

Water, wastewater, vaccines, and priority populations: Field epidemiology in Victoria, Australia during the COVID-19 pandemic

Aidan Yuen

M.Sc. B.Sc.(Hons) B.Sc.(Adv)

A thesis submitted for the degree of
Master of Philosophy (Applied Epidemiology)
at the Australian National University

Submitted for examination October 2022

Corrections submitted May 2023

Field placement

Department of Health, State Government of Victoria

Academic supervisor

Dr. Davoud Pourmarzi

Field supervisor

Dr. Jim Black



Australian
National
University



Department
of Health

© Copyright by Aidan Yuen 2022

All Rights Reserved

Originality statement

I hereby declare that this submission is my own work. To the best of my knowledge, it contains no materials that have been accepted for the award of any other degree or diploma at any educational institution, except where due acknowledgement is made in the thesis. Any contribution made to the research by others is explicitly acknowledged. I also declare that the intellectual content of this thesis is the product of my own work; assistance from others in the projects' design and conception or in style, presentation or linguistic expression is acknowledged.

A handwritten signature in black ink, reading "Aidan Yuen". The signature is written in a cursive, flowing style with a large initial 'A' and a long horizontal stroke extending to the right.

Aidan Yuen

28 October 2022

Acknowledgements

I would like to acknowledge the many people who have helped me along the way.

I am especially grateful to Dr. Davoud Pourmarzi, my academic supervisor, for his kind support and sound advice throughout the program. Our interactions always left me feeling invigorated and inspired—a testament to his calm demeanour, and his infectious passion for public health. Thanks also to Dr. Jim Black, my field supervisor, for sharing his expertise with me, and for always encouraging me to push my boundaries. His intelligence, integrity and decisiveness were paramount to my progress.

At the State Government of Victoria's Department of Health, I want to thank Lucinda Franklin and Alvin Lee, my managers, for their guidance and for dealing with my endless paperwork. Thanks also to the SynSurv Team for their friendship and invaluable support throughout my candidature. To my many collaborators, thank you for the countless learnings. I am especially grateful to Stacey Rowe, Dr. Sheena Sullivan and Mohana Baptista for giving me the opportunity to assist with the COVID-19 Response, and for facilitating my secondment to the Western Public Health Unit (WPHU), where I investigated a COVID-19 outbreak. To the WPHU staff, thank you for the warm welcome—I especially want to thank Dr. Frances Ampt and Gabrielle Hales for their excellent mentorship.

Thanks also to the MAE staff for devising and delivering this enriching and challenging program. To the MAE 2021 cohort—and especially to my MAE twin, Al Gomez—thank you for all the laughs and WhatsApp chats. A special shout-out also goes to Meg Dalmau and Zoe Joo, who I had the joy of travelling to Panama with for the 11th TEPHINET Global Scientific Conference. Thank you for the week of giggles and gluttony—this was easily the highlight of my MAE! To everyone else involved in the MAE, I am grateful for the times you have generously offered your assistance.

Finally, I wish to thank my friends and family for their continued support. A special thanks goes out to my late friend, Nate Kai, for always giving me the time and space to vent my frustrations about the program (and about life in general 😊). This thesis is dedicated to you.

Abstract

This thesis demonstrates my fulfilment of the requirements of the Master of Philosophy in Applied Epidemiology (MAE) program at the Australian National University. My MAE placement was with the State Government of Victoria's Department of Health from February 2021 to December 2022. Chapter one describes a test of the utility of interrupted time series segmented regression analysis for detecting point-source and continuous-source waterborne disease outbreaks. Building on from chapter one, chapter two details the deployment of a syndromic surveillance system for monitoring and evaluating the public health impacts of drinking water contamination events using data from public hospital emergency departments. The third chapter describes an estimation of the accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people. Chapter four details an investigation of a COVID-19 outbreak at a residential aged-care facility, while chapter five comprises a mixed-methods systematic review on the COVID-19 vaccine attitudes of racial and ethnic minorities. The sixth and final chapter includes a portfolio of my teaching commitments and other public health activities, including an FAQ on monkeypox following the outbreak in May 2022. I present each chapter with a reflective discussion of my role, my lessons learnt, and the projects' public health impacts.

Contents

Introduction	1
Chapter 1: Interrupted time series segmented regression analysis for detecting waterborne disease outbreaks by syndromic surveillance.....	5
Prologue.....	5
My role.....	5
Lessons learnt	6
Public health impacts	6
Abstract	8
1. Introduction	9
2. Methods	11
2.1. Study design	11
2.2. Data sources	11
2.3. Interrupted time series analysis	12
3. Results	14
3.1. Suspected contamination event.....	14
3.2. Simulated outbreaks.....	14
4. Discussion.....	16
5. Additional information.....	18
5.1. Acknowledgements	18
5.2. Author details	18
5.3. Statements	18
6. References.....	19
Appendix	21
Chapter 2: Establishing a syndromic surveillance system for detecting gastroenteritis outbreaks following drinking water contamination events in Victoria, Australia	22
Prologue.....	22
My role.....	22
Lessons learnt	23
Public health impacts	24
Abstract	25
1. Introduction	26
2. Methods	28
2.1. Surveillance system design	28
2.2. Incidence thresholds to identify possible outbreaks	29
2.3. Surveillance system attributes	30

3. Results	31
4. Discussion	35
4.1. Surveillance system attributes	35
4.2. Limitations and future directions	38
4.3. Conclusions.....	38
5. Additional information	39
5.1. Acknowledgements	39
5.2. Author details	39
5.3. Statements	39
6. References	40
Chapter 3: Estimating the accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in catchments in Victoria, Australia	42
Prologue.....	42
My role	42
Lessons learnt	43
Public health impacts	43
Abstract	45
1. Introduction	46
2. Methods	48
2.1. Study design	48
2.2. Data sources	48
2.3. Data analysis.....	49
3. Results	51
3.1. Accuracy estimates	51
3.2. Estimated probability of detection.....	52
4. Discussion.....	56
5. Additional information	59
5.1. Acknowledgements	59
5.2. Funding statement.....	59
5.3. Ethical statement.....	59
6. References.....	60
Appendix	63
Chapter 4: Investigation of a COVID-19 outbreak at the Arcare Maidstone residential aged-care facility.....	64
Prologue.....	64
My role	64
Lessons learnt	65

Public health impacts	65
Abstract	66
1. Introduction	68
1.1. COVID-19.....	68
1.2. Variants of concern.....	68
1.3. Transmission.....	68
1.4. Diagnosis	69
1.5. Treatment.....	69
1.6. Vaccination.....	70
1.7. Residential aged-care facilities (RACFs)	70
1.8. COVID-19 outbreak at the Arcare Maidstone RACF in May 2021	70
1.9. Aims and objectives	71
2. Methods	72
2.1. Ethics	72
2.2. Governance.....	72
2.3. Epidemiological investigation	73
2.4. Genomic investigation	76
2.5. Public health actions	77
3. Results	80
3.1. Descriptive Epidemiology	80
3.2. Genomic analysis.....	84
3.3. Outline of public health actions.....	85
4. Discussion.....	88
4.1. Key learnings	88
4.2. Conclusions.....	90
5. References.....	91
Chapter 5: COVID-19 vaccine hesitancy among racial and ethnic minorities and foreign-born populations in high-income English-speaking countries: A mixed-methods systematic review	95
Prologue.....	95
My role.....	95
Lessons learnt	96
Public health impacts	96
Abstract.....	97
1. Introduction	98
2. Methods	99
2.1. Inclusion criteria	99

2.2.	Search strategy	99
2.3.	Assessment of methodological quality	99
2.4.	Data extraction	99
2.5.	Data synthesis.....	100
3.	Results	101
3.1.	Search results	101
3.2.	Methodological quality appraisal.....	101
3.3.	Characteristics of included studies	102
3.4.	Quantitative synthesis	102
3.5.	Qualitative synthesis	104
3.6.	Synthesised findings	106
4.	Discussion.....	107
4.1.	Strengths and limitations	108
4.2.	Recommendations for future research.....	108
4.3.	Conclusions.....	109
5.	Declarations	110
5.1.	Ethics approval and consent to participate	110
5.2.	Consent for publication.....	110
5.3.	Availability of data and materials	110
5.4.	Competing interests	110
5.5.	Funding	110
5.6.	Authors' contributions.....	110
5.7.	Acknowledgements	110
6.	References.....	111
7.	Tables	117
Chapter 6:	Other public health activities	128
1.	Teaching to first-year Scholars	128
2.	Lessons from the field	128
3.	Evidence-based Medicine—London School of Paediatrics Day	129
4.	11 th TEPHINET Global Scientific Conference	129
5.	Casual/Sessional Academic post.....	129
6.	Monkeypox FAQ.....	130
Appendices		131

Introduction

This thesis demonstrates my fulfilment of the requirements of the Master of Philosophy in Applied Epidemiology (MAE) program at the Australian National University (ANU). My candidature involved a full-time placement at the State Government of Victoria's Department of Health (the Department) from February 2021 to December 2022. I was supervised by Dr. Davoud Pourmarzi at the ANU and Dr. Jim Black at the Department. The MAE requires that Scholars demonstrate core competencies in field epidemiology in accordance with its accreditation under the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET). This thesis is organised into six chapters. Chapters one through four each detail a project addressing the four major MAE competencies. I address all minor competencies in chapters five and six, and at various points throughout the thesis (Table 1).

Chapter one describes an analysis of a public health dataset. The Department is currently building its syndromic surveillance capabilities for rapidly detecting gastroenteritis outbreaks following drinking water contamination events to prevent large-scale morbidity and mortality, and associated costs. In deploying this system, I tested the utility of interrupted time series segmented regression analysis for detecting point-source and continuous-source waterborne disease outbreaks following such events. This involved retrospectively analysing a past lapse in water treatment. Given the absence of recent events leading to outbreaks, we then simulated outbreaks of various sizes to determine the number of excess presentations needed for such methods to statistically signal a detection. The models demonstrated high specificity, while sensitivity was dose dependent.

Building on from chapter one, chapter two details the establishment of a surveillance system for drinking water contamination events. Most Victorians are currently supplied with potable water by retail water corporations; these agencies have a legislative requirement to notify the Department of any known or suspected contamination events. To help monitor and evaluate these notifications, we deployed a syndromic surveillance system that statistically signals potential gastroenteritis outbreaks in affected postcodes using the methods described in chapter one. The system comprises a report/dashboard that ingests data on gastroenteritis presentations at public hospital EDs, which are updated daily. When used in conjunction with microbiological testing and consultation with key stakeholders, such as OzFoodNet epidemiologists, this system can help inform public health decision-making, including the issuing, and lifting of boil water advisories.

The third chapter details an epidemiological study. In Victoria, wastewater surveillance was initially implemented to facilitate COVID-19 case finding. Wastewater samples are collected from sewage and analysed for SARS-CoV-2 fragments shed by infected people. Of note,

Introduction

viral shedding from the digestive system often persists longer than one's infectious period, which may limit the program's utility. To estimate its accuracy—considering its limitations—we conducted a diagnostic test accuracy study, through which, the program showed high specificity and moderate sensitivity. We then forecasted the detection probability for varying numbers of infected people at varying periods of potential shedding. Probabilities were elevated for catchments with any number of infected people than catchments with no infected people, even for periods up to 84 days following symptom onset/testing date—a likely consequence of persistent faecal shedding. Our findings were shared with colleagues who are now evaluating the program to ensure efficiency and appropriate resource allocation, and to potentially extend its uses to other pathogens.

The fourth chapter describes a COVID-19 outbreak investigation at the Arcare Maidstone residential aged-care facility (RACF). The outbreak was declared on 29 May 2021 when the index case was notified to the Department. I was subsequently deployed to the Western Public Health Unit (WPHU) to help investigate the outbreak, which involved collecting and analysing key epidemiological and genomic data to inform decision-making, and to enact rapid control measures to prevent further transmission. With this, the outbreak was stood down on 21 June 2021. My findings were captured in a report for WPHU and the Department, which was used to inform subsequent RACF-outbreaks.

Chapter five details a mixed-methods systematic review on the prevalence of, and reasons for, COVID-19 vaccine hesitancy among racial and ethnic minorities and foreign-born populations in high-income English-speaking countries. These populations can experience lower access and acceptance of COVID-19 vaccines, despite facing a disproportionate burden of COVID-19. Addressing hesitancy among such populations can therefore improve health outcomes, promote health equity, and help countries reach and exceed their vaccination targets, which provided the impetus for this project. Through our systematic review, we found that hesitancy could be attributed to a mistrust in institutions, health concerns, and a lack of access, though these were not exclusive to minorities. That said, certain groups did report greater mistrust in governments, and greater concerns about vaccine safety and effectiveness as drivers of hesitancy. My findings were subsequently used to inform the Department's vaccine outreach initiatives and policy interventions.

Finally, chapter six comprises a portfolio of my other public health activities during my candidature. To meet the MAE teaching requirements, my fellow MAE 2021 Scholars and I delivered a lecture on antimicrobial resistance and healthcare-associated infections to the 2022 cohort. I also conducted a peer-to-peer teaching session ("lessons from the field") where I discussed the use of diagnostic test accuracy studies for estimating the accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in

Introduction

catchments. In addition to the MAE requirements, I also: 1) delivered a lecture on interpreting diagnostic test accuracy studies to paediatric trainees at a workshop organised by the *Royal Society of Medicine UK*; 2) facilitated a workshop on adult learning principles and experiential learning theories for field epidemiology trainers at the *11th TEPHINET Global Scientific Conference*; and 3) facilitated population health tutorials and problem-based learning sessions for first- and second-year Doctor of Medicine and Surgery (MChD) students at the ANU. To meet the lay summary minor competency, I prepared an FAQ on monkeypox to assist the Department's social media team with their public engagements following the monkeypox outbreak in May 2022.

This thesis demonstrates my competencies in outbreak investigation, public health surveillance, analysis of public health data, and research design and methods—all of which are crucial to best practice epidemiology. But above all, the MAE has taught me perseverance. The COVID-19 pandemic provided a challenging backdrop for which to complete the MAE. Despite the personal and professional hurdles it brought to my candidature, I am proud to have produced this thesis. I first learnt about the MAE at the end of high school and thought how cool it would be to work as a boots-on-the-ground disease detective. A decade later, and I will soon graduate from that very program!

Table 1. Master of Philosophy in Applied Epidemiology (MAE) competencies and relevant thesis chapters.

MAE competencies	Thesis chapters					
	Chapter 1: Interrupted time series analysis of water events	Chapter 2: Syndromic surveillance for water events	Chapter 3: SARS-CoV-2 wastewater surveillance accuracy	Chapter 4: COVID-19 outbreak in aged-care	Chapter 5: COVID-19 vaccine hesitancy in minorities	Chapter 6: Other public health activities
<i>Major competencies</i>						
Investigation of an acute public health problem or threat				✓		
Analysis of a public health dataset	✓					
Establish or evaluate a surveillance system or other health information system		✓				
Design and conduct an epidemiological study			✓			
<i>Minor competencies</i>						
Literature review					✓	
Lay summary						✓
Conference presentation	✓		✓			
Peer-reviewed publication	✓	✓	✓		✓	
Teaching field epidemiology						✓

Chapter 1: Interrupted time series segmented regression analysis for detecting waterborne disease outbreaks by syndromic surveillance

Prologue

This chapter meets the MAE major competency on completing an “analysis of a public health dataset”. The Department is currently building its syndromic surveillance capabilities for rapidly detecting gastroenteritis outbreaks following drinking water contamination events to prevent large-scale morbidity and mortality, and associated costs. In deploying this system, I tested the utility of interrupted time series segmented regression analysis for detecting point-source and continuous-source waterborne disease outbreaks following such events. This involved retrospectively analysing a past lapse in water treatment. Given the absence of recent events leading to outbreaks, we then simulated outbreaks of various sizes to determine the number of excess presentations needed for such methods to statistically signal a detection. The models demonstrated high specificity, while sensitivity was dose dependent; it was therefore used to determine incidence thresholds to identify potential outbreaks in the syndromic surveillance system detailed in chapter two.

This project was largely conceptualised by Dr. Jim Black, my field supervisor, and was born out of the broader SynSurv project, which is the Department’s syndromic surveillance system. Syndromic surveillance is used in many jurisdictions worldwide, including the United States, the United Kingdom and France. In Victoria, the first version of SynSurv was developed for the 2006 Commonwealth Games in Melbourne. It currently comprises a set of tools to answer specific questions on behalf of “clients” to help inform public health actions for which they are responsible. At present, modules have been deployed for thunderstorm asthma and point-source smoke hazards, among others. A new module for drinking water contamination events—detailed in chapters one and two—was conceptualised to build the Department’s capacity for monitoring and evaluating such events and to inform subsequent interventions, including the issuing, and lifting of boil water advisories.

My role

This project began with a thorough review of the academic and grey literature of existing syndromic surveillance systems and their analytical approaches for determining incidence thresholds to identify potential outbreaks. I also consulted other SynSurv epidemiologists and reviewed operating documents for existing SynSurv modules—including those for thunderstorm asthma and point-source smoke hazards—to learn their approaches. This was

used to inform my own study protocol and data analysis plan. Ethical approval was then sought from the State Government of Victoria's Department of Health and Department of Family, Fairness and Housing Human Research Ethics Committee. Upon approval, I performed data cleaning and linkage across multiple datasets and data types—including spatial data—and conducted descriptive and inferential statistical analyses using R.

Our findings were drafted into a scientific manuscript and submitted to *Communicable Disease Intelligence* for peer-review on 17 August 2022; the contents of this manuscript form the body of this chapter. I also presented our findings at the *Communicable Diseases and Immunisation Conference* in Sydney on 22 June 2022; the slides are included in this chapter's appendix (Appendix A). Both works meet the MAE minor competencies on preparing a "peer-reviewed publication" and a "conference presentation".

Lessons learnt

Through this project, I developed a newfound appreciation for how data can be a key communication tool with stakeholders and for driving decision-making. If stakeholders know how big a problem is—for example, in a drinking water contamination event—they are more likely to become engaged and to allocate resources to that problem.

I also learnt about the value of adopting analytical techniques from other disciplines to applied epidemiology. Interrupted time series analysis is typically used to evaluate the impact of policy interventions in a population. But as this chapter highlights, this approach also has potential for informing incidence thresholds in syndromic surveillance systems.

This project also taught me how to repurpose data for public health surveillance. ICD-10 codes, for example, are used in public and private hospitals in Australia to classify episodes of admitted patient care. These codes are then used by the Independent Hospital Pricing Authority to fund hospitals based on the mix of patients they treat. But as this chapter demonstrates, ICD-10 codes also have utility in monitoring and evaluating the impacts of public health hazards.

Public health impacts

In retrospectively analysing a past lapse in drinking water treatment, our study demonstrated the utility of interrupted time series segmented regression analysis for detecting waterborne disease outbreaks through the syndromic surveillance of gastroenteritis presentations to public hospital emergency departments (EDs). We also simulated outbreaks of various sizes—given the absence of recent events leading to outbreaks—and demonstrated the ability for segmented regressions to statistically signal a detection, even without a large excess in presentations. Its sensitivity was also dose-dependent, i.e., a small outbreak may go

undetected with this approach. This should not pose major ramifications to public health as such events will likely see low morbidity. In contrast, this approach will likely detect large outbreaks, which should prompt rapid and localised public health actions to resolve the issue. The simulations also showed that this approach is highly specific, with a false-positive detection rate of less than 10%. Our study therefore supports the use of such analyses for informing Victoria's syndromic surveillance system for such events, when used in conjunction with timely public hospital ED data.

Abstract

Introduction

Pathogens can enter the drinking water supply and cause gastroenteritis outbreaks. Such events can affect many people in a short time, making them a high risk for public health. In Australia, the State Government of Victoria's Department of Health is deploying a syndromic surveillance system for drinking water contamination events. We assessed the utility of segmented regression analyses for detecting such events and determined the number of excess presentations needed for such methods to signal a detection.

Methods

The study involved an interrupted time series study of a past lapse in water treatment. The baseline period comprised the four weeks before the minimum incubation period of suspected pathogens, set at two days post-event. The surveillance period comprised the week after. We used segmented linear regression to compare the count of gastroenteritis presentations to public hospital emergency departments (EDs) between the surveillance and baseline periods. We then simulated events resulting in varying excess presentations. These were superimposed onto the ED data over fifty different dates across 2020. Using the same regression, we calculated the detection probability at $P < 0.05$ for each outbreak size.

Results

In the retrospective analysis, there was strong evidence for an increase in presentations shortly after the event. In the simulations, with no excess presentations—i.e., with the ED data as is—the models signalled 8% detections. The models returned 50% detections with 28 excess presentations and 100% detections with 78 excess presentations.

Conclusions

The transient increase in presentations after the event may be attributed to microbiological hazards or increased health seeking behaviour following the issuing of boil water advisories. The simulations demonstrated the ability for segmented regressions to signal a detection, even without a large excess in presentations. The approach also demonstrated high specificity and should therefore be considered for informing Victoria's syndromic surveillance system.

Keywords

Drinking water contamination; syndromic surveillance; waterborne disease outbreaks.

1. Introduction

In drinking water contamination events, pathogens—such as Shiga toxin-producing *Escherichia coli* (STEC) and *Cryptosporidium*—can cause outbreaks of acute gastroenteritis (1-3). Such outbreaks can affect many people in a short time, making them a high risk for public health (4). Recognising and responding to such outbreaks quickly can therefore mitigate downstream morbidity and mortality, and associated costs (5,6). In the Milwaukee, Wisconsin cryptosporidiosis outbreak of 1993, for example, up to 85% of the 403,000 cases could have been avoided had surveillance systems detected it earlier (7).

One avenue for early detection is syndromic surveillance. Syndromic surveillance uses pre-clinical and clinical pre-diagnostic data, and proxy measures—such as hospital admission reports and over-the-counter pharmaceutical sales—to identify potential outbreaks (8-11). Syndromic surveillance can therefore detect outbreaks earlier than surveillance systems that rely on laboratory-confirmed cases (5,6). In the Milwaukee outbreak, for example, calls to nurse hotlines reported a four-fold increase in diarrhoeal disease; this was observed one day before local pharmacists noticed that over-the-counter anti-diarrhoeal drugs were selling out, and five days before the local public health unit was notified of a potential outbreak (12,13). Although the impetus for its initial expansion was for bioterrorism preparedness, the Milwaukee event demonstrated the utility of syndromic surveillance for detecting waterborne disease outbreaks (14).

Victoria, Australia also experiences sporadic drinking water contamination events. In such events, water agencies are required to report to the State Government of Victoria's Department of Health (the Department) any known or suspected contamination, in accordance with the *Safe Drinking Water Act 2003*. One such occasion occurred in 2020, when a storm caused a power outage, which then caused a generator to fail. Undisinfected water subsequently entered the water distribution zones of the two affected water agencies, resulting in the issuing of boil water advisories. Although there is little evidence that this event—or any other recent events—have resulted in outbreaks, preparedness for future outbreaks is important to avoid situations like the Milwaukee event.

Given this, the Department is building its capacity for the syndromic surveillance of such events by using rapidly acquired but non-specific information on gastroenteritis presentations to public hospital emergency departments (EDs). This system will consider incorporating inferential statistics to help signal the occurrence of potential outbreaks. One potential analytical approach is interrupted time series segmented regression analysis, which is a powerful statistical method typically used to evaluate policy interventions (15). In this paper, we adapted this approach to the study of drinking water contamination events.

Chapter 1

By retrospectively analysing the 2020 event, we aimed to answer the following question: What is the utility of applying interrupted time series segmented regression analyses for detecting excess gastroenteritis presentations to public hospital EDs following a drinking water contamination event?

Given there is little evidence of recent events resulting in outbreaks, we then simulated outbreaks of various sizes to answer the following question: What number of excess presentations to public hospital EDs are needed for such methods to statistically signal a detection?

2. Methods

2.1. Study design

This study involved an ecological time series study of secondary panel data stratified by postcode and days. The study population included all people resident in the affected Victorian postcodes for the period from 1 January 2020 to 31 December 2020.

2.2. Data sources

Shapefiles of the various water distribution zones were provided by each water agency. By layering these zones over Victorian postcodes, we determined which postcodes are served by which agencies (Figure 1). Because some postcodes are served by multiple agencies, or only partially served by an agency, we defined two different analyses:

- An “inclusive” option, where postcodes are considered part of a zone if they are served at least in part by a water agency; and
- A “core” option, where postcodes are considered part of a zone if they are only served by a water agency, and wholly served by that agency.

Of note, not all postcodes are served by a water agency. And of those that are, not all areas in that postcode are connected to the network. Unserved populations commonly access their drinking water from bores, wells, and rainwater collections.

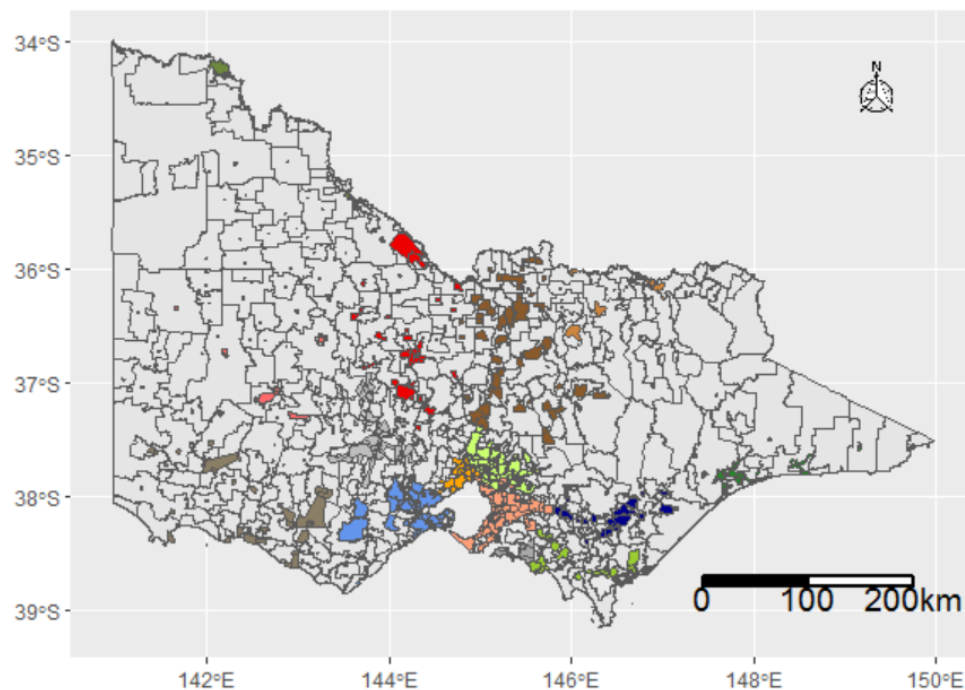


Figure 1. Water distribution zones of water agencies overlaying Victorian postcodes (grey borders). Each colour represents the area served by a different water agency.

ED presentations were retrieved from the VEMD, which includes de-identified demographic, administrative and clinical data detailing presentations at Victorian public hospitals EDs. Residential addresses for each presentation were mapped to their corresponding water distributions zones. Gastroenteritis presentations were identified using diagnosis fields that included an ICD-10 code with the prefix "A0".

2.3. Interrupted time series analysis

2.3.1. Suspected contamination event

The dataset was restricted to those postcodes served by the affected water agencies for both the “inclusive” and “core” definitions described above.

The baseline period was defined as the four weeks before the minimum incubation period of pathogens commonly implicated in such events, like *Cryptosporidium* and STEC (17,18); this was set at two days post-event. The surveillance period was defined as the week after that minimum incubation period. Interrupted time series analysis was used to test the hypothesis that the count of gastroenteritis presentations is different between the baseline and surveillance periods. The following segmented linear regression model was used for our interrupted time series analysis:

$$Y_t = \beta_0 + \beta_1 T + \beta_2 X_t + \beta_3 TX_t$$

This model required three key variables:

1. T : the days since the start of the study period.
2. X_t : a dummy variable indicating the baseline and surveillance periods.
3. Y_t : the outcome at time t .

Upon entering these variables into the model, we retrieved the following coefficients for analysis:

- β_0 : is the constant—i.e., the value at which the regression crosses the y-axis.
- β_1 : the baseline trend—i.e., the change in presentations with a time unit increase in the baseline period.
- β_2 : the level change, i.e.—the immediate change in presentations in the surveillance period compared to the baseline period; this coefficient can signal a point-source outbreak.
- β_3 : the slope change, i.e.—the change in the regression gradient of the surveillance period compared to the baseline period; this coefficient can signal a continuous-source outbreak.

2.3.2. Simulated outbreaks

To help interpret negative and positive results of future analyses, we simulated single-day water contamination events causing point-source outbreaks of log-normal distribution, resulting in varying numbers of excess gastroenteritis presentations to public hospital EDs (Figure 2). Given the absence of recent events leading to outbreaks, these excess presentations were then superimposed onto the existing VEMD data for the same postcodes as in the previous analysis, but over a different date. We reran the same segmented regression model and used $P < 0.05$ for the β_2 coefficient to signal a detection. We repeated this process for 50 different dates across 2020 and calculated the proportion of positive detections for each outbreak size simulated in Figure 2.

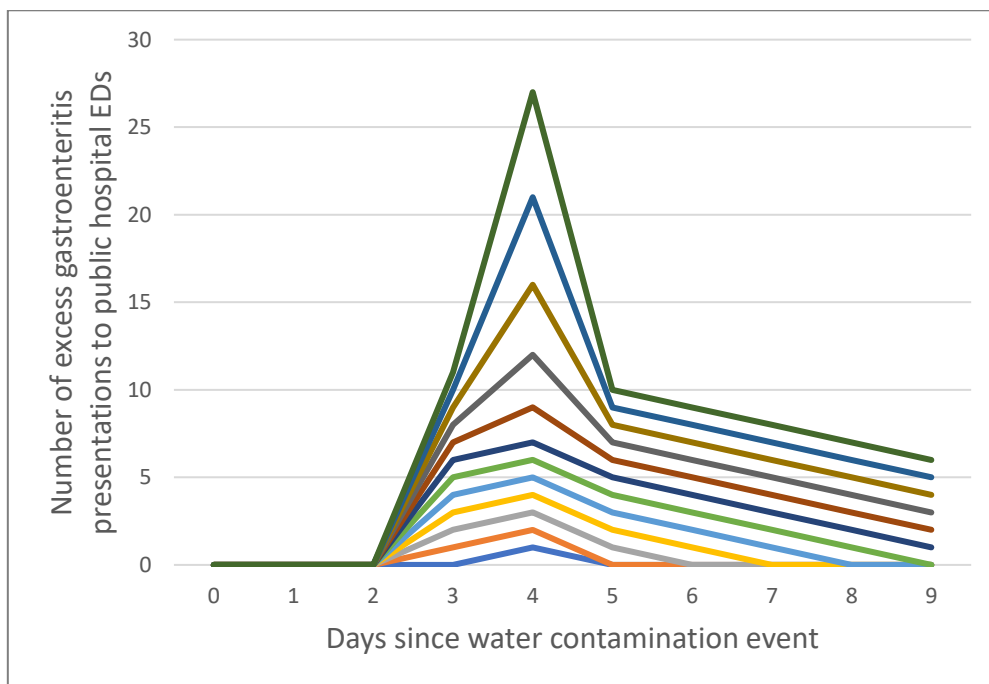


Figure 2. Simulated point-source outbreaks of Shiga-toxin producing *Escherichia coli* following a single-day water contamination event resulting in excess gastroenteritis presentations to public hospital emergency departments (EDs). The number of excess presentations in each outbreak is as follows: blue (1), orange (3), light grey (6), yellow (10), light blue (15), light green (21), dark blue (28), dark brown (36), dark grey (45), light brown (55), dark blue (66) and dark green (78).

3. Results

3.1. Suspected contamination event

The “inclusive” analysis included 237 postcodes. There were approximately 15 gastroenteritis presentations to public hospital EDs at the beginning of the study ($\beta_0=15.52$), with little evidence for a change in rate across the baseline period, which comprised the four weeks before the minimum incubation period of suspected pathogens, set at two days post-event ($\beta_7=-0.08$, $P=0.33$). There was very strong evidence for a level change in approximately 11 additional presentations immediately following the minimum incubation period of suspected pathogens ($\beta_7=10.94$, $P<0.001$), with strong evidence showing a subsequent decrease in presentations over the surveillance week ($\beta_3=-1.67$, $P=0.02$) (Figure 3).

The “core” analysis included 97 postcodes. The beginning of the study period saw approximately 7 presentations ($\beta_0=6.56$), with little evidence for a change in rate across the baseline period ($\beta_7=-0.03$, $P=0.68$). There was strong evidence for an immediate increase in presentations following the minimum incubation period of suspected pathogens ($\beta_7=7.39$, $P=0.01$), and some evidence to show a subsequent decrease in presentations over the surveillance week ($\beta_3=-1.04$, $P=0.07$) (Figure 3).

3.2. Simulated outbreaks

Over fifty runs of the simulated outbreaks for the “inclusive” analysis, with no excess presentations—i.e., with the ED data as is—the models signalled a detection 8% of the time. The models returned 50% detections with 28 excess presentations, and 100% detections with 78 excess presentations (Table 1). For the “core” analysis, with no excess presentations, the models signalled a detection 6% of the time. The models returned over 50% detections with 21 excess presentations, and 100% detections with 45 excess presentations (Table 1).

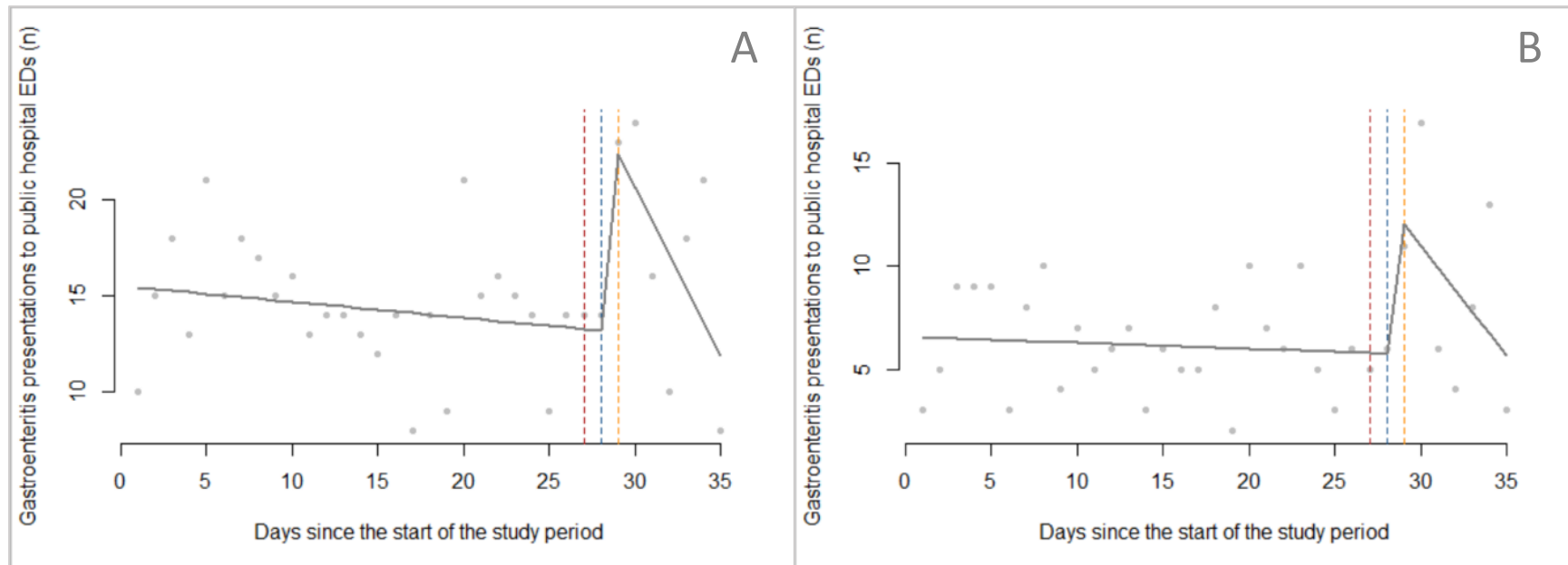


Figure 3. Interrupted time series study of gastroenteritis presentations to public hospital emergency departments (EDs) before and after a suspected contamination event in affected postcodes in Victoria, Australia (2020). A: includes postcodes that are served at least in part by the affected source. B: includes postcodes that are only served, and wholly served, by the affected source. The contamination event (red line), boil water advisory (blue line) and the minimum incubation period of suspected pathogens (yellow line) are depicted.

Table 1. The probability of detection in an interrupted time series study of gastroenteritis presentations to public hospital emergency departments (EDs) before and after simulated outbreaks of various sizes in affected postcodes in Victoria, Australia (2020). Details of the simulated outbreaks and resultant excess presentations are given in Figure 2.

Excess presentations to public hospital EDs (n)	0	1	3	6	10	15	21	28	36	45	55	66	78
Proportion detected for the “inclusive” ¹ analysis	8%	8%	10%	18%	24%	32%	44%	50%	58%	76%	88%	94%	100%
Proportion detected for the “core” ² analysis	6%	10%	14%	20%	36%	44%	60%	78%	88%	100%	100%	100%	100%

¹ Includes postcodes that are served at least in part by the affected source

² Includes postcodes that are only served, and wholly served, by the affected source

4. Discussion

This study demonstrated the utility of applying segmented regression analysis to an interrupted time series study of gastroenteritis presentations to public hospital EDs before and after a suspected drinking water contamination event. We also simulated outbreaks of various sizes—given the absence of recent events leading to outbreaks—and demonstrated the ability of segmented regressions to statistically signal a detection, even without a large excess in presentations. Our study therefore supports the use of interrupted time series analysis for informing Victoria’s syndromic surveillance system for such events in conjunction with timely public hospital ED data.

In this study, the suspected contamination event saw a transient increase in presentations, but indicator microorganisms were undetected in samples taken from the affected waterbodies. We recognise there are limitations to monitoring extensively for specific pathogens in large water distribution networks, like those implicated in this event. It therefore remains possible that the transient increase in presentations could be attributed to microbiological hazards. Alternatively, our findings may be ascribed to increased health seeking behaviour following the issuing of boil water advisories (3).

The segmented regressions also signalled detections when applied to other dates in the VEMD—a likely consequence of random error (19). With a false-positive rate of less than 10% for both the “inclusive” and “core” analyses, a positive detection is therefore suggestive of a gastroenteritis outbreak in a defined geographical setting, which may be attributed to a water contamination event. Its sensitivity, i.e., its true-positive detection rate, was dose-dependent. This is consistent with other syndromic surveillance approaches that use health insurance data, telephone triage and over-the-counter pharmacy sales (8,20).

Of note, our study period occurred during the COVID-19 pandemic. ED presentations likely fluctuated with stay-at-home orders, which may have introduced additional noise to the baseline rates of gastroenteritis presentations. By restricting the baseline period to four weeks, we were able to retain sufficient data to establish a robust baseline, while minimising the impact of variable lockdowns and seasonal variability.

Our analyses did have some limitations. Firstly, gastroenteritis syndromes were identified using ICD-10 codes, which can be subject to misclassification. Similarly, there is likely misclassification in how we determined which postcodes are served by which water source. The “inclusive” definition will have captured all affected postcodes, with the drawback being the inclusion of unaffected populations in sections served by other zones. The “core” definition has the advantage of restricting analyses to postcodes completely affected by the event, at the expense of excluding affected postcodes served additionally by other zones.

The misclassification in ICD-10 codes and postcodes are likely non-differential between the baseline and surveillance periods, thus biasing the effect estimates towards the null. As such, the sensitivity estimates of our models are likely minimum estimates of the true value.

Furthermore, some people may have ingested water in the affected postcodes, but gotten ill in another, thereby reducing case ascertainment. This was minimised by the presence of stay-at-home orders during the study period. However, we recognise that this limitation will be exacerbated in its future applications to syndromic surveillance during non-lockdown contexts.

Our retrospective analysis was also limited to a single water contamination event as the model for a waterborne disease outbreak. This is sufficient for a proof of concept of the methods—which was the principal aim of the paper—but is limited by the uncertainties around whether the event was the cause of any illness. These methods should therefore be tested against other water events to better assess its accuracy for detecting such outbreaks.

Our simulation was also run over 50 different dates across 2020; the results may therefore lack precision and may benefit from additional runs. Furthermore, all simulations were modelled after single-day water contamination events leading to point-source outbreaks of STEC. Therefore, our findings may not be generalisable to outbreaks with different characteristics. Future simulations could incorporate other pathogens and other outbreak types, including continuous-source outbreaks, to better assess the model's sensitivity and specificity. Future studies could also explore the utility of interrupted times series analysis applied to other outcome data, such as telephone triage, web-based queries, and over-the-counter pharmaceutical sales (8). One key assumption in our discussion is that the boil water advisories may have increased health seeking behaviour. However, there is a dearth of literature to support this assumption, which presents another avenue for novel research.

In closing, this study demonstrated the utility of interrupted time series analysis for the early detection of waterborne disease outbreaks when used in conjunction with timely public hospital ED data. This approach will therefore be considered for informing Victoria's syndromic surveillance system for monitoring and evaluating such events.

5. Additional information

5.1. Acknowledgements

The authors acknowledge the contributions of the staff at the State Government of Victoria's Department of Health and the Victorian water agencies.

