline: 31254076]
50. Walther D, Kampen H. The citizen science project 'Mueckenatlas' helps monitor the distribution and spread of invasive mosquito species in Germany. J Med Entomol 2017 Nov 07;54(6):1790-1794 [FREE Full text] [doi: 10.1093/jme/tjx166] [Medline: 29029273]
51. Munakamwe Z, Constantine A, McInerney C. The Victorian weed spotters: Recruitment and training of citizen scientists. In: Proceedings of the 21st Australasian Weeds Conference. 2018 Presented at: The 21st Australasian Weeds Conference; September 9-13, 2018; Sydney, Australia p. 193-196 URL: http://caws.org.nz/old-site/awc/2018/awc201811931.pdf
52. Crow P, de Groot M. Using citizen science to monitor the spread of tree pests and diseases: Outcomes of two projects in Slovenia and the UK. Manag Biol Invasion 2020;11(4):703-719. [doi: 10.3391/mbi.2020.11.4.06]
53. Schmidt C, Phippard A, Olsen JM, Wirt K, Riviera A, Crawley A, et al. Kidenga: Public engagement for detection and prevention of Aedes-borne viral diseases. In: Proceedings of the 15th International Society for Disease Surveillance Conference. 2017 Presented at: The 15th International Society for Disease Surveillance Conference; December 6-8, 2016; Atlanta, GA p. e111 URL: https://journals.uic.edu/ojs/index.php/ojphi/article/view/7694/6214
54. Fernando ONN, Rathnayake VS, Vijaykumar S, Lwin MO, Foo S. Mo-Buzz: Socially-mediated collaborative platform for ubiquitous location based service. In: Proceedings of the 15th International Conference on Human Interface and the Management of Information. Berlin, Germany: Springer; 2013 Presented at: The 15th International Conference on Human Interface and the Management of Information; July 21-26, 2013; Las Vegas, NV p. 373-382. [doi: 10.1007/978-3-642-39215-3_44]
55. Masiira B, Nakiire L, Kihembo C, Katushabe E, Natseri N, Nabukenya I, et al. Evaluation of integrated disease surveillance and response (IDSR) core and support functions after the revitalisation of IDSR in Uganda from 2012 to 2016. BMC Public Health 2019 Jan 09;19(1):46 [FREE Full text] [doi: 10.1186/s12889-018-6336-2] [Medline: 30626358]
56. Hewitt MJ, Hourston M, McDonald JI. A long way from home: Biosecurity lessons learnt from the impact of La Niña on the transportation and establishment of tropical portunid species. PLoS One 2018;13(8):e0202766 [FREE Full text] [doi: 10.1371/journal.pone.0202766] [Medline: 30133520]
57. Hourston M, McDonald J, Hewitt M. Public engagement for the detection of the introduced marine species Charybdis japonica in Western Australia. Manag Biol Invasion 2015 Sep;6(3):243-252. [doi: 10.3391/mbi.2015.6.3.03]

58. Crop acreage data. Farm Service Agency, US Department of Agriculture. 2022. URL: https://fsa.usda.gov/news-room/efoia/electronic-reading-room/frequently-requested-information/crop-acreage-data/index [accessed 2022-07-13]
59. Lu L, Zhang J, Xie Y, Gao F, Xu S, Wu X, et al. Wearable health devices in health care: Narrative systematic review. JMIR Mhealth Uhealth 2020 Nov 09;8(11):e18907 [FREE Full text] [doi: 10.2196/18907] [Medline: 33164904]
60. Hobbs EC, Colling A, Gurung RB, Allen J. The potential of diagnostic point-of-care tests (POCTs) for infectious and zoonotic animal diseases in developing countries: Technical, regulatory and sociocultural considerations. Transbound Emerg Dis 2021 Jul;68(4):1835-1849 [FREE Full text] [doi: 10.1111/tbed.13880] [Medline: 33058533]
61. Neethirajan S. Recent advances in wearable sensors for animal health management. Sens Biosensing Res 2017 Feb;12:15-29. [doi: 10.1016/j.sbsr.2016.11.004]
62. Ending Pandemics. URL: http://endingpandemics.org [accessed 2022-07-13]

## Abbreviations

**AVADAR:** Audio-Visual Acute Flaccid Paralysis Detection and Reporting
**CAHO:** Community-Based Animal Health Outreach
**CORDS:** Connecting Organizations for Regional Disease Surveillance
**EDDMapS:** Early Detection and Distribution Mapping System
**FAO:** Food and Agriculture Organization of the United Nations
**IWOPS:** International Workshop on Participatory Surveillance
**OIE:** World Organisation for Animal Health; formerly, Office International des Epizooties
**SMART:** Spatial Monitoring and Reporting Tool
**TEPHINET:** Training Programs in Epidemiology and Public Health Interventions Network

*Edited by A Mavragani, T Sanchez; submitted 07.04.22; peer-reviewed by E Lau, J Olsen, M Raimi; comments to author 30.04.22; revised version received 11.05.22; accepted 28.06.22; published 05.08.22.*

*Please cite as:*
*McNeil C, Verlander S, Divi N, Smolinski M*
*The Landscape of Participatory Surveillance Systems Across the One Health Spectrum: Systematic Review*
*JMIR Public Health Surveill 2022;8(8):e38551*
*URL: https://publichealth.jmir.org/2022/8/e38551*
*doi:10.2196/38551*
*PMID:35930345*

Original Paper

# Impact of COVID-19 Social Distancing Mandates on Gastrointestinal Pathogen Positivity: Secondary Data Analysis

Tanner Palmer[1,2], MSPH; L Scott Benson[1], MPH, MD, PhD; Christina Porucznik[1], MSPH, PhD; Lisa H Gren[1], MSPH, PhD

[1]Division of Public Health, Department of Family and Preventive Medicine, University of Utah School of Medicine, Salt Lake City, UT, United States
[2]bioMérieux, Inc, Salt Lake City, UT, United States

**Corresponding Author:**
Tanner Palmer, MSPH
bioMérieux, Inc
515 Colorow Drive
Salt Lake City, UT, 84108
United States
Phone: 1 801 736 6354 ext 2398
Email: tanner.palmer@biomerieux.com

## Abstract

**Background:** Acute gastrointestinal (GI) illnesses are of the most common problems evaluated by physicians and some of the most preventable. There is evidence of GI pathogen transmission when people are in close contact. The COVID-19 pandemic led to the sudden implementation of widespread social distancing measures in the United States. There is strong evidence that social distancing measures impact the spread of SARS-CoV-2, and a growing body of research indicates that these measures also decrease the transmission of other respiratory pathogens.

**Objective:** This study aims to investigate the impact of COVID-19 social distancing mandates on the GI pathogen positivity rates.

**Methods:** Deidentified GI Panel polymerase chain reaction test results from a routinely collected diagnostic database from January 1, 2019, through August 31, 2020, were analyzed for the GI pathogen positivity percentage. An interrupted time series analysis was performed, using social distancing mandate issue dates as the intervention date. The following 3 target organisms were chosen for the final analysis to represent different primary transmission routes: adenovirus F40 and 41, norovirus GI and GII, and *Escherichia coli* O157.

**Results:** In total, 84,223 test results from 9 states were included in the final data set. With the exception of *E coli* O157 in Kansas, Michigan, and Nebraska, we observed an immediate decrease in positivity percentage during the week of social distancing mandates for all other targets and states. Norovirus GI and GII showed the most notable drop in positivity, whereas *E coli* O157 appeared to be least impacted by social distancing mandates. Although we acknowledge the analysis has a multiple testing problem, the majority of our significant results showed significance even below the .01 level.

**Conclusions:** This study aimed to investigate the impact of social distancing mandates for COVID-19 on GI pathogen positivity, and we discovered that social distancing measures in fact decreased GI pathogen positivity initially. The use of similar measures may prove useful in GI pathogen outbreaks. The use of a unique diagnostic database in this study exhibits the potential for its use as a public health surveillance tool.

***(JMIR Public Health Surveill 2022;8(8):e34757)*** doi:10.2196/34757

**KEYWORDS**

social distancing; gastrointestinal; COVID-19; gastroenteritis; surveillance; epidemiology; pathogen transmission; respiratory pathogen; public health; pathogen outbreak; outbreak; surveillance tool; diagnostic database

## Introduction

Acute gastrointestinal (GI) illnesses are of the most common problems evaluated by physicians, and they are also some of the most preventable [1]. There is evidence of GI pathogen transmission when people are in close contact, such as at mass gatherings and in group childcare [2-4]. Common infection control measures such as handwashing and limiting contact with sick individuals can lead to a decrease in GI pathogen transmission and illness [1]. Still, the United States alone sees 311 to 375 million episodes of acute GI illnesses per year, leading to more than 900,000 hospitalizations and 6000 deaths [1]. These illnesses are not only a burden to health systems, but they can also be incredibly uncomfortable, and in some instances, dangerous for the patient.

The COVID-19 pandemic led to the sudden implementation of widespread public health measures in the United States, including 6-feet social distancing protocols, messaging around effective hand hygiene, stay-at-home orders, large gathering bans, and the closures of public areas (eg, schools, restaurants, and nonessential businesses) [5-7]. There is strong evidence that social distancing measures impact the spread of SARS-CoV-2, and a growing body of research indicates that these measures also considerably decreased the transmission of influenza, respiratory syncytial virus, and respiratory enterovirus [8-13]. There was a reduction of reportable GI illnesses observed during the COVID-19 pandemic in countries that implemented public health measures, and data from the National Outbreak Reporting System showed a reduction in GI illnesses in the United States from 2019 to 2020 [14-16]. With this study, we hope to add to the growing knowledge base that public health measures meant to control COVID-19 also impacted other diseases.

Identification of GI pathogens has routinely relied on contemporary diagnostic microbiology; however, many laboratories are adopting rapid polymerase chain reaction (PCR) tests for the identification of GI pathogens from stool samples [17]. Adoption of rapid PCR tests, such as the BioFire FilmArray GI Panel (referred to as GI Panel), in conjunction with participation in automated diagnostic databases, like BioFire Syndromic Trends (referred to as Trend), allows for the investigation and monitoring of GI pathogen positivity rates at the level of communities or states [18].

Using Trend, this study aims to investigate the impact of COVID-19 social distancing mandates on the GI pathogen positivity rates in different states. Understanding the impact of the mandates on GI pathogens may allow for the expanded utility of these measures to control pathogens in the future. We hypothesize that social distancing measures meant to limit the transmission of COVID-19 also resulted in decreased GI pathogen positivity.

# Methods

## Ethical Considerations

This study was reviewed by the University of Utah Institutional Review Board (IRB) and was determined not to meet the definitions of Human Subjects Research according to Federal regulations (IRB_00142577). Therefore, the study did not require IRB oversight.

## Data Source and Collection

### Test Results

To determine changes in positivity rates of pathogens, deidentified test results from the GI Panel from January 1, 2019, through August 31, 2020, were analyzed. The GI Panel is a widely deployed rapid PCR test, typically used in the hospital setting, designed to detect the most common pathogens associated with gastroenteritis [19]. To test on the GI panel, stool specimens are collected in Cary Blair transport medium from patients with gastroenteritis, and they are tested for 22 targets including bacteria, viruses, and parasites [19]. Three target organisms were chosen for this study: adenovirus F40 and 41, norovirus GI and GII, and *Escherichia coli* O157. These targets were selected because they represent different primary transmission routes. Adenovirus (types F40 and 41) is transmitted via aerosolized droplets and has a high prevalence in children. Norovirus (GI and GII) is mainly transmitted through the fecal-oral route and is highly contagious. *E coli* O157, although rare, is a cause of foodborne bacterial illnesses, and because of the severity of the disease, it is likely to be tested for and detected when it occurs [1,20].

Deidentified test results including the date of the test, the target organism species, the number of positive tests for that target, and the total number of tests were automatically recorded in the Trend database [18]. All participating laboratories were hospital- or clinic-based and accredited by the Clinical Laboratory Improvement Amendments. Reference laboratories were excluded. Laboratory verification or quality control runs were automatically excluded from Trend. Data used in this study were only from laboratories in the United States. For the purposes of data deidentification, 3 laboratories must participate in Trend in a state for that state to be included in the database. As such, 9 states were included in this study: California, Colorado, Illinois, Kansas, Michigan, Nebraska, Ohio, Texas, and Wisconsin.

### Social Distancing Mandates

The start dates of individual state COVID-19 social distancing mandates were obtained from the State COVID-19 Data and Policy Actions data curated by the Kaiser Family Foundation [21]. The following 4 key mandates were chosen to be included in this analysis: (1) stay-at-home orders, (2) restaurant closures, (3) nonessential business closures, and (4) large gathering bans.

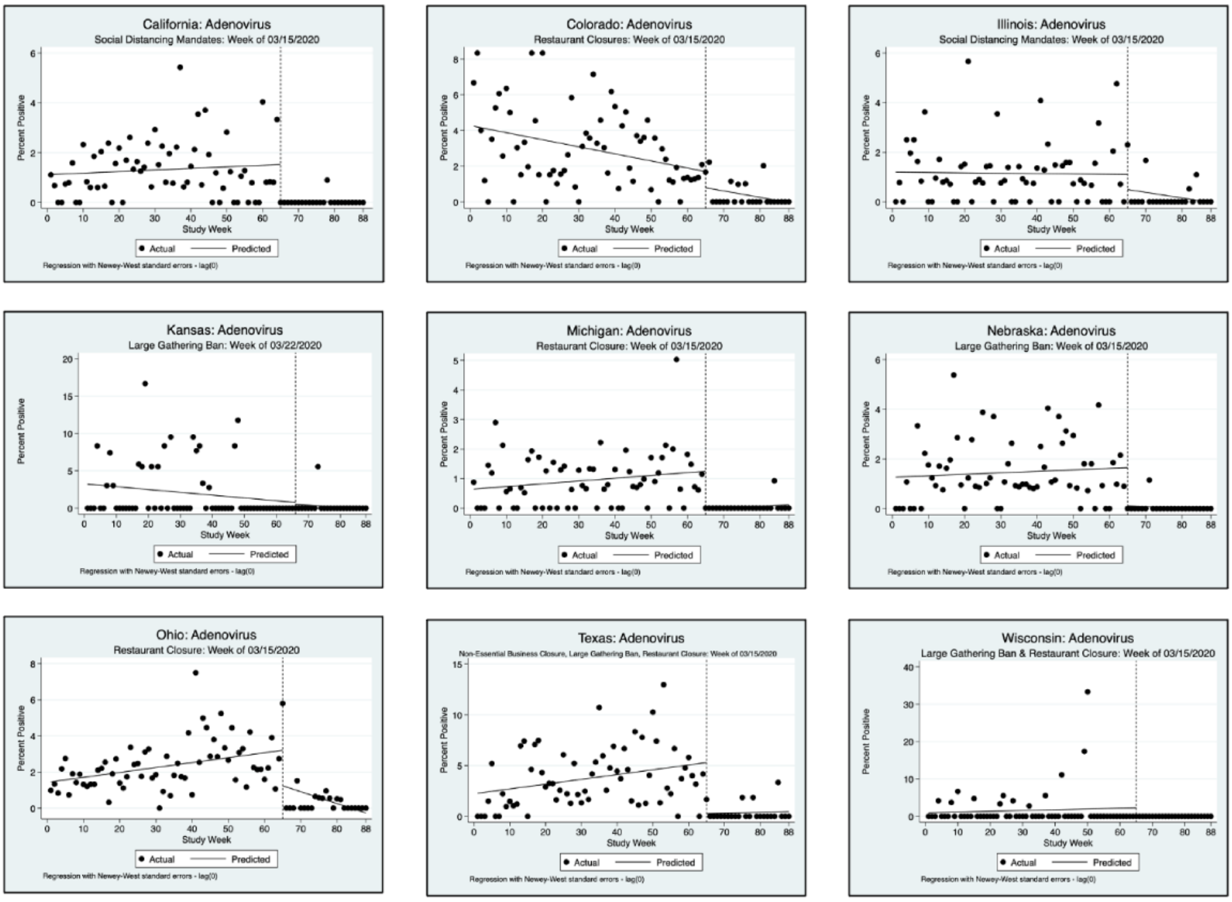
Mask mandates were not included in the analysis.

## Statistical Analysis

Data analysis was performed using Stata/IC (version 16.1; StataCorp). Daily test results were provided in the Trend database. Days when no GI Panel tests were performed in a state were excluded from the analysis. The daily test results were summed to weekly test results, and subsequently, weekly positivity percentages for each state and target were analyzed.

An interrupted time series analysis (ITSA) was performed for each of the 3 pathogens of interest and each state, using a downloadable Stata package (Figures 1-6) [22]. Figures 1-6 show the percent positivity before social distancing mandates went into effect (solid black dots before the vertical dashed line) and after social distancing mandates went into effect (solid black dots after the vertical dashed line). The best fit positivity percentage is represented by the solid horizontal line. We were most interested in the difference between the best fit positivity percentage before social distancing mandates and immediately after social distancing mandates. The time of intervention for the ITSA was the week that social distancing mandates went into effect for each individual state. In most states, multiple mandates went into effect in the same week; thus, the ITSA was performed only once for mandates occurring in the same week. Mandates occurring in separate weeks required a separate ITSA.

**Figure 1.** Interrupted time series analysis (ITSA) graphs for adenovirus F40 and 41. With the exception of California and Illinois, a second ITSA was performed for the second week in which social distancing mandates were issued. Refer to Figure 2 for the second ITSA.



California: Adenovirus
Social Distancing Mandates: Week of 03/15/2020

Colorado: Adenovirus
Restaurant Closures: Week of 03/15/2020

Illinois: Adenovirus
Social Distancing Mandates: Week of 03/15/2020

Kansas: Adenovirus
Large Gathering Ban: Week of 03/22/2020

Michigan: Adenovirus
Restaurant Closure: Week of 03/15/2020

Nebraska: Adenovirus
Large Gathering Ban: Week of 03/15/2020

Ohio: Adenovirus
Restaurant Closure: Week of 03/15/2020

Texas: Adenovirus
Non-Essential Business Closure, Large Gathering Ban, Restaurant Closure: Week of 03/15/2020

Wisconsin: Adenovirus
Large Gathering Ban & Restaurant Closure: Week of 03/15/2020

Regression with Newey-West standard errors - lag(0)

**Figure 2.** Interrupted time series analysis (ITSA) graphs for adenovirus F40 and 41 for the second week in which social distancing mandates were issued.

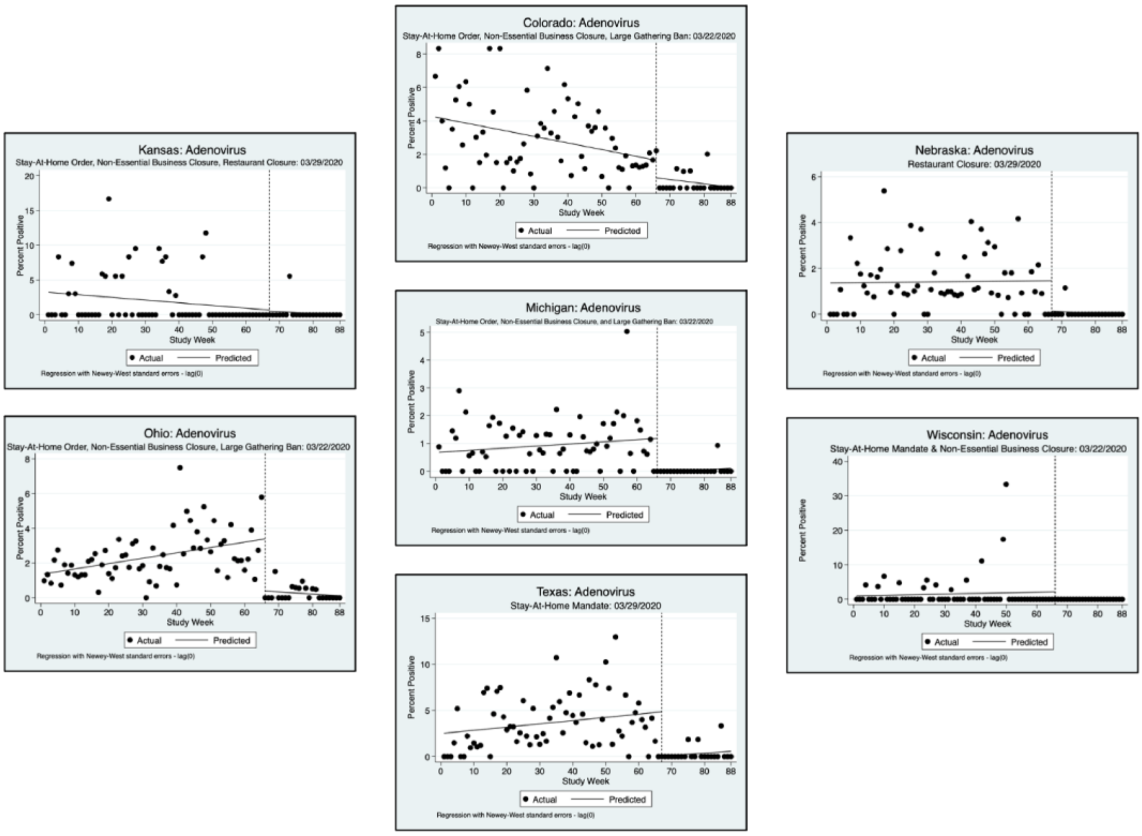


**Figure 3.** Interrupted time series analysis (ITSA) graphs for *Escherichia coli* O157. With the exception of California and Illinois, a second ITSA was performed for the second week in which social distancing mandates were issued. Refer to Figure 4 for the second ITSA.

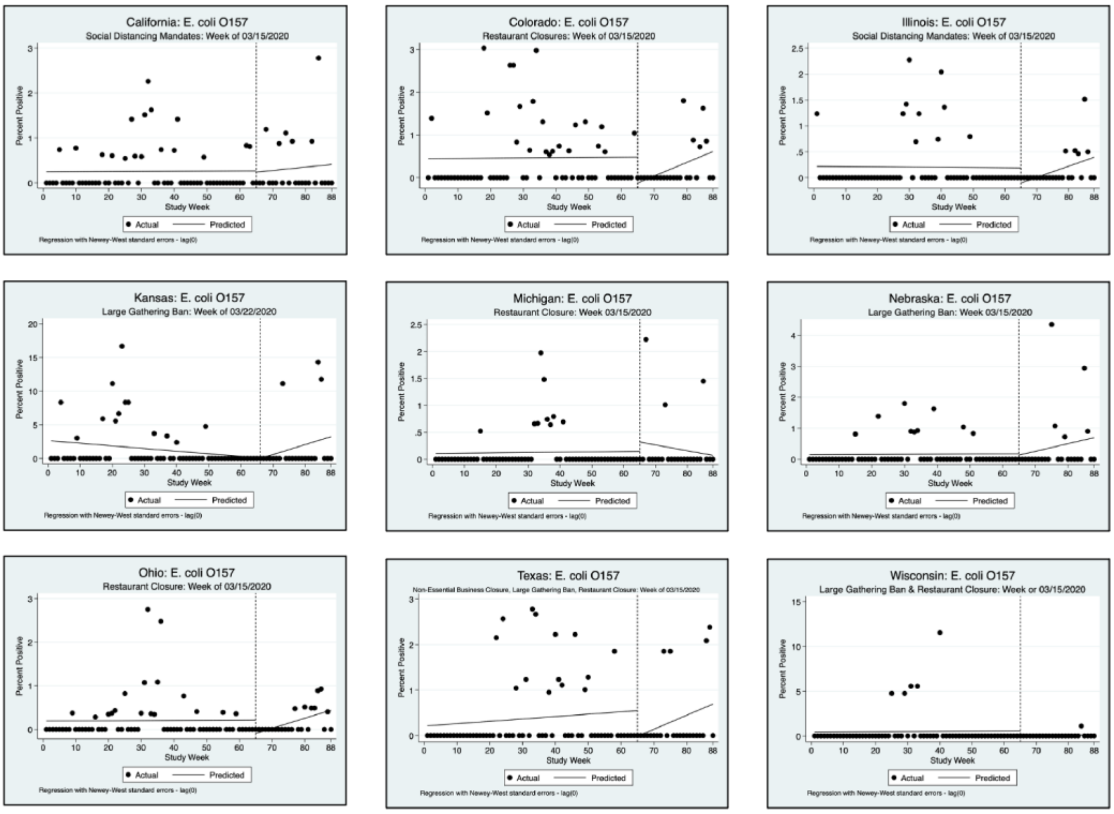


**Figure 4.** Interrupted time series analysis (ITSA) graphs for *Escherichia coli* O157 for the second week in which social distancing mandates were issued.

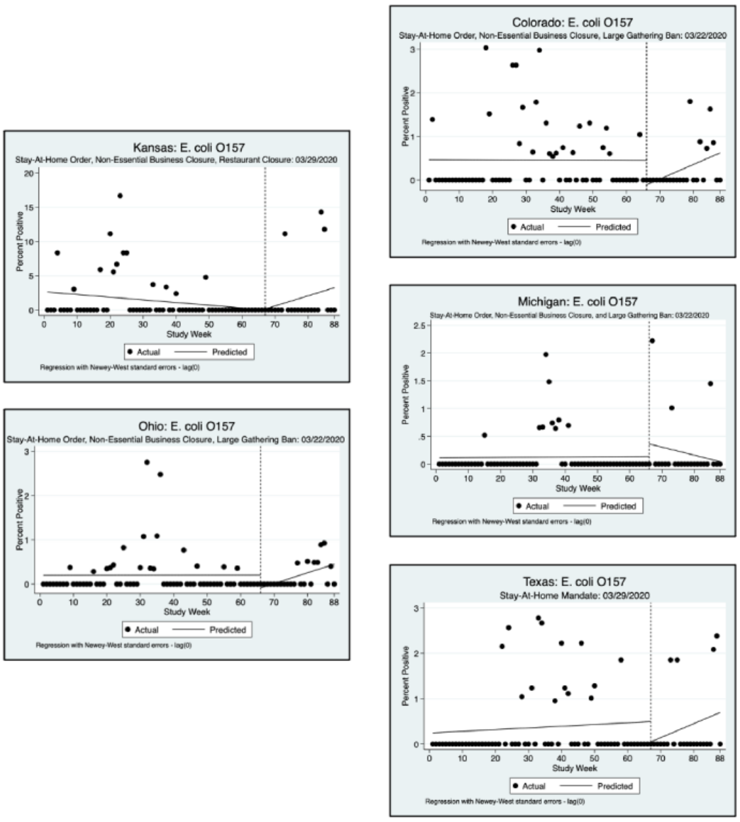


**Figure 5.** Interrupted time series analysis (ITSA) graphs for norovirus GI and GII. With the exception of California and Illinois, a second ITSA was performed for the second week in which social distancing mandates were issued. Refer to Figure 6 for the second ITSA.

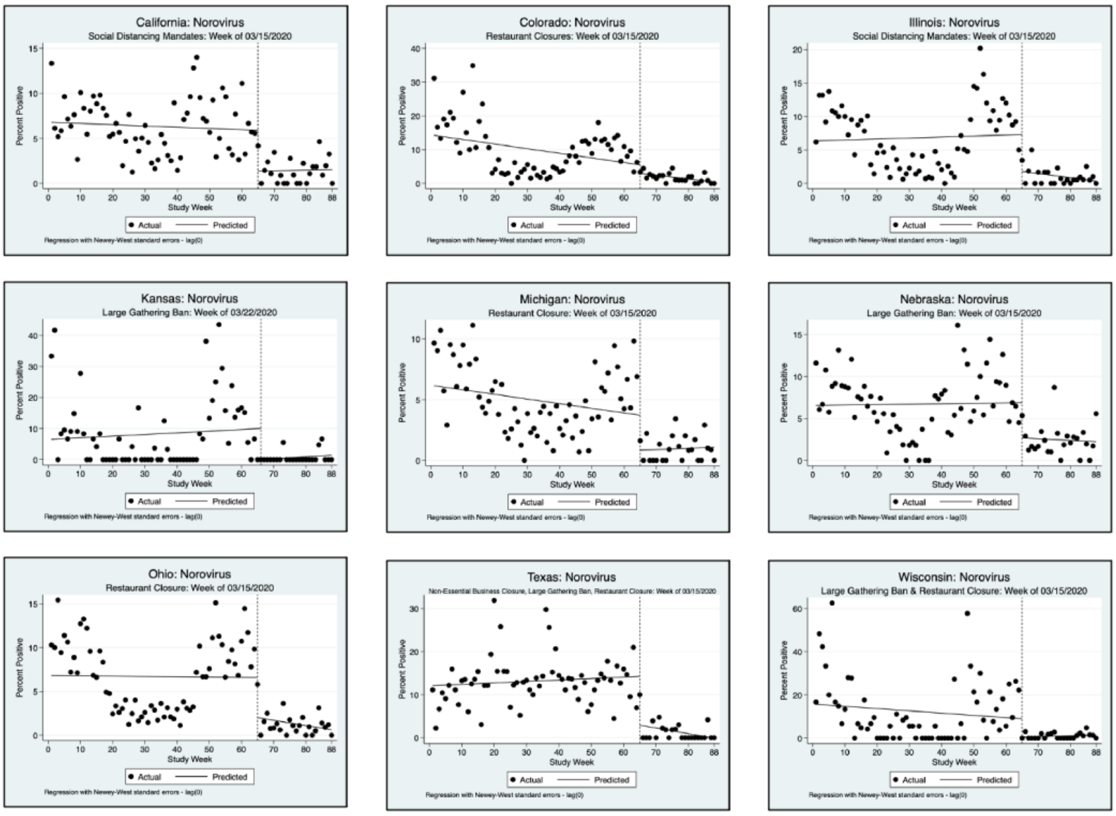
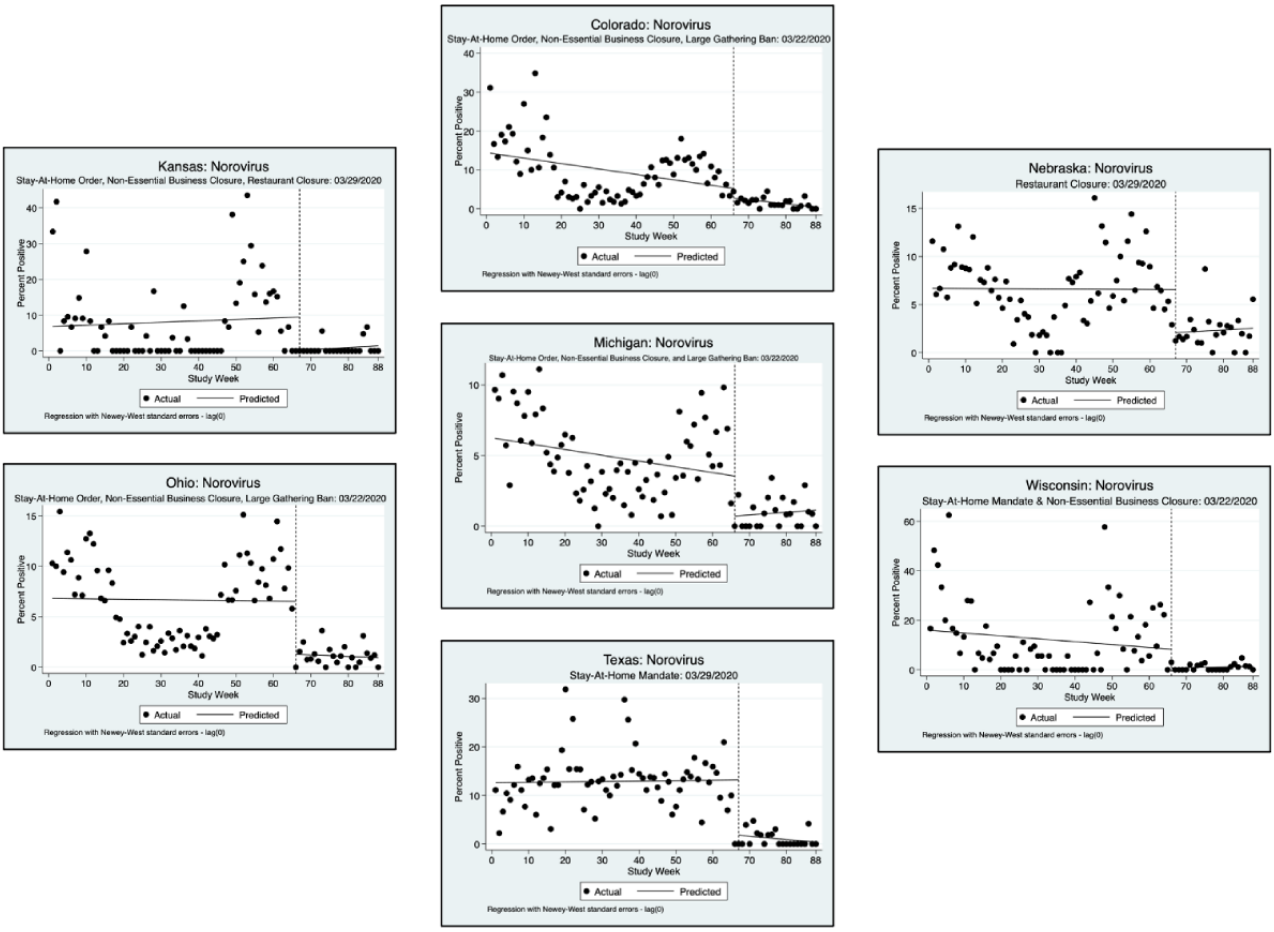


**Figure 6.** Interrupted time series analysis (ITSA) graphs for Norovirus GI and GII for the second week in which social distancing mandates were issued.



## Results

### Data Overview

A total of 84,223 tests from 9 states were included in the final data set (Table 1). Norovirus GI and GII had a higher overall positivity percentage compared to adenovirus F40 and 41 and *E coli* O157.

All states included in the analyses mandated social distancing policies in March of 2020 between the weeks beginning March 15, 2020, and March 29, 2020 (Table 2). Social distancing mandates occurred across two separate weeks for most states, with the exception of California and Illinois, where all mandates were announced in a single week. According to the Kaiser Family Foundation, Nebraska was the only state in the analysis that did not mandate nonessential business closures or a stay-at-home order.

**Table 1.** Distribution of total tests and positive tests.

| States | Total tests, n | Positive tests | | |
|---|---|---|---|---|
| | | Adenovirus F40 and 41, n (%) | Norovirus GI and GII, n (%) | *Escherichia coli* O157, n (%) |
| California | 11,400 | 124 (1.09) | 614 (5.39) | 32 (0.28) |
| Colorado | 9879 | 222 (2.25) | 693 (7.01) | 45 (0.46) |
| Illinois | 11,268 | 104 (0.92) | 594 (5.27) | 25 (0.22) |
| Kansas | 1674 | 26 (1.55) | 109 (6.51) | 24 (1.43) |
| Michigan | 11,458 | 88 (0.77) | 486 (4.24) | 16 (0.14) |
| Nebraska | 8814 | 97 (1.10) | 489 (5.55) | 20 (0.23) |
| Ohio | 21,049 | 404 (1.92) | 1171 (5.56) | 45 (0.21) |
| Texas | 6103 | 195 (3.20) | 685 (11.22) | 24 (0.39) |
| Wisconsin | 2588 | 20 (0.77) | 173 (6.68) | 8 (0.31) |

**Table 2.** Timing of social distancing mandates in analyzed states.

| State | Week of mandate | | | |
|---|---|---|---|---|
| | Stay-at-home order | Restaurant closures | Nonessential business closures | Large gathering bans |
| California | 3/15/20 | 3/15/20 | 3/15/20 | 3/15/20 |
| Colorado | 3/22/20 | 3/15/20 | 3/22/20 | 3/22/20 |
| Illinois | 3/15/20 | 3/15/20 | 3/15/20 | 3/15/20 |
| Kansas | 3/29/20 | 3/29/20 | 3/29/20 | 3/22/20 |
| Michigan | 3/22/20 | 3/15/20 | 3/22/20 | 3/22/20 |
| Nebraska | N/A[a] | 3/29/20 | N/A | 3/15/20 |
| Ohio | 3/22/20 | 3/15/20 | 3/22/20 | 3/22/20 |
| Texas | 3/29/20 | 3/15/20 | 3/15/20 | 3/15/20 |
| Wisconsin | 3/22/20 | 3/15/20 | 3/22/20 | 3/15/20 |

[a] N/A: not applicable; according to the Kaiser Family Foundation, Nebraska did not mandate nonessential business closures or a stay-at-home order.

## Immediate Effect

With the exception of *E coli* O157 in Kansas, Michigan, and Nebraska, we observed an immediate decrease in positivity percentage during the week of social distancing mandates. Norovirus GI and GII showed the most notable drop in positivity, whereas *E coli* O157 appeared to be least impacted by social distancing mandates (Figure 7; Table 3). Although we acknowledge the analysis has a multiple testing problem, the majority of our significant results showed significance even below the .01 level (Table 3).

**Figure 7.** Immediate change in positivity percentage during the week of social distancing mandates.

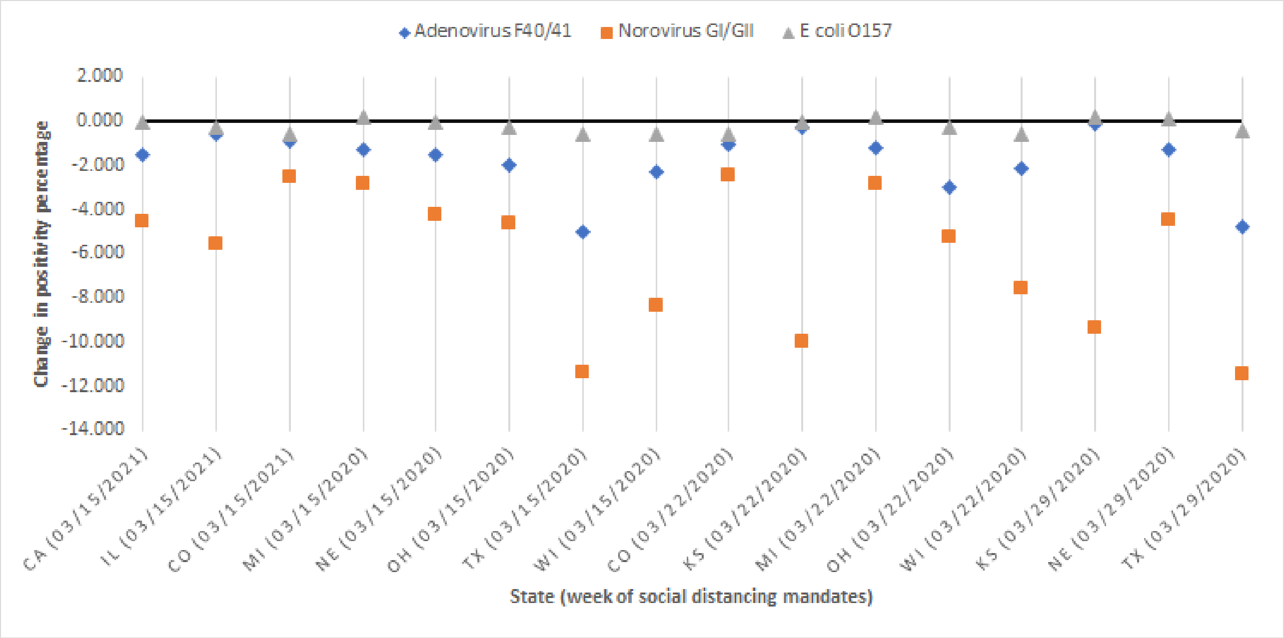


**Table 3.** Immediate change in positivity percentage during the week of social distancing mandate issuance.

| State (week of mandate) | Adenovirus F40 and 41 | | Norovirus GI and GII | | *Escherichia coli* O157 | |
|---|---|---|---|---|---|---|
| | Change (%) | *P* value | Change (%) | *P* value | Change (%) | *P* value |
| California (3/15/20) | –1.499 | <.001 | –4.507 | <.001 | –0.027 | .90 |
| Illinois (3/15/20) | –0.607 | .22 | –5.527 | <.001 | –0.290 | .02 |
| Colorado (3/15/20) | –0.901 | .08 | –2.560 | .08 | –0.601 | .001 |
| Michigan (3/15/20) | –1.278 | <.001 | –2.870 | .001 | 0.171 | .58 |
| Nebraska (3/15/20) | –1.536 | <.001 | –4.195 | .001 | –0.042 | .89 |
| Ohio (3/15/20) | –1.963 | .03 | –4.583 | .001 | –0.307 | .004 |
| Texas (3/15/20) | –5.016 | <.001 | –11.347 | <.001 | –0.564 | .049 |
| Wisconsin (3/15/20) | –2.279 | .16 | –8.364 | .03 | –0.582 | .10 |
| Colorado (3/22/20) | –1.048 | .04 | –2.471 | .09 | –0.561 | .001 |
| Kansas (3/22/20) | –0.283 | .73 | –9.986 | .003 | –0.075 | .95 |
| Michigan (3/22/20) | –1.210 | <.001 | –2.827 | .001 | 0.224 | .50 |
| Ohio (3/22/20) | –3.009 | <.001 | –5.252 | <.001 | –0.287 | .006 |
| Wisconsin (3/22/20) | –2.159 | .16 | –7.569 | .046 | –0.549 | .11 |
| Kansas (3/29/20) | –0.133 | .87 | –9.361 | .004 | 0.228 | .93 |
| Nebraska (3/29/20) | –1.320 | <.001 | –4.475 | <.001 | 0.082 | .82 |
| Texas (3/29/20) | –4.777 | <.001 | –11.428 | <.001 | –0.447 | .15 |

## Discussion

### Principal Findings

The results from this study indicate that public health measures meant for COVID-19 can initially decrease GI pathogen positivity. In most instances, we observed an immediate decrease in positivity percentage, suggesting that social distancing measures can very quickly decrease GI pathogen transmission. Similar results have been observed in previous studies, demonstrating that these public health measures can decrease transmission of other pathogens transmitted through the respiratory route, such as influenza, respiratory syncytial virus, and respiratory enterovirus; this study additionally demonstrates that they are also effective against GI pathogens on a national scale [8-13].