5.2. Author details

Authors

Mr. Aidan Yuen (<http://orcid.org/0000-0002-8642-8619>)^{1,2}, Dr. Davoud Pourmarzi¹, Ms. Suzie Sarkis², Ms. Carmela Luisetto², Mr. Kamal Khatri², Dr. Angie Bone², Dr. Jim Black²

Affiliations

1. National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australian Capital Territory 2600, Australia
2. Department of Health, State Government of Victoria, Melbourne, Victoria 3000, Australia

Corresponding author

- Name: Aidan Yuen
- Email: aidan.yuen@anu.edu.au

5.3. Statements

Ethical statement

Ethical approval was obtained from the State Government of Victoria's Department of Health and Department of Families, Fairness and Housing Human Research Ethics Committee (ref: HREC/80437/DOH-2021-294619).

Funding statement

This research did not receive any specific funding.

Data availability

Data requests can be directed to the corresponding author.

Conflict of interest

We declare no known competing interests that could have influenced this work.

6. References

1. Pignata C, S, Bonetta S, Cacciò SM, Sannella AR, Gilli G, et al. Cryptosporidium Oocyst Contamination in Drinking Water: A Case Study in Italy. *Int J Environ Res Public Health* [Internet]. 2019 Jun 10;16(11):2055. Available from: <https://pubmed.ncbi.nlm.nih.gov/31185673>
2. Reynolds C, Checkley S, Chui L, Otto S, Neumann NF. Evaluating the risks associated with Shiga-toxin-producing *Escherichia coli* (STEC) in private well waters in Canada. *Can J Microbiol*. 2020 May;66(5):337-50.
3. Lin CJ, Richardson DB, Hilborn ED, Weinberg H, Engel LS, Wade TJ. Emergency Department Visits for Acute Gastrointestinal Illness After a Major Water Pipe Break in 2010. *Epidemiology*. 2019 Nov;30(6):893-900.
4. Mackenzie WR, Hoxie NJ, Proctor ME, Gradus MS, Blair KA, Peterson DE, et al. A Massive Outbreak in Milwaukee of *Cryptosporidium* Infection Transmitted through the Public Water Supply. *New England Journal of Medicine* [Internet]. 1994 Jul 21;331(3):161-7. Available from: <https://doi.org/10.1056/NEJM199407213310304>
5. Paterson BJ, Durrheim DN. The remarkable adaptability of syndromic surveillance to meet public health needs. *J Epidemiol Glob Health* [Internet]. 2013;3(1):41-7. Available from: <https://doi.org/10.1016/j.jegh.2012.12.005>
6. Nygård K, Schimmer B, Søbstad Ø, Walde A, Tveit I, Langeland N, et al. A large community outbreak of waterborne giardiasis- delayed detection in a non-endemic urban area. *BMC Public Health* [Internet]. 2006;6(1):141. Available from: <https://doi.org/10.1186/1471-2458-6-141>
7. Eisenberg JN, Seto EY, Colford JMJ, Olivieri A, Spear RC. An analysis of the Milwaukee cryptosporidiosis outbreak based on a dynamic model of the infection process. *Epidemiology*. 1998 May;9(3):255-63.
8. Andersson T, Bjelkmar P, Hulth A, Lindh J, Stenmark S, Widerström M. Syndromic surveillance for local outbreak detection and awareness: evaluating outbreak signals of acute gastroenteritis in telephone triage, web-based queries and over-the-counter pharmacy sales. *Epidemiol Infect*. 2014 Feb;142(2):303-13.
9. Groeneveld GH, Dalhuijsen A, Kara-Zaitri C, Hamilton B, de Waal MW, van Dissel JT, et al. ICARES: a real-time automated detection tool for clusters of infectious diseases in the Netherlands. *BMC Infect Dis*. 2017 Mar;17(1):201.

10. Shortridge JE, Guikema SD. Public health and pipe breaks in water distribution systems: analysis with internet search volume as a proxy. *Water Res.* 2014 Apr;53:26-34.
11. Pivette M, Mueller JE, Crépey P, Bar-Hen A. Drug sales data analysis for outbreak detection of infectious diseases: a systematic literature review. *BMC Infect Dis* [Internet]. 2014;14(1):604. Available from: <https://doi.org/10.1186/s12879-014-0604-2>
12. Proctor ME, Blair KA, Davis JP. Surveillance data for waterborne illness detection: an assessment following a massive waterborne outbreak of *Cryptosporidium* infection. *Epidemiol Infect.* 1998 Feb;120(1):43-54.
13. Rodman JS, Frost F, Jakubowski W. Using nurse hot line calls for disease surveillance. *Emerg Infect Dis* [Internet]. 1998;4(2):329-32. Available from: <https://pubmed.ncbi.nlm.nih.gov/9621209>
14. Berger M, Shiao R, Weintraub JM. Review of syndromic surveillance: implications for waterborne disease detection. *J Epidemiol Community Health* (1978) [Internet]. 2006 Jun;60(6):543-50. Available from: <https://pubmed.ncbi.nlm.nih.gov/16698988>
15. Schober P, Vetter TR. Segmented Regression in an Interrupted Time Series Study Design. *Anesth Analg* [Internet]. 2021;132(3). Available from: https://journals.lww.com/anesthesia-analgesia/Fulltext/2021/03000/Segmented_Regression_in_an_Interrupted_Time_Series.aspx
16. Victoria State Government Department of Health. Victorian Emergency Minimum Dataset (VEMD) User Manual [Internet]. 2013. p. 1-11. Available from: <https://www.health.vic.gov.au/data-reporting/victorian-emergency-minimum-dataset-vemd>
17. Onyango LA, Quinn C, Tng KH, Wood JG, Leslie G. A Study of Failure Events in Drinking Water Systems as a Basis for Comparison and Evaluation of the Efficacy of Potable Reuse Schemes. *Environ Health Insights* [Internet]. 2015 Jan 1;9s3:EHI.S31749. Available from: <https://doi.org/10.4137/EHI.S31749>
18. Motlagh AM, Yang Z. Detection and occurrence of indicator organisms and pathogens. *Water Environ Res.* 2019 Oct;91(10):1402-8.
19. Hyllestad S, Amato E, Nygård K, Vold L, Aavitsland P. The effectiveness of syndromic surveillance for the early detection of waterborne outbreaks: a systematic review. *BMC Infect Dis* [Internet]. 2021;21(1):696. Available from: <https://doi.org/10.1186/s12879-021-06387-y>
20. Mouly D, Gorla S, Mounié M, Beaudeau P, Galey C, Gallay A, et al. Waterborne Disease Outbreak Detection: A Simulation-Based Study. *Int J Environ Res Public Health.* 2018 Jul;15(7).

Appendix

Appendix A. Oral presentation at the *Communicable Diseases and Immunisation Conference* in Sydney, Australia on 22 June 2022.

Using interrupted time series segmented regression models to detect waterborne disease outbreaks

Aidan Yuen (aidan.yuen@anu.edu.au)

Master of Philosophy in Applied Epidemiology Scholar

Supervisors: Davoud Pourmarzi & Jim Black

Australian National University | Victorian Department of Health



Australian
National
University



Department
of Health

OFFICIAL

Background – water contamination events

Milwaukee, Wisconsin cryptosporidiosis outbreak of 1993



<https://omilwaukee.com/articles/ebolaimilwaukee>

Silvan Reservoir contamination event on 27 August 2020



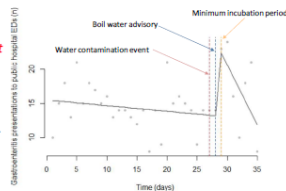
<https://www.abc.net.au/news/2020-08-29/victoria-hundreds-of-homes-went-without-power-overnight/12608286>

OFFICIAL

Methods – interrupted time series analysis of the Silvan Reservoir contamination event

$$Y_t = \beta_0 + \beta_1 T + \beta_2 X_t + \beta_3 TX_t$$

- T : days since the start of the study
- Y_t : outcome at time t
- X_t : dummy variable indicating the pre-event period (coded 0) and the post-event period (coded 1)

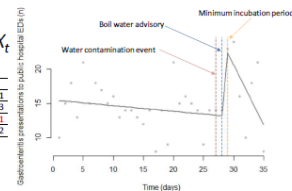


OFFICIAL

Results – interrupted time series analysis of the Silvan Reservoir contamination event

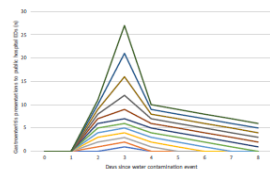
$$Y_t = \beta_0 + \beta_1 T + \beta_2 X_t + \beta_3 TX_t$$

Coefficient	Description	Estimate	P-value
β_0	Intercept	15.52	<0.001
β_1	Pre-event trend	-0.08	0.33
β_2	Level change	10.94	<0.001
β_3	Slope change	-1.67	0.02



OFFICIAL

Methods & results – simulated water contamination events



Gastro presentations to public hospital EDs	0	1	3	5	10	15	21	28	36	45	55	66	78
% Detections at $P < 0.05$ for β_2	8%	8%	10%	18%	24%	32%	44%	50%	58%	76%	88%	94%	100%

OFFICIAL

Conclusions & acknowledgements

- Interrupted time series analyses are useful for detecting waterborne disease outbreaks!
- With thanks to:
 - Davoud Pourmarzi (Australian National University)
 - Jim Black (Victorian Department of Health)
 - Staff at both institutions



Australian
National
University



Department
of Health

OFFICIAL

Chapter 2: Establishing a syndromic surveillance system for detecting gastroenteritis outbreaks following drinking water contamination events in Victoria, Australia

Prologue

This chapter meets the MAE major competency to “establish or evaluate a surveillance system or other health information system”. Building on from chapter one, chapter two details the establishment of a surveillance system for drinking water contamination events. Most Victorians are supplied with potable water from retail corporations; these agencies have a legislative requirement to notify the State Government of Victoria's Department of Health (the Department) of any known or suspected contamination events. To help monitor and evaluate these notifications, we deployed a syndromic surveillance system that statistically signals potential gastroenteritis outbreaks in affected postcodes using the methods described in chapter one. The system was built in accordance with the USA Centers for Disease Control and Prevention (CDC) *Updated Guidelines for Evaluating Public Health Surveillance Systems*. The system comprises a report/dashboard that ingests data on gastroenteritis presentations at public hospital EDs, which are updated daily. When used in conjunction with microbiological testing of the affected waterbody, and consultation with key stakeholders, such as OzFoodNet epidemiologists, this system can help inform public health decision-making, including the issuing, and lifting of boil water advisories.

As with chapter one, this project was largely conceptualised by Dr. Jim Black, my field supervisor, and forms part of the Department's broader SynSurv project. The impetus for this project was born out of the Department's lack of capacity to monitor and evaluate the public health impacts of drinking water contamination events. This chapter introduces the data sources used, our analytical approach for determining incidence thresholds to identify possible outbreaks, a demonstration of the report/dashboard, and ends with a discussion of the system's efficiency and effectiveness.

My role

I was responsible for leading all consultations with key stakeholders, including SynSurv epidemiologists, OzFoodNet epidemiologists and members of the Water Unit—all of whom were identified as the primary end-users of the system. In doing so, I could determine their end-user needs, which helped in drafting a clear protocol for the subsequent design of the system. Our protocol was also informed by a thorough review of the academic and grey

literature, and operating documents for other SynSurv modules, including those for thunderstorm asthma and point-source smoke hazards.

Chapter one details a pilot study that I led, which demonstrated the utility of interrupted time series analysis for detecting waterborne disease outbreaks through the syndromic surveillance of gastroenteritis presentations to public hospital EDs. This analytical approach was subsequently incorporated into this system to help determine incidence thresholds to identify possible outbreaks. I authored the R code for cleaning, linking, and analysing the data, and built the report/dashboard using Microsoft Power BI.

Upon completion, the final system was presented to all key stakeholders, and training was provided on how to operate the report/dashboard. I also acted as the central source of knowledge and advice and was responsible for resolving and troubleshooting any issues that arose; these included issues with the underlying R and DAX code that drive the report/dashboard. The Manager of the Communicable Diseases Epidemiology and Surveillance unit at the Department also invited me to present the system at the weekly surveillance meeting, which was attended by over 100 people from across the Department and Local Public Health Units.

Our findings were drafted into a scientific manuscript for peer-review in *Communicable Disease Intelligence*; the contents of this manuscript form the body of this chapter. This manuscript meets the MAE minor competency on preparing a “peer-reviewed publication”.

Lessons learnt

Establishing a surveillance system can be a difficult task, and this project was no exception. This project proved to be the most challenging to complete, which made for many lessons learnt along the way.

For example, I learnt much about project management and leading stakeholder consultations. Early in the project, I presented a business case with well-documented case studies, which proved instrumental in securing early stakeholder buy-in and subsequent engagement. Engaging stakeholders throughout the course of the project was also essential for delivering a product that was appropriate and acceptable for the end-users’ needs. It was particularly challenging engaging those with many responsibilities and priorities. Scheduling meetings well in advance proved useful for securing a time in their busy calendars. It was also important to come to these meetings prepared to capitalise on the limited time I had with these stakeholders.

The more technical aspects of the project also taught me much about R coding and DAX programming in Microsoft Power BI. Above all, the project taught me to appreciate the intricacies and complexities that go into establishing a new surveillance system.

Public health impacts

This syndromic surveillance system provides an accessible tool for the Department to monitor and evaluate the public health impacts of drinking water contamination events. Water agencies have a legislative requirement to notify the department of any known or suspected events. Upon receiving such notifications, the Department can use this report/dashboard to visualise the temporal and spatial distribution of gastroenteritis presentations in the affected postcodes. The users will also receive alerts when syndromes exceed certain statistical thresholds that could signal an outbreak. When used in conjunction with microbiological testing of the affected waterbody, and consultation with key stakeholders, including OzFoodNet epidemiologists, this system can help inform timely and localised public health actions, including the issuing, and lifting of boil water advisories.

Abstract

Background

In Victoria, Australia, water agencies supply most Victorians with potable water, and have a legislative requirement to notify the State Government of Victoria's Department of Health (the Department) of any known or suspected contamination. This project established a syndromic surveillance system for such events using gastroenteritis presentations to public hospital emergency departments (EDs).

Methods

The system report/dashboard was built using R and Microsoft Power BI. ED presentations per residential postcode were derived from the Victorian Emergency Minimum Dataset. Gastroenteritis syndromes were flagged using ICD-10 codes. We superimposed the shapefiles of each agency's water distribution zones over shapefiles of Victorian postcodes to determine which postcodes are served by which agencies, and therefore, which postcodes are implicated in contamination events. Following implementation, we then discussed the system's efficiency and effectiveness against the USA Centers for Disease Control and Prevention (CDC) *Updated Guidelines for Evaluating Public Health Surveillance Systems*.

Results

Using the parameters of an event, the report/dashboard will plot the count of gastroenteritis presentations for a selected pre- and post-event period. Interrupted time series segmented regression models will test the hypothesis that counts are statistically different between the pre- and post-event periods. If there is strong evidence that the post-event count is higher than the pre-event count, the user is alerted to a potential outbreak.

Conclusions

Upon receiving a notification for a contamination event, the Department can use this report to monitor and evaluate the short-term public health impacts of these events. When used in conjunction with microbiological testing of the affected waterbody, and consultation with key stakeholders, including OzFoodNet epidemiologists, this report can inform subsequent public health actions, including the issuing, or lifting of boil water advisories.

1. Introduction

Water-related gastroenteritis outbreaks can affect many people in a short time, thus making them a high risk for public health (1). The early detection and resolution of such outbreaks is therefore crucial for mitigating downstream morbidity and mortality, and associated costs (2,3). In Australia, reports of waterborne gastroenteritis outbreaks are rare (4). Most Australians are supplied with potable water by retail water corporations. This water is often disinfected, which—together with filtration—is credited with substantial reductions in waterborne disease (5). Disinfection reduces the risk of microbial contaminants which may enter the supply through point sources of pollution (e.g., human, and industrial waste discharges) and diffuse sources (e.g., agricultural and animal husbandry activities) (6).

In Victoria, water agencies are required to notify the State Government of Victoria's Department of Health (the Department) any known or suspected contamination events pursuant to Sections 18 or 22 of the *Safe Drinking Water Act 2003 (Victoria)*. Following such events, the Department may issue boil water advisories; these are public announcements advising that drinking water should be boiled (or otherwise disinfected) prior to consumption until the issue is rectified (6).

The Department is currently building its syndromic surveillance capabilities to monitor and evaluate the public health impacts of these events. Syndromic surveillance uses pre-clinical and clinical pre-diagnostic data, and proxy measures—such as hospital admission reports and over-the-counter pharmaceutical sales—to identify potential outbreaks (7-10). Syndromic surveillance can therefore detect outbreaks earlier than surveillance systems that rely on laboratory-confirmed cases (2,3).

Interest in syndromic surveillance increased after the cryptosporidiosis outbreak in Milwaukee, Wisconsin in 1993, which resulted in more than 400,000 cases of diarrhoeal disease and over 100 preventable deaths (1). The outbreak remained undetected by both the water quality monitoring system and the notifiable disease surveillance system until it was already widespread. An estimated 85% of cases could have been avoided had surveillance systems detected the outbreak at the earliest point in the illness course (11). Another study of a Swedish cryptosporidiosis outbreak in 2011 similarly suggested that detection at the earliest signal (via calls to a health line) could have reduced the total outbreak size from 18,500 cases to 2,300 cases (12).

Syndromic surveillance is now used in many jurisdictions worldwide, including the United States, the United Kingdom and France. In Victoria, the first version of SynSurv was developed for the 2006 Commonwealth Games in Melbourne. It currently comprises a set of tools to answer specific questions on behalf of “clients” to help inform public health actions

for which they are responsible. At present, modules have been deployed for thunderstorm asthma and point-source smoke hazards, among others.

This paper details the establishment of a SynSurv module for drinking water contamination events using rapidly acquired but non-specific information on gastroenteritis presentations to public hospital emergency departments (EDs). This project was informed by the USA Centers for Disease Control and Prevention (CDC) *Updated Guidelines for Evaluating Public Health Surveillance Systems* (13). The objectives of the project were to:

1. Build a technical platform that ingests existing (near real-time) data from public hospital EDs;
2. Monitor gastroenteritis syndromes following drinking water contamination events in affected postcodes, and to generate alerting of potential outbreaks; and
3. Determine how the report will be used by the Department and other stakeholders to inform public health decision-making.

2. Methods

2.1. Surveillance system design

2.1.1. Stakeholder engagement

Multiple stakeholders were consulted for establishing and operationalising the technical platform. Firstly, we liaised with members of the Water Unit, OzFoodNet and SynSurv at the Department to define the system objectives and to establish their end-user needs for the final report/dashboard. SynSurv epidemiologists were also consulted to brainstorm different analytical approaches for determining incidence thresholds to identify possible outbreaks.

2.1.2. Data sources

Each water agency provided us with shapefiles of their water distribution zones. By layering these zones over Victorian postcodes, we determined which postcodes are served by which agencies, and therefore, which postcodes are implicated in contamination events (Figure 1).

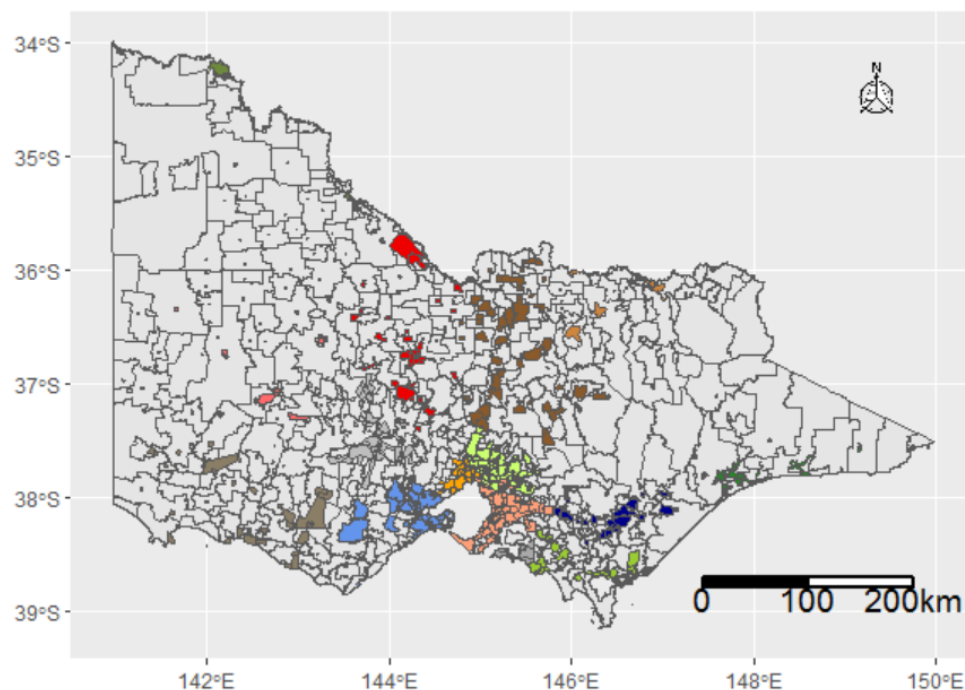


Figure 1. Water distribution zones of water agencies overlaying Victorian postcodes (grey borders). Each colour represents the area served by a different water agency.

ED presentations were retrieved from the VEMD, which includes de-identified demographic, administrative and clinical data detailing presentations at Victorian public hospital EDs. Residential addresses for each presentation were mapped to their corresponding water distributions zones. Because some postcodes are served by multiple agencies, or only partially served by an agency, we defined two different analyses:

- An “inclusive” option, where postcodes are considered part of a zone if they are served at least in part by a water agency; and
- A “core” option, where postcodes are considered part of a zone if they are only served by a water agency, and wholly served by that agency.

2.1.3. Syndrome definition

Gastroenteritis presentations were identified using diagnosis fields that included an ICD-10 code with the prefix "A0".

2.1.4. Software

The system report/dashboard ingests data from the VEMD, which is refreshed daily. R (a programming language for statistical computing and graphics) was used for data cleaning, linkage, and analysis. Microsoft Power BI (an interactive data visualisation software product) was used for generating the data visualisations.

2.2. Incidence thresholds to identify possible outbreaks

2.2.1. Pilot study

A pilot study was conducted to test the utility of interrupted time series segmented regression analysis for detecting waterborne disease outbreaks by syndromic surveillance. This involved retrospectively analysing a past lapse in water treatment. Here, we observed strong statistical evidence for an increase in gastroenteritis presentations to public hospital EDs shortly after the event. This may indicate a point-source outbreak attributed to microbiological hazards, or it may reflect increased health seeking behaviour following the issuing of boil water advisories. We also simulated outbreaks of various sizes—given the absence of recent events leading to outbreaks—and demonstrated the ability of segmented regressions to statistically signal a detection, even without a large excess in presentations. The model's sensitivity was dose dependent, while its specificity was high—and was therefore considered for incorporation into the present system.

2.2.2. Implementation

The system uses interrupted time series analysis to test the hypothesis that the count of gastroenteritis presentations in a selected surveillance period is different to a given baseline period; the baseline and surveillance periods represent the days before and after the minimum incubation period of the suspected pathogen(s) implicated in the event. The baseline period was set at 28 days; this is long enough to establish a robust baseline, but short enough to minimise the effects of seasonal variability and variable lockdowns. Users have the option of selecting a surveillance period that spans 7 to 14 days. Selecting a period

of less than 7 days would increase the chance of random error; the analysis is then compromised. Options for periods exceeding 14 days is unnecessary, as the system is principally interested in the early detection of events and in the evaluation of recent events.

The following segmented linear regression model is used for our interrupted time series analysis:

$$Y_t = \beta_0 + \beta_1 T + \beta_2 X_t + \beta_3 TX_t$$

This model requires three key variables:

- T : the days since the start of the study period.
- X_t : a dummy variable indicating the baseline and surveillance periods.
- Y_t : the outcome at time t .

Upon entering these variables into the model, we retrieve the following coefficients for analysis:

- β_0 : the constant—i.e., the value at which the regression crosses the y-axis.
- β_1 : the baseline trend—i.e., the change in presentations with a time unit increase in the baseline period.
- β_2 : the level change, i.e.—the immediate change in presentations in the surveillance period compared to the baseline period; this coefficient can signal a point-source outbreak.
- β_3 : the slope change, i.e.—the change in the regression gradient of the surveillance period compared to the baseline period; this coefficient can signal a continuous-source outbreak.

2.3. Surveillance system attributes

This system was built in accordance with the attributes outlined in the USA CDC *Guidelines for Evaluating Surveillance Systems*. These attributes are usefulness, simplicity, flexibility, data quality, acceptability, sensitivity, predictive value positive, representativeness, timeliness, and stability (13). We discuss the system's efficiency and effectiveness against these guidelines. In building this system, we considered how we could achieve the best results for each of these attributes. Future evaluations of this system should be made against these criteria by a neutral third party for best practice epidemiology.

3. Results

Upon receiving a notification for a known or suspected contamination event, stakeholders can use this report/dashboard to monitor and evaluate the event's impact on gastroenteritis presentations to public hospital EDs in the affected postcodes. The user is required to supply the parameters of the event into the control panel, including the date of the contamination event, the days since the first public health actions were issued, and the minimum incubation period of the suspected pathogens. Take cryptosporidiosis for example; its incubation period spans one to 14 days, with a median of seven days. We cannot miss any potential outbreaks, so we should select one for this parameter. However, the implicated pathogens are often unknown, in which case, the users are advised to select a number at the lower end of the given options. The user must also select the desired surveillance period, which represents the days following that minimum incubation period. Finally, the user must select the water agencies implicated in the event (Figure 2).

Control Panel

Select the date of the contamination event

Wednesday, 21 September 2022
 Thursday, 22 September 2022
 Friday, 23 September 2022
 Saturday, 24 September 2022

Select the number of days before the first public health actions were issued

0 1 2 3
 4 5 6 7

Select the minimum incubation period (days) of the suspected pathogen(s) in the event

0 1 2 3
 4 5 6 7

Select the desired surveillance period (days) following that minimum incubation period

7 8 9 10
 11 12 13 14

Select the affected water agencies

☒ Select all
☐ Barwon Water
☐ Central Highlands Water
☐ City West Water
☐ Coliban Water
☐ East Gippsland
☐ Gippsland Water
☐ Golburn Valley Water
☐ Grampians Wimmera Mallee
☐ Lower Murray
☐ North East Water
☒ South East Water
☐ South Gippsland Water
☐ Wannon Water
☐ Western Port Water
☒ Yarra Valley Water

Parameters for subsequent analyses

Baseline period	26 August 2022	to	22 September 2022
Surveillance period	23 September 2022	to	2 October 2022

Figure 2. Control panel of the SynSurv module for drinking water contamination events.

Based on the water agencies selected, the report will then determine which postcodes are affected by the event for both the “inclusive” and “core” definitions as defined in the Methods (Figure 3).

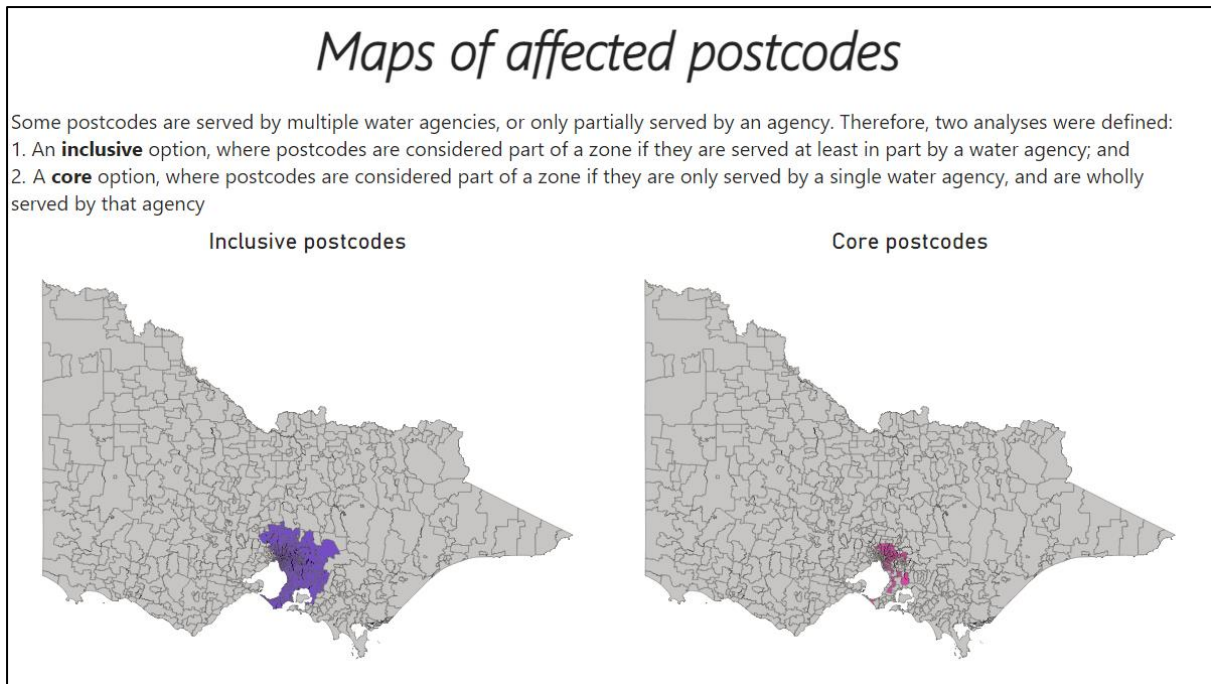


Figure 3. Maps of affected postcodes.

With the affected postcodes identified for both the “inclusive” and “core” definitions, the report will then aggregate the count of gastroenteritis presentations per day for the period identified in the control panel (Figure 4). Of note, the “inclusive” analysis captures all affected postcodes, but also captures unaffected populations in sections of postcodes served by other zones (i.e., there is likely overcounting). The “core” analysis is restricted to postcodes completely affected by the event, but excludes affected postcodes served additionally by other zones (i.e., there is likely undercounting). The true number of presentations in affected populations therefore exists somewhere between the “inclusive” and “core” analyses.

Using the plot for the “inclusive” analysis, the report then runs an interrupted time series segmented regression to test the hypothesis that the surveillance period is statistically different to the baseline period. The report will signal a potential point-source outbreak if there is strong evidence for an immediate increase (level change) in presentations in the surveillance period. It will signal a potential continuous-source outbreak if slope of the surveillance period is greater than that of the baseline period ($P < 0.05$) (Figure 5). The same analysis is then repeated for the plots for the “core” analysis (Figure 6).

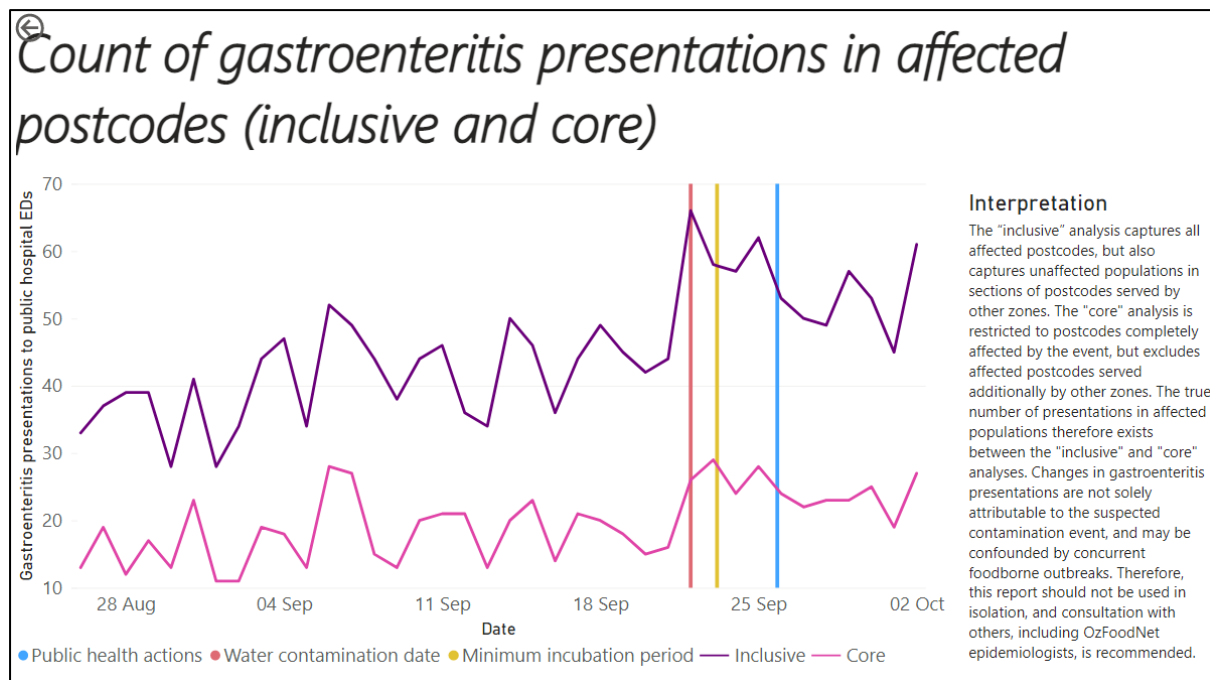


Figure 4. Count of gastroenteritis presentations in affected postcodes (inclusive and core).

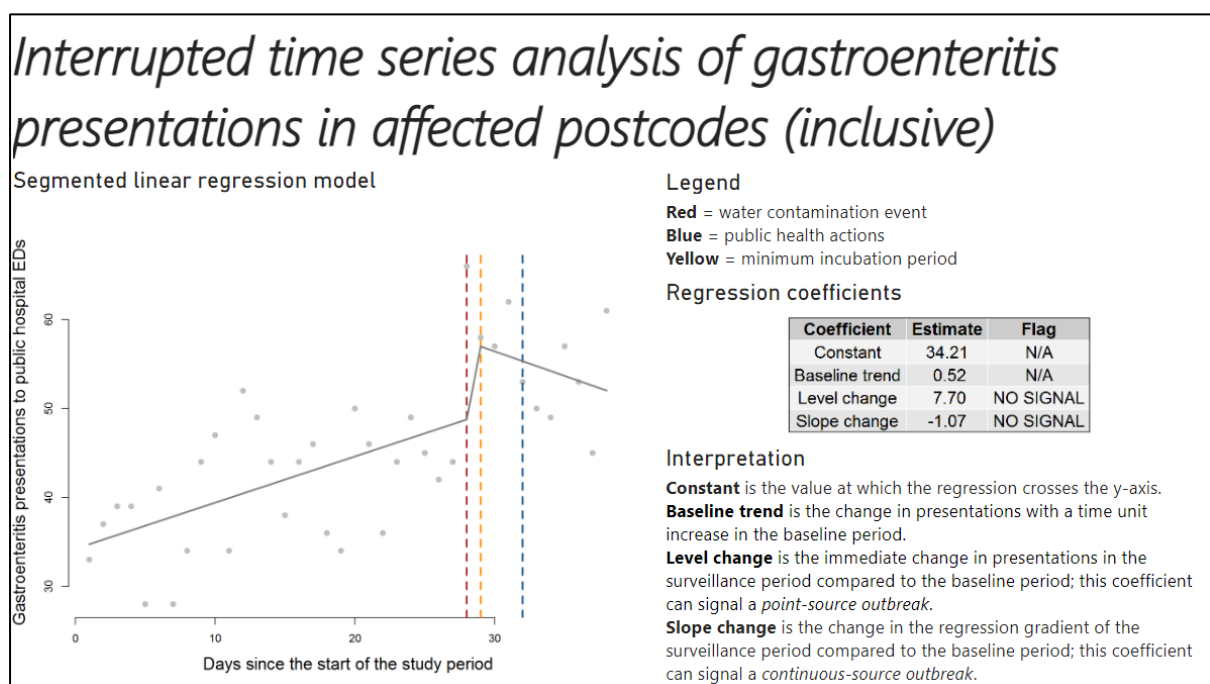


Figure 5. Interrupted time series analysis of gastroenteritis presentations in affected postcodes (inclusive).

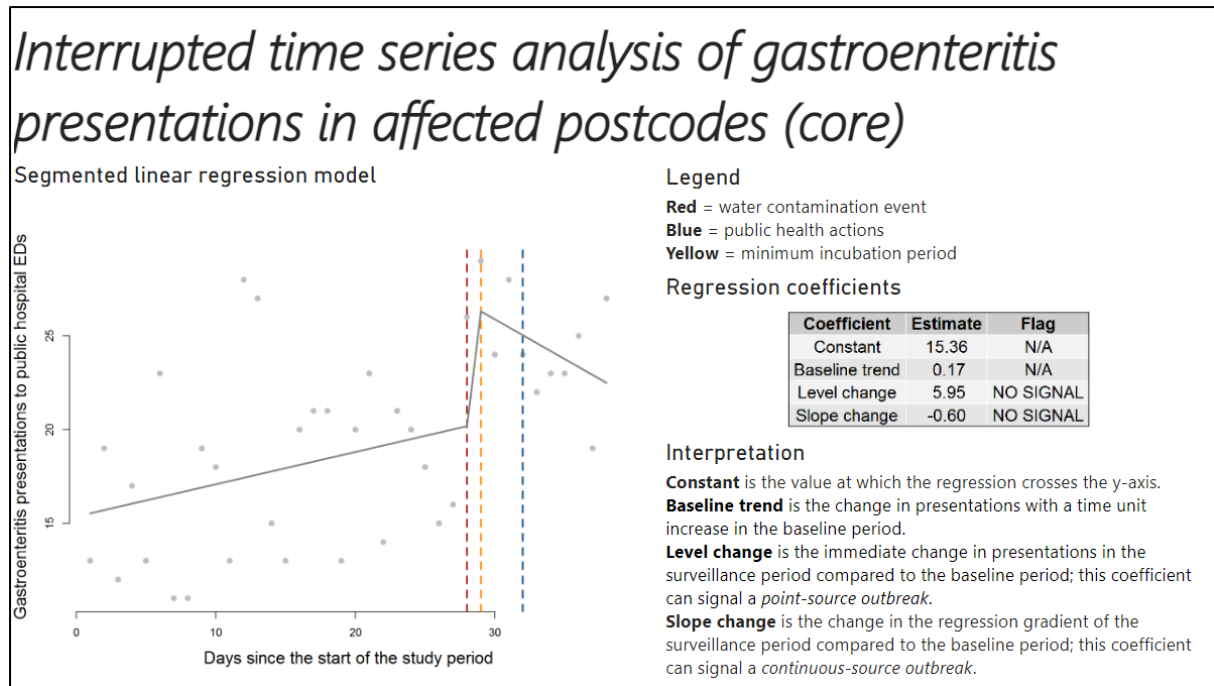


Figure 6. Interrupted time series analysis of gastroenteritis presentations in affected postcodes (core).

4. Discussion

This project established a syndromic surveillance system for drinking water contamination events. The system comprises a report/dashboard that ingests data on gastroenteritis presentations at public hospital EDs, which are updated daily. After inputting the required parameters for the analysis, the users are then alerted to potential outbreaks when incidence thresholds are breached, which can help inform public health decision making, such as the issuing, and lifting of boil water advisories. Note that this analysis is intended to be run when the Department is notified of a water contamination incident and is not run and reviewed proactively to detect water contamination incidents.

4.1. Surveillance system attributes

In this section, we discuss the system's efficiency and effectiveness against the USA Centers for Disease Control and Prevention (CDC) *Updated Guidelines for Evaluating Public Health Surveillance Systems*. Please note this is not a formal evaluation of the system as it is intrinsically biased, given that we built the system and authored this report. This section functions as a pilot piece to inform future evaluations, which would require a neutral third party for best practice epidemiology.

4.1.1. Usefulness

Usefulness refers to the system's ability to contribute to the prevention and control of adverse health events (13). While benefits realisation is beyond the scope of this project—as delivery of benefits is a long-term endeavour—this surveillance system is anticipated to:

1. Provide novel information and detect trends signalling acute changes in gastroenteritis incidence following known or suspected contamination events;
2. Assist with the mobilisation of rapid and localised responses to such events—e.g., the issuing of boil water advisories—to reduce morbidity and mortality; and
3. Provide data to stakeholders for later evaluations of events and interventions.

These key benefits also support the Department in achieving its vision that Victorians are the healthiest people in the world.

Of note, the system should not be used in isolation. Changes in gastroenteritis epidemiology following contamination events may be attributed to microbiological hazards, or they may be confounded by concurrent foodborne outbreaks. They may also reflect increased health seeking behaviour following the issuing of boil water advisories. This report should therefore be used in conjunction with microbiological testing of the affected waterbody, and consultation with key stakeholders, such as OzFoodNet epidemiologists, to help inform public health decision-making.

A key weakness of the system is the requirement that all parameters be entered for the analyses to run. This issue is moot where pathogen(s) implicated in an event are known. Oftentimes, however, this information is unknown. In such cases, the users are required to input parameters based on their best judgement. The conclusions drawn from this system may in turn lack accuracy and may be inappropriate for informing public health actions.

4.1.2. Simplicity

Simplicity relates to the design and size of the system (13). The underlying code to program the system is complex, and alterations to the algorithms requires familiarity with R and DAX (the programming language in Power BI). That said, all code has been adequately annotated, so that others can easily contribute changes to the system. The report/dashboard itself is also simple to use. Upon supplying the required parameters, it then conducts the data cleaning, linkage, and analysis, and generates the visualisations.

4.1.3. Flexibility

Flexibility refers to the system's ability to adapt to changing information needs or operating conditions (13). Following implementation, we received stakeholder requests for more granular water distribution zones, which were not available at the time. Securing these shapefiles from each water agency will likely be timely, but upon acquisition, the implementation of such zones should be relatively simple for someone familiar with R. Likewise, ICD-11 codes will soon be implemented in the VEMD, upon which, the gastroenteritis syndromes will have to be redefined. Again, this should be relatively simple for someone familiar with R.

The system is also flexible with changing operating needs. In particular, the report/dashboard was built to accommodate the many ways a water contamination event can manifest. For example, the system can account for a suite of implicating pathogens, and their corresponding minimum incubation periods.

4.1.4. Data quality

Data quality reflects the care taken in managing data systems (13). The VEMD—the source of outcome data—is likely accurate, as it is subject to various quality assurance checks. Data submitted by health services are subject to a validation process, which includes checks for valid values and compliance with VEMD business rules. The Department also performs monthly data quality checks on ED-only admissions, overlapping ED presentation times and admission times, and VEMD length of stays of over 24 hours. Health services are required to correct the data where anomalies are detected.

4.1.5. Acceptability

Acceptability refers to the system's ability to reflect the willingness of the end users to accept and use the data generated through the system (13). All end-users were involved in defining the system objectives, and were consulted throughout the design, development, and implementation of the system. We therefore anticipate high acceptance among users in SynSurv, the Water Unit and OzFoodNet. The system has already demonstrated high short-term acceptability; following implementation, the system has been used to monitor and evaluate several suspected contamination events. We must continually engage with users to assess its long-term acceptability.

4.1.6. Sensitivity and predictive value positive

Sensitivity and predictive value positive both measure the system's ability to accurately detect an outbreak (13). In our pilot study, the segmented regression models had a false-positive rate of less than 10% for both the "inclusive" and "core" analyses. Given its high specificity, a positive detection is therefore suggestive of a gastroenteritis outbreak in a defined geographical setting, which may be attributed to a water contamination event. Its sensitivity, i.e., its true-positive detection rate, was dose-dependent. This should not pose major ramifications to public health. A small event that is resolved quickly will unlikely signal a detection. However, a large event—involving high morbidity and mortality—will likely be detected, upon which, public health actions and appropriate resources can be mobilised to resolve the event.

4.1.7. Representativeness

Representativeness refers to the system's ability to describe the occurrence of the condition over time and to characterise the distribution of disease in the population by place and person (13). The system currently provides information on the geographical and temporal distribution of presentations, but not on age and sex. Future iterations of the system will incorporate such variables to better understand the epidemiology of such presentations.

4.1.8. Timeliness

Timeliness reflects the speed between steps in a public health surveillance system (13). The system report/dashboard ingests data from the VEMD, which is updated by health services daily—which makes for a timely system. However, it currently defines syndromes using ICD-10 codes, which are only assigned at discharge and are therefore subject to lags. Future iterations will identify syndromes using triage text, which are submitted to the Department shortly after a patient presents at a triage desk, thus improving its timeliness.

4.1.9. *Stability*

Stability refers to the reliability and availability of the public health surveillance system (13). Leave or illness among staff should not pose an issue to the system's performance. All the underlying code for the data cleaning, linkage and analysis is adequately annotated and backed up to provide extra stability. Unfortunately, all SynSurv staff are employed on short-term fixed-term contracts. If contracts are not renewed, the functionality of SynSurv and its modules may suffer, particularly in the event of unforeseen system failures. Therefore, increased competency in R and DAX amongst epidemiologists across the Department is paramount for this system's long-term stability.

4.2. Limitations and future directions

The current SynSurv module has potential for improved timeliness. Other SynSurv modules—like the thunderstorm asthma module—currently receive data from public hospital EDs at near real-time. This includes data on the hospital/site name, presentation date and time, patient age, patient gender, patient postcode and triage text detailing the admit reason. Natural language processing is then used to rapidly classify this text into syndromes, which enables analysis and insight faster than traditional syndromic surveillance approaches. We hope to use this approach in the present module to improve its timeliness.

We also hope to assign syndromes using data from the state's nurse-on-call line. This data includes a free-text field akin to triage text and is amenable to the same natural language processing techniques. Nurse-on-call data provides a valuable addition to the emergency department data, helping to bridge geographic and temporal gaps. Therefore, incorporating such data into the current system can improve its usefulness and representativeness.

4.3. Conclusions

This syndromic surveillance system provides an accessible tool for the Department to monitor and evaluate the public health impacts of drinking water contamination events. Water agencies have a legislative requirement to notify the department of any known or suspected events. Upon receiving such notifications, the Department can use this report/dashboard to visualise the temporal and spatial distribution of gastroenteritis presentations in the affected postcodes. The users will receive alerts when syndromes exceed certain statistical thresholds that could indicate an outbreak. When used in conjunction with microbiological testing of the affected waterbody, and consultation with key experts—including OzFoodNet epidemiologists—this system can help inform timely and localised public health actions, including the issuing, and lifting of boil water advisories.

5. Additional information

5.1. Acknowledgements

The authors acknowledge the contributions of the staff at the State Government of Victoria's Department of Health, especially those in the Water Unit, SynSurv and OzFoodNet.

5.2. Author details

Authors

Mr. Aidan Yuen (<http://orcid.org/0000-0002-8642-8619>)^{1,2}, Dr. Davoud Pourmarzi¹, Dr. Jim Black²

Affiliations

1. National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australian Capital Territory 2600, Australia
2. Department of Health, State Government of Victoria, Melbourne, Victoria 3000, Australia

Corresponding author

- Name: Aidan Yuen
- Email: aidan.yuen@anu.edu.au

5.3. Statements

Ethical statement

Ethical approval was obtained from the Australian National University Human Research Ethics Committee (Protocol 2017/909).

Funding statement

This research did not receive any specific funding.

Data availability

Data requests can be directed to the corresponding author.

Conflict of interest

We declare no known competing interests that could have influenced this work.

6. References

1. Mackenzie WR, Hoxie NJ, Proctor ME, Gradus MS, Blair KA, Peterson DE, et al. A Massive Outbreak in Milwaukee of *Cryptosporidium* Infection Transmitted through the Public Water Supply. *New England Journal of Medicine* [Internet]. 1994 Jul 21;331(3):161-7. Available from: <https://doi.org/10.1056/NEJM199407213310304>
2. Paterson BJ, Durrheim DN. The remarkable adaptability of syndromic surveillance to meet public health needs. *J Epidemiol Glob Health* [Internet]. 2013;3(1):41-7. Available from: <https://doi.org/10.1016/j.jegh.2012.12.005>
3. Nygård K, Schimmer B, Søbstad Ø, Walde A, Tveit I, Langeland N, et al. A large community outbreak of waterborne giardiasis- delayed detection in a non-endemic urban area. *BMC Public Health* [Internet]. 2006;6(1):141. Available from: <https://doi.org/10.1186/1471-2458-6-141>
4. Dale K, Kirk M, Sinclair M, Hall R, Leder K. Reported waterborne outbreaks of gastrointestinal disease in Australia are predominantly associated with recreational exposure. *Aust N Z J Public Health*. 2010 Oct;34(5):527-30.
5. Cutler D, Miller G. The role of public health improvements in health advances: the twentieth-century United States. *Demography*. 2005 Feb;42(1):1-22.
6. National Water Quality Management Strategy. Australian Drinking Water Guidelines 6 [Internet]. Canberra, Australia; 2017. Available from: <https://www.nhmrc.gov.au/sites/default/files/documents/reports/aust-drinking-water-guidelines.pdf>
7. Andersson T, Bjelkmar P, Hulth A, Lindh J, Stenmark S, Widerström M. Syndromic surveillance for local outbreak detection and awareness: evaluating outbreak signals of acute gastroenteritis in telephone triage, web-based queries and over-the-counter pharmacy sales. *Epidemiol Infect*. 2014 Feb;142(2):303-13.
8. Groeneveld GH, Dalhuijsen A, Kara-Zaitri C, Hamilton B, de Waal MW, van Dissel JT, et al. ICARES: a real-time automated detection tool for clusters of infectious diseases in the Netherlands. *BMC Infect Dis*. 2017 Mar;17(1):201.
9. Shortridge JE, Guikema SD. Public health and pipe breaks in water distribution systems: analysis with internet search volume as a proxy. *Water Res*. 2014 Apr;53:26-34.
10. Pivette M, Mueller JE, Crépey P, Bar-Hen A. Drug sales data analysis for outbreak detection of infectious diseases: a systematic literature review. *BMC Infect Dis* [Internet]. 2014;14(1):604. Available from: <https://doi.org/10.1186/s12879-014-0604-2>

11. Eisenberg JN, Seto EY, Colford JMJ, Olivieri A, Spear RC. An analysis of the Milwaukee cryptosporidiosis outbreak based on a dynamic model of the infection process. *Epidemiology*. 1998 May;9(3):255-63.
12. Bjelkmar P, Hansen A, Schönning C, Bergström J, Löfdahl M, Lebbad M, et al. Early outbreak detection by linking health advice line calls to water distribution areas retrospectively demonstrated in a large waterborne outbreak of cryptosporidiosis in Sweden. *BMC Public Health* [Internet]. 2017;17(1):328. Available from: <https://doi.org/10.1186/s12889-017-4233-8>
13. German RR, Lee LM, Horan JM, Milstein RL, Pertowski CA, Waller MN. Updated guidelines for evaluating public health surveillance systems: recommendations from the Guidelines Working Group. *MMWR Recomm Rep*. 2001 Jul;50(RR-13):1-7.

Chapter 3: Estimating the accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in catchments in Victoria, Australia

Prologue

This chapter meets the MAE major competency to “design and conduct an epidemiological study”. In Victoria, wastewater surveillance was initially implemented to facilitate COVID-19 case finding. Wastewater samples are collected from sewage and analysed for SARS-CoV-2 fragments shed by infected people. Of note, viral shedding from the digestive system often persists longer than one's infectious period, which may limit the program's utility. To estimate its accuracy—considering its limitations—we conducted a diagnostic test accuracy study, through which, the program showed high specificity and moderate sensitivity. We then forecasted the detection probability for varying numbers of infected people at varying periods of potential shedding. Probabilities were elevated for catchments with any number of infected people than catchments with no infected people, even for periods up to 84 days following symptom onset/testing date—a likely consequence of persistent faecal shedding. Our findings were shared with colleagues who are now evaluating the program to ensure efficiency and appropriate resource allocation, and to potentially extend its uses to other pathogens.

This project was largely conceptualised by Dr. Jim Black, my field supervisor, who had conducted an earlier study to estimate the accuracy of SARS-CoV-2 wastewater surveillance. This study was conducted during low caseloads, and so its findings may not translate to contexts involving high transmission—prompting the conceptualisation of the present project. This chapter introduces the data sources used, our study design and methods, key calculations of test accuracy, and a discussion of our findings' implications on the program's future.

My role

I was responsible for coordinating every stage of the project cycle; this included leading and chairing meetings with the SARS-CoV-2 wastewater surveillance team. Using the results of my consultation—together with a review of the current literature on wastewater-based epidemiology—I was able to draft a study protocol and data analysis plan. Ethical approval was then obtained from the State Government of Victoria's Department of Health and Department of Family, Fairness and Housing Human Research Ethics Committee.

I then designed and conducted a diagnostic test accuracy study. In cross-classifying the wastewater test results with the presence of known SARS-CoV-2 infected people resident in

catchments, we could estimate the accuracy of the program. I conducted all data cleaning, linkage, and analysis in R. In mid-2021, I also volunteered with the SARS-CoV-2 wastewater surveillance team to assist with the program's operations; this was instrumental in understanding the implications of my results.

Our findings were drafted into a scientific manuscript and submitted to *Science of the Total Environment* for peer-review on 13 August 2022; the contents of this manuscript form the body of this chapter. I also presented our findings at the *11th TEPHINET Global Scientific Conference* in Panama on 9 September 2022; the poster is included in this chapter's appendix (Appendix A). Both works meet the MAE minor competencies on preparing a "peer-reviewed publication" and a "conference presentation".

Lessons learnt

This project took the longest time for me to complete, and I learnt many lessons in the process. Multidisciplinary collaborations are an exciting opportunity for knowledge exchange, but they also bring about specific challenges. For example, my stakeholders and I initially had trouble reaching a consensus on the project scope. As the project coordinator, I had to exercise facilitation, coaching and mediation to ultimately reach an acceptable middle-ground. I also learnt the importance of clear communication and in leveraging meeting minutes at every point in the project lifecycle. The latter was particularly useful for resolving conflicts around actions, deadlines, and accountabilities.

I also learnt much about data management. The datasets I worked with were complex and required much cleaning and manipulation, such as merging multiple datasets and transforming datasets from wide to long. This was incredibly useful for developing my proficiency with R. With the push towards bigger and more detailed datasets, these lessons will stand me in good stead for future analyses.

Public health impacts

This study provides novel insights into the accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in Victoria. Given its high specificity, catchments with positive detections likely contain infected residents, and should be—and have been—targeted for rapid and localised public health action. Its variable sensitivity is biologically plausible, as faecal shedding is variable between individuals, and among those who shed, the virus may degrade in sewage. Passive sampling produced higher sensitivity estimates than grab sampling, and similar estimates to composite sampling; this is reassuring as it currently predominates the program and is cheaper, safer, and easier than

composite sampling. Our findings were shared with colleagues at the Department who are now evaluating the program to ensure efficiency and appropriate resource allocation.

Wastewater surveillance was initially implemented to facilitate COVID-19 case detections. However, in the current context of high caseloads, this is less informative. That said, the program—with the already established infrastructure—can be leverage for potentially detecting incursions of new variants in the community. Wastewater surveillance can also help understand disease prevalence by correlating viral concentrations with community case levels. With the infrastructure already in place, the Department can potentially leverage the program for other viable pathogens, including influenza.

Abstract

Background

In Australia, the State Government of Victoria uses wastewater surveillance to detect new incursions of COVID-19. The Government is now evaluating the program to ensure efficiency and appropriate resource allocation. This study estimated the accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in catchments. We also estimated the detection probability for varying numbers of infected people at varying periods around symptom onset/testing date.

Methods

We conducted a diagnostic test accuracy study from 25 August 2020 to 27 September 2021 in Victoria, Australia. Sensitivity and specificity were estimated by cross-classifying wastewater test results (index test) with the presence of known SARS-CoV-2 infected people resident on each catchment sampling day (reference test). Estimates were then stratified by days with/without lockdowns and sampling methods. The detection probability was estimated using logistic regression.

Results

Sensitivity was moderate and specificity was high for detecting people at -2 to +7 days around symptom onset/testing date. Sensitivity was higher during lockdowns than non-lockdowns, and with multi-day passive sampling than single-day grab sampling. The estimated detection probability was elevated for catchments with any number of infected people than catchments with no infected people, even for periods up to 84 days following symptom onset/testing date.

Conclusions

Given its high specificity, catchments with positive detections likely contain infected residents, and should be targeted for public health action. Its moderate sensitivity is biologically plausible, as faecal shedding is variable between individuals, and among those who shed, the virus may degrade in sewage. Sensitivity estimates are also likely closer to the true value during lockdowns, as there is less misclassification between the index and reference tests. The higher sensitivity estimated with passive sampling is reassuring as it currently predominates the program. The increased probability of detection beyond the infectious period may be attributed to persistent faecal shedding.

Keywords

COVID-19; SARS-CoV-2; wastewater surveillance; wastewater-based epidemiology.

1. Introduction

At the end of 2019, a novel coronavirus—severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—emerged in Wuhan, China, causing an outbreak of unusual viral pneumonia (1). The novel outbreak was declared a pandemic of “coronavirus disease 2019” (COVID-19) by the World Health Organization on 11 March 2020 (2). In response to the pandemic, the State Government of Victoria’s Department of Health (the Department) implemented wastewater surveillance to help detect new incursions of COVID-19 in communities.

Wastewater samples are collected from sewer networks and analysed for SARS-CoV-2 fragments (3). Catchments with positive SARS-CoV-2 detections and no recent SARS-CoV-2 infected residents or visitors have been targeted for rapid and localised public health action. Wastewater sampling does not hinge on individual action—such as recognising symptoms and seeking diagnostic tests—and can therefore contribute important information about COVID-19 transmission that cannot be obtained otherwise, particularly for individuals who are asymptomatic, pre-symptomatic or undiagnosed (4).

The Department’s wastewater surveillance program uses three different sampling methods. Grab sampling provides a crude point-in-time sample (3). Composite sampling uses autosamplers and flow meters to take frequent flow- and time-proportional samples (5). Finally, passive sampling involves deploying a device in a waterbody for a period to allow for pollutants to interact with the device (5). Short passive sampling involves a deployment of less than four hours and is typically used following an urgent trigger. Long passive sampling—often over a few days—is otherwise preferred. Following sampling, wastewater samples are then analysed for SARS-CoV-2 fragments using reverse transcription quantitative polymerase chain reaction (RT-qPCR) (3).

Of note, viral shedding from the digestive system often persists longer than one’s infectious period (6). For example, one infected individual was found to excrete the virus in faeces for up to 20 weeks (7). One study showed that the odds of detection in wastewater was elevated even at 55 days after symptom onset or testing date for symptomatic and asymptomatic individuals, respectively (“symptom onset/testing date” hereafter) (3). Positive detections could therefore be the product of one’s non-infectious shedding period, which limits the program’s utility for case finding. Viral excretion in faeces also varies between individuals, with limited data showing wide variability (8). And among those who do shed in faeces, the virus is likely to degrade in wastewater, especially at higher ambient temperatures and in the presence of detergents and other substances (9).

Despite these limitations, wastewater surveillance has been integral to the Department’s COVID-19 response. The Department is now evaluating the program to ensure efficiency

and appropriate resource allocation, and to potentially extend its uses to other pathogens. As part of this evaluation, we aimed to answer the following research questions:

- What is the estimated accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in catchments?
- How does accuracy vary with different sampling methods and catchment properties?
- What is the probability of detection for varying numbers of infected people at varying periods around symptom onset/testing date?

2. Methods

2.1. Study design

We conducted a diagnostic test accuracy study for the period 25 August 2020 to 27 September 2021 in Victoria, Australia.

2.2. Data sources

Data were sourced from the Department's COVID-19 surveillance databases, including data on (1) SARS-CoV-2 wastewater surveillance test results, and (2) known SARS-CoV-2 infected people.

2.2.1. SARS-CoV-2 wastewater surveillance

The study included all RT-qPCR tests for SARS-CoV-2 sub-genomes in wastewater samples. The testing algorithm defined a positive detection as any RT-qPCR amplification using the PerkinElmer kit that included both Orf1ab and N gene signals or a single gene signal that was independently confirmed by sequencing. A negative detection was defined as the absence of any gene signal in RT-qPCR. A single gene detection that was not independently confirmed by sequencing was considered a negative detection. Laboratory methods are further described elsewhere (3).

Wastewater test results were analysed per catchment sampling day, i.e., each day of deployment was considered an individual observation. For example, a passive sampler deployed from 5 June 2021 to 7 June 2021 provides three observations—one for each day it was deployed for—while a grab sampler deployed and retrieved on 8 June 2021 provides one observation.

Catchments designated as site types 1 and 4, were excluded. Site type 1 includes effluent treatment plants and water treatment plants; these are large catchments serving over a million people and receive in-flows from network catchments, and therefore have a greater likelihood of containing SARS-CoV-2 contributions from infected people at various stages of infection. Including such catchments in analyses would likely distort the accuracy estimates.

In contrast, site level 4 catchments are smaller and only sampled following a trigger at a higher level, particularly at levels 2 and 3. Site level 4 catchments are often large industrial areas or small residential areas that have lower likelihoods of detection; including such catchments would also distort the estimates. Given this, we also excluded catchments with populations less than 30 residents and those with unknown populations.

2.2.2. SARS-CoV-2 infected people

The study included all known SARS-CoV-2 infected people in Victoria until 27 September 2021. The latitude and longitude of the people's residences were used to identify the wastewater treatment plant and/or sewage network catchment they are served by. The number of infected people per catchment sampling day was aggregated and joined to the wastewater surveillance data to determine the presence and/or count of infected people for each wastewater test result.

2.3. Data analysis

2.3.1. Accuracy estimates

The index test was the wastewater test result, while the reference test was the presence or absence of known infected people in catchments. Residential addresses were used as the best proxy for where infected people may have been using the bathroom, and potentially shedding SARS-CoV-2 into sewage. Accuracy was estimated by cross classifying the index test with the reference test (10).

Sensitivity and specificity were the proportion of positive and negative reference test results with matching index test results, i.e., the true-positive and true-negative proportions, respectively. The positive predictive value (PPV) and negative predictive value (NPV) were the proportion of index test results with matching reference test results.

Stratified analysis by days with/without lockdowns

The dataset was restricted to long passive sampling and composite sampling, as these methods were the preferred sampling methods at the time of writing. Infected people were included at -2 to +7 days around symptom onset/testing date. Accuracy estimates were then stratified by days with or without lockdown (stay-at-home orders).

Stratified analysis by sampling methods

The dataset was restricted to lockdown days to reduce the misclassification of where infected people were using bathrooms, resulting in more accurate estimates of the true sensitivity and specificity. Infected people were included at -2 to +7 days around symptom onset/testing date. Calculations were subsequently stratified by sampling methods (grab, composite, and short and long passive sampling).

Stratified analysis by catchment properties

The dataset was restricted to both lockdown days, and to long passive and composite sampling methods. Infected people were included at -2 to +7 days around symptom

onset/testing date. Calculations were then stratified by catchment properties (site region, site type, catchment size, catchment population).

Accuracy estimates for varying numbers of infected people at varying periods of shedding

Using the same restricted dataset, we then calculated the estimated sensitivity and specificity for catchment sampling days with a single known infected person, few (≤ 5) known infected people, and any number of infected people at -2 to +7, +14, +21, and +28 days around symptom onset/testing date. Given limitations with the dataset, we did not conduct calculations for catchments with >5 known infected people.

2.3.2. Estimated probability of detection

The outcome variable was the wastewater test result, and the exposure variable was the count of known SARS-CoV-2 infected people resident per catchment sampling day.

Shedding periods were defined as having begun two days before symptom onset/testing date. Upper limits of shedding were defined at seven-day intervals, from +7 to +84 days.

Analyses were conducted using univariate logistic regression, given the binary outcome.

Separate models were fitted with the outcome variable and the various definitions of the exposure. The “predict” function in R was used to estimate the detection probability for each definition of the exposure for varying numbers of infected people present in catchments.

3. Results

3.1. Accuracy estimates

This study focused on sensitivity and specificity, rather than the predictive values. The latter—although useful for interpreting positive and negative wastewater test results—are affected by prevalence and do not translate well to other contexts (10).

3.1.1. Stratified analysis by days with/without lockdowns

The non-overlapping confidence intervals suggest strong evidence that lockdowns had a higher sensitivity estimate and a lower specificity estimate than non-lockdowns (Table 1).

Table 1. Accuracy estimates of wastewater surveillance (index test) for detecting the presence of known SARS-CoV-2 infected people resident per catchment sampling day (reference test) from 25 August 2020 to 27 September 2021 in Victoria, Australia; infected people were included at -2 to +7 days around symptom onset/testing date.

Lockdown (n)	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
No (16,665)	0.30 (0.27, 0.33)	0.96 (0.96, 0.97)	0.32 (0.29, 0.35)	0.96 (0.96, 0.96)
Yes (8,477)	0.49 (0.47, 0.52)	0.83 (0.82, 0.83)	0.38 (0.36, 0.41)	0.88 (0.87, 0.89)

3.1.2. Stratified analysis by sampling methods

There was strong evidence to show that long passive sampling had a higher sensitivity than grab sampling. Composite sampling and short passive sampling showed little evidence for a difference in sensitivity compared to both grab and long passive sampling given the overlapping confidence intervals. Composite sampling had a higher estimated specificity than grab and long passive sampling (Table 2).

Table 2. Accuracy estimates of wastewater surveillance (index test) using different sampling methods for detecting the presence of known SARS-CoV-2 infected people resident per catchment sampling day (reference test) from 25 August 2020 to 27 September 2021 in Victoria, Australia; infected people were included at -2 to +7 days around symptom onset/testing date.

Sampling method (n)	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Grab (1,652)	0.36 (0.29, 0.43)	0.83 (0.81, 0.85)	0.23 (0.19, 0.28)	0.90 (0.89, 0.92)
Composite (303)	0.50 (0.31, 0.69)	0.92 (0.88, 0.95)	0.39 (0.24, 0.57)	0.94 (0.91, 0.97)
Short passive (113)	0.33 (0.19, 0.51)	0.87 (0.77, 0.94)	0.55 (0.32, 0.76)	0.74 (0.63, 0.82)
Long passive (8,174)	0.49 (0.47, 0.52)	0.82 (0.81, 0.83)	0.38 (0.36, 0.41)	0.88 (0.87, 0.89)

3.1.3. Stratified analysis by catchment properties

There was strong evidence that sensitivity was higher in metropolitan areas than regional areas, in influent sites than network sites, and in the smallest quartile of catchment size. For catchment population, the estimated sensitivity was lowest for the largest quartile; all other quartiles showed little evidence for a difference. There was strong evidence that specificity was higher in regional areas than metropolitan areas, in influent sites than network sites, and in the largest quartiles of catchment size and catchment population (Table 3).

3.1.4. Accuracy estimates for varying numbers of infected people at varying periods of shedding

There was strong evidence that sensitivity was higher for catchments with any number of infected people present, than for catchments with few infected people or with a single infected person (Table 4). Estimates were also higher for periods up to +7 days after symptom onset/testing date, than for periods up to +14, +21 and +28 days (Table 4).

Specificity estimates showed little evidence for a difference across catchments with a single, few, or any number of infected people. Estimates were also similar for periods up to +7, +14, +21 and +28 days after symptom onset/testing date (Table 5).

3.2. Estimated probability of detection

With no known infected people resident, wastewater surveillance had an estimated 19% probability of detection for all periods around symptom onset/testing date. The estimated probability of detection was elevated for catchments with any number of infected people than

catchments with no infected people, even for periods up to 84 days following symptom onset/testing date. Catchment sampling days with more known infected people resident had higher probabilities of detection. In the presence of 100 known infected residents, catchments had an estimated 100% probability of detection at -2 to +7 days around symptom onset/testing date; this dropped to approximately 50% with 15 to 20 people. Probabilities generally decreased with increasing days following symptom onset/testing date (Table 6).

Chapter 3

Table 3. Accuracy estimates of wastewater surveillance (index test) with different catchment properties for detecting the presence of known SARS-CoV-2 infected people resident per catchment sampling day (reference test) from 25 August 2020 to 27 September 2021 in Victoria, Australia; infected people were included at -2 to +7 days around symptom onset/testing date.

Catchment property (n)		Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Region	Regional (1,087)	0.17 (0.07, 0.34)	0.98 (0.97, 0.99)	0.25 (0.10, 0.47)	0.97 (0.96, 0.98)
	Metro (7,390)	0.50 (0.47, 0.53)	0.80 (0.79, 0.81)	0.39 (0.36, 0.41)	0.86 (0.85, 0.87)
Site type	Influent (2,291)	0.58 (0.53, 0.64)	0.89 (0.88, 0.90)	0.49 (0.44, 0.53)	0.92 (0.91, 0.94)
	Network (6,186)	0.47 (0.44, 0.49)	0.80 (0.79, 0.81)	0.36 (0.33, 0.38)	0.86 (0.85, 0.87)
Catchment size (quartiles)	1 (Largest) (2,120)	0.42 (0.38, 0.46)	0.91 (0.89, 0.92)	0.64 (0.59, 0.69)	0.80 (0.78, 0.82)
	2 (2,119)	0.56 (0.52, 0.60)	0.77 (0.75, 0.79)	0.43 (0.39, 0.47)	0.85 (0.83, 0.87)
	3 (2,119)	0.44 (0.38, 0.49)	0.78 (0.76, 0.80)	0.29 (0.25, 0.33)	0.87 (0.86, 0.89)
	4 (Smallest) (2,119)	0.79 (0.69, 0.87)	0.85 (0.83, 0.86)	0.19 (0.15, 0.23)	0.99 (0.98, 0.99)
Catchment population (quartiles)	1 (Largest) (2,120)	0.40 (0.36, 0.44)	0.86 (0.84, 0.87)	0.57 (0.52, 0.61)	0.75 (0.73, 0.77)
	2 (2,119)	0.56 (0.52, 0.60)	0.78 (0.76, 0.80)	0.54 (0.50, 0.58)	0.79 (0.77, 0.82)
	3 (2,119)	0.58 (0.49, 0.66)	0.78 (0.76, 0.79)	0.15 (0.12, 0.18)	0.96 (0.95, 0.97)
	4 (Smallest) (2,119)	0.64 (0.50, 0.77)	0.88 (0.87, 0.90)	0.12 (0.09, 0.17)	0.99 (0.98, 0.99)

Table 4. Estimated sensitivity (95% CI) of wastewater surveillance (index test) for detecting the presence of known SARS-CoV-2 infected people resident per catchment sampling day (reference test) from 25 August 2020 to 27 September 2021 in Victoria, Australia.

Days around symptom onset ¹ /testing date ²	Single infected person	Few infected people (≤ 5)	Any number of infected people
-2 to +7	0.11 (0.08, 0.15)	0.25 (0.22, 0.29)	0.49 (0.47, 0.52)
-2 to +14	0.09 (0.06, 0.13)	0.21 (0.18, 0.24)	0.45 (0.43, 0.48)
-2 to +21	0.08 (0.05, 0.12)	0.17 (0.14, 0.19)	0.42 (0.40, 0.44)
-2 to +28	0.08 (0.05, 0.11)	0.15 (0.13, 0.18)	0.40 (0.38, 0.42)

¹ Applicable to symptomatic individuals

² Applicable to asymptomatic individuals

Table 5. Estimated specificity (95% CI) of wastewater surveillance (index test) for detecting the presence of known SARS-CoV-2 infected people resident per catchment sampling day (reference test) from 25 August 2020 to 27 September 2021 in Victoria, Australia.

Days around symptom onset ¹ /testing date ²	Single infected person	Few infected people (≤ 5)	Any number of infected people
-2 to +7	0.83 (0.82, 0.83)	0.83 (0.82, 0.83)	0.83 (0.82, 0.83)
-2 to +14	0.82 (0.81, 0.83)	0.82 (0.81, 0.83)	0.82 (0.81, 0.83)
-2 to +21	0.82 (0.81, 0.83)	0.82 (0.81, 0.83)	0.82 (0.81, 0.83)
-2 to +28	0.82 (0.81, 0.83)	0.82 (0.81, 0.83)	0.82 (0.81, 0.83)

¹ Applicable to symptomatic individuals

² Applicable to asymptomatic individuals

Table 6. Estimated probability of detection for varying numbers of infected people at varying periods around symptom onset/testing date in Victoria, Australia from 25 August 2020 to 27 September 2021.

Days around symptom onset ¹ /testing date ²	Number of infected people present									
	0	1	5	10	15	20	25	50	75	100
-2 to +7	19%	20%	26%	35%	45%	55%	65%	93%	99%	100%
-2 to +14	19%	20%	24%	29%	35%	42%	49%	79%	94%	98%
-2 to +21	19%	20%	23%	28%	33%	38%	43%	71%	89%	96%
-2 to +28	19%	20%	23%	27%	31%	36%	41%	67%	86%	95%
-2 to +35	19%	20%	23%	26%	30%	35%	39%	63%	82%	93%
-2 to +42	19%	20%	22%	26%	29%	33%	38%	60%	79%	91%
-2 to +49	19%	20%	22%	25%	29%	33%	37%	58%	77%	89%
-2 to +56	19%	20%	22%	25%	29%	32%	36%	57%	76%	88%
-2 to +63	19%	20%	22%	25%	28%	32%	36%	56%	75%	87%
-2 to +70	19%	20%	22%	25%	28%	31%	35%	55%	73%	86%
-2 to +77	19%	20%	22%	25%	28%	31%	35%	54%	72%	85%
-2 to +84	19%	20%	22%	25%	28%	31%	34%	54%	72%	85%

¹ Applicable to symptomatic individuals

² Applicable to asymptomatic individuals

4. Discussion

This study provides new evidence on the accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in Victoria, Australia. Sensitivity was moderate and specificity was high for detecting people at -2 to +7 days around symptom onset/testing date. Sensitivity was higher during lockdowns than non-lockdowns, and with multi-day passive sampling than single-day grab sampling. The estimated detection probability was elevated for catchments with any number of infected people than catchments with no infected people, even for periods up to 84 days following symptom onset/testing date.

The estimated sensitivity and specificity are consistent with a similar study conducted for the period 25 August 2020 to 27 October 2020 (3). Its moderate sensitivity—i.e., its moderate true-positive and false-negative proportions—is biologically plausible, as faecal shedding is variable between individuals (8), and of those who shed, the virus may degrade in sewage (9). Negative tests therefore only provide some confidence in the absence of infected people. With its high specificity—i.e., its high true-negative and low false-positive proportions—catchments with positive wastewater tests likely contain infected residents (11), and should be, and have been, targeted for public health action in low case load settings.

Estimates are likely closer to the true values during lockdowns; people are shedding in their places of residence, resulting in less misclassification between the index test and the reference test. Given this, sensitivity estimates were expectedly higher during lockdowns. The applications of wastewater surveillance may therefore be limited in future contexts where large geographical lockdowns are no longer imposed.

Specificity was lower in lockdowns; this may be attributed to higher wastewater detections of viral contributions by persistent shedders, which increases the false-positive proportion. Alternatively, people may have been reluctant to, or lacked access to COVID-19 testing during lockdowns, thereby reducing case ascertainment, and increasing the false-positive proportion, which may also explain the lower specificity observed.

Long passive sampling produced higher sensitivity estimates than grab sampling, and similar estimates to composite sampling; this is reassuring as it currently predominates the program and is cheaper, safer, and easier than composite sampling (5). Grab sampling resulted in the lowest sensitivity estimates. In catchments with few infected people close to the sampling site, viral fragments may pass as a bolus and evade detection. Detections with grab sampling are likely hinged on fortuitous timing (3).

Sensitivity estimates were also higher in influent catchments than network catchments. Influent catchments are larger and receive in-flows from various networks and therefore—

depending on the sampling methods used—have greater opportunity for receiving SARS-CoV-2 contributions. With greater opportunities for detection, the higher estimated sensitivity is biologically plausible.

The smallest quartile of catchment size produced the highest sensitivity estimates; the smallest catchments are those located in metropolitan Melbourne, where population density is higher than in regional Victoria. Such catchments are therefore more likely to have multiple persons shedding into the catchment, thereby increasing the probability of detection through wastewater surveillance, which may explain the higher sensitivity.

This study presented some limitations. The elevated probability of detection beyond the infectious period, and the elevated probabilities in the absence of known infected residents, may be attributed to false-positive detections of SARS-CoV-2 contributions from persistent shedders (12), which were not ascertained for this study. False-positive detections may also include contributions from undiagnosed infected people. This misclassification was minimised by high testing rates and contact tracing at the time of data collection (3). Nonetheless, our specificity estimates are likely a minimum estimate of the true value.

Furthermore, our reference test and outcome variable were defined according to the residences of known infected people. This is not always correct, as people may be using toilets and bathrooms—and contributing to sewage—outside of their residences. This misclassification was minimised by restricting most analyses to lockdown days, where people were most likely shedding in their places of residence, resulting in lower misclassification between the index and reference tests. The reference test is also hinged on people getting tested. As there are multiple influences on testing behaviour, which can vary over time and with different populations, using notifications as a reference test may affect the validity of our conclusions.

In the current context of high caseloads, detections of new incursions of COVID-19 into the community is less informative. However, the program—with its moderate sensitivity, coupled with the high caseloads—has potential for rapidly detecting incursions of new variants in the community. This was demonstrated in New York, where wastewater surveillance detected the Omicron variant before the first documented clinical case (13). Wastewater surveillance can also help understand disease prevalence by correlating viral concentrations with community case levels. RNA loads have also been used to predict hospitalisations in Attica, Greece, which can be useful for informing workforce policy and planning (14).

Prior to the pandemic, wastewater surveillance was used to detect the presence of poliovirus (15). With the infrastructure already in place, the Victorian wastewater surveillance program could be leveraged for other pathogens. One study quantified influenza A virus RNA in

wastewater during an active outbreak; RNA concentrations were strongly associated with reported clinical cases and reflected the outbreak pattern and magnitude, suggesting its viability for wastewater surveillance (16,17). Organisms transmitted via the faecal-oral route, such as norovirus and Salmonella, are usually excreted in large numbers in faeces, making them likely contenders too (18).

In closing, this study provides novel insights into the accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in Victoria. Given its high specificity, catchments with positive detections likely contain infected residents, and should be—and have been—targeted for rapid and localised public health action. Its variable sensitivity is biologically plausible, as faecal shedding is variable between individuals, and among those who shed, the virus may degrade in sewage. Passive sampling produced higher sensitivity estimates than grab sampling, and similar estimates to composite sampling; this is reassuring as it currently predominates the program and is cheaper, safer, and easier than composite sampling. Our findings were shared with colleagues at the Department who are now evaluating the program to ensure efficiency and appropriate resource allocation, and to potentially extend its uses to other pathogens.

5. Additional information

5.1. Acknowledgements

The authors acknowledge the contributions of the staff at the State Government of Victoria's Department of Health, especially those in the COVID-19 division, the collaborating water agencies, the Australian Laboratory Services, the University of Melbourne, Monash University, Victorian Infectious Diseases Reference Laboratory, and the Walter and Eliza Hall Institute. All collaborating groups are members of the Collaboration on Sewage Surveillance for SARS-CoV-2 (ColoSSoS) project, coordinated by Water Research Australia.

5.2. Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

5.3. Ethical statement

Ethical approval was obtained from the State Government of Victoria's Department of Health and Department of Families, Fairness and Housing Human Research Ethics Committee (ref: AM/78425/DOH-2022-305096).