To provide context for our results on the effects of the mode of transmission of the pathogens, we chose 3 pathogens with different routes of transmission. Interestingly, our results show norovirus GI and GII was most impacted by the social distancing mandates. This may be due to the contagious nature of the pathogen, suggesting that social distancing mandates may be most effective against highly contagious GI pathogens that are most commonly spread person to person. The reduced person-to-person contact resulting from social distancing mandates could have decreased the transmission of norovirus GI and GII. Conversely, social distancing mandates showed a minimal impact on *E coli* O157 positivity rates. The results of *E coli* O157 positivity may be due to the incubation period of the bacterial infection, typically longer than viral infections, as we did not account for lag time in our analysis; however, this could be investigated in future studies. Additionally, as restaurants closed to dine-in service, take-out service typically remained available, which could have contributed to the minimal impact observed in our results. The social distancing mandates exhibited a moderate effect on the positivity percentage of adenovirus F40 and 41, more so than on *E coli* O157, but not as extreme as on norovirus GI and GII. It is possible that limited person-to-person contact impacted one route of transmission for adenovirus F40 and 41, but the virus was still spreading through other routes of transmission (eg, a fecal-oral route) leading to the observed moderate impact.

Our results show variability in the change of positivity percentage between states. This study did not aim to analyze this variability; however, differences in health behaviors of state residents and the enforcement of social distancing mandates may be contributing causes of this variability. An area of focus for future studies could be investigating differences between states.

The most notable strength of this study is the database itself, Trend. This study is a novel use of this unique diagnostic database that allowed us access to a large sample size of routinely collected, deidentified data. The large sample size consisting of test results across the nation should allow for generalizability to many communities. During the COVID-19 pandemic, social distancing mandates were universally used as a public health measure to control transmission, permitting us to use them as a variable in the analysis and compare states. The ITSA analysis allowed us to investigate the immediate impact of COVID-19–related social distancing measures on the positivity percentage of GI pathogens.

Although this study presents interesting findings using a unique diagnostic database, it is not without limitations. The BioFire

Trend database is expansive, and not all laboratories in a state may be participating, introducing the possibility of selection bias. However, the data set represents data from 9 states in different regions across the United States, allowing for some generalizability. There is possibility for diagnostic bias if a clinician chooses not to use the GI Panel, but most provider institutions will have testing algorithms established, that likely include the GI Panel if the patient is showing acute GI illness symptoms. Additionally, key social distancing measures were only measured on a statewide basis, which does not account for differences between counties or cities, nor did we have available data about compliance with social distancing mandates. However, given the time frame of our study, compliance is likely high, since our analysis period covers the time when the only measures available to prevent COVID-19 were social distancing measures. Hand hygiene was not investigated in this study, and it may have impacted the transmission of GI pathogens during the COVID-19 pandemic; future studies should investigate the effect of hand hygiene. BioFire Trend does not collect demographic data, and further studies are needed to investigate the effects of gender, age, race or ethnicity, and other demographic variables on GI pathogen positivity percentages.

## Conclusions

We investigated the impact of social distancing mandates for COVID-19 on GI pathogen positivity, and we discovered that social distancing measures did, in fact, decrease GI pathogen positivity. Our results show the possible utility of social distancing measures to reduce the spread of GI pathogens. The use of similar measures may prove useful in GI pathogen outbreaks. In addition to anecdotal evidence of decreased illness during the COVID-19 pandemic, the findings from this study can be used to reinforce that social distancing interventions can be used to reduce GI pathogen transmission.

The use of a unique diagnostic database, Trend, exhibits the potential for its use as a public health surveillance tool. We have only demonstrated one use of this routinely collected data, but we imagine it could be used for algorithms, models, and tools for early detection of diseases and monitoring the impact of different interventions to control outbreaks. Further research should not only investigate additional applications of Trend but also the impact of different public health measures between different communities. Further studies could assess whether GI pathogen positivity also decreased on a global scale during the COVID-19 time frame, further investigate the impact of COVID-19 mandates on pathogen positivity with the addition of contextual information, and observe long-term GI pathogen positivity after social distancing mandates went into effect.

## Acknowledgments

Tanner Palmer would like to express his sincere gratitude to the graduate committee Dr Lisa Gren, Dr Christy Porucznik, and Dr Scott Benson for their support and feedback throughout the graduate program and this study. The authors would also like to thank BioFire Diagnostics Medical Affairs for allowing this study to be conducted and the BioFire Diagnostics Syndromic Trends team for providing the data required. Special thanks to Camille Cook for introducing the contacts required to begin this study and for her mentorship at the beginning of this research.

## Authors' Contributions

TP conceptualized and refined the research idea, performed the statistical analysis with guidance from LHG, performed the literature review, and wrote the manuscript. LHG, LSB, and CP conceptualized and refined the research idea, and reviewed and revised the manuscript prior to submission.

## Conflicts of Interest

TP is an employee of bioMérieux, Inc. bioMérieux markets the BioFire FilmArray GI Panel and BioFire Syndromic Trends. This study was not sponsored by bioMérieux.

## References

1. Mahon C, Lehman D, Manuselis G. Textbook of Diagnostic Microbiology, 5th edition. New York: Saunders; 2015.
2. Gautret P, Steffen R. Communicable diseases as health risks at mass gatherings other than Hajj: what is the evidence? Int J Infect Dis 2016 Jun;47:46-52 [FREE Full text] [doi: 10.1016/j.ijid.2016.03.007] [Medline: 26987476]
3. Hoang V, Gautret P. Infectious diseases and mass gatherings. Curr Infect Dis Rep 2018 Aug 28;20(11):44 [FREE Full text] [doi: 10.1007/s11908-018-0650-9] [Medline: 30155747]
4. Collins J, Shane A. 3 - Infections associated with group childcare. In: Principles and Practice of Pediatric Infectious Diseases. Philadelphia: Elsevier; 2018:25-32.
5. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/social-distancing.html [accessed 2020-10-05]
6. Courtemanche C, Garuccio J, Le A, Pinkston J, Yelowitz A. Strong social distancing measures in the United States reduced the COVID-19 growth rate. Health Aff (Millwood) 2020 Jul 01;39(7):1237-1246. [doi: 10.1377/hlthaff.2020.00608] [Medline: 32407171]

7. Handwashing and making a solution for handwashing in Global, low-resource settings. Centers for Disease Control Prevention. URL: https://www.cdc.gov/coronavirus/2019-ncov/global-covid-19/handwashing.html [accessed 2022-07-05]
8. Chiu N, Chi H, Tai Y, Peng C, Tseng C, Chen C, et al. Impact of wearing masks, hand hygiene, and social distancing on influenza, enterovirus, and all-cause pneumonia during the coronavirus pandemic: retrospective national epidemiological surveillance study. J Med Internet Res 2020 Aug 20;22(8):e21257 [FREE Full text] [doi: 10.2196/21257] [Medline: 32750008]
9. Choe YJ, Lee J. The impact of social distancing on the transmission of influenza virus, South Korea, 2020. Osong Public Health Res Perspect 2020 Jun;11(3):91-92 [FREE Full text] [doi: 10.24171/j.phrp.2020.11.3.07] [Medline: 32494566]
10. Kuitunen I, Artama M, Mäkelä L, Backman K, Heiskanen-Kosma T, Renko M. Effect of social distancing due to the COVID-19 pandemic on the incidence of viral respiratory tract infections in children in Finland during early 2020. Pediatr Infect Dis J 2020 Dec;39(12):e423-e427. [doi: 10.1097/INF.0000000000002845] [Medline: 32773660]
11. Wiese A, Everson J, Grijalva C. Social distancing measures: evidence of interruption of seasonal influenza activity and early lessons of the SARS-COV-2 pandemic. Clin Infect Dis 2021 Jul 01;73(1):e141-e143 [FREE Full text] [doi: 10.1093/cid/ciaa834] [Medline: 32562538]
12. Edwards KM. The impact of social distancing for severe acute respiratory syndrome coronavirus 2 on respiratory syncytial virus and influenza burden. Clin Infect Dis 2021 Jun 15;72(12):2076-2078 [FREE Full text] [doi: 10.1093/cid/ciaa1543] [Medline: 33038221]
13. Nawrocki J, Olin K, Holdrege MC, Hartsell J, Meyers L, Cox C, et al. The effects of social distancing policies on non-SARS-COV-2 respiratory pathogens. Open Forum Infect Dis 2021 Jul;8(7):ofab133 [FREE Full text] [doi: 10.1093/ofid/ofab133] [Medline: 34322558]
14. Steffen R, Lautenschlager S, Fehr J. Travel restrictions and lockdown during the COVID-19 pandemic-impact on notified infectious diseases in Switzerland. J Travel Med 2020 Dec 23;27(8):1-3 [FREE Full text] [doi: 10.1093/jtm/taaa180] [Medline: 33152761]
15. Adegbija O, Walker J, Smoll N, Khan A, Graham J, Khandaker G. Notifiable diseases after implementation of COVID-19 public health prevention measures in Central Queensland, Australia. Commun Dis Intell (2018) 2021 Feb 26;45:1-5 [FREE Full text] [doi: 10.33321/cdi.2021.45.11] [Medline: 33632091]
16. National outbreak reporting system. Centers for Disease Control and Prevention. URL: https://wwwn.cdc.gov/norsdashboard/ [accessed 2022-02-20]
17. Bloomfield MG, Balm MND, Blackmore TK. Molecular testing for viral and bacterial enteric pathogens: gold standard for viruses, but don't let culture go just yet? Pathology 2015 Apr;47(3):227-233. [doi: 10.1097/PAT.0000000000000233] [Medline: 25719855]
18. Meyers L, Ginocchio CC, Faucett AN, Nolte FS, Gesteland PH, Leber A, et al. Automated real-time collection of pathogen-specific diagnostic data: syndromic infectious disease epidemiology. JMIR Public Health Surveill 2018 Jul 06;4(3):e59 [FREE Full text] [doi: 10.2196/publichealth.9876] [Medline: 29980501]
19. The BioFire® FilmArray® gastrointestinal (GI) panel. BioFire Diagnostics. URL: https://www.biofiredx.com/products/the-filmarray-panels/filmarraygi/ [accessed 2021-02-03]
20. Sell J, Dolan B. Common gastrointestinal infections. Prim Care 2018 Sep;45(3):519-532. [doi: 10.1016/j.pop.2018.05.008] [Medline: 30115338]
21. State COVID-19 data and policy actions. KFF. 2022 Feb 10. URL: https://www.kff.org/report-section/state-covid-19-data-and-policy-actions-policy-actions/#socialdistancing [accessed 2021-05-21]
22. Linden A. Conducting interrupted time-series analysis for single- and multiple-group comparisons. The Stata Journal 2015 Jun 01;15(2):480-500. [doi: 10.1177/1536867x1501500208]

---

## Abbreviations

**GI:** gastrointestinal
**IRB:** institutional review board
**ITSA:** interrupted time series analysis
**PCR:** polymerase chain reaction

*Edited by T Sanchez; submitted 29.11.21; peer-reviewed by CY Lin, R Steffen; comments to author 06.01.22; revised version received 10.04.22; accepted 03.05.22; published 24.08.22.*

*Please cite as:*
*Palmer T, Benson LS, Porucznik C, Gren LH*
*Impact of COVID-19 Social Distancing Mandates on Gastrointestinal Pathogen Positivity: Secondary Data Analysis*
*JMIR Public Health Surveill 2022;8(8):e34757*
*URL: https://publichealth.jmir.org/2022/8/e34757*
*doi:10.2196/34757*
*PMID:35507923*

Corrigenda and Addenda

# Correction: Relationship Between Protein Intake in Each Traditional Meal and Physical Activity: Cross-sectional Study

Takae Shinto[1], MSc; Saneyuki Makino[1], MSc; Yu Tahara[1], PhD; Lyie Nitta[1], MSc; Mai Kuwahara[1], MSc; Ayako Tada[2], BA; Nanako Abe[2], BA; Mikiko Michie[2], BA; Shigenobu Shibata[1], PhD

[1]Department of Bioscience and Engineering, Waseda University, Tokyo, Japan

[2]Asken Inc, Tokyo, Japan

**Corresponding Author:**
Shigenobu Shibata, PhD
Department of Bioscience and Engineering
Waseda University
Wakamatsu-cho 2-2
Shinjuku-ku
Tokyo, 162-0056
Japan
Phone: 81 +81353697318
Email: shibatas@waseda.jp

**Related Article:**

Correction of: https://publichealth.jmir.org/2022/7/e35898/

***(JMIR Public Health Surveill 2022;8(8):e41460)*** doi:10.2196/41460

In “Relationship Between Protein Intake in Each Traditional Meal and Physical Activity: Cross-sectional Study” (JMIR Public Health Surveill 2022;8(7):e35898), four errors were noted.

1. Due to a system error, in the originally published web version of the article, the name of one author, Lyie Nitta, was replaced with the name of another author, Mai Kuwahara. The order of authors appeared as follows:

> *Takae Shinto, Saneyuki Makino, Yu Tahara, Mai Kuwahara, Mai Kuwahara, Ayako Tada, Nanako Abe, Mikiko Michie, Shigenobu Shibata*

This has been corrected to:

> *Takae Shinto, Saneyuki Makino, Yu Tahara, Lyie Nitta, Mai Kuwahara, Ayako Tada, Nanako Abe, Mikiko Michie, Shigenobu Shibata*

2. In the originally published PDF version of the article, author Lyie Nitta's name appeared incorrectly as Lie Nitta. It has now been corrected in the article.

3. In the originally published web version of the article, author Mai Kuwahara was incorrectly linked to author Lyie Nitta’s ORCID iD. This discrepancy has now been corrected in the article.

4. In the originally published article, the copyright statement erroneously appeared as follows:

> ©*Takae Shinto, Saneyuki Makino, Yu Tahara, Mai Kuwahara, Mai Kuwahara, Ayako Tada, Nanako Abe, Mikiko Michie, Shigenobu Shibata.*

This has been corrected to:

> ©*Takae Shinto, Saneyuki Makino, Yu Tahara, Lyie Nitta, Mai Kuwahara, Ayako Tada, Nanako Abe, Mikiko Michie, Shigenobu Shibata.*

The correction will appear in the online version of the paper on the JMIR Publications website on August 4, 2022, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

*Submitted 26.07.22; this is a non–peer-reviewed article;accepted 26.07.22; published 04.08.22.*

*Please cite as:*
*Shinto T, Makino S, Tahara Y, Nitta L, Kuwahara M, Tada A, Abe N, Michie M, Shibata S*
*Correction: Relationship Between Protein Intake in Each Traditional Meal and Physical Activity: Cross-sectional Study*
*JMIR Public Health Surveill 2022;8(8):e41460*
*URL: https://publichealth.jmir.org/2022/8/e41460*
*doi:10.2196/41460*
*PMID:35926187*

Original Paper

# Colorectal Cancer Incidence, Inequalities, and Prevention Priorities in Urban Texas: Surveillance Study With the “surveil” Software Package

Connor Donegan[1,2], MA; Amy E Hughes[1], PhD; Simon J Craddock Lee[3], MPH, PhD

[1]Department of Population and Data Sciences, University of Texas Southwestern Medical Center, Dallas, TX, United States
[2]Department of Geospatial Information Sciences, The University of Texas at Dallas, Dallas, TX, United States
[3]Department of Population Health, University of Kansas Medical Center, Kansas City, KS, United States

**Corresponding Author:**
Connor Donegan, MA
Department of Population and Data Sciences
University of Texas Southwestern Medical Center
5323 Harry Hines Blvd
Dallas, TX, 75390
United States
Phone: 1 214 648 9400
Email: Connor.Donegan@UTSouthwestern.edu

## Abstract

**Background:** Monitoring disease incidence rates over time with population surveillance data is fundamental to public health research and practice. Bayesian disease monitoring methods provide advantages over conventional methods including greater flexibility in model specification and the ability to conduct formal inference on model-derived quantities of interest. However, software platforms for Bayesian inference are often inaccessible to nonspecialists.

**Objective:** To increase the accessibility of Bayesian methods among health surveillance researchers, we introduce a Bayesian methodology and open source software package, surveil, for time-series modeling of disease incidence and mortality. Given case count and population-at-risk data, the software enables health researchers to draw inferences about underlying risk and derivative quantities including age-standardized rates, annual and cumulative percent change, and measures of inequality.

**Methods:** We specify a Poisson likelihood for case counts and model trends in log-risk using the first-difference (random-walk) prior. Models in the surveil R package were built using the Stan modeling language. We demonstrate the methodology and software by analyzing age-standardized colorectal cancer (CRC) incidence rates by race and ethnicity for non-Latino Black (Black), non-Latino White (White), and Hispanic/Latino (of any race) adults aged 50-79 years in Texas’s 4 largest metropolitan statistical areas between 1999 and 2018.

**Results:** Our analysis revealed a cumulative decline of 31% (95% CI –37% to –25%) in CRC risk among Black adults, 17% (95% CI –23% to –11%) for Latino adults, and 35% (95% CI –38% to –31%) for White adults from 1999 to 2018. None of the 3 observed groups experienced significant incidence reduction in the final 4 years of the study (2015-2018). The Black-White rate difference (per 100,000) was 44 (95% CI 30-57) in 1999 and 35 (95% CI 28-43) in 2018. Cumulatively, the Black-White gap accounts for 3983 CRC cases (95% CI 3746-4219) or 31% (95% CI 29%-32%) of total CRC incidence among Black adults in this period.

**Conclusions:** Stalled progress on CRC prevention and excess CRC risk among Black residents warrant special attention as cancer prevention and control priorities in urban Texas. Our methodology and software can help the public and health agencies monitor health inequalities and evaluate progress toward disease prevention goals. Advantages of the methodology over current common practice include the following: (1) the absence of piecewise linearity constraints on the model space, and (2) formal inference can be undertaken on any model-derived quantities of interest using Bayesian methods.

***(JMIR Public Health Surveill 2022;8(8):e34589)*** doi:10.2196/34589

**KEYWORDS**

Bayesian analysis; cancer prevention; colorectal cancer; health equity; open source software; public health monitoring; time-series analysis

## Introduction

Monitoring disease incidence rates is fundamental to public health research and practice. Vital statistics systems, cancer registries, and other disease-specific monitoring programs provide critical data resources for public health research, and valid interpretation of these data requires formal modeling.

Joinpoint regression modeling (JRM) is a commonly employed, National Cancer Institute–endorsed method for monitoring incidence and mortality rates [1-4]. JRM fits a piecewise linear time trend to (log-) incidence rates. Nonetheless, piecewise linearity conflicts with subject matter expertise insofar as we "do not really believe that cancer rates change abruptly" [1] and some trends are "obviously nonlinear" [3]. Further, standard JRM methodology systematically underreports the uncertainty of estimates because the SEs are conditional on an iterative model selection procedure [5].

We present a Bayesian methodology and open source software package for routine disease surveillance. The models are appropriate for time-series count data aggregated across evenly spaced time periods. The models assign the Poisson likelihood to observed counts conditional on unknown risk; time trends in risk are modeled by assigning the first-difference (random-walk) prior distribution to the log-rates. Binomial models for nonrare events are also implemented. Strengths of the method include its parsimony, the absence of linearity constraints, and the use of Bayesian inference [6-12] to summarize knowledge of disease risk as well as model-derived quantities of interest, such as age-standardized rates and measures of inequality [9,11,12]. The methodology is freely available through the surveil R software package [13,14].

We demonstrate use of the surveil R package by analyzing urban colorectal cancer (CRC) incidence in Texas. "Eliminating cancer disparities" is purportedly a "cross-cutting aim" of the Cancer Prevention and Research Institute of Texas's (CPRIT's) *2018 Texas Cancer Plan*, but the plan conspicuously lacks disparity-related goals and metrics [15]. Racial-ethnic inequalities in CRC are of long-standing concern, including the Black-White incidence and mortality differences that emerged in the early 1990s [16,17]. We examine CRC incidence by race and ethnicity in the 4 largest metropolitan areas in Texas, using our Poisson time-series models. We also examine CRC incidence inequalities and their change over time [18]. We conclude with comments on CRC prevention priorities for Texas, lessons from successful CRC screening efforts, and limitations of this analysis.

## Methods

### Model Specification

The surveil R package implements Poisson random-walk models. For time period $t=\{1,\ldots,n\}$, we assign the Poisson probability distribution to the observed case counts, $y_t$, conditional on a given level of risk, $\exp(\eta_t)$, and population at risk, $P_t$:

$$y_t \sim \text{Pois}(P_t * \exp(\eta_t))$$

Alternatively, the binomial likelihood may be used:

$$y_t \sim \text{Binom}(P_t, g^{-1}(\eta_t)),$$

where $g^{-1}(x)=\exp(x)/(1+\exp(x))$ is the inverse-logit function.

We assign the first-difference (random-walk) model to the log- or logit-transformed risk parameters, consistent with our knowledge that disease risk tends to vary smoothly over time:

$$\eta_t \sim \text{Gau}(\eta_{t-1}, \tau^2),\ t>1$$

This and related intrinsic Gaussian Markov random field specifications are extensively studied models for time trend analyses [19,20].

By default, surveil prior distributions are diffuse for most applications, and users can adjust them to match their subject matter knowledge. The log- or logit-transformed risk for $t=1$ ($\eta_1$), requires a prior distribution (because $t=0$ does not exist). For a rare disease, the following prior is diffuse:

$$\eta_1 \sim \text{Gau}(-5, 5^2)$$

It is centered on a rate of $e^{-5}$=673 per 100,000 and spreads the prior probability across a wide range of values. Changes in log-rates are small, such that surveil's following default prior is also diffuse:

$$\tau \sim \text{Gau}^+(0, 1^2)$$

This base model specification may be extended for multiple correlated time series, such as observations of multiple demographic groups. If $\boldsymbol{\eta}_t$ is the vector of log-rates for $k$ groups at time $t$, then

$$\boldsymbol{\eta}_t \sim \text{Gau}(\boldsymbol{\eta}_{t-1}, \Sigma)$$

introduces a covariance structure through the multivariate normal distribution [21]. We decompose the $k$-by-$k$ covariance matrix, $\Sigma$, into a vector of scale parameters and a correlation matrix, and use the LKJ distribution as a prior for the correlation matrix [22].

### Bayesian Inference

The models were built in Stan, a state-of-the-art platform for Bayesian inference with Markov chain Monte Carlo (MCMC) [22,23]. Stan uses a Hamiltonian Monte Carlo algorithm to draw samples from user-specified joint probability distributions [9,11,24]. Model results are summarized by surveil, which reports estimates (means of marginal posterior distributions) with 95% CIs (Textbox 1).

**Textbox 1.** The surveil R package.

The surveil R package is freely available and archived on the Comprehensive R Archive Network. Basic use of the software requires only introductory-level R programming skills. Tables downloaded from the CDC Wonder database are automatically in the expected format. The model-fitting function, stan_rw, returns a summary of results (estimates with 95% CIs) and Markov chain Monte Carlo (MCMC) samples.

The package supports a streamlined workflow for analyzing disease incidence data. It produces publication-quality visualizations using ggplot2 [25] and enables researchers to make health equity an integral component of surveillance research. The models were built in the Stan modeling language, a robust, stable, state-of-the-art platform for Bayesian inference, providing built-in MCMC diagnostics and visualization methods.

Using MCMC, probability statements can be made about any quantity of interest that is derived from model parameters [9,11,12]. Functions in the surveil package return probability distributions for model-derived quantities such as annual and cumulative percent change, age-standardized rates, the Theil inequality index [26], and a variety of pairwise inequality measures (Textbox 2). The Theil index measures discrepancies between each group's share of disease burden and their share of the population; owing to its fractal structure, it can be used to measure inequality across geographically nested populations [27-29].

When working with age-standardized rates, excess cases (ECs) must be calculated separately for each age stratum and then summed across age groups (Textbox 3). Dividing the resulting ECs by total risk provides an age-standardized measure of proportion attributable risk (PAR). For age-standardized rates, this method of calculating the PAR may be preferred over the rate ratio (RR) as a measure of relative inequality because the PAR better reflects the actual age distribution. If an RR is still preferred and the PAR is less than 1, the PAR can be converted to its equivalent RR using RR=(1/PAR)/(1/PAR-1).

**Textbox 2.** Measures of pairwise inequality provided by surveil.

Rate ratio (RR)=$R_d/R_a$, where R is the incidence rate, and subscripts "a" and "d" represent the advantaged and disadvantaged demographic groups, respectively.

- Rate difference (RD)=$R_d-R_a$
- Proportion attributable risk (PAR)=RD/$R_d$
- Excess cases (EC)=RD×$P_d$, where P represents the populations at risk.
- Cumulative EC=$\Sigma_t$ $EC_t$, where the subscript "t" represents the time period.
- Cumulative PAR=$\Sigma_t EC_t/\Sigma_t (R_{dt}\times P_{dt})$

**Textbox 3.** Age-standardized measures of pairwise inequality provided by surveil.

Rate ratio (RR)=$SR_d/SR_a$, where "SR" is the age-standardized incidence rate, and subscripts "a" and "d" represent the advantaged and disadvantaged demographic groups, respectively.

- Rate difference=$SR_d-SR_a$
- Excess cases (EC)=$\Sigma_i (R_{di}-R_{ai})\times P_{di}$, where "P" represents the populations at risk, and subscript "i" represents the age groups.
- Proportion attributable risk (PAR)=$EC/\Sigma_i R_{di}\times P_{di}$
- Cumulative EC=$\Sigma_t$ $EC_t$, where "t" represents the time periods.
- Cumulative PAR=$\Sigma_t EC_t/\Sigma_t \Sigma_i (R_{dit}\times P_{dit})$

## CRC Incidence in Urban Texas

We gathered publicly available age-specific (50-79 years) data on CRC incidence and population at risk, between 1999 and 2018, by race and ethnicity in the 4 largest metropolitan statistical areas (MSAs) in Texas (centered in Austin, Dallas, Houston, and San Antonio). Uncensored data for this age range are publicly available at the level of 5-year age groups for Hispanic/Latino (all racial groups combined), non-Latino Black or African American (Black), and non-Latino White (White) populations. CRC data for Asian Pacific Islanders are not available for 5-year age groups but are available for the aggregate 50-79–year-old population. Data for American Indians/Alaska Natives are not available [30].

We modeled CRC incidence by race-ethnicity and 5-year age group for the 4 MSAs combined using surveil's Poisson first-difference models. We calculated age-standardized rates using direct age-standardization and the 2000 US standard million population [12]. While remaining cognizant of data limitations, we also modeled age-specific (50-79 years) CRC incidence with Poisson first-difference models in order to examine CRC risk among Asian Pacific Islander residents.

We examined rates of change by calculating the average annual percent change (AAPC) per 4-year period. The sole purpose of aggregating to 4-year periods is to stabilize the estimates. We measure Black-White inequality by the rate difference (RD), PAR, and ECs. Probability distributions for all quantities of interest were obtained using MCMC analysis. For each model, we drew 6000 samples from each of 4 MCMC chains, discarding the first 3000 samples of each chain as warm-up. Before analyzing the results, we confirm that MCMC samples converge on a single distribution using the split R-hat statistic and that MCMC SEs are sufficiently small [11]. We summarize posterior distributions using the mean and 95% CI.

## Results

### Aggregate MSA Trends

CRC incidence declined substantially between 1999 and 2018 (Figure 1 and Table 1). Age-standardized CRC risk declined 31% (95% CI –37% to –25%) for Black adults from a rate per 100,000 of 188 (95% CI 176-201) in 1999 to 129 (95% CI 123-136) in 2018. CRC risk among White adults decreased by 35% (95% CI –38% to –31%), from 144 per 100,000 (95% CI 140-150) in 1999 to 94 (95% CI 91-98) in 2018. Among Latino adults, CRC risk decreased by 17% (95% CI –23% to –11%), from 116 (95% CI 109-123) in 1999 to 96 (95% CI 92-100) in 2018. Results from the age-specific models (Table 2), while subject to some amount of confounding by age, indicate that CRC risk was lower for Asian Pacific Islanders than for the other groups examined and that Asian Pacific Islanders experienced the smallest cumulative change in risk (if any), which was –11% (95% CI –25% to 3%).

**Figure 1.** Age-standardized incidence rates of colorectal cancer (CRC) per 100,000 by race-ethnicity among adults aged 50-79 years between 1999 and 2018 in 4 Texas metropolitan statistical areas.

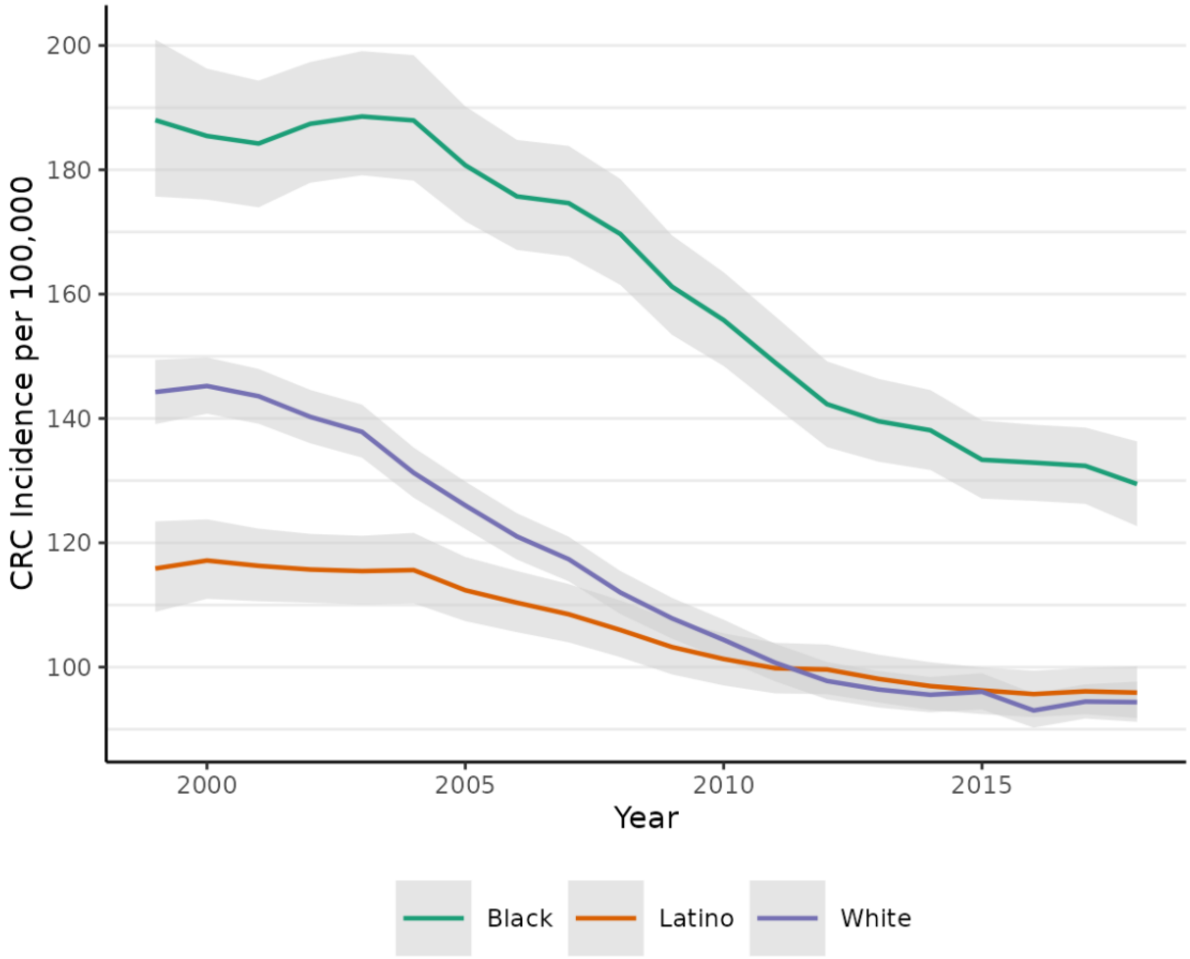


**Table 1.** Levels and cumulative percent change of age-standardized risk of colorectal cancer (CRC) per 100,000 among adults aged 50-79 years, in Texas's 4 largest metropolitan statistical areas between 1999 and 2018.

| | Age-standardized CRC risk in 1999, risk (95% CI) | Age-standardized CRC risk in 2018, risk (95% CI) | Percent (%) change (95% CI) |
|---|---|---|---|
| Black | 188 (176 to 201) | 129 (123 to 136) | –31 (–37 to –25) |
| Latino | 116 (109 to 123) | 96 (92 to 100) | –17 (–23 to –11) |
| White | 144 (140 to 150) | 94 (91 to 98) | –35 (–38 to –31) |

**Table 2.** Levels and cumulative percent change of age-specific risk of colorectal cancer (CRC) per 100,000 among adults aged 50-79 years (not age-standardized), in Texas's 4 largest metropolitan statistical areas between 1999 and 2018.

| | Non–age-standardized CRC risk in 1999, risk (95% CI) | Non–age-standardized CRC risk in 2018, risk (95% CI) | Percent (%) change (95% CI) |
|---|---|---|---|
| Asian Pacific Islander | 75 (66 to 88) | 67 (61 to 73) | –11 (–25 to 3) |
| Black | 170 (160 to 182) | 122 (115 to 128) | –28 (–34 to –22) |
| Latino | 103 (97 to 109) | 86 (83 to 90) | –16 (–22 to –9) |
| White | 135 (130 to 140) | 95 (91 to 98) | –30 (–34 to –26) |

AAPC by 4-year period shows that the most rapid progress on CRC prevention was achieved (roughly) between 2003 and 2014, and that progress appears to have stalled since then (Figure 2). For example, from 2007 to 2010, AAPC for Black, Latino, and White residents, respectively, was –3.7 (95% CI –5.5 to –1.5), –2.2 (95% CI –3.9 to –0.5), and –3.7 (95% CI –4.9 to –2.4). Of these 3 groups, none experienced any robust reduction in CRC risk over the most recent period (2015-2018).

By multiple measures, aggregate Black-White inequality increased between 1999 and 2008 and then decreased or stabilized by 2018 (Figure 3). The RD increased from 44 per 100,000 (95% CI 30-57) in 1999 to 58 (95% CI 49-67) by 2008 and then decreased to 35 (95% CI 28-43) by 2018. Expressed in relative terms as a percentage of total risk among Black adults (PAR), the Black-White gap increased from 25% (95% CI 19%-30%) in 1999 to 35% (95% CI 31%-38%) in 2008 and then decreased to 28% (95% CI 23%-32%) by 2018. Cumulatively, the Black-White gap accounts for 3983 CRC cases (95% CI 3746-4219) or 31% (95% CI 29%-32%) of CRC incidence among Black residents aged 50-79 years. The EC count is a function of both the RD and size of the population at risk; owing to a combination of Black population growth and the persistence of the Black-White gap, the annual number of excess cases increased from 117 (95% CI 85-150) in 1999 to 230 (95% CI 183-276) in 2018. These represent the number of cases that would have been avoided had the level of risk for Black residents equaled that of White residents each year.

**Figure 2.** Average annual percent change (AAPC) in age-standardized incidence rates of colorectal cancer (CRC) by 4-year period between 1999 and 2018.

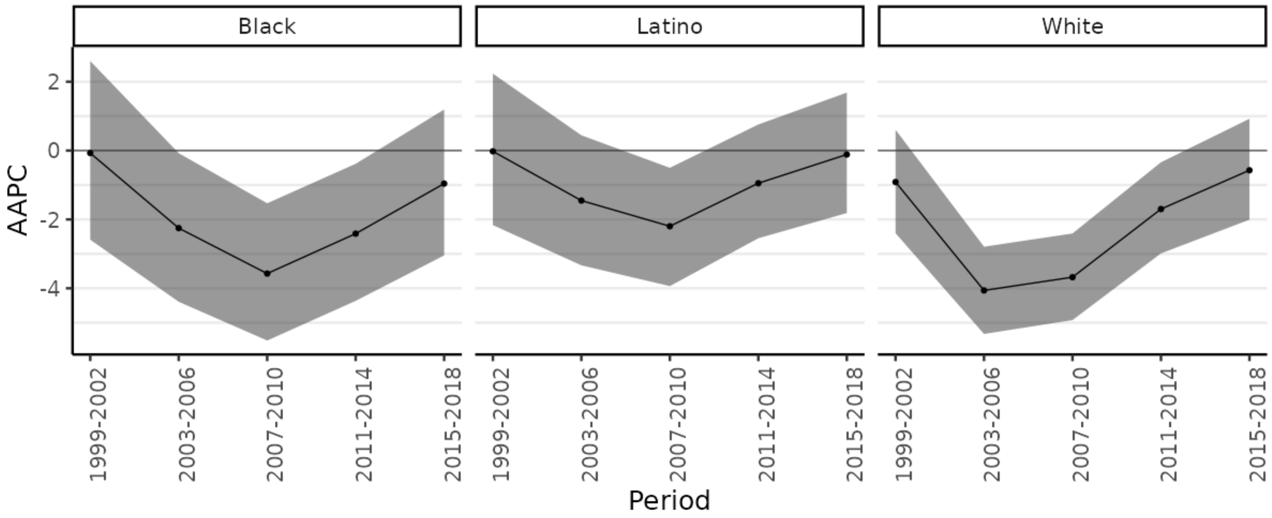
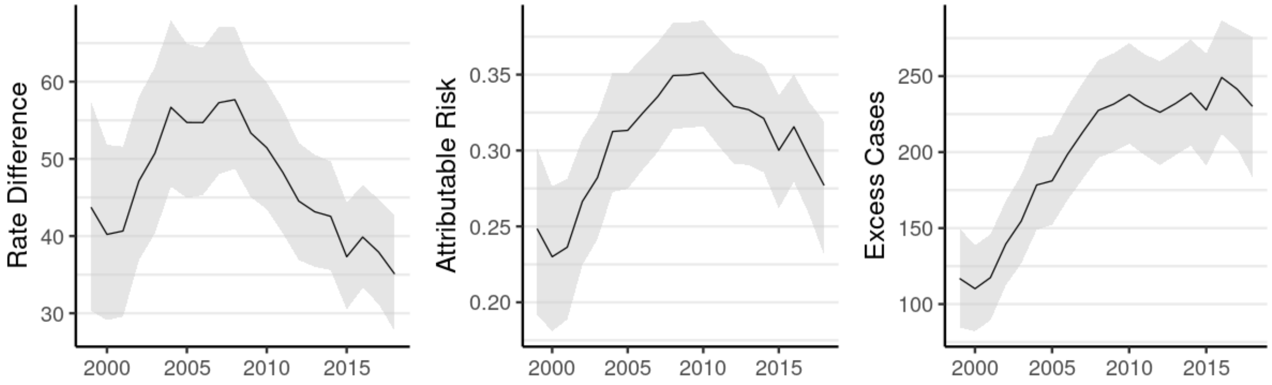


**Figure 3.** Black-White inequality in the incidence rates of colorectal cancer between 1999 and 2018: rate difference per 100,000, proportion attributable risk, and excess cases.



## Discussion

### Methodological Contributions

Monitoring disease incidence is a crucial public health task. The ubiquitous JRM method has notable shortcomings, including linearity constraints and overconfident SEs. This paper presents a parsimonious methodology grounded in Bayesian time-series analysis and accessible through the surveil R package. The package also returns probability distributions for annual and cumulative percent change, measures of pairwise inequality, and the Theil inequality index. Using standard MCMC analysis techniques, users may also conduct inference on any user-defined quantity of interest that is a function of model parameters, such as the AAPC. This project aims to make Bayesian analysis accessible to a wider range of researchers while making robust analyses of health inequality integral to surveillance research. The Poisson models discussed here are appropriate for "rare" events (generally, rates of <0.04). Binomial models for nonrare events are also implemented in surveil. The models are designed for the analysis of data from high-quality surveillance or vital statistics systems that have been aggregated across evenly spaced time periods.

### CRC Prevention Priorities

Between 1999 and 2013, robust CRC risk reduction occurred for White and Black residents, the highest-risk racial-ethnic groups for which data are publicly available, while more modest progress was achieved for Latino and Asian Pacific Islander populations. Excess CRC risk among Black adults is the most burdensome and urgent health inequality identified in this analysis. Black-White inequality increased in relative terms before falling toward its previous level, while annual excess cases increased by approximately 190%. From 2015 to 2018, none of the observed groups experienced any substantial progress in terms of CRC risk reduction.

CRC screening by colonoscopy can prevent CRC through the removal of precancerous polyps [31]. Organized CRC screening programs implemented by, respectively, the state of Delaware and Kaiser Permanente Northern California were followed by substantial reductions in CRC incidence and the practical elimination of Black-White differences in CRC incidence rates [32,33]. New York's Citywide Colon Cancer Control Coalition (C5) provides a third example of an effective and equitable CRC screening program. The C5 effort included, among other things, a public advertising campaign to promote colonoscopy, a patient navigation system, and a voluntary colonoscopy quality improvement initiative with 230 participating gastroenterologists [34].

Given claims that racial segregation is a driver of Black-White cancer inequalities [35-37], it would be insightful and useful to learn how much of the Black-White gap in metropolitan Texas is accounted for by segregated and high-poverty areas. Ongoing research aims to address important limitations of this analysis using the geostan R package—surveil's spatially oriented companion for public health research [38,39].

### Limitations

Major limitations of this analysis include the absence of data by social class or income, aggregation of data across distinct MSAs, exclusion of the El Paso metropolitan area, and exclusive focus on the highest-risk age groups.

### Conclusions

Public accountability for public health goals requires routine monitoring of health outcomes and inequalities. surveil can help health agencies and the public in defining goals and monitoring outcomes. Our analysis of CRC incidence in 4 Texas MSAs finds that prevention progress has stalled and that little to no progress on Black-White CRC inequality was achieved from 1999 to 2018. Texans have voted twice—first in 2007, and again in 2019—to establish and fund CPRIT, making cancer prevention a public priority. CPRIT recently identified ending cancer disparities as a priority [15]. Initiation of a new period of robust and widespread CRC prevention and closure of the Black-White gap warrant urgent attention from the *Texas Cancer Plan* as well as Texas cancer researchers. Ambitious and well-resourced CRC screening initiatives have succeeded elsewhere and may provide important lessons for Texas.

## Acknowledgments

This research was supported by the Texas Health Resources Clinical Scholars Program and Cancer Prevention and Research Institute of Texas (CPRIT PP180018).