6. References

1. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol* [Internet]. 19(3):141-54. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwtV3Pa9swFBZbx2CXsnW_0m6td9lgQ2n0w5Z02CGkLS2UFNKK7CZkWYYd6pQmOfS_75MIO0566Q67CCNsy7zv8fQ9S-8TQoz2B3grJjhpOeeWmFLawpYmo1zSXOa8Elo4bjbPhmmIANd9_xV46APofSHtP4DfvhQ64BpcAFpwAmif5QajLUFmX6MynFzj0fwG03r
2. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. *Acta Biomed* [Internet]. 2020 Mar 19;91(1):157-60. Available from: <https://pubmed.ncbi.nlm.nih.gov/32191675>
3. Black J, Aung P, Nolan M, Roney E, Poon R, Hennessy D, et al. Epidemiological evaluation of sewage surveillance as a tool to detect the presence of COVID-19 cases in a low case load setting. *Sci Total Environ* [Internet]. 2021;786:147469. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwtV3Nb9MwFLdGJyQkhKAwjfEh36tEdeLGzmGHaQQxLiDYELfIcRzRaU3Q0jLtxL_Oe7HjpAUJduASJVbt1H0_Pf_e6_sgJI7CebCjE4zUnHPNVCV1qSuVRfXGhSx4KVJmuNruDbPX13scxv6r4GEMRI-JtHcQvl8UBuAelABXAAFc_wkG2dABthPHUN0baWJrbjB
4. Aparna K, C. HX, Marisa H. Developing a Flexible National Wastewater Surveillance System for COVID-19 and Beyond. *Environ Health Perspect* [Internet]. 2022 Apr 20;129(4):45002. Available from: <https://doi.org/10.1289/EHP8572>
5. Schang C, Crosbie ND, Nolan M, Poon R, Wang M, Jex A, et al. Passive Sampling of SARS-CoV-2 for Wastewater Surveillance. *Environ Sci Technol*. 2021 Aug;55(15):10432-41.
6. Xu Y, Li X, Zhu B, Liang H, Fang C, Gong Y, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med* [Internet]. 2020;26(4):502-5. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwpV1Lb9QwELZoK1AvPAqUQimGCxJS2MRxsvYJLatWcKCg3dKrZcdOW6IKIk0Wqf--M2snbHpASJw9ec545kvmmxICUvYxju74BCcKznmR6FIUtih1zrhgRhhuxzJxXA9nw3hylZbGBHV3XnLtum1d4F_zEQQbyeJcZuLT4leEc6Qw3xqGamyRHQDbEmx-5_Px6Y9
7. Cho SM, Ha GY. A Case of COVID-19 in a 45-Day-Old Infant with Persistent Fecal Virus Shedding for More Than 12 Weeks. *Yonsei Med J* [Internet]. 2020;61(10):901-3. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwtV07b9swECbSFCi6FH03fYEowC6GXJOiLXLolMkOmiHIECdAJ0EPMnHTyIVjD_n3vRNFS0laIB26CBR1oijdz_K78_FIS

CiGo-DWmGBUKaUseW5VWZU2nwipRKEKWUWaG5nf3Btmx2_x2dX9V8VDHageF9L-g_K3jUIFIAECcAQQwPFeMlgHae7c9enR6cE04Bo

8. Guo M, Tao W, Flavell RA, Zhu S. Potential intestinal infection and faecal-oral transmission of SARS-CoV-2. *Nat Rev Gastroenterol Hepatol* [Internet]. 2021/02/15. 2021 Apr;18(4):269-83. Available from: <https://pubmed.ncbi.nlm.nih.gov/33589829>
9. Silverman AI, Boehm AB. Systematic Review and Meta-Analysis of the Persistence and Disinfection of Human Coronaviruses and Their Viral Surrogates in Water and Wastewater. *Environ Sci Technol Lett* [Internet]. 2020;7(8):544-53. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwjV07T8MwELagLIDEG1Fe8shA2thxE2esChULUwsdI9uxpSwpyoP_wT_m7CSIVAh1i62T5TgX32ff3XclBXTgext7guaKMaaIMFylyoiQMk4IlyyNYqKZ-F0b5id3fcOhT8IQqHKgrQe0qga-ctSDu2iPwmnc1i8YT2arGxY_jkBDA1ddjnIPDLpf0Q79PY41UKp
10. Sitch AJ, Dekkers OM, Scholefield BR, Takwoingi Y. Introduction to diagnostic test accuracy studies. *Eur J Endocrinol* [Internet]. 2021;184(2):E5-9. Available from: <https://eje.bioscientifica.com/view/journals/eje/184/2/EJE-20-1239.xml>
11. Trevethan R. Sensitivity, Specificity, and Predictive Values: Foundations, Plausibilities, and Pitfalls in Research and Practice. *Front Public Health* [Internet]. 2017 Nov 20;5:307. Available from: <https://pubmed.ncbi.nlm.nih.gov/29209603>
12. Zhang N, Gong Y, Meng F, Shi Y, Wang J, Mao P, et al. Comparative study on virus shedding patterns in nasopharyngeal and fecal specimens of COVID-19 patients. *Sci China Life Sci* [Internet]. 2021;64(3):486-8. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwtV1Li9swEBZplklvpU-6faFeemhwsGRhy4ceirtLC0u3sEnpTcjyeJvDKkucFPbfd2RJsP0sD304ocwNsw3noek-YaQjM_T5JZNAGmEEIbpVprGtDrnQvJa1qIpSgZCH_aGmUTWnGHswvKPYwi9K6T9B_D3L8UBvEYVwCMqAR7vpAbViN278wTSdvZ7tdl1s-4
13. Kirby AE, Welsh RM, Marsh ZA, Yu AT, Vugia DJ, Boehm AB, et al. Notes from the Field: Early Evidence of the SARS-CoV-2 B.1.1.529 (Omicron) Variant in Community Wastewater - United States, November-December 2021. *MMWR Morb Mortal Wkly Rep* [Internet]. 2022 Jan 21;71(3):103-5. Available from: <https://pubmed.ncbi.nlm.nih.gov/35051130>
14. Galani A, Aalizadeh R, Kostakis M, Markou A, Alygizakis N, Lytras T, et al. SARS-CoV-2 wastewater surveillance data can predict hospitalizations and ICU admissions. *Sci Total Environ* [Internet]. 2021/09/07. 2022 Jan 15;804:150151. Available from: <https://pubmed.ncbi.nlm.nih.gov/34623953>

15. Ivanova OE, Yarmolskaya MS, Ereemeeva TP, Babkina GM, Baykova OY, Akhmadishina L v, et al. Environmental Surveillance for Poliovirus and Other Enteroviruses: Long-Term Experience in Moscow, Russian Federation, 2004-2017. *Viruses* [Internet]. 2019 May 8;11(5):424. Available from: <https://pubmed.ncbi.nlm.nih.gov/31072058>
16. D'Souza RS, Wolfe I. COVID-19 vaccines in high-risk ethnic groups. *The Lancet* [Internet]. 2021;397(10282):1348. Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-85103752401&doi=10.1016%2FS0140-6736%2821%2900624-3&partnerID=40&md5=3f695d459083685ae1dbaf8332822e40>
17. Wolfe MK, Duong D, Bakker KM, Ammerman M, Mortenson L, Hughes B, et al. Wastewater-based detection of an influenza outbreak. *medRxiv* [Internet]. 2022 Jan 1;2022.02.15.22271027. Available from: <http://medrxiv.org/content/early/2022/02/19/2022.02.15.22271027.abstract>
18. Sinclair RG, Choi CY, Riley MR, Gerba CP. Pathogen Surveillance Through Monitoring of Sewer Systems. In: *Advances in Applied Microbiology* [Internet]. San Diego, CA: Elsevier Science & Technology; 2008. p. 249-69. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwnV3dS8MwED9kIMgEv3V-jD7qw1ybZmnyqOLwSYRtzyVNE9xLN6ab-N9713QfFQXxpVBS2nIX7n5J7n4_gJjdhp1vMcFKwzk3kXbS5MZpwbhkmcx4nqjlcl3XhoHuLwf6vrWX6rIQ5V-H8oboRFSHGLdjERJ1vny-W22xEFdmuCYPZ4n0asnLF5QMOyxOOMZkUZH

Appendix

Appendix A. Poster and oral presentation at the 11th TEPHINET Global Scientific Conference in Panama City, Panama on 9 September 2022.



SARS-CoV-2 wastewater surveillance has moderate sensitivity and high specificity in Victoria, Australia



Aidan Yuen (aidan.yuen@anu.edu.au)^{1,2}, Davoud Pourmarzi¹ & Jim Black²

¹National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australian Capital Territory 2600, Australia

²Department of Health, State Government of Victoria, Melbourne, Victoria 3000, Australia



Background

- In **Victoria, Australia**, wastewater surveillance is used to detect new incursions of COVID-19.
- The program uses **grab, composite** and **passive sampling**.
- The Government is now evaluating the program to ensure efficiency and appropriate resource allocation.
- This study **estimated the accuracy** of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people.



Methods

- We conducted a **diagnostic test accuracy study** from 25 August 2020 to 27 September 2021 in Victoria, Australia.
- Sensitivity** and **specificity** were estimated by cross-classifying wastewater results (**index test**) with the presence of known infected people resident on each catchment sampling day (**reference test**).
- Estimates were then **stratified** by lockdown days and sampling methods.
- The **detection probability** was estimated using univariate logistic regression.

		Known infected people resident in catchments	
		Present	Absent
Wastewater test result	+ve	True +ve (a)	False +ve (b)
	-ve	False -ve (c)	True -ve (d)
Sensitivity = a/(a+c)			
Specificity = d/(b+d)			

Lockdown (n)	Sensitivity (95% CI)	Specificity (95% CI)
No (16,665)	0.30 (0.27, 0.33)	0.96 (0.96, 0.97)
Yes (8,477)	0.49 (0.47, 0.52)	0.83 (0.82, 0.83)
Sampling method (n)	Sensitivity (95% CI)	Specificity (95% CI)
Grab (1,652)	0.36 (0.29, 0.43)	0.83 (0.81, 0.85)
Composite (303)	0.50 (0.31, 0.69)	0.92 (0.88, 0.95)
Short passive (113)	0.33 (0.19, 0.51)	0.87 (0.77, 0.94)
Long passive (8,174)	0.49 (0.47, 0.52)	0.82 (0.81, 0.83)

Days around symptom onset/ testing date	Number of infected people present									
	0	1	5	10	15	20	25	50	75	100
Estimated detection probability (%)										
-2 to +7	19	20	26	35	45	55	65	93	99	100
-2 to +14	19	20	24	29	35	42	49	79	94	98
-2 to +21	19	20	23	28	33	38	43	71	89	96
-2 to +28	19	20	23	27	31	36	41	67	86	95
-2 to +35	19	20	23	26	30	35	39	63	82	93
-2 to +42	19	20	22	26	29	33	38	60	79	91
-2 to +49	19	20	22	25	29	33	37	58	77	89
-2 to +56	19	20	22	25	29	32	36	57	76	88
-2 to +63	19	20	22	25	28	32	36	56	75	87
-2 to +70	19	20	22	25	28	31	35	55	73	86
-2 to +77	19	20	22	25	28	31	35	54	72	85
-2 to +84	19	20	22	25	28	31	34	54	72	85

Results

- The program showed **moderate sensitivity** and **high specificity** for detecting the presence of infected people at -2 to +7 days around symptom onset/testing date.
- Sensitivity was higher during **lockdowns** than non-lockdowns, and with **long passive sampling** than grab sampling.
- The detection probability was elevated even for periods **up to 84 days** following symptom onset/testing date.

Conclusions

- High specificity** → catchments with detections likely contain infected residents → target for public health action.
- Moderate sensitivity** → biologically plausible, as faecal shedding is variable, and the virus may degrade in sewage.
- Accuracy estimates are closer to the true value during **lockdowns** → index and reference tests have less misclassification.
- Long passive sampling** currently predominates the program.
- Increased detection probability beyond the infectious period → may be attributed to **persistent faecal shedding**.



Australian National University



Department of Health



Chapter 4: Investigation of a COVID-19 outbreak at the Arcare Maidstone residential aged-care facility

Prologue

This chapter meets the MAE major competency to complete an “investigation of an acute public health problem or threat”. This chapter describes a COVID-19 outbreak investigation at the Arcare Maidstone residential aged-care facility (RACF). The outbreak was declared on 29 May 2021 when the index case was notified to the Department. I was subsequently deployed to the Western Public Health Unit (WPHU) to help investigate the outbreak, which involved collecting and analysing key epidemiological and genomic data to inform decision-making, and to enact rapid control measures to prevent further transmission at the site. With this, the outbreak was stood down on 21 June 2021. My findings were captured in a report for WPHU and the Department, which was used to inform subsequent RACF-outbreaks.

This project was conceptualised by Dr. Jim Black, my field supervisor, and:

- Stacey Rowe, Director, COVID-19 Response, Department of Health;
- Dr. Sheena Sullivan, Senior Public Health Officer, COVID-19 Response, Department of Health;
- Mohana Baptista, Director, COVID-19 Response, Department of Health;
- Dr. Frances Ampt, Epidemiologist, WPHU, Western Health; and
- Gabrielle Hales, Epidemiologist, WPHU, Western Health.

My role

I was deployed to WPHU to co-lead the investigation with Dr. Frances Ampt and Gabrielle Hales. My responsibilities during the investigation were to attend key meetings as the lead epidemiologist. I also developed an ad hoc surveillance system for monitoring the movements of all attendees at the site during the outbreak period and implemented revisions to the system to additionally capture testing data, vaccination records and QR code attestations. I also prepared dynamic situational reports and responded to ad hoc requests for intelligence relating to the outbreak. Protocols for the retrospective analysis of the outbreak—including calculations of attack rates—were prepared. Upon analysing the epidemiological and genomic data, I prepared the final outbreak management report for both internal and external stakeholders. Throughout my secondment, I supervised three Data Assurance Officers, and oversaw their data collection and cleaning duties.

Lessons learnt

This project taught me about the complexity and urgency of COVID-19 outbreak investigations. Outbreaks at RACFs are particularly sensitive, and often undergo strict public scrutiny, given the disproportionate COVID-19 morbidity and mortality at such facilities. Considering this, our investigation focused on rapidly recognising cases and enacting control measures to prevent further transmission at the site. Through these efforts, the outbreak resulted in zero deaths.

I also learnt about the importance of accurate data collection at all points in the investigation. Knowing who was attending the site throughout the outbreak period was imperative for case finding. Genomic analysis—although costly in terms of time and money—provided confidence in the epidemiological links between cases; it also confirmed the variant responsible for the outbreak. Testing data was used to determine if transmission was still occurring at the site, and when transmission had ceased, thus allowing for the outbreak to be stood down.

However, some of the data—particularly the sign-in sheets and rosters—were compromised by spelling errors and missing fields. This made surveillance particularly challenging, especially when linking records across multiple datasets, including testing data, vaccination records and QR code check-ins. As such, much time was spent manually cleaning the data.

Public health impacts

The investigation of the Arcare Maidstone RACF outbreak was essential for understanding the transmission patterns of SARS-CoV-2 at the site. This information provided the evidence base for enacting public health measures to mitigate further spread of the virus within the site, and within the broader Victorian community. The methodology and analyses captured in this report were used to inform future COVID-19 outbreak investigations.

Abstract

Background

An outbreak at the Arcare Maidstone RACF was declared on 29 May 2021 when the index case was notified to the State Government of Victoria's Department of Health (the Department). The index case was an employee who developed symptoms on 28 May. They were tested on the same day and diagnosed on 29 May. The individual had worked in the facility on the Magnolia unit—a high-care non-dementia ward that housed 36 residents—while likely infectious on 26 and 27 May. The investigation aimed to collect and analyse key epidemiological and genomic data to inform public health decision-making, and to enact rapid control measures to prevent further transmission at the site.

Methods

Upon notification of the index case, an Outbreak Management Team (OMT) meeting was convened on 30 May to monitor and manage the outbreak. WPHU was the lead public health entity and acted on behalf of, and as part of, the Department's COVID-19 response. Case finding and surveillance involved reviewing lists of staff, contractors, visitors, and residents who attended the site during the outbreak period. The acquisition source was investigated by comparing the acquisition sites of the index case with exposure sites generated by cases from concurrent outbreaks in Victoria. Epidemiological links were established by reviewing the acquisition sites and exposure sites of cases and identifying places where they may have intersected. Whole genome sequencing helped verify these epidemiological links and identified the variant responsible for the outbreak. Public health actions were enacted to mitigate further transmission at the site. The OMT aimed to stand down the outbreak at 14 days after the last case was onsite and to close the outbreak after 28 days.

Results

The outbreak period was defined as having begun two days before the first symptom onset date (i.e., on 26 May), and as having ended two incubation periods after the last infected person onsite went into isolation on 5 June (i.e., 3 July). At the beginning, there were 79 residents and 110 staff onsite; 72 residents were left by the end. A total of 406 attendees were accounted for during the entire outbreak period. The outbreak resulted in 12 cases and 245 close contacts. Three (25%) were residents, five (42%) were staff members and four (33%) were household contacts. Residents presented an attack rate of 3.8% (3/79), while staff presented an attack rate of 1.0% (4/405, excluding the staff index case). Genomic analysis confirmed that all cases were of the B.1.617.1 variant. Public health actions included zoning, cohorting, movement restrictions, use of tier 3 PPE, cleaning and

disinfection, and vaccinations. Transmission was attributed to breaches in infection prevention and control measures, all of which were addressed at notice. The outbreak was stood down on 21 June 2021, upon which all enhanced public health actions were ceased.

Conclusion

The Arcare Maidstone outbreak experienced relatively low morbidity and no mortality—a testament to the rapid response. This investigation will serve as a precedent and a learning tool for future COVID-19 outbreaks in RACFs.

1. Introduction

1.1. COVID-19

At the end of 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China, causing an outbreak of unusual viral pneumonia (1). The novel outbreak was eventually declared a pandemic of “coronavirus disease 2019” (COVID-19) by the World Health Organization on 11 March 2020 (2). Initial estimates of the mean incubation period of COVID-19 ranged from 5.6 (95% CI: 5.2-6.0) to 6.7 days (95% CI: 6.0-7.4) (3). At the time of writing, symptoms included cough, fever, fatigue, and headache, while some cases also experienced rhinorrhoea, diarrhoea, and altered smell and taste. It was also fatal in a relatively small proportion of cases with early estimates of the fatality rate ranging from 0.17% to 1.7% (4).

1.2. Variants of concern

SARS-CoV-2, like other RNA viruses, is prone to genetic evolution while adapting to their new human hosts. Such adaptive mutations can result in variants with different pathogenicity to the ancestral strain (5). Multiple variants of SARS-CoV-2 have been identified, most of which are considered variants of interest, as opposed to variants of concern (VOCs)—the latter of which pose greater risks to public health. VOCs are marked by enhanced transmissibility or virulence, reduced neutralisation by antibodies, the ability to evade detection, and/or decrease the effectiveness of therapeutics and vaccination. As of 22 June 2021, the WHO identified four SARS-CoV-2 VOCs:

- Alpha (B.1.1.7)—first VOC identified in the UK in late December 2020;
- Beta (B.1.351)—first reported in South Africa in December 2020;
- Gamma (P.1)—first reported in Brazil in January 2021; and
- Delta (B.1.617.2)—first reported in India in December 2020 (6-9).

At the time of writing, outbreaks in Victoria since May—including the Arcare Maidstone residential aged-care facility (RACF) outbreak—have been of the delta variant.

1.3. Transmission

Respiratory transmission through droplets from coughing or sneezing, or airborne transmission through the inhalation of aerosol droplets exhaled by an infected person, are the dominant forms of transmission, with transmission risk being predicated on proximity and ventilation (10-12). Vertical transmission (13) and transmission from minks (14) have also been documented, but rarely occur. Fomite transmission is also possible but is difficult to demonstrate directly (10,11). Live virus has been isolated from saliva (15) and stool (16) and

viral RNA has been isolated from semen (17) and blood (18), but there are no reported cases of transmission via faecal-oral, sexual, or bloodborne routes (11). Cases show heterogeneous transmission dynamics, i.e., most people do not transmit the virus, while some can cause many secondary cases (superspreading events) (19).

1.4. Diagnosis

1.4.1. *Specimen collection*

COVID-19 is typically diagnosed through laboratory tests. Specimens for virus detection are acquired through nasopharyngeal and oropharyngeal swabs, but may also involve broncho-alveolar lavage, sputum, stool, urine, and blood, depending on the clinical manifestation of the individual (20,21).

1.4.2. *Nucleic acid test*

The current gold standard for detecting SARS-CoV-2 is nucleic acid testing (NAT), such as real-time reverse transcription-polymerase chain reaction (RT-PCR), which aims to detect SARS-CoV-2 RNA in samples (22). NAT is both sensitive and specific; for example, the nasopharyngeal swab NAT has a reported sensitivity of 85.7% (95% CI=76.5%-93.4%) and a specificity of 98.9% (95%CI=97.4%-99.7%) (23). Of note, false-negative results can arise if viral genome is insufficient or if the optimal time-window of viral replication is missed. False-positive results can arise when RT-PCR detects residual RNA in non-infectious convalescent individuals (24).

1.4.3. *Antigen test*

Antigen-based tests can use specific monoclonal antibodies to bind to specific SARS-CoV-2 antigens in samples. These tests typically target structural proteins, such as spike, membrane, envelope and nucleocapsid proteins. However, given its lower sensitivity and specificity, antigen-based tests are not considered the gold standard (25).

1.4.4. *Serological assays*

Serological assays aim to detect specific antibodies (IgG and IgM) produced against SARS-CoV-2 in serum, plasma, or whole blood. Such antibodies are usually detected one to three weeks after symptom onset, and so serology tests are limited to detecting infections later in the infection course, and for identifying people with immunity against the disease (26).

1.5. Treatment

At the time of writing, therapeutic options included the following (29):

- Antiviral drugs, e.g., remdesivir;

- Anti-SARS-CoV-2 monoclonal antibodies, e.g., bamlanivimab/etesevimab and casirivimab/imdevimab;
- Convalescent plasma from recovered COVID-19 patients;
- Anti-inflammatory drugs, e.g., dexamethasone; and
- Immunomodulating agents, e.g., baricitinib and tocilizumab.

COVID-19 cases with associated respiratory insufficiency should also be monitored with continuous pulse oximetry and administered with oxygen supplementation via nasal cannula or Venturi mask. Non-invasive treatments such as High-Flow Nasal Cannula or Non-invasive Positive Pressure Ventilation should be considered for cases where there is no clinical improvement or worsening of symptoms or oxygen saturation (30).

1.6. Vaccination

Vaccines work by stimulating the body to produce specific antibodies against SARS-CoV-2; individuals will then experience an anamnestic response when the body is exposed to SARS-CoV-2 again (31). They are crucial for achieving herd immunity to attenuate the COVID-19 pandemic (32).

Vaccine development was expedited rapidly at the outset of the pandemic, with more than 150 candidate vaccines in development within the first 5 months of 2020 (33). By the end of February 2021, more than 40 countries and regions were working on developing COVID-19 vaccines. At the time of writing, among those in clinical trials, two vaccines from the United States (Moderna and Johnson & Johnson/Janssen), one codeveloped by the United States (Pfizer) and Germany (BioNTech), one from the UK (AstraZeneca/Oxford), four from China, and one from Russia have been granted conditional authorisations in one or more countries (34). As of 10 April 2021, the top five countries with vaccination programs were the United States (6.129 million), China (4.052 million), the European Union (2.66 million), the United Kingdom (1.82 million) and India (1.084 million) (31).

1.7. Residential aged-care facilities (RACFs)

By the end of 2020, Australia recorded over 27,000 COVID-19 cases, the bulk of which occurred in Victoria between May and October 2020. In Victoria, approximately 2,000 cases occurred in RACFs, which saw 647 deaths. At the time, 75% of the country's deaths occurred in such facilities (35).

1.8. COVID-19 outbreak at the Arcare Maidstone RACF in May 2021

The Arcare Maidstone RACF is located at 31 Hampstead Rd, Maidstone, Victoria 3012. Its 110 staff work on dedicated assignments, where they each care for the same few residents.

The site includes 90 suites sectioned into three zones. The facility has an al fresco café, a movie theatre, hair salon, worship room, dining rooms, and two courtyards.

An outbreak at the Arcare Maidstone RACF was declared on 29 May 2021 when the presumed index case was notified to the State Government of Victoria's Department of Health (the Department). They were an employee who developed symptoms on 28 May. They were tested on the same day and diagnosed on 29 May. The individual worked on the Magnolia unit—a high-care non-dementia ward that housed 36 residents—during their presumed infectious period (26 to 27 May).

1.9. Aims and objectives

The investigation aimed to collect and analyse key epidemiological and genomic data to inform public health decision-making, and to enact rapid control measures to prevent further transmission at the site. The investigation also aimed to stand down the outbreak after one full incubation period of SARS-CoV-2 (i.e., 14 days), and to close the outbreak after two full incubation periods (i.e., 28 days) from the date the last infected case was onsite.

The strategic intent and objectives of the investigation were to:

- Describe the epidemiology and genomics of the Arcare Maidstone outbreak;
- Manage infection prevention and control measures to prevent further transmission;
- Conduct critical contact tracing and testing to identify all at-risk individuals;
- Arrange vaccinations for unvaccinated residents and staff; and
- Organise priorities and logistics for the care of the residents.

2. Methods

2.1. Ethics

Ethical approval was obtained from the Australian National University Human Research Ethics Committee (Protocol 2017/909). All data were collected, stored, and destroyed under the provisions of the *Public Health and Wellbeing Act 2008 (Victoria)*.

The main ethical considerations were related to the use of raw data that contained the patients' re-identifiable IDs; patient confidentiality could have been compromised at any point in the investigation. Several mitigation strategies were in place to prevent such breaches. All the data were stored and analysed within the Microsoft Azure virtual machine within the Department's firewall and Western Health servers. Both are only accessible to employees who use the same data as part of their normal duties. Therefore, the collection, storage, and eventual destruction of the data in this study do not create any new ethical considerations. To avoid identification of individual patients, all results have been presented in aggregate form; at meetings, cases were identified by the first two letters of their first and last names.

2.2. Governance

Upon notification of the index case, an Outbreak Management Team (OMT) meeting was convened on 30 May to monitor and manage the outbreak. The Western Public Health Unit (WPHU) at Western Health was the lead public health entity and acted on behalf of, and as part of, the Department's COVID-19 response. The chair of the Outbreak Management Team (OMT) was either the Director or the Medical Lead at WPHU.

The OMT meeting occurred daily and was attended by representatives of the following:

- The Arcare Maidstone RACF, who have approved provider obligations under the Aged Care Act and are responsible for enacting the outbreak management plan;
- WPHU, who have a legislative responsibility for declaring the outbreak, managing the public health aspects of the outbreak, standing down the outbreak, and co-ordinating resident hospital transfers when required for public health reasons;
- The Department's COVID-19 Investigation Case Contact Outbreak Management (ICCOM) division, including the Infection Prevention and Control Advisory Response (IPCAR);
- The Victorian State COVID-19 operations team of the Australian Government Department of Health, including The Aged Care Quality and Safety Commission;
- Sonic Pathology (Melbourne Pathology) who was responsible for onsite testing;
- Melbourne Health (the Aged Care Hub);

- Western Health Chronic and Complex Care;
- The Victorian Aged Care Response Centre; and
- Aspen, who was responsible for onsite vaccinations.

2.3. Epidemiological investigation

The epidemiological investigation was conducted in accordance with the Victorian Residential Aged-Care Facility COVID-19 Outbreak Management Guidelines (“Victorian guidelines” hereafter).

2.3.1. National case definitions

As per national guidelines, COVID-19 case definitions are outlined in Table 1.

2.3.2. Outbreak case and contact definitions

In the Arcare Maidstone outbreak, confirmed cases, close contacts and surveillance contacts were defined as follows.

Confirmed case

A person with a definitive laboratory test for COVID-19 with an epidemiological link to a confirmed case of the Arcare Maidstone RACF outbreak, with symptom onset (or infectious period) on/after 14 May 2021 (14 days prior to symptom onset of the earliest confirmed case).

Close contact

Up until 5 June 2021, the tier 1A primary close contact (PCC) definition for staff, contractors and visitors was defined as:

- Any staff member, contractor or visitor in/to the facility and attended Unit 2 between 7 am and 1:30 pm on 26 May or 27 May (including handovers, etc.); OR
- Any staff member, contractor or visitor in/to the facility who shared communal facilities (e.g., tearoom or office space) with a confirmed case between 7 am and 1:30 pm on 26 May or 27 May.

On 6 June, PCC definitions for staff, contractors and visitors were amended to:

- Any person who had been on the Magnolia Unit since 7am on 26 May 2021 (the date the index case was likely first infectious); OR
- Any staff member, contractor or visitor in/to the facility who shared communal facilities (e.g., tearoom or office space) with a confirmed case on or after 7am on 26 May 2021.

Table 1. COVID-19 case definitions as prescribed by the Communicable Disease Network for Australia (CDNA) national guidelines for public health units (6 June 2021); source: <https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-novel-coronavirus.htm>.

Category	Criteria	Supplementary information
Confirmed case	Laboratory definitive evidence (where not classified as a historical case)	<i>Laboratory definitive evidence:</i> 1. Detection of SARS-CoV-2 by nucleic acid testing OR 2. Isolation of SARS-CoV-2 in cell culture, with confirmation using a nucleic acid test OR 3. SARS-CoV-2 IgG seroconversion or a four-fold or greater increase in SARS-CoV-2 antibodies of any immunoglobulin subclass including 'total' assays in acute and convalescent sera, in the absence of vaccination.
Historical case	Laboratory suggestive evidence; AND either: 1. Previous (prior to the past 14 days) clinical evidence OR 2. Previous (prior to the past 14 days) epidemiological evidence. A historical case should not have symptoms of COVID-19 (or not have had symptoms of COVID-19 for the past 14 days).	<i>Laboratory suggestive evidence:</i> 1. Detection of SARS-CoV-2 by polymerase chain reaction (PCR) on two specimens at least 24 hours apart with results suggestive of a historical infection on both specimens AND detection of IgG or total antibody, in the absence of vaccination OR 2. Negative SARS-CoV-2 PCR AND detection of IgG or total antibody, in the absence of vaccination OR 3. Detection of SARS-CoV-2 by PCR with initial test results suggestive of a historical infection AND a subsequent PCR is negative, taken at least 24 hours apart. <i>Clinical evidence:</i> 1. Fever ($\geq 37.5^{\circ}\text{C}$) or history of fever (e.g., night sweats, chills) OR 2. Acute respiratory infection (e.g., cough, shortness of breath, sore throat) OR 3. Loss of smell or loss of taste.
Probable case	A person who meets the above clinical AND epidemiological criteria. Clinical and public health judgement should be used in assessing if hospitalised patients with non-specific signs of infection and/or patients who do not meet the clinical or epidemiological criteria should be considered suspect cases.	<i>Epidemiological evidence:</i> • Close contact with a confirmed case • International travel • Workers supporting designated COVID-19 quarantine and isolation services • International border staff • Air and maritime crew • Health, aged or residential care workers and staff with potential COVID-19 contact • People who have been in a setting where there is a COVID-19 case • People who have been in areas with recent local transmission of SARS-CoV-2.

Throughout the outbreak period, the tier 1A PCC definition for residents included any resident who attended or was at Arcare Maidstone in any part of the facility from 26 May.

Tier 2 casual contacts were defined as any other attendance at the Arcare Maidstone RACF since 7am from 26 May.

Surveillance

Attendees since 7am on 26 May 2021 were all registered with WPHU for surveillance awareness and oversight.

2.3.3. Testing

Up until 5 June 2021, testing teams were onsite every 48 hours to test staff and residents who were present at the time. Symptomatic residents were tested at notice. As of 6 June, all attendees were classified into three categories for testing:

- Daily testing for regular staff onsite at 9 am;
- Surveillance testing (3 per week) for those deemed high risk (e.g., irregular staff); and
- PCC testing at notice and at day 13.

As of 8 June, daily testing was instigated for all staff onsite, including night shift staff, to improve case finding. The final round of testing (day 13 since last case was onsite) was conducted on 19 June.

2.3.4. Case finding and contact tracing

Contacts were identified through various measures. Arcare Maidstone RACF provided lists of staff, contractors, visitors, and residents during the outbreak period to the WPHU Medical Lead and Epidemiologists. Staff at Arcare Maidstone RACF were also briefed verbally and in writing to raise awareness and to check staff against contact definitions. Contact definitions were also provided to families to identify visitors. Contact definitions were published on the Department's exposure sites website to assist with identifying visitors and contractors who may have attended during the outbreak period. Using this information, attack rates for residents and staff were calculated using the population at-risk as the denominator.

2.3.5. Case interviews

All confirmed cases were interviewed by Public Health Officers at WPHU. Under *the Public Health and Wellbeing Act Victoria (2008)*, cases were required to answer all questions, but could refuse if their answers would incriminate them. Cases were asked for their demographic information, whether they wished to receive a once-off \$1,500 support payment (if eligible), information on their general practitioner, questions about conditions that may

place them at an increased risk of COVID-19 complications, questions about contact with a confirmed case, symptoms, movements in the 14 days prior to symptom onset for symptomatic cases or testing date for asymptomatic individuals, information about close contacts during acquisition and infectious periods, and finally advice on isolation. Cases were also followed up with welfare checks and with reminders for day 13 testing.

2.3.6. Staff Attestation and Visitor Registration (SAVR) application

SAVR is an electronic application that rapidly screens for COVID-19 symptoms and records the details of any attendees at Victorian health facilities. The SAVR tool was implemented at the Arcare Maidstone RACF on 9 June 2021 to assist with contact tracing, and in the surveillance of attendees. Scanners were required to fill in their first and last names, their phone numbers, and the unit they were working on (Jasmine or Magnolia). Compliance with SAVR was calculated by cross-classifying the number of attendees who checked in via SAVR against the number of attendees on rosters and sign-in sheets.

2.3.7. Wastewater surveillance

As part of the Department's COVID-19 response, wastewater surveillance was introduced to facilitate case detection. Wastewater samples are collected from sewage and analysed for SARS-CoV-2 fragments shed via an infected person's saliva, sputum, stool, or urine. Daily targeted testing was initiated on 16 June 2020.

2.3.8. Acquisition source and epidemiological links

The index case's acquisition sites were compared with existing exposure sites generated by cases from concurrent outbreaks in Victoria to identify the acquisition source of the outbreak. Epidemiological links were established by reviewing the acquisition sites and exposure sites of cases in the current outbreak to identify places where cases may have intersected.

2.4. Genomic investigation

All viruses recovered from cases were forwarded to the Microbiological Diagnostic Unit Public Health Laboratory (MDU PHL). The laboratory genetically sequenced SARS-CoV-2 viral specimens from the cases to identify links between cases in the outbreak, and with cases in concurrent outbreaks in Victoria.

2.5. Public health actions

2.5.1. Isolation

Throughout the outbreak period, confirmed cases and close contacts were instructed to isolate or quarantine for 14 days. Casual contacts were instructed to test and isolate until they received a negative result.

2.5.2. Immediate tasks

As per Victorian guidelines, the OMT was advised to commence all public health actions outlined in Table 2 within 24 hours of the COVID-19 outbreak being declared. Table 3 lists the initial stakeholder allocated to key tasks.

Table 2. Key tasks to be completed within the first 24 hours of a COVID-19 outbreak in a residential aged-care facility.

Domain	Action
Infection prevention and control	Isolate residents and cease communal activities
	Staff to wear Tier 3 personal protective equipment (PPE) (P2/N95 mask, eye protection, gown, and gloves) for all resident interactions
	Institute spotters to observe PPE use
	Set up donning and doffing stations
	Organise a deep clean of the facility
Staff	Advise close contacts to quarantine
	Allocate staff to work only in a specific area across their entire shift and for different shifts, including for tea breaks
	Ensure staff are not working across other residential aged-care facilities
	Address critical staffing issues
	Ensure all communal staff spaces meet the density quotient, and that staff are 1.5 meters apart in staff communal spaces
Logistics	Ensure PPE and alcohol-based hand rub stocks are adequate
	Ensure waste disposal is adequate
	Ensure meal provisions are adequate
	Ensure adequate provision of medications and equipment to support the clinical needs of residents, e.g., oxygen
Resident care	Check if any residents need a clinical review
	Transfer residents who have been recommended for public health reasons
	Cease all new admissions and transfers into the facility
	Cease all visitation (except for end-of-life care) and advise visitors currently on site to leave and isolate at home until further advised
Testing	Test all residents and staff for COVID-19
Vaccinations	If possible, vaccinate all residents and staff

Table 3. Stakeholder allocations to key tasks; RACF=residential aged-care facility.

Key task	Primary stakeholder initially allocated	Alternative stakeholder if primary stakeholder is unable/unlikely to complete the task within 24 hours
Infection prevention and control	RACF management and Infection Prevention Lead working with the Health Service Aged Care Representative	RACF Management and Infection Prevention Lead working with the Department Outbreak Squad
Close contact definition determined/ resident hospital transfer plan for public health reasons	WPHU	
Complete close contact spreadsheet	RACF Management	Once returned, WPHU will generate a list of close contacts who will be contacted for further instructions regarding testing and quarantine
Workforce planning	RACF management	The Australian Government Case Manager can coordinate surge staffing; this is likely unavailable on day 0, and alternative staff pools may be accessible via the Health Service Cluster and the Department
Ensuring PPE stock/ waste disposal and food and equipment (e.g., oxygen) is adequate	RACF Management	Australian Government Case Manager
Resident's care	RACF staff and residents' General Practitioners	Escalation to Local Health Service Residential in Reach team if needed
Initial testing	The Australian Government will coordinate site testing through Sonic Pathology (Melbourne Pathology)	If testing via the Department/ Australian Government cannot be performed within 24 hours, the Health Service Cluster may be asked to perform

2.5.3. Standing down the outbreak

Public health actions—including zoning, cohorting, movement restrictions, use of tier 3 PPE, cleaning and disinfection, and vaccinations—were initiated to mitigate any further transmission onsite, with the goal of standing down the outbreak at 14 days after the last case was on site. This required certain criteria to be met, as per Victorian guidelines.

Chapter 4

Standing down an outbreak (previously called “transitioning to enhanced surveillance”) would cease all enhanced public health actions. This is generally considered when:

- At least 14 days have elapsed since the last infectious staff member was on site AND
- At least 14 days have passed since the last resident case on-site was considered infectious (i.e., the date the resident was deemed eligible for ‘release from isolation’ or the date of death or transfer out of the facility) AND
- A final round of testing has been conducted for all workers and residents on or at about 13 days from the last potential infectious exposure on-site (either since the last infectious staff member was on site or the last resident case on-site was considered infectious, whichever is later) and returned negative results AND
- All negative residents remain asymptomatic.

3. Results

3.1. Descriptive Epidemiology

The outbreak period was defined as having begun two days before the first symptom onset date (i.e., on 26 May), and as having ended two incubation periods after the last infected person onsite went into isolation on 5 June (i.e., 3 July). At the beginning, there were 79 residents and 110 staff onsite. By the end, there were 72 residents left onsite. Seven were transferred offsite for reasons related, or unrelated, to COVID-19 or were deceased. A total of 406 workers were onsite across the entire outbreak period.

The outbreak resulted in 12 cases and 245 close contacts (Table 4, Figure 1). Case 1—the suspected index case—was linked to two household contacts who eventually became confirmed cases. Case 3 was also a close contact of case 1, as they worked onsite on the same days. The resident cases—case 4, 5 and 8—were all considered close contacts of the presumed index case (Figure 1). Cases were spread across six households, including the Arcare Maidstone RACF, and linked to three other concurrent Victorian outbreaks (Figure 1).

Table 4. High-level summary of the epidemiology of the Arcare Maidstone residential aged-care facility outbreak (2021).

Variable	Value
Confirmed cases (n)	12
Close contacts (n)	245
Date of first diagnosis	29 May 2021
Date of first symptom onset	28 May 2021
Date of last symptom onset	09 June 2021
Date of last isolation start	13 June 2021

Half of cases were female, and half were male. The median age was 34 years, with a range of 19 to 99 years. No cases identified as Indigenous. Half (50%) spoke English at home, and nine (75%) were born outside of Australia. Three cases (25%) were hospitalised, and no cases were deceased (Table 5). Half (n=6) were symptomatic, i.e., ever developed symptoms during their infectious period (Figure 2). Three cases (25%) were residents, five (42%) were staff members, including agency staff, and four (33%) were household contacts (Figure 3). Residents presented an attack rate of 3.8% (3/79). All attendees were considered at risk and presented an attack rate of 1.0% (4/405). Attack rates were not calculated for household contacts due to the absence of denominator data.

Chapter 4

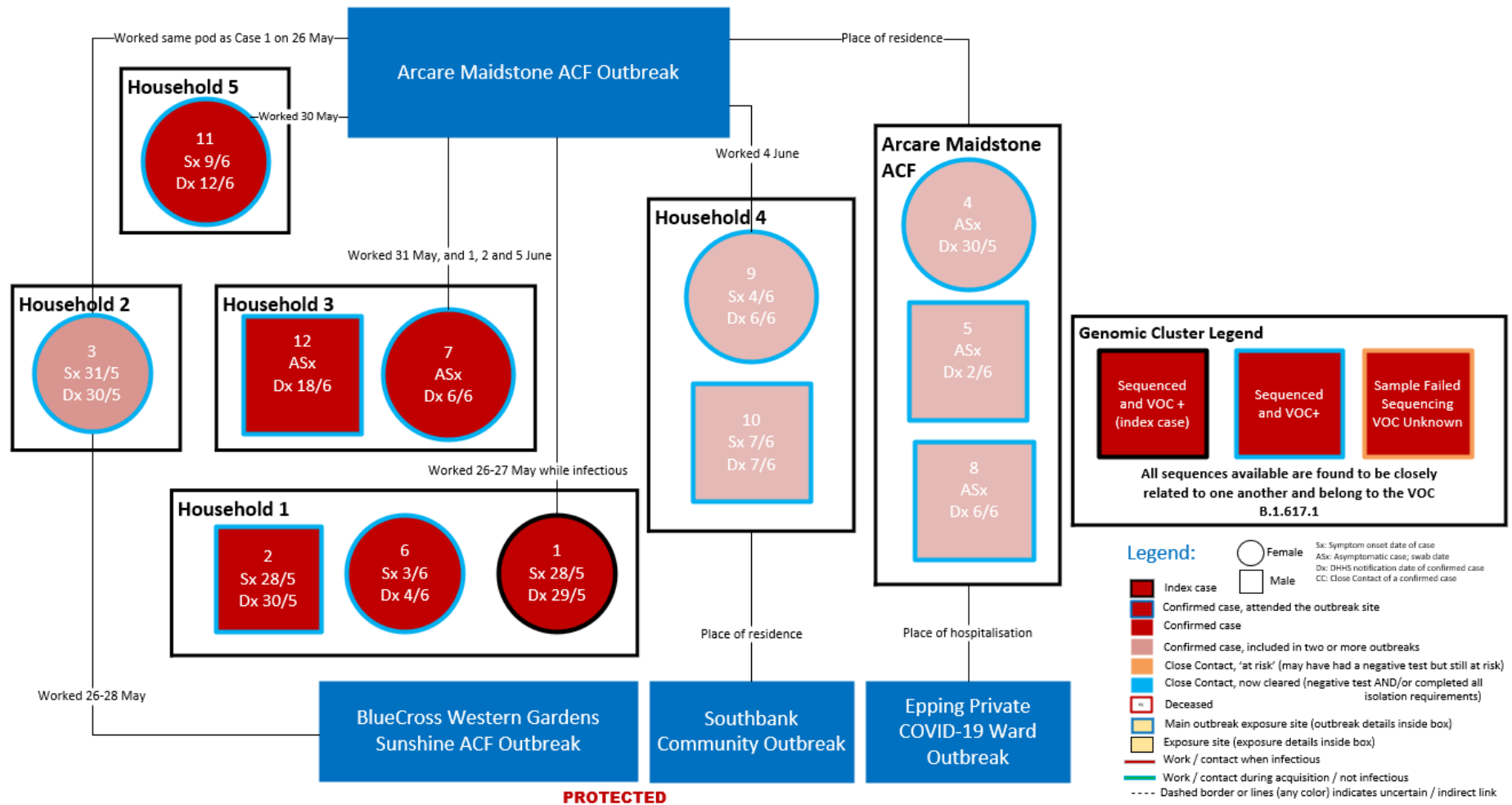


Figure 1. Social-location networks/epidemiological links in the Arcare Maidstone residential aged-care facility outbreak (2021). Red circles and squares represent confirmed cases (see legend for more information). Blue boxes show outbreaks that cases are linked to. Black boxes show which households cases belong to. Lines joining cases/households to outbreaks also describe key events relating to potential transmission.

Table 5. Summary of the demographics and clinical outcomes of cases linked to the Arcare Maidstone residential aged-care facility outbreak (2021).