## Conflicts of Interest

None declared.

## References

1. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000 Feb 15;19(3):335-351. [doi: 10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z] [Medline: 10649300]
2. Tiwari RC, Cronin KA, Davis W, Feuer EJ, Yu B, Chib S. Bayesian model selection for join point regression with application to age-adjusted cancer rates. J Royal Statistical Soc C 2005 Nov;54(5):919-939. [doi: 10.1111/j.1467-9876.2005.00518.x]
3. Fay MP, Tiwari RC, Feuer EJ, Zou Z. Estimating average annual percent change for disease rates without assuming constant change. Biometrics 2006 Sep;62(3):847-854. [doi: 10.1111/j.1541-0420.2006.00528.x] [Medline: 16984328]

4. Joinpoint Trend Analysis Software. National Cancer Institute. Division of Cancer Control & Population Sciences. URL: https://surveillance.cancer.gov/joinpoint/ [accessed 2021-10-07]
5. Ghosh P, Ghosh K, Tiwari RC. Bayesian approach to cancer-trend analysis using age-stratified Poisson regression models. Stat Med 2011 Jan 30;30(2):127-139. [doi: 10.1002/sim.4077] [Medline: 20839366]
6. Jeffreys H. Theory of Probability. Oxford: Oxford University Press; 1939.
7. Cox R. The Algebra of Probable Inference. Baltimore, MD: The Johns Hopkins Press; 1961.
8. Jaynes E. Probability Theory The Logic of Science. Cambridge: Cambridge University Press; 2003.
9. MacKay D. Information Theory, Inference and Learning Algorithms. Cambridge: Cambridge University Press; 2003.
10. Sivia D. Data Analysis: A Bayesian Tutorial. Oxford: Oxford University Press; 2006.
11. Gelman A, Carlin J, Stern H, Dunson D, Vehtari A, Rubin D. Bayesian Data Analysis. Boca Raton, FL: CRC Press; 2013.
12. Broemeling L. Bayesian Methods in Epidemiology. Boca Raton, FL: CRC Press; 2014.
13. Donegan C. surveil: Public Health Surveillance. R package version 0.2.0. 2022. URL: https://cran.r-project.org/package=surveil [accessed 2022-07-26]
14. R Core Team. R: A Language and Environment for Statistical Computing. The R Foundation. URL: https://www.r-project.org/ [accessed 2022-07-26]
15. 2018 Texas Cancer Plan. Cancer Prevention & Research Institute of Texas. URL: https://www.cprit.texas.gov/media/1457/tcp2018_web_09192018.pdf [accessed 2022-07-26]
16. Howlader N, Noone A, Krapcho M, Miller D, Brest A, Yu M, et al. SEER Cancer Statistics Review (CSR) 1975-2017. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. URL: https://seer.cancer.gov/csr/1975_2017/ [accessed 2022-07-26]
17. Wailoo K. How Cancer Crossed the Color Line. Oxford: Oxford University Press; 2011.
18. Menvielle G, Kulhanaova I, Machenbach JP. Assessing the impact of a public health intervention to reduce social inequalities in cancer. In: Vaccarella S, Lortet-Tieulent J, Saracci R, editors. Reducing social inequalities in cancer: evidence and priorities for research. Lyon: International Agency for Research on Cancer; 2019.
19. Clayton DG. Generalized linear mixed models. In: Gilks WR, Richardson S, Spiegelhalter D, editors. Markov Chain Monte Carlo in Practice. New York, NY: Chapman and Hall/CRC; 1995.
20. Rue H, Held L. Gaussian Markov Random Fields: Theory and Applications. Boca Raton, FL: CRC Press; 2005.
21. Brandt P, Williams J. Multiple Time Series Models. Thousand Oaks, CA: Sage Publications; 2007.
22. Stan Development Team. Stan Modeling Language Users Guide and Reference Manual, 2. URL: https://mc-stan.org/ [accessed 2022-07-26]
23. Carpenter B, Gelman A, Hoffman MD, Lee D, Goodrich B, Betancourt M, et al. Stan: A Probabilistic Programming Language. J Stat Soft 2017;76(1). [doi: 10.18637/jss.v076.i01]
24. Betancourt M, Girolami M. Hamiltonian Monte Carlo for Hierarchical Models. In: Upadhyay SK, Singh U, Dey DK, Loganathan A, editors. Current Trends in Bayesian Methodology with Applications. New York, NY: Chapman and Hall/CRC; 2015.
25. Wickham H. ggplot2: Elegant Graphics for Data Analysis. Cham: Springer; 2016:189-201.
26. Theil H. Statistical Decomposition Analysis: With Applications in the Social and Administrative Sciences (volume 14). Amsterdam: North-Holland Publishing Company; 1972.
27. Conceicao PN, Galbraith JK, Bradford P. The Theil index in sequences of nested and hierarchic grouping structures. Eastern Economic Journal 2001;27(4):491-514.
28. Berner M, Galbraith JK. 2 - Measuring Inequality and Industrial Change. In: Galbraith JK, Berner M, editors. Inequality and Industrial Change: A Global View. Cambridge: Cambridge University Press; 2001.
29. Galbraith J. Inequality and Instability: A Study of the World Economy Just Before the Great Crisis. Oxford: Oxford University Press; 2012.
30. United States and Puerto Rico Cancer Statistics, 1999-2017 Incidence Archive Request. Centers for Disease Control and Prevention. URL: http://wonder.cdc.gov/cancer-v2017.html [accessed 2022-01-12]
31. Ladabaum U, Dominitz JA, Kahi C, Schoen RE. Strategies for colorectal cancer screening. Gastroenterology 2020 Jan;158(2):418-432. [doi: 10.1053/j.gastro.2019.06.043] [Medline: 31394083]
32. Doubeni CA, Corley DA, Zhao W, Lau Y, Jensen CD, Levin TR. Association between improved colorectal screening and racial disparities. N Engl J Med 2022 Feb 24;386(8):796-798. [doi: 10.1056/nejmc2112409]
33. Grubbs SS, Polite BN, Carney J, Bowser W, Rogers J, Katurakes N, et al. Eliminating racial disparities in colorectal cancer in the real world: It took a village. JCO 2013 Jun 01;31(16):1928-1930. [doi: 10.1200/jco.2012.47.8412]
34. Itzkowitz SH, Winawer SJ, Krauskopf M, Carlesimo M, Schnoll-Sussman FH, Huang K, et al. New York Citywide Colon Cancer Control Coalition: A public health effort to increase colon cancer screening and address health disparities. Cancer 2016 Jan 15;122(2):269-277 [FREE Full text] [doi: 10.1002/cncr.29595] [Medline: 26595055]
35. Pruitt SL, Davidson NO, Gupta S, Yan Y, Schootman M. Missed opportunities: racial and neighborhood socioeconomic disparities in emergency colorectal cancer diagnosis and surgery. BMC Cancer 2014 Dec 09;14(1):927 [FREE Full text] [doi: 10.1186/1471-2407-14-927] [Medline: 25491412]

36. Landrine H, Corral I, Lee JGL, Efird JT, Hall MB, Bess JJ. Residential segregation and racial cancer disparities: a systematic review. J Racial Ethn Health Disparities 2017 Dec 30;4(6):1195-1205. [doi: 10.1007/s40615-016-0326-9] [Medline: 28039602]
37. Krieger N, Wright E, Chen J, Waterman P, Huntley E, Arcaya M. Cancer stage at diagnosis, historical redlining, and current neighborhood characteristics: breast, cervical, lung, and colorectal cancers, Massachusetts, 2001-2015. Am J Epidemiol 2020 Oct 01;189(10):1065-1075 [FREE Full text] [doi: 10.1093/aje/kwaa045] [Medline: 32219369]
38. Donegan C, Chun Y, Griffith DA. Modeling community health with areal data: bayesian inference with survey standard errors and spatial structure. Int J Environ Res Public Health 2021 Jun 26;18(13):6856 [FREE Full text] [doi: 10.3390/ijerph18136856] [Medline: 34206725]
39. Donegan C. geostan: Bayesian spatial analysis. R package version 0.3.0. 2022. URL: https://cran.r-project.org/package=geostan [accessed 2022-07-26]

---

## Abbreviations

**AAPC:** average annual percent change
**C5:** Citywide Colon Cancer Control Coalition
**CPRIT:** Cancer Prevention and Research Institute of Texas
**CRC:** colorectal cancer
**EC:** excess case
**JRM:** Joinpoint regression modeling
**MCMC:** Markov chain Monte Carlo
**MSA:** metropolitan statistical area
**PAR:** proportion of attributable risk
**RD:** rate difference
**RR:** rate ratio

---

*Edited by Y Khader; submitted 18.11.21; peer-reviewed by DW Waqar Ali, X Huang; comments to author 06.05.22; revised version received 30.06.22; accepted 06.07.22; published 16.08.22.*

*Please cite as:*
*Donegan C, Hughes AE, Lee SJC*
*Colorectal Cancer Incidence, Inequalities, and Prevention Priorities in Urban Texas: Surveillance Study With the “surveil” Software Package*
*JMIR Public Health Surveill 2022;8(8):e34589*
*URL: https://publichealth.jmir.org/2022/8/e34589*
*doi:10.2196/34589*
*PMID:35972778*

Original Paper

# Investigating Linkages Between Spatiotemporal Patterns of the COVID-19 Delta Variant and Public Health Interventions in Southeast Asia: Prospective Space-Time Scan Statistical Analysis Method

Wei Luo[1*], PhD; Zhaoyin Liu[1*], BSc; Yuxuan Zhou[1*], BSc; Yumin Zhao[2], MS; Yunyue Elita Li[3], PhD; Arif Masrur[4], PhD; Manzhu Yu[4], PhD

[1]Department of Geography, National University of Singapore, Singapore, Singapore
[2]Department of Civil and Environmental Engineering, National University of Singapore, Singapore, Singapore
[3]Department of Earth, Atmospheric, and Planetary Sciences, Purdue University, West Lafayette, IN, United States
[4]Department of Geography, Pennsylvania State University, State College, PA, United States
[*]these authors contributed equally

**Corresponding Author:**
Wei Luo, PhD
Department of Geography
National University of Singapore
1 Arts Link, #04-32 Block AS2
Singapore, 117570
Singapore
Phone: 65 65163851
Email: geowl@nus.edu.sg

## Abstract

**Background:** The COVID-19 Delta variant has presented an unprecedented challenge to countries in Southeast Asia (SEA). Its transmission has shown spatial heterogeneity in SEA after countries have adopted different public health interventions during the process. Hence, it is crucial for public health authorities to discover potential linkages between epidemic progression and corresponding interventions such that collective and coordinated control measurements can be designed to increase their effectiveness at reducing transmission in SEA.

**Objective:** The purpose of this study is to explore potential linkages between the spatiotemporal progression of the COVID-19 Delta variant and nonpharmaceutical intervention (NPI) measures in SEA. We detected the space-time clusters of outbreaks of COVID-19 and analyzed how the NPI measures relate to the propagation of COVID-19.

**Methods:** We collected district-level daily new cases of COVID-19 from June 1 to October 31, 2021, and district-level population data in SEA. We adopted prospective space-time scan statistics to identify the space-time clusters. Using cumulative prospective space-time scan statistics, we further identified variations of relative risk (RR) across each district at a half-month interval and their potential public health intervention linkages.

**Results:** We found 7 high-risk clusters (clusters 1-7) of COVID-19 transmission in Malaysia, the Philippines, Thailand, Vietnam, and Indonesia between June and August, 2021, with an RR of 5.45 ($P<.001$), 3.50 ($P<.001$), 2.30 ($P<.001$), 1.36 ($P<.001$), 5.62 ($P<.001$), 2.38 ($P<.001$), 3.45 ($P<.001$), respectively. There were 34 provinces in Indonesia that have successfully mitigated the risk of COVID-19, with a decreasing range between –0.05 and –1.46 due to the assistance of continuous restrictions. However, 58.6% of districts in Malaysia, Singapore, Thailand, and the Philippines saw an increase in the infection risk, which is aligned with their loosened restrictions. Continuous strict interventions were effective in mitigating COVID-19, while relaxing restrictions may exacerbate the propagation risk of this epidemic.

**Conclusions:** The analyses of space-time clusters and RRs of districts benefit public health authorities with continuous surveillance of COVID-19 dynamics using real-time data. International coordination with more synchronized interventions amidst all SEA countries may play a key role in mitigating the progression of COVID-19.

***(JMIR Public Health Surveill 2022;8(8):e35840)*** doi:10.2196/35840

**KEYWORDS**

COVID-19; Delta variant; space-time scan; intervention; Southeast Asia

## Introduction

COVID-19 is a global epidemic caused by SARS-CoV-2. SARS-CoV-2 is highly contagious as it easily spreads across humans, animals, and the environment via contact, droplets, air, fomites, and other transmission modes [1]. In December 2019, COVID-19 was first identified in Wuhan, a transportation and communication hub located in central China, and rapidly spread to surrounding regions in China. Although governments took a certain level of precautions and control regulation, international cases managed to emerge along with significant outbreaks worldwide. As of December 12, 2021, the disease had infected over 200 million people worldwide [2].

Countries in Southeast Asia (SEA) saw unprecedented challenges in health and social care systems, tourism, trade, and the service industry with the outbreak of COVID-19 [3]. Many countries in SEA made efforts to recover the economy during late 2020 and early 2021 by progressively easing lockdowns and strengthening export orders, but they were hammered by the wave of the new COVID-19 Delta variant [4]. The Delta variant is estimated to be 2 or even 4 times more transmissible than the original virus, with a reproductive number (R0) over 5, which means that more than 5 people can be further infected by each infected individual [5]. Since April 2021, SEA observed an exponential increase in new cases due to the Delta variant and has become an emerging hotspot of COVID-19 [6]. This new outbreak of the Delta variant heavily burdened national and international business in SEA. Interruption of the supply chain of many products (eg, garments, automobile parts, semiconductors) had a substantial impact on the manufacturing industries in SEA, especially for countries relying on them (ie, Vietnam, Malaysia, Thailand, Indonesia, and the Philippines) [4]. Due to these economic pressures, a growing number of countries in SEA planned to live with the virus and adjusted their public health intervention policies. [7]. Under this circumstance, monitoring outbreaks and identifying the space-time clusters of infection have become significant for a coordinated response to the epidemic in SEA.

Spatiotemporal analysis has been widely used in research of COVID-19 propagation to illustrate the characteristics and mechanism of COVID-19 spatial propagation. It can provide public health authorities with important information about the pandemic to enable better management under the situation [8-10]. Among diverse spatiotemporal methods, space-time scanning is one of the most popular methods adopted by many studies to explore spatiotemporal clusters in different regions worldwide, such as Mainland China [11], the United States [12], Mexico [13], Spain [14], Malaysia [15], Bangladesh [16], Brazil [17], and South Korea [18]. In SEA, previous studies have applied this analysis to investigate the first wave of COVID-19 cases [19,20]. However, these studies have mainly focused on each individual country without exploring propagation patterns and progression characteristics with collective public health interventions at the regional scale. Previous research has shown that regional coordination could interrupt the transmission of COVID-19 in an effective way [10,17,21-23]. To contain the emerging epidemic of COVID-19 and minimize its risk, countries in SEA have deployed various preventive and containment measures, such as lockdowns, social distancing restrictions, and mandatory tracking and trace methods [24,25].

Delta variant transmission has shown significant spatial heterogeneity in SEA because different countries adopted different interventions as the virus spread. Hence, this paper aims to identify the space-time clusters of outbreaks of COVID-19 caused by the SARS-CoV-2 Delta variant in SEA. We utilized district-scale daily confirmed cases of 7 SEA countries from June to October 2021 to identify the active and emerging clusters of the disease and summarized relative policies to investigate the potential linkage between government interventions and pandemic progression. Our work will contribute to regional surveillance of COVID-19 progression in SEA and provides essential information about COVID-19 propagation to public health authorities, which is beneficial for timely policymaking according to the dynamic COVID-19 situation.

## Methods

### Study Areas and Relevant Interventions

Our study focused on the COVID-19 Delta variant in SEA. Due to the constraint of relevant data availability, we were only able to include 7 countries, namely (1) Indonesia, (2) Malaysia, (3) the Philippines, (4) Singapore, (5) Thailand, (6) Vietnam, and (7) Brunei, as they disclosed data of daily confirmed cases at a district level. During the second COVID-19 outbreak caused by the Delta variant, the dynamic of interventions implemented by different countries along the way may have caused a fluctuation in transmission. For example, Thailand, Singapore, Malaysia, the Philippines, and Vietnam began to relax their restrictions around August 2021, which may have caused significant changes in the pandemic patterns (Table 1). The diverse policies will help explain the progression and transmission of the Delta variant of COVID-19 in the following analysis. The interventions were aggregated by the Center for Strategic & International Studies (CSIS) [26].

**Table 1.** Major public health interventions in SEA[a,b].

| Duration | Interventions |
|---|---|
| **Indonesia** | |
| June 1-14, 2021 | Micro community activity restrictions (*Pemberlakuan Pembatasan Kegiatan Masyarakat* [PPKM] in Indonesian) implemented, which include guidance on travel, work-from-home policies, online teaching, the restaurant industry, and gatherings |
| June 14-28, 2021 | Community activity restrictions (ie, the PPKM) extended |
| July 2-20, 2021 | Emergency public activity restrictions implemented across Java and Bali |
| July 7-September 20, 2021 | The PPKM extended covering the entire country |
| August 31-September 6, 2021 | COVID-19 restrictions relaxed |
| September 7-October 31, 2021 | COVID-19 restrictions eased for tourists across most of Java |
| October 5-18, 2021 | Community restrictions extended in Java and Bali |
| October 19-31, 2021 | PPKM restrictions eased to level 2 in Jakarta and Tangerang |
| **Thailand** | |
| July 17-September 30, 2021 | Nationwide emergency imposed |
| August 1-31, 2021 | Tighter restrictions imposed, including travel curbs, curfews, and travel from other regions |
| August 16-30, 2021 | Lockdown measures extended for 2 weeks |
| August 23-October 31, 2021 | The country's strategy to shifted "learning to live with COVID-19" by relaxing some restrictions and reopening its borders to vaccinated visitors gradually |
| September 1-October 31, 2021 | Domestic flights from and to Bangkok and other high-risk areas allowed to resume |
| October 1-31, 2021 | Restrictions in dark-red provinces (highest-risk regions) eased |
| October 16-31, 2021 | Curfew shortened |
| **Singapore** | |
| June 21-July 22, 2021 | Indoor dining resumed |
| July 22-August 8, 2021 | Returned to phase 2 (heightened alert) status, putting in place enhanced restrictions, including limiting social gatherings to 2 people and banning indoor and outdoor dining |
| August 8-September 27, 2021 | Restrictions relaxed for fully vaccinated people |
| August 19-September 27, 2021 | Workforce allowed to return to their offices |
| August 20-October 31, 2021 | Border restrictions eased |
| September 14-October 31, 2021 | Nationwide booster shot campaign further strengthened |
| September 27-October 31, 2021 | In-person gathering limited from 5 to 2 people but border restrictions further eased for fully vaccinated people |
| **Malaysia** | |
| June 1-28, 2021 | Nationwide lockdown implemented |
| July 3-September 14, 2021 | Lockdowns in Kelantan, Pahang, Perak, Perlis, and Terengganu relaxed |
| August 1-October 31, 2021 | Extending the country's state of emergency ended |
| August 2-September 14, 2021 | Restrictions further loosened in Perlis, Sarawak, and Labuan |
| August 8-September 14, 2021 | Some restrictions relaxed for fully vaccinated people in 8 states |
| August 21-September 14, 2021 | Social distancing measures loosened for outdoor sports and in-person dining for fully vaccinated people |
| September 10-14, 2021 | Travel, dining, and tourism restrictions relaxed in Kuala Lumpur, Selangor, and Putrajaya |
| September 9-October 31, 2021 | Creative industry reopened |
| September 14-October 1, 2021 | COVID-19 lockdown restrictions further eased |
| October 1-31, 2021 | Movement restrictions relaxed |
| **The Philippines** | |
| June 1-30, 2021 | Travel restrictions extended on inbound travelers coming from India and 6 other countries |
| June 29-July 15, 2021 | Movement restrictions in the capital and surrounding provinces extended |

| Duration | Interventions |
|---|---|
| July 25-31, 2021 | Travel from Malaysia and Thailand suspended, restrictions in the Manila area tightened |
| August 13-31, 2021 | Ban on travelers from India, Pakistan, Bangladesh, Sri Lanka, Nepal, the UAE, Oman, Thailand, Malaysia, and Indonesia extended |
| August 6-20, 2021 | Reverted to the strictest level of lockdown in Metro Manila |
| August 21-31, 2021 | COVID-19 restrictions eased in the Manila capital region |
| September 7-15, 2021 | Movement restrictions extended in Manila |
| September 16-October 1, 2021 | Wide-scale restrictions eased in Manila despite direct warnings from the World Health Organization (WHO) against reopening certain businesses |
| October 1-31, 2021 | Movement restrictions eased in the Manila capital region |
| October 13-31, 2021 | Curfew hours shortened in Metro Manila |
| October 16-31, 2021 | Alert level lowered in the National Capital Region from level 4 to 3 |
| **Vietnam** | |
| June 14-30, 2021 | Social distance measures extended in Ho Chi Minh City |
| July 7-21, 2021 | 2-week lockdown implemented in Ho Chi Minh City |
| July 18-August 1, 2021 | 2-week lockdown imposed in 16 southern provinces |
| August 15-September 15, 2021 | Social distancing requirements extended in Ho Chi Minh City |
| September 16-30, 2021 | COVID-19 restriction extended in Ho Chi Minh City |
| September 23-October 31, 2021 | Lockdown restrictions eased in several provinces |
| October 1-31, 2021 | Select economic activities resumed in Ho Chi Minh City |
| October 13-31, 2021 | Coach buses to resume operations allowed in Ho Chi Minh City between the city and nearby provinces |
| October 15-31, 2021 | Risk level reduced in Ho Chi Minh City |
| **Brunei** | |
| August 8-October 3, 2021 | COVID-19 restrictions implemented |
| September 1-15, 2021 | Travel restrictions to and from India, Nepal, Sri Lanka, Pakistan, and Bangladesh extended |
| October 4-17, 2021 | Movement restrictions tightened |
| October 13-31, 2021 | Nightly curfew extended |

[a] SEA: Southeast Asia.

[b] Note that up to October 31, 2021, some of the interventions were still continuously effective. We therefore defined the ending date of the duration of such interventions as the last day of our study period.

## COVID-19 Daily Cases and Populations

We obtained or extracted data of COVID-19–confirmed cases from the official websites of public health authorities in the 7 countries and Johns Hopkins University's Center for Systems Science and Engineering GIS dashboard (Table 2). From March to May 2021, the 7 countries in SEA successively identified the Delta variant, which dominated mass infections in the next few months (Table 3) [27-33]. Figure 1 shows the substantial growth of confirmed cases of COVID-19 in the 7 countries from June 2021, and most of the countries experienced apparent fluctuations of daily confirmed cases from June to October 2021. Therefore, we adopted data from June 1 to October 31, 2021, which is the approximate date of the second COVID-19 outbreak in these 7 countries in SEA. We aggregated the data at the first administrative level, except for those in Singapore and Brunei, which were aggregated at the country level, considering the similar magnitude of area and population in each analytic unit. We obtained or extracted population data from statistical reports and yearbooks from those countries (Table 2).

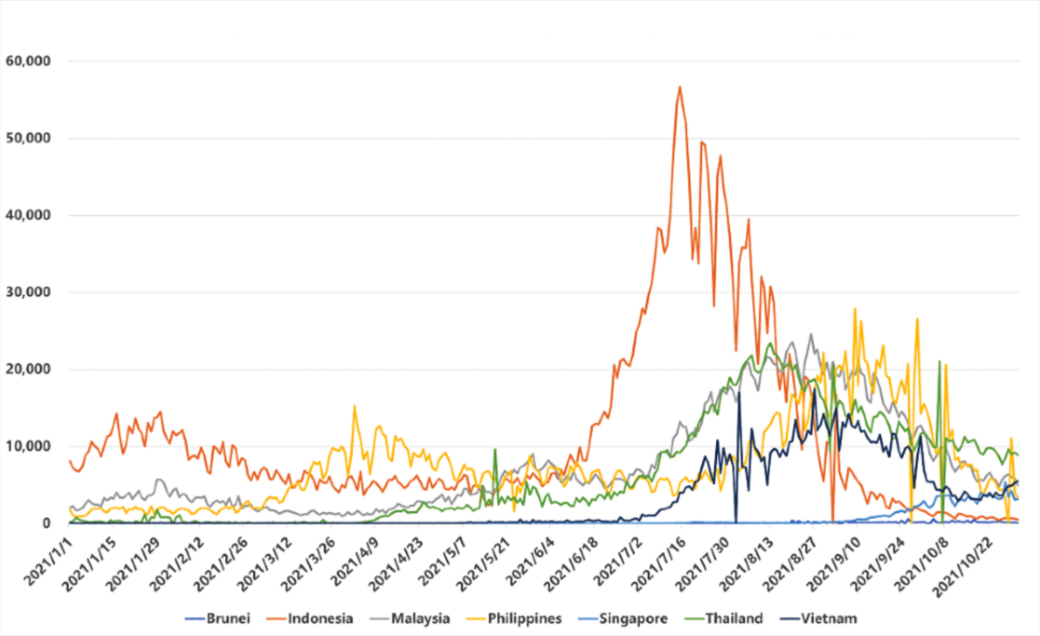
**Table 2.** Collected data and their sources.

| Country | Case source | Population source |
|---|---|---|
| Indonesia | KAWALCOVID19 and the National Board of Confirmed Case Development [34] | Statistics Indonesia [35] |
| Malaysia | Official data on the COVID-19 epidemic in Malaysia [36] | Department of Statistics Malaysia [37] |
| The Philippines | Department of Health, the Philippines [38] | Philippine Statistics Authority [39] |
| Singapore | Ministry of Health, Singapore [40] | Department of Statistics, Singapore [41] |
| Thailand | Ministry of Public Health, Department of Disease Control Situational Reports [42] | National Statistical Office of Thailand [43] |
| Brunei | Johns Hopkins University's Center for Systems Science and Engineering COVID-19 data [44] | Department of Economic Planning and Statistics [45] |
| Vietnam | Ministry of Health, Vietnam [46] | General Statistics Office of Vietnam [47] |

**Table 3.** Month of identification of the Delta variant in 7 countries.

| Country | Month of first confirmed case of Delta variant |
|---|---|
| Indonesia | March 2021 |
| Thailand | May 2021 |
| Singapore | April 2021 |
| Malaysia | May 2021 |
| The Philippines | May 2021 |
| Vietnam | April 2021 |
| Brunei | August 2021 |

**Figure 1.** Daily confirmed new COVID-19 cases in Southeast Asia (SEA) from January 1 to October 31, 2021.



## Space-Time Scan Statistical Analysis

To explore emerging and active space-time clusters of COVID-19 cases in SEA, we conducted prospective space-time scan statistical analysis using SaTScan version 9.6 [48], which is often used to detect spatial clusters of infectious diseases [49,50]. Using space-time scan statistics, we identified and mapped significant clusters of the Delta variant in SEA, considering the uneven distribution of population size. The space-time scan statistics adopted a cylinder to detect potential space-time clusters in SEA, which can cover each possible location, size, and period [51]. For each cylinder, the base represented space, the height represented time, and the center represented the centroids of study units throughout SEA. The size of the cylindrical window was expanded until reaching specific maximum spatial and temporal upper bounds, which were set to 10% of the population risk and 50% of the study period, respectively, in this study. We set the minimum duration of each cluster to 2 days for surveillance of the continuously existing clusters. The minimum number of cases in each cluster was set to 3 in order to ensure that there must be at least 3 cases in each cluster.

We assumed that the COVID-19 cases follow a Poisson distribution according to the population of study units in SEA. The null hypothesis ($H_0$) indicates that the model reflects infection of COVID-19 having a constant intensity $\mu$ within or outside the cylinder, which is proportional to the at-risk population. The alternative hypothesis ($H_A$) indicates that the observed cases are more than expected cases, which reflects an increased risk within a cylinder. Expected cases were calculated by Equation (1) [12]:

where $p$ represents the population within a study unit, $C$ represents the total COVID-19 cases in our study area (ie, 7 countries in SEA), and $P$ represents the total estimated population within our study area.

A maximum likelihood ratio test was performed to evaluate the null and alternative hypotheses. It identified scanning windows with an elevated risk for COVID-19, which was defined by Equation (2) [17,52]:

where $L(Z)$ represents the likelihood function for cylinder $Z$, $L_0$ represents the likelihood function for $H_0$, $n_Z$ represents the number of COVID-19 cases in a cylinder, $\mu(Z)$ represents the number of expected cases in cylinder $Z$, and N represents the total number of observed cases for the 7 countries in SEA across all periods. When the likelihood ratio is greater than 1, there is an elevated risk in the cylinder, and the cylinder with the maximum likelihood ratio should be the most likely cluster.

The relative risk (RR) of COVID-19 was assumed homogeneous throughout different districts within the same cluster. To make the results more reasonable, we calculated the RR for each study unit within a cluster to explore the spatial heterogeneity of the RR of COVID-19, as given by Equation (3) [53]:

where $c$ represents the total number of COVID-19 in a study unit, $e$ represents the total number of expected cases in a study unit, and $C$ represents the total number of observed cases in the 7 countries of SEA. The formula indicates that the RR represents the estimated risk in a study unit, divided by the risk outside that unit. Specifically, if a location (cluster or study unit) has an RR of 3, the population within the location is three times more likely to be exposed to COVID-19 infection than its outside. The high-risk clusters are characterized by higher observed than expected COVID-19 cases (RR>1), while the low-risk clusters are characterized by higher expected than observed COVID-19 cases (RR<1).

The following sections reveal significant emerging clusters of COVID-19 cases in 7 countries of SEA from June 1 to October 31, 2021. Considering that some SEA countries (eg, Malaysia, the Philippines, Singapore, Thailand) started loosening their restrictions from August 2021, along with strengthening their vaccination plan, we divided the timeline into 2 parts (ie, June 1-August 31, 2021, and June 1-October 31, 2021) in order to identify the dynamics of the clusters. Additionally, we explored the variation in the RR across each district in each half-month, which is approximately equal to the incubation period of an infection [54], using a cumulative half-month prospective scanning approach. Next, we compared the interventions with the discovered space-time characteristics to identify the potential linkage between political intervention and the progression of the Delta variant of COVID-19.

## Results

### Dynamics of District-Level Merging Clusters in SEA

#### *Results From June 1 to August 31, 2021*

As shown in Table 4, 14 significant space-time clusters were identified from June 1 to August 31, 2021, in SEA, including 7 (50%) high-risk clusters (RR>1) and 7 (50%) low-risk clusters (RR<1). Most of the high-risk clusters emerged between mid-July and late August 2021, which means the situation of COVID-19 in SEA became severe during this period. Specifically, cluster 1 was the most likely, and a transnational cluster, containing 39 (83%) high-risk districts (RR>1) out of 47 districts of Malaysia and Thailand. This cluster had the highest RR of 5.45, which means people in this cluster were 5.45 times more likely to be exposed to COVID-19 than in other regions. Similarly, cluster 2 had an RR of 5.62 and contained 2 districts of Vietnam, namely Binh Duong and Ho Chi Minh City. Another transnational cluster was cluster 4, with an RR of 3.50, containing 6 districts of Malaysia, Indonesia, and Brunei. Additionally, north Thailand and the north Philippines also emerged as high-risk clusters from July 22 to August 31, 2021, and from August 11-31, 2021, respectively. There were also 2 clusters emerging in Indonesia, and they contained only 1 district, which was Jakarta, with an RR of 2.38, and Daerah Istimewa Yogyakarta (DIY), with an RR of 3.88. In addition, 3 high-risk clusters in Indonesia revealed that the population within a number of regions in Indonesia was more likely to be exposed to COVID-19 compared to other regions in SEA during this period. Additionally, there were 7 low-risk clusters distributed across other regions of SEA (eg, north of Vietnam, south of the Philippines, and some other districts of Indonesia), which means the population within these clusters was less likely to be exposed to COVID-19. Note that cluster 10, with an RR of 0.60, contained 2 high-risk districts of the Philippines (ie, region VII, with an RR of 1.07, and region X, with an RR of 1.08). Figure 2 shows the distribution of each cluster. There were a number of small-scale clusters in south Indonesia, while the largest-scale cluster appeared across southern Thailand and north Malaysia. From the results, the Delta variant of COVID-19 had a wider influence in Malaysia and Indonesia in the early phase, while some regions in Vietnam and the Philippines had relatively high risk as well.

**Table 4.** Space-time clusters of COVID-19 from June 1 to August 31, 2021.

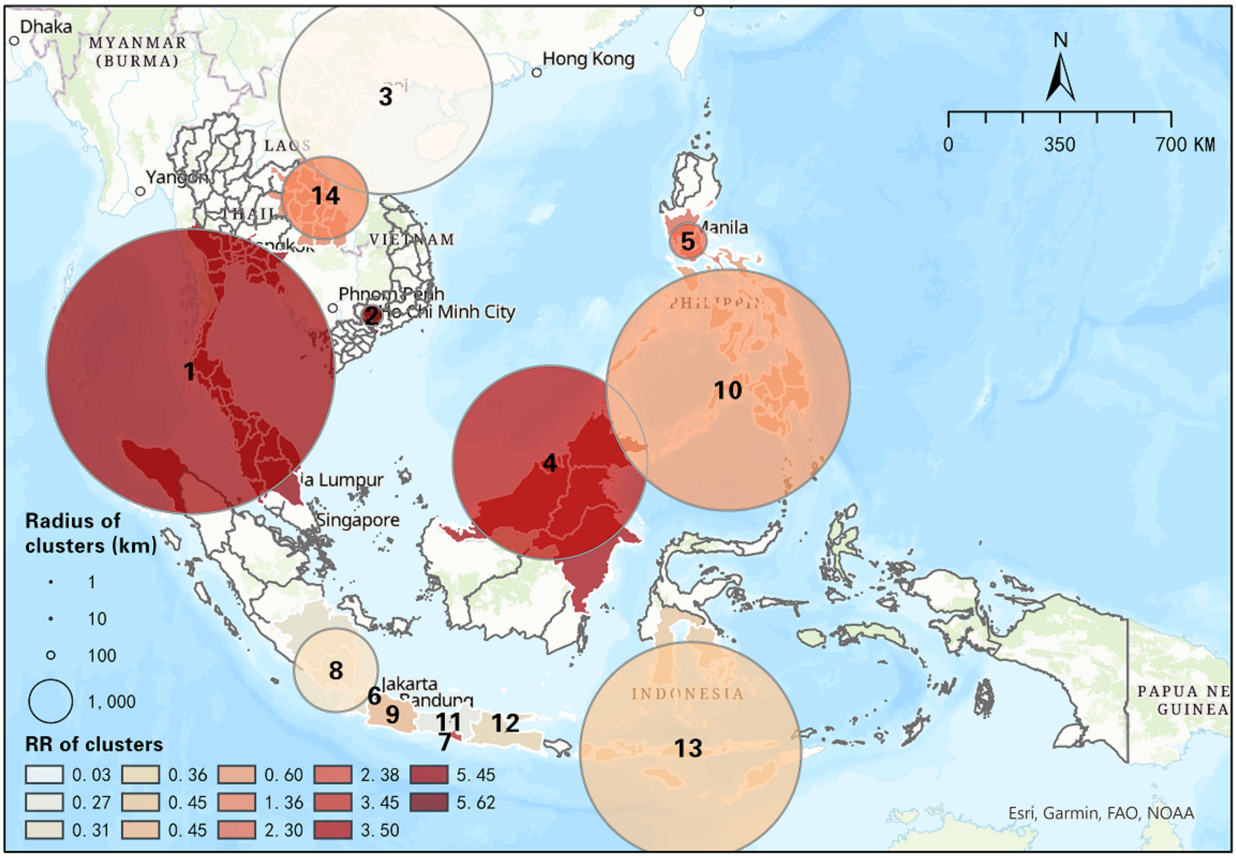
| Cluster | Duration (days) | Total districts, N | *P* value | Observed | Expected | RR[a] | Districts (RR>1), n (%) |
|---|---|---|---|---|---|---|---|
| 1 | July 17-August 31 | 47 | <.001 | 1,246,176 | 278,375.06 | 5.45[b] | 39 (83) |
| 2 | July 18-August 31 | 2 | <.001 | 300,418 | 55,874.66 | 5.62[b] | 2 (100) |
| 3 | July 17-August 31 | 30 | <.001 | 6335 | 223,562.03 | 0.03 | 0 |
| 4 | July 22-August 31 | 6 | <.001 | 184,097 | 53,834.73 | 3.50[b] | 4 (67) |
| 5 | August 11-31 | 3 | <.001 | 196,693 | 87,355.91 | 2.30[b] | 3 (100) |
| 6 | July 17-August 31 | 1 (Jakarta) | <.001 | 123,567 | 52,481.33 | 2.38[b] | 1 (100) |
| 7 | July 17-August 31 | 1 (DIY[c]) | <.001 | 62,476 | 18,229.28 | 3.45[b] | 1 (100) |
| 8 | August 7-31 | 3 | <.001 | 24,861 | 79,338.99 | 0.31 | 0 |
| 9 | August 7-31 | 1 (Jawa Barat) | <.001 | 59,194 | 130,362.28 | 0.45 | 0 |
| 10 | July 17-August 31 | 11 | <.001 | 158,665 | 259,719.07 | 0.60 | 2 (18) |
| 11 | August 18-31 | 1 (Jawa Tengah) | <.001 | 15,132 | 55,221.58 | 0.27 | 0 |
| 12 | August 15-31 | 1 (Jawa Timur) | <.001 | 26,939 | 74,674.85 | 0.36 | 0 |
| 13 | August 15-31 | 4 | <.001 | 18,415 | 41,030.60 | 0.45 | 0 |
| 14 | July 22-August 31 | 14 | <.001 | 82,443 | 60,927.09 | 1.36[b] | 11 (79) |

[a] RR: relative risk.

[b] High-risk clusters.

[c] DIY: Daerah Istimewa Yogyakarta.

**Figure 2.** Spatial distribution of space-time clusters of COVID-19 from June 1 to August 31, 2021. RR: relative risk.



### Results From June 1-October 31, 2021

In total, 11 significant clusters were detected from June 1 to October 31, 2021, which was 3 less than the early phase. Among the 11 clusters, there were only 4 (36%) high-risk clusters (RR>1), decreasing from 7 in the previous period (Table 5). The most likely cluster was the same as in the previous period, which covered partial districts of Thailand and Malaysia. The RR of cluster 1, however, decreased from 5.45 to 3.91 in this period, while the number of high-risk districts increased from 39 to 45, which implies that more districts were affected by COVID-19. Cluster 2 was also the same as in the previous period, containing Binh Duong and Ho Chi Minh City. In addition, cluster 7 evolved from cluster 4 in the previous period, with the exclusion of Kalimantan Timur. The RR of this cluster increased from 3.50 to 4.62, indicating that people in this cluster were more likely to be infected in this period. Similarly, the Cordillera Administrative Region, region II, and region I merged with 1 high-risk cluster in the north Philippines and formed a larger cluster. The rest of the clusters were low-risk clusters with RR<1. Figure 3 visualizes the distribution of clusters in this period, which shows directly that some of the clusters remained between 2 continuous periods, while a number of clusters in the previous period disappeared and some new clusters appeared in this period. Especially in Indonesia, high-risk clusters in Jakarta and DIY disappeared, which emerged as low-risk clusters with other districts. Overall, the space-time scan statistic results show the transmission and dispersal of the Delta variant of COVID-19 in SEA from 2 different periods.

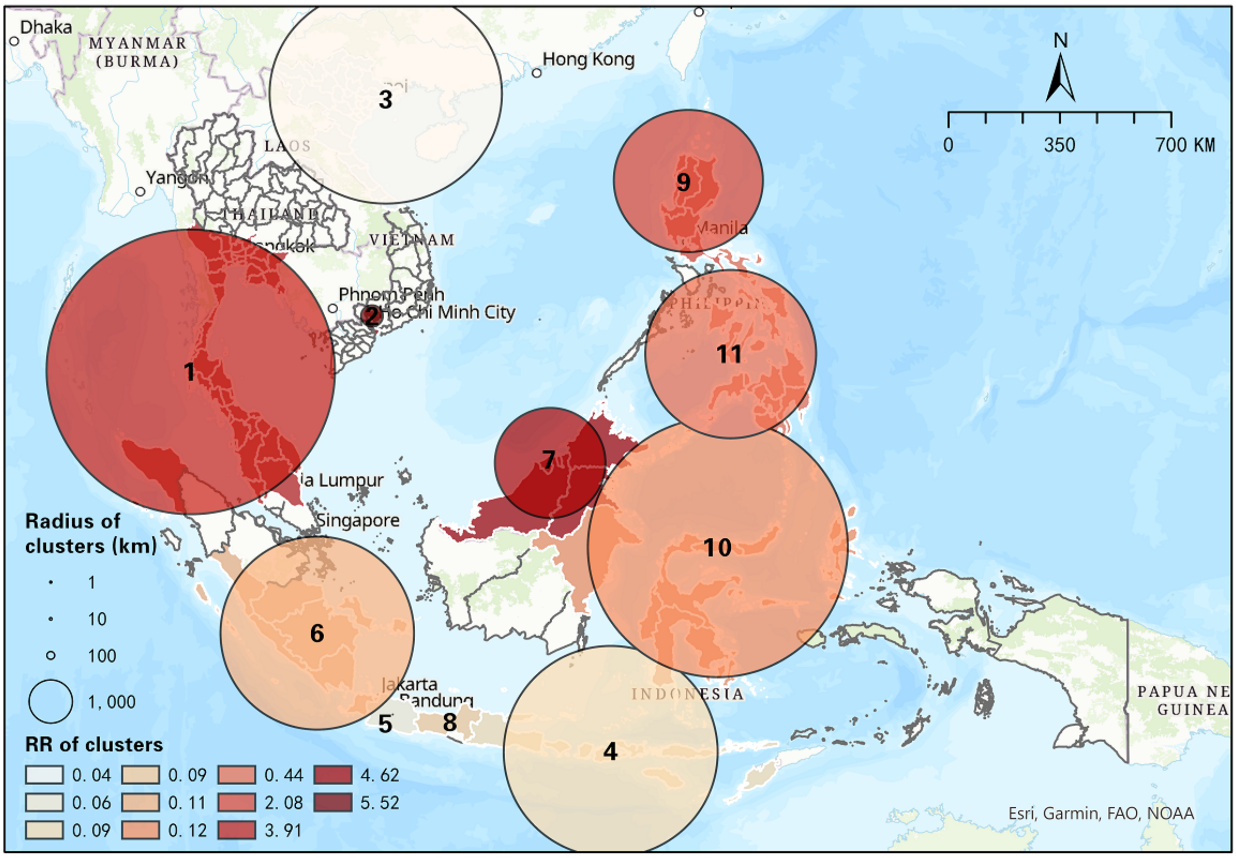
**Table 5.** Space-time clusters of COVID-19 from June 1 to October 31, 2021.

| Cluster | Duration (days) | Total districts, N | *P* value | Observed | Expected | RR[a] | Districts (RR>1), n (%) |
|---|---|---|---|---|---|---|---|
| 1 | August 17-October 31 | 47 | <.001 | 1,441,175 | 421,090.26 | 3.91[b] | 45 (96) |
| 2 | August 17-October 31 | 2 | <.001 | 456,029 | 86,398.28 | 5.52[b] | 2 (100) |
| 3 | August 17-October 31 | 33 | <.001 | 13,724 | 355,228.49 | 0.04 | 0 |
| 4 | August 28-October 31 | 4 | <.001 | 34,492 | 357,601.25 | 0.09 | 4 (100) |
| 5 | August 27-October 31 | 1 (Jawa Barat) | <.001 | 19,419 | 315,097.51 | 0.06 | 0 |
| 6 | August 27-October 31 | 8 | <.001 | 37,326 | 342,621.73 | 0.11 | 0 |
| 7 | August 17-October 31 | 5 | <.001 | 283,690 | 63,058.92 | 4.62[b] | 4 (80) |
| 8 | August 21-October 31 | 1 (Jawa Tengah) | <.001 | 24,989 | 260,017.41 | 0.09 | 0 |
| 9 | August 17-October 31 | 6 | <.001 | 728,003 | 366,113.53 | 2.08[b] | 6 (100) |
| 10 | September 3-October 31 | 8 | <.001 | 17,783 | 145,558.63 | 0.12 | 0 |
| 11 | October 4-31 | 10 | <.001 | 60,614 | 136,535.58 | 0.44 | 0 |

[a] RR: relative risk.

[b] High-risk clusters.

**Figure 3.** Spatial distribution of space-time clusters of COVID-19 from June 1 to October 31, 2021. RR: relative risk.



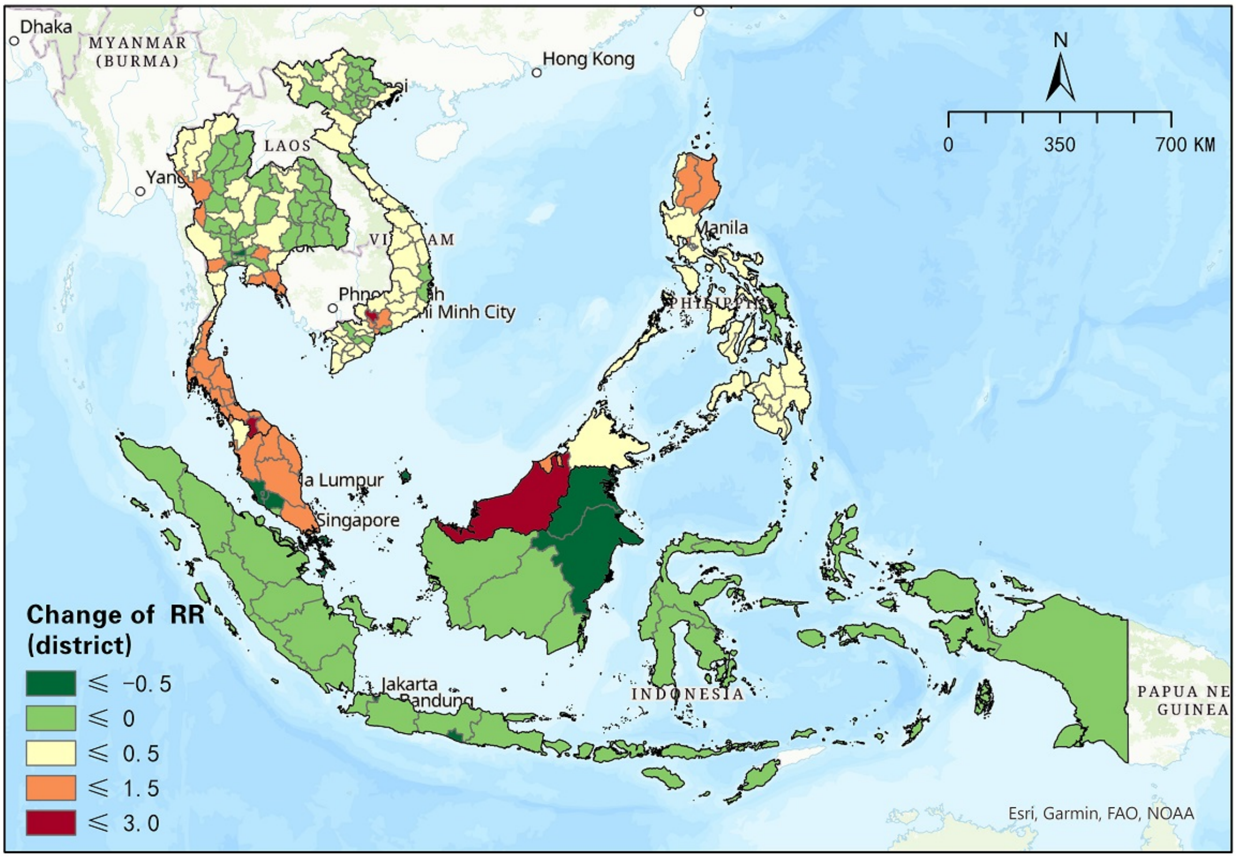
## Temporal Progression of the RR of COVID-19 in SEA

Figure 4 presents changes in the district RR of COVID-19 in SEA between 2 outbreak periods, June 1-August 31 and June 1-October 31, 2021. Overall, this temporal change in the RR manifests different space-time characteristics in terms of COVID-19 progression before and after the countries changed their intervention strategies in handling COVID-19 in July and August 2021. Among the 7 countries in SEA, Indonesia was the only one that showed an overall positive trend of a decreasing RR in every district, while alarming changes of an increasing RR were frequently seen in the other 6 countries, especially in Singapore, the Philippines, Malaysia, and Vietnam.

Specifically, all districts of Indonesia observed a decrease in the RR to different extents. Although the RR in most districts of Indonesia slightly decreased by 0.05-0.5, the other 5 districts (ie, Jakarta, DIY, Kalimantan Utara, Kalimantan Timur, and Kepulauan Riau) manifested a rather significant decrease (≤–0.5), in which the highest difference (–1.4) between the 2 periods was seen in Jakarta, the capital of Indonesia. Note that Jakarta was one of the major emerging risk districts early in the second outbreak and still faced a relatively high RR (2.79) until the end of our study period. On the contrary, the RR of all districts in the Philippines increased between the 2 outbreak periods, indicating an overall deterioration in the risk impact of COVID-19. Fortunately, among a total of 17 districts in the Philippines, 14 (82%) showed minor increases (≤0.5). The other 3 districts, namely the National Capital Region, region II, and the Cordillera Administrative Region, manifested an increase from 0.59 to 1.23. Meanwhile, no significant increase (>1.5) was observed, indicating that the most severe variation in the RR did not occur in the Philippines.

Other countries including Singapore, Malaysia, Brunei, Thailand, Vietnam, in contrast, showed a variety of RR changes in different districts, approximately half of which (n=39, 51%) showed increases in the RR, and half decreased among the 77 districts in Thailand. It is obvious that coastal areas in the south of the country faced a more elevated RR than inland areas in the central, eastern, and northern districts. The RR in almost all districts in Vietnam slightly changed, ranging from –0.08 to 0.28, except for 3 connected cities (ie, Dong Nai: 0.63, Ho Chi Minh City: 0.72, and Binh Duong: 1.73). As for Malaysia, 10 (63%) of 16 districts showed an increase in the RR and took up a major proportion of the country. Labuan and Kuala Lumpur observed the most obvious decrease among SEA districts. It should be noted that they were also the districts most severely threatened by COVID-19 risks early in the study period (RR>10) and had the relatively highest RR in SEA until the end of the study. Additionally, Singapore saw an increased RR of 1.43. The RR in Brunei also increased but still remained less than 1.

**Figure 4.** Changes in the relative risk (RR) of COVID-19 (district level) between two periods (June 1-August 31 and June 1-October 31, 2021).



Furthermore, we detected progression of the RR at a half-month interval, and a sum of 10 intervals was used to illustrate the progression of the Delta variant from June to October 2021 (Figures 5-9). In the first half of June 2021, elevated risks were identified in the middle south of Thailand, many states in Malaysia, and many districts in the Philippines, while 70% (44/63) of the districts in Vietnam manifested RR=0 during this period (Figure 5). These patterns revealed that the potential new wave of the pandemic was more likely to emerge in those high-risk districts. From then on, the Delta variant spread in SEA, and the capital areas of several countries were severely affected in SEA (eg, Bangkok Metropolis and surrounding areas, Kuala Lumpur and surrounding areas, Jakarta and surrounding areas). On the contrary, the RR in the Manila capital region in the Philippines decreased (Figure 6). By the middle of August 2021, Thailand had been influenced by the expansion of COVID-19, and most districts showed an elevated risk. Additionally, most high-risk areas in the previous months remained severe during this time, although the RR of some districts slightly declined (eg, Bangkok, Samut Sakhon, Jakarta, Riau, Sarawak). This phenomenon also reflected a high infection capability of the Delta variant (Figure 7). In the next 1.5 months (ie, August 15-September 30, 2021), the situation in Indonesia improved. North Philippines, however, showed an increased RR on September 15, 2021 (Figures 7 and 8). In the next month, the RR of Singapore increased from 0.44 to 1.53, and the RR of northern Malaysia and southern Thailand worsened as well (Figure 9). Up to October 31, 2021, the situation of Thailand, Malaysia, Singapore, Ho Chi Minh City in Vietnam, and capital areas in the Philippines was still alarming, and further studies should focus on this.

**Figure 5.** Spatial patterns of progression of the COVID-19 RR in SEA (June 1-15 and June 1-30, 2021). RR: relative risk; SEA: Southeast Asia.

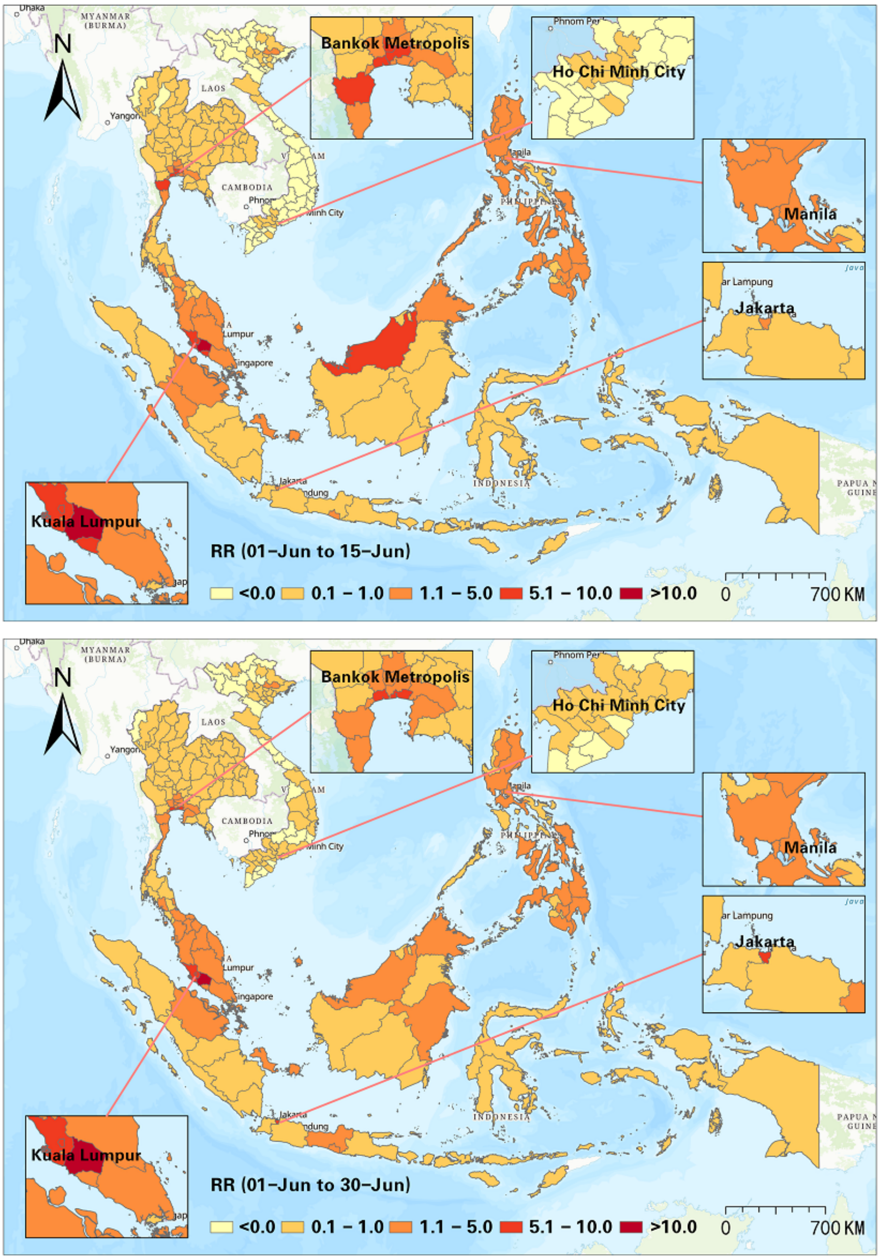


**Figure 6.** Spatial patterns of progression of the COVID-19 RR in SEA (June 1-July 15 and June 1-July 31, 2021). RR: relative risk; SEA: Southeast Asia.

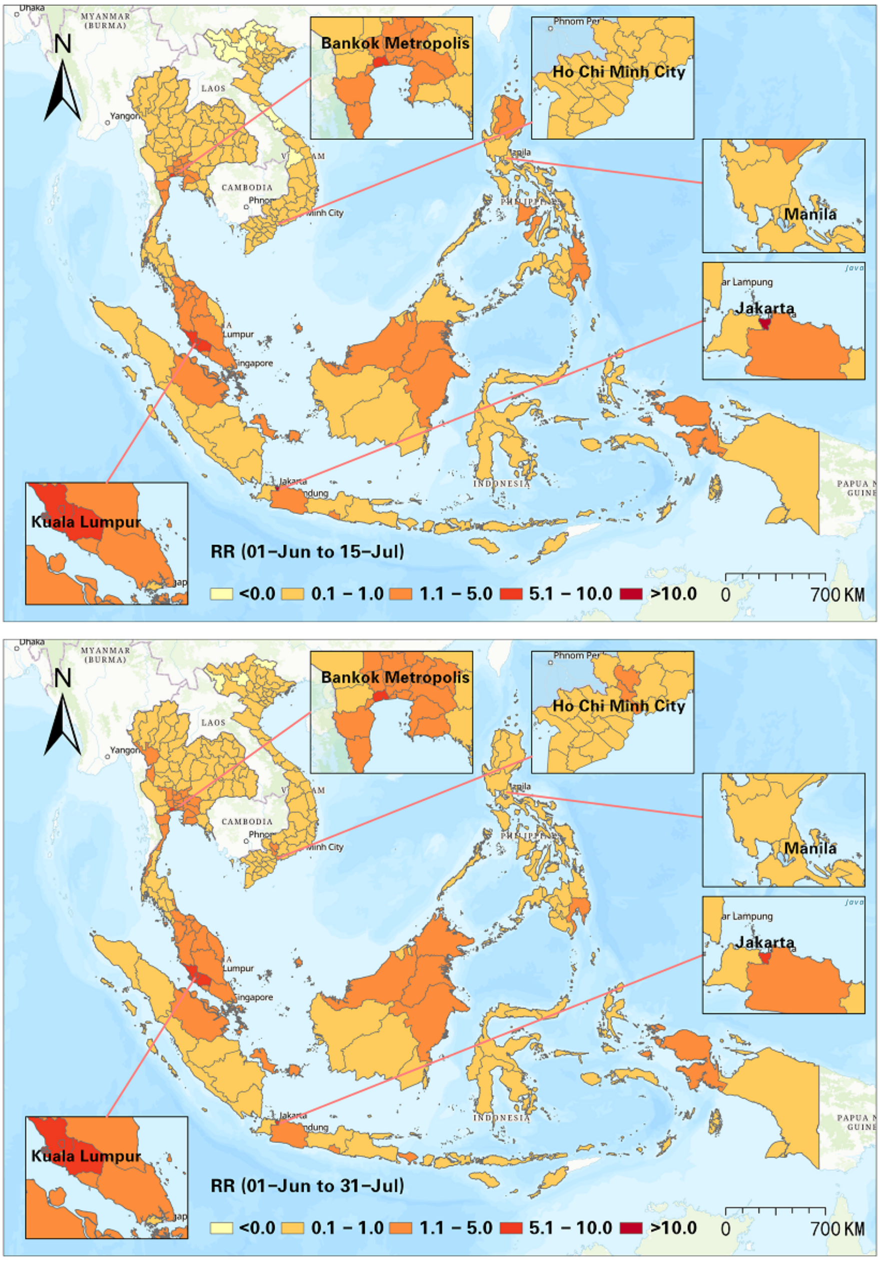


**Figure 7.** Spatial patterns of progression of the COVID-19 RR in SEA (June 1-August 15 and June 1-August 31, 2021). RR: relative risk; SEA: Southeast Asia.

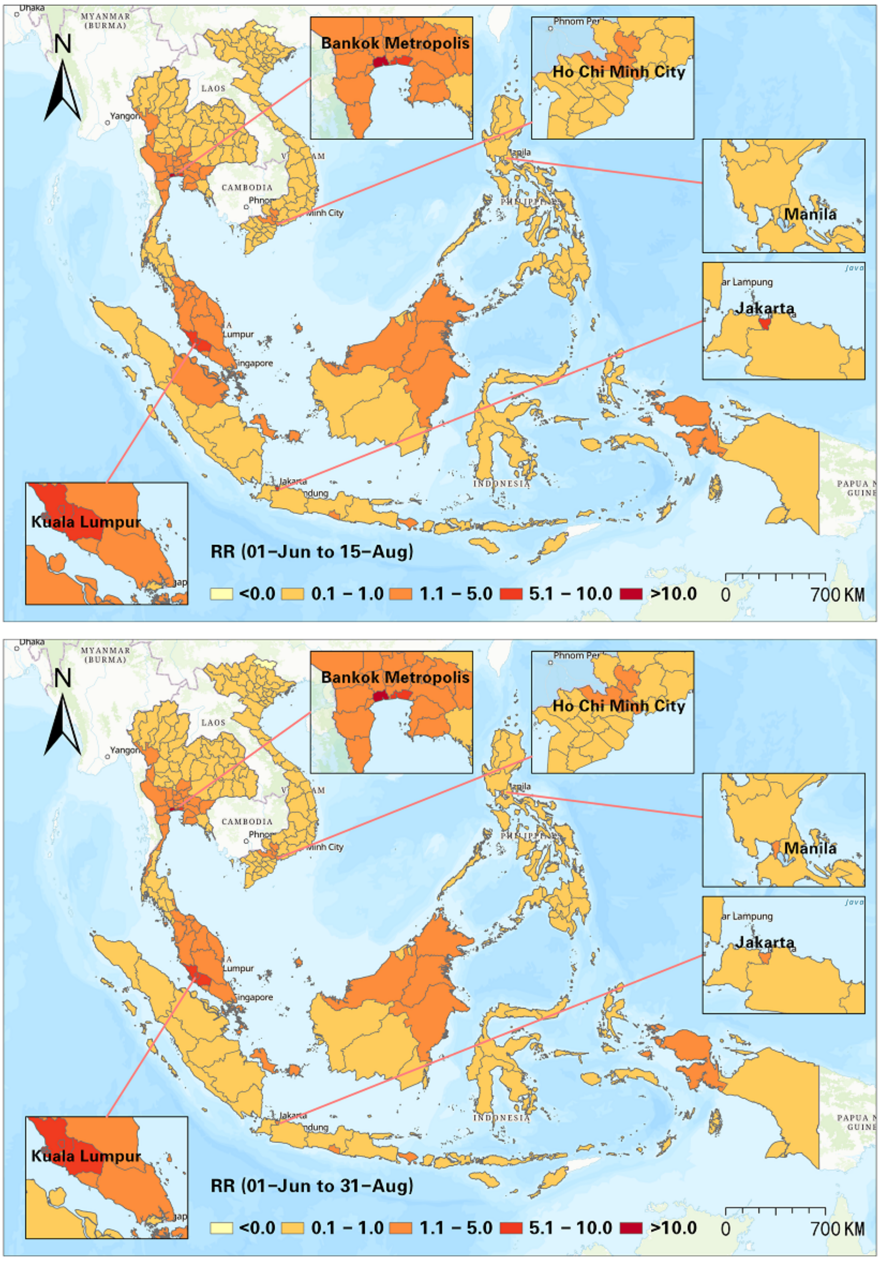


**Figure 8.** Spatial patterns of progression of the COVID-19 RR in SEA (June 1-September 15 and June 1-September 30, 2021). RR: relative risk; SEA: Southeast Asia.

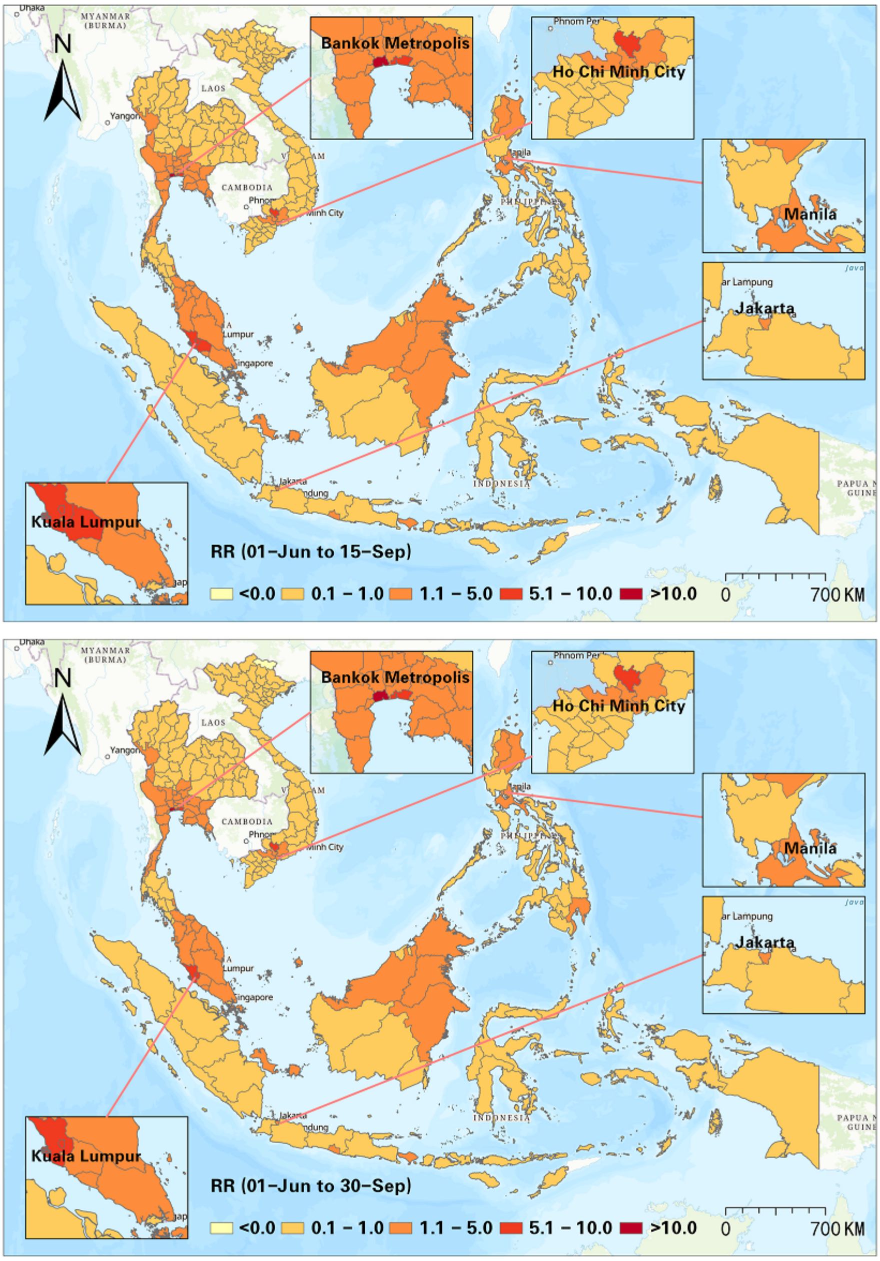
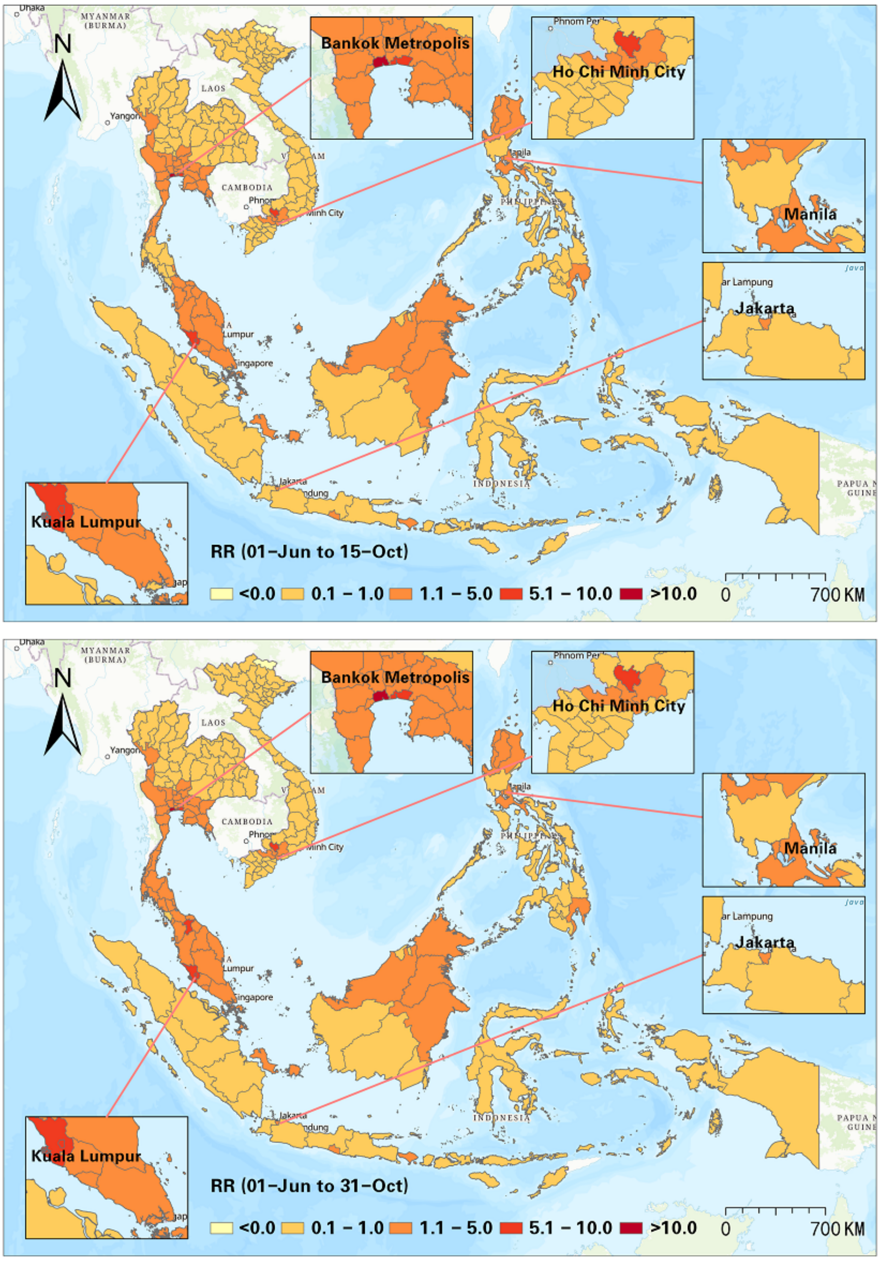


**Figure 9.** Spatial patterns of progression of the COVID-19 RR in SEA (June 1-October 15 and June 1-October 31, 2021). RR: relative risk; SEA: Southeast Asia.



## Discussion

### Principal Findings

In this study, we utilized prospective space-time scan statistics to detect the emerging and existing space-time clusters of COVID-19 in SEA. We found that most districts in Malaysia and the Philippines, Ho Chi Minh City and Binh Duong in Vietnam, the capital and its surrounding areas in Thailand, and Indonesia exhibited a high risk of COVID-19 transmission in the early phase (June-August 2021). Space-time clusters and the RR of districts changed along with the dynamics of government interventions implemented by each country after August 2021. Indonesia mitigated the risk of pandemic transmission throughout the study period. This may be attributed to the implemented and extended the *Pemberlakuan Pembatasan Kegiatan Masyarakat* (PPKM), including policies of mandatory working from home, guidance on online teaching, and restrictions of dine-in, social gathering, and interprovince and international traveling. For example, characterized as the largest city nationwide with a high population density, Jakarta’s success in preventing exacerbation of the risk impact of COVID-19 is most likely to be related to its persistent restrictions and unchanged strategy toward COVID-19 [55].

In most of the countries where restrictions were not consistent, the RR showed an increase after they loosened restrictions. For instance, the Philippines imposed border and movement restrictions, including the strictest level of lockdown and online teaching, that managed to mitigate the pandemic RR between June and August 2021. In contrast, the Manila capital region temporally eased the movement restriction from August 21 to 31, 2021; reopened restaurants and churches; and replaced a large-scale coronavirus restriction from September 15, 2021.

The results showed that the RR in the capital regions of the Philippines elevated thereafter, and the gradually intensified risks of districts in the Philippines should receive continuous attention. Particularly, although a series of regulations and restrictions, including lockdowns, curfews, and social distancing measures, had been specifically implemented in Ho Chi Minh City, the city still manifested overall worsen symptoms. This may be related to the high contagiousness of the Delta variant and overloaded health care system in Ho Chi Minh City [56]. In addition, Ho Chi Minh City has a larger population with a more economic development level than other districts, which resulted in more infections via contact with a relatively larger number of crowds. It has been suggested that population density and contact intensity are the main drivers for the propagation and amplification of this virus [57]. Moreover, the continuous high risk in Malaysia was probably because the government gradually adopted more loose measures than the other countries in SEA, with its phase development of the National Recovery Plan since the beginning of our study period. Singapore began intermittently relaxing social restrictions since early August 2021, and the RR showed an increase since September 2021.

## Comparison With Prior Work

To the best of our knowledge, this is the first attempt to use prospective space-time scan statistics to explore the space-time progression of the COVID-19 Delta variant outbreak in SEA, as well as summarize the potential linkage between the epidemic dynamics and public health interventions. Prior studies have adopted methods including the time-series forecasting model and the modified susceptible exposed infected and recovered (SEIR) model to investigate the risk of COVID-19 propagation [58,59]. Consistent with the findings of these studies, our study proved that appropriate nonpharmaceutical interventions (NPIs) are an effective way to mitigate the transmission of COVID-19, especially in Indonesia, which implemented multiple interventions (PPKM). In contrast, loosened restrictions may increase human mobility and further raise the risk of COVID-19 transmission [60,61]. Our results indicated that easing restrictions could lead to long-term existence of high-risk clusters and recurrent high risk in certain districts. Furthermore, previous studies on modeling linkages between NPIs and COVID-19 transmission were generally retrospective or predictive analyses and often focused on a single country [62-66]. The advantage of this study over prior works is that we provided a novel insight for timely and cross-nation surveillance of the dynamics and characteristics of the Delta variant at the district level in SEA. The perspective space-time scanning method used in this study can help detect spatiotemporal dynamics of COVID-19 propagation after the implementation of interventions in real time, which is beneficial for adjusting interventions and preventing COVID-19 transmission in time.

Moreover, previous studies have indicated that the propagation of COVID-19 was influenced by diverse factors. For example, population density, human movement, and environmental factors are proven to positively influence the spread of COVID-19 [67-69]. In addition, a severe COVID-19 outbreak is more likely to occur in regions with poor socioeconomic status [70-72]. Despite this, our study further emphasized the importance of public health interventions. Hence, we suggested that continuous strict restrictions are beneficial for epidemic control, especially for developing regions with weak public health systems and relatively low vaccination rates. Furthermore, to better understand the progression of COVID-19 transmission, the detection of space-time clusters could be adjusted with covariates, such as income, age, air quality, and vaccination status, which could improve evaluation of COVID-19 transmission [16,73].

## Implications and Recommendations

Public health interventions play an important role in epidemic containment, in which social restriction policies effectively mitigate the propagation of COVID-19 [37]. Restrictions of mass gathering and travel, keeping a social distance, and reducing human mobility are beneficial to control COVID-19 because these measures can reduce the probability of exposure to virus infection [74,75]. Our study discovered the potential linkage between the dynamics of COVID-19 outbreaks and interventions. This indicated that although continuously strict restrictions contribute to preventing exacerbation of the pandemic, temporary or continuous relaxation may result in acceleration of epidemic propagation. Appropriate restriction policies are key to preventing the pandemic, because high transmission of the COVID-19 variant would lead to worse situations [76]. In addition, if the number of community cases exceeds imported cases, border restrictions would be less valuable than domestic measures. In this case, authorities should emphasize more on domestic intervention in order to reduce community transmission [77]. Nevertheless, intervention measures against COVID-19 require adequate resources and good socioeconomic status. When implementing the intervention, economic and social justification is one of the priorities that governments should consider [78]. Hence, it is a challenge for all countries to weigh the balance between epidemic development and socioeconomic loss [79].

Considering domestic social and economic status, most countries in SEA gradually changed their strategies from the elimination of cases to living with COVID-19 since August 2021 [7]. A concurrent trend observed in SEA is that all countries except for Indonesia have been gradually loosening social restrictions, allowing international communications, while boosting vaccination to achieve group immunity. For instance, the Singapore Ministry of Health believes that with the assistance of a high vaccination rate, the economy and social norms could be restored without causing uncontrollable disease outbreaks or breakdown in the hospital system [80]. Vaccination is increasingly essential to protect the crowd from the exacerbating threat of morbidity and mortality of this Delta variant and future variants [81-84]. However, a previous study found that the effectiveness of available vaccines against the Delta variant (B.1.617.2) showed a reduction compared to previous virus variants [85], implying that current vaccination is likely to become ineffective against future variants [86]. Considering the fragile health systems in SEA, implementations including contact tracing, quick isolation, and strict restriction are still essential to prevent potential future outbreaks [87,88].

International coordination also plays an important role in responding to the pandemic. This includes information sharing, vaccine donation, medical support, and industry cooperation [89,90]. The Association of Southeast Asian Nations (ASEAN) countries are advised to exploit the strong socioeconomic connectivity to adopt collaborative policies in response to COVID-19. To facilitate cooperation among countries in SEA, regional surveillance is indispensable as it provides necessary information about emerging risks in the event of potential outbreaks due to new variants. This approach supports more precise prevention and mitigation of COVID-19, thus minimizing the cost of relevant resources. It was reported that Singapore and Vietnam provided medical equipment and support to neighboring countries [3], and we hope that there will be more multilateral collaborations among countries in SEA, especially considering the long-term challenges brought about by emerging new COVID-19 variants.

## Limitations

Despite the insights from our study, there are notable limitations in the COVID-19 data. To begin with, only 7 of 12 countries provided data at the primary administrative district level, so we were not able to explore the complete propagation process in SEA. In fact, many previous studies also faced a shortage or loss of available data (ie, insufficient pediatrics data) [91-93]. Additionally, although this study and many previous studies adopted COVID-19 case report data for analysis, these data may be confounded by underreporting. Due to insufficient testing data, this study did not account for different spatiotemporal screening rates [94,95]. In addition, if higher spatial resolution data were available (ie, city, county, and even block or subzone), more specific and detailed patterns could be revealed. Insufficient knowledge of the data or dynamics would lead to invalidity and unreliability of responses to COVID-19 [96]. Therefore, we strongly suggest that public health authorities in SEA should disclose more representative and reliable data [97,98]. Furthermore, although this study focused on the Delta variant of COVID-19, the data we adopted inevitably included cases from all variants. Although the Delta variant dominated the second outbreak in SEA since June 2021, this may result in uncertainty, in that proportion of cases caused by the Delta variants were not the same in different countries. Moreover, COVID-19 transmission and its impacts have shown environmental inequality in terms of household income, education level, age, gender, etc [99,100]. The potential correlation between environmental inequality and COVID-19 should be further studied using diverse data in order to obtain significant insights into resource allocation and regional prevention.

## Conclusion

The prospective space-time scan statistics revealed the potential linkages between public health interventions and the risk of the Delta variant of COVID-19 transmission. Regions that continuously adopted strict restrictions have witnessed a decreasing risk of pandemic progression, whereas some countries that implemented loosened interventions have shown a relatively higher risk. Moreover, our approach can be used to monitor the dynamics of COVID-19 with the latest data and support timely adjustments of domestic and interregional public health interventions to prevent further deterioration of the pandemic situation.

## Acknowledgments

This research was partially funded by the National University of Singapore Start-up Grant (#A-0003623-00-00) awarded to WL.

## Conflicts of Interest

None declared.