Variable		Number	Percentage (%)
Total		12	100
Sex	Female	6	50
	Male	6	50
Age group (years)	0-14	0	0
	15-24	1	8
	25-34	5	42
	35-44	1	8
	45-54	2	17
	55-64	0	0
	65+	3	25
Indigenous status	Indigenous	0	0
	Non-Indigenous	9	75
	Unknown	3	25
Language	English	6	50
	Filipino/Tagalog	2	17
	Missing/Unknown	4	33
Country of birth	Australia	3	25
	Brazil	1	8
	India	2	17
	Philippines	3	25
	United Kingdom	3	25
Clinical outcomes	Hospitalised	3	25
	Not hospitalised	9	75

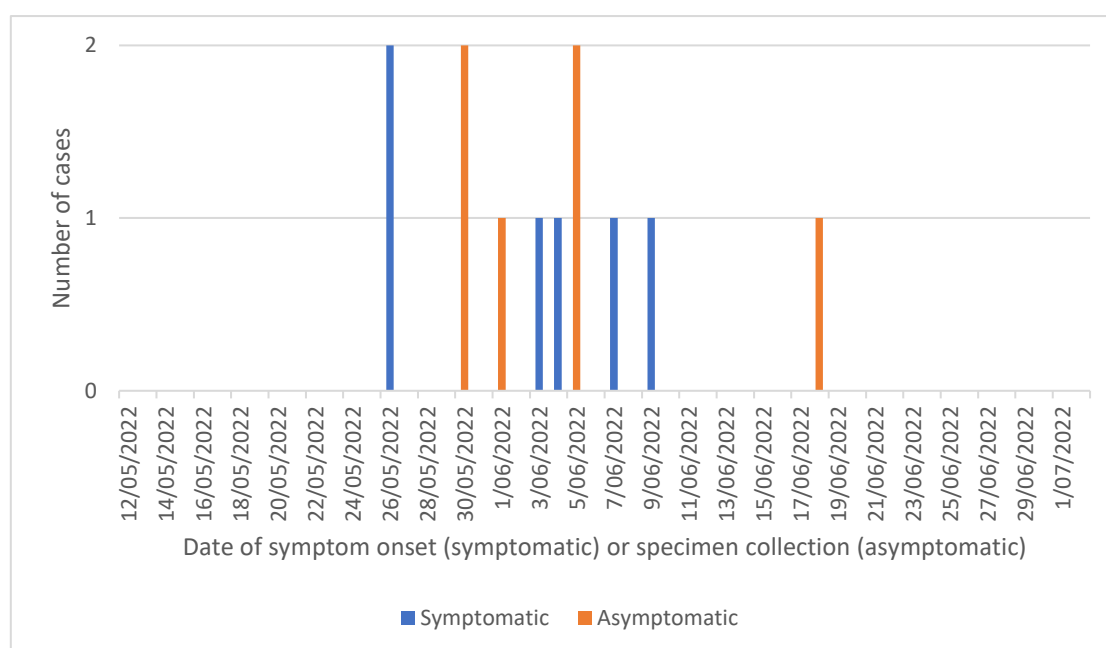


Figure 2. Epidemic curve for the Arcare Maidstone residential aged-care facility outbreak (2021).

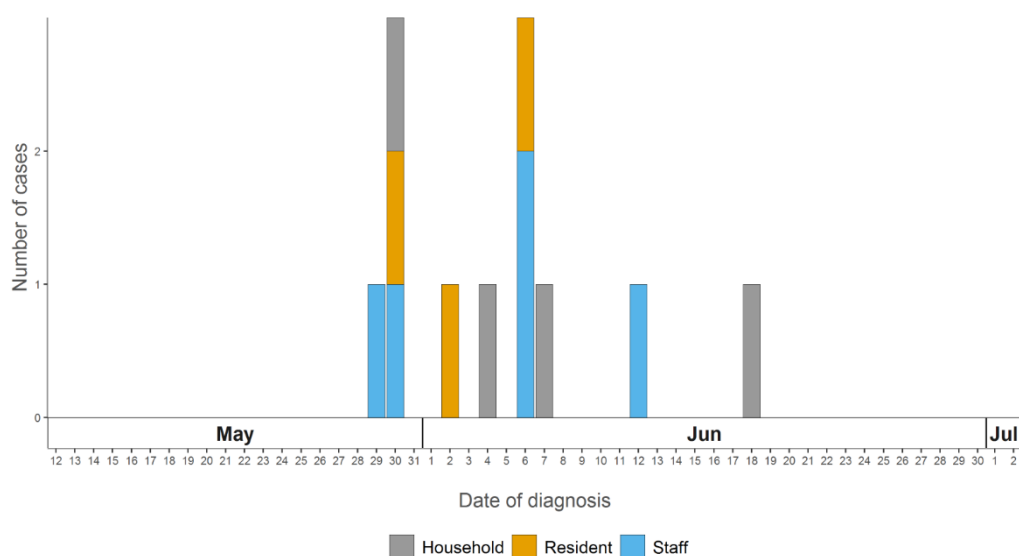


Figure 3. Epidemic curve for the Arcare Maidstone residential aged-care facility outbreak by diagnosis date and case type (household, resident, or staff) (2021).

3.1.1. SAVR compliance

Following its inception on 9 June 2021, QR code check-ins via the SAVR application saw an average daily compliance of around 20%. The lowest compliance was observed on 10 June 2021, the day after its inception, at 6%. In contrast, the greatest compliance was observed on 14 June 2021 at 30% (Table 6). An upward trend in compliance was observed throughout the outbreak period (Figure 4). Approximately 7% of attendees checked in via QR codes but were not accounted for on agency lists each day (Table 6).

Table 6. Number of attendees on logs and attendees who checked in via the Staff Attestation and Visitor Registration (SAVR) application per day of the Arcare Maidstone residential aged-care facility outbreak (2021); SAVR was instituted on 9 June 2021.

Date	10 Jun	11 Jun	12 Jun	13 Jun	14 Jun	15 Jun	16 Jun	17 Jun	18 Jun	19 Jun
Attendees on logs	57	105	105	78	108	111	121	100	109	129
Attendees checked in via SAVR app	17	24	25	21	39	36	35	35	29	30
Attendees on logs OR SAVR app	70	110	113	87	113	116	127	112	112	131
Attendees on logs AND SAVR app	4	19	17	12	34	31	29	23	26	28
Percentage attendees on logs AND SAVR app (%)	6	17	15	14	30	27	23	21	24	21

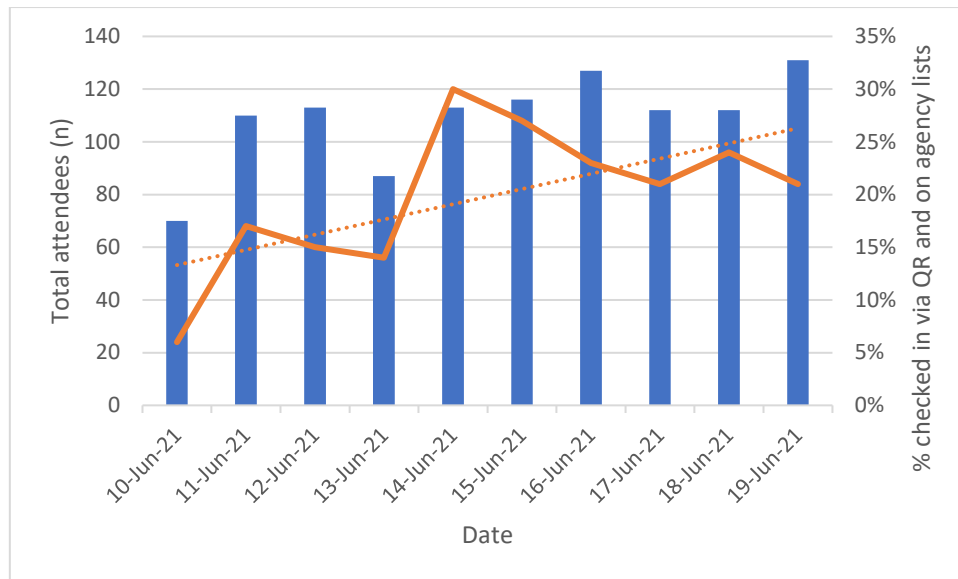


Figure 4. QR code check-ins via the Staff Attestation and Visitor Registration (SAVR) application during the Arcare Maidstone residential aged-care facility outbreak (2021); SAVR was instituted on 9 June 2021. The total number of recorded attendees is shown in blue; the proportion who checked-in via SAVR is shown in orange.

3.1.2. Wastewater surveillance

Daily wastewater testing was instigated from 16 June 2021 until the outbreak was stood down on 21 June 2021. Testing returned negative results on each day, which provided reassurance in the absence of SARS-CoV-2 infected people on the premises.

3.1.3. Acquisition source

Case 1 was the suspected index case; they were a personal care assistant and became symptomatic on 28 May 2021. The case was swabbed that same day and tested positive on 29 May 2021. The staff member reported working at the facility exclusively on 26 and 27 May 2021, i.e., during their probable infectious period. Their acquisition source was investigated, but no epidemiological links with cases in concurrent Victorian outbreaks were established. Case 2, a household contact of Case 1, was also investigated as the potential index case; their symptom onset date was the same as Case 1, but again, acquisition was undetermined.

3.2. Genomic analysis

As of 13 June 2021, sequencing data was available for all twelve cases to help establish transmission chains through genomic analysis. All cases were B.1.617.1 and were thus related to each other. The virus recovered from the index case was closely related to viruses recovered from cases linked to an earlier community outbreak in Whittlesea (Figure 1). However, no epidemiological links were established between the two outbreaks. All viruses

in the Arcare Outbreak sat within cluster B.1, a sub cluster of the larger Cluster B that was associated with the Reservoir Workplace Transmission site in the City of Whittlesea Community Outbreak.

A sample from the later Southbank Community outbreak was closely related to samples from the Arcare Maidstone RACF outbreak. Epidemiological links were also established between the two outbreaks, thus supporting the hypothesis that the Arcare Maidstone RACF outbreak seeded this outbreak. These outbreaks were managed separately.

3.3. Outline of public health actions

3.3.1. Timeline of public health actions

Outbreak control measures were enacted to prevent further transmission at the Arcare Maidstone RACF. Measures were enacted in accordance with Victorian guidelines, and included zoning, cohorting, movement restrictions, use of tier 3 PPE, cleaning and disinfection, and vaccinations. A timeline of key public health actions, infection prevention and control breaches and other key events is given in Table 7.

3.3.2. Standing down the outbreak

The outbreak was stood down after meeting the following criteria on 21 June 2021. All enhanced public health actions were subsequently ceased.

Criterion 1—14 days have elapsed since the last infectious staff member was onsite

The last infectious staff member was onsite on Friday 4 June 2021.

Criterion 2—14 days have elapsed since the last infectious resident was onsite

The last infectious resident was onsite on Sunday 6 June 2021.

Criterion 3a—all residents are negative for COVID-19 on day 13 testing since the last potential infectious exposure onsite

As of 20 June 2021, there were 72 residents at the Arcare Maidstone RACF, of whom, 71 were tested from late Friday 18 June until Saturday 19 June (day 13 testing) and were negative. One resident had a saliva test, which returned a negative test on the same day. The OMT deemed the result acceptable for standing down the outbreak.

Chapter 4

Table 7. Timeline of key events and public health actions taken during the Arcare Maidstone residential aged-care facility outbreak (2021).

Date	Event
29 May	First case diagnosed in a staff member
	First outbreak management team (OMT) convened
	Primary close contact (PCC) definition established
	Facility in lockdown
	Cohorting and tier 3 personal protective equipment (PPE) in place for resident interactions
	Donning/doffing stations implemented with infection prevention and control (IPC) nurse and quality support nurses in place
30 May	Vaccination offered for previously unvaccinated residents/staff
	Commonwealth to aid with staffing, and preference expressed for Aspen and agencies before moving staff from acute hospitals
	First terminal clean conducted and additional cleaning contractors sourced
	Onsite testing
	Three additional cases diagnosed (household, resident, and staff)
31 May	Aspen attended for further vaccination of residents (Pfizer)
	Resident case transferred to Epping Private Hospital
	Staff case moved to hotel quarantine unit
	All clinical placements ceased
1 June	Western Public Health Unit (WPHU) received initial lists of primary close contacts (PCC) for contact tracing and surveillance
	IPC Advice and Response (IPCAR) and Royal Melbourne Hospital (RMH) onsite to advise new staff on IPC
2 June	No PPE spotters or IPC leads onsite
	Resident case diagnosed and transferred out to Epping Private Hospital
3 June	Genomics test results received, and outbreak strain identified as the same strain as other Melbourne outbreaks
	Arcare provided raw attestation data to WPHU
	All staff now only at the Arcare Maidstone RACF and no other site
4 June	One household case diagnosed (related to case 1)
6 June	PCC definition amended
	One resident diagnosed and transferred to Epping Private Hospital, and two staff cases (cleaner and RN) diagnosed
	IPCAR review completed; spotter and PPE expertise deficiency noted
7 June	Household case diagnosed (related to case 7)
	Staff case (case 9) transferred to hotel quarantine unit (HQU)
8 June	Two teams of senior nursing staff sourced to work alongside Arcare team
	Daily testing instigated
	WPHU begins efforts to reconcile all attendees onsite since 26 May 2021
	PCC clearance underway by WPHU
9 June	QR code sign-ins via Staff Attestation and Visitor Registration (SAVR) application implemented
	Final IPCAR report submitted; new recommendations on donning and doffing in the carpark, and IPC education
10 June	WPHU expressed the requirement for accurate attestation of all staff entering the site
11 June	Testers not compliant with PPE protocol; escalated to Sonic
	Diagnosis of case related to Arcare case, triggering Kings Park Southbank outbreak
12 June	Staff case diagnosed
13 June	Yesterday's case referred to Household Engagement Programme (HEP)
	Cleaner and household case (case 7 and 10) transferred to HQU
14 June	Barrier wall erected for staff to don PPE
15 June	Repatriation of resident PCC to Arcare
	Daily wastewater testing instigated for 16 June
	No repatriation of cases or PCCs from Epping Private to Arcare
16 June	Day 13 testing of staff
	Diagnosis of case related to Arcare cases, triggering Epping Private Hospital outbreak
17 June	Arcare staff moving from 12-hour to 8-hour shifts
18 June	Household case diagnosed
19 June	Final round of testing (day 13 testing)
	Expert Review Panel (ERP) for residents in Epping Private Hospital
21 June	Outbreak stood down
3 July	Outbreak closed

Criterion 3b—where possible all aged care workers who have attended the facility since the last potential infectious exposure onsite (06/06/2021) have been tested and found to be negative for COVID-19

As of 20 June 2021, 270 people were identified as having attended in any capacity as an aged care worker since 6 June 2021. Of the 270 people:

- 266 (99%) had a negative test since 6 June 2021; four had no recorded test result.
- 238 (88%) had a negative test since 16 June 2021, i.e., in the five days prior to standing down the outbreak.

Negative test results were returned by 200 (74%) on either 19 or 20 June; Arcare and Aspen showed the highest rates of testing on these dates, with close to 80% of employees being tested (Table 8).

Criterion 4—any negative residents remain asymptomatic

On 20 June 2021, two residents on the Jasmine Unit were unwell in the preceding 24 hours. Both were confirmed to be non-COVID-19 cases on 21 June 2021, allowing for the outbreak to be stood down.

Table 8. Breakdown of workers who attended the Arcare Maidstone residential aged-care facility and returned a negative test from 6 June 2021 to 20 June 2021; IPCAR=Infection Prevention and Control Advisory Response, DH=Department of Health (Victoria).

Employer	Total	Number tested since 16 June 2021 (%)	Number tested on 19/20 June 2021 (%)
Arcare	204	183 (90)	161 (79)
Aspen	24	22 (92)	19 (79)
IPCAR & DH	1	0 (0)	0 (0)
Melbourne Health	7	5 (71)	3 (43)
Sonic	22	19 (86)	12 (55)
Western Health	12	9 (75)	5 (42)
Total attendees	270	238 (88)	200 (74)

4. Discussion

An outbreak at the Arcare Maidstone RACF was declared on 29 May 2021. The outbreak period was defined as having begun on 26 May, and as having ended on 3 July. At the beginning, there were 79 residents and 110 staff onsite; 72 residents were left by the end. A total of 406 attendees were accounted for during the entire outbreak period. The outbreak resulted in 12 cases and 245 close contacts. Three were residents, five were staff members and four were household contacts. Genomic analysis confirmed that all cases were of the B.1.617.1 variant.

Public health actions included zoning, cohorting, movement restrictions, use of tier 3 PPE, cleaning and disinfection, and vaccinations. Transmission was attributed to breaches in infection prevention and control measures, all of which were addressed at notice. The outbreak was stood down on 21 June 2021, upon which all enhanced public health actions were ceased. Given the dearth of literature on COVID-19 outbreak investigations in RACFs at the time, we did not conduct a comparison with other similar outbreaks.

4.1. Key learnings

4.1.1. Case definitions

On 6 June 2021, primary close contact (PCC) definitions were broadened mid-outbreak to capture as many at-risk people as possible for surveillance. However, this caused a sudden furlough of many key staff, including PPE spotters and quality support officers at donning and doffing stations, thus leaving gaps in infection prevention and control (IPC). In response, Arcare had to employ approximately 100 new staff to assist at very short notice. In future, PCC definitions should be confirmed early in the outbreak, and attention needs to be paid sooner to the need for replacement staff, to prevent critical staff shortages.

Of note, all staff and resident cases arose within 14 days of initial exposure. This outbreak may therefore have been characterised by a single exposure event—in which case, all the evolving outbreak measures, such as changing the contact definitions, were unnecessary.

4.1.2. Case finding

This outbreak was the first RACF outbreak in Victoria to have robust denominator data for calculating attack rates—a testament to the investigation's thorough case finding and surveillance. However, this was not without its challenges.

At the time, Directions required RACFs to record all attendees onsite. In this outbreak, all agencies were required to supply rosters and sign-in sheets to WPHU every day. At the beginning, WPHU had to manually digitise the documents, as many were handwritten.

Compiling these logs everyday proved time-consuming, particularly for Arcare Maidstone and WPHU, but was the only way to accurately monitor attendees.

The SAVR app was implemented mid-outbreak to help automate and digitise the surveillance process, but at best, saw 30% compliance on any given day. The low compliance meant that SAVR could not be used for surveillance, and hence why paper-based logs were relied upon throughout the outbreak. The use of QR codes has clear advantages over logs in providing a single source of information. The electronic nature of SAVR also makes it less vulnerable to being destroyed or made unavailable compared to other paper-based alternatives. QR codes were mandated for all RACFs soon after this outbreak, and with high compliance, can be an effective and efficient tool for outbreak management and control.

4.1.3. Infection Prevention and Control

Several IPC approaches proved effective throughout the outbreak. Positive residents were transferred offsite and cared for in hospital, so that staff working onsite had less risk of contracting COVID-19 and of being furloughed. Although this proved beneficial at mitigating transmission at the RACF, it did however trigger an outbreak at one of the participating healthcare facilities. Future transfers should therefore be assessed on a case-by-case basis with consideration for the risks of triggering another outbreak.

IPC issues were addressed often, e.g., mask testing and fitting performed by Western Health and Melbourne Health. However, a formal review of IPC practices at the investigation debrief determined that IPC breaches at the beginning of the outbreak were likely responsible for continued transmission among residents and staff. These early breaches may be attributed to conflicting advice at the initial OMTs, particularly around donning and doffing practices. These issues were discussed at a “lessons learnt” session after the outbreak was stood down. Future IPC advice should be consistent and documented to establish clarity and accountability to mitigate breaches.

4.1.4. Vaccinations

The RACF relied on self-reports to gauge people’s vaccination statuses, given there were issues with accessing the Australian Immunisation Records throughout the outbreak period. Despite the inaccuracies inherent to self-reports, this was the best available evidence for informing the many vaccination campaigns. Unfortunately, this information was unavailable at the time of writing and has not been captured in this report.

4.1.5. Communication

Several issues with communication were identified during the outbreak. At one point, Senate estimates included information about the Arcare Maidstone RACF outbreak, and the public was notified of positive cases before Arcare was. A public apology was issued by government officials and should not happen again.

Additionally, the OMT meeting times changed frequently throughout the outbreak period, which affected Arcare's ability to attend. There was also contention around who could attend the OMTs. At times, the OMT actions and deadlines were also impractical and confusing. For example, some OMT actions were sent after 5 pm, but required that actions be met by 5 pm. Future OMTs should be consistent, and minutes should be sent shortly after the close of the meeting, so that all parties are aware of what actions they are responsible for and when.

4.2. Conclusions

The Arcare Maidstone RACF outbreak experienced relatively low morbidity and mortality for an RACF—a testament to the rapid response. Transmission likely occurred due to breaches to infection prevention and control measures—e.g., a lack of PPE spotters and low compliance with PPE requirements—which were addressed at notice. The facility eventually achieved zero transmission and was successfully stood down. The lessons learnt from this outbreak investigation should help inform future COVID-19 outbreaks in RACFs as COVID-19 remains a considerable burden globally.

5. References

1. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol* [Internet]. 19(3):141-54. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwtV3Pa9swFBZbx2CXsnW_0m6td9lgQ2n0w5Z02CGkLS2UFNKk7CZkWYYd6pQmOfS_75MIO0566Q67CCNsy7zv8fQ9S-8TQoz2B3grJjhpOeeWmFLawpYmo1zSXOa8Elo4bjbPhmmIANd9_xV46APofSHtP4DfvhQ64BpcAFpwAmif5QajLUFmX6MynFzj0fwG03r
2. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. *Acta Biomed* [Internet]. 2020 Mar 19;91(1):157-60. Available from: <https://pubmed.ncbi.nlm.nih.gov/32191675>
3. Quesada JA, López-Pineda A, Gil-Guillén VF, Arriero-Marín JM, Gutiérrez F, Carratala-Munuera C. Incubation period of COVID-19: A systematic review and meta-analysis. *Rev Clin Esp* [Internet]. 2020/11/28. 2021 Feb;221(2):109-17. Available from: <https://pubmed.ncbi.nlm.nih.gov/33998486>
4. Meyerowitz-Katz G, Merone L. A systematic review and meta-analysis of published research data on COVID-19 infection fatality rates. *International Journal of Infectious Diseases* [Internet]. 2020;101:138-48. Available from: <https://www.sciencedirect.com/science/article/pii/S1201971220321809>
5. Giovanetti M, Benedetti F, Campisi G, Ciccozzi A, Fabris S, Ceccarelli G, et al. Evolution patterns of SARS-CoV-2: Snapshot on its genome variants. *Biochem Biophys Res Commun*. 2021 Jan;538:88-91.
6. Planas D, Veyer D, Baidaliuk A, Staropoli I, Guivel-Benhassine F, Rajah MM, et al. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. *Nature*. 2021 Aug;596(7871):276-80.
7. Faria NR, Mellan TA, Whittaker C, Claro IM, Candido D da S, Mishra S, et al. Genomics and epidemiology of a novel SARS-CoV-2 lineage in Manaus, Brazil. *medRxiv* [Internet]. 2021 Mar 3;2021.02.26.21252554. Available from: <https://pubmed.ncbi.nlm.nih.gov/33688664>
8. Tegally H, Wilkinson E, Giovanetti M, Iranzadeh A, Fonseca V, Giandhari J, et al. Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa. *medRxiv* [Internet]. 2020 Jan 1;2020.12.21.20248640. Available from: <http://medrxiv.org/content/early/2020/12/22/2020.12.21.20248640.abstract>

9. Davies N, Abbott S, Barnard R, Jarvis C, Kucharski A, Munday J, et al. Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England [Internet]. medRxiv; 2020. Available from: <http://europepmc.org/abstract/PPR/PPR258079>
10. Noorimotlagh Z, Jaafarzadeh N, Martínez SS, Mirzaee SA. A systematic review of possible airborne transmission of the COVID-19 virus (SARS-CoV-2) in the indoor air environment. Environ Res [Internet]. 2020/12/10. 2021 Feb;193:110612. Available from: <https://pubmed.ncbi.nlm.nih.gov/33309820>
11. Meyerowitz EA, Richterman A, Gandhi RT, Sax PE. Transmission of SARS-CoV-2: A Review of Viral, Host, and Environmental Factors. Ann Intern Med [Internet]. 2020/09/17. 2021 Jan;174(1):69-79. Available from: <https://pubmed.ncbi.nlm.nih.gov/32941052>
12. Bazant MZ, Bush JWM. A guideline to limit indoor airborne transmission of COVID-19. Proceedings of the National Academy of Sciences [Internet]. 2021 Apr 27;118(17):e2018995118. Available from: <http://www.pnas.org/content/118/17/e2018995118.abstract>
13. Kotlyar AM, Grechukhina O, Chen A, Popkhadze S, Grimshaw A, Tal O, et al. Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis. Am J Obstet Gynecol [Internet]. 2020/07/31. 2021 Jan;224(1):35-53.e3. Available from: <https://pubmed.ncbi.nlm.nih.gov/32739398>
14. Shuai L, Zhong G, Yuan Q, Wen Z, Wang C, He X, et al. Replication, pathogenicity, and transmission of SARS-CoV-2 in minks. Natl Sci Rev [Internet]. 2021 Mar 1;8(3). Available from: <https://doi.org/10.1093/nsr/nwaa291>
15. To KKW, Tsang OTY, Leung WS, Tam AR, Wu TC, Lung DC, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis [Internet]. 2020 May 1;20(5):565-74. Available from: [https://doi.org/10.1016/S1473-3099\(20\)30196-1](https://doi.org/10.1016/S1473-3099(20)30196-1)
16. Meng XJ, Liang TJ. SARS-CoV-2 Infection in the Gastrointestinal Tract: Fecal-Oral Route of Transmission for COVID-19? Gastroenterology [Internet]. 2021/01/07. 2021 Apr;160(5):1467-9. Available from: <https://pubmed.ncbi.nlm.nih.gov/33422479>
17. Li D, Jin M, Bao P, Zhao W, Zhang S. Clinical Characteristics and Results of Semen Tests Among Men With Coronavirus Disease 2019. JAMA Netw Open [Internet]. 2020 May 7;3(5):e208292-e208292. Available from: <https://doi.org/10.1001/jamanetworkopen.2020.8292>

18. Chang L, Zhao L, Gong H, Wang L, Wang L. Severe Acute Respiratory Syndrome Coronavirus 2 RNA Detected in Blood Donations. *Emerg Infect Dis* [Internet]. 2020/06/21. 2020 Jul;26(7):1631-3. Available from: <https://pubmed.ncbi.nlm.nih.gov/32243255>
19. Althouse BM, Wenger EA, Miller JC, Scarpino S v, Allard A, Hébert-Dufresne L, et al. Superspreading events in the transmission dynamics of SARS-CoV-2: Opportunities for interventions and control. *PLoS Biol* [Internet]. 2020 Nov 12;18(11):e3000897. Available from: <https://doi.org/10.1371/journal.pbio.3000897>
20. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ* [Internet]. 2020 Feb 19;368:m606. Available from: <http://www.bmj.com/content/368/bmj.m606.abstract>
21. Yüce M, Filiztekin E, Özkaya KG. COVID-19 diagnosis -A review of current methods. *Biosens Bioelectron* [Internet]. 2020/10/24. 2021 Jan 15;172:112752. Available from: <https://pubmed.ncbi.nlm.nih.gov/33126180>
22. Böger B, Fachi MM, Vilhena RO, Cobre AF, Tonin FS, Pontarolo R. Systematic review with meta-analysis of the accuracy of diagnostic tests for COVID-19. *Am J Infect Control* [Internet]. 2020/07/10. 2021 Jan;49(1):21-9. Available from: <https://pubmed.ncbi.nlm.nih.gov/32659413>
23. Butler-Laporte G, Lawandi A, Schiller I, Yao M, Dendukuri N, McDonald EG, et al. Comparison of Saliva and Nasopharyngeal Swab Nucleic Acid Amplification Testing for Detection of SARS-CoV-2: A Systematic Review and Meta-analysis. *JAMA Intern Med* [Internet]. 2021 Mar 1;181(3):353-60. Available from: <https://doi.org/10.1001/jamainternmed.2020.8876>
24. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *New England Journal of Medicine* [Internet]. 2020 Feb 19;382(12):1177-9. Available from: <https://doi.org/10.1056/NEJMc2001737>
25. Grant BD, Anderson CE, Williford JR, Alonzo LF, Glukhova VA, Boyle DS, et al. SARS-CoV-2 Coronavirus Nucleocapsid Antigen-Detecting Half-Strip Lateral Flow Assay Toward the Development of Point of Care Tests Using Commercially Available Reagents. *Anal Chem* [Internet]. 2020/08/05. 2020 Aug 18;92(16):11305-9. Available from: <https://pubmed.ncbi.nlm.nih.gov/32605363>

26. Yi-Wei T, E. SJ, H. PD, W. SC, J. MA. Laboratory Diagnosis of COVID-19: Current Issues and Challenges. *J Clin Microbiol* [Internet]. 2021 Jun 13;58(6):e00512-20. Available from: <https://doi.org/10.1128/JCM.00512-20>
27. Burki TK. Testing for COVID-19. *Lancet Respir Med* [Internet]. 2020/05/29. 2020 Jul;8(7):e63-4. Available from: <https://pubmed.ncbi.nlm.nih.gov/32479792>
28. Chen H, Ai L, Lu H, Li H. Clinical and imaging features of COVID-19. *Radiol Infect Dis* [Internet]. 2020/04/27. 2020 Jun;7(2):43-50. Available from: <https://pubmed.ncbi.nlm.nih.gov/32346593>
29. Shang L, Lye DC, Cao B. Contemporary narrative review of treatment options for COVID-19. *Respirology* [Internet]. 2021 Aug 1;26(8):745-67. Available from: <https://doi.org/10.1111/resp.14106>
30. Coopersmith CM, Antonelli M, Bauer SR, Deutschman CS, Evans LE, Ferrer R, et al. The Surviving Sepsis Campaign: Research Priorities for Coronavirus Disease 2019 in Critical Illness. *Crit Care Med*. 2021 Apr;49(4):598-622.
31. Yan ZP, Yang M, Lai CL. COVID-19 Vaccines: A Review of the Safety and Efficacy of Current Clinical Trials. *Pharmaceuticals (Basel)* [Internet]. 2021 Apr 25;14(5):406. Available from: <https://pubmed.ncbi.nlm.nih.gov/33923054>
32. Day M. Covid-19: four fifths of cases are asymptomatic, China figures indicate. *BMJ*. 2020 Apr;369:m1375.
33. Umakanthan S, Chattu VK, Ranade A v, Das D, Basavarajegowda A, Bukelo M. A rapid review of recent advances in diagnosis, treatment and vaccination for COVID-19. *AIMS Public Health* [Internet]. 2021 Feb 1;8(1):137-53. Available from: <https://pubmed.ncbi.nlm.nih.gov/33575413>
34. Li Y, Tenchov R, Smoot J, Liu C, Watkins S, Zhou Q. A Comprehensive Review of the Global Efforts on COVID-19 Vaccine Development. *ACS Cent Sci* [Internet]. 2021/03/29. 2021 Apr 28;7(4):512-33. Available from: <https://pubmed.ncbi.nlm.nih.gov/34056083>
35. Cousins S. Experts criticise Australia's aged care failings over COVID-19. *Lancet* [Internet]. 2020/10/22. 2020;396(10259):1322-3. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7581404/>

Chapter 5: COVID-19 vaccine hesitancy among racial and ethnic minorities and foreign-born populations in high-income English-speaking countries: A mixed-methods systematic review

Prologue

This chapter meets the MAE minor competency to complete a “literature review”. This chapter details a systematic review on the prevalence of, and reasons for, COVID-19 vaccine hesitancy among racial and ethnic minorities in high-income English-speaking countries. These populations can experience lower access and acceptance of COVID-19 vaccines, despite facing a disproportionate burden of COVID-19. Addressing hesitancy among such populations can therefore improve health outcomes, promote health equity, and help countries reach and exceed their vaccination targets, which provided the impetus for this project. Through our systematic review, we found that hesitancy could be attributed to a mistrust in institutions, health concerns, and a lack of access, though these were not exclusive to minorities. That said, certain groups did report greater mistrust in governments, and greater concerns about vaccine safety and effectiveness, as drivers of hesitancy. My findings were subsequently used to inform the Department’s vaccine outreach initiatives.

This project was conceptualised through a mutual interest in migrant health between me and my academic supervisor, Dr. Davoud Pourmarzi. As a migrant himself, Davoud is intimately acquainted with the structural barriers that can impinge a migrant’s access to healthcare and health information. I have also witnessed such inequities firsthand, having come from a family of migrants and refugees. This topic therefore presented an excellent opportunity for which to complete this MAE competency.

My role

For this project, I formulated the research question, registered the protocol, defined the inclusion and exclusion criteria, conducted the literature search, screened for eligible studies, extracted the data, evaluated the risk of bias, and interpreted and discussed the results. Our findings were drafted into a scientific manuscript and submitted to *BMC Globalization and Health* for peer-review on 4 August 2022; the contents of this manuscript form the body of this chapter. This manuscript meets the MAE minor competency on preparing a “peer-reviewed publication”.

Lessons learnt

As my first ever systematic review, this experience came with many lessons learnt. Firstly, systematic reviews are a mammoth task! The PRISMA guidelines were incredibly useful for managing the project pipeline, and for breaking it down into manageable bite-sized tasks.

Defining appropriate inclusion criteria was essential for ensuring the project could be completed within the confines of the MAE, without compromising the review's quality. We had to change criteria several times, given the surplus of papers retrieved with the initial searches. Upon refinement, the exercise became more feasible. I also developed a better understanding of how using Boolean operators, quotation marks and database filters in search strategies can yield papers that are most relevant to the research question.

Screening and data extraction can be timely and requires excellent document version control. I often felt disheartened by the long arduous process, but I am lucky to have Dr. Davoud Pourmarzi as a supervisor, as he was incredibly understanding and supportive throughout the project. I also discovered how Rayyan (a free web-tool) can be useful for screening papers, while Excel can be useful for data extraction and synthesis.

This project also gave me a newfound appreciation for qualitative research, which I had little prior experience with. Qualitative research can provide a wealth of knowledge that cannot be obtained otherwise. Given this, I hope to incorporate more qualitative methods—including qualitative systematic reviews—in my future public health practice.

Public health impacts

By systematically reviewing the current literature, this review provides insights into the vaccine attitudes that are unique to, or more prevalent, amongst racial and ethnic minorities and foreign-born populations. Given the higher disease burden experienced by minorities, the Department required urgent solutions and strategies to improve their vaccine uptake, and in turn, attenuate transmission in the community. Our findings support the use of clear, accessible, and tailored information campaigns led by trusted and collaborative healthcare and community networks. Our findings were shared with the Department to help inform targeted outreach initiatives and policy interventions, to improve health outcomes, promote health equity, and help the Government reach and exceed its vaccination targets. Our findings may have implications throughout the entire COVID-19 vaccination campaign course—including the administration of subsequent boosters—and may remain salient for future vaccination campaigns.

Abstract

Background

Vaccine acceptance is crucial for attenuating COVID-19 disease and transmission, and associated costs. Racial and ethnic minorities and foreign-born populations in high-income English-speaking countries may experience lower access to, and acceptance of, vaccines despite facing a disproportionate burden of COVID-19. Addressing hesitancy among such populations can therefore improve health outcomes, promote health equity, and help countries reach and exceed their vaccination targets. With this, we conducted a mixed-methods systematic review to synthesise the current evidence on the prevalence of, and reasons for, COVID-19 vaccine hesitancy among racial and ethnic minorities and foreign-born populations in high-income English-speaking countries.

Methods

The search was conducted on 22 September 2021. Quantitative and qualitative studies were sought from Scopus, PsycInfo and PubMed, and included if they provided analysis on the study population. Inclusion was limited to papers published in English and after 2019. The quantitative component was further limited to papers with data collection during or after the US Food and Drug Administration approved the first COVID-19 vaccine on 11 December 2020. Methodological quality was assessed using Joanne Briggs Institute tools. Quantitative findings were synthesised using narrative review, and qualitative findings were meta-aggregated and meta-synthesised.

Results

Of the 537 papers screened, 22 quantitative and five qualitative studies were included. Nineteen studies were from the USA and others were from the UK and Canada. Compared to White populations, Black populations exhibited higher hesitancy. This was true for other groups, but to a lesser extent. Hesitancy can be attributed to a mistrust in institutions, health concerns, and a lack of access; these reasons were not exclusive to minorities. Black populations reported greater mistrust in governments, and greater concerns about vaccine safety and effectiveness, as drivers of hesitancy.

Conclusions

By systematically synthesising the current literature, this study provides insights that may help inform policy interventions to improve vaccine uptake among priority populations. Our findings have implications throughout the entire COVID-19 vaccination campaign course—including the administration of boosters—and will likely remain relevant beyond COVID-19.

1. Introduction

Vaccine acceptance is crucial for attenuating COVID-19 disease and transmission, and associated costs (1). Vaccination efforts are impeded by vaccine hesitancy, defined as the “delay in acceptance or refusal of vaccination” (2). Hesitancy exists on a continuum; strategies to engage hesitant populations must therefore be nuanced to meet diverse needs (2). Hesitant individuals are more likely to exhibit caution than outright rejection (3,4), which suggests opportunities to influence behaviour and promote uptake (5).

Racial and ethnic minorities and foreign-born populations in high-income English-speaking countries may experience lower access to, and acceptance of, COVID-19 vaccines, despite facing a disproportionate burden of COVID-19 (6,7). Addressing hesitancy can therefore improve health outcomes, promote health equity, and help countries reach and exceed their vaccination targets.

Racial and ethnic minorities encompass a diverse group. In general, race refers to categories of people divided by ancestry and physicality, while ethnicity refers to a person’s cultural, linguistic, customary, and religious identities (8). Both terms are shaped by geographical, cultural, and socio-political forces, and continue to evolve (8,9). These constructs may be useful for studying disparities in health and healthcare (9).

Foreign-born populations include migrants, refugees, and asylum seekers. Migrants are a heterogeneous group with no formal definition; they generally refer to persons moving within or between countries for economic and social reasons (10). Refugees are formally defined in the 1951 Refugee Convention and includes people residing outside their countries of nationality owing to fears of persecution, while asylum seekers are those awaiting decisions on their applications for refugee status (10).

Past reviews have described vaccine attitudes across various populations (11-15). Hesitancy can be ascribed to a mistrust in institutions, concerns around vaccine safety and effectiveness, and a lack of access to information and vaccination points (11,12).

Understanding the attitudes that are unique to, or more prevalent among, priority populations can help inform targeted policy solutions to improve uptake. This systematic review therefore aimed to synthesise the quantitative and qualitative evidence on the prevalence of—and reasons for—COVID-19 vaccine hesitancy among racial and ethnic minorities and foreign-born populations in high-income English-speaking countries.

2. Methods

The protocol was registered on PROSPERO (ref: PROSPERO 2021 CRD42021278450).

2.1. Inclusion criteria

We included quantitative and qualitative studies conducted in countries where English is spoken as a first language by most of the population; these include Australia, Canada, Ireland, New Zealand, Singapore, the United Kingdom (UK) and the United States of America (USA). Inclusion was restricted to studies published in peer-reviewed journals and preprints. Papers were included if they provided analysis, or sub-group analysis, on those who matched the study population. We only included papers written in English and published after 2019. The quantitative component was further restricted to papers with data collection during or after the first COVID-19 vaccine was approved by the USA Food and Drug Administration (FDA) on 11 December 2020.

2.2. Search strategy

The search was conducted on 22 September 2021. Published studies were sought from Scopus, PsycInfo and PubMed. The search strategy in PubMed was as follows:

(COVID-19 OR SARS-CoV-2 OR coronavirus) AND (vaccin) AND (accep* OR uptake OR hesitan* OR attitude OR inten* OR willin*) AND (race OR racial OR ethni* OR migran* OR migrat* OR refuge* OR asylum OR minorit* OR colour OR color OR "language other than")*

2.3. Assessment of methodological quality

Methodological quality was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal tools by one author and independently reviewed by a second author. Disagreements were resolved through discussion until a consensus was reached.

2.4. Data extraction

Quantitative outcomes for vaccine hesitancy (prevalence of, and reasons for) were extracted. Outcomes for vaccine acceptance were used instead where measures of hesitancy were absent. For the qualitative component, the reasons for hesitancy and their supporting quotes were extracted. Their credibility was established by assessing the congruency between the supporting data and the authors' analytic interpretations using the following scale (16):

- Unequivocal: findings accompanied by an illustration that is beyond reasonable doubt and therefore not open to challenge.

- Equivocal: findings accompanied by an illustration lacking clear association with it and therefore open to challenge.
- Unsupported: findings not supported by the data.

The extracted data were reviewed independently by two of the authors, and differences were discussed until a consensus was reached.

2.5. Data synthesis

Data synthesis methods were adapted from the JBI convergent segregated approach, which maintains a clear distinction between the quantitative and qualitative evidence. Quantitative findings were synthesised in narrative form. Qualitative findings and their supporting quotes were meta-aggregated into categories based on their similarity; these were then further synthesised (17).

3. Results

3.1. Search results

Among 760 identified titles, 537 were screened, of which, 22 quantitative studies and five qualitative studies were included for data extraction (Figure 1).