## References

1. World Health Organization. Transmission of SARS-CoV-2: Implications for Infection Prevention Precautions. Scientific Brief, 09 July 2020. URL: https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions/ [accessed 2022-05-19]
2. 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. [doi: 10.1016/s1473-3099(20)30120-1]
3. Amul GG, Ang M, Kraybill D, Ong SE, Yoong J. Responses to COVID‐19 in Southeast Asia: diverse paths and ongoing challenges. Asian Econ Policy Rev 2021 Aug 11;17(1):90-110. [doi: 10.1111/aepr.12362]
4. ASEAN Economies Hit Hard by Escalating Covid Delta Waves. URL: https://ihsmarkit.com/research-analysis/asean-economies-hit-hard-by-escalating-covid-delta-waves-sep21.html/ [accessed 2021-12-17]
5. Liu Y, Rocklöv J. The reproductive number of the Delta variant of SARS-CoV-2 is far higher compared to the ancestral SARS-CoV-2 virus. J Travel Med 2021 Oct 11;28(7):taab124 [FREE Full text] [doi: 10.1093/jtm/taab124] [Medline: 34369565]
6. Chookajorn T, Kochakarn T, Wilasang C, Kotanan N, Modchang C. Southeast Asia is an emerging hotspot for COVID-19. Nat Med 2021 Sep 16;27(9):1495-1496. [doi: 10.1038/s41591-021-01471-x] [Medline: 34400842]
7. Zainuddin A. Southeast Asia Nations Plan to 'Live With Virus' As Delta Surges. URL: https://thediplomat.com/2021/09/southeast-asia-nations-plan-to-live-with-virus-as-delta-surges/ [accessed 2021-12-17]
8. Franch-Pardo I, Napoletano BM, Rosete-Verges F, Billa L. Spatial analysis and GIS in the study of COVID-19. A review. Sci Total Environ 2020 Oct 15;739:140033 [FREE Full text] [doi: 10.1016/j.scitotenv.2020.140033] [Medline: 32534320]

9. Yin L, Zhang H, Li Y, Liu K, Chen T, Luo W, et al. A data driven agent-based model that recommends non-pharmaceutical interventions to suppress Coronavirus disease 2019 resurgence in megacities. J R Soc Interface 2021 Aug 25;18(181):20210112 [FREE Full text] [doi: 10.1098/rsif.2021.0112] [Medline: 34428950]
10. Lai S, Ruktanonchai NW, Zhou L, Prosper O, Luo W, Floyd JR, et al. Effect of non-pharmaceutical interventions to contain COVID-19 in China. Nature 2020 Sep 04;585(7825):410-413 [FREE Full text] [doi: 10.1038/s41586-020-2293-x] [Medline: 32365354]
11. Xu M, Cao C, Zhang X, Lin H, Yao Z, Zhong S, et al. Fine-scale space-time cluster detection of COVID-19 in Mainland China using retrospective analysis. Int J Environ Res Public Health 2021 Mar 30;18(7):3583 [FREE Full text] [doi: 10.3390/ijerph18073583] [Medline: 33808290]
12. Desjardins M, Hohl A, Delmelle E. Rapid surveillance of COVID-19 in the United States using a prospective space-time scan statistic: detecting and evaluating emerging clusters. Appl Geogr 2020 May;118:102202 [FREE Full text] [doi: 10.1016/j.apgeog.2020.102202] [Medline: 32287518]
13. Benita F, Gasca-Sanchez F. The main factors influencing COVID-19 spread and deaths in Mexico: a comparison between phases I and II. Appl Geogr 2021 Sep;134:102523 [FREE Full text] [doi: 10.1016/j.apgeog.2021.102523] [Medline: 34334843]
14. Rosillo N, Del-Águila-Mejía J, Rojas-Benedicto A, Guerrero-Vadillo M, Peñuelas M, Mazagatos C, et al. Real time surveillance of COVID-19 space and time clusters during the summer 2020 in Spain. BMC Public Health 2021 May 21;21(1):961 [FREE Full text] [doi: 10.1186/s12889-021-10961-z] [Medline: 34016076]
15. Ullah S, Mohd Nor NH, Daud H, Zainuddin N, Gandapur MSJ, Ali I, et al. Spatial cluster analysis of COVID-19 in Malaysia (Mar-Sep, 2020). Geospat Health 2021 May 05;16(1) [FREE Full text] [doi: 10.4081/gh.2021.961] [Medline: 33969966]
16. Masrur A, Yu M, Luo W, Dewan A. Space-time patterns, change, and propagation of COVID-19 risk relative to the intervention scenarios in Bangladesh. Int J Environ Res Public Health 2020 Aug 14;17(16):5911 [FREE Full text] [doi: 10.3390/ijerph17165911] [Medline: 32824030]
17. Martines MR, Ferreira RV, Toppa RH, Assunção LM, Desjardins MR, Delmelle EM. Detecting space-time clusters of COVID-19 in Brazil: mortality, inequality, socioeconomic vulnerability, and the relative risk of the disease in Brazilian municipalities. J Geogr Syst 2021 Mar 08;23(1):7-36 [FREE Full text] [doi: 10.1007/s10109-020-00344-0] [Medline: 33716567]
18. Kim S, Castro MC. Spatiotemporal pattern of COVID-19 and government response in South Korea (as of May 31, 2020). Int J Infect Dis 2020 Sep;98:328-333 [FREE Full text] [doi: 10.1016/j.ijid.2020.07.004] [Medline: 32634584]
19. Zhu M, Kleepbua J, Guan Z, Chew SP, Tan JW, Shen J, et al. Early spatiotemporal patterns and population characteristics of the COVID-19 pandemic in Southeast Asia. Healthcare (Basel) 2021 Sep 16;9(9):1220 [FREE Full text] [doi: 10.3390/healthcare9091220] [Medline: 34574997]
20. Salman AM, Ahmed I, Mohd MH, Jamiluddin MS, Dheyab MA. Scenario analysis of COVID-19 transmission dynamics in Malaysia with the possibility of reinfection and limited medical resources scenarios. Comput Biol Med 2021 Jun;133:104372 [FREE Full text] [doi: 10.1016/j.compbiomed.2021.104372] [Medline: 33864970]
21. Bouchnita A, Jebrane A. A hybrid multi-scale model of COVID-19 transmission dynamics to assess the potential of non-pharmaceutical interventions. Chaos Solitons Fractals 2020 Sep;138:109941 [FREE Full text] [doi: 10.1016/j.chaos.2020.109941] [Medline: 32834575]
22. Nian F, Shi Y, Cao J. COVID-19 propagation model based on economic development and interventions. Wirel Pers Commun 2022 Aug 18;122(3):2355-2365 [FREE Full text] [doi: 10.1007/s11277-021-08998-9] [Medline: 34421225]
23. Ruktanonchai NW, Floyd JR, Lai S, Ruktanonchai CW, Sadilek A, Rente-Lourenco P, et al. Assessing the impact of coordinated COVID-19 exit strategies across Europe. Science 2020 Sep 18;369(6510):1465-1470 [FREE Full text] [doi: 10.1126/science.abc5096] [Medline: 32680881]
24. Khairulbahri M. Lessons learned from three Southeast Asian countries during the COVID-19 pandemic. J Policy Model 2021 Nov;43(6):1354-1364 [FREE Full text] [doi: 10.1016/j.jpolmod.2021.09.002] [Medline: 34690384]
25. Arnakim LY, Kibtiah TM. Response of ASEAN member states to the spread of COVID-19 in Southeast Asia. In: IOP Conference Series: Earth and Environmental Science. Bristol, UK: IOP Publishing; Apr 01, 2021:012100.
26. Southeast Asia Covid-19 Tracker. URL: https://www.csis.org/programs/southeast-asia-program/projects/southeast-asia-covid-19-tracker/ [accessed 2021-12-17]
27. Delta Sub-variant Pushes up Covid-19 Tally in Some Indonesian Cities. URL: https://www.straitstimes.com/asia/se-asia/delta-sub-variant-pushes-up-covid-19-tally-in-some-indonesian-cities [accessed 2022-05-19]
28. Mallapaty S. Delta threatens rural regions that dodged earlier COVID waves. Nature 2021 Aug 06;596(7872):325-326. [doi: 10.1038/d41586-021-02146-w] [Medline: 34354278]
29. IN FOCUS: The Rapid Rise of the Delta Variant and How It Is Shaping Singapore's COVID-19 Fight. URL: https://www.channelnewsasia.com/singapore/covid-19-delta-variant-virus-vaccine-moh-2082741 [accessed 2022-05-19]
30. Malaysia Reports First case of Indian COVID-19 Variant. URL: https://www.reuters.com/world/india/malaysia-reports-first-case-indian-covid-19-variant-2021-05-02/ [accessed 2022-05-19]
31. Philippines Tightens Curbs after Detecting First Local Cases of Delta Variant. URL: https://www.reuters.com/world/asia-pacific/philippines-detects-first-local-transmission-delta-variant-2021-07-16/ [accessed 2022-05-19]

32. Thu H. Delta Variant Outbreak Challenges Vietnam’s COVID-19 Response Strategy. URL: https://www.brookings.edu/blog/order-from-chaos/2021/08/11/delta-variant-outbreak-challenges-vietnams-covid-19-response-strategy/ [accessed 2022-05-19]
33. Brunei Confirms COVID-19 Delta Variant as Daily Cases Exceed 100 for 8 Days. URL: http://www.news.cn/english/2021-08/26/c_1310150959.htm [accessed 2022-05-19]
34. KAWALCOVID19, National Board of Confirmed Case Development. URL: https://covid19.go.id/ [accessed 2022-05-19]
35. Statistics Indonesia. URL: https://www.bps.go.id/ [accessed 2022-05-19]
36. Official Data on the COVID-19 Epidemic in Malaysia. URL: https://github.com/MoH-Malaysia/covid19-public [accessed 2022-05-19]
37. Department of Statistics Malaysia. URL: https://www.dosm.gov.my/v1/index.php [accessed 2022-05-19]
38. Department of Health, the Philippines. URL: https://doh.gov.ph/covid19tracker [accessed 2022-05-19]
39. Philippine Statistics Authority. URL: https://psa.gov.ph/ [accessed 2022-05-19]
40. Ministry of Health, Singapore. URL: https://www.moh.gov.sg/covid-19 [accessed 2022-05-19]
41. Department of Statistics Singapore. URL: https://www.singstat.gov.sg/ [accessed 2022-05-19]
42. Ministry of Public Health, Department of Disease Control Situational Reports. URL: https://covid19.ddc.moph.go.th/en [accessed 2022-05-19]
43. National Statistical Office of Thailand. URL: http://web.nso.go.th/ [accessed 2022-05-19]
44. COVID-19 Data Repository by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. URL: https://github.com/CSSEGISandData/COVID-19 [accessed 2022-07-29]
45. Department of Economic Planning and Statistics, Brunei. URL: http://www.deps.gov.bn/Theme/Home.aspx [accessed 2022-05-19]
46. Ministry of Health, Vietnam. URL: https://covid19.gov.vn [accessed 2022-05-19]
47. General Statistics Office of Vietnam. URL: https://www.gso.gov.vn/en/homepage/ [accessed 2022-05-19]
48. Kulldorff M. SaTScanTM User Guide. URL: https://www.satscan.org/cgi-bin/satscan/register.pl/SaTScan_Users_Guide.pdf?todo=process_userguide_download/ [accessed 2021-12-17]
49. Kulldorff M. Prospective time periodic geographical disease surveillance using a scan statistic. J R Stat Soc Ser A Stat Soc 2002 Jan 06;164(1):61-72. [doi: 10.1111/1467-985x.00186]
50. Kulldorff M. A spatial scan statistic. Commun Stat Theory Methods 2007 Jun 27;26(6):1481-1496. [doi: 10.1080/03610929708831995]
51. Hohl A, Delmelle EM, Desjardins MR, Lan Y. Daily surveillance of COVID-19 using the prospective space-time scan statistic in the United States. Spat Spatiotemporal Epidemiol 2020 Aug;34:100354 [FREE Full text] [doi: 10.1016/j.sste.2020.100354] [Medline: 32807396]
52. Desjardins M, Whiteman A, Casas I, Delmelle E. Space-time clusters and co-occurrence of chikungunya and dengue fever in Colombia from 2015 to 2016. Acta Trop 2018 Sep;185:77-85. [doi: 10.1016/j.actatropica.2018.04.023] [Medline: 29709630]
53. Kan Z, Kwan M, Wong MS, Huang J, Liu D. Identifying the space-time patterns of COVID-19 risk and their associations with different built environment features in Hong Kong. Sci Total Environ 2021 Jun 10;772:145379 [FREE Full text] [doi: 10.1016/j.scitotenv.2021.145379] [Medline: 33578150]
54. Yang L, Dai J, Zhao J, Wang Y, Deng P, Wang J. Estimation of incubation period and serial interval of COVID-19: analysis of 178 cases and 131 transmission chains in Hubei Province, China. Epidemiol Infect 2020 Jun 19;148:e117 [FREE Full text] [doi: 10.1017/S0950268820001338] [Medline: 32594928]
55. Pemerintah Terapkan PPKM Mikro Di Seluruh Provinsi Mulai 1 Juni. Cabinet Secretariat of the Republic of Indonesia. URL: https://diskominfo.anambaskab.go.id/berita/pemerintah-terapkan-ppkm-mikro-di-seluruh-provinsi-mulai-1-juni/ [accessed 2021-12-17]
56. What the Delta Variant Did to South-East Asia. URL: https://www.economist.com/asia/what-the-delta-variant-did-to-south-east-asia/21804360/ [accessed 2021-12-17]
57. Rocklöv J, Sjödin H. High population densities catalyse the spread of COVID-19. J Travel Med 2020 May 18;27(3):taaa038 [FREE Full text] [doi: 10.1093/jtm/taaa038] [Medline: 32227186]
58. Feng L, Zhang T, Wang Q, Xie Y, Peng Z, Zheng J, et al. Impact of COVID-19 outbreaks and interventions on influenza in China and the United States. Nat Commun 2021 May 31;12(1):3249 [FREE Full text] [doi: 10.1038/s41467-021-23440-1] [Medline: 34059675]
59. Ejigu BA, Asfaw MD, Cavalerie L, Abebaw T, Nanyingi M, Baylis M. Assessing the impact of non-pharmaceutical interventions (NPI) on the dynamics of COVID-19: a mathematical modelling study of the case of Ethiopia. PLoS One 2021;16(11):e0259874 [FREE Full text] [doi: 10.1371/journal.pone.0259874] [Medline: 34784379]
60. Inferring the Effectiveness of Government Interventions against COVID-19. URL: https://www.science.org/doi/full/10.1126/science.abd9338 [accessed 2022-05-19]
61. Xiong C, Hu S, Yang M, Luo W, Zhang L. Mobile device data reveal the dynamics in a positive relationship between human mobility and COVID-19 infections. Proc Natl Acad Sci U S A 2020 Nov 03;117(44):27087-27089 [FREE Full text] [doi: 10.1073/pnas.2010836117] [Medline: 33060300]

62. Manabe T, Phan D, Nohara Y, Kambayashi D, Nguyen TH, Van Do T, et al. Spatiotemporal distribution of COVID-19 during the first 7 months of the epidemic in Vietnam. BMC Infect Dis 2021 Oct 30;21(1):1124 [FREE Full text] [doi: 10.1186/s12879-021-06822-0] [Medline: 34717588]
63. Purwanto P, Utaya S, Handoyo B, Bachri S, Astuti IS, Utomo KSB, et al. Spatiotemporal analysis of COVID-19 spread with emerging hotspot analysis and space–time cube models in East Java, Indonesia. IJGI 2021 Mar 03;10(3):133. [doi: 10.3390/ijgi10030133]
64. Yeung AY, Roewer-Despres F, Rosella L, Rudzicz F. Machine learning-based prediction of growth in confirmed COVID-19 infection cases in 114 countries using metrics of nonpharmaceutical interventions and cultural dimensions: model development and validation. J Med Internet Res 2021 Apr 23;23(4):e26628 [FREE Full text] [doi: 10.2196/26628] [Medline: 33844636]
65. Ebrahim S, Ashworth H, Noah C, Kadambi A, Toumi A, Chhatwal J. Reduction of COVID-19 incidence and nonpharmacologic interventions: analysis using a US county-level policy data set. J Med Internet Res 2020 Dec 21;22(12):e24614 [FREE Full text] [doi: 10.2196/24614] [Medline: 33302253]
66. Jayaweera M, Dannangoda C, Dilshan D, Dissanayake J, Perera H, Manatunge J, et al. Grappling with COVID-19 by imposing and lifting non-pharmaceutical interventions in Sri Lanka: a modeling perspective. Infect Dis Model 2021;6:820-831 [FREE Full text] [doi: 10.1016/j.idm.2021.06.004] [Medline: 34250320]
67. Han Y, Yang L, Jia K, Li J, Feng S, Chen W, et al. Spatial distribution characteristics of the COVID-19 pandemic in Beijing and its relationship with environmental factors. Sci Total Environ 2021 Mar 20;761:144257 [FREE Full text] [doi: 10.1016/j.scitotenv.2020.144257] [Medline: 33352341]
68. Wang Q, Dong W, Yang K, Ren Z, Huang D, Zhang P, et al. Temporal and spatial analysis of COVID-19 transmission in China and its influencing factors. Int J Infect Dis 2021 Apr;105:675-685 [FREE Full text] [doi: 10.1016/j.ijid.2021.03.014] [Medline: 33711521]
69. Poirier C, Luo W, Majumder MS, Liu D, Mandl KD, Mooring TA, et al. The role of environmental factors on transmission rates of the COVID-19 outbreak: an initial assessment in two spatial scales. Sci Rep 2020 Oct 12;10(1):17002 [FREE Full text] [doi: 10.1038/s41598-020-74089-7] [Medline: 33046802]
70. Lone NI, McPeake J, Stewart NI, Blayney MC, Seem RC, Donaldson L, Scottish Intensive Care Society Audit Group. Influence of socioeconomic deprivation on interventions and outcomes for patients admitted with COVID-19 to critical care units in Scotland: a national cohort study. Lancet Reg Health Eur 2021 Mar;1:100005 [FREE Full text] [doi: 10.1016/j.lanepe.2020.100005] [Medline: 34173618]
71. Ehlert A. The socio-economic determinants of COVID-19: a spatial analysis of German county level data. Socioecon Plann Sci 2021 Dec;78:101083 [FREE Full text] [doi: 10.1016/j.seps.2021.101083] [Medline: 34007090]
72. Garnier R, Benetka JR, Kraemer J, Bansal S. Socioeconomic disparities in social distancing during the COVID-19 pandemic in the United States: observational study. J Med Internet Res 2021 Jan 22;23(1):e24591 [FREE Full text] [doi: 10.2196/24591] [Medline: 33351774]
73. Nigussie TZ, Zewotir TT, Muluneh EK. Detection of temporal, spatial and spatiotemporal clustering of malaria incidence in northwest Ethiopia, 2012-2020. Sci Rep 2022 Mar 07;12(1):3635 [FREE Full text] [doi: 10.1038/s41598-022-07713-3] [Medline: 35256698]
74. Yin H, Sun T, Yao L, Jiao Y, Ma L, Lin L. Association between population density and infection rate suggests the importance of social distancing and travel restriction in reducing the COVID-19 pandemic. Environ Sci Pollut Res 2021:1-7. [doi: 10.1101/2020.09.04.20187849]
75. Zhang S, Wang Z, Chang R, Wang H, Xu C, Yu X, et al. COVID-19 containment: China provides important lessons for global response. Front Med 2020 Apr 25;14(2):215-219 [FREE Full text] [doi: 10.1007/s11684-020-0766-9] [Medline: 32212059]
76. Jusup M, Holme P, Kanazawa K, Takayasu M, Romić I, Wang Z, et al. Social physics. Phys Rep 2022 Feb;948:1-148. [doi: 10.1016/j.physrep.2021.10.005]
77. Jayant M. Delta Variant Makes COVID-19 Border Closures Unsustainable in Southeast Asia. URL: https://www.channelnewsasia.com/commentary/border-closures-delta-variant-vaccination-rates-vaccinated-travel-lanes-2234886/ [accessed 2021-12-17]
78. Boettke PJ, Powell B. The political economy of the COVID-19 pandemic. South Econ J 2021 Apr;87(4):1090-1106 [FREE Full text] [doi: 10.1002/soej.12488] [Medline: 33821055]
79. Zhu R, Anselin L, Batty M, Kwan M, Chen M, Luo W, et al. The effects of different travel modes and travel destinations on COVID-19 transmission in global cities. Sci Bull (Beijing) 2022 Mar 30;67(6):588-592 [FREE Full text] [doi: 10.1016/j.scib.2021.11.023] [Medline: 34868708]
80. Ministry of Health Singapore. Preparing for Our Transition towards COVID Resilience. URL: https://www.moh.gov.sg/news-highlights/details/preparing-for-our-transition-towards-covid-resilience/ [accessed 2021-12-17]
81. Corey L, Mascola JR, Fauci AS, Collins FS. Science 2020 May 29;368(6494):948-950. [doi: 10.1126/science.abc5312] [Medline: 32393526]
82. Fowlkes A, Gaglani M, Groover K, Thiese MS, Tyner H, Ellingson K, HEROES-RECOVER Cohorts. Effectiveness of COVID-19 vaccines in preventing SARS-CoV-2 infection among frontline workers before and during B.1.617.2 (Delta)

variant predominance - eight U.S. locations, December 2020-August 2021. Morb Mortal Wkly Rep 2021 Aug 27;70(34):1167-1169 [FREE Full text] [doi: 10.15585/mmwr.mm7034e4] [Medline: 34437521]
83. Leshem E, Wilder-Smith A. COVID-19 vaccine impact in Israel and a way out of the pandemic. Lancet 2021 May;397(10287):1783-1785. [doi: 10.1016/s0140-6736(21)01018-7]
84. Makhoul M, Chemaitelly H, Ayoub HH, Seedat S, Abu-Raddad LJ. Epidemiological differences in the impact of COVID-19 vaccination in the United States and China. Vaccines (Basel) 2021 Mar 05;9(3):223 [FREE Full text] [doi: 10.3390/vaccines9030223] [Medline: 33807647]
85. Keegan L, Truelove S, Lessler J. Progress of the Delta variant and erosion of vaccine effectiveness, a warning from Utah. medRxiv 2022. [doi: 10.1101/2021.08.09.21261554]
86. Bewick S. Viral variants and vaccinations: if we can change the COVID-19 vaccine, should we? medRxiv 2022. [doi: 10.1101/2021.01.05.21249255]
87. Albouy-Llaty M, Martin C, Benamouzig D, Bothorel E, Munier G, Simonin C, et al. Positioning digital tracing applications in the management of the COVID-19 pandemic in France. J Med Internet Res 2021 Oct 07;23(10):e27301 [FREE Full text] [doi: 10.2196/27301] [Medline: 34313588]
88. Wong CKH, Wong JYH, Tang EHM, Au CH, Lau KTK, Wai AKC. Impact of national containment measures on decelerating the increase in daily new cases of COVID-19 in 54 countries and 4 epicenters of the pandemic: comparative observational study. J Med Internet Res 2020 Jul 22;22(7):e19904 [FREE Full text] [doi: 10.2196/19904] [Medline: 32658858]
89. The Lancet. COVID-19: where do we go from here? Lancet 2021 Dec;398(10318):2207. [doi: 10.1016/s0140-6736(21)02790-2]
90. Singh S, McNab C, Olson R, Bristol N, Nolan C, Bergstrøm E, et al. How an outbreak became a pandemic: a chronological analysis of crucial junctures and international obligations in the early months of the COVID-19 pandemic. Lancet 2021 Dec;398(10316):2109-2124 [FREE Full text] [doi: 10.1016/s0140-6736(21)01897-3]
91. Leon-Abarca JA. Obesity and immunodeficiencies are the main pre-existing conditions associated with mild to moderate COVID-19 in children. Pediatr Obes 2020 Dec 12;15(12):e12713 [FREE Full text] [doi: 10.1111/ijpo.12713] [Medline: 32789994]
92. Noh JY, Yoon JG, Seong H, Choi WS, Sohn JW, Cheong HJ, et al. Asymptomatic infection and atypical manifestations of COVID-19: comparison of viral shedding duration. J Infect 2020 Nov;81(5):816-846 [FREE Full text] [doi: 10.1016/j.jinf.2020.05.035] [Medline: 32445728]
93. Woolf SH, Chapman DA, Sabo RT, Zimmerman EB. Excess deaths from COVID-19 and other causes in the US, March 1, 2020, to January 2, 2021. JAMA 2021 Apr 02;325(17):1786 [FREE Full text] [doi: 10.1001/jama.2021.5199] [Medline: 33797550]
94. Bermudi PMM, Lorenz C, Aguiar BSD, Failla MA, Barrozo LV, Chiaravalloti-Neto F. Spatiotemporal ecological study of COVID-19 mortality in the city of São Paulo, Brazil: shifting of the high mortality risk from areas with the best to those with the worst socio-economic conditions. Travel Med Infect Dis 2021 Jan;39:101945 [FREE Full text] [doi: 10.1016/j.tmaid.2020.101945] [Medline: 33278610]
95. Rampal L, Liew BS, Choolani M, Ganasegeran K, Pramanick A, Vallibhakara SA, et al. Battling COVID-19 pandemic waves in six South-East Asian countries: a real-time consensus review. Med J Malaysia 2020 Nov;75(6):613-625 [FREE Full text] [Medline: 33219168]
96. Hirabayashi A, Kajihara T, Yahara K, Shibayama K, Sugai M. Impact of the COVID-19 pandemic on the surveillance of antimicrobial resistance. J Hosp Infect 2021;117:147-156 [FREE Full text] [doi: 10.1016/j.jhin.2021.09.011]
97. Lange K. The prevention of COVID-19 and the need for reliable data. Mov Nutr Health Dis 2020:4. [doi: 10.5283/mnhd.25]
98. Dron L, Dillman A, Zoratti MJ, Haggstrom J, Mills EJ, Park JJH. Clinical trial data sharing for COVID-19-related research. J Med Internet Res 2021 Mar 12;23(3):e26718 [FREE Full text] [doi: 10.2196/26718] [Medline: 33684053]
99. Mollalo A, Vahedi B, Rivera KM. GIS-based spatial modeling of COVID-19 incidence rate in the continental United States. Sci Total Environ 2020 Aug 01;728:138884 [FREE Full text] [doi: 10.1016/j.scitotenv.2020.138884] [Medline: 32335404]
100. Spotswood EN, Benjamin M, Stoneburner L, Wheeler MM, Beller EE, Balk D, et al. Nature inequity and higher COVID-19 case rates in less-green neighbourhoods in the United States. Nat Sustain 2021 Oct 11;4(12):1092-1098. [doi: 10.1038/s41893-021-00781-9]

---

## Abbreviations

**DIY:** Daerah Istimewa Yogyakarta
**NPI:** nonpharmaceutical intervention
**PPKM:** Pemberlakuan Pembatasan Kegiatan Masyarakat
**RR:** relative risk
**SEA:** Southeast Asia

*Edited by T Sanchez, A Mavragani; submitted 20.12.21; peer-reviewed by ECY Su, A Joseph; comments to author 10.05.22; revised version received 19.05.22; accepted 19.07.22; published 09.08.22.*

*Please cite as:*
*Luo W, Liu Z, Zhou Y, Zhao Y, Li YE, Masrur A, Yu M*
*Investigating Linkages Between Spatiotemporal Patterns of the COVID-19 Delta Variant and Public Health Interventions in Southeast Asia: Prospective Space-Time Scan Statistical Analysis Method*
*JMIR Public Health Surveill 2022;8(8):e35840*
*URL: https://publichealth.jmir.org/2022/8/e35840*
*doi:10.2196/35840*
*PMID:35861674*

Original Paper

# Preferences for Attributes of Initial COVID-19 Diagnosis in the United States and China During the Pandemic: Discrete Choice Experiment With Propensity Score Matching

Yimin Zhang[1*], MBBS; Taoran Liu[2*], BS; Zonglin He[3*], MBBS; Sze Ngai Chan[4], MBBS, MPH, PhD; Babatunde Akinwunmi[5,6], MD, MPH; Jian Huang[7], MPH, PhD; Tak-Hap Wong[2], MBBS, MMed; Casper J P Zhang[8*], MPH, PhD; Wai-Kit Ming[2*], MD, PhD, MPH

[1]School of Medicine, Jinan University, Guangzhou, China
[2]Department of Infectious Diseases and Public Health, City University of Hong Kong, Hong Kong, China
[3]Division of Life Science, Hong Kong University of Science and Technology, Hong Kong, Hong Kong
[4]Department of Obstetrics and Gynaecology, First Affiliated Hospital of Jinan University, Guangzhou, China
[5]Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Boston, MA, United States
[6]Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, United States
[7]Singapore Institute for Clinical Sciences, Agency for Science, Technology and Research, Singapore, Singapore
[8]School of Public Health, University of Hong Kong, Hong Kong, China
[*]these authors contributed equally

**Corresponding Author:**
Wai-Kit Ming, MD, PhD, MPH
Department of Infectious Diseases and Public Health
City University of Hong Kong
Room 1A-503, 5/F, Block 1, To Yuen Building
31 To Yuen Street
Hong Kong
China
Phone: 852 3442 6956
Email: wkming2@cityu.edu.hk

## Abstract

**Background:** China and the United States play critical leading roles in the global effort to contain the COVID-19 virus. Therefore, their population's preferences for initial diagnosis were compared to provide policy and clinical insights.

**Objective:** We aim to quantify and compare the public's preferences for medical management of fever and the attributes of initial diagnosis in the case of presenting symptoms during the COVID-19 pandemic in China and the United States.

**Methods:** We conducted a cross-sectional study from January to March 2021 in China and the United States using an online discrete choice experiment (DCE) questionnaire distributed through Amazon Mechanical Turk (MTurk; in the United States) and recruited volunteers (in China). Propensity score matching (PSM) was used to match the 2 groups of respondents from China and the United States to minimize confounding effects. In addition, the respondents' preferences for different diagnosis options were evaluated using a mixed logit model (MXL) and latent class models (LCMs). Moreover, demographic data were collected and compared using the chi-square test, Fisher test, and Mann-Whitney *U* test.

**Results:** A total of 9112 respondents (5411, 59.4%, from China and 3701, 40.6%, from the United States) who completed our survey were included in our analysis. After PSM, 1240 (22.9%) respondents from China and 1240 (33.5%) from the United States were matched for sex, age, educational level, occupation, and annual salary levels. The segmented sizes of 3 classes of respondents from China were 870 (70.2%), 270 (21.8%), and 100 (8.0%), respectively. Meanwhile, the US respondents' segmented sizes were 269 (21.7%), 139 (11.2%), and 832 (67.1%), respectively. Respondents from China attached the greatest importance to the type of medical institution (weighted importance=40.0%), while those from the United States valued the waiting time (weighted importance=31.5%) the most. Respondents from China preferred the emergency department (coefficient=0.973, reference level: online consultation) and fever clinic (a special clinic for the treatment of fever patients for the prevention and control of acute infectious diseases in China; coefficient=0.974, reference level: online consultation), while those from the United States preferred private clinics (general practices; coefficient=0.543, reference level: online consultation). Additionally, shorter waiting times, COVID-19 nucleic acid testing arrangements, higher reimbursement rates, and lower costs were always preferred.

**Conclusions:** Improvements in the availability of COVID-19 testing and medical professional skills and increased designated health care facilities may help boost potential health care seeking during COVID-19 and prevent unrecognized community spreading of SARS-CoV-2 in China and the United States. Moreover, to better prevent future waves of pandemics, identify undiagnosed patients, and encourage those undiagnosed to seek health care services to curb the pandemic, the hierarchical diagnosis and treatment system needs improvement in China, and the United States should focus on reducing diagnosis costs and raising the reimbursement rate of medical insurance.

***(JMIR Public Health Surveill 2022;8(8):e37422)*** doi:10.2196/37422

**KEYWORDS**

COVID-19; public health; discrete choice experiment; patient preference; propensity score matching; patients with fever

## Introduction

COVID-19 was first reported in Wuhan, Hubei Province, China. It is caused by SARS-CoV-2 [1]. COVID-19, which had spread to more than 200 countries and regions as of May 2, 2022, was declared a public health emergency of international concern by the World Health Organization (WHO), with over 511 million confirmed cases and around 6 million confirmed deaths worldwide [2], having a devastating impact on the global economy, public health system, and health care services.

Patients with COVID-19 typically reported fever as the primary symptom, together with symptoms of upper respiratory tract infection, including cough, fatigue, and dyspnea, similar to the common cold and influenza [1,3,4]. Thus, researchers and clinicians faced numerous difficulties in quickly and accurately distinguishing COVID-19 from other respiratory infectious diseases in the early stages of the epidemic [5,6], especially when increasingly more infected individuals were asymptomatic [7,8]. So far, the COVID-19 nucleic acid test remains the gold standard for diagnosing COVID-19 and serves as the foundation for identifying, tracing, and isolating infected individuals [9]. With only enhanced surveillance and public health and social measures (PHSMs) to guard against COVID-19, a large proportion of those infected may still be undiagnosed and constantly spreading the virus in the community [10]. Therefore, it would be important to investigate the motivation of the public to undergo COVID-19 nucleic testing if infection were suspected.

China and the United States implemented different PHSMs during COVID-19. Compared with the United States, China enacted stricter actions, quickly locking down cities with confirmed community transmission, requiring face masks in public, and declaring national health insurance pay for all COVID-19–related costs [11-13]. Different types and levels of PHSMs may lead to differed attitudes toward, preferences for, and practices in the management of COVID-19 infection, leading to different transmission patterns of COVID-19 in the community. There is also an abundance of differences between the 2 countries in terms of medical structures (especially the health care system) and medical treatment, as well as others. These differences may lead to different preferences and variations among people in the 2 countries concerning medical treatment options, hence influencing their health-seeking behavior during COVID-19.

Factors have been identified that could influence the health care–seeking and utilization behavior of the patients [14,15]. On the one hand, the perception of disease severity and fear of infection, as well as the availability of appropriate health care facilities, lay the foundation of health-seeking behavior [16]. On the other hand, the delay in obtaining urgent health care may be due to personal experiences and anxieties over the COVID-19 pandemic, mandatory quarantines, national halt of mobility, mandatory lockdowns, and loss of income [17]. Moreover, the health-seeking behavior of those with fever during the pandemic may also be compromised by the potential stigma and discrimination [18]. The need to eliminate uncertainty motivates people to seek information and health care [19,20], and health care seeking can assist the patients better in making health decisions [21]. During COVID-19, a run on the medical resources was well noted in the world, and the failure to implement nucleic acid testing in the early stage led to widespread SARS-CoV-2 in the community and the late imposing of identification-tracing-isolation of those infected [22,23]. With medical resources directed to compensate for these newly emerging infectious diseases and health care facilities crowded with infectious patients, studies have identified the difficulties and burdens patients with diseases other than COVID-19 faced during the pandemic [24,25]. Nevertheless, the health-seeking behavior of those potentially infected with COVID-19 during the pandemic was not explored.

Therefore, given the political and cultural differences between China and the United States, as well as the 2 countries' disparate approaches to COVID-19 prevention and general medical insurance policies, our study aimed to investigate the preferences and choices of patients with fever for initial diagnosis in China and the United States during the COVID-19 pandemic using propensity score matching (PSM) and discrete choice experiment (DCE) analysis. This study focused on the availability of health care services that may influence the health care–seeking behavior of patients with fever during the pandemic, which may provide policymakers with insights to reform the health care system, better reallocate medical resources, and promote campaigns to encourage undiagnosed patients to undergo testing and may also provide practical guidance for preparing for any other future outbreaks.

# Methods

## Overview

This self-administered online cross-sectional study was conducted in China and the United States from January to March 2021. The questionnaire was constructed and administered using Lighthouse Studio version 9.8.1 (Sawtooth Software Inc). In the questionnaire, a total of 12 demographic questions and 7 DCE questions were included. First, demographic and socioeconomic information was collected, including age, sex, education level, annual income, and occupation, followed by 1 set of DCEs to investigate the respondents' preferences for the initial diagnosis of fever during the COVID-19 pandemic using simulated scenarios of different diagnosis and treatment attributes. The questionnaire generally included 7 scenarios, with 1 fixed scenario and 6 hypothetical scenarios with fixed attributes and random levels, where the respondents were required to choose 1 option of 3 in each scenario.

First, the demographic idiosyncrasy of the 2 groups of respondents before and after PSM was presented. Later, the general preferences of the 2 groups of respondents were presented to show population-wide preferences for the initial diagnosis of fever during the pandemic; moreover, to compare the 2 groups of respondents from China and the United States, PSM was utilized to 1-to-1-match the respondents for 5 confounding variables (sex, age, income level, occupations, and educational level), aimed at comparing the preferences without being influenced by the confounding variables and demographic factors.

## Selection of Attributes and Levels

DCEs are now widely used in the fields of health care and public health [26,27]. The literature indicates that patients' preferences strongly correlate with their willingness to use diagnosis, treatment services, and follow-up treatment [28]. By consulting several public health experts and reviewing the relevant literature [29-32], this study identified the following 6 attributes concerning diagnoses and treatment services, as well as their corresponding levels: (1) diagnosis and treatment medical institutions, (2) diagnosis and treatment personnel, (3) waiting time, (4) whether to test the nucleic acid of COVID-19 immediately, (5) medical expenses, and (6) reimbursement rate of medical expenses. The detailed attributes and their respective levels are presented in Table 1.

**Table 1.** Diagnosis attributes and their respective levels in this DCE[a] (January-March 2021).

| Diagnosis attribute | Description and levels |
|---|---|
| Types of clinics | • Description: types of health care institutions that provide medical services during the COVID-19 pandemic<br>• Levels: telephone consultation, online consultation, emergency room, fever clinic, and private clinic (general practices) |
| Medical staff | • Description: types of health care workers who can provide medical services, including diagnosis and treatment, for patients during the COVID-19 pandemic<br>• Levels: doctor, nurse, and paramedic |
| Waiting time | • Description: time needed for a patient to receive medical consultation or other medical services to diagnose their fever during the COVID-19 pandemic<br>• Levels: 0, 15, 30, 45, 60, and 75 minutes |
| Immediate COVID-19 nucleic acid testing | • Description: whether to undergo the SARS-CoV-2 nucleic acid test upon receiving medical services for fever during the COVID-19 pandemic<br>• Levels: Yes and no |
| Reimbursement ratio | • Description: how much (%) of the medical expenses that patients spend on their medical services for fever could be reimbursed during the COVID-19 pandemic<br>• Levels: 0%, 20%, 40%, 60%, 80%, and 100% |
| Cost | • Description: direct cost for medical services the patients receive for diagnosing and treating fever during the COVID-19 pandemic<br>• Levels: US $0, US $25, US $50, US $75, and US $100 |

[a] DCE: discrete choice experiment.

## Questionnaire and DCE Instrument Design

The questionnaire took 5-10 minutes to complete. Upon completing the questionnaire, each respondent immediately got a randomly generated 6-digit code without filling in any personal information. With this code, they received a preset US $0.10 on the Amazon Mechanical Turk (MTurk) platform as a reward. All respondents were required to be at least 18 years old and consented to participate by clicking the "agree to participate in the questionnaire" option before formally starting to answer the questionnaire. Before completing the questionnaire, all respondents were fully informed that this questionnaire was completely anonymous. Once the respondents agreed to take the questionnaire survey, they were informed that they voluntarily agreed to participate in the study and the questionnaire answers would be protected by privacy laws.

In the first part of the questionnaire, respondents were required to provide basic demographic information, including sex, age, educational level, occupation, annual salary, and marital status. In addition to the basic demographic information, respondents were also asked whether they had ever been infected with COVID-19 and whether their acquaintances had ever been infected with COVID-19. The second part asked the respondents to consider a preferred treatment plan among 3 options in a task-choice scenario. Each scenario required the respondents to imagine themselves in a fever state and asked how they would seek health care services. This questionnaire included 6 attributes with a maximum of 6 levels, 7 scenarios per respondent, 3 alternatives per scenario. One example of the task-choice scenario is shown in Figure 1. See Multimedia Appendices 1 and 2 for the English and Chinese questionnaires, respectively.

Internal validity was evaluated using the program developed by Johnson et al [33], which includes stability (with repeated questions), within-set dominated pairs, across-set dominated pairs, transitivity, and attribute dominance (noncompensatory preferences). Multimedia Appendix 3, Table S9, shows information regarding the attributes of the DCE questionnaire, and Multimedia Appendix 1, Table S10, summarizes the test summaries. The internal validity test results and the summary results are shown in Multimedia Appendix 1, Tables S11-S13. According to the relevant research [34,35], our results showed that our questionnaire is efficient.

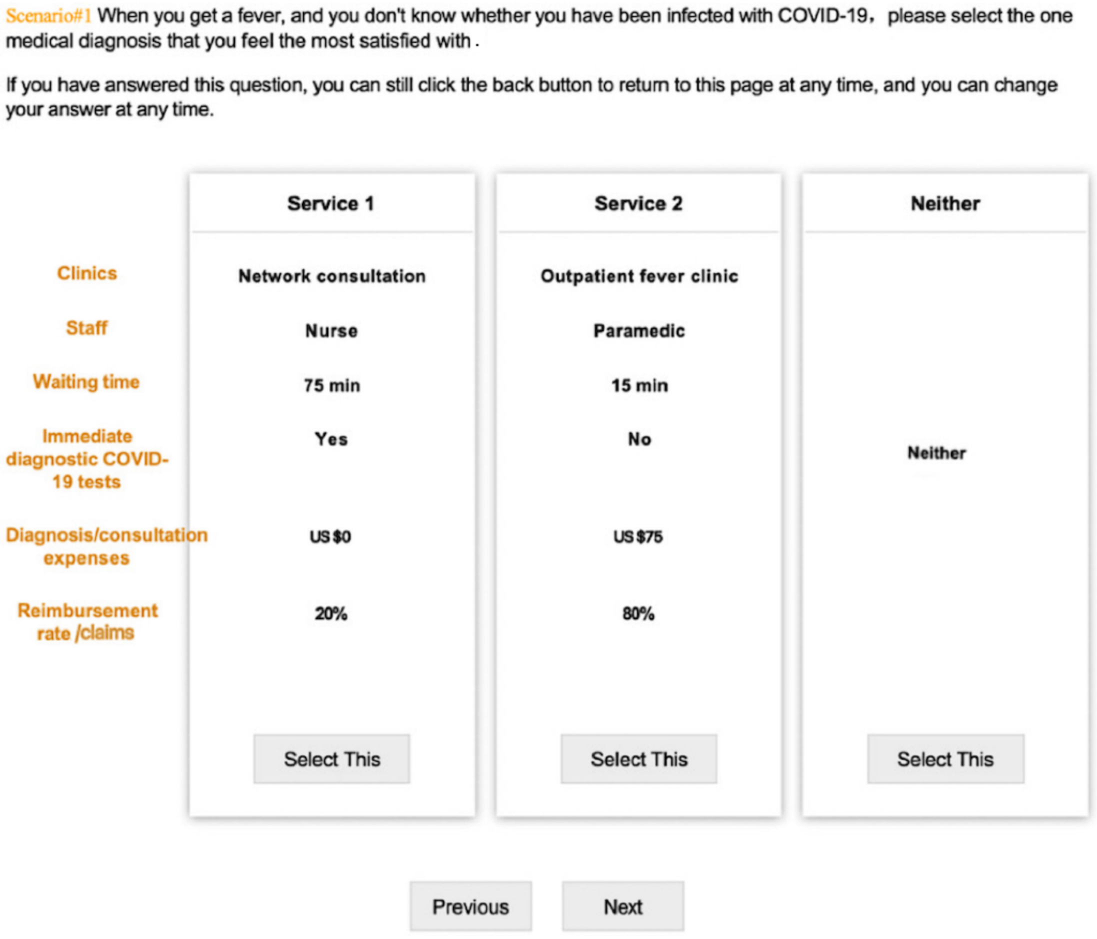


**Figure 1.** An example scenario of a choice-based conjoint in the questionnaire (January-March 2021).

Scenario#1 When you get a fever, and you don't know whether you have been infected with COVID-19, please select the one medical diagnosis that you feel the most satisfied with .

If you have answered this question, you can still click the back button to return to this page at any time, and you can change your answer at any time.

| | Service 1 | Service 2 | Neither |
|---|---|---|---|
| Clinics | Network consultation | Outpatient fever clinic | Neither |
| Staff | Nurse | Paramedic | |
| Waiting time | 75 min | 15 min | |
| Immediate diagnostic COVID-19 tests | Yes | No | |
| Diagnosis/consultation expenses | US $0 | US $75 | |
| Reimbursement rate /claims | 20% | 80% | |

## Data Collection

Questionnaires were distributed via multiple international online panel providers (for data collection in the United States) and recruited volunteers (for data collection across China) from January to March 2021 [36,37]. Specifically, MTurk was used for data collection in the United States, and stratified sampling by age and geological locations was used for data collection in China [38]. MTurk was found to provide census-level sampling data during ongoing social events [39-41]. In total, 10,921 respondents participated in the survey, but only 9112 (83.4%) finished all the questions. Therefore, a total of 9112 respondents were included in the study, with 5411 (59.4%) respondents from China and 3701 (40.6%) from the United States. According to the rule of thumb [42], the sample size of a DCE depends on the number of choice tasks (t), the number of alternatives (a), and the number of analysis cells (c). According to the equation

when considering the main effects, c equals the largest number of levels for any attribute. For this study, c=6, t=7, and a=3; thus, a minimum of 143 respondents were required.

## Statistical Analysis

Sociodemographic data were analyzed using descriptive statistics of frequency and percentage. Comparisons between the respondents from China and the United States were conducted using the chi-square test, and the results were presented as frequencies and percentages. Statistical significance was set at *P*<.05 (2-tailed). All the results were analyzed using STATA version 14.0 (Stata Corp), except the latent class models (LCMs) and assessment of internal validity of the DCE, which were analyzed using Lighthouse Studio version 9.12.1.

For the DCE, a mixed logit model (MXL) was first used to quantify the preferences of the respondents for the attributes and levels of an initial diagnosis of fever during COVID-19 in their trade-off in general. After using the MXL, we dummy-coded all the attribute levels, with the levels with the lowest model parameter $\beta$ as the reference level in each attribute, by which we could enhance the interpretation of the preference weights by specifying the difference between 2 random coefficients.