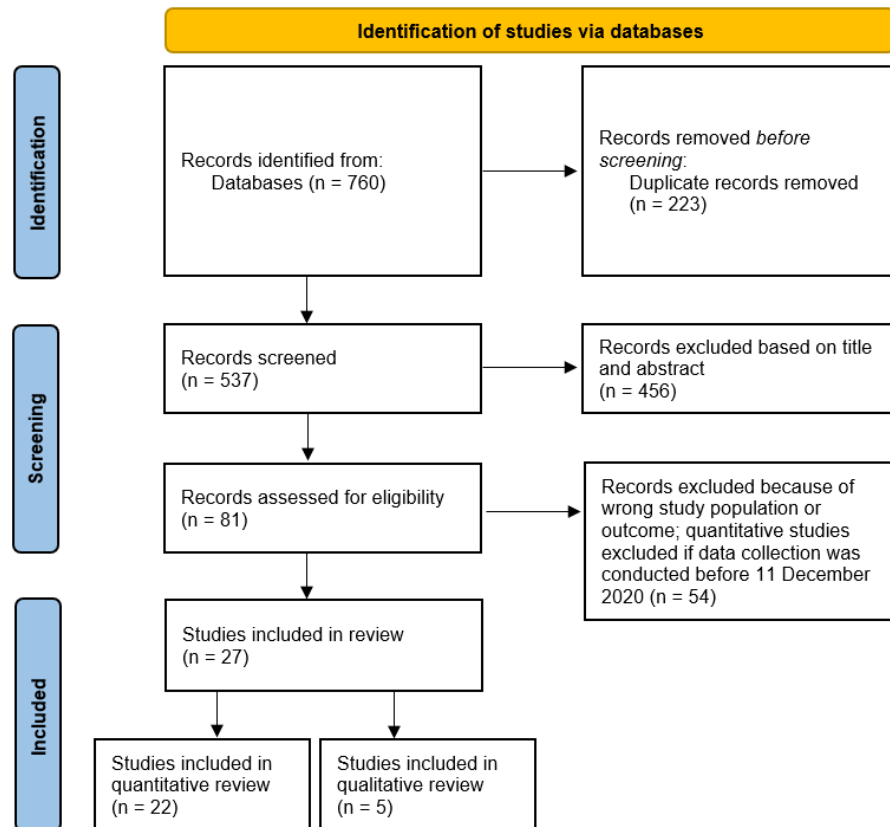


Figure 1. PRISMA flow diagram of search and study selection process.

3.2. Methodological quality appraisal

3.2.1. Quantitative studies

Among the 22 quantitative studies, one was a preprint (18); the rest were peer-reviewed articles. All were cross-sectional studies: two were nested within cohort studies (19,20), and one was incorrectly identified as a cohort study (18). One study did not clearly define their inclusion criteria (18); confounders were not identified in two studies (5,21); all other criteria were met by all studies.

3.2.2. Qualitative studies

Among the five qualitative studies, one was a preprint (22) and all others were published peer-reviewed articles. One paper reported the researchers' cultural or theoretical positions (23). All other criteria were met by all studies (22-26).

3.3. Characteristics of included studies

3.3.1. Quantitative studies

Data collection ranged from March 2020 to April 2021. Nineteen studies were from the USA, one was from the UK (27), one was from both the UK and the USA (18), and one was from Canada (28). One paper included adult refugees who recently arrived in the USA (29); another paper included adults who self-identified as Asian American or Pacific Islander in the USA (30); and one included members of the 100 Black Men of Augusta, a local chapter of a national non-profit community organisation in the USA (20). One paper had an unspecified population (18). All other papers included the general adult population of their study settings. All studies retrieved their samples using convenience and snowball sampling (Table 1). See section 7 for tables.

3.3.2. Qualitative studies

Data collection spanned June 2020 to March 2021. Three studies were from the USA and two were from the UK (Table 2). In the USA-based studies, one included Hispanic/Latinx adults in the East Coachella Valley of the farm-working community along the Salton Sea (22). One study included Black or Latinx individuals in New Jersey (25), while another study recruited Black barbershop owners in West Philadelphia (26). The two UK-based papers included migrants older than 18 years, and who resided in the UK for less than 10 years (23,24). One was further restricted to those with precarious immigration statuses (24). All studies retrieved their samples using convenience or snowball sampling (Table 2).

3.4. Quantitative synthesis

3.4.1. Vaccine hesitancy

Fourteen studies reported outcomes on vaccine hesitancy. Ten studies reported the prevalence (3,5,18,20,21,28,29,31-33). Six papers reported prevalence ratios or odds ratios (3,4,18,31,32,34); all used White populations as the reference group, except one (34). All studies used a single question to measure hesitancy. Of the fourteen studies, seven defined "hesitancy" as those who probably or definitely would not get vaccinated

(3,4,20,21,28,34,35); seven studies additionally included those who were unsure (5,18,27,29,31-33) (Table 1).

In studies reporting hesitancy in the USA, prevalence among White populations ranged from 7.4% to 62.7%, and from 27.8% to 74.0% among Black populations, 15.6% to 59.5% among Hispanic/Latinx population, 6.5% to 36.0% among Asians, and 16.6% to 68.0% among those who identified as multiracial or other (3,5,18,21,31-33). In one study on racial and ethnic minority men—predominantly Black men—15.6% were hesitant (20) (Table 1).

In the USA, Black populations had 1.2 (1.0-1.5) to 3.3 (2.2-5.0) times the odds of hesitancy than White populations (3,4,18,31). Odds ratios ranged from 0.9 (0.7-1.2) to 2.1 (1.2-3.6) for Latinx/Hispanic populations (3,18,31), 0.3 (0.3-0.4) to 1.3 (1.2-1.5) for Asians, and 1.5 (1.4-1.6) to 3.6 (1.4-9.1) for multiracial or other populations, relative to White populations (3,4,18). One paper reported that Hispanic/Latinx ethnicities had 0.6 (0.5-0.6) times the odds of hesitancy compared to non-Hispanic/Latinx ethnicities (4) (Table 1).

In one UK study, prevalence was 5.1% among white populations, 18.4% among Black populations, 9.8% among South Asians, 11.1% among Middle Eastern and East Asians, and 9.4% among multiracial or other populations (18). Compared to White populations, Black populations had 2.8 (2.7-3.0) times the odds of hesitancy. Odds ratios were 1.7 (1.6-1.8) for South Asians, 1.8 (1.7-2.0) for Middle Eastern and East Asians, and 1.5 (1.4-1.6) for multiracial or other populations, relative to White populations (18) (Table 1).

A Canadian study showed that hesitancy was higher among visible minorities (12.3%)—defined as “persons, other than Aboriginal peoples, who are non-Caucasian in race or non-white in colour”—than non-minorities (8.8%) ($P<0.0001$). Hesitancy was also higher among Indigenous (14.6%) than non-Indigenous populations (8.7%) ($P<0.0001$) (28) (Table 1).

3.4.2. Vaccine acceptance

Among the eight studies that did not report vaccine hesitancy, seven reported results for vaccine acceptance, of which, five reported the prevalence or odds ratios in the USA (19,36-39). All seven papers measured the outcome with a single question; acceptance was defined as probable or definite intent and excluded those who were unsure (19,36-41) (Table 1).

Vaccine acceptance in the USA ranged from 59.6% to 73.5% among White populations, 38.7% to 65.0% among Black populations, 55.3% to 71.9% among Hispanic/Latinx populations, and 73% to 91.5% among Asians (36-39). Compared to White populations, the odds ratio of acceptance ranged from 0.3 (0.2-0.4) to 2.0 (1.4-3.0) for Black populations, 0.6 (0.4-0.7) to 1.5 (1.0-2.3) for Hispanic/Latinx populations, and 0.6 (0.3-1.1) to 1.2 (1.2-1.2) for Asians (19,36-38) (Table 1).

3.4.3. Reasons for vaccine hesitancy

Eight studies reported reasons for vaccine hesitancy in the USA (3,4,21,29,30,35,40,41); reasons included a mistrust in vaccines and institutions, concerns about vaccine effectiveness, concerns about their safety and side effects, among other reasons (Table 3).

Mistrust in vaccines and institutions

Compared to White populations, Black and other racial/ethnic groups reported more mistrust towards COVID-19 vaccines ($P<0.05$) (21), and experienced more circumspection and low confidence in vaccines ($P<0.05$) (35). Black and Hispanic/Latinx populations were also more likely than White populations to report concerns that vaccines were rushed; they also preferred to wait to see how the vaccines worked first ($P<0.05$) (3,21). Fear of the vaccines was also lower among White populations than minority populations ($P<0.05$) (40) (Table 3).

Mistrust in the government to develop COVID-19 vaccines was also higher among non-Hispanic Black populations than non-Hispanic White populations ($P<0.05$) (3), while mistrust in pharmaceutical companies was not statistically different between groups ($P>0.05$) (3). One study showed that mistrust in vaccines, government and the medical establishment was lowest among Asians (4) (Table 3).

Concerns about vaccine safety and side effects

Compared to White populations, Black populations reported greater concerns about vaccine safety and side effects and were more likely to believe that they could cause COVID-19 or were more harmful than COVID-19 ($P<0.05$) (21,41). Some studies reported little evidence for a difference in concerns about safety across groups ($P>0.05$) (3,41). Among refugees, concerns about side effects were the most cited reason for hesitancy (29) (Table 3).

Concerns about vaccine effectiveness

Compared to White populations, Black populations were more likely to report concerns about vaccine effectiveness ($P<0.05$); the same study observed little evidence for a difference between White, Hispanic/Latinx and Asian groups ($P>0.05$) (21). Another study observed little evidence for a difference across all groups for such concerns ($P>0.05$) (3) (Table 3).

3.5. Qualitative synthesis

Of the five qualitative studies, two used focus groups, two used semi-structured interviews, and one used both for data collection. All studies analysed data using thematic analysis. Thirty-six findings were extracted; 33 were unequivocal and the rest were equivocal. Hesitancy was attributed to a mistrust in the government, mistrust in medical science,

concerns about the safety and effectiveness of COVID-19 vaccines, personal philosophies on health, social norms, lack of access to information or access to conflicting information, and a lack of financial or geographical access (Table 4).

3.5.1. Mistrust in the government

Among Black and Hispanic/Latinx populations in the USA, vaccine hesitancy was attributed to the political environment (26). There were fears the government had implanted another deadly virus, or a microchip to monitor and control behaviour (22). For those with precarious immigration statuses in the UK, there were fears of being the last to receive the vaccine (23), or of being excluded completely (24). One paper described fears that immigration statuses would be shared with the Home Office (24). There were also fears of being charged, and of immigration checks at access points (24) (Table 4).

3.5.2. Mistrust in medical science

Black and Hispanic/Latinx populations in the USA reported uneasiness about the short timelines for testing; some felt disbelief a vaccine could be developed so rapidly (25,26). Participants also felt they were under-represented in clinical trials (23). There were concerns they were being used for medical experiments, and some preferred to wait to see how others would respond first (23,25). Some participants also cited historical medical experimentation and mistreatment towards the Black community (25,26), and unethical research practices on prison populations, as reasons for hesitancy (26). Beliefs that COVID-19 was a hoax also deterred vaccine uptake (23) (Table 4).

3.5.3. Concerns about the safety and effectiveness of COVID-19 vaccines

Hesitancy was attributed to concerns about the effectiveness of vaccines for Black and Hispanic/Latinx populations in the USA (26). Some viewed COVID-19 vaccines as unsafe and harmful (22,23), with some describing concerns about the short- and long-term repercussions (25). There were also concerns about how they could affect fertility (25). Hesitant attitudes were also attributed to beliefs that existing medications, like hydroxychloroquine, were more appropriate, though this was equivocal (26) (Table 4).

3.5.4. Personal philosophies on health

Among minorities and migrants in the USA and UK, complacency towards the severity and duration of the COVID-19 pandemic contributed to hesitancy (26), as did the idea that COVID-19 was less likely to affect certain groups (23). Some participants preferred to improve their health using home remedies to protect against COVID-19 (23,26) (Table 4).

3.5.5. Social norms

Black Americans reported that their social networks contributed to hesitancy (26). Recommendations to take the vaccine from famous individuals and role models of similar cultural backgrounds would not contribute to vaccine uptake among some participants (26). Those considering vaccinations were considered foolish, less educated, or unable to make unbiased decisions, though this finding was equivocal (26) (Table 4).

3.5.6. Lack of access to information or access to conflicting information

The inaccessibility of sufficiently understandable materials among minorities and migrants in the USA and UK contributed to hesitancy (24). Some participants sought information in their own languages (24), and information specific to their communities (25). Some expressed an inability to distinguish real news from fake news (24) (Table 4).

3.5.7. Lack of financial or geographical access

Financial or geographical access can also affect one's attitude towards vaccination. In the UK, the potential costs of the vaccines contributed to hesitancy among migrants (24). There were also preferences for settings requiring minimal travel (24) (Table 4).

3.6. Synthesised findings

Compared to White populations, Black populations exhibited higher hesitancy, while Asians exhibited lower hesitancy. Hesitancy was attributed to a mistrust in the government, mistrust in medical science, concerns about the safety and effectiveness of the vaccines, personal philosophies on health, social norms, lack of access to information or access to conflicting information, and a lack of financial or geographical access; however, these were not exclusive to minorities. That said, Black populations did report greater mistrust in governments, and greater concerns about vaccine safety and effectiveness.

4. Discussion

This review provides insights on the prevalence of, and reasons for, COVID-19 vaccine hesitancy among racial and ethnic minorities and foreign-born populations in high-income English-speaking countries. Compared to White populations, Black populations—and to a lesser extent, other groups—were more likely to be hesitant. These findings are not unique to COVID-19 and have also been observed for HPV, pneumococcal and influenza vaccines (42-44).

While mistrust exists across sociodemographic, geographic, and political contexts (11,12), it is consistently higher among Black populations. Black Americans, for example, are more likely to mistrust the government's motives—sentiments that likely stem from historical inequities (45). Black Americans also exhibit greater mistrust in health services and medical science, which may be rooted in past exploitation by physicians and researchers, such as the syphilis study at Tuskegee, where hundreds of Black men were withheld treatment (22,23). Institutions should therefore acknowledge and address how racist structures and interactions have fostered mistrust among Black Americans (39,46). For minorities and migrants more broadly, addressing anti-immigration and xenophobic sentiments may also improve trust and reduce hesitancy (22).

Some minorities are also more likely to express concerns about the safety and effectiveness of COVID-19 vaccines. Studies show that a provider's recommendation is a key driving factor for vaccine uptake (48,49), and racial and ethnic minorities are more accepting of healthcare regulations when engaged by providers of the same cultural background (50). Diverse healthcare spokespeople are therefore key in vaccination campaigns (21).

Uptake may also be improved by debunking notions that COVID-19 is not severe, or less likely to affect certain races and ethnicities (23,51). Demystifying notions around the effectiveness of home remedies and alternative options may also prove fruitful.

Social norms as a reason for hesitancy was highlighted in the current review, but not in other reviews of broader populations (11,12). Therefore, this finding may be unique to—or more prevalent among—some minority communities. Given the influence of social networks on vaccine attitudes, uptake among individuals may have a ripple effect on their peers (26). Engaging minorities and migrant groups in co-designing interventions to facilitate uptake is therefore crucial (23). Initiatives should be expedited through trusted networks, such as religious leaders, teachers, nursery workers and advice workers (47).

Poor access to information is a key driver of hesitancy, and can be ameliorated with clear, honest, and responsive information that is culturally and religiously sensitive (52). Publishing

in various languages can better engage linguistically diverse groups (23). Accessibility may be improved through online platforms that translate resources and provide language-specific advice. For individuals who lack access and skills to use technology, multiple communication channels should be considered, such as letters and posters in local community hubs (23). The Swedish “corona lines”—a telephone service offering advice in various languages—is an example of good practice (53).

Geographical access can be improved with trusted and well-defined access points, such as mobile services, and walk-in clinics in community centres and places of worship.

Collaborations with existing networks can help broadcast these access points (24).

Addressing financial burdens, including travel costs, should also improve uptake (24).

4.1. Strengths and limitations

By systematically reviewing the current literature, this review provides insights into the vaccine attitudes that are unique to, or more prevalent, amongst racial and ethnic minorities and foreign-born populations. Our findings may prove useful in informing policy interventions and outreach initiatives throughout the COVID-19 vaccination campaign course, including the administration of boosters (51). The implications of these findings may also remain salient for future vaccination campaigns (24).

However, there are limitations that need to be acknowledged. Firstly, most papers were from the USA. Given the varied countrywide COVID-19 responses, results from this review may not be generalisable to other contexts. This review also collected data at a single point period. As vaccination programs have progressed, participants who were initially hesitant may now hold more positive attitudes (12). In all included studies, vaccination status and intentions were self-reported and are thus subject to social desirability bias. Response rates across the studies were also variable; one study reported a response rate of about 15% and is therefore subject to non-response bias (32). All studies recruited participants using convenience sampling or snowball sampling, and therefore, samples may not be representative of their target populations. As most studies used internet-based surveys in English, a section of the computer-averse or non-English-speaking population were excluded, thus furthering selection bias.

4.2. Recommendations for future research

This review has identified potential avenues for future research. Firstly, racial, and ethnic minorities and foreign-born populations come from different cultural, linguistic, and religious backgrounds across various socioeconomic strata, with varying proficiencies in English (47).

Therefore, our findings may not be generalisable to each distinct subgroup (21). Qualitative research could be useful for elucidating differences between groups.

Due to data limitations, some priority groups were not studied. For example, COVID-19 has disproportionately impacted Indigenous Americans, yet little is known about their vaccine intentions (39). Similarly, Middle Eastern and North African populations are underrepresented in research on health disparities in the USA, despite increasing evidence that this group—particularly Arab Americans—can experience barriers to care, including group-based medical mistrust and perceived discrimination (54,55). Future studies should therefore adopt sampling strategies to explore vaccine attitudes among such groups (39).

Furthermore, there is currently a dearth of literature on how vaccine attitudes translate into actually getting vaccinated. Longitudinal studies may help elucidate such questions.

Interventional studies on policies and programs that aim to reduce barriers to vaccine uptake may also prove insightful.

4.3. Conclusions

In closing, this review provides insight into the prevalence of, and reasons for, COVID-19 vaccine hesitancy among racial and ethnic minorities and foreign-born populations in high-income English-speaking countries. Urgent solutions and strategies to improve vaccine uptake among such priority populations are needed to improve health outcomes, promote health equity, and to help governments reach and exceed their vaccination targets. These findings have implications throughout the vaccination campaign course and are salient beyond the COVID-19 pandemic.

5. Declarations

5.1. Ethics approval and consent to participate

Not applicable.

5.2. Consent for publication

Not applicable.

5.3. Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

5.4. Competing interests

The authors declare that they have no competing interests.

5.5. Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Aidan Yuen and Keeley Allen are Master of Philosophy in Applied Epidemiology Scholars at the Australian National University and are funded by the Master of Philosophy in Applied Epidemiology Scholarship.

5.6. Authors' contributions

AY: formulated the research question, registered the protocol, defined the inclusion and exclusion criteria, conducted the literature search, screened for eligible studies, extracted the data, evaluated the risk of bias, interpreted, and discussed the results, and wrote the paper.

KA: reviewed the paper.

DP: formulated the research question, registered the protocol, defined the inclusion and exclusion criteria, conducted the literature search, screened for eligible studies, extracted the data, evaluated the risk of bias, and reviewed the paper.

5.7. Acknowledgements

We wish to acknowledge the contributions of Dr. Jim Black for reviewing the initial drafts of this review.

6. References

1. Anderson RM, Vegvari C, Truscott J, Collyer BS. Challenges in creating herd immunity to SARS-CoV-2 infection by mass vaccination. *The Lancet* [Internet]. 2020 Nov 21;396(10263):1614-6. Available from: [https://doi.org/10.1016/S0140-6736\(20\)32318-7](https://doi.org/10.1016/S0140-6736(20)32318-7)
2. MacDonald NE. Vaccine hesitancy: Definition, scope and determinants. *Vaccine*. 2015 Aug;33(34):4161-4.
3. Saluja S, Nok Lam C, Wishart D, McMorris A, Cousineau MR, Kaplan CM. Disparities in COVID-19 vaccine hesitancy among Los Angeles County adults after vaccine authorization. *Prev Med Rep*. 2021 Dec;24:101544.
4. Tram KH, Saeed S, Bradley C, Fox B, Eshun-Wilson I, Mody A, et al. Deliberation, Dissent, and Distrust: Understanding distinct drivers of COVID-19 vaccine hesitancy in the United States. *Clin Infect Dis*. 2021 Jul;
5. Daly M, Jones A, Robinson E. Public trust and willingness to vaccinate against COVID-19 in the US from October 14, 2020, to March 29, 2021. *Daly Kapteyn, Lopez, Robinson, Szilagyi G, editor. JAMA: Journal of the American Medical Association* [Internet]. 2021;325(23):2397-9. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=psyc17&NEWS=N&AN=2021-59074-001>
6. Sze S, Pan D, Nevill CR, Gray LJ, Martin CA, Nazareth J, et al. Ethnicity and clinical outcomes in COVID-19: A systematic review and meta-analysis. *EClinicalMedicine* [Internet]. 2020 Dec 1;29. Available from: <https://doi.org/10.1016/j.eclinm.2020.100630>
7. Hayward SE, Deal A, Cheng C, Crawshaw A, Orcutt M, Vandrevalla TF, et al. Clinical outcomes and risk factors for COVID-19 among migrant populations in high-income countries: A systematic review. *J Migr Health*. 2021;3:100041.
8. Flanagan A, Frey T, Christiansen SL, Committee AMAM of S. Updated Guidance on the Reporting of Race and Ethnicity in Medical and Science Journals. *JAMA* [Internet]. 2021 Aug 17;326(7):621-7. Available from: <https://doi.org/10.1001/jama.2021.13304>
9. Borrell LN, Elhawary JR, Fuentes-Afflick E, Witonsky J, Bhakta N, Wu AHB, et al. Race and Genetic Ancestry in Medicine – A Time for Reckoning with Racism. *New England Journal of Medicine* [Internet]. 2021 Jan 6;384(5):474-80. Available from: <https://doi.org/10.1056/NEJMms2029562>

10. Douglas P, Cetron M, Spiegel P. Definitions matter: migrants, immigrants, asylum seekers and refugees. *J Travel Med* [Internet]. 2019 Feb 1;26(2). Available from: <https://doi.org/10.1093/jtm/taz005>
11. Wang Q, Yang L, Jin H, Lin L. Vaccination against COVID-19: A systematic review and meta-analysis of acceptability and its predictors. *Prev Med (Baltim)* [Internet]. 2021;150:106694. Available from: <https://www.sciencedirect.com/science/article/pii/S0091743521002632>
12. Cascini F, Pantovic A, Al-Ajlouni Y, Failla G, Ricciardi W. Attitudes, acceptance and hesitancy among the general population worldwide to receive the COVID-19 vaccines and their contributing factors: A systematic review. *EClinicalMedicine*. 2021 Oct;40:101113.
13. Sallam M. COVID-19 Vaccine Hesitancy Worldwide: A Concise Systematic Review of Vaccine Acceptance Rates. *Vaccines (Basel)* [Internet]. 2021 Feb 16;9(2):160. Available from: <https://pubmed.ncbi.nlm.nih.gov/33669441>
14. Mose A, Haile K, Timerga A. COVID-19 vaccine hesitancy among medical and health science students attending Wolkite University in Ethiopia. *PLoS One* [Internet]. 2022 Jan 25;17(1):e0263081. Available from: <https://doi.org/10.1371/journal.pone.0263081>
15. Yasmin F, Najeeb H, Moeed A, Naeem U, Asghar MS, Chughtai NU, et al. COVID-19 Vaccine Hesitancy in the United States: A Systematic Review [Internet]. Vol. 9, *Frontiers in Public Health*. 2021. Available from: <https://www.frontiersin.org/article/10.3389/fpubh.2021.770985>
16. Munn Z, Porritt K, Lockwood C, Aromataris E, Pearson A. Establishing confidence in the output of qualitative research synthesis: the ConQual approach. *BMC Med Res Methodol* [Internet]. 2014;14(1):108. Available from: <https://doi.org/10.1186/1471-2288-14-108>
17. Pearson A, White H, Bath-Hextall F, Apostolo J, Salmond S, Kirkpatrick P. The Joanna Briggs Institute Reviewers Manual: Methodology for JBI mixed methods systematic reviews. Adelaide, Australia; 2014.
18. Nguyen LH, Joshi AD, Drew DA, Merino J, Ma W, Lo CH, et al. Racial and ethnic differences in COVID-19 vaccine hesitancy and uptake. *medRxiv: the preprint server for health sciences*. 2021.
19. Grumbach K, Judson T, Desai M, Jain V, Lindan C, Doernberg SB, et al. Association of Race/Ethnicity With Likelihood of COVID-19 Vaccine Uptake Among Health Workers and the General Population in the San Francisco Bay Area. *JAMA Intern Med*. 2021 Jul;181(7):1008-11.

20. Moore JX, Gilbert KL, Lively KL, Laurent C, Chawla R, Li C, et al. Correlates of COVID-19 Vaccine Hesitancy among a Community Sample of African Americans Living in the Southern United States. *Vaccines (Basel)*. 2021 Aug;9(8).
21. Kricorian K, Turner K. COVID-19 Vaccine Acceptance and Beliefs among Black and Hispanic Americans. *PLoS One*. 2021;16(8):e0256122.
22. Gehlbach D, Vázquez E, Ortiz G, Li E, Sánchez CB, Rodríguez S, et al. COVID-19 Testing and Vaccine Hesitancy in Latinx Farm-Working Communities in The Eastern Coachella Valley. *Research square*. 2021.
23. Knights F, Carter J, Deal A, Crawshaw AF, Hayward SE, Jones L, et al. Impact of COVID-19 on migrants' access to primary care and implications for vaccine roll-out: a national qualitative study. *Br J Gen Pract*. 2021 Aug;71(709):e583-95.
24. Deal A, Hayward SE, Huda M, Knights F, Crawshaw AF, Carter J, et al. Strategies and action points to ensure equitable uptake of COVID-19 vaccinations: A national qualitative interview study to explore the views of undocumented migrants, asylum seekers, and refugees. *J Migr Health*. 2021;4:100050.
25. Jimenez ME, Rivera-Núñez Z, Crabtree BF, Hill D, Pellerano MB, Devance D, et al. Black and Latinx Community Perspectives on COVID-19 Mitigation Behaviors, Testing, and Vaccines. *JAMA Netw Open*. 2021 Jul;4(7):e2117074.
26. Momplaisir F, Haynes N, Nkwihoreze H, Nelson M, Werner RM, Jemmott J. Understanding Drivers of COVID-19 Vaccine Hesitancy Among Blacks. *Clin Infect Dis*. 2021 Feb;
27. Allington D, McAndrew S, Moxham-Hall V, Duffy B. Coronavirus conspiracy suspicions, general vaccine attitudes, trust and coronavirus information source as predictors of vaccine hesitancy among UK residents during the COVID-19 pandemic. *Psychol Med*. 2021 Apr;1-12.
28. Tang X, Gelband H, Nagelkerke N, Bogoch II, Brown P, Morawski E, et al. COVID-19 vaccination intention during early vaccine rollout in Canada: a nationwide online survey. *Lancet Regional Health Americas*. 2021 Aug;100055.
29. Zhang M, Gurung A, Anglewicz P, Subedi P, Payton C, Ali A, et al. Acceptance of COVID-19 Vaccine Among Refugees in the United States. *Public Health Rep*. 2021 Sep;333549211045838.

30. Ta Park V, Dougan M, Meyer O, Nam B, Tzuang M, Park L, et al. Differences in COVID-19 Vaccine Concerns Among Asian Americans and Pacific Islanders: The COMPASS Survey. *J Racial Ethn Health Disparities*. 2021 Apr;1-13.
31. Doherty IA, Pilkington W, Brown L, Billings V, Hoffler U, Paulin L, et al. COVID-19 Vaccine Hesitancy in Underserved Communities of North Carolina. *medRxiv: the preprint server for health sciences*. 2021.
32. McElfish PA, Willis DE, Shah SK, Bryant-Moore K, Rojo MO, Selig JP. Sociodemographic Determinants of COVID-19 Vaccine Hesitancy, Fear of Infection, and Protection Self-Efficacy. *J Prim Care Community Health*. 2021;12:21501327211040744.
33. Thompson HS, Manning M, Mitchell J, Kim S, Harper FWK, Cresswell S, et al. Factors Associated With Racial/Ethnic Group-Based Medical Mistrust and Perspectives on COVID-19 Vaccine Trial Participation and Vaccine Uptake in the US. *JAMA Netw Open*. 2021 May;4(5):e2111629.
34. Savoia E, Piltch-Loeb R, Goldberg B, Miller-Idriss C, Hughes B, Montrond A, et al. Predictors of COVID-19 Vaccine Hesitancy: Socio-Demographics, Co-Morbidity, and Past Experience of Racial Discrimination. *Vaccines (Basel)*. 2021 Jul;9(7).
35. Liu R, Li GM. Hesitancy in the time of coronavirus: Temporal, spatial, and sociodemographic variations in COVID-19 vaccine hesitancy. *SSM Popul Health*. 2021 Sep;15:100896.
36. Mondal P, Sinharoy A, Su L. Sociodemographic predictors of COVID-19 vaccine acceptance: a nationwide US-based survey study. *Public Health*. 2021 Jul;198:252-9.
37. Nguyen KH, Nguyen K, Corlin L, Allen JD, Chung M. Changes in COVID-19 vaccination receipt and intention to vaccinate by socioeconomic characteristics and geographic area, United States, January 6 - March 29, 2021. *Ann Med*. 2021 Dec;53(1):1419-28.
38. Szilagyi PG, Thomas K, Shah MD, Vizueta N, Cui Y, Vangala S, et al. The role of trust in the likelihood of receiving a COVID-19 vaccine: Results from a national survey. *Prev Med (Baltim)*. 2021 Jul;153:106727.
39. Niño MD, Hearne BN, Cai T. Trajectories of COVID-19 vaccine intentions among U.S. adults: The role of race and ethnicity. *SSM Popul Health*. 2021 Sep;15:100824.
40. Killgore WDS, Cloonan SA, Taylor EC, Dailey NS. The COVID-19 Vaccine Is Here-Now Who Is Willing to Get It? *Vaccines (Basel)*. 2021 Apr;9(4).

41. Kreps SE, Goldfarb JL, Brownstein JS, Kriner DL. The Relationship between US Adults' Misconceptions about COVID-19 Vaccines and Vaccination Preferences. *Vaccines (Basel)*. 2021 Aug;9(8).
42. Fu LY, Haimowitz R, Thompson D. Community members trusted by African American parents for vaccine advice. *Hum Vaccin Immunother*. 2019;15(7-8):1715-22.
43. Katz IT, Bogart LM, Fu CM, Liu Y, Cox JE, Samuels RC, et al. Barriers to HPV immunization among blacks and latinos: a qualitative analysis of caregivers, adolescents, and providers. *BMC Public Health [Internet]*. 2016;16(1):874. Available from: <https://doi.org/10.1186/s12889-016-3529-4>
44. Harris LM, Chin NP, Fiscella K, Humiston S. Barrier to pneumococcal and influenza vaccinations in Black elderly communities: mistrust. *J Natl Med Assoc [Internet]*. 2006 Oct;98(10):1678-84. Available from: <https://pubmed.ncbi.nlm.nih.gov/17052061>
45. Taylor-Clark KA, Viswanath K, Blendon RJ. Communication inequalities during Public Health disasters: Katrina's wake. *Health Commun*. 2010 Apr;25(3):221-9.
46. Tanne JH. Covid-19: FDA panel votes to authorise Pfizer BioNTech vaccine. *BMJ [Internet]*. 2020 Dec 11;371:m4799. Available from: <http://www.bmj.com/content/371/bmj.m4799.abstract>
47. Kamal A, Hodson A, Pearce JM. A Rapid Systematic Review of Factors Influencing COVID-19 Vaccination Uptake in Minority Ethnic Groups in the UK. Vol. 9, *Vaccines* . 2021.
48. Head KJ, Kasting ML, Sturm LA, Hartsock JA, Zimet GD. A National Survey Assessing SARS-CoV-2 Vaccination Intentions: Implications for Future Public Health Communication Efforts. *Sci Commun [Internet]*. 2020 Sep 23;42(5):698-723. Available from: <https://doi.org/10.1177/1075547020960463>
49. Reiter PL, Katz ML. Racial/Ethnic Differences in Knowledge, Attitudes, and Beliefs About COVID-19 Among Adults in the United States. *Front Public Health*. 2021;9:653498.
50. Shepherd SM, Willis-Esqueda C, Paradies Y, Sivasubramaniam D, Sherwood J, Brockie T. Racial and cultural minority experiences and perceptions of health care provision in a mid-western region. *Int J Equity Health [Internet]*. 2018;17(1):33. Available from: <https://doi.org/10.1186/s12939-018-0744-x>
51. Momplaisir FM, Kuter BJ, Ghadimi F, Browne S, Nkwihoreze H, Feemster KA, et al. Racial/Ethnic Differences in COVID-19 Vaccine Hesitancy Among Health Care Workers in 2 Large Academic Hospitals. *JAMA Netw Open*. 2021 Aug;4(8):e2121931.

52. Biasio LR. Vaccine hesitancy and health literacy. *Hum Vaccin Immunother* [Internet]. 2016/11/03. 2017 Mar 4;13(3):701-2. Available from: <https://pubmed.ncbi.nlm.nih.gov/27808587>
53. Valeriani G, Sarajlic Vukovic I, Lindegaard T, Felizia R, Mollica R, Andersson G. Addressing Healthcare Gaps in Sweden during the COVID-19 Outbreak: On Community Outreach and Empowering Ethnic Minority Groups in a Digitalized Context. *Healthcare (Basel)* [Internet]. 2020 Nov 1;8(4):445. Available from: <https://pubmed.ncbi.nlm.nih.gov/33139619>
54. Abuelezam NN, El-Sayed AM, Galea S. The Health of Arab Americans in the United States: An Updated Comprehensive Literature Review. *Front Public Health* [Internet]. 2018 Sep 11;6:262. Available from: <https://pubmed.ncbi.nlm.nih.gov/30255009>
55. Jaffee K, Cohen M, Azaiza F, Hammad A, Hamade H, Thompson H. Cultural Barriers to Breast Cancer Screening and Medical Mistrust Among Arab American Women. *J Immigr Minor Health*. 2021 Feb;23(1):95-102.

7. Tables

Table 1. Characteristics of and data from quantitative studies (prevalence of vaccine hesitancy/acceptance)

Paper	Study design and study population	Date of data collection	Sample size	Measurement tool	Vaccine hesitancy/acceptance measurement
Allington et al., 2021 (27)	Cross-sectional study of residents aged 18-75, UK	21 November to 21 December 2020	N=4343: 91% white, 7% other ethnicity	Tool: "If a vaccine for coronavirus becomes available, how likely or unlikely would you personally be to get the vaccine/if you were offered it?" Hesitancy: Fairly likely, not very likely, not at all likely, definitely not, don't know	Fully adjusted linear rank order model; White=ref.; Other ethnicity: Est.=0.05, Low=0.00, High=0.11, P=0.048
Daly et al., 2021 (5)	Cross-sectional study of adults, USA	March 2021	N=6035	Tool: Participants were asked how likely they were to get vaccinated against COVID-19 Hesitancy: Unsure or somewhat/very unlikely to vaccinate	Prevalence (95% CI); White=34.8% (32.8%-36.8%), Hispanic=36.4% (31.2%-41.7%), Black=43.0% (37.3%-48.7%), other=20.4% (14.3%-26.6%)
Doherty et al., 2021 (31)	Cross-sectional study of adults at 34 COVID-19 testing sites in 9 counties of North Carolina, USA	27 August to 15 December 2020	N=859: 28.4% White, 58.7% Black, 12.9% Latinx	Tool: "Would you get vaccinated against COVID-19 as quickly as possible when the vaccine becomes available?" Hesitancy: No or don't know/not sure	Prevalence (P-value); White=62.7% (ref.), Black=74.0% (P=0.002), Latinx=59.5% (P=0.560) Multivariate logistic regression, OR (95% CI) (P-value); White=ref., Black=1.68 (1.16-2.45) (P=0.006), Latinx=1.14 (0.67-1.91) (P=0.634)
Grumbach et al., 2021 (19)	Cross-sectional study of the general population in 6 counties of the San Francisco Bay Area, USA	27 November 2020 to 15 January 2021	N=3161	Tool: "How likely are you to get an approved COVID-19 vaccine when it becomes available?" Acceptance: Scoring ≥ 3 on 1-7 Likert scale anchored at "not at all likely" and "very likely"	Adjusted OR (95% CI); White=ref., Black=0.29 (0.20-0.43), Latinx=0.55 (0.43-0.71), Asian=0.57 (0.47-0.70), other=0.62 (0.38-1.02), multiple races=0.65 (0.46-0.92)
Killgore et al., 2021 (40)	Cross-sectional study of English-speaking adults, USA	10 to 15 December 2020	N=1017: 75.7% White, 11.1% Black/African American, 4.7% Hispanic/Latino, 5.4% Asian, 0.7% Native American/American Indian/Alaska Native, 0.3% Native Hawaiian/Pacific, 2.2% other	Tool: "I will get the new COVID-19 vaccine as soon as it is offered to me" Acceptance: 7-point Likert scale from "totally disagree" to "totally agree"	Stepwise multiple linear regression; race/ethnicity (White): B=0.068, P=0.009

Chapter 5

Kreps et al., 2021 (41)	Cross-sectional study of the adult population, USA	11 to 15 February 2021	N=1027: 65% White, 11% Black, 15% Latinx, 4% Asian, 6% Other	Tool: "Once a vaccine to prevent COVID-19 is available to you, would you...?" Acceptance: 4-point scale (definitely will vaccinate to definitely will not vaccinate)	Ordered logit regression, coefficient (95% CI) (P-value); White=ref., Black=-1.17 (-1.73-0.61) (P=0.00); Latinx=-0.38 (-0.93-0.17) (P=0.17)
Kricorian & Turner, 2021 (21)	Cross-sectional study of adults, USA	January 2021	N=1950: 63.8% White, 12.1% Black, 10.5% Hispanic, 2.7% Asian, 6.7% Other	Tool: "After the COVID-19 vaccine is broadly available, how long do you plan to wait to get the vaccine?" Hesitancy: "I do not plan to get the COVID-19 vaccine"	Prevalence; White (ref.)=18.7%, Black=27.8%*, Hispanic=16.7%, Asian=6.5%; other=35.1%* *P<0.05
Liu & Li, 2021 (35)	Cross-sectional study of the Household Pulse Survey, USA	6 January to 29 March 2021	N=443680: 75% White, 4.7% Asian, 7.2% Black, 9.7% Hispanic, 3.5% other/mixed	Tool: Intention to get a vaccine once it becomes available Hesitancy: "probably not" or "definitely not"	Multilevel models, log odds estimation (P-value); White=ref., Asian=-0.93 (P<0.001), Black=0.33 (P<0.001), Hispanic=-0.29 (P<0.001), other/mixed=0.29 (P<0.001)
McElfish et al., 2021 (32)	Cross-sectional study of adults in Arkansas, USA	30 October 2020 to 16 January 2021	N=754; 747 with race/ethnicity data: 17.14% Black/African American, 70.41% White, 8.17% other race or multiracial, 4.28% Hispanic/Latinx	Tool: "If a vaccine for COVID-19 were available today, what is the likelihood that you would get vaccinated?" Hesitancy: "don't know/not sure," "unlikely," or "very unlikely"	Prevalence; Black/African American=63.03%, White=31.24%, other/multiracial=46.43, Hispanic/Latinx=51.72%, P<0.001 Full-information maximum likelihood logistic regression, OR (P-value); White=ref., Black/African American=3.08 (P=0.000), other/multiracial=1.77 (P=0.65), Hispanic/Latinx = 2.19 (P=0.059)
Mondal et al., 2021 (36)	Nationwide cross-sectional study of adults, USA	May 2020 and January 2021	N=2978; 2874 with race/ethnicity data: 4.5% Asian, 6.9% African American, 7.1% Hispanic, 77.1% White, 4.5% Others	Tool: "Would you like to get the COVID-19 vaccine, if available?" Acceptance: Yes	Prevalence; Asian=91.47%, African American=64.97%, Hispanic=71.92%, White=72.66%, others=84.12%, P<0.001 Stepwise backward logistic regression, OR (95% CI) (P-value); White=ref., Asian=0.56 (0.27-1.14) (P=0.11), Black=2.04 (1.37-3.04) (P<0.001), Hispanic=1.52 (1.01-2.28) (P=0.04), others=1.77 (1.10-2.85) (P=0.02)
Moore et al., 2021 (20)	Cross-sectional study of adult members of the 100 Black Men of Augusta organisation, USA	January to April 2021	N=257; 69.5% Black	Tool: "If given to you for free, how likely are you to take a COVID-19 vaccination?" Hesitancy: neutral Resistance: unlikely and very unlikely	Prevalence of hesitancy=15.6% Prevalence of resistance=16.3%
K. H. Nguyen et al., 2021 (37)	Cross-sectional study of adults, USA	17 March to 29 March 2021	N=77104	Tool: "Once a vaccine to prevent COVID-19 is available to you, would you...definitely, probably, probably not, or definitely not get a vaccine". Acceptance: "definitely or probably" be vaccinated	Weighted prevalence (95% CI); Non-Hispanic White (ref.)=73.5 (72.9-74.2); non-Hispanic Black=64.1 (61.7-66.4)*; Hispanic=70.8 (68.4-73.1)*; non-Hispanic Asian=86.0 (83.8-88.2)*; non-Hispanic other/multiple races=64.2 (59.7-68.7)* *P<0.05

Chapter 5

					Adjusted prevalence ratio (95% CI); Non-Hispanic White = ref.; non-Hispanic Black=0.86 (0.85-0.88); Hispanic=1.08 (1.06-1.09); non-Hispanic Asian=1.17 (1.16-1.19); non-Hispanic other/multiple races=0.93 (0.90-0.95)
L. H. Nguyen et al., 2021 (18)	USA and UK	24 March 2020 to 16 February 2021	N=1341682 USA: 64144 White, 2179 Black, 3235 Hispanic, 3089 Asian, 1003 more than one/other UK: 1110544 White, 8787 Black, 15199 South Asian, 6946 Middle East/East Asian, 13512 more than one/other	Tool: Participant willingness to obtain a COVID-19 vaccine if it was offered to them Hesitancy: unsure/not willing	Prevalence; USA: White=7.4%, Black=28.0%, Hispanic=15.6%, Asian=10.0%, more than one/other=16.6% UK: White=5.1%, Black=18.4%, South Asian=9.8%, Middle East/East Asian=11.1%, more than one/other=9.4% Multivariable-adjusted OR (95% CI); USA: White=ref., Black=3.15 (2.86-3.47), Hispanic=1.42 (1.28-1.58), Asian=1.34 (1.18-1.52), more than one/other=2.02 (1.70-2.39) UK: White=1.0 (ref.), Black=2.84 (2.69-2.99), South Asian=1.66 (1.57-1.76), Middle East/East Asian=1.84 (1.7-1.98), more than one/other=1.48 (1.39-1.57)
Nino et al., 2021 (39)	Cross-sectional study from the national Understanding America Study, USA	9 December 2020 to 6 January 2021	N=5023	Tool: "How likely are you to get vaccinated for coronavirus once a vaccination is available to the public?" Acceptance: somewhat likely/very likely=1	Prevalence; overall=61%, Latina/o=58%, Asian/Pacific Islander=73%, Black=40%, White=64%
Park et al., 2021 (30)	Cross-sectional study of Asian Americans and Pacific Islanders, USA.	24 October to 11 December 2020	N=1646: 97.6% Asian, 2.4% Native Hawaiian/Pacific Islanders	Not measured	
Saluja et al., 2021 (3)	Cross-sectional study of adults living in Los Angeles County, USA	5 December 2020 and 10 January 2021	N=1984: 20.0% Non-Hispanic White, 15.0% Asian, 17.1% Black, 46.5% Hispanic, 1.4% other	Tool: "Would you be willing to get the COVID-19 vaccine once it is available" Hesitancy: "probably" or "definitely" not on a 4-item scale	Prevalence; total=28.4%, non-Hispanic White=21.7% (ref.), Asian=17.8%, Black=42.1%*, Hispanic=30.7%*, other=68.0%* * P<0.05 Logistic regression, adjusted OR (95% CI) (P-value); non-Hispanic White=ref., Asian=0.8 (0.5-1.5) (P=0.51), Black=3.3 (2.2-5.0) (P<0.001), Hispanic=2.1 (1.2-3.6) (P=0.008), other=3.6 (1.4-9.1)
Savoia et al., 2021 (34)	Cross-sectional study of adults, USA	13 December to 23 December 2020	N=2650: 66.2% non-Hispanic White, 14.3% Black, 7.8% Hispanic, 4.9% non-Hispanic	Tool: Respondents were asked how likely they would be to take a COVID-19 vaccine if offered to them at no cost within two months.	Association with vaccine hesitancy, crude OR (95% CI); all other races=ref., non-Hispanic white=0.94 (0.81-1.10), non-Hispanic Black=1.22 (1.00-1.48), non-Hispanic Asian=0.87 (0.63-1.20), Hispanic=0.92 (0.71-1.20)

Chapter 5

			Asian, 4.6% 2+ races, 1.5% prefer not to say, 0.7% other	Hesitancy: unspecified; measured by a Likert-type scale; 1 (low hesitancy) to 6 (high hesitancy)	
Szilagyi et al., 2021 (38)	Cross-sectional study of non-institutionalised adults, USA	23 December 2020 to 19 January 2021	Weighted: N=6066: 62.4% White, 16.6% Hispanic, 12.0% Black, 5.3% Asian, 3.5% other	Tool: "How likely are you to get vaccinated for coronavirus once a vaccine is available to the public?" Acceptance: "somewhat or very likely"	Prevalence; White=59.6%, Hispanic=55.3%, Black=38.7%, Asian=77.5%, other=59.9% Multivariate analysis of likelihood of vaccination, adjusted RR (95% CI); White=ref., Hispanic=1.04 (0.95-1.13), Black=0.97 (0.87-1.10), Asian=1.12 (1.02-1.23), other=1.10 (0.98-1.23)
Tang et al., 2021 (28)	Cross-sectional study of adult panel members from the Angus Reid Forum, Canada	December 2020 to February 2021	N=14621: 65.7% Not visible minority, 14.3% visible minority; 91.1% not Indigenous, 8.9% Indigenous	Tool: "When a vaccine against the coronavirus becomes available to you, will you get vaccinated or not?" Hesitancy: "Will not vaccinate"	Prevalence (P-value); not visible minority=8.8% (ref.), visible minority=12.3% (P<0.0001); not Indigenous=8.7% (ref.), Indigenous=14.6% (P<0.0001)
Thompson et al., 2021 (33)	Cross-sectional study of adults in Michigan, USA	June to December 2020	N=1835: 52% White, 21% Black, 5% Arab, Chaldean, Middle Eastern, or North African (MENA), 5% Hispanic, 5% Asian, 11% other	Tool: "If you were offered a coronavirus vaccine that had been approved by the US Food and Drug Administration today, would you agree to be vaccinated?" Hesitancy: Definitely no, probably no, or unsure	Prevalence; total=52%, White=43%; Black=72%, MENA=62%; Hispanic=58%; Asian=36%, multiracial or other=57% Path analysis modelling, B (SE) (P-value); Black=0.51 (0.08) (P<0.001), MENA=0.19 (0.14) (P=0.18), Hispanic=-0.02 (0.13) (P=0.86), Asian=-0.63 (0.14) (P<0.001), White=-0.20 (0.07) (P=0.005)
Tram et al., 2021 (4)	Cross-sectional study of adults, USA	6 January to 29 March 2021	N=459235: Black=7.7%, White=82.5%, Asian=5.1%, >=2 races/other=4.7%; Hispanic/Latino (of any race)=9.6%, not Hispanic/Latino=90.4%	Tool: Whether they planned on getting a vaccine Hesitancy: "probably not" or "definitely not"	Adjusted OR (95% CI) (P-value); White=ref.; Black=1.25 (1.19-1.32) (P<0.001); Asian=0.34 (0.30,0.38) (P<0.01); >=2 races/other=1.50 (1.39-1.61) (P<0.001); non-Hispanic=ref., Hispanic=0.55 (0.52-0.58) (P<0.001)
Zhang et al., 2021 (29)	Cross-sectional study of recently arrived refugees aged ≥8, USA	December 2020 to January 2021	N=435: 15.6% Afghanistan, 38.2% Nepal, 26.0% Somalia, 9.0% South Sudan, 7.8% Burma/ Myanmar, 3.4% others	Tool: "If a vaccine against COVID-19 becomes available, do you plan to get vaccinated?" Hesitancy: unsure/no	Prevalence=7.6% did not plan to receive a vaccine, and 22.1% were unsure.

Table 2. Characteristics of qualitative studies.

Paper	Methodology, method, and data analysis	Date of data collection	Inclusion criteria and setting	Study participants
Deal et al., 2021 (24)	Qualitative study, semi-structured interviews, thematic analysis	4 September 2020 to 8 March 2021	Recently arrived migrants (foreign-born, >18 years old; <10 years in the UK) with precarious immigration status; UK	N=32; 3 refugees, 19 asylum seekers, 8 undocumented migrants and 2 with limited leave to remain from 15 different countries
Gehlbach et al., 2021 (22)	Community-based participatory study, focus groups, thematic analysis	November to December 2020	1) ≥18 years, 2) lived in the East Coachella Valley, California and/or farm-working community along the Salton Sea, 3) self-identified as Hispanic, Latinx and/or indigenous from Latin America, and 4) spoke Spanish and/or Purépecha; USA	N=55; 44 Hispanic/Latinx and 9 Purépecha
Jimenez et al., 2021 (25)	Community-engaged qualitative study, group/individual interviews, thematic analysis	19 November 2020 to 5 February 2021	Black and Latinx individuals in New Jersey counties (Essex, Middlesex, Passaic, and Union); USA	N=111; 68 Black and 43 Latinx
Knights et al., 2021 (23)	Qualitative study, semi-structured interviews, thematic analysis	18 June to 30 November 2020	Newly arrived migrants (born overseas, aged >18 years, and <10 years in the UK); UK	N=17; 15 asylum seekers, and 2 refugees
Momplaisir et al., 2021 (26)	Qualitative study, focus groups, thematic analysis (modified grounded theory approach)	July to August 2020	Black barbershop and salon owners in West Philadelphia, USA	N=24

Table 3. Data from quantitative studies (reasons for vaccine hesitancy).

Paper	Analyses, measures, and additional information	Reasons for vaccine hesitancy	Results
Killgore et al., 2021 (40)	Stepwise multiple linear regression, B coefficient (P-value)	Feeling afraid	Race/ethnicity (White): B=-0.121, P=0.0000
Kreps et al., 2021 (41)	Ordered logit regression, coefficient (95% CI) (P-value)	Perceived side effect severity	White=ref., Black=0.71 (0.14-1.28) (P=0.02), Latinx=0.16 (-0.33-0.64) (P=0.53)
		Estimated clinical trial size	White=ref., Black=-0.40 (-1.00-0.19), (P=0.18), Latinx=-0.35 (-0.77-0.07) (P=0.10)
		Perception that vaccines have live virus	White=ref., Black=0.12 (-0.60-0.85) (P=0.74), Latinx=0.17 (-0.57-0.90) (P=0.65)
Kricorian & Turner, 2021 (21)	Prevalence, % *P<0.05	Going to be effective	White=55.1%, Black=38.7%*, Hispanic=49.3%, Asian=60.6%, other=40.8%*
		Going to be safe	White=42.7%, Black=33.6%*, Hispanic=41.1%, Asian=50.0%, other=32.8%*
		Being rushed out too quickly	White=30.1%, Black=47.7%*, Hispanic=42.1%*, Asian=25.0%, other=46.9*
		Just not something I trust	White=23.7%, Black=34.0%*, Hispanic=27.0%, Asian=15.2%, other=31.5%*
		Not worth the risk	White=15.6%, Black=18.3%, Hispanic=17.1%, Asian=9.1%, other=25.4%*
		Dangerous	White=10.0%, Black=16.2%*, Hispanic=13.5%, Asian=6.3%, other=13.7%
		More harmful than getting COVID-19	White=7.8%, Black=12.3%*, Hispanic=8.6%, Asian=6.1%, other=11.5%
Liu & Li, 2021 (35)	Multilevel models, log odds estimation (P-value) *P<0.001	Going to cause people to catch COVID-19	White=6.4%, Black=14.0%*, Hispanic=7.9%, Asian=3.1%, other=16.8%*
		Confidence	White=ref., Asian=-1.10*, Black=0.32*, Hispanic=-0.31*, other/mixed=0.35*
		Circumspection	White=ref., Asian=-0.88*, Black=0.35*, Hispanic=-0.25*, other/mixed=0.26*
Park et al., 2021 (30)	Prevalence, % This study only included Asian Americans and Pacific Islanders	Complacency	White=ref., Asian=-1.39*, Black=-0.38*, Hispanic=-0.55*, other/mixed=0.12*
		Side effects only	34.1%
		Unsafe only	6.0%
	Prevalence, %	Multiple reasons	36.4%
		Safety concerns	Non-Hispanic White=60.6%, Asian=58.3%, Black=54.4%, Hispanic=60.7%, other=53.3%

Chapter 5

Saluja et al., 2021 (3)	*P<0.05, ref.=non-Hispanic White	Don't think the vaccine will work	Non-Hispanic White=21.4%, Asian=8.9%, Black=26.3%, Hispanic=18.6%, other=23.3%
		Don't trust the government to develop a COVID-19 vaccine	Non-Hispanic White=22.1%, Asian=34.8%, Black=36.1%*, Hispanic=33.1%, other=33.0%
		Don't trust pharmaceutical companies to develop a COVID-19 vaccine	Non-Hispanic White=31.2%, Asian=26.4%, Black=27.1%, Hispanic=20.8%, other=23.3%
		Want to wait to see how it works	Non-Hispanic White=27.3%, Asian=44.6%, Black=41.2%*, Hispanic=42.0%*, other=38.6%
		Don't believe in getting vaccinated in general	Non-Hispanic White=18.6%, Asian=8.6%, Black=13.3%, Hispanic=15.2%, other=16.5%
		Don't think I will get COVID-19	Non-Hispanic White=10.0%, Asian=6.2%, Black=15.8%, Hispanic=9.1%, other=23.3%
Tram et al., 2021 (4)	Prevalence, % (95% CI)	Deliberation	Black=84.1 (83.0-85.2), White=85.2 (84.8-85.6), Asian=89.4 (87.4-91.1), ≥2 races/other=83.3 (81.3-85.0); Hispanic/Latino= 87.5 (86.5-88.4), not Hispanic/Latino=84.4 (84.1-84.8)
		Dissent	Black=11.1 (10.3-12.1), White=14.8 (14.3-15.3), Asian=8.3 (6.9-9.9), ≥2 Races/other=18.5 (17.0-20.2); Hispanic/Latino=11.2 (10.2-12.3), not Hispanic/Latino=14.9 (14.5-15.3)
		Distrust	Black=32.8 (31.5-34.2), White=30.7 (30.2-31.2), Asian=15.0 (13.4-16.7), ≥2 Races/other=35.1 (33.1-37.1); Hispanic/Latino=25.7 (24.6-26.8), not Hispanic/Latino=32.0 (31.5-32.5)
Zhang et al., 2021 (29)	Prevalence, % This study only included recently arrived refugees aged ≥18	Side effects	71.3%
		Don't think vaccines work well	12.4%
		Don't like needles	8.5%
		COVID-19 is not serious	5.4%
		Believe in natural/traditional remedies	5.4%
		Allergic to vaccines	3.1%
		Religious reasons	2.3%
		Don't have time	0.8%

Table 4. Meta-aggregation and meta-synthesis of qualitative findings; findings were rated as unequivocal (U) or equivocal (E).

Findings	Supporting quotes	Categories	Synthesised findings
The political environment and the vaccines' association with President Trump (U)	"You see what's going on with police brutality and things, things have been caught on tape and it's not being addressed, so [it's not so] weird in thinking that the vaccines that go to zip codes 19131, 19139, 19104 would be tainted." (p. 3) (26)	Mistrust in the government	Hesitancy can be attributed to a mistrust in the government, mistrust in medical science, concerns about the safety and effectiveness of the vaccines, personal philosophies on health, social norms, lack of access to information or access to conflicting information, and a lack of financial or geographical access.
The vaccines contain a microchip to control and monitor behaviour, or contain another virus (U)	"My neighbors say 'No' [to getting the vaccine], because they [the government] are going to put a chip in them, or because they might put another virus [in them]." (p. 9) (22)		
Concerns about being the last to receive the vaccine (U)	"We have that feeling we'd be the last to have the vaccination" (p. 592) (23)		
Concerns about being excluded from the vaccine rollout (U)	"I listened that it [COVID-19 vaccinations] will come in UK. They will give the British people first and we asylum seekers will come in the end." (p. 4) (24)		
Fears around being charged for the vaccines (U)	"And government should not come and hunt you that you are owing them. Because you took the vaccine you are owing them " (p. 3) (24)		
Fears around immigration checks during vaccination (U)	"They don't need to put the word documents [in Covid vaccine adverts] because what if I don't have it, I'm undocumented. And you said okay come on have your vaccine, we're not going to check you...I won't go because I don't know to what extent is true." (p. 3) (24)		
Fears that immigration statuses will be shared with the Home Office (U)	"The prime minister has said we want everybody to be vaccinated. But he did not say no information will be given to the home office. He did not give that safety blanket and security to people that are afraid to give information away." (p. 5) (24)		

Chapter 5

Concerns that testing was rushed (U)	"No, I will not be taking a [COVID-19] vaccine...One, they didn't have enough studies. It takes at least a year and a half, two years or three years for them to complete a study and they did it in four months." (p. 2) (26)	Mistrust in medical science	
Concerns about how the vaccine could be developed so rapidly (U)	"It's a lot of things that have been out here for hundreds of years that you couldn't find a vaccine for, but this here, in less than a year, you come up with a vaccine that's supposed to cure it. So how do you have the vaccine so fast?" (p. 7) (25)		
Beliefs that their communities were under-represented in clinical trials (U)	"The main problem is that we not having the same community participating too much in the trials." (p. 591) (23)		
Concerns they would be used for medical experiments (U)	'If I go there [for a vaccine] they might be using me as a guinea pig or I don't know." (p. 591-592) (23)		
Wanting to see how others respond first (U)	"The only way I would get the vaccine would be if the same scientists who created it, and the executives and owners of the companies who created the vaccine, and the President and the entire Cabinet got the vaccine, then I would get the vaccine." (p. 7) (25)		
Mistrust based on historic mistreatment (U)	"I'm paranoid, I keep getting, when I hear that Tuskegee experiment. But I stay away from that. I wouldn't get a vaccine." (p. 3) (26)		
Mistrust based on unethical research practices (U)	"You have more people in prisons have gotten this [COVID-19]. People are trying to get help. But I see them trying to go to a place like that to try this stuff on which is what they used to do with vaccines, try it on prisoners and see how they respond." (p. 3) (26)		
The idea that COVID-19 is a hoax (U)	"Some of the people, culturally, they don't believe that such a virus exists. They think that it's 5G or something else." (p. 590) (23)		
Uncertainty about vaccine effectiveness in general (U)	"They don't know if you're going to get it, like you know how you could still get the flu even if you get a flu shot." (p. 3) (26)	Concerns about the safety and effectiveness	
Concerns that the vaccine is unsafe (U)	"There is fears about vaccine safety, people are scared of it, is it safe? Isn't it safe?" (p. 591) (23)		

Chapter 5

Concerns that the vaccine is harmful (U)	"If we get vaccinated, we might get more sick, or are going to die." (p. 9) (22)	of the vaccines	
Concerns about the short-term side-effects (U)	"I'm just like really interested in the adverse outcomes and the changes...we may react to it differently. So I'm really concerned about that." (p. 5) (25)		
Concerns about the long-term side-effects (U)	"I wouldn't feel confident about the vaccine because I wouldn't know what the long-term side effects would be." (p. 7) (25)		
Concerns about the effects on reproductive health (U)	"... and they had gave this vaccine to a woman ... they were saying that she may have some fertility issues. That's one of the side effects... I'm thinking about my children, how will it affect them...?" (p. 5) (25)		
Beliefs that existing medications are more appropriate than COVID-19 vaccines (E)	"A vaccine, that's just being made up as we speak like with no data, no—no real testing, but yet hydroxychloroquine has been approved by FDA treated for malaria for—for 57 years or 67 years and we already know, the effects and what it does and what it, what it is good for." (p. 4) (26)		
Complacency towards COVID-19 (U)	"I don't think that COVID will remain a threat for us for a long time...So why should I put extra artificial materials in my body?" (p. 4) (24)	Personal philosophies on health	
The idea that COVID-19 is less likely to affect racial and ethnic minorities (U)	"Most of the African-descended origin genes are resistant to the COVID." (p. 590) (23)		
The focus should be on improving baseline health (U)	"You have alkaline foods that you can put in your body that fight off the virus, you have immune support vitamins out here that can fight off virus." (p. 4) (26)		
Reliance on home remedies to protect against COVID-19 (U)	"You just give one teaspoon honey with seven flaxseeds every morning just give them, just to protect from viral." (p. 590) (23)		
Low vaccine uptake among social networks (U)	"Everybody that I spoke with, every individual that I spoke with was against the vaccine." (p. 4-5) (26)	Social norms	

Chapter 5

Recommendation from famous individuals and/or role-models would not persuade them (U)	"I was just speaking on Obama, like if he advocated for [a COVID-19 vaccine] I would still – I have to say no way, so I would think it will be still under that umbrella of evil." (p. 5) (26)		
Those willing to take a vaccine were considered foolish, less educated, or unable to make unbiased decisions (E)	"I have a few aunts that would take [a COVID-19 vaccine]...They are not from the sharper side of the family." (p. 5) (26)		
Lack of access to sufficiently understandable information (U)	"I don't know how the government receive it [COVID-19 information] at first, because I think... like I said, because they are giving a lot of confusion to the society. They are passing a lot of confusion " (p. 5) (24)		
More information needed in their own language (U)	"Some people can speak and some they can't understand about the English... I suggest that all these things should be in other languages as well." (p. 5) (24)	Lack of access to reliable information	
Wanting information specific to their communities (U)	"... for example, our Hispanic community, which is different from the African or White communities—how has it affected us, what are our risks..." (p. 7) (25)		
Inability to distinguish between real news and fake news (U)	"... I don't know if it's real, I don't know if it's fake. When you take it, it will change the DNA.... A lot of stories are flying." (p. 4) (24)		
Feeling conflicted about which sources to trust (U)	"For me, I would like to take the vaccine if that will make everything better. But the fake news is scaring me, so I don't know." (p. 4) (24)		
Concerns about costs associated with the vaccine (U)	"They should just make it equal for everybody to take the vaccine freely. Because some cannot afford to pay to take the vaccine." (p. 5) (24)	Lack of financial or geographical access	
Preference for familiar settings requiring minimal travel (E)	"It depends on the distance. Because as I said, we are not able to offer ourself to transport, we cannot pay for it." (p. 5) (24)		

Chapter 6: Other public health activities

This chapter comprises a portfolio of my other public health activities that meet the MAE minor competencies on “teaching field epidemiology” and completing a “lay summary”.

1. Teaching to first-year Scholars

As part of the MAE, second-year Scholars are required to deliver a lecture to first-year Scholars during their first courseblock. My fellow 2021 Scholars Keeley Allen, Justine Marshall, Jane McAllister, and Erin Flynn, and I delivered an online lecture entitled “Forget COVID! Why you should be afraid of AMR and what to do about it” on 11 March 2022. We collectively agreed on this topic given the growing threat that anti-microbial resistance (AMR) poses to the effective prevention and treatment of infections. Our lecture outlined why AMR is a public health issue, and described AMR surveillance systems in different jurisdictions, using Carbapenemase-producing Enterobacterales (CPE) as an example. I was the last speaker, and my section involved several quizzes that reinforced the participants’ understanding of the earlier sections. Because our lecture was running overtime, I had to rush my part. Despite this, the post-evaluation survey was largely positive, with fifteen of sixteen respondents reporting that they were “satisfied” or “very satisfied” with the lecture. There was some expected feedback on better time management, which I will keep in mind for future lectures. Overall, this was both enjoyable and enlightening; I am glad to have had this opportunity to teach others about this pressing public health issue (Appendix A).

2. Lessons from the field

The MAE also requires that Scholars develop a case study of a public health problem encountered in the field to maximise opportunities for peer-to-peer teaching and learning. My case study was based on my research in chapter three and involved a discussion of the applications of diagnostic test accuracy studies for estimating the accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people. I developed all lesson materials and distributed them to seven MAE 2021 Scholars. These included background readings on diagnostic test accuracy studies and wastewater-based epidemiology, and exercises involving calculations of sensitivity, specificity, and predictive values. I then facilitated the lesson via Zoom on 29 April 2022, where we discussed the participants’ responses and recapped the key learnings. Feedback at the end was very positive; however, these were not formally captured in a post-event evaluation, which I will make sure to do in future trainings. A key takeaway from this exercise was the power of teach-back; in teaching my peers, I was able to develop a better grasp of the concepts (Appendix B).

3. Evidence-based Medicine—London School of Paediatrics Day

During my candidature, I was invited by Dr. Lakmal Mudalige of the Royal Society of Medicine UK to speak at the *Evidence-based Medicine—London School of Paediatrics Day* on 27 October 2021. This workshop aimed to promote the application of evidence-based medicine within paediatrics and child health, and provide participants with an update on relevant tools, resources, and databases. My lecture explained how to critically appraise and design diagnostic test accuracy studies. Despite delivering the lecture at 01:00 AEST—while I was half asleep—the lecture was well-received. In the post-event evaluation, all participants thought the lecture was useful for their clinical practice. I take great satisfaction in sharing my knowledge about public health research and practice, and hope to incorporate more teaching in my future career (Appendix C).

4. 11th TEPHINET Global Scientific Conference

In 2022, the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET) held its 11th Global Scientific Conference in Panama from 4th to 9th September. This event provided a forum for TEPHINET-accredited Field Epidemiology Training Program (FETP) residents, graduates, and mentors worldwide to come together and learn about the latest in applied epidemiology from one another. As part of the event, Zoe Joo (a fellow MAE 2021 Scholar) and I were invited by Matthew Griffith (a PhD student at the ANU) to help design and facilitate a workshop entitled “Beyond principles: How do we use learning theories to facilitate learning experiences for FETP trainees?” This workshop aimed to address gaps in knowledge of experiential learning theories and adult learning principles among FETP trainers. To prepare for the workshop, we met weekly over the course of three months. We conceptualised an experience that was multi-modal, involving small-group discussions, poster presentations and a short lecture, as well as intermittent icebreakers and energisers to help keep the day engaging. The workshop was attended by eight people, half of whom were country FETP directors. In the post-event evaluation survey, all participants thought the workshop was useful for informing their respective FETP curricula. Through this experience, I became intimately acquainted with the time and energy required for delivering an engaging workshop. Furthermore, much of the materials I presented were new to me and were incredibly useful for informing my own teaching practice (Appendix D).

5. Casual/Sessional Academic post

During the MAE, I also held a Casual/Sessional Academic post at the ANU, where I delivered part of the medical curriculum to first- and second-year Doctor of Medicine and Surgery (MChD) students. The MChD is underpinned by four themes: 1) medical sciences,

2) clinical skills, 3) population health, and 4) professionalism and leadership. The first two years of the curriculum are built around problem-based learning (PBL) sessions that help consolidate the students' learnings from the four themes. Each week, the students are presented with a PBL case study, where they work through hypotheses and diagnoses in a scientific manner. My role involved leading population health tutorials and PBL sessions. This role has taught me how to exercise facilitation, coaching and mediation to empower my students to be creative and analytical thinkers, as well as cooperative and self-directed learners.

6. Monkeypox FAQ

Since mid-May 2022, monkeypox cases have been reported in multiple countries that are not endemic for monkeypox virus—including Australia—with reports of local transmission. In Victoria, a limited number of smallpox vaccines became available at the time of writing, prompting an influx of enquiries to the State Government of Victoria's Department of Health. To assist the social media team with their public engagements, I developed an FAQ on 16 August 2022. This involved translating biological and epidemiological concepts into a format digestible for a lay audience, noting sensitivities around the outbreak's disproportionate impact on men who have sex with men. My FAQ has since been used extensively by the social media team and exists as a live document that is updated as needed (Appendix E).

Appendices

Appendix A. Teaching to first-year Scholars: Forget COVID! Why you should be afraid of AMR and what to do about it.



FORGET COVID!

Why you should be afraid of AMR and what to do about it

OFFICIAL



LEARNING OBJECTIVE

By the end of the session, scholars will be able to **describe** why antimicrobial resistance (AMR) is a public health issue and **describe** the components of the Australian AMR surveillance system, using carbapenemase-producing enterobacteriales (CPE) as an example

OFFICIAL

HOW DO WE KNOW IF YOU REACH THE OBJECTIVE?

FORMATIVE LEARNING ASSESSMENT

Each section will have a short learning objective at the start

You will be asked at the end of each section if you feel you have met that objective. Please use one of the below Zoom reactions



I got this



Raise Hand

I'm almost there and I have a question to help me meet the section objective



I don't got this

There is time at the end of each section to ask questions to help you meet the objective

We will also do a check in at the end against the section learning objective

OFFICIAL



AMR in public health

What is AMR and why should epis care

01

AMR/MRO surveillance

How do we conduct surveillance for AMR in Australia?

02

AMR and genomics

A crash course in the microbiology of AMR

03

Example: CPE surveillance in SA

Detecting CPE outbreaks

04

Example: Epidemiology in Vic

A world-leading study combining genomics and epi

05

OFFICIAL



01. AMR in public health

OFFICIAL



SECTION OBJECTIVE

By the end of this section, scholars will be able to:

- Define antimicrobial resistance (AMR)
- Describe at least three reasons why AMR is a public health issue

OFFICIAL

TIME FOR SOME DEFINITIONS!

Antimicrobial resistance (AMR): **process** when a microorganism that once responded to a drug changes over time and no longer responds to that drug.

WHO - Antimicrobial resistance 2021

Multidrug resistant organism (MRO or MDRO): a **microorganism** that is resistant to one or more antimicrobial agent.

CDC - MDRO Definition 2015

WE ARE



MROS

Susceptible to drug





Resistant to drug (an MRO)



Source: Amineza Talehkhani

OFFICIAL

SO WHAT?

Why should field epidemiologists care about antimicrobial resistance?

<https://pollev.com/forgetcovid813>

Because who doesn't love a poll??

OFFICIAL

CHECK IN!

SECTION OBJECTIVE

By the end of this section, scholars will be able to:

- Define antimicrobial resistance (AMR)
- Describe at least three reasons why AMR is a public health issue



 Raise Hand



OFFICIAL



02. AMR surveillance

OFFICIAL

By the end of this section, scholars will be able to:

By the end of this section, scholars will be able to:

- ## SECTION OBJECTIVE

By the end of this section, scholars will be able to:

 - Understand some of the different ways in which surveillance for AMR operates in Australia
 - Identify some of the issues and challenges with surveillance for AMR



OFFICIAL

How do we conduct surveillance for AMR?



Multidrug resistant organisms (MROs)

How Antibiotic Resistance Happens

The infographic is titled "How Antibiotic Resistance Happens" in a large, bold, black font. Below the title, there are four numbered steps, each with a text box and a corresponding illustration in a hexagonal frame. Step 1: "Lots of germs. A few are drug resistant." shows a mix of blue and pink rod-shaped bacteria. Step 2: "Antibiotics kill bacteria causing the illness, as well as good bacteria protecting the body from infection." shows blue bacteria being killed by 'X' marks, while pink bacteria survive. Step 3: "The drug-resistant bacteria are now allowed to grow and take over." shows only pink bacteria remaining. Step 4: "Some bacteria give their drug-resistance to other bacteria, causing more problems." shows a pink bacteria with a red arrow pointing to another pink bacteria, indicating the transfer of resistance.

- 1.** Lots of germs. A few are drug resistant.
- 2.** Antibiotics kill bacteria causing the illness, as well as good bacteria protecting the body from infection.
- 3.** The drug-resistant bacteria are now allowed to grow and take over.
- 4.** Some bacteria give their drug-resistance to other bacteria, causing more problems.

Source: Centers for Disease Control and Prevention

OFFICIAL

Multidrug resistant organisms

Microorganisms (mostly bacteria) are resistant to one or more classes of antimicrobials

E.g. Methicillin-resistant *Staphylococcus aureus* (MRSA)

CPE



Official

What is CPE?

Carbapenemase-producing Enterobacterales

Enterobacterales

Order

Family

Genus

Species

Order	Family	Genus	Species
Enterobacterales	Enterobacteriaceae	Citrobacter	Citrobacter amalonitidis Citrobacter braakii Citrobacter freundii Citrobacter koseri
		Enterobacter	Enterobacter cloacae Enterobacter gergoviae Enterobacter sakazakii
		Escherichia	Escherichia coli Escherichia fergusonii
		Klebsiella	Klebsiella pneumoniae Klebsiella oxytoca Klebsiella terrigena
		Morganellaceae	Morganella morganii Morganella morganii Morganella morganii
	Yersiniaceae	Yersinia	Yersinia enterocolitica Yersinia enterocolitica
		Serratia	Serratia marcescens

What is CPE?

Carbapenemase-producing *Enterobacteriales*

Amber data

CPE: the five most

Accession number	Species	CPE	CPE type
U00096	<i>E. coli</i>	+	KPC
U00097	<i>E. coli</i>	+	KPC
U00098	<i>E. coli</i>	+	KPC
U00099	<i>E. coli</i>	+	KPC
U00100	<i>E. coli</i>	+	KPC
U00101	<i>E. coli</i>	+	KPC
U00102	<i>E. coli</i>	+	KPC
U00103	<i>E. coli</i>	+	KPC
U00104	<i>E. coli</i>	+	KPC
U00105	<i>E. coli</i>	+	KPC
U00106	<i>E. coli</i>	+	KPC
U00107	<i>E. coli</i>	+	KPC
U00108	<i>E. coli</i>	+	KPC
U00109	<i>E. coli</i>	+	KPC
U00110	<i>E. coli</i>	+	KPC
U00111	<i>E. coli</i>	+	KPC
U00112	<i>E. coli</i>	+	KPC
U00113	<i>E. coli</i>	+	KPC
U00114	<i>E. coli</i>	+	KPC
U00115	<i>E. coli</i>	+	KPC
U00116	<i>E. coli</i>	+	KPC
U00117	<i>E. coli</i>	+	KPC
U00118	<i>E. coli</i>	+	KPC
U00119	<i>E. coli</i>	+	KPC
U00120	<i>E. coli</i>	+	KPC
U00121	<i>E. coli</i>	+	KPC
U00122	<i>E. coli</i>	+	KPC
U00123	<i>E. coli</i>	+	KPC
U00124	<i>E. coli</i>	+	KPC
U00125	<i>E. coli</i>	+	KPC
U00126	<i>E. coli</i>	+	KPC
U00127	<i>E. coli</i>	+	KPC
U00128	<i>E. coli</i>	+	KPC
U00129	<i>E. coli</i>	+	KPC
U00130	<i>E. coli</i>	+	KPC
U00131	<i>E. coli</i>	+	KPC
U00132	<i>E. coli</i>	+	KPC
U00133	<i>E. coli</i>	+	KPC
U00134	<i>E. coli</i>	+	KPC
U00135	<i>E. coli</i>	+	KPC
U00136	<i>E. coli</i>	+	KPC
U00137	<i>E. coli</i>	+	KPC
U00138	<i>E. coli</i>	+	KPC
U00139	<i>E. coli</i>	+	KPC
U00140	<i>E. coli</i>	+	KPC
U00141	<i>E. coli</i>	+	KPC
U00142	<i>E. coli</i>	+	KPC
U00143	<i>E. coli</i>	+	KPC
U00144	<i>E. coli</i>	+	KPC
U00145	<i>E. coli</i>	+	KPC
U00146	<i>E. coli</i>	+	KPC
U00147	<i>E. coli</i>	+	KPC
U00148	<i>E. coli</i>	+	KPC
U00149	<i>E. coli</i>	+	KPC
U00150	<i>E. coli</i>	+	KPC
U00151	<i>E. coli</i>	+	KPC
U00152	<i>E. coli</i>	+	KPC
U00153	<i>E. coli</i>	+	KPC
U00154	<i>E. coli</i>	+	KPC
U00155	<i>E. coli</i>	+	KPC
U00156	<i>E. coli</i>	+	KPC
U00157	<i>E. coli</i>	+	KPC
U00158	<i>E. coli</i>	+	KPC
U00159	<i>E. coli</i>	+	KPC
U00160	<i>E. coli</i>	+	KPC
U00161	<i>E. coli</i>	+	KPC
U00162	<i>E. coli</i>	+	KPC
U00163	<i>E. coli</i>	+	KPC
U00164	<i>E. coli</i>	+	KPC
U00165	<i>E. coli</i>	+	KPC
U00166	<i>E. coli</i>	+	KPC
U00167	<i>E. coli</i>	+	KPC
U00168	<i>E. coli</i>	+	KPC
U00169	<i>E. coli</i>	+	KPC
U00170	<i>E. coli</i>	+	KPC
U00171	<i>E. coli</i>	+	KPC
U00172	<i>E. coli</i>	+	KPC
U00173	<i>E. coli</i>	+	KPC
U00174	<i>E. coli</i>	+	KPC
U00175	<i>E. coli</i>	+	KPC
U00176	<i>E. coli</i>	+	KPC
U00177	<i>E. coli</i>	+	KPC
U00178	<i>E. coli</i>	+	KPC
U00179	<i>E. coli</i>	+	KPC
U00180	<i>E. coli</i>	+	KPC
U00181	<i>E. coli</i>	+	KPC

Figure 1. Global distribution of carbapenemases in Enterobacteriaceae, by country and region.

Legend:

Carbapenemase	IMP	KPC	NDM	OXA	VIM
Endemic/nationwide distribution	Red dot	Green dot	Blue dot	Purple dot	Pink dot
Significant outbreak/ regional spread	Red dot with border	Green dot with border	Blue dot with border	Purple dot with border	Pink dot with border
Sporadic outbreak/ acquisition	Red dot with border	Green dot with border	Blue dot with border	Purple dot with border	Pink dot with border

Bar chart: Percentage of countries with carbapenemase spread by region.

Region	Percentage
Europe	~45%
Africa	~35%
Asia	~25%
Oceania	~15%

Source: JACM, Volume 210, November 1, 15 (2017), <https://doi.org/10.1093/jac/dkx322>

OFFICIAL

JACM, Volume 210, November 1, 15 (2017)

OXFORD

How does it work in NSW?



OFFICIAL

What is notifiable in NSW?

Carbapenemase-producing *Enterobacteriales* (CPE) infection or colonisation – since Feb 2019

Case definition in NSW
Confirmed CPE Case: A person with a species of *Enterobacteriales* isolated from routine clinical or screening specimens (infection or colonisation) where a carbapenemase gene is detected in a sample or isolate irrespective of phenotypic susceptibility.

Candida auris infection and colonisation – since June 2020

In NSW:

- We count the organism, not the gene
- We don't collect any enhanced surveillance info – travel history, previous hospitalisation
- We don't know if a notification is a colonisation or an infection
- Can be colonised for years

OFFICIAL

When do specimens get collected?

Screening varies between facilities

What is the problem with this?

Which criteria/settings trigger testing?
Are these uniform?
Agreed statewide set of 'moments for testing'?
Are these suitable (clinical/surveillance)?
Who could we be missing?

OFFICIAL

Colonisation vs infection

Specimens from NON-STERILE sites, e.g. faeces

In most cases, people carry CPE in their gut without it causing any symptoms or an infection. This is known as colonisation.

If you have CPE, extra precautions will need to be taken on admission to a health care or residential care facility to prevent CPE spreading to other people

Specimens from normally sterile sites, e.g. blood

What do we do with the knowledge that there are 100 colonized people? Or 100 infections? Are these different, or can we lump them together?

OFFICIAL

Challenges of surveillance for MROs

The shift from health care facility to statewide

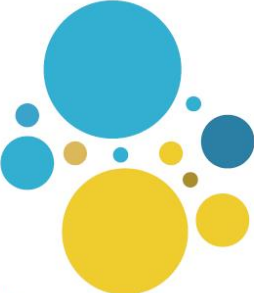
Shame, stigma and secrecy!

Without combining epi and genomics, you can't solve the problem



OFFICIAL

What about other jurisdictions?



OFFICIAL

What about other jurisdictions?



WESTERN AUSTRALIA
Carbapenem-resistant *Enterobacteriaceae* (CRE) infection or colonisation
Mecillin-resistant *Staphylococcus aureus* (MRSA) infection or colonisation
Vancomycin-resistant enterococci (VRE) infection or colonisation

SOUTH AUSTRALIA
Candida aurtis
Carbapenemase-producing *Enterobacteriales* (CPE)

TASMANIA
Carbapenemase-producing *Enterobacteriaceae*
Staphylococcus aureus bacteraemia
Vancomycin Resistant *Enterococcus*

VICTORIA
Candida aurtis - Urgent
Carbapenemase-producing *Acinetobacter* spp. - Routine
Carbapenemase-producing *Enterobacteriales* - Routine
Carbapenemase-producing *Pseudomonas* spp. - Routine
VanA-type vancomycin-resistant *Enterococcus* (VRE) - Routine

OFFICIAL

AURA & CARAlerts

www.safetyandquality.gov.au

AUSTRALIAN COMMISSION on SAFETY and QUALITY in HEALTH CARE

National Alert System for Critical Antimicrobial Resistances (CARAlert)

The National Alert System for Critical Antimicrobial Resistances (CARAlert) collects data on nationally agreed priority organisms with critical resistance to first-line antimicrobials, agreed to provide timely information and advice to regional clinicians, policy makers and system managers in regard to antimicrobial resistance in Australia.

Antimicrobial Use and Resistance in Australia (AURA) Surveillance System provides data and information to support Australia's strategic response to AMR. Established in 2014.

The AURA Surveillance System collects data from hospital and community settings to provide a comprehensive national and regional picture of antimicrobial usage and AMR.

CAR Alerts – reporting on high priority MROs

Voluntary, national surveillance

OFFICIAL

Public health actions arising from MRO surveillance

What are we trying to achieve?

- Estimate scope and magnitude of MROs
- Review the geographic and demographic distribution
- Detect outbreaks
- Evaluate control measures
- Program monitoring
- Health system monitoring for resource allocation
- Policy analysis
- Generate hypothesis and stimulate applied research

Tracking MROs across facilities – we know that transmission occurs in different facilities, if we want to break transmission chains we need to have that higher view – and we need to combine the epi and the genomics...

How do we do that?

OFFICIAL

CHECK IN!