PSM was performed to minimize the confounding bias of respondents from the United States and China that arose from the discrepancy of the demographic characteristics in both groups [38]. Specifically, the covariates were identified through the pairwise Pearson correlation matrix, and the final set of covariates for PSM was decided by minimizing the residual confounding factors as much as possible, where a logistic regression model was conducted to estimate the propensity scores for each group of respondents. Later, we conducted 1-to-1 matching without replacement so that a candidate respondent in the United States could be matched to only 1 respondent in China, after which the distribution of the covariates between the 2 groups would be the same [43]. Finally, a total of 2480 respondents, with 1240 (50%) from China and the other half from the United States, were matched from the total 9112 respondents, with the covariates being sex, age, occupation, educational level, and annual income. The flowchart of the PSM is shown in Multimedia Appendix 3, Figure S1.

The MXL was used to quantify the preference importance and weights of the various attributes of the DCE in the respondents' trade-offs. Additionally, the utility that the coefficients and SD used measured the levels of each attribute. The attribute cost was transformed into a continuous variable. Other parameters were assigned with a normal distribution, and we generated 1000 Halton draws for each population. We assumed that the attribute levels with *P*<.05 were statistically significant. We calculated each attribute preference's general estimated weight to identify its importance. The formula is:

$$\text{Weighted importance} = \text{Coefficient of attribute X/Sum of coefficients of all attributes except the cost attribute}$$

LCMs were used to explore the preference heterogeneity among the populations from the United States and China; this study also presented an LCM analysis, which divided the respondent population from the United States and China into a fixed proportion. Moreover, the number of latent groups was identified using the Akaike information criterion (AIC) and the Bayesian information criterion (BIC) [44]. In this study, 3 groups of the respondent population from China and 3 from the United States were identified and included in further research. In the study [45], we compared the models with 2-5 classes according to the AIC, the BIC, and the consistency information criterion (CAIC). Multimedia Appendix 3, Tables S3 and S4, show the AIC, BIC, and CAIC values of different classes in China and the United States.

The willingness to pay (WTP) is a measure used to capture the upper limit of the amount of money that people are willing to sacrifice to obtain the benefits of a particular medical service, diagnosis, and treatment plan—that is, the highest amount of money that respondents were willing to sacrifice when they chose their preferred diagnosis and treatment service in this study. Our study analyzed the WTP of the respondents to determine the homogeneity or heterogeneity caused by the cost in the choice of treatment options. We estimated the WTP:

$$\text{WTPx} = (\text{vx}_1 - \text{vx}_0)/{-\beta_{\text{cost}}},$$

where $\beta_{\text{cost}}$ is the coefficient on the cost parameter and $\text{vx}_0$ and $\text{vx}_1$ are the coefficient before and after a change in the level of attribute x, respectively. For each reference attribute, $\text{vx}_0$ was considered 0.

### Ethical Considerations

The respondents provided informed consent before filling in the questionnaire and agreed to participate in screening and to the use and publication of their data in journal papers. The questionnaire was completely anonymous, and the answers were protected by privacy law. During the process of filling in the questionnaire, all respondents could withdraw from the survey at any time. The study was conducted according to the guidelines of the 1964 Declaration of Helsinki and was approved by the Jinan University Medical Ethics Committee (JNUKY-2021-004). All procedures performed involving human respondents were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

## Results

### Data Acquisition and Demographic Characteristics

A total of 9112 respondents from China and the United States were included in the final analysis, the demographic characteristics of whom are shown in Table 2. Of these respondents, 5411 (59.4%) respondents were from China and 3701 (40.6%) respondents were from the United States. After PSM, 1240 (22.9%) respondents from China and 1240 (33.5%) from the United States were matched, and no apparent differences were found between the 2 groups of respondents (*P*>.05 for all sociodemographic factors), as shown in Table 2.

After PSM, of the 1240 respondents from China, 1188 (95.8%) were between 18 and 60 years old and 706 (56.9%) were female. Of those from the United States, 1182 (95.3%) were between 18 and 60 years old, 705 (56.9%) were female, and 18 (1.5%) had a postgraduate degree.

**Table 2.** Demographic characteristics of nonmatched and propensity score–matched respondents from China and the United States (January-March 2021).

| Baseline matching characteristics | Nonmatched respondents | | Propensity score–matched respondents | |
|---|---|---|---|---|
| | China (n=5411), n (%) | United States (n=3701), n (%) | China (n=1240), n (%) | United States (n=1240), n (%) |
| **Sex (nonmatched *P*=.003; propensity score–matched *P*=.99)** | | | | |
| Male | 2400 (44.4) | 1765 (47.7) | 534 (43.1) | 535 (43.1) |
| Female | 2993 (55.3) | 1918 (51.8) | 706 (56.9) | 705 (56.9) |
| Other | 18 (0.3) | 18 (0.5) | 0 | 0 |
| **Age (nonmatched *P*<.001; propensity score–matched *P*=.99)** | | | | |
| 18-25 | 1127 (20.8) | 501 (13.5) | 164 (13.2) | 162 (13.1) |
| 26-30 | 762 (14.1) | 762 (20.6) | 235 (19.0) | 234 (18.9) |
| 31-35 | 704 (13.0) | 750 (20.3) | 244 (19.7) | 251 (20.2) |
| 36-40 | 490 (9.1) | 505 (13.6) | 152 (12.3) | 152 (12.3) |
| 41-45 | 520 (9.6) | 368 (9.9) | 139 (11.2) | 136 (10.9) |
| 46-50 | 632 (11.7) | 241 (6.5) | 105 (8.5) | 103 (8.3) |
| 51-55 | 434 (8.0) | 174 (4.7) | 89 (7.2) | 84 (6.8) |
| 56-60 | 349 (6.4) | 154 (4.2) | 60 (4.8) | 60 (4.8) |
| >60 | 393 (7.3) | 246 (6.7) | 52 (4.2) | 58 (4.7) |
| **Highest educational level (nonmatched *P*<.001; propensity score–matched *P*=.87)** | | | | |
| Preprimary education or primary school education | 404 (7.5) | 2 (0.1) | 1221 (98.5; nonpostgraduate) | 1222 (98.5; nonpostgraduate) |
| Middle school education | 596 (11.0) | 15 (0.4) | N/A[a] | N/A |
| High school education | 939 (17.4) | 675 (18.2) | N/A | N/A |
| Vocational school education | 896 (16.6) | 508 (13.7) | N/A | N/A |
| Bachelor's degree | 2027 (37.5) | 1710 (46.2) | N/A | N/A |
| Master's degree | 428 (7.9) | 711 (19.2) | N/A | N/A |
| PhD | 121 (2.2) | 80 (2.2) | 19 (1.5; postgraduate) | 18 (1.5; postgraduate) |
| **Occupation and working area (nonmatched *P*<.001; propensity score–matched *P*=.99)** | | | | |
| Students | 1238 (22.9) | 249 (6.7) | 139 (11.2) | 132 (10.6) |
| Managers | 685 (12.7) | 5419 (14.6) | 178 (14.4) | 174 (14.0) |
| Professionals | 775 (14.3) | 93 (2.5) | 250 (20.2) | 250 (20.2) |
| Technicians and associate professionals | 798 (14.8) | 423 (11.4) | 148 (11.9) | 157 (12.7) |
| Clerical support workers | 232 (4.3) | 318 (8.6) | 121 (9.8) | 122 (9.8) |
| Service and sales workers | 521 (9.6) | 453 (12.2) | 185 (14.9) | 188 (15.2) |
| Skilled agricultural, forestry, and fishery workers | 378 (7.0) | 43 (1.2) | 14 (1.1) | 14 (1.1) |
| Craft and related trade workers | 122 (2.3) | 78 (2.1) | 27 (2.2) | 28 (2.3) |
| Plant and machine operators and assemblers | 184 (3.4) | 32 (0.9) | 11 (0.9) | 11 (0.9) |
| Elementary occupations | 133 (2.5) | 75 (2.0) | 16 (1.3) | 14 (1.1) |
| Armed forces occupations | 73 (1.4) | 19 (0.5) | 6 (0.5) | 4 (0.3) |
| Other | 272 (5.0) | 477 (12.9) | 145 (11.7) | 146 (11.8) |
| **Annual salary level (US $; nonmatched *P*<.001; propensity score–matched *P*=.99)** | | | | |
| <10,000 | 2272 (48.1) | 398 (11.0) | 335 (27.0) | 333 (26.9) |
| 10,001-20,000 | 1232 (26.1) | 382 (10.6) | 257 (20.7) | 259 (20.9) |
| 20,001-30,000 | 564 (11.9) | 481 (13.3) | 236 (19.0) | 236 (19.0) |

| Baseline matching characteristics | Nonmatched respondents | | Propensity score–matched respondents | |
|---|---|---|---|---|
| | China (n=5411), n (%) | United States (n=3701), n (%) | China (n=1240), n (%) | United States (n=1240), n (%) |
| 30,001-40,000 | 297 (6.3) | 472 (13.1) | 192 (15.5) | 193 (15.6) |
| 40,001-50,000 | 164 (3.5) | 456 (12.6) | 91 (7.3) | 92 (7.4) |
| 50,001-60,000 | 55 (1.7) | 464 (12.8) | 41 (3.3) | 40 (3.2) |
| 60,001-70,000 | 47 (1.0) | 331 (9.2) | 23 (1.9) | 24 (1.9) |
| >70,000 | 94 (2.0) | 630 (17.4) | 65 (5.2) | 63 (5.1) |

[a] N/A: not applicable.

## General MXL Results

The comparison of relative attribute importance between China and the United States before and after PSM is shown in Figure 2. After PSM, respondents from China attached the most importance to the types of the medical institutions (39.9%), followed by the reimbursement rate (34.3%), and the waiting time was the least essential attribute (6.5%). For respondents from the United States, the reimbursement rate was the most important attribute (34.6%), followed by the waiting time (25.3%).

The MXL results depicting the levels of each attribute of respondents' preferences in China and the United States for an initial diagnosis of fever during the COVID-19 pandemic before and after PSM are shown in Tables 3 and 4, respectively. Respondents from China strongly preferred going to a fever clinic (utility coefficient=0.974) or the emergency department (utility coefficient=0.973) compared to a network consultation. In contrast, US respondents preferred private clinics (general practices) the most. The more negative correlation of cost for the Chinese respondents showed that they cared more about the cost than the US respondents did. In addition, both populations showed a similar preference for immediate COVID-19 nucleic acid tests with a high reimbursement rate, which indicates that people consistently prefer low-consumption treatment plans.

**Figure 2.** General estimated weighted importance of attribute preference in pre-PSM and PSM respondents in China and the United States (January-March 2021). PSM: propensity score matching.

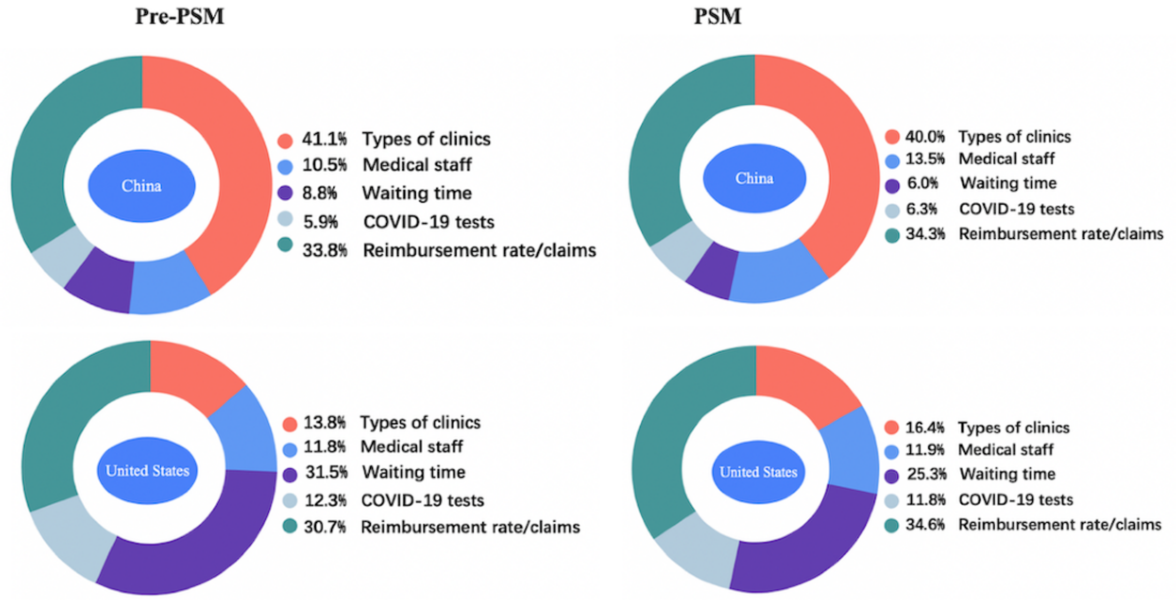


**Table 3.** Pre-PSM[a] results of the MLX[b] model of the preferences of respondents in China (N=5411) and the United States (N=3701) for initial diagnosis of fever during COVID-19 (January-March 2021).

| Attributes and levels | China | | | | The United States | | | |
|---|---|---|---|---|---|---|---|---|
| | Coefficient | SD | SE | *P* value | Coefficient | SD | SE | *P* value |
| **Mean** | | | | | | | | |
| Opt out (respondents chose neither of the two options) | –2.690 | 4.361 | 0.122 | <.001 | –2.344 | 4.134 | 0.136 | <.001 |
| **Types of clinics** | | | | | | | | |
| Online consultation | Reference | N/A[c] | N/A | N/A | Reference | N/A | N/A | N/A |
| Private clinic | 0.028 | 1.008 | 0.040 | .48 | 0.471 | 0.679 | 0.047 | <.001 |
| Telephone consultation | 0.292 | 0.364 | 0.036 | <.001 | 0.030 | 0.948 | 0.048 | .54 |
| Fever clinic | 1.124 | 1.103 | 0.045 | <.001 | 0.322 | 0.298 | 0.044 | <.001 |
| Emergency room | 1.011 | 0.804 | 0.043 | <.001 | 0.050 | 0.698 | 0.046 | .28 |
| **Medical staff** | | | | | | | | |
| Paramedic | Reference | N/A | N/A | N/A | Reference | N/A | N/A | N/A |
| Nurse | 0.127 | 0.245 | 0.027 | <.001 | 0.209 | 0.209 | 0.033 | <.001 |
| Doctor | 0.499 | 0.785 | 0.030 | <.001 | 0.533 | 0.732 | 0.038 | <.001 |
| **Waiting time (minutes)** | | | | | | | | |
| 75 | Reference | N/A | N/A | N/A | Reference | N/A | N/A | N/A |
| 0 | 0.172 | 0.509 | 0.041 | <.001 | 0.631 | 0.635 | 0.053 | <.001 |
| 15 | 0.175 | 0.388 | 0.041 | <.001 | 0.530 | 0.395 | 0.051 | <.001 |
| 30 | 0.093 | 0.477 | 0.041 | .02 | 0.431 | 0.415 | 0.051 | <.001 |
| 45 | 0.055 | 0.280 | 0.041 | .18 | 0.260 | 0.305 | 0.051 | <.001 |
| 60 | 0.030 | 0.182 | 0.040 | .46 | 0.140 | 0.349 | 0.051 | .006 |
| **COVID-19 nucleic acid testing** | | | | | | | | |
| No | Reference | N/A | N/A | N/A | Reference | N/A | N/A | N/A |
| Yes | 0.350 | 0.899 | 0.024 | <.001 | 0.774 | 1.111 | 0.037 | <.001 |
| **Reimbursement ratio (%)** | | | | | | | | |
| 0 | Reference | N/A | N/A | N/A | Reference | N/A | N/A | N/A |
| 20 | 0.130 | 0.377 | 0.041 | .002 | 0.029 | 0.431 | 0.051 | .56 |
| 40 | 0.187 | 0.338 | 0.041 | <.001 | 0.176 | 0.194 | 0.049 | <.001 |
| 60 | 0.340 | 0.054 | 0.041 | <.001 | 0.346 | 0.137 | 0.050 | <.001 |
| 80 | 0.584 | 0.523 | 0.042 | <.001 | 0.560 | 0.591 | 0.052 | <.001 |
| 100 | 0.776 | 0.928 | 0.045 | <.001 | 0.825 | 1.119 | 0.057 | <.001 |
| Cost | –6.53 | 2.05 | 0.190 | <.001 | –5.74 | 1.78 | 0.144 | <.001 |

[a] PSM: propensity score matching.

[b] MXL: mixed logit model.

[c] N/A: not applicable.

**Table 4.** Post-PSM[a] results of the MLX[b] model of the preferences of respondents in China (N=1240) and the United States (N=1240) for initial diagnosis of fever during COVID-19 (January-March 2021).

| Attributes and levels | China | | | | The United States | | | |
|---|---|---|---|---|---|---|---|---|
| | Coefficient | SD | SE | *P* value | Coefficient | SD | SE | *P* value |
| **Mean** | | | | | | | | |
| Opt out (respondents chose neither of the two options) | –2.663 | 4.066 | 0.245 | <.001 | –2.045 | 4.550 | 0.239 | <.001 |
| **Types of clinics** | | | | | | | | |
| Online consultation | Reference | N/A[c] | N/A | N/A | Reference | N/A | N/A | N/A |
| Private clinic | 0.054 | 1.054 | 0.084 | .52 | 0.543 | 0.854 | 0.091 | <.001 |
| Telephone consultation | 0.208 | 0.181 | 0.076 | .01 | 0.070 | 1.131 | 0.093 | .45 |
| Fever clinic | 0.974 | 1.140 | 0.096 | <.001 | 0.434 | 0.581 | 0.087 | <.001 |
| Emergency room | 0.973 | 0.757 | 0.091 | <.001 | 0.069 | 0.931 | 0.090 | .44 |
| **Medical staff** | | | | | | | | |
| Paramedic | Reference | N/A | N/A | N/A | Reference | N/A | N/A | N/A |
| Nurse | 0.136 | 0.151 | 0.056 | .02 | 0.237 | 0.496 | 0.064 | <.001 |
| Doctor | 0.609 | 0.981 | 0.070 | <.001 | 0.570 | 0.838 | 0.074 | <.001 |
| **Waiting time (minutes)** | | | | | | | | |
| 75 | Reference | N/A | N/A | N/A | Reference | N/A | N/A | N/A |
| 0 | 0.144 | 0.566 | 0.087 | .10 | 0.136 | 0.875 | 0.095 | .16 |
| 15 | 0.154 | 0.643 | 0.088 | .08 | 0.136 | 0.535 | 0.099 | .17 |
| 30 | 0.032 | 0.254 | 0.085 | .71 | 0.397 | 0.176 | 0.097 | <.001 |
| 45 | -0.017 | 0.439 | 0.087 | .85 | 0.401 | 0.665 | 0.097 | <.001 |
| 60 | 0.020 | 0.357 | 0.086 | .82 | 0.649 | 0.063 | 0.103 | <.001 |
| **COVID-19 nucleic acid testing** | | | | | | | | |
| No | Reference | N/A | N/A | N/A | Reference | N/A | N/A | N/A |
| Yes | 0.348 | 0.902 | 0.051 | <.001 | 0.801 | 1.126 | 0.069 | <.001 |
| **Reimbursement ratio (%)** | | | | | | | | |
| 0 | Reference | N/A | N/A | N/A | Reference | N/A | N/A | N/A |
| 20 | 0.103 | 0.540 | 0.089 | .25 | 0.107 | 0.843 | 0.100 | .28 |
| 40 | 0.198 | 0.429 | 0.087 | .02 | 0.310 | 0.364 | 0.096 | .001 |
| 60 | 0.286 | 0.217 | 0.085 | .001 | 0.449 | 0.146 | 0.096 | <.001 |
| 80 | 0.566 | 0.513 | 0.089 | <.001 | 0.549 | 0.885 | 0.100 | <.001 |
| 100 | 0.742 | 1.037 | 0.098 | <.001 | 0.935 | 0.994 | 0.108 | <.001 |
| Cost | –6.81 | 1.98 | 0.37 | <.001 | –5.52 | 1.86 | 0.196 | <.001 |

[a] PSM: propensity score matching.

[b] MXL: mixed logit model.

[c] N/A: not applicable.

## Willingness-to-Pay Results

A WTP greater than 0 indicates that the WTP can ensure a change in the reference level, while a WTP less than 0 indicates the patients are willing to pay to avoid a change in the reference level. Through the analysis, it was evident that the Chinese respondents preferred hospital emergency and fever clinics, for which they were willing to pay US $0.14 (reference level: online consultation US $0) and US $0.14 (reference level: online consultation US $0) to receive services from these 2 types of medical institutions. At the same time, they are willing to pay US $0.09 (reference level: paramedic US $0) for the treatment provided by doctors. Compared to the WTP of the respondents from China, the respondents from the United States were more willing to pay US $0.10 (reference level: online consultation US $0) and US $0.08 (reference level: online consultation US

$0) for treatment in private hospitals and fever clinics, revealing a preference discrepancy with China. Both US and Chinese respondents were willing to pay US $0.15 and US $0.05 for immediate COVID-19 nucleic acid testing (Tables 5 and 6). They were willing to pay a certain amount for a shorter waiting time and a higher reimbursement rate, indicating that a diagnosis service with an immediate COVID-19 nucleic acid test, shorter waiting time, and lower cost is more acceptable for respondents. Specifically, the interaction test indicated that cost and reimbursement rate have a significant interaction. This indicates that the effects of choice obtained with the 2 attributes vary together (Multimedia Appendix 3, Tables S5-S8).

**Table 5.** Respondents' WTP[a] in China (January-March 2021).

| Attribute and change | WTP (US $) |
|---|---|
| **Types of clinics** | |
| Online consultation–private clinic | 0.01 |
| Online consultation–telephone consultation | 0.03 |
| Online consultation–fever clinic | 0.14 |
| Online consultation–the emergency room | 0.14 |
| **Medical staff** | |
| Paramedic-nurse | 0.02 |
| Paramedic-doctor | 0.09 |
| **Waiting time (minutes)** | |
| 75-0 | 0.02 |
| 75-15 | 0.02 |
| 75-30 | 0.00 |
| 75-45 | 0.00 |
| 75-60 | 0.00 |
| **COVID-19 nucleic acid testing** | |
| No-yes | 0.05 |
| **Reimbursement ratio (%)** | |
| 0-20 | 0.02 |
| 0-40 | 0.03 |
| 0-60 | 0.04 |
| 0-80 | 0.08 |
| 0-100 | 0.11 |

[a] WTP: willingness to pay.

**Table 6.** Respondents' WTP[a] in the United States (January-March 2021).

| Attribute and change | WTP (US $) |
|---|---|
| **Types of clinics** | |
| Online consultation–private clinic | 0.10 |
| Online consultation–telephone consultation | 0.01 |
| Online consultation–fever clinic | 0.08 |
| Online consultation–the emergency room | 0.01 |
| **Medical staff** | |
| Paramedic-nurse | 0.04 |
| Paramedic-doctor | 0.10 |
| **Waiting time (minutes)** | |
| 75-0 | 0.02 |
| 75-15 | 0.02 |
| 75-30 | 0.07 |
| 75-45 | 0.07 |
| 75-60 | 0.12 |
| **COVID-19 nucleic acid testing** | |
| No-yes | 0.15 |
| **Reimbursement ratio (%)** | |
| 0-20 | 0.02 |
| 0-40 | 0.06 |
| 0-60 | 0.08 |
| 0-80 | 0.10 |
| 0-100 | 0.17 |

[a] WTP: willingness to pay.

## LCM Results

After comparing the AIC and BIC, we determined 3 classes for respondents from China and 3 for those from the United States. The segmented sizes of the 3 classes of respondents from China were 870 (70.2%), 270 (21.8%), and 100 (8.0%), respectively. The US respondents' segmented sizes were 269 (21.7%), 139 (11.2%), and 832 (67.1%), respectively.

Figure 3 shows the heterogeneities of attribute importance of different classes of respondents from China and the United States, and Figure 4 shows preference weights stratified by group and class. Class 1 of respondents from China ranked reimbursement rate and claims as the first important attribute, while classes 2 and 3 thought that the importance of the types of clinics is the most critical factor affecting their medical preference. Meanwhile, classes 1 and 3 of respondents from China considered the waiting time the least important, while class 2 of respondents from China ranked the immediate COVID-19 test as the least important attribute.

For the classes of respondents from the United States, classes 1 and 2 ranked cost as the first important attribute, while class 3 attached the most importance to the reimbursement rate and claims. For these 3 classes of respondents from the United States, the least important attributes were waiting time, types of staff, and types of clinics, respectively. Cost had overwhelming importance in class 2 compared to the other 2 classes.

**Figure 3.** Weighted importance of diagnosis attributes in China and the United States, as determined by the LCM (January-March 2021). LCM: latent class model.

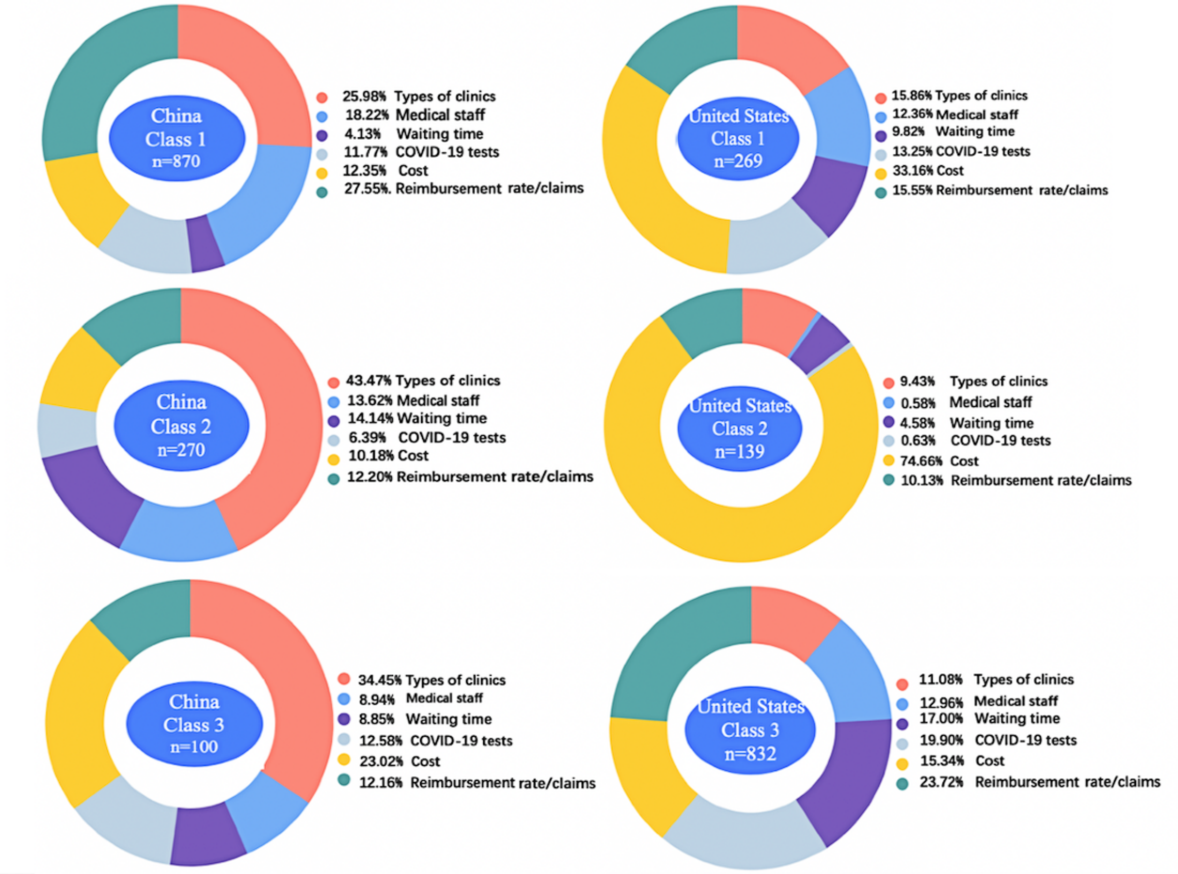
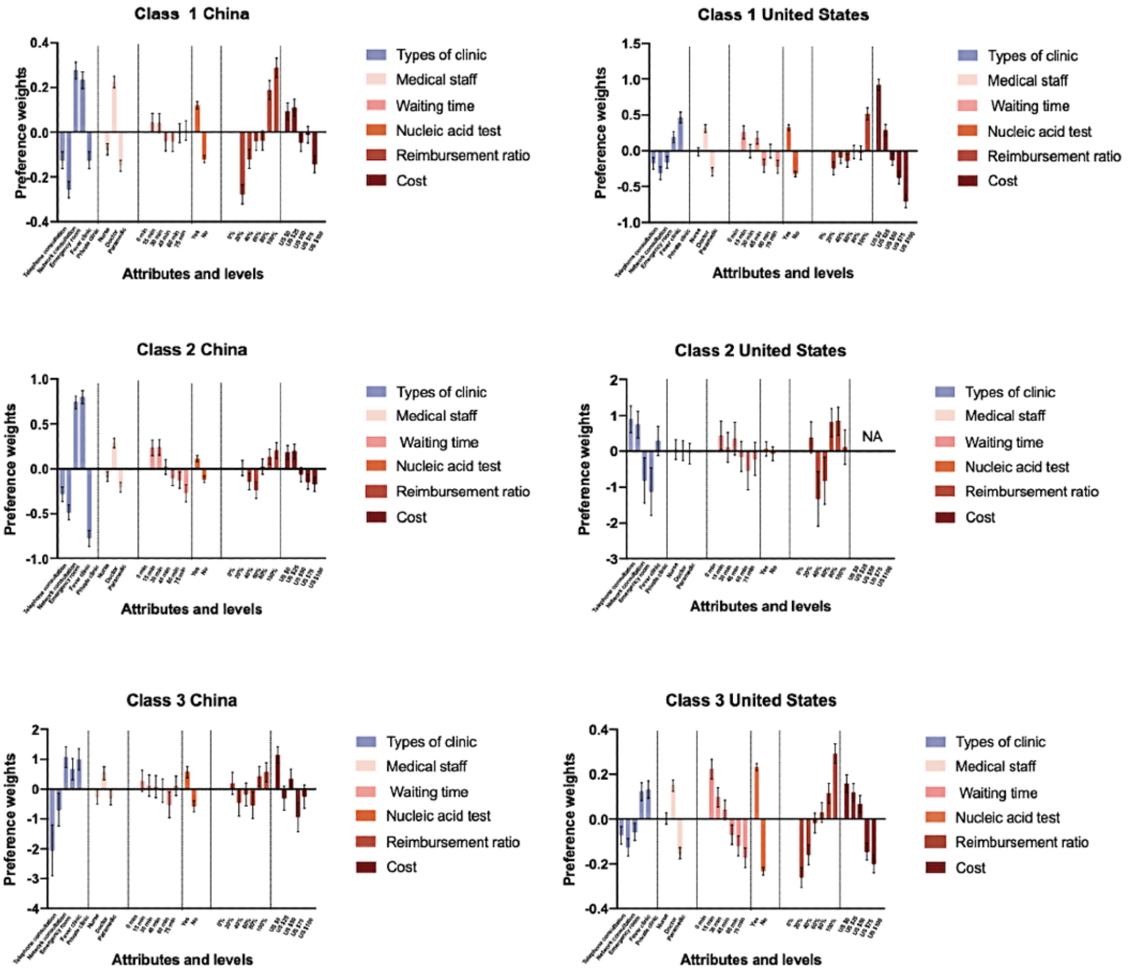


**Figure 4.** Preference weights stratified by group and class in China and the United States (January-March 2021).



# Discussion

## Principal Findings

The study found that respondents from China and the United States had distinctly different preferences for attributes regarding the initial diagnosis of fever during the COVID-19 pandemic. Types of medical institutions were the most important factor for Chinese respondents, while those from the United States thought that cost was the most important factor when seeking medical services for fever during the pandemic. In addition, both populations highlighted the importance of the reimbursement rate. These heterogeneities and homogeneities may result from differences in the medical systems, health care services provided, COVID-19–mitigating strategies, and medical insurance systems between China and the United States.

## Comparison With Prior Work

DCEs can be used to understand people's underlying psychological situations, and the influencing factors and weights of choice preferences can be obtained through the hypothetical medical choice [46]. DCEs are also widely used in a series of aspects such as epidemic prevention, control, and supervision [47-49]. To the best of our knowledge, this is the first study to explore the preferences for health care services for the initial diagnosis of patients with fever during the COVID-19 pandemic. Our previous work found that respondents in China had a rather considerable basic knowledge of the detection methods of SARS-CoV-2 and the types of testing kits, even if they have no experience in contracting the virus or undergoing screening tests [50]. Nevertheless, considering that during the pandemic, everyone in China seeking health care services for fever, together with those accompanying them, would be screened by the SARS-CoV-2 nucleic acid test [51], the Chinese respondents placed the least importance on the necessity of immediate nucleic acid tests, while for the US respondents, COVID-19 tests accounted for 12.3% of the relative importance.

According to Caldow et al [52], patients prefer medical services provided by doctors, which is consistent with our results that doctors are preferred over nurses and paramedics for diagnosing fever [52]. During the pandemic, to relieve the consultation pressure of fever clinics in hospitals and prevent cross-infection, online fever clinics, an internet-based clinic system, were utilized in China, where a study enrolling more than 60,000 patients found that online fever clinics may efficiently ease patients' worry and clinicians can educate patients who are suspected of having COVID-19 to isolate and protect themselves [53]. Online and telephone consultation services have the characteristics of convenience and rapidity and can transcend distances to achieve preliminary medical services. In the case of future outbreaks, public health guidelines and policymaking may incorporate these 2 services into the first step of medical services to quickly divert different patients to curb the population contact transmission of infectious diseases. Although the respondents did not readily choose and prefer online clinics, Zhao et al [54] found that during the pandemic, many patients had trouble obtaining offline health care services and relied heavily on the internet for health information [54].

### China and the United States Hold Distinctly Different Organization and Governance of the Health System

Chinese respondents regarded the medical institution type as the most important preference factor, especially public medical institutions, while respondents from the United States preferred private medical institutions, as shown in Table 4. The phenomenon may be attributable to the different medical and health service systems of China and the United States [55].

In China, health care providers include hospitals, primary health care institutions, and specialized public health institutions, where government-owned public hospitals and health institutions remain dominant in providing health care services, accounting for around 60% of all hospitals [56]. Nevertheless, the US health care system is more a combination of multiple systems operating individually but synergically, where nongovernment entities play a vital role in building the industry standard, fostering health accessibility, improving the quality of life, and controlling costs at various levels. With more than 6000 hospitals registered in the United States, only about 200 hospitals are owned by the federal government. The majority (more than 5000) of the hospitals are community hospitals, which include nonfederal hospitals, short-term general hospitals, and other special hospitals [57].

In this sense, it would be reasonable to assume that Chinese citizens would choose government-owned health institutions, while US citizens would prefer private-owned hospitals, which corresponds to the notion that government-owned hospitals predominate in China and community hospitals prevail in the United States. This fact consistently correlates with our results in Table 3, which show that Chinese respondents preferred fever clinics (designated public hospitals specializing in managing feverish patients during the pandemic), while the US respondents tended to choose private clinics.

According to LCM results, all respondents (from both China and the United States) were more willing to accept the diagnosis and treatment scheme with immediate nucleic acid testing, lower treatment costs, and higher reimbursement rates. In the LCM results, class 3 in China showed a preference for private medical institutions, and class 2 in the United States was more willing to receive telephone consultations than to travel to medical institutions; these findings differed from the overall performances of the Chinese and US groups.

Since the health system reform was enacted in 2009, more private-owned hospitals and health institutions have been established to provide the general population with equal access to basic health care [58-60]. According to a report by the China Statistical Information Center, from January to February 2021, the outpatient volume in China reached 960 million people, including 510 million in public hospitals and 90 million in private hospitals [61].

Despite its uneven distribution of medical resources in urban and rural areas, China is gradually beginning to promote internet hospitals. Telephone and online consultations have grown rapidly during the COVID-19 pandemic. Internet hospitals enable patients to consult doctors from large university-affiliated public hospitals for treatment through other internet hospitals [62]. During the pandemic, the application of internet hospitals in China, together with a remote drug delivery platform, has helped maintain constant health care services and provide for those in need, specifically those with chronic and mild diseases. This has been considered a potent tool to optimize medical resource distribution by relieving offline hospitals and catering to those in need without contracting the virus [63].

However, telephone and online consultations are still in their early stage of development. Because of the lack of standardized diagnosis and treatment standards, poor operation, and management issues, these 2 consultation schemes cannot wholly replace the conventional diagnostic process. Compared to traditional face-to-face medical schemes, the number of patients they serve is still small [64-66]. Nevertheless, the low selection rate of these 2 consultation modes may be attributable to the respondents having no idea of how these 2 types of consultation work and how they provide health care services [67].

COVID-19 is inherently not a disease that can solely be diagnosed via symptoms and signs, and the internet hospital is still in its exploration stage, where various issues remain unsolved. Thus, not being preferred does not necessarily mean that the internet hospital is suboptimal in guiding patients toward effective medical treatment.

### Distinctly Different Financing Methods for Health Care Services in China and the United States

Additionally, for respondents from the United States, cost was the most important factor affecting preference. This may be caused by the differences in the treatment costs and medical reimbursement systems in China and the United States.

In the United States, only around 30% of the population is covered by the public financing system, mainly via Medicare and Medicaid, and around 54% of the population receives private health insurance [68]. Nevertheless, one-sixth of Americans are uninsured, and high out-of-pocket expenditure still may put a heavy burden on some of those receiving insurance, hindering timely health care and medications.

Nevertheless, in China, the Information Office of the State Council of the People's Republic of China announced that the cost of COVID-19 in China would be covered by the national free treatment policy [69,70]. Therefore, it is reasonable that the respondents from China do not attach the maximum importance to the cost of diagnosis and treatment is the most important factor. This may be due to the national free treatment policy, which helps eliminate the burden of treatment costs on the public.

COVID-19 patients with severe and nonsevere complications were admitted to hospitals at an average cost of US $20,292 according to data provided by the Kaiser Family Foundation in the United States, and this is about 8.5 times the average cost in China. At the same time, although there is a medical insurance system in the United States, even after Medicare reimbursement, the average out-of-pocket expenses of patients may exceed US $1300 [71]. Experts have recommended that new federal legislation should be established to expend federal funds on emergency responses, hiring and training of personnel, and distribution of diagnostic tests, therapeutic approaches, and vaccines at different levels and, most importantly, to expand the coverage rate of medical insurance for diagnosing, treating, and following up patients with COVID-19 [72]. During COVID-19, a wide range of previously unavailable telehealth services were covered by Medicare and Medicaid, allowed by the Section 1135 waiver in the United States [73]. Moreover, the havoc COVID-19 caused on the economy resulted in a 15% unemployment rate in May 2020 [74], which increased the rate of the uninsured and enrollment in Medicaid, and hence some have addressed the need to put forward “Medicare for All” [75]. Nevertheless, scholars have addressed that ensuring effective government action with sensible private sector regulation may be a preferable option over turning to insurance to pay for COVID-19–related medical costs [76]. Generally, we believe that both expanding the coverage of insurance to those uninsured or with low insurance for COVID-19–related health care costs and ensuring the federal mandate for free access to COVID-19 testing and treatment can effectively motivate those potentially infected to undergo testing and proper treatments.

### Encouraging Undiagnosed Patients to Test for COVID-19 is Important for Curbing the Pandemic

Identification, tracing, and isolation of those infected are vital for containing the community spread of COVID-19. Nevertheless, if those infected remain untested and no universal nucleic test programs are conducted, then the infected citizens may still be constantly spreading the virus in the community. Therefore, identifying potential COVID-19–infected patients in the community and encouraging them to undergo testing and quarantine is important for curbing COVID-19 spread in the community.

In China, large-scale community nucleic acid testing can be implemented to identify potentially infected people due to the state's attitude toward early diagnosis, early isolation, and early treatment of COVID-19. The willingness of the public to participate in screening tests depends on their awareness of the risks and benefits. The governmental entities stipulate that residents in controlled areas must participate in community nucleic acid testing and those who do not participate without good cause may suffer legal consequences and difficulties in daily life [51]. This is in line with the general policy of “dynamic zero COVID-19 strategies” for preventing and controlling the former COVID-19 pandemic in China [77].

For the United States and other noncentralized countries where large-scale community-wide mass screening tests are difficult to implement, it is difficult to identify those infected in the community unless they undergo screening tests voluntarily. However, some people still avoid nucleic acid testing as they are afraid of testing positive for the disease and other factors [78]. Although the Centers for Disease Control and Prevention (CDC) and other institutions have issued a series of guidelines on coping with COVID-19 [79], according to Park et al [80], the psychological pressure of contracting COVID-19 may reduce the rate of public compliance with official health guidelines. Therefore, it is recommended that the public be encouraged to participate in screening tests, either nucleic acid tests or antigen tests, in a number of ways, including broadcasting public messages by medical and health experts, providing information on social media, and distributing small gifts to those who participate in testing, to make every resident aware of the importance and obligation of nucleic acid screening [81,82]. Improving the participation rate in those screening, testing, and detecting of those infected may help control the spread of COVID-19. We advocate the use of publicity campaigns in the media, the spread of rigorous scientific information, the promotion of culturally sensitive psychological counseling, and other related services to account for different needs and to encourage the public to be willing to participate in screening tests. Regarding the stigma and discrimination related to being diagnosed as COVID-19 positive, it is necessary to provide social support to relieve the potential stigma and social unrest. To make this possible, multidisciplinary teams comprising experts from clinics, social sciences, government entities, communication, and the media are needed [83].