SECTION OBJECTIVE

By the end of this section, scholars will be able to:

- Understand some of the different ways in which surveillance for AMR operates in Australia
- Identify some of the issues and challenges with surveillance for AMR

OFFICIAL

03. AMR and genomics

OFFICIAL

SECTION OBJECTIVE

By the end of this section, scholars will be able to:

- Describe the mechanisms by which bacteria acquire resistance
- Identify basic concepts and terminology around AMR genomics and whole genome sequencing
- Describe how genomics can be used for AMR surveillance and some of the current challenges.

OFFICIAL

WORDLE TIME!!!

<https://mywordle.strivemath.com/?word=csehd>

HINT: WHERE IS RESISTANCE FOUND?

NEVER ENOUGH WORDLE

OFFICIAL

INTRO TO THE BACTERIAL GENOME

Chromosome

- Contains majority of bacterial DNA

Mobile genetic elements

The most important for AMR:

- Plasmids
- Transposons

OFFICIAL

HOW DO BACTERIA ACQUIRE RESISTANCE?

Intrinsic resistance

- Bacterial species can naturally have resistance genes in the genome or lack the antibiotic target

Acquired resistance

Vertical transmission

- chromosomal mutation/gene acquisition and clonal expansion

Horizontal transmission

- Can result in gene transfer between same or different species
- Multiple resistance genes can be carried by the same mobile genetic elements
- Possible to evolve towards multi-drug resistance, hyper virulence

Source: Davies G, and Summers M (2014) How to fight back against antibiotic resistance. *Science* 345:40-41.

OFFICIAL

HOW IS RESISTANCE DETECTED?

Culture based antimicrobial susceptibility testing (AST)

Phenotypic

Question: How do organisms respond to antibiotics?

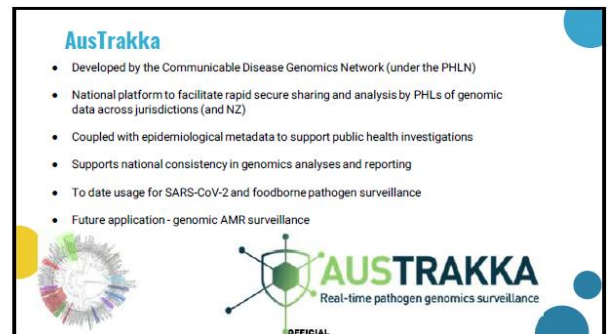
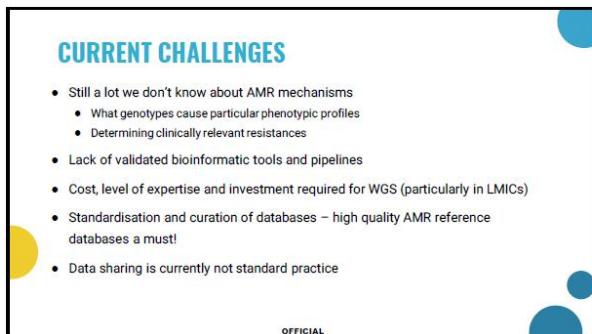
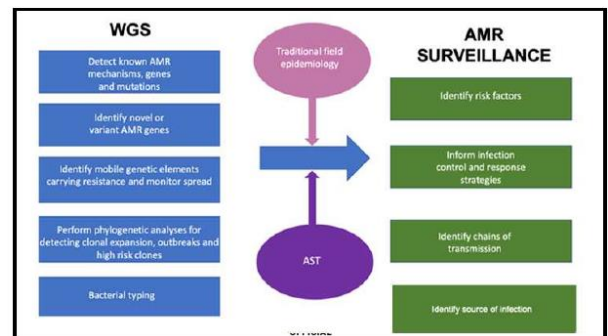
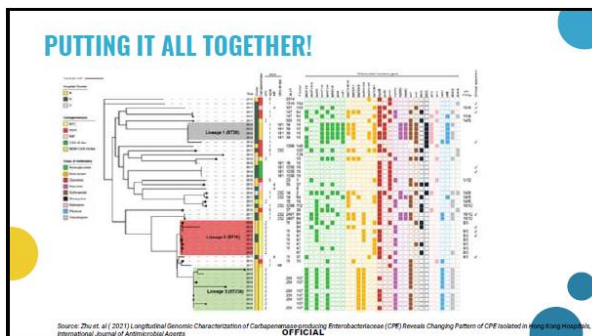
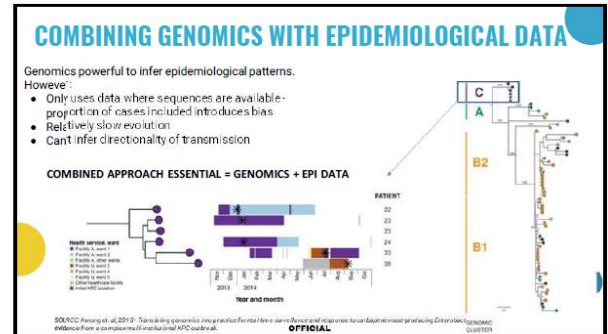
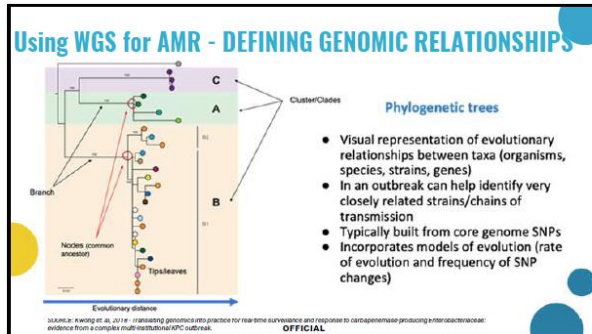
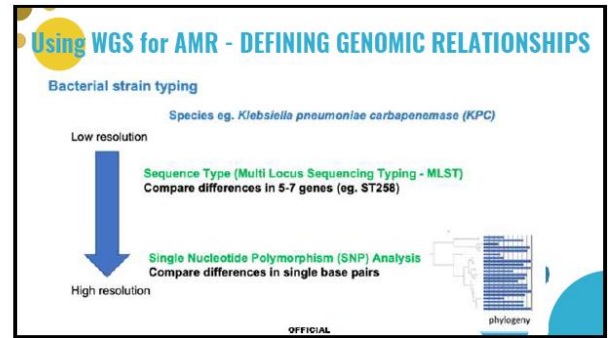
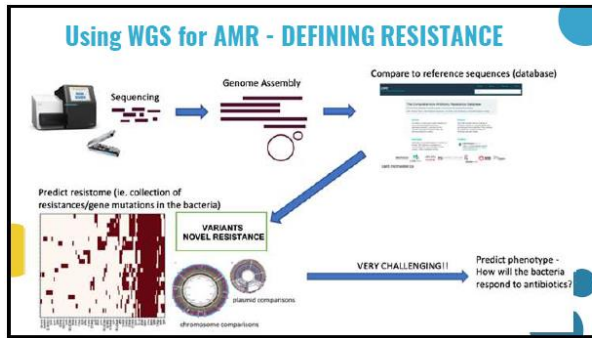
Molecular methods

Genotypic

Question: Is there a resistance gene or mechanism present?

Whole Genome Sequencing – can tell you the resistance genes and so much more!

OFFICIAL



CHECK IN!

SECTION OBJECTIVE

By the end of this section, scholars will be able to:

- Describe the mechanisms by which bacteria acquire resistance
- Identify basic concepts and terminology around genomics and whole genome sequencing
- Describe how genomics can be used for AMR surveillance and describe some of the current challenges

👍 Raise Hand

04. Example: CPE surveillance in South Australian

OFFICIAL

SECTION OBJECTIVE

By the end of this lesson, scholars will be able to describe the utility of WGS for CPE surveillance and outbreak investigations

OFFICIAL

Clinical characteristics of CPE

- Once colonised with CPE long-term carriage is likely
- Silent colonisation may result in a source patient screening positive after a patient(s) whom they transmitted to
- The rate of infection following exposure/colonisation with CPE higher compared with bacteria of the same species that do not produce carbapenemases
- Plasmids that carry genes encoding for carbapenemase enzymes can be highly mobile, transferring resistance to new species
- Abx therapy increases the susceptibility of non-colonised patients becoming colonised on exposure to CPE
- Abx therapy increases the shedding of CPE by patients already colonised
- Release of Abx into the healthcare environment, especially drains, can promote persistent carriage in the environment

Outbreak investigation

Epidemiologic Steps of an Outbreak Investigation

1. Prepare for field work
2. **Establish the existence of an outbreak**
3. **Verify the diagnosis**
4. **Construct a working case definition**
5. **Find cases systematically and record information**
6. Perform descriptive epidemiology
7. Develop hypotheses
8. Evaluate hypotheses epidemiologically
9. As necessary, reconsider, refine, and re-evaluate hypotheses
10. Compare and reconcile with laboratory and/or environmental studies
11. **Implement control and prevention measures**
12. Initiate or maintain surveillance
13. Communicate findings

Establish the existence of an outbreak

- See positive isolates from 2017/2018
- Check with the laboratories to see if there were any changes in testing
- Where have the isolates come from
- Confirm CPE screening and reporting activities

Is this an outbreak?

www.poller.com/forgetcovid183

Confirmed CPE positive isolates by species type, South Australia, April 2018 - Jan 2021

Number of isolates positive for Carbapenemase resistant genes

Month of onset

■ *K. pneumoniae* ■ *E. coli* ■ *K. oxytoca* ■ *A. baumannii* ■ *K. aerogenes* ■ *E. cloacae* ■ Unknown

Establish the existence of an outbreak

Appears to be an increase in NDM positive isolates in 2019

Confirmed CPE positive isolates by resistant gene type, South Australia, April 2018 - Jan 2021

Number of isolates positive for Carbapenemase resistant genes

Month of onset

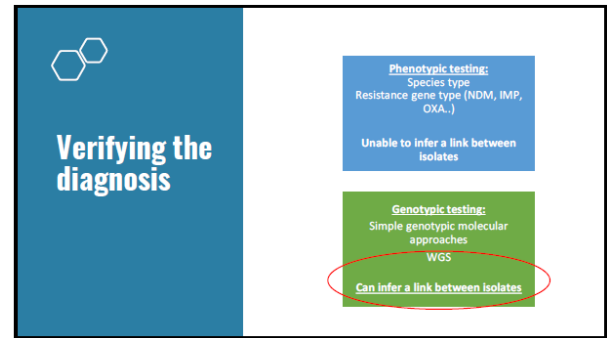
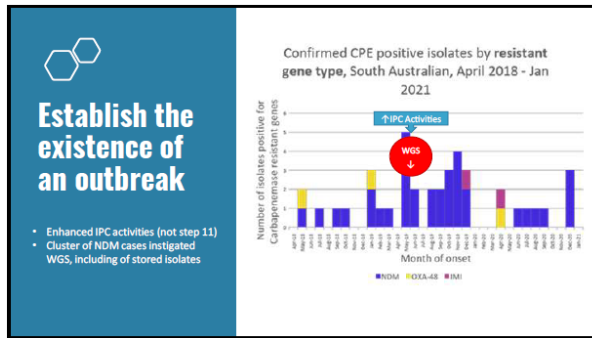
■ NDM ■ GES-48 ■ IMI

Establish the existence of an outbreak

14 cases reported to CARAlert in 2017 and 2018 combine

Most cases related to interstate and overseas travel or hospitalisation

By July 2019 there were 12 CPE cases in a single hospital



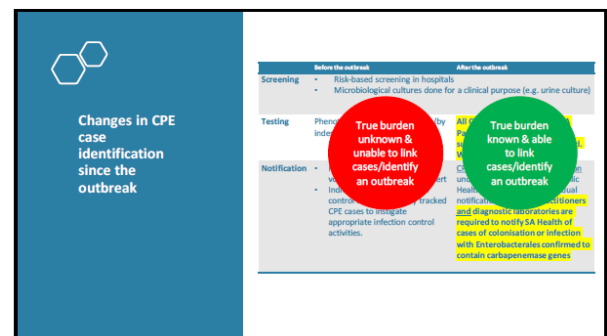
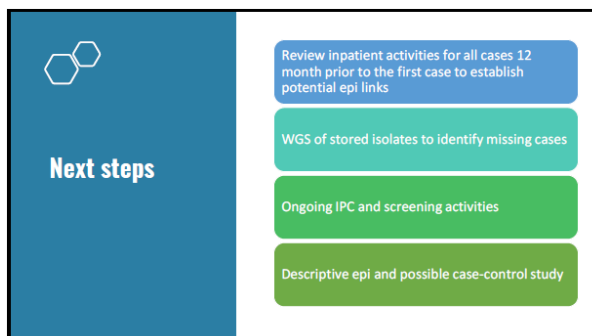
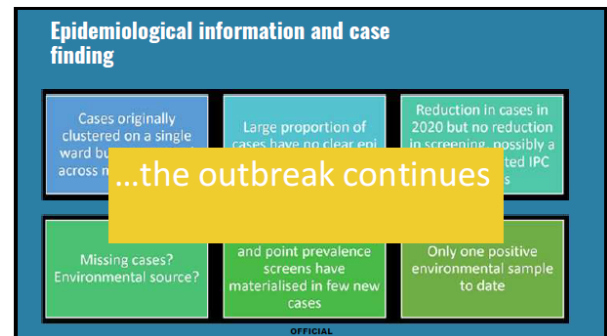
Outbreak cases

- WGS identified 25 patients carried the same NDM-4 resistance gene
- Most cases due to one strain of *K. pneumoniae* (37/39)
- Multiple species - evidence of horizontal transfer (including in the same patient)
- Same plasmid (IncFII) present among nearly all cases

Case definition: inpatients with NDM-4 CPE isolated from clinical or screening specimens during the outbreak period

Carbapenemase		Organism	Sequence type	IncFII plasmid		Total
Gene allele	Species			Res	No/Unknown	
NDM-4	<i>K. pneumoniae</i>	29	17	1	17	
		26	2	1	3	
	Unidentified	1			1	
	<i>E. coli</i>	Unidentified	4	2	6	
	<i>E. aerogenes</i>	Unidentified	1		1	
	Unidentified	1			1	
		27	3		29*	

*No patients isolated with multiple species carrying the NDM-4 resistance gene



CHECK IN!

SECTION OBJECTIVE

By the end of this lesson, scholars will be able to describe the utility of WGS for CPE surveillance and outbreak investigations

👍 Raise Hand

OFFICIAL

05. Example: Integrated Genomic & Epidemiological Surveillance in Victoria

OFFICIAL

SECTION OBJECTIVE

By the end of the section, scholars will be able to:

- To briefly describe Victoria's integrated genomic and epidemiological surveillance system for CPE
- To interpret figures to describe the epidemiology of CPE in Victoria from 2016 to 2018

OFFICIAL

Search and Genetic Impact of an Integrated Genomic and Epidemiological Surveillance and Response Program for Control of Carbapenemase-producing Enterobacteriaceae

- A prospective multimodal intervention including active screening, carrier isolation, centralised case investigation, and comparative pathogen genomics was implemented in 2015
- All diagnostic labs referred suspected CPE isolates to the state reference lab for confirmatory testing, whole-genome sequencing, and investigation
- Epidemiological data were collected for all persons from whom an isolate with a confirmed carbapenemase gene originated
- Trends in CPE incidence and clinical presentation, risk factors, and local transmission over the program's first 3 years (2016–2018) were analysed in this paper

OFFICIAL

QUIZ TIME!!!

www.pollev.com/forgetcovid183

OFFICIAL

RISK FACTORS FOR CPE ACQUISITION

Carbapenemase gene group	N cases	Suspected source of acquisition	Travel, previous four years	N male (%)	Median Age (IQR)
IMP	142	Overseas acquisition ^a 65%, Local cluster 15%, Local outbreak 10%, Unable to determine source 10%	No travel 65%, Unknown 15%, South and central Asia 10%, South-east Asia 10%, Middle East 10%, Europe 10%, Multiple or other 10%	85 (60%)	65 (46 - 77)
NDM	114	Overseas acquisition ^a 65%, Local cluster 15%, Local outbreak 10%, Unable to determine source 10%	No travel 65%, Unknown 15%, South and central Asia 10%, South-east Asia 10%, Middle East 10%, Europe 10%, Multiple or other 10%	69 (61%)	60 (30 - 60)
OXA-48-like	75	Overseas acquisition ^a 65%, Local cluster 15%, Local outbreak 10%, Unable to determine source 10%	No travel 65%, Unknown 15%, South and central Asia 10%, South-east Asia 10%, Middle East 10%, Europe 10%, Multiple or other 10%	38 (51%) ^a	63 (36 - 73)
KPC	45	Overseas acquisition ^a 65%, Local cluster 15%, Local outbreak 10%, Unable to determine source 10%	No travel 65%, Unknown 15%, South and central Asia 10%, South-east Asia 10%, Middle East 10%, Europe 10%, Multiple or other 10%	27 (59%)	70 (59 - 78)
NDM, OXA-48-like	7	Overseas acquisition ^a 65%, Local cluster 15%, Local outbreak 10%, Unable to determine source 10%	No travel 65%, Unknown 15%, South and central Asia 10%, South-east Asia 10%, Middle East 10%, Europe 10%, Multiple or other 10%	4 (57%)	68 (56 - 77)
Other	18	Overseas acquisition ^a 65%, Local cluster 15%, Local outbreak 10%, Unable to determine source 10%	No travel 65%, Unknown 15%, South and central Asia 10%, South-east Asia 10%, Middle East 10%, Europe 10%, Multiple or other 10%	7 (39%)	58 (43 - 70)

OFFICIAL

LOCAL ACQUISITION OF CPEs IN VICTORIA

OFFICIAL

CASE STUDY - OUTBREAK INVESTIGATION

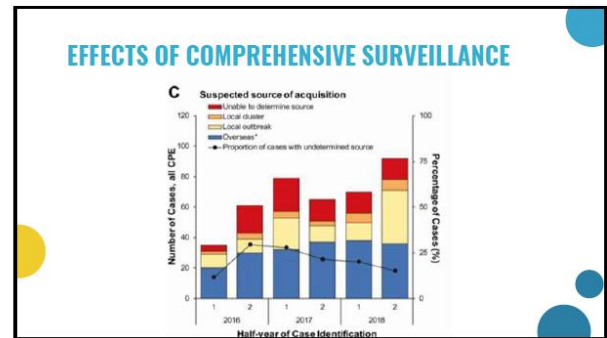
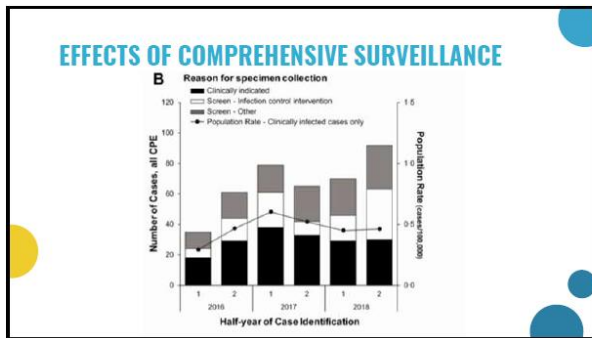
OFFICIAL

CASE STUDY - OUTBREAK INVESTIGATION

OFFICIAL

EFFECTS OF COMPREHENSIVE SURVEILLANCE

OFFICIAL



CONCLUSIONS

Centralised CPE control programs can:

- Increase case ascertainment
- Resolve risk factors
- Identify local transmission through prospective genomic and epidemiological surveillance.

Methodologies are transferable to low-prevalence settings and MROs globally.

OFFICIAL

CHECK IN!

SECTION OBJECTIVE

By the end of the section, scholars will be able to:

- Briefly describe Victoria's integrated genomic and epidemiological surveillance system for CPE
- Interpret figures to describe the epidemiology of CPE in Victoria from 2016 to 2018

🔴 Raise Hand 🗨️

OFFICIAL

FINAL CHECK IN!

LEARNING OBJECTIVE

By the end of the session, scholars will be able to **describe** why antimicrobial resistance (AMR) is a public health issue and **describe** the components of the Australian AMR surveillance system, using carbapenemase-producing enterobacteriales (CPE) as an example

🔴 Raise Hand 🗨️

OFFICIAL

THANK YOU!

Final evaluation (thank you in advance!)

https://anu.au1.qualtrics.com/jfe/form/SV_dpo06mikhac0e

Don't be a stranger!

keely.allen@anu.edu.au
justine.marshall@anu.edu.au
jane.mcallister@anu.edu.au
erin.flynn@anu.edu.au
aidan.yuen@anu.edu.au

OFFICIAL

Appendix B. Lessons from the field: Estimating the test accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in catchments.

Lessons from the field: Estimating the test accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in catchments

Learning outcomes:

- **Describe** how wastewater surveillance can serve as a diagnostic test for the presence of SARS-CoV-2 infected people in catchments
- **Apply** diagnostic test accuracy studies to estimate the accuracy of wastewater surveillance
- **Calculate** and **interpret** key measures of test accuracy

Wastewater-based epidemiology

As part of the State Government of Victoria's COVID-19 response, wastewater surveillance was implemented to help detect new incursions of COVID-19. Wastewater samples are collected from sewer networks and analysed for SARS-CoV-2 fragments using Quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR) (1). Given the high sensitivity and specificity of qRT-PCR, wastewater surveillance can serve as a diagnostic test for the presence of SARS-CoV-2 infected people in the community (2,3).

Catchments that have positive SARS-CoV-2 detections with no known recent SARS-CoV-2 infected residents or visitors have been targeted for rapid and localised public health action. Wastewater sampling does not hinge on individual action—such as recognising symptoms and seeking nasopharyngeal tests—and can therefore contribute important information about COVID-19 transmission that cannot be obtained otherwise, particularly for individuals who are asymptomatic, pre-symptomatic or undiagnosed (1).

Viral shedding into wastewater may occur directly (e.g., coughing in a shower or using the toilet) or indirectly (e.g., washing hands and clothes that contain virus) (4). Viral shedding from the digestive system often continues beyond the symptomatic period (5). For example, one infected individual was found to excrete the virus in faeces for up to 20 weeks (6).

A positive SARS-CoV-2 detection in wastewater could therefore be the result of an individual's non-infectious shedding period; this then poses a limitation to the program's utility for case detection. Viral excretion in faeces also varies between individuals, with limited data showing wide variability (7-9). And of those who do shed SARS-CoV-2 in their

faeces, the virus is likely to degrade rapidly in wastewater, especially at higher ambient temperatures and in the presence of detergents and other substances (10).

Considering these limitations, how can we evaluate the accuracy of wastewater surveillance for detecting SARS-CoV-2 infected people? Elucidating this question will help us understand its utility as a primary early detection tool to inform timely public health action.

Diagnostic test accuracy studies

This is where diagnostic test accuracy studies come in! These studies aim to assess the accuracy of a diagnostic test. They typically involve a sample population who are given the index test—i.e., the test the researchers are evaluating. The participants are also given a reference test, or “gold standard”, which can verify the presence or absence of the target condition. By cross classifying the results of the index test against those of the reference test, we can work out the accuracy of that index test (11) (Figure 1).

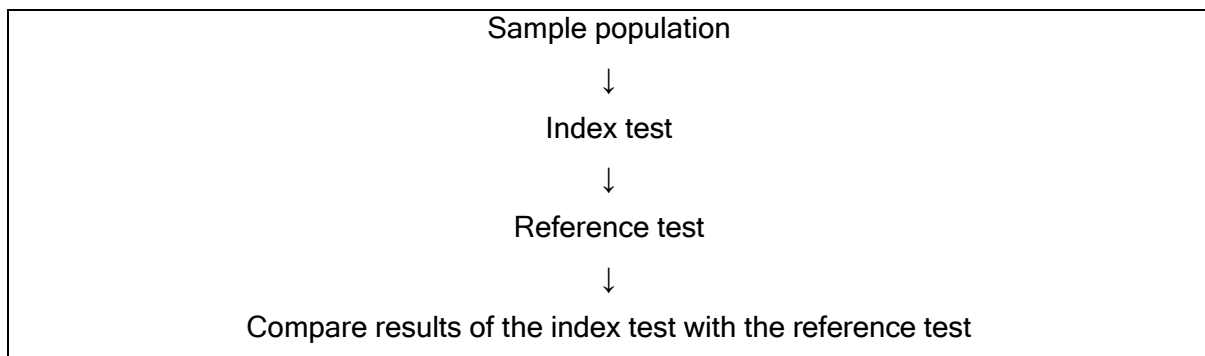


Figure 1. Schematic of diagnostic test accuracy study designs.

This produces a two-by-two table giving the number of true positives, false positives, false negatives, and true negatives (Table 1).

Table 1. Two-by-two table comparing results of an index test against those of a reference test.

		Reference test	
		Outcome +	Outcome -
Index test	Test +	True positive (a)	False positive (b)
	Test -	False negative (c)	True negative (d)

Measures of test accuracy

Sensitivity measures the proportion of participants with the target condition (positive reference test) who also return a positive index test result, i.e., the true-positive proportion. Specificity measures the proportion of participants without the target condition (negative reference test) who also return a negative index test result, i.e., the true-negative proportion. The positive predictive value (PPV) is the proportion of participants with a positive index test result who have the target condition (positive reference test). The negative predictive value (NPV) is the proportion of participants with a negative index test result who do not have the target condition (negative reference test). Calculations for these measures of test accuracy are given in Figure 2.

Sensitivity = $a/(a + c)$
Specificity = $d/(b + d)$
PPV = $a/(a + b)$
NPV = $d/(c + d)$

Figure 2. Calculations for accuracy measures using the two-by-two table given in Table 1.

Sensitivity and specificity are unaffected—while PPV and NPV *are* affected—by the prevalence of the outcome. Sensitivity and specificity are therefore inherent to a diagnostic test. A useful mnemonic for applying sensitivity and specificity calculations to practice is the SPIN/SNOUT mnemonic (Figure 3).

Figure 3. SPIN/SNOUT mnemonic for applying sensitivity and specificity calculations.

SPIN: <i>Specific</i> test is <i>P</i>ositive → rules the outcome <i>IN</i> SNOUT: <i>S</i>ensitive test is <i>N</i>egative → rules the outcome <i>OUT</i>
--

Scenario

You've been tasked by the State Government of Victoria's Department of Health to evaluate the accuracy of wastewater surveillance for detecting the presence of SARS-CoV-2 infected people in catchments. For this project, you've opted to conduct a diagnostic test accuracy study for the period 25 August 2020 to 27 September 2021. The index test is the wastewater test result, while the reference test is the presence or absence of known infected people in catchments. You don't know the exact locations of where infected people were using the bathroom and shedding in catchments (obviously!), so you used their residential addresses as the best proxy (Table 2).

Table 2. Two-by-two table comparing wastewater test results against the presence of known SARS-CoV-2 infected people resident in catchments.

		Known SARS-CoV-2 infected people resident in catchments (reference test)	
		Present	Absent
Wastewater test result (index test)	Positive	True positive (a)	False positive (b)
	Negative	False negative (c)	True negative (d)

Crude analysis

When people are assumed to shed at -2 to +7 days around symptom onset for symptomatic individuals and testing date for asymptomatic individuals, the results of the two-by-two table are given in Table 3.

Table 3. Two-by-two table comparing wastewater test results against the presence of known SARS-CoV-2 infected people resident in catchments.

		Known SARS-CoV-2 infected people resident in catchments (reference test)	
		Present	Absent
Wastewater test result (index test)	Positive		
	Negative		

Exercise 1. Calculate the sensitivity, specificity, PPV and NPV of SARS-CoV-2 wastewater surveillance using the two-by-two table in Table 3 and describe your results.

Exercise 2. Considering the SPIN/SNOUT mnemonic (Figure 3), how should wastewater surveillance be best used in the COVID-19 response?

Stratified analysis (lockdowns)

Victoria was subject to variable stay-at-home orders throughout the study period. We can stratify our dataset to assess the accuracy of wastewater surveillance during non-lockdown (Table 4) and lockdown days (Table 5).

Table 4. Two-by-two table comparing wastewater test results against the presence of known SARS-CoV-2 infected people resident in catchments during days without lockdowns.

		Known SARS-CoV-2 infected people resident in catchments (reference test)	
		Present	Absent
Wastewater test result (index test)	Positive		
	Negative		

Table 5. Two-by-two table comparing wastewater test results against the presence of known SARS-CoV-2 infected people resident in catchments during days with lockdowns.

		Known SARS-CoV-2 infected people resident in catchments (reference test)	
		Present	Absent
Wastewater test result (index test)	Positive		
	Negative		

Exercise 3. Calculate the sensitivity and specificity of wastewater surveillance during days with and without stay-at-home orders and discuss the possible reasons for any differences observed (TIP: consider the limitations with the reference test).

Stratified analysis (sampling methods)

The program uses three different sampling methods. Grab sampling provides a crude point-in-time sample. In a low caseload context, wide dispersal of the virus in smaller catchments is not expected. Rather, bolus type dispersal is likely to predominate, so only intermittent positive tests with fortuitous timing would be expected from grab samples (12) (Table 6).

Composite sampling uses autosamplers and flow meters to take frequent flow- and time-proportional samples (13). Its utility is often limited by installation and maintenance costs, equipment availability, safety concerns, and excessive sampling depths (Table 7).

Finally, in passive sampling, a device is deployed in a waterbody for a period to allow for pollutants to interact with the device (13). This presents a cheap, safe, and easy alternative to composite sampling, and currently predominates the program (Table 8).

Table 6. Two-by-two table of wastewater test results using grab sampling, compared to the presence of known SARS-CoV-2 infected people resident in catchments.

		Known SARS-CoV-2 infected people resident in catchments (reference test)	
		Present	Absent
Wastewater test result (index test)	Positive		
	Negative		

Table 7. Two-by-two table of wastewater test results using composite sampling, compared to the presence of known SARS-CoV-2 infected people resident in catchments.

		Known SARS-CoV-2 infected people resident in catchments (reference test)	
		Present	Absent
Wastewater test result (index test)	Positive		
	Negative		

Table 8. Two-by-two table of wastewater test results using passive sampling, compared to the presence of known SARS-CoV-2 infected people resident in catchments.

		Known SARS-CoV-2 infected people resident in catchments (reference test)	
		Present	Absent
Wastewater test result (index test)	Positive		
	Negative		

Exercise 4. Calculate the sensitivity and specificity of SARS-CoV-2 wastewater surveillance for each sampling method.

Using all the evidence presented, evaluate the pros and cons for each sampling method.

References

1. Black J, Aung P, Nolan M, Roney E, Poon R, Hennessy D, et al. Epidemiological evaluation of sewage surveillance as a tool to detect the presence of COVID-19 cases in a low case load setting. *Sci Total Environ* [Internet]. 2021;786:147469. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwtV3Nb9MwFLdGJyQkhKAwjfEh36tEdeLGzmGHaQQxLiDYELflcRzRaU3Q0jLtxL_Oe7HjpAUJduASJVbt1H0_Pf_e6_sgJI7CebCjE4zUnHPNVCV1qSuVRFxGhSx4KVJmuNruDbPX13scxv6r4GEMRI-JtHcQvI8UBuAelABXAAFc_wkG2dABthPHUN0baWJrbjB
2. Larson RC, Berman O, Nourinejad M. Sampling manholes to home in on SARS-CoV-2 infections. *PLoS One* [Internet]. 2020;15(10):e0240007-e0240007. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwrV1LT9wwELaq7aWqVEFfpFDk9tL2kCXxl3GOC2LVSIWL2Jar5ScgFWdFdv8_48S7VRASFy45xD7YM5mZb5zxNwhRMi3yez7BCcMYM6XywljjVUWYIFpoZuumdEyNe8P87_wVS8QGtuBBjkfc1qostl5ABDIZJaiveV02GgJx4fRw65eyTW41uGQw6qpK9-ZoXR4
3. Randazzo W, Truchado P, Cuevas-Ferrando E, Simón P, Allende A, Sánchez G. SARS-CoV-2 RNA in wastewater anticipated COVID-19 occurrence in a low prevalence area. *Water research (Oxford)* [Internet]. 2020;181:115942. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwtV3Pb9MwFLZGd4ED4vfGBvKJS-WqcdwkPnDoSifGAVC7btwix3a0TFuCuLab9tfznp0fZSANKlikld36Vc9f7c_Pz58JCflgyO6MCTbRQggdqDzRRucq4iLhWZlJE8vACvXz3TBbzW1pXdl_7Xgog67Hg7R_0fto1AA7wEC8AQQwPOPYDAfz-ZsUp0w3p99HmN
4. Sinclair RG, Choi CY, Riley MR, Gerba CP. Pathogen Surveillance Through Monitoring of Sewer Systems. In: *Advances in Applied Microbiology* [Internet]. San Diego, CA: Elsevier Science & Technology; 2008. p. 249-69. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwnV3dS8MwED9kIMgEv3V-jD7qw1ybZmnyqOLwSYRtzyVNE9xLN6ab-N9713QfFQXxpVBS2nIX7n5J7n4_gJjdhp1vMcFKwzk3kXbS5MZpwbhkmcx4nqjlcI3XhoHuLwf6vrWX6rlQ5V-H8oboRFSHGLdjERJ1vny-W22xEFdmuCYPZ4n0asnLF5QMOyxOOMZkUZH
5. Xu Y, Li X, Zhu B, Liang H, Fang C, Gong Y, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med* [Internet]. 2020;26(4):502-5. Available from: <http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwpV1Lb9QwELZoK1AvPAqU>

QimGCxJS2MRxsvYJLatWcKCg3dKrZcdOW6IKlk0Wqf--
M2snbHpASJw9ec545kvmmxICUvYxju74BCcKznmR6FIUtih1zrhgRhhuxzJxXA9nw3hylZbG
BHV3XnLtum1d4F_zEQQbyeJcZuLT4leEc6Qw3xqGamyRHQDbEmx-5_Px6Y9

6. Cho SM, Ha GY. A Case of COVID-19 in a 45-Day-Old Infant with Persistent Fecal Virus Shedding for More Than 12 Weeks. *Yonsei Med J* [Internet]. 2020;61(10):901-3. Available from:
http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwtV07b9swECbSFCi6FH03fYEowC6GXJOiLXLolMkOmiHIECdAJ0EPMnHTyIVjD_n3vRNFS0laIB26CBR1oijdZ_K78_FISCiGo-DWmGBUKaUseW5VWZU2nwipRKEKWUWaG5nf3Btmx2_x2dX9V8VDHageF9L-g_K3jUIFIAECcAQQwPFeMlgHae7c9enR6cE04Bo
7. Parasa S, Desai M, Thoguluva Chandrasekar V, Patel HK, Kennedy KF, Roesch T, et al. Prevalence of Gastrointestinal Symptoms and Fecal Viral Shedding in Patients With Coronavirus Disease 2019: A Systematic Review and Meta-analysis. *JAMA Netw Open* [Internet]. 2020 Jun 1;3(6):e2011335-e2011335. Available from:
<https://pubmed.ncbi.nlm.nih.gov/32525549>
8. Fontana L, Villamagna A, Sikka M, McGregor J. Understanding viral shedding of severe acute respiratory coronavirus virus 2 (SARS-CoV-2): Review of current literature. *Infection control and hospital epidemiology* U6 - ctx_ver=Z3988-2004&ctx_enc=info%3Aofi%2Fenc%3AUTF-8&rft_id=info%3Aid%2Fsummon.serialssolutions.com&rft_val_fmt=info%3Aofi%2Ffmt%3Akev%3Amtx%3Ajournal&rft.genre=article&rft.atitle=Understanding+viral+shed [Internet]. 2020;1-10. Available from:
http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwtV3dS8MwEA86EQQRP_Gb-KAoo7JkWT8EH4Y4FlaC29S30SYXJmgznziH-916WdG31RR98CSVpU9pfuPvi7nJHSJ2f1rxvMgFCKYSQLNahVFLHPhchT8JEqCBilOJybZiZbN-Y9_0r8NiH0JuDtH8AfzopduA1LgFscRFg-6tl0CsdXjERvc_V0QCUctHOqBjBuBC
9. Zheng S, Fan J, Yu F, Feng B, Lou B, Zou Q, et al. Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study. *BMJ* [Internet]. 2020;369:m1443-m1443. Available from:
http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwhV1Lb9QwEB5BkRAX3o-Fthrg2rTxY70Ot1K1QpUWoS30wCWyHRu2okmV3a3ET-HfMo6z7S6qyi2OR05sjz2fPfY3AILv5tk_c4LXTkrpmAnaVS4YxaXmVltZjQrmpVmPDQPvb3boM6H27PnZ7jmtAsRdAkN5ZMufjl-v595V9Eu6dp3QSoieWWitGLIp9LxulW6

10. Silverman AI, Boehm AB. Systematic Review and Meta-Analysis of the Persistence and Disinfection of Human Coronaviruses and Their Viral Surrogates in Water and Wastewater. *Environ Sci Technol Lett* [Internet]. 2020;7(8):544-53. Available from: http://anu.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwjV07T8MwELagLIDEG1Fe8shA2thxE2esChULUwsdI9uxpSwpyoP_wT_m7CSIVAh1i62T5TgX32ff3XclBXTgext7guaKMaaIMFylyoiQMk4IlyyNYqKZ-F0b5id3fcOhT8lQqHKgrQe0qga-ctSDu2iPwmnc1i8YT2arGxY_jkBDA1ddjnIPDLpf0Q79PY41UKp
11. Sitch AJ, Dekkers OM, Scholefield BR, Takwoingi Y. Introduction to diagnostic test accuracy studies. *Eur J Endocrinol* [Internet]. 2021;184(2):E5-9. Available from: <https://eje.bioscientifica.com/view/journals/eje/184/2/EJE-20-1239.xml>
12. O'Reilly KM, Allen DJ, Fine P, Asghar H. The challenges of informative wastewater sampling for SARS-CoV-2 must be met: lessons from polio eradication. *Lancet Microbe* [Internet]. 2020 Sep 1;1(5):e189-90. Available from: [https://doi.org/10.1016/S2666-5247\(20\)30100-2](https://doi.org/10.1016/S2666-5247(20)30100-2)
13. Schang C, Crosbie ND, Nolan M, Poon R, Wang M, Jex A, et al. Passive Sampling of SARS-CoV-2 for Wastewater Surveillance. *Environ Sci Technol*. 2021 Aug;55(15):10432-41.

Appendix C. Evidence-based Medicine—London School of Paediatrics Day: Interpreting diagnostic test accuracy studies.


Interpreting diagnostic test accuracy studies
 Aidan Yuen
 Field Epidemiology Training Program (FETP)
 The Australian National University | Department of Health, State Government of Victoria

OFFICIAL

Acknowledgment of Country



OFFICIAL

Outcomes

- Describe diagnostic test studies and their methods
- **Appraise** diagnostic test studies
- Calculate and interpret **key measures** of diagnostic test studies
- Understand the **practical considerations** of applying diagnostic tests in practice

OFFICIAL

How do clinicians make diagnoses?

- **Aim:** identify the strategies and methods used by GPs in routine clinical consultations
- **Method:** six GPs collected and recorded strategies used on 300 patients

Stage	Strategy
Initiation of the diagnosis	• Spot diagnoses • Self labelling • Presenting complaint • Pattern recognition trigger
Refinement	• Restricted rule-outs • Stepwise refinement • Probabilistic reasoning • Pattern recognition fit • Clinical prediction rule
Defining the final diagnosis	• Known diagnosis • Further tests ordered • Test of treatment • Test of time • No label applied

Heneghan C, Glasziou P, Thompson M, et al. Diagnostic strategies used in primary care. *BMJ*. 2009;338:b946. Published 2009 Apr 20. doi:10.1136/bmj.b946

OFFICIAL

What are diagnostic tests used for?

- Increase certainty about presence/absence of disease
- Understand disease severity
- Monitor clinical course
- Assess prognosis – risk/stage within diagnosis
- Plan treatment, e.g. location

OFFICIAL

What are the roles of new tests?

- **Replacement** – new replaces old
 - E.g. CT colonography for barium enema
- **Triage** – new determines need for old
 - E.g. B-natriuretic peptide for echocardiography
- **Add-on** – new combined with old
 - E.g. ECG and myocardial perfusion scan

OFFICIAL

What are diagnostic test studies?

```

graph TD
    A[Series of patients] --> B[Index test]
    B --> C[Reference test "gold standard"]
    C --> D[Compare results of the index test with the gold standard]
  
```

OFFICIAL

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

Journal homepage: www.elsevier.com/locate/ijid

Original Article

Diagnostic accuracy of a SARS-CoV-2 rapid antigen test in real-life clinical settings

Sabrina Jegerlehner, MD, MSc^{1,*}, Franziska Suter-Riniker, PhD^{2,3}, Philipp Jent, MD³, Pascal Bittel, PhD⁴, Michael Nagler, MD, PhD, MSc^{1,4}

¹Department of Emergency Medicine, Inselspital, Bern University Hospital, Bern, Switzerland
²Institute for Infectious Diseases, University of Bern, Bern, Switzerland
³Department of Infectious Diseases, Bern University Hospital, Bern, Switzerland
⁴University Institute of Clinical Chemistry, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland

ARTICLE INFO

Article history:
 Received 4 May 2021
 Received in revised form 10 June 2021
 Accepted 7 July 2021

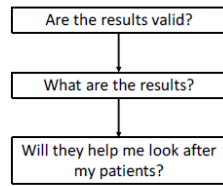
ABSTRACT

Background: Laboratory tests are a mainstay in managing the COVID-19 pandemic, and high hopes are placed on rapid antigen tests. However, the accuracy of rapid antigen tests in real-life clinical settings is unclear