## Limitations

There are limitations of our research. First, the nature of this cross-sectional study inherently led to reporting bias, information bias, and confounding bias. In the study, we used a closed-end, self-administered questionnaire to prevent missed data and used online an panel platform (MTurk) to prevent selection bias, as a previous study proved the census-level quality of survey data collected via MTurk [61,84]. Nevertheless, selection bias may still exist. PSM was used to control the confounding effects when directly comparing the 2 cohorts of respondents. However, as various factors may underlie the respondents' decision-making in the 2 distinctly different countries, the scale differences may not be completely accounted for, and the results should be interpreted with caution. Moreover, as the DCE asked participants to make choices between hypothetical scenarios, which may not reflect real-world situations and hypothetical bias may exist, and we did not investigate external validity in the study, the results of the study should be interpreted cautiously. Our questionnaire involves the treatment modes of telephone and online consultations, which some respondents may not have experienced and may have led to selection bias. Moreover, we did not include questions on past experience with online/telephone consultation as well as previous experience with COVID-19 testing or treatment, so how such underlying factors may influence preferences could not be distinguished and need future exploration. In addition, we did not include the investigation of how different ethnicities and residence locations (urban and rural) may affect the respondents' preferences, which can be further explored in a future study. The significant interactions between cost and reimbursement rate render interpreting these 2 attributes difficult, so the WTP should be interpreted cautiously.

## Conclusion

Improvements in the availability of COVID-19 testing, medical professional skills, and designated health care facilities may help boost potential health care seeking during COVID-19 and prevent unrecognized community spread of SARS-CoV-2 in China and the United States. Moreover, to better prevent future waves of pandemics, identify undiagnosed patients, and encourage them to seek health care services to curb the pandemic, it is suggested that the hierarchical diagnosis and treatment system be improved in China and that the United States focus on reducing medical costs and raising the reimbursement rate of medical insurance. Second, online and telephone consultations may serve as patients' primary medical services, which may triage suspected and nonsuspected patients of infectious diseases, reducing the possible cross-infection during the pandemic.

## Authors' Contributions

YZ, TL, and W-KM were responsible for conceptualization and investigation; YZ, TL, ZH, and W-KM for methodology; YZ for visualization; W-KM for supervision; YZ and TL for writing—original draft preparation; and YZ, TL, ZH, W-KM, CSN, JH, BOA, and CJPZ for writing—review and editing. CJPZ (casperz1@connect.hku.hk) is co-corresponding author. All authors have read and agreed to the published version of the manuscript.

## Conflicts of Interest

None declared.

Multimedia Appendix 1
DCE questionnaires in English.
[PDF File (Adobe PDF File), 3043 KB - publichealth_v8i8e37422_app1.pdf ]

Multimedia Appendix 2
DCE questionnaires in Chinese.
[PDF File (Adobe PDF File), 3162 KB - publichealth_v8i8e37422_app2.pdf ]

Multimedia Appendix 3
The new version of appendix for the manuscript .
[DOCX File , 142 KB - publichealth_v8i8e37422_app3.docx ]

## References

1. 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] [Medline: 31986264]
2. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. URL: https://covid19.who.int/ [accessed 2021-09-01]
3. Habas K, Nganwuchu C, Shahzad F, Gopalan R, Haque M, Rahman S, et al. Resolution of coronavirus disease 2019 (COVID-19). Expert Rev Anti Infect Ther 2020 Dec;18(12):1201-1211. [doi: 10.1080/14787210.2020.1797487] [Medline: 32749914]
4. 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] [Medline: 31994742]
5. Chotpitayasunondh T, Fischer TK, Heraud J, Hurt AC, Monto AS, Osterhaus A, et al. Influenza and COVID-19: what does co-existence mean? Influenza Other Respir Viruses 2021 May;15(3):407-412 [FREE Full text] [doi: 10.1111/irv.12824] [Medline: 33128444]
6. World Health Organization. Coronavirus Disease (COVID-19): Similarities and Differences with Influenza. URL: https://tinyurl.com/3kjb63kx [accessed 2021-09-01]
7. Sakurai A, Sasaki T, Kato S, Hayashi M, Tsuzuki S, Ishihara T, et al. Natural history of asymptomatic SARS-CoV-2 infection. N Engl J Med 2020 Aug 27;383(9):885-886 [FREE Full text] [doi: 10.1056/NEJMc2013020] [Medline: 32530584]
8. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, China Novel Coronavirus Investigating Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020 Feb 20;382(8):727-733 [FREE Full text] [doi: 10.1056/NEJMoa2001017] [Medline: 31978945]
9. Mercer TR, Salit M. Testing at scale during the COVID-19 pandemic. Nat Rev Genet 2021 Jul 04;22(7):415-426 [FREE Full text] [doi: 10.1038/s41576-021-00360-w] [Medline: 33948037]
10. Yang B, Tsang TK, Gao H, Lau EHY, Lin Y, Ho F, et al. Universal community nucleic acid testing for COVID-19 in Hong Kong reveals insights into transmission dynamics: a cross-sectional and modelling study. Clin Infect Dis 2021 Oct 28:ciab925. [doi: 10.1093/cid/ciab925] [Medline: 34718464]

11. Hartley DM, Perencevich EN. Public health interventions for COVID-19: emerging evidence and implications for an evolving public health crisis. JAMA 2020 May 19;323(19):1908-1909. [doi: 10.1001/jama.2020.5910] [Medline: 32275299]
12. Jernigan DB, CDC COVID-19 Response Team. Update: public health response to the coronavirus disease 2019 outbreak - United States, February 24, 2020. Morb Mortal Wkly Rep 2020 Feb 28;69(8):216-219 [FREE Full text] [doi: 10.15585/mmwr.mm6908e1] [Medline: 32106216]
13. 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] [Medline: 32275295]
14. Andersen RM, Rice TH, Kominski GF. Changing the U.S. Health Care System: Key Issues in Health Services Policy and Management, 3rd ed. San Francisco, CA: Jossey-Bass; 2007.
15. Andersen R, Davidson P. Improving Access to Care in America: Individual and Contextual Indicators. San Francisco, CA: Jossey-Bass; 2007:3-31.
16. Liu Y, Zhong L, Yuan S, van de Klundert J. Why patients prefer high-level healthcare facilities: a qualitative study using focus groups in rural and urban China. BMJ Glob Health 2018;3(5):e000854 [FREE Full text] [doi: 10.1136/bmjgh-2018-000854] [Medline: 30258653]
17. Onchonga D, Alfatafta H, Ngetich E, Makunda W. Health-seeking behaviour among pregnant women during the COVID-19 pandemic: a qualitative study. Heliyon 2021 Sep;7(9):e07972 [FREE Full text] [doi: 10.1016/j.heliyon.2021.e07972] [Medline: 34541362]
18. Villa S, Jaramillo E, Mangioni D, Bandera A, Gori A, Raviglione MC. Stigma at the time of the COVID-19 pandemic. Clin Microbiol Infect 2020 Nov;26(11):1450-1452 [FREE Full text] [doi: 10.1016/j.cmi.2020.08.001] [Medline: 32777361]
19. Lin W, Zhang X, Song H, Omori K. Corrigendum to “Health information seeking in the Web 2.0 age: trust in social media, uncertainty reduction, and self-disclosure” [Computers in Human Behavior 56 (2016) 289–294]. Comput Hum Behav 2016 Aug;61:690. [doi: 10.1016/j.chb.2016.01.040]
20. Skarpa PE, Garoufallou E. Information seeking behavior and COVID-19 pandemic: a snapshot of young, middle aged and senior individuals in Greece. Int J Med Inform 2021 Jun;150:104465. [doi: 10.1016/j.ijmedinf.2021.104465] [Medline: 33887589]
21. Lambert SD, Loiselle CG. Health information seeking behavior. Qual Health Res 2007 Oct;17(8):1006-1019. [doi: 10.1177/1049732307305199] [Medline: 17928475]
22. Blumenthal D, Fowler EJ, Abrams M, Collins SR. Covid-19 - implications for the health care system. N Engl J Med 2020 Oct 08;383(15):1483-1488. [doi: 10.1056/NEJMsb2021088] [Medline: 32706956]
23. Schneider EC. Failing the test - the tragic data gap undermining the U.S. pandemic response. N Engl J Med 2020 Jul 23;383(4):299-302. [doi: 10.1056/NEJMp2014836] [Medline: 32412704]
24. Chou Y, Yen Y, Chu D, Hu H. Impact of the COVID-19 pandemic on healthcare-seeking behaviors among frequent emergency department users: a cohort study. Int J Environ Res Public Health 2021 Jun 11;18(12):6351 [FREE Full text] [doi: 10.3390/ijerph18126351] [Medline: 34208194]
25. Westgard BC, Morgan MW, Vazquez-Benitez G, Erickson LO, Zwank MD. An analysis of changes in emergency department visits after a state declaration during the time of COVID-19. Ann Emerg Med 2020 Nov;76(5):595-601 [FREE Full text] [doi: 10.1016/j.annemergmed.2020.06.019] [Medline: 33008651]
26. Soekhai V, de Bekker-Grob EW, Ellis AR, Vass CM. Discrete choice experiments in health economics: past, present and future. Pharmacoeconomics 2019 Feb;37(2):201-226 [FREE Full text] [doi: 10.1007/s40273-018-0734-2] [Medline: 30392040]
27. Webb EJD, Meads D, Lynch Y, Judge S, Randall N, Goldbart J, et al. Attribute selection for a discrete choice experiment incorporating a best-worst scaling survey. Value Health 2021 Apr;24(4):575-584 [FREE Full text] [doi: 10.1016/j.jval.2020.10.025] [Medline: 33840436]
28. Marshall DA, Johnson FR, Kulin NA, Ozdemir S, Walsh JME, Marshall JK, et al. How do physician assessments of patient preferences for colorectal cancer screening tests differ from actual preferences? A comparison in Canada and the United States using a stated-choice survey. Health Econ 2009 Dec;18(12):1420-1439 [FREE Full text] [doi: 10.1002/hec.1437] [Medline: 19191268]
29. Quill TE, Arnold R, Back AL. Discussing treatment preferences with patients who want "everything". Ann Intern Med 2009 Sep 01;151(5):345-349. [doi: 10.7326/0003-4819-151-5-200909010-00010] [Medline: 19721022]
30. Cunningham CE, Deal K, Rimas H, Campbell H, Russell A, Henderson J, et al. Using conjoint analysis to model the preferences of different patient segments for attributes of patient-centered care. Patient 2008 Dec 01;1(4):317-330. [doi: 10.2165/1312067-200801040-00013] [Medline: 22272999]
31. Jouyani Y, Bahrampour M, Barouni M, Dehnavieh R. Patient preferences for hospital quality: case study of iran. Iran Red Crescent Med J 2013 Sep;15(9):804-808 [FREE Full text] [doi: 10.5812/ircmj.12851] [Medline: 24616790]
32. Hanson K, McPake B, Nakamba P, Archard L. Preferences for hospital quality in Zambia: results from a discrete choice experiment. Health Econ 2005 Jul;14(7):687-701. [doi: 10.1002/hec.959] [Medline: 15619273]
33. Johnson FR, Yang J, Reed SD. The internal validity of discrete choice experiment data: a testing tool for quantitative assessments. Value Health 2019 Feb;22(2):157-160 [FREE Full text] [doi: 10.1016/j.jval.2018.07.876] [Medline: 30711059]

34. Janssen EM, Marshall DA, Hauber AB, Bridges JFP. Improving the quality of discrete-choice experiments in health: how can we assess validity and reliability? Expert Rev Pharmacoecon Outcomes Res 2017 Dec;17(6):531-542. [doi: 10.1080/14737167.2017.1389648] [Medline: 29058478]
35. Whitty JA, Walker R, Golenko X, Ratcliffe J. A think aloud study comparing the validity and acceptability of discrete choice and best worst scaling methods. PLoS One 2014;9(4):e90635 [FREE Full text] [doi: 10.1371/journal.pone.0090635] [Medline: 24759637]
36. Shank DB. Using crowdsourcing websites for sociological research: the case of Amazon Mechanical Turk. Am Soc 2015 Mar 14;47(1):47-55. [doi: 10.1007/s12108-015-9266-9]
37. Chandler J, Shapiro D. Conducting clinical research using crowdsourced convenience samples. Annu Rev Clin Psychol 2016;12:53-81. [doi: 10.1146/annurev-clinpsy-021815-093623] [Medline: 26772208]
38. Liu T, He Z, Huang J, Yan N, Chen Q, Huang F, et al. A comparison of vaccine hesitancy of COVID-19 vaccination in China and the United States. Vaccines (Basel) 2021 Jun 14;9(6):649 [FREE Full text] [doi: 10.3390/vaccines9060649] [Medline: 34198716]
39. Hauser DJ, Schwarz N. Attentive Turkers: MTurk participants perform better on online attention checks than do subject pool participants. Behav Res Methods 2016 Mar 12;48(1):400-407. [doi: 10.3758/s13428-015-0578-z] [Medline: 25761395]
40. Park S, Boatwright B, Johnson Avery E. Information channel preference in health crisis: exploring the roles of perceived risk, preparedness, knowledge, and intent to follow directives. Public Relat Rev 2019 Dec;45(5):101794. [doi: 10.1016/j.pubrev.2019.05.015]
41. Huff C, Tingley D. “Who are these people?” Evaluating the demographic characteristics and political preferences of MTurk survey respondents. Res Politics 2015 Sep 10;2(3):205316801560464. [doi: 10.1177/2053168015604648]
42. de Bekker-Grob EW, Donkers B, Jonker MF, Stolk EA. Sample size requirements for discrete-choice experiments in healthcare: a practical guide. Patient 2015 Oct;8(5):373-384 [FREE Full text] [doi: 10.1007/s40271-015-0118-z] [Medline: 25726010]
43. He Z, Tang Y, Xie H, Lin Y, Liang S, Xu Y, et al. Economic burden of IADPSG gestational diabetes diagnostic criteria in China: propensity score matching analysis from a 7-year retrospective cohort. BMJ Open Diabetes Res Care 2020 Aug 26;8(1):e001538 [FREE Full text] [doi: 10.1136/bmjdrc-2020-001538] [Medline: 32847843]
44. Vrieze SI. Model selection and psychological theory: a discussion of the differences between the Akaike information criterion (AIC) and the Bayesian information criterion (BIC). Psychol Methods 2012 Jun;17(2):228-243 [FREE Full text] [doi: 10.1037/a0027127] [Medline: 22309957]
45. Katare B, Zhao S, Cuffey J, Marshall MI, Valdivia C. Preferences toward COVID-19 diagnostic testing features: results from a national cross-sectional survey. Am J Health Promot 2022 Jan;36(1):185-189. [doi: 10.1177/08901171211034093] [Medline: 34284644]
46. McGrady ME, Pai ALH, Prosser LA. Using discrete choice experiments to develop and deliver patient-centered psychological interventions: a systematic review. Health Psychol Rev 2021 Jun;15(2):314-332 [FREE Full text] [doi: 10.1080/17437199.2020.1715813] [Medline: 31937184]
47. Frimpong JA, Helleringer S. Strategies to increase downloads of COVID-19 exposure notification apps: a discrete choice experiment. PLoS One 2021;16(11):e0258945 [FREE Full text] [doi: 10.1371/journal.pone.0258945] [Medline: 34723981]
48. Homaie Rad E, Hajizadeh M, Yazdi-Feyzabadi V, Delavari S, Mohtasham-Amiri Z. How much money should be paid for a patient to isolate during the COVID-19 outbreak? A discrete choice experiment in Iran. Appl Health Econ Health Policy 2021 Sep;19(5):709-719 [FREE Full text] [doi: 10.1007/s40258-021-00671-3] [Medline: 34312818]
49. Krauth C, Oedingen C, Bartling T, Dreier M, Spura A, de Bock F, et al. Public preferences for exit strategies from COVID-19 lockdown in Germany: a discrete choice experiment. Int J Public Health 2021;66:591027 [FREE Full text] [doi: 10.3389/ijph.2021.591027] [Medline: 34744560]
50. Lan R, Sujanto R, Lu K, He Z, Zhang CJP, Ming W. Perceived effectiveness, safety, and attitudes toward the use of nucleic tests of SARS-CoV-2 among clinicians and general public in China. Front Public Health 2020 Dec 17;8:599862 [FREE Full text] [doi: 10.3389/fpubh.2020.599862] [Medline: 33392138]
51. Li Z, Liu F, Cui J, Peng Z, Chang Z, Lai S, et al. Comprehensive large-scale nucleic acid-testing strategies support China's sustained containment of COVID-19. Nat Med 2021 May 15;27(5):740-742. [doi: 10.1038/s41591-021-01308-7] [Medline: 33859409]
52. Caldow J, Bond C, Ryan M, Campbell NC, Miguel FS, Kiger A, et al. Treatment of minor illness in primary care: a national survey of patient satisfaction, attitudes and preferences regarding a wider nursing role. Health Expect 2007 Mar;10(1):30-45 [FREE Full text] [doi: 10.1111/j.1369-7625.2006.00422.x] [Medline: 17324193]
53. Li G, Fan G, Chen Y, Deng Z. What patients "see" doctors in online fever clinics during COVID-19 in Wuhan? J Am Med Inform Assoc 2020 Jul 01;27(7):1067-1071 [FREE Full text] [doi: 10.1093/jamia/ocaa062] [Medline: 32524147]
54. Zhao X, Fan J, Basnyat I, Hu B. Online health information seeking using "#COVID-19 patient seeking help" on Weibo in Wuhan, China: descriptive study. J Med Internet Res 2020 Oct 15;22(10):e22910 [FREE Full text] [doi: 10.2196/22910] [Medline: 33001838]
55. Chinese Academy of Social Sciences. Teaching You to Understand American Medical System. URL: http://www.casscppr.org/article/yiliaogaige/other/1683.html [accessed 2021-09-06]

56. National Health Commission of the People's Republic of China. 56. Notice on Issuing "Hospital Infection Management Standard (Trial)". URL: http://www.nhc.gov.cn/wjw/gfxwj/201304/3660a9b180ce4c49910f516b30d3768f.shtml [accessed 2021-09-06]
57. American Hospital Association. Fast Facts on U.S. Hospitals, 2022. URL: https://www.aha.org/statistics/fast-facts-us-hospitals [accessed 2022-07-12]
58. Ministry of Health. Health Statistics Yearbook 2012. URL: http://www.nhfpc.gov.cn/htmlfiles/zwgkzt/ptjnj/year2012/index2012.html [accessed 2022-07-12]
59. Ministry of Health. Health Statistics Yearbook 2013. URL: http://www.nhfpc.gov.cn/htmlfiles/zwgkzt/ptjnj/year2012/index2012.html [accessed 2022-07-12]
60. World Health Organization. People's Republic of China Health System Review. 2015. URL: https://apps.who.int/iris/handle/10665/208229 [accessed 2022-07-12]
61. Jensen-Doss A, Patel ZS, Casline E, Mora Ringle VA, Timpano KR. Using Mechanical Turk to study parents and children: an examination of data quality and representativeness. J Clin Child Adolesc Psychol 2022 Jan 15;51(4):428-442. [doi: 10.1080/15374416.2020.1815205] [Medline: 33448875]
62. Tu J, Wang C, Wu S. The internet hospital: an emerging innovation in China. Lancet Global Health 2015 Aug;3(8):e445-e446 [FREE Full text] [doi: 10.1016/S2214-109X(15)00042-X] [Medline: 26187488]
63. Ding L, She Q, Chen F, Chen Z, Jiang M, Huang H, et al. The internet hospital plus drug delivery platform for health management during the COVID-19 pandemic: observational study. J Med Internet Res 2020 Aug 06;22(8):e19678 [FREE Full text] [doi: 10.2196/19678] [Medline: 32716892]
64. "2020 Internet Hospital Report" Is Here!. URL: https://www.cn-healthcare.com/articlewm/20200805/content-1135596.html [accessed 2022-07-12]
65. 2021 China Internet Hospital Development Report. URL: https://inf.news/en/economy/ae10a366ea32aa6d07ee74d1ee162e7b.html [accessed 2022-07-12]
66. Telehealth: A Quarter-Trillion-Dollar Post-COVID-19 Reality?. URL: https://www.mckinsey.com/industries/healthcare-systems-and-services/our-insights/telehealth-a-quarter-trillion-dollar-post-covid-19-reality [accessed 2022-04-30]
67. Chen Q. How to Go Further in the Construction of Internet Hospitals in China. URL: https://epaper.gmw.cn/gmrb/html/2021-06/15/nw.D110000gmrb_20210615_3-02.htm [accessed 2022-07-12]
68. Rice T, Rosenau P, Unruh L, Barnes A, Saltman R, van Ginneken E. United States of America: health system review. Health Syst Transit 2013;15(3):1-431. [Medline: 24025796]
69. National Medical Insurance Bureau: Take the People as the Center, Effectively Guarantee the Medical Expenses of Patients. URL: http://www.xinhuanet.com/politics/2020-03/29/c_1125784154.htm [accessed 2022-07-12]
70. The State Council Information Office of the People's Republic of China. Fighting Covid-19: China in Action. URL: https://www.mfa.gov.cn/ce/cehr/eng/gdxw/t1786877.htm [accessed 2022-07-12]
71. New Analysis Finds Inpatient Coronavirus Treatment Costs Could Top $20K for Patients with Employer Coverage. URL: https://tinyurl.com/bf495zpu [accessed 2021-09-06]
72. No authors listed. Erratum for [Covid-19 - implications for the health care system. Blumenthal D, Fowler EJ, Abrams M, Collins SR. N Engl J Med. 2020 Oct 8;383(15):1483-1488]. N Engl J Med 2020 Oct 22;383(17):1698. [doi: 10.1056/NEJMx200018] [Medline: 32706957]
73. Menon DU, Belcher HME. COVID-19 pandemic health disparities and pediatric health care: the promise of telehealth. JAMA Pediatr 2021 Apr 01;175(4):345-346. [doi: 10.1001/jamapediatrics.2020.5097] [Medline: 33284346]
74. National & State Historic Unemployment Claims. URL: https://usafacts.org/visualizations/weekly-unemployment-claims/ [accessed 2022-06-20]
75. Pines JM. COVID-19, Medicare for all, and the uncertain future of emergency medicine. Ann Emerg Med 2020 Oct;76(4):459-461 [FREE Full text] [doi: 10.1016/j.annemergmed.2020.06.034] [Medline: 32747081]
76. Duggal R, Hooda S. COVID-19, health insurance and access to healthcare. Econ Polit Wkly 2021:10-12.
77. National Health Commission of the People's Republic of China. We Should Always Adhere to the General Policy of Dynamic Zeroing. URL: http://www.chinanews.com.cn/shipin/cns-d/2022/04-19/news923592.shtml [accessed 2022-04-30]
78. [Epidemic Prevention and Control] Those Who Do Not Participate in Nucleic Acid Testing for No Reason Will Bear Legal Consequences!. URL: https://m.thepaper.cn/baijiahao_17546807 [accessed 2022-04-30]
79. Centers for Disease Control and Prevention (CDC). What to Do If You Are Sick. URL: https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/steps-when-sick.html [accessed 2022-04-30]
80. Park CL, Russell BS, Fendrich M, Finkelstein-Fox L, Hutchison M, Becker J. Americans' COVID-19 stress, coping, and adherence to CDC guidelines. J Gen Intern Med 2020 Aug;35(8):2296-2303 [FREE Full text] [doi: 10.1007/s11606-020-05898-9] [Medline: 32472486]
81. Wu Jinglei: From the Screening Point of View, Infected People Show Dot Regional Aggregation, and There Is a Hidden Transmission Chain. URL: https://m.gmw.cn/baijia/2022-03/20/1302855193.html [accessed 2022-07-12]
82. 128,437 People Were Inspected Every Day! "Xindu Speed" in Nucleic Acid Testing Exercise for All Staff. URL: http://jsnews.jschina.com.cn/yc/a/202203/t20220309_2959858.shtml [accessed 2022-07-12]

83. Hyer RN, Covello VT. Effective Media Communication during Public Health Emergencies: a WHO Field Guide. URL: https://apps.who.int/iris/bitstream/handle/10665/43477/WHO_CDS_2005.31a_eng.pdf?sequence=1&isAllowed=y [accessed 2022-07-12]
84. McCredie MN, Morey LC. Who are the turkers? A characterization of MTurk workers using the Personality Assessment Inventory. Assessment 2019 Jul;26(5):759-766. [doi: 10.1177/1073191118760709] [Medline: 29490470]

## Abbreviations

**AIC:** Akaike information criterion
**BIC:** Bayesian information criterion
**CAIC:** consistency information criterion
**CDC:** Centers for Disease Control and Prevention
**DCE:** discrete choice experiment
**LCM:** latent class model
**MTurk:** Mechanical Turk
**MXL:** mixed logit model
**PHSM:** public health and social measure
**PSM:** propensity score matching
**WTP:** willingness to pay

---

*Edited by A Mavragani, T Sanchez; submitted 20.02.22; peer-reviewed by Y Xie, J Ong; comments to author 27.03.22; revised version received 14.05.22; accepted 23.06.22; published 16.08.22.*

*Please cite as:*
*Zhang Y, Liu T, He Z, Chan SN, Akinwunmi B, Huang J, Wong TH, Zhang CJP, Ming WK*
*Preferences for Attributes of Initial COVID-19 Diagnosis in the United States and China During the Pandemic: Discrete Choice Experiment With Propensity Score Matching*
*JMIR Public Health Surveill 2022;8(8):e37422*
*URL: https://publichealth.jmir.org/2022/8/e37422*
*doi:10.2196/37422*
*PMID:35759683*

Original Paper

# Birth and Death Notifications for Improving Civil Registration and Vital Statistics in Bangladesh: Pilot Exploratory Study

Tazeen Tahsina[1,2], MSc; Afrin Iqbal[1], MPH; Ahmed Ehsanur Rahman[1], PhD; Suman Kanti Chowdhury[1], MPH; Atique Iqbal Chowdhury[1], MSc; Sk Masum Billah[1], MPH; Ataur Rahman[1], MPH; Monira Parveen[3], MBBS; Lubana Ahmed[4], MBBS; Qazi Sadequr Rahman[1], MSc; Shah Ali Akbar Ashrafi[5], MPH; Shams El Arifeen[1], DPH

[1]International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh
[2]School of Health and Related Research, University of Sheffield, Sheffield, United Kingdom
[3]UNICEF, Dhaka, Bangladesh
[4]Cowatersogema, Dhaka, Bangladesh
[5]Civil Registration and Vital Statistics, Dhaka, Bangladesh

**Corresponding Author:**
Tazeen Tahsina, MSc
International Centre for Diarrhoeal Disease Research, Bangladesh
68, Shahid Tajuddin Ahmed Sarani, Mohakhali
Dhaka, 1212
Bangladesh
Phone: 880 9827077
Email: tahsina.tazeen@gmail.com

## Abstract

**Background:** Effective health policy formulation requires sound information of the numerical data and causes of deaths in a population. Currently, in Bangladesh, neither births nor deaths are fully and promptly registered. Birth registration in Bangladesh is around 54% nationally. Although the legal requirements are to register within 45 days of an event, only 4.5% of births and 35.9% of deaths were reported within the required time frame in 2020. This study adopted an innovative digital notification approach to improve the coverage of registration of these events at the community level.

**Objective:** Our primary objective was to assess (1) the proportion of events identified by the new notification systems (success rate) and the contribution of the different notifiers individually and in combination (completeness) and (2) the proportion of events notified within specific time limits (timeliness of notifications) after introducing the innovative approach.

**Methods:** We conducted a pilot study in 2016 in 2 subdistricts of Bangladesh to understand whether accurate, timely, and complete information on births and deaths can be collected and notified by facility-based service providers; community health workers, including those who routinely visit households; local government authorities; and key informants from the community. We designed a mobile technology–based platform, an app, and a call center through which the notifications were recorded. All notifications were verified through the confirmation of events by family members during visits to the concerned households. We undertook a household survey–based assessment at the end of the notification period.

**Results:** Our innovative system gathered 13,377 notifications for births and deaths from all channels, including duplicate reports from multiple sources. Project workers were able to verify 92% of the births and 93% of the deaths through household visits. The household survey conducted among a subsample of the project population identified 1204 births and 341 deaths. After matching the notifications with the household survey, we found that the system was able to capture over 87% of the births in the survey areas. Health assistants and family welfare assistants were the primary sources of information. Notifications from facilities were very low for both events.

**Conclusions:** The Global Civil Registration and Vital Statistics: Scaling Up Investment Plan 2015-2024 and the World Health Organization reiterated the importance of building an evidence base for improving civil registration and vital statistics. Our pilot innovation revealed that it is possible to coordinate with the routine health information system to note births and deaths as the first step to ensure registration. Health assistants could capture more than half of the notifications as a stand-alone source.

***(JMIR Public Health Surveill 2022;8(8):e25735)*** doi:10.2196/25735

**KEYWORDS**

notification; registration; birth; death; CRVS; mobile phone; mobile app; mobile technology; technology-based platform; community health; low- and middle-income countries; mHealth; Bangladesh

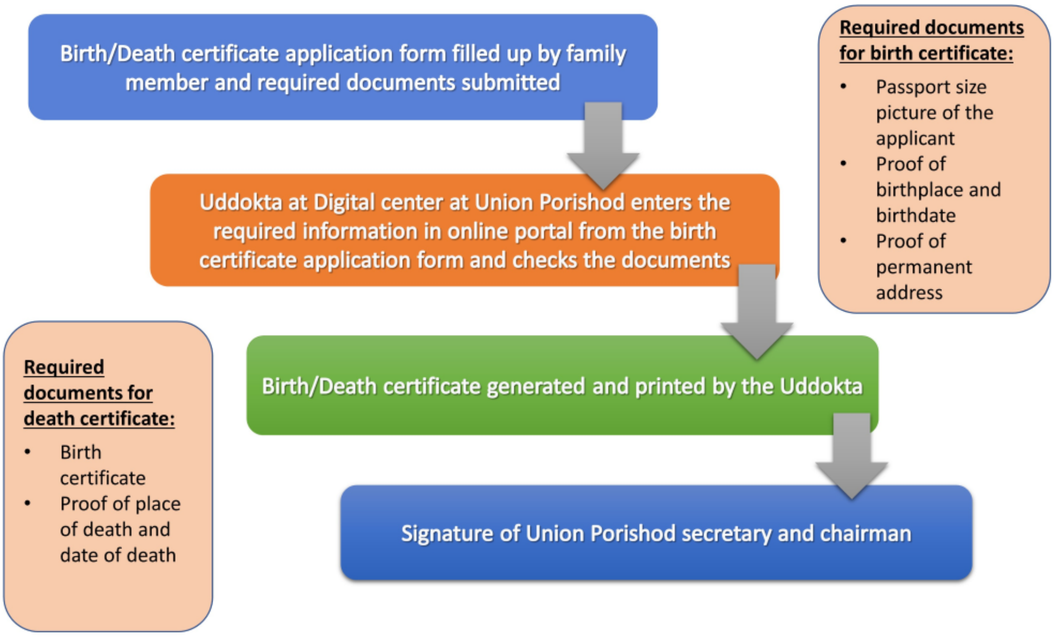
## *Introduction*

“No one should be without a legal identity. No life should be allowed to remain invisible to policymakers. No person should fall between the cracks of incomplete official data” [1]; this statement stresses the Sustainable Development Goal 16.9 agenda and the recommendations of the United Nations Commission on Information and Accountability for Women and Children's Health, thereby ensuring legal identity for all [2-5]. Births, deaths, marriages, divorce, adoption, and causes of death are the vital events that constitute a country’s civil registration and vital statistics (CRVS). Vital registration is fundamental to the logical operation of health care services, thereby ensuring equity, empowerment, and improved economic productivity [6-11]. Birth registration is an essential human right, acknowledging individual existence and identity. It also helps ensure health care, social protection, and education [9]. Death registration aids the estimation of disease burden and provides an understanding of the cause of death in communities, which is critical for prioritizing strategies and designing interventions addressing specific health needs [12,13].

Birth registration in Bangladesh is around 54% nationally, while death registration only covered 14.5% of deaths [14]. In 2010, the Office of the Registrar General of Birth and Death Registration launched an online registration system, but the coverage has still been low. Out of those registered, only 4.5% of births and 35.9% of deaths were registered within 45 days in 2020 [15,16]. In 2016, the Birth Registration Information System recorded that only 2% of births were registered within 45 days and death registration covered 13% of the national deaths [15]. There are multiple ministries within the government that are involved in the identification of vital events. An interministerial approach labelled as “CRVS++” has been undertaken by the cabinet division since 2014 [17]. The country is still working toward developing a unique ID system and linking it to the service delivery processes of various ministries, including the Ministry of Health and Family Welfare. Efforts are being scaled up to generate the cause of death from health care facilities, and a pilot study was initiated in the Kaliganj subdistrict for community-level workers to conduct verbal autopsies [16,17]. Coverage data on the pilot initiatives are yet to be visible through the CRVS tracker. However, the minimal effort directed toward the identification of cause of death has resulted in large changes in the timely reporting of death events [16].

In Bangladesh, the birth and death registration process involves 2 steps: (1) identification and notification and (2) registration [18]. The Birth and Death Registration Act 2014 [19] promotes notification within 45 days and identifies a set of entities as possible notifiers across different government bodies and the community [20]. The second part, the registration, is a mechanical process of availing and distributing a legal document, the certificate, for individual records (Figure 1). The notification of births and deaths can be the first step toward increasing the coverage of registration. The health sector can play a pivotal role in improving the notification of births and deaths through innovations [21].

**Figure 1.** Mechanical process of availing and distributing a legal document for individual record.



There is a dearth of evidence regarding the feasibility and functionality of using different sources as potential notifiers, particularly the health sector. Every additional source adds an extra level of complexity to the overall system and its accountability and sustainability. The published literature focuses on the need for and importance of a well-functioning

CRVS system for countries [6,8,10,13,22-25]. Two country-specific studies and 1 regional study have explained ways to improve the coverage of certificates and how the health system can help improve the CRVS [13,23,26]. However, these tend to be passive notification systems that underperform; none focused on a more proactive and innovative method to improve notification. There is scope for research and innovation to identify an efficient notification process and acknowledge the importance of having an optimum number of notifiers. Once that part is done, the mechanical challenges associated with the registration system can be assessed in the next stage.

Our primary objective was to assess (1) the proportion of events identified by the new notification systems (success rate) and the contribution of different notifiers individually and in combination (completeness) and (2) the proportion of events notified within specific time limits (timeliness of notifications) after introducing the innovative approach. We also aimed to understand whether the system excluded individuals belonging to any specific sociodemographic characteristics or located within specific geographic boundaries from the reporting system.

## Methods

### Description of the Notification Process

Following the Birth and Death Registration Act [19], we identified a list of individuals and authorities eligible to notify an event of birth and death (Table 1). The notifiers, selected in consultation with the Ministry of Health and Family Welfare and local government representatives, fall into 3 groups. These include public facility–level health care service providers (nursing supervisor/nurse and resident medical officer), community-level domiciliary health and family planning workers (health assistants, family welfare assistants, and community health care providers [CHCPs]), and local government representatives, namely, the Uddoktas (a community volunteer who facilitates birth and death registration at the union level), village police, imams (religious leaders), and households. Private sector facilities were not included in the notification process.

**Table 1.** List of channels for the notification of births and deaths in 2 rural subdistricts of Bangladesh from January to October 2016.

| Notification interface, institute, work station, and notifiers | Catchment area | Notification interface |
|---|---|---|
| **Web-based app** | | |
| **Directorate General of Health Services** | | |
| Domiciliary service, health assistant | Ward level: for every 5000-6000 people | Government of Bangladesh–provided tablets (Basail) and project mobile phones (Kasba) |
| **Upazila Health Complex** | | |
| Resident medical officer | Upazila-facility deaths only | Project mobile phones |
| Nursing supervisor | Upazila-facility deaths in the entire upazila | Project mobile phones |
| **Directorate General of Family Planning** | | |
| Domiciliary service, family planning assistant (family welfare assistant) | Ward level: for every 5000-6000 people | Government of Bangladesh–provided tablets (Basail) and project mobile phones (Kasba) |
| **Local government body** | | |
| Union Digital Center, Uddokta | Union level | Project mobile phones |
| Union Parishad, female member | Union level: 25,000 people | Project mobile phones |
| **Call center** | | |
| Local government body, union parishad, village police | Ward level | Call center operator |
| **Self-notification** | | |
| Family members | Household | Call center operator |
| Imam | Households surrounding the mosques | Call center operator |

### Notification Platform

To facilitate the notification process, we designed 2 platforms: the direct system used an Android smartphone–based app and the indirect one received notifications through a call center. The health assistants, family welfare assistants, resident medical officers, nursing supervisors, members, and Uddoktas notified directly through the app. The village police, imam, and family members notified by calling the call center (Table 1).

To enable notifiers to provide the notifications, the project provided mobile phones preloaded with the app to select notifiers in the Kasba upazila (subdistrict) where the government did not provide tablets for routine data collection among the community health and family planning workers. Project mobile phones were also given to nursing supervisors, female members, and Uddoktas in both upazilas.

### Mobile App

The mobile app was simple and kept to a minimum set of information required for identifying an individual's household for verification. Our notification system collected information on the identification of an individual birth and death event, date and place of the event, detailed address, and contact. Each entry was stored in the mobile device and the central server. The notification records were made available to the devices of project staff responsible for verification through household visits. The app allowed all notifications to be stored as a new entry, even if there were repeat notifications of the same events (Multimedia Appendix 1).

### Call Center

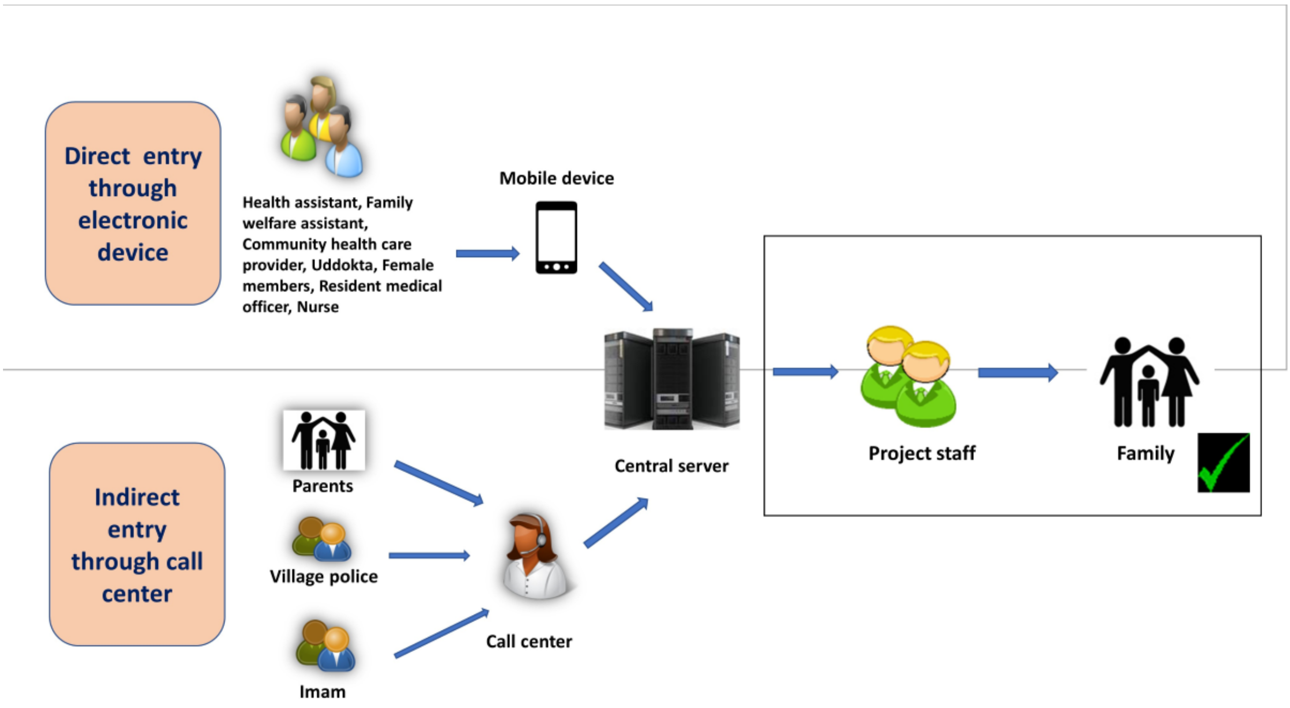
The call center was based in Dhaka, with 1 operator working between 9 AM and 5 PM. Communication materials were distributed to all households and community informants with the call center number. They left missed calls to the number and they were called back to collect necessary information. For each call, BDT 50 (1 BDT is equivalent to 0.011 USD) was transferred in the form of mobile recharge to families and BDT 20 for imams and village police as incentives. This system also accommodated repeat records from multiple notifiers.

### Household Visit for Verification and Identification of Repeat Notifications

There was no built-in mechanism in the system to flag repeat notifications. It allowed for as many repeat notifications as done by the various notifiers. Each notification was given a unique number generated by the system. We developed a verification system so that we could identify repeat notifications and identify multiple entries for the same individuals. All notifications were verified through confirmation of events by family members during a visit by project staff (a verifier) to the respective household. Verifiers also used a mobile-based platform to collect additional information other than the notifications. They were trained on using the data collection tool and the mobile-based system and given refresher training at regular intervals to ensure quality.

To understand how the verification system worked, let us assume that 3 different sources notified a single event: a health assistant, the household itself, and an Uddokta. If a notification was first received from the health assistant, our field staff visited the household, collected information to confirm the event and the date and place of the event, and left a calendar at the household with an ID number generated by the system at the first verification visit. This ID number on the calendar helped to identify duplicate notifications during subsequent visits. Assuming that the second notification was received from the household, the field staff went back to the same house and verified the notification. If the event was previously reported by a health assistant, instead of providing a new calendar, he/she would enter the identification number from the existing calendar in the household. The same process would be repeated for the third notification by the Uddokta. Figure 2 entails the notification and verification processes.

**Figure 2.** Notification flow and validation.



### Settings

This project took place in 2 upazilas in Bangladesh: Basail (Tangail district) and Kasba (Brahmanbaria district). We included 5 unions from each upazila for piloting the notification system, covering ~280,000 people from October 2015 to September 2016.

### Assessment of the Functionality of the Notifiers

To assess how well the notification system worked, we conducted a household survey at the end of the notification period between October and December 2016. As this was a pilot, the survey was not designed to measure the accuracy of the different notifiers. Rather, it aimed to assess the coverage/completeness of the notification system that we piloted. Timeliness was measured from the notification system itself through collection of dates of an event during the verification visits. Notifiers could report an event at any time point during our study period. We estimated the time lag between the date of the event and the date of the notification for each notifier. This also helped to identify the notifier who had the shortest time lag between the event and reporting.

For the household survey, we assumed a death rate of 6 per 1000 people and a birth rate of 21 per 1000 people, a recall period of 12 months, and that our notifiers could capture 80% of the birth and death events. An estimated sample of 56,000 people covering 14,000 households was required to assess the notification channels. We defined clusters in the 2 upazilas by using the probability proportionate to size sampling technique. All births and deaths taking place in the surveyed households, accounting for about 20% of total households in the 2 subdistricts between January and October 2016, were recorded. We estimated the number of birth and death events that took place in this random subsample. All households within the selected areas were listed and asked whether any birth or death event took place within the household during the time period mentioned above. If the response was yes, detailed information on the household socioeconomic characteristics, background characteristics of respondents, and the birth and death events was collected. Written consent was obtained from those attending the interview and no monetary compensation was made. There were separate modules for birth and death events. For birth, the women who gave birth were interviewed, while for death, household heads were interviewed. The survey tools are provided in Multimedia Appendices 2 and 3.

### Data Analysis

We used descriptive statistics to elaborate the notification system and the household survey. We entered data into the project database by using Microsoft SQL Server 2005 with Visual Basic 6.0 for the user interface. We used STATA (version 12; StataCorp LLC) for the statistical analysis.

First, we assessed the performance of individual notifiers in terms of proportion of birth/death events notified by each compared to the total unique number of notifications. We also explored coverage reached by the combination of notifiers to identify sources that can reach maximum coverage. The unique notifications were identified based on the calendar ID collected during the repeat verification visits. We also assessed how well each notifier performed in terms of timeliness. Date of event was captured during household verification of each event from household members. Notification coverage was analyzed by notifications received any time after an event and by the first source of notification to understand which source was the quickest in reporting the events.

The next step was to assess the performance of the notifiers compared to the data in the household survey. Using the calendar identification number that was left at the household during the verification visits, we matched the notifications to the information obtained from the household survey. Assuming the survey captured all births and deaths that took place over the study period, we then compared the total births and deaths captured as an overall proportion reported through the notification system to the number reported through the survey. Next, we stratified the birth and death notifications by the source of notification and the place of occurrence of the event.

We compared the demographic characteristics between births and deaths captured and missed by our notification system. We looked at some background characteristics of mothers who gave birth and of household heads who had a deceased member in the family. We separated the analysis by those captured and not captured by our notification channels. We included place of birth, age, sex of child, wealth quintile of household, education, and occupation of mothers who gave birth.

We also tried to investigate any possible geographical pockets where the noncaptured births and deaths took place. We also produced geographical information system–based maps to see whether the events not captured in the notification channels were clustered within any geographic area.

### Ethics Approval

Ethics approval to conduct the study was obtained from the Institutional Review Board of the International Centre for Diarrhoeal Disease Research, Bangladesh (PR 15099).

## Results

### Notifier Performance: Coverage (Proportion of Notifications Done by Each Channel From the Notification Database)

Between January and October 2016, there were 13,377 notifications of births (n=10,816) and deaths (n=2561) received from all channels. All notifications were verified through household visits even in cases of duplicate reports. The verification success rate was 92% for births and 93% for deaths. Health assistants, family welfare assistants, CHCPs, and families were the predominant channels of notification (Figure 3).

Health assistants were the most successful in capturing birth and death events. They covered 76.8% of all births. This was followed by family welfare assistants and CHCPs. Families reported 12.6% of births to the call center. Health assistants were the first to notify 60.4% of the births. Family welfare assistants were the second best performers in terms of notifying births followed by households. A very low proportion of births was notified by facility-level health care providers, namely, nursing supervisors and resident medical officers (Table 2).

Health assistants captured 53.6% (n=778) of all deaths. This was followed by family welfare assistants and CHCPs. Health assistants notified 37.2% (n=540) of deaths before other sources, followed by CHCPs and family welfare assistants. Around 10.1% (n=147) deaths were first notified by family members (Table 2).

**Figure 3.** Notification and verification status.

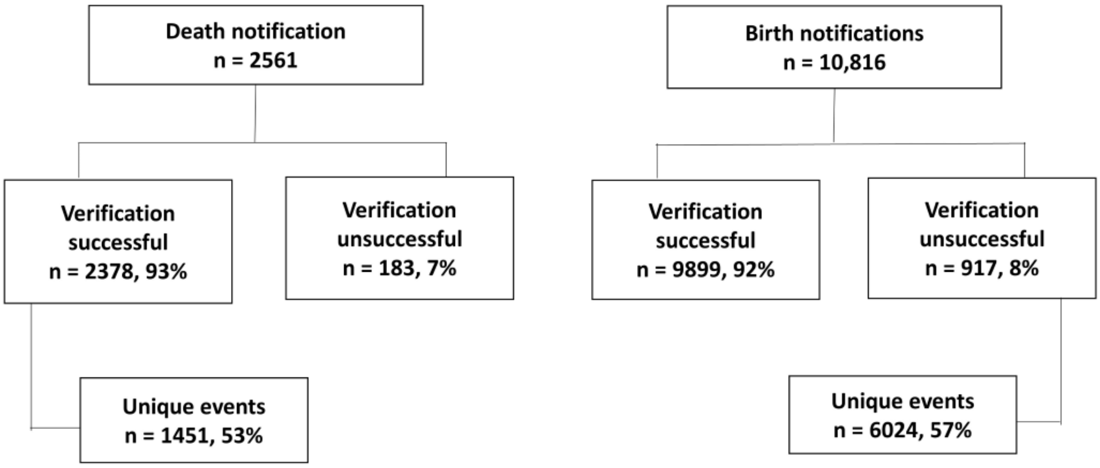


**Table 2.** Proportion of births and deaths captured by the individual notification channel in 2 rural subdistricts of Bangladesh from January to October 2016.

| Notification processes and channels | Notified anytime | | First notifier | |
|---|---|---|---|---|
| | Birth (N=6024), n (%) | Death (N=1451), n (%) | Birth (N=6024), n (%) | Death (N=1451), n (%) |
| **Android app** | | | | |
| Health assistant | 4626 (76.8) | 778 (53.6) | 3638 (60.4) | 540 (37.2) |
| Family welfare assistant | 1536 (25.5) | 402 (27.7) | 910 (15.1) | 207 (14.3) |
| Community health care provider | 1012 (16.8) | 379 (26.1) | 578 (9.6) | 254 (17.5) |
| Resident medical officer | 0 (0) | 73 (5) | 0 (0) | 1 (0.1) |
| Nursing supervisor | 96 (1.6) | 174 (12) | 30 (0.5) | 4 (0.3) |
| Uddokta | 48 (0.8) | 3 (0.2) | 60 (1) | 115 (7.9) |
| Female member | 90 (1.5) | 81 (5.6) | 78 (1.3) | 55 (3.8) |
| **Call center** | | | | |
| Imam | 72 (1.2) | 68 (4.7) | 54 (0.9) | 49 (3.4) |
| Village police | 42 (0.7) | 115 (7.9) | 30 (0.5) | 77 (5.3) |
| Parents/family | 759 (12.6) | 190 (13.1) | 645 (10.7) | 147 (10.1) |

## Notifier Performance: Timeliness

Around 8.4% (n=506) of births were notified on the first day and 71.5% (n=4307) of births were notified within the legally recommended time of 45 days. The median time taken to notify births was 27 (IQR 11-50) days. The median time of notifications via call center was 8 days for births (Table 3). Overall, 31.7% (n=460) of deaths were notified within 1 day while 89.3% (n=1296) were notified within 45 days. The median time taken to notify deaths was 5 (IQR 1-23) days, which was as low as 3 days via the call center (Table 3).

When we consider the timeliness and the source of notification together, median time taken by health assistants to notify births was 34 (IQR 18-55 days). Health assistants notified almost half of these events within 45 days followed by family welfare assistants (Table 3). Median number of days Health assistants took to notify deaths was 9 days and they notified 45% (n=653) of death events within 45 days. Together, health assistants and family welfare assistants notified 55% (n=798) of death events within 45 days (Table 3).

**Table 3.** Notification timeliness by different channels of notification in 2 rural subdistricts of Bangladesh from January to October 2016.

| Timeliness | Births (N=6024) | Deaths (N=1451) |
|---|---|---|
| **Notification timeliness and source, n (%)** | | |
| Within 24 hours | 506 (8.4) | 460 (31.7) |
| Within 72 hours | 747 (12.4) | 634 (43.7) |
| Within 15 days | 1928 (32) | 1006 (69.3) |
| Within 45 days | 4307 (71.5) | 1296 (89.3) |
| Health assistant | 2861 (47.6) | 653 (45) |
| Family welfare assistant | 1145 (19) | 353 (24.3) |
| **Android-based app, all notifiers (n=168[a]), days, median (IQR)** | 27 (11-50) | 5 (1-23) |
| Health assistant (n=41) | 34 (18-55) | 9 (3-31) |
| Family welfare assistant (n=49) | 17 (6-35) | 3 (1-14) |
| Community health care provider (n=34) | 27 (11-48) | 5 (1-23) |
| Uddokta (n=10) | 23 (7- 49) | 5 (1-25) |
| Nursing supervisor (n=2) | 1 (0-4) | 0 (0) |
| Resident medical officer (n=1) | 0 (0) | 143 (141-146) |
| **Call center, days, median (IQR)** | 8 (2-33) | 3 (1-14) |
| Imam | 5 (2-12) | 1 (0-8) |
| Village police | 26 (7-62) | 3 (1-17) |
| Parents/family | 8 (1-34) | 4 (1-14) |

[a] Family members who notified from the community via the call center are not considered among the 168 notifiers.

## Notification Coverage: Findings From Household Survey

The household survey identified 1204 births between January and October 2016. When matched with the notifications, the majority of these births (87.3%, n=1051) were captured by our notification system. Overall, more than half of the births took place in facilities and the rest at home. Among the facility births, a large proportion was notified by community health and family planning workers. The majority (n=367, 65.6%) were notified by health assistants. This was followed by family welfare assistants (n=97, 17.4%), CHCPs (n=86, 15.4%), and households through the call center (n=74, 13.2%). Out of the total 64 deliveries that took place in public facilities, only 2 were notified by the nursing supervisors stationed at the hospitals (n=3, 0.18%) (Table 4). Similarly, among home births, most were notified by health assistants (n=378, 76.8%) followed by family welfare assistants (n=127, 25.8%) and CHCPs (n=69, 14.1%) (Table 4).

**Table 4.** Proportion of births and deaths captured by individual notification channel and place of event in 2 rural subdistricts of Bangladesh from January to October 2016.

| Notification process and channels | Household survey | | | | | |
|---|---|---|---|---|---|---|
| | Birth (N=1204), n (%) | Home birth (N=547), n (%) | Facility birth (N=657), n (%) | Death (N=341), n (%) | Home death (N=256), n (%) | Facility death (N=85), n (%) |
| Total | 1204 (100) | 248 (45.4) | 359 (54.6) | 341 (100) | 192 (75.1) | 21 (24.9) |
| **Android app** | | | | | | |
| Health assistant | 743 (70.7) | 378 (76.8) | 367 (65.6) | 109 (49.2) | 91 (51.6) | 19 (42.4) |
| Family welfare assistant | 223 (21.2) | 127 (25.8) | 97 (17.4) | 42 (18.8) | 32 (17.9) | 10 (21.2) |
| Community health care provider | 156 (14.8) | 69 (14.1) | 86 (15.4) | 48 (21.4) | 39 (21.9) | 9 (20) |
| Resident medical officer | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Nursing supervisor | 4 (0.4) | 1 (0.2) | 3 (0.5) | 1 (0.3) | 1 (0.4) | 0 (0) |
| Uddokta | 11 (1) | 3 (0.6) | 8 (1.4) | 5 (2.4) | 3 (1.9) | 2 (3.5) |
| Female member | 12 (1.1) | 3 (0.7) | 8 (1.4) | 12 (5.6) | 10 (5.5) | 3 (5.9) |
| **Call center** | | | | | | |
| Imam | 8 (0.8) | 1 (0.2) | 7 (1.2) | 17 (7.6) | 14 (8.2) | 3 (5.9) |
| Village police | 9 (0.9) | 1 (0.2) | 8 (1.4) | 9 (4.1) | 8 (4.7) | 1 (2.4) |
| Parents/family | 141 (13.4) | 66 (13.5) | 74 (13.2) | 22 (9.7) | 16 (8.9) | 5 (11.8) |
| Total, all sources | 1051 (87.3) | 492 (89.9) | 559 (85.1) | 222 (65.1) | 176 (68.8) | 46 (54.1) |

A total of 341 deaths were identified in the household survey. After matching, we found that 65.1% (n=222) of these were captured by our notification system. When analyzed by source of notification, most (n=19, 42.4%) facility deaths were captured by health assistants followed by family welfare assistants. More than half of home deaths were captured by health assistants. This was followed by family welfare assistants (n=32, 17.9%) and CHCPs (n=48, 21.4%) (Table 4).

Among events that were captured both by the notification channels and the survey, 82% (n=4938) of births were notified by health assistants and family welfare assistants combined. Nearly 80% (n=4819) of births were captured by health assistants and CHCPs combined. The proportion increased to 88% (n=5301) for births when the 3 channels were combined. The rest of the sources together could cover around 50% (n=3012) of births and deaths. Nearly 80% (n=1158) of the deaths were captured by health assistants and CHCPs combined. Health assistants, family welfare assistants, and CHCPs together notified 86% (n=1247) of the deaths in the survey. All the remaining sources together covered only around 50% of deaths.

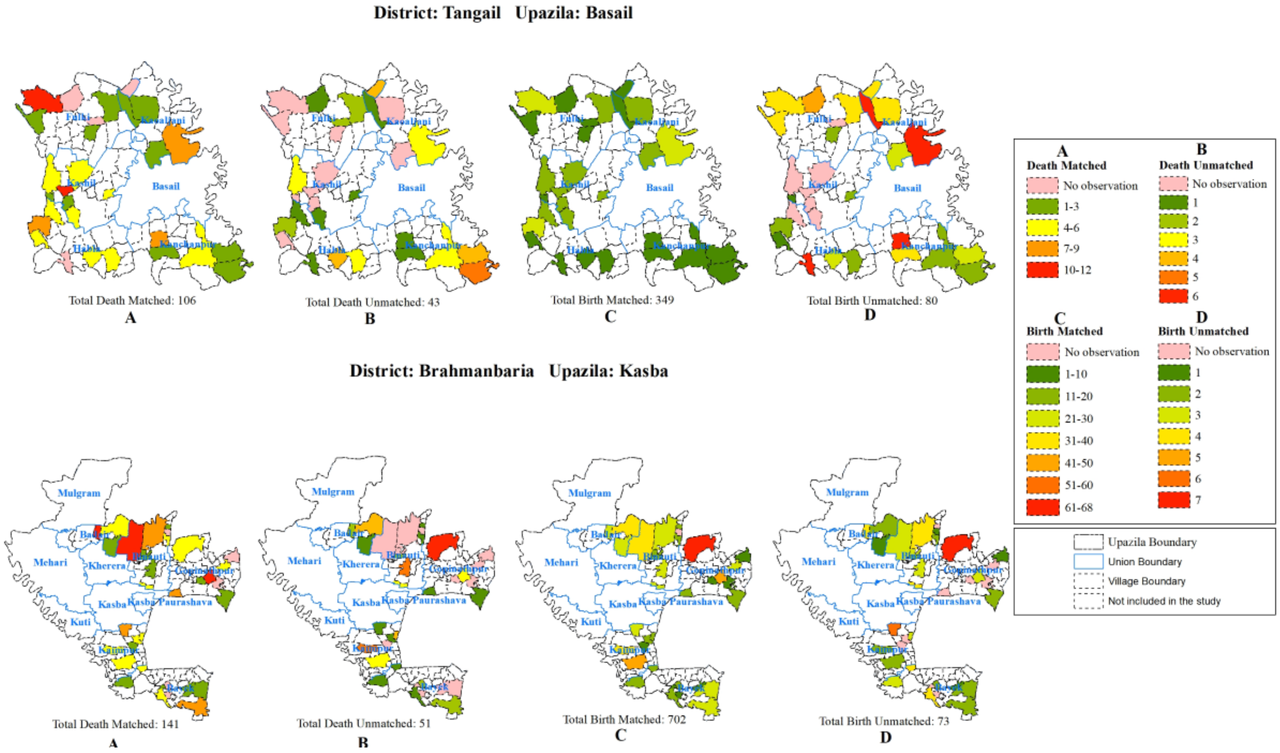
Distribution within the notified and nonnotified births in terms of all these determinants are reported in Table 5. Place of death, sex of deceased, household wealth quintile, education, and occupation of the household head were compared between the notified and nonnotified deaths. A similar distribution pattern was observed in the 2 groups. Statistical significance was not reported owing to the low number of samples in the noncaptured group (Table 5).

Our geographical information system maps also suggested no geographic clustering among the nonnotified cases identified during the household survey. Some areas performed better than others, but the untapped birth and death events were evenly scattered around the areas covered by our notifiers (Figure 4).

**Table 5.** Background characteristics of the mothers who gave birth and of decedents in 2 rural subdistricts of Bangladesh from January to October 2016.

| | Birth | | Death | |
|---|---|---|---|---|
| | Captured by notification channels (N=1051), n (%) | Not captured by notification channels (N=153), n (%) | Captured by notification channels (N=248), n (%) | Not captured by notification channels (N=94), n (%) |
| **Place of event** | | | | |
| Facility | 559 (53.2) | 98 (64.1) | 54 (21.7) | 31 (32.9) |
| Home | 492 (46.8) | 55 (35.9) | 194 (78.1) | 63 (67) |
| **Age in years of mother/decedent by cohort** | | | | |
| <20 | 209 (19.9) | 39 (25.5) | 21 (8.5) | 1 (0.8) |
| 20-29 | 665 (63.3) | 92 (60.1) | 37 (14.9) | 24 (24.5) |
| 30-39 | 166 (15.8) | 20 (13.1) | 55 (22.3) | 24 (25.5) |
| 40-49 | 12 (1.1) | 2 (1.3) | 64 (25.9) | 20 (21.3) |
| 50-59 | 0 (0) | 0 (0) | 49 (19.8) | 7 (7.5) |
| ≥60 | 0 (0) | 0 (0) | 40 (16.2) | 11 (11.7) |
| Missing | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| **Sex** | | | | |
| Male | 554 (52.7) | 86 (56.2) | 136 (54.9) | 36 (37.8) |
| Female | 491 (46.7) | 66 (43.1) | 107 (43.2) | 35 (36.9) |
| Missing | 6 (0.6) | 1 (0.7) | 5 (1.8) | 24 (25.2) |
| **Wealth quintile** | | | | |
| Lowest | 186 (17.7) | 18 (11.8) | 55 (22.1) | 21 (22.7) |
| Second | 197 (18.7) | 17 (11.1) | 38 (15.3) | 19 (20.2) |
| Middle | 159 (15.1) | 38 (24.8) | 48 (19.4) | 24 (25.2) |
| Fourth | 167 (15.9) | 26 (16.9) | 57 (22.9) | 13 (14.3) |
| Highest | 203 (19.3) | 28 (18.3) | 50 (20.3) | 17 (17.7) |
| **Education (mother/household head)** | | | | |
| Primary or below | 272 (25.9) | 31 (20.3) | 235 (94.7) | 92 (97.9) |
| Secondary | 508 (48.3) | 68 (44.4) | 12 (4.9) | 2 (2.1) |
| Higher | 269 (25.6) | 54 (35.3) | 1 (0.4) | 0 (0) |
| **Occupation** | | | | |
| Unskilled labor | 4 (0.4) | 0 (0) | 27 (10.9) | 10 (10.6) |
| Skilled worker | 34 (3.2) | 4 (2.6) | 37 (14.9) | 18 (19.2) |
| Business/trade | 3 (0.3) | 0 (0) | 35 (14.2) | 11 (11.7) |
| Service holder | 3 (0.3) | 3 (1.9) | 19 (7.7) | 3 (3.2) |
| Professional | 8 (0.8) | 0 (0) | 5 (2.1) | 2 (2.1) |
| Unemployed | 1000 (95.1) | 146 (95.4) | 15 (6.1) | 2 (2.1) |

**Figure 4.** Distribution of births and deaths identified in household surveys across Mouzas (above from left: Basail death notified, death nonnotified, birth notified, birth nonnotified; below from left: Kasba death notified, death nonnotified, birth notified, birth nonnotified).



### Missed Events

Among nonnotified births (n=156), about 35% (n=55) happened outside the project area. One-fifth of the mothers were at their maternal home with newborns. The rest included outmigration (n=41, 26%), false notification (n=16, 10%), and early newborn death (n=9, 6%). Among nonnotified deaths (n=93), approximately 86% (n=80) of the households were not aware of the need for death notification.

## Discussion

### Principal Findings and Policy Recommendations

Our pilot notification system was developed with the aim of identifying a single channel or combination of channels to help improve the notification of birth and death events. Although the notifications from health facilities were very low for both births and deaths, community-level sources, especially the health assistants and family welfare assistants, could together cover more than 80% of the events within their catchment population. Health assistants were the champions in notifying births and deaths with the shortest time lag from the time of the event. Our findings revealed that community-based staff within the routine health system can ensure complete and timely notification of births and deaths [27].

Health assistants and family welfare assistants showcased promising performance in notifying births and deaths within 45 days. Our study identified that coverage can reach as high as 83%, a massive improvement from the 4.5% currently captured in the online birth registration information system [15]. Death notifications have already seen massive improvement as a result of the medical certification of the cause of death and verbal autopsy scale-up initiatives by the government. However, this can also rise drastically from its current state to about 66% through a notification system. We need to keep in mind that the project provided minimal training and facilitation for collecting the notifications. The health sector will be able to achieve even better notification and registration coverage of vital events with proper guidance and regulations from the relevant authorities.

The use of an electronic system and integrating such tools with the current data capture system in Bangladesh can be an effective means to facilitate the notification process. Mobile-based electronic systems for registering births and deaths have been successfully tried out in other countries. In Tanzania, the registrars used a mobile app to collect and upload data to a central system [26]. In Pakistan, marriage contractors, female health workers, and Telenor mobile phone network agents were selected as mobile gatekeepers to reach universal coverage for the national identity scheme [26]. It is also not an additional burden or a completely new system, as Bangladesh itself has done exceptionally well in developing electronic data capture and storage systems. The health assistants and family welfare assistants have already been provided with tablets and training on electronic data capture systems. Once the CRVS++ under the leadership of the cabinet division is in place and running, it will become much easier to accumulate information from the various agents across different ministries, including health, and connect them to the central CRVS database [17].

Poor notifications from facilities emphasize the need to introduce and maintain an accountability mechanism in all public and private facilities for immediate birth and death reporting. Nationally, 37% of births now occur in facilities and 22% of these are in the private sector [27]. Nearly 55% of the deliveries in our survey area took place in facilities. As reported in the household survey, half of these deliveries were conducted in private sector facilities, partly explaining the low level of public facility notification. Although community-level providers captured most of the births and deaths in the study area, health care providers stationed at facilities are much better positioned to provide immediate information on births and deaths. Both private and public facilities are required to report births and deaths in the District Health Information System, which needs a lot of improvements. As an initial step, medical certification of the cause of death forms at both public and private health facilities and verbal autopsy in the community through health assistants have been launched as a pilot to identify the cause of death for generating death certificates [17]. Both these initiatives have played a crucial role in improving death reporting within 45 days.

Although a large proportion of the births still occur at home, frontline domiciliary workers of the government are the best source to inform these events. Domiciliary health and family planning workers have a comparative advantage of “local knowledge” within the community, and notification of births and deaths is part of their day-to-day job. Through regular interaction with households, health assistants and family welfare assistants should be able to quickly and easily learn about important events like births and deaths [28]. This leaves the opportunity for collecting information on births and deaths with a minimum time interval from event occurrence [28].

Our findings indicate some untapped opportunities among CHCPs and Uddoktas in reporting both birth and death events. Fixed duty stations lack delivery facilities, which limits provider-people interactions and is perhaps one of the reasons underlying the low level of reporting by other cadres such as CHCPs or Uddoktas. Although CHCPs work closely with health assistants/family welfare assistants, their work stations and community clinics are a curative platform offering very limited services. Uddoktas, however, are stationed at Union Digital Centers located at the Union Parishad Office, which limits their role to proactively identifying births and deaths. As a demand-side effort, a nationwide campaign on the importance of early registration of births and deaths will increase awareness and accountability within the system [26]. Such mechanisms can be useful for hard-to-reach areas or areas without a dedicated health assistant/family welfare assistant.

The effectiveness of the health sector as a source of birth and death notification, as demonstrated by this study, also opens the door to linking these sources to the local and national level registrar’s office where the registration process will be completed. There are multiple ongoing national initiatives in Bangladesh where digital data systems within the health sector are already underway through introduction of the District Health Information Software and the electronic Management Information System [29,30]. This system can be sustainable, as the Management Information System within the Directorate General of Health Services in Bangladesh is providing handheld tablets to all health assistants. The CHCPs are also equipped with laptop computers. Technical and mechanical difficulties are taken care of by the Management Information System and the Directorate General of Health Services; however, the shortage of adequate monitoring and supervisory bodies as well as technical assistance does slow the digital data input process nationally.

Bangladesh is rich in data in terms of household surveys conducted every 2 or 3 years [24]. Although censuses and household surveys act as a source of vital statistics, these are unable to provide continuous administrative data at the national or subnational level, permitting the production of statistics on population dynamics and health and inequities in service delivery [12]. Moving forward, a complete and functioning notification system based on health sector information relevant to vital events can eventually help replace surveys and censuses. Data collection through surveys and its transition to readable data makes translation of evidence into policy a lengthy process [31]. With declining trends in maternal, newborn, and child mortality, surveys are becoming increasingly resource-intensive, and alternate measures are needed [32,33]. Previous studies suggest that strong CRVS data have been used to estimate maternal mortality, replacing surveys in other settings [34,35].

Simplification of the registration will save time and smoothen the certification process with no hidden fees and can improve registration as seen in a study conducted in Indonesia [23]. Once data are entered in the system, birth and death notifications can be shared in the respective local government offices for processing the birth and death certificates. The notification systems captured all the required information for issuing a certificate. Discussions have already taken place on incorporating all these information fields into the individual tracker in the District Health Information Software-2 and the electronic Management Information System. The only remaining step would be for a family member to physically visit the respective facilities and receive the certificates. Currently, there is no tangible benefit or sense of obligation for parents or individuals for the early registration of births and deaths. Although the government initiated a pilot in Kaligonj subdistrict by using an updated child immunization card to include birth registration numbers, the first vaccine dose is not required until 42 days after birth [36]. This poses the risk of missing early neonatal deaths and stillbirths, which are also commonly missed in household surveys.

Countries with better CRVS systems perform better in terms of their health indicators [10]. Accurate, timely, relevant, comparable, and easily available statistical information is essential for effective program design beyond health [37]. The Vital Statistics Performance Index of Bangladesh is very low [25]. As the country has mandated to strengthen its civil registration system, quick short surveys can eventually be used as a quality check to identify under- or overreporting of births and deaths [7,22]. There is a huge opportunity for capturing deaths through the domiciliary health and family planning workforce. This becomes a much-required and desirable task in a pandemic situation like COVID-19. Our findings suggest that health assistants and family welfare assistants can play a pivotal role in conducting mortality surveillance and support policy makers with the necessary information in mitigation planning [38].

## Limitations

Our study required the verification of every birth/death event by physically visiting each household, which may not be feasible when done nationally. We assessed the innovative digital notification approach by using a sample household survey, whereas conducting a complete census of all households in the study area would be ideal. This was not possible owing to resource constraints, thereby limiting our ability to achieve the objective of matching every birth and death event case by case. This limited our analysis for testing the validity of routine sources and determining an inflation factor for measuring mortality. We also could not include private sector facilities, where a large proportion of facility births take place. However, this was a pilot to test as many sources as possible, and covering a large number of small private clinics was beyond our scope in terms of government-enlisted notifiers. The government in its pilot phase for the identification of cause of death has included private sector facilities. We are also undertaking one new research study to validate the routine health information system in the identification and reporting of adult female mortality. We have included all public and private sector facilities in 2 upazilas. The study, once complete, will add a lot more information to our findings in this paper.

One key limitation for the scale-up of such a program is the lack of information on how to identify duplicates without involving additional human resources. However, much improvement in the national identification card has been made since we conducted our study, and a national identification system will be the key to merging data from various sources and removing duplicates. Another initiative by the government to introduce and implement unique IDs for every individual may facilitate the removal of duplicates in greater capacity as unique IDs include individuals aged 0-18 years as opposed to the national identification card, where the age of eligibility is 18 years.

There are potential sources of bias in reporting births and deaths from the notifiers. We tried addressing that by including as many notifiers as possible from the community. Further, each type of notifier is dedicated to a specific geographical region. To see if there were biases in reporting births and deaths, household characteristics from the survey were compared between notified and missed events. Since a statistical significance test could not be conducted owing to very low numbers, we also looked at the geographic location of the notified and nonnotified events and ensured there was no clustering in reporting. Another source of bias could be the person within the household who was interviewed. There were clear instructions on how to select the respondent (women for birth and household head for death) to minimize such bias.

Finally, this study was undertaken in 2016 and since then, there has been a lot of development in the national CRVS program. The CRVS++ system is under development, and pilot studies to identify the cause of death both from facilities and communities are underway. The pilot study revealed how the routine health information system can be a source of notification for the CRVS system and integration of the two is underway. Through our collaboration with the cabinet division, we have shared our learnings and fed into the pilot that was undertaken in Kaligonj [36]. Our findings will be a very useful addition to evidence-based decision-making for policy makers involved in improving birth and death registration. Apart from improving CRVS, the pilot study also showed ways to improve the measurements and evidence-based decision-making by using the routine health data sources. A larger validation study is ongoing, building onto the pilot study to measure the mortality of female adults from routine sources of information.

## Conclusion

Our pilot study revealed that it is possible to tap into the routine health information system for notification on births and deaths as the first step to ensuring registration. Health assistants captured more than half of the notifications as a stand-alone source and this could be further improved when family welfare assistants are also involved. Timely notification of birth and death events using an innovative communications approach with community-based staff can be a crucial step in improving the registration of births and deaths. Once the notification part is ensured with all the required fields for the certificate made available, the mechanical procedures of certification can easily be completed through the respective local government offices. It can shorten the time needed to issue a certificate and make the process of certification simple and efficient.

## Acknowledgments

This study was funded by Global Affairs Canada through Co-water Inc. None of the funders were involved in the design, implementation, analysis, or interpretation of the data.

## Conflicts of Interest

None declared.

Multimedia Appendix 1
Supplementary table.
[DOCX File , 52 KB - publichealth_v8i8e25735_app1.docx ]

Multimedia Appendix 2
Census: birth and death module.

[PDF File (Adobe PDF File), 1586 KB - publichealth_v8i8e25735_app2.pdf ]

---

Multimedia Appendix 3
Census: death module.
[PDF File (Adobe PDF File), 1347 KB - publichealth_v8i8e25735_app3.pdf ]

---

## References

1. Chowdhury AI. Civil Registration and Vital Statistics in Asia and the Pacific. Get Everyone in the Picture. URL: https://getinthepicture.org/ [accessed 2015-05-12]
2. Sustainable Development Goals 2015. United Nations Development Programme. URL: http://www.undp.org/content/undp/en/home/sustainable-development-goals.html [accessed 2015-05-17]
3. Goal 3 Targets 2015. United Nations Development Programme. URL: http://www.undp.org/content/undp/en/home/sustainable-development-goals/goal-3-good-health-and-well-being/targets/ [accessed 2016-07-02]
4. Goal 16 Indicators. United Nations Development Programme. 2015. URL: https://www.sdg16hub.org/landing-page/sdg-16-indicators [accessed 2017-09-17]
5. Accountability for Women's and Children's Health 2014 Progress Report. Implementing the Commission on Information and Accountability Recommendations. 2014. URL: https://www.everywomaneverychild.org/wp-content/uploads/2016/11/COIA_report_2014.pdf [accessed 2017-10-09]
6. AbouZahr C, de Savigny D, Mikkelsen L, Setel PW, Lozano R, Nichols E, et al. Civil registration and vital statistics: progress in the data revolution for counting and accountability. Lancet 2015 Oct 03;386(10001):1373-1385 [FREE Full text] [doi: 10.1016/S0140-6736(15)60173-8] [Medline: 25971224]
7. Hill K, Lopez AD, Shibuya K, Jha P, Monitoring of Vital Events (MoVE). Interim measures for meeting needs for health sector data: births, deaths, and causes of death. Lancet 2007 Nov;370(9600):1726-1735. [doi: 10.1016/S0140-6736(07)61309-9] [Medline: 18029005]
8. Hill K, Thomas K, AbouZahr C, Walker N, Say L, Inoue M, Maternal Mortality Working Group. Estimates of maternal mortality worldwide between 1990 and 2005: an assessment of available data. Lancet 2007 Oct 13;370(9595):1311-1319. [doi: 10.1016/S0140-6736(07)61572-4] [Medline: 17933645]
9. National Institute of Population Research and Training. Bangladesh Demographic and Health Survey, 2011. 2010. URL: https://dhsprogram.com/pubs/pdf/fr265/fr265.pdf [accessed 2016-05-01]
10. Phillips DE, AbouZahr C, Lopez AD, Mikkelsen L, de Savigny D, Lozano R, et al. Are well functioning civil registration and vital statistics systems associated with better health outcomes? Lancet 2015 Oct 03;386(10001):1386-1394. [doi: 10.1016/S0140-6736(15)60172-6] [Medline: 25971222]
11. Wang H, Dwyer-Lindgren L, Lofgren KT, Rajaratnam JK, Marcus JR, Levin-Rector A, et al. Age-specific and sex-specific mortality in 187 countries, 1970-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012 Dec 15;380(9859):2071-2094. [doi: 10.1016/S0140-6736(12)61719-X] [Medline: 23245603]
12. Registering millions: Celebrating the success and potential of Bangladesh's civil registration and vital statistics system. Get in the picture. 2011. URL: https://getinthepicture.org/resource/registering-millions-celebrating-success-and-potential-bangladeshs-civil-registration-and [accessed 2016-08-09]
13. Abouzahr C, Azimi S, Bersales L, Chandramouli C, Hufana L, Khan K. Strengthening civil registration and vital statistics in the Asia-Pacific region: learning from country experiences. Asia-Pacific Population Journal 2012;29(1):39-73. [doi: 10.18356/a906ccf5-en]
14. United Nations Childrens Fund. Under-five Mortality (U5MR). Childinfo: Monitoring the situation of children and women. 2009. URL: https://data.unicef.org/resources/data_explorer/unicef_f/?ag=UNICEF&df=GLOBAL_DATAFLOW&ver=1.0&dq=BGD.PT_CHLD_Y0T4_REG.&startPeriod=1970&endPeriod=2022 [accessed 2022-08-14]
15. Office of Registrar General. URL: http://180.211.213.83/brisreport/ReportPage.aspx?rpno=7 [accessed 2015-05-06]
16. Cabinet Division BS, Dhaka. CRVS in Bangladesh and COVID-19 Response. URL: https://getinthepicture.org/system/files/sites/default/files/CRVS_in_Bangladesh_Midterm_CRVS_report_28Jun2021.pdf [accessed 2021-09-08]
17. CRVS in Bangladesh. CRVS Secretariat CD. URL: http://crvs.gov.bd/about/crvs-in-bangladesh [accessed 2019-07-09]
18. The World Bank. Global Civil Registration and Vital Statistics: Scaling up Investment Plan 2015-2024. 2014. URL: https://www.worldbank.org/content/dam/Worldbank/document/HDN/Health/CRVSScaling-upoverview5-28-14web.pdf, [accessed 2020-02-02]
19. Bangladesh National Parliament. The Births and Deaths Registration Act. Bangladesh: Bangladesh National Parliament; 2014. URL: https://www.refworld.org/docid/511b54192.html [accessed 2016-02-02]
20. Local Government Division. URL: hhttps://www.dpp.gov.bd/bgpress/index.php/document/extraordinary_gazettes/285 [accessed 2022-08-09]
21. World Health Organization. Strengthening Civil Registration and Vital Statistics Systems through Innovative Approaches in the Health Sector: Guiding Principles and Good Practices. URL: https://getinthepicture.org/sites/default/files/resources/crvs_meeting_dec2013_report.pdf [accessed 2016-04-02]

22. AbouZahr C, Cleland J, Coullare F, Macfarlane SB, Notzon FC, Setel P, Monitoring of Vital Events (MoVE) writing group, et al. The way forward. Lancet 2007 Nov 24;370(9601):1791-1799. [doi: 10.1016/S0140-6736(07)61310-5] [Medline: 18029003]
23. Duff P, Kusumaningrum S, Stark L. Barriers to birth registration in Indonesia. Lancet Glob Health 2016 Apr;4(4):e234-e235 [FREE Full text] [doi: 10.1016/S2214-109X(15)00321-6] [Medline: 27013307]
24. Setel PW, Macfarlane SB, Szreter S, Mikkelsen L, Jha P, Stout S, Monitoring of Vital Events. A scandal of invisibility: making everyone count by counting everyone. Lancet 2007 Nov 03;370(9598):1569-1577. [doi: 10.1016/S0140-6736(07)61307-5] [Medline: 17992727]
25. Mikkelsen L, Phillips DE, AbouZahr C, Setel PW, de Savigny D, Lozano R, et al. A global assessment of civil registration and vital statistics systems: monitoring data quality and progress. Lancet 2015 Oct 03;386(10001):1395-1406. [doi: 10.1016/S0140-6736(15)60171-4] [Medline: 25971218]
26. Innovations in Mobile Birth Registration: Insights from Tigo Tanzania and Telenor Pakistan. 2017. URL: https://www.gsma.com/mobilefordevelopment/wp-content/uploads/2017/01/Innovations-in-Mobile-Birth-Registration_Insights-from-Tigo-Tanzania-and-Telenor-Pakistan.pdf [accessed 2018-05-14]
27. National Institute of Population Research and Training. Bangladesh Demographic and Health Survey, 2014. Dhaka, Bangladesh. 2013. URL: https://dhsprogram.com/pubs/pdf/FR311/FR311.pdf [accessed 2018-06-05]
28. Yanow D. Translating local knowledge at organizational peripheries. Br J Management 2004 Mar;15(S1):9-25. [doi: 10.1111/j.1467-8551.2004.00397.x]
29. District Health Information Software. DGHS. URL: https://dghs.gov.bd/index.php/en/home/113-english-root/dhis2, [accessed 2020-02-02]
30. How eMIS Tools are expanding in different districts of Bangladesh. Routine Health Information System. 2020 Feb 02. URL: http://www.rhis.net.bd/ [accessed 2020-02-02]
31. Hounton S, De Bernis L, Hussein J, Graham WJ, Danel I, Byass P, et al. Towards elimination of maternal deaths: maternal deaths surveillance and response. Reprod Health 2013 Jan 02;10:1 [FREE Full text] [doi: 10.1186/1742-4755-10-1] [Medline: 23279882]
32. Graham W, Ahmed S, Stanton C, Abou-Zahr C, Campbell O. Measuring maternal mortality: an overview of opportunities and options for developing countries. BMC Med 2008 May 26;6:12 [FREE Full text] [doi: 10.1186/1741-7015-6-12] [Medline: 18503716]
33. Shiffman J. Generating political priority for maternal mortality reduction in 5 developing countries. Am J Public Health 2007 May;97(5):796-803. [doi: 10.2105/AJPH.2006.095455] [Medline: 17395848]
34. Sankoh O, Byass P. Time for civil registration with verbal autopsy. Lancet Glob Health 2014 Dec;2(12):e693-e694 [FREE Full text] [doi: 10.1016/S2214-109X(14)70340-7] [Medline: 25433624]
35. Bongaarts J. WHO, UNICEF, UNFPA, World Bank Group, and United Nations Population Division Trends in Maternal Mortality: 1990 to 2015 Geneva: World Health Organization, 2015. Population and Development Review 2016 Dec 20;42(4):726-726. [doi: 10.1111/padr.12033]
36. Uddin M, Ashrafi SAA, Azad AK, Chowdhury A, Chowdhury HR, Riley ID, et al. Improving coverage of civil registration and vital statistics, Bangladesh. Bull World Health Organ 2019 Sep 01;97(9):637-641 [FREE Full text] [doi: 10.2471/BLT.18.219162] [Medline: 31474777]
37. Mahapatra P, Shibuya K, Lopez AD, Coullare F, Notzon FC, Rao C, Monitoring Vital Events. Civil registration systems and vital statistics: successes and missed opportunities. Lancet 2007 Nov 10;370(9599):1653-1663. [doi: 10.1016/S0140-6736(07)61308-7] [Medline: 18029006]
38. Setel P, AbouZahr C, Atuheire EB, Bratschi M, Cercone E, Chinganya O, et al. Mortality surveillance during the COVID-19 pandemic. Bull World Health Organ 2020 Jun 01;98(6):374 [FREE Full text] [doi: 10.2471/BLT.20.263194] [Medline: 32514207]

## Abbreviations

**CHCP:** community health care provider
**CRVS:** civil registration and vital statistics

*Edited by T Sanchez; submitted 13.11.20; peer-reviewed by C Reis, P Streathfield, A Mangharam, C Abouzahr; comments to author 10.05.21; revised version received 31.08.21; accepted 01.04.22; published 29.08.22.*

*Please cite as:*
*Tahsina T, Iqbal A, Rahman AE, Chowdhury SK, Chowdhury AI, Billah SM, Rahman A, Parveen M, Ahmed L, Rahman QS, Ashrafi SAA, Arifeen SE*
*Birth and Death Notifications for Improving Civil Registration and Vital Statistics in Bangladesh: Pilot Exploratory Study*
*JMIR Public Health Surveill 2022;8(8):e25735*
*URL: https://publichealth.jmir.org/2022/8/e25735*
*doi:10.2196/25735*
*PMID:36036979*

Publisher:
JMIR Publications
130 Queens Quay East.
Toronto, ON, M5A 3Y5
Phone: (+1) 416-583-2040
Email: support@jmir.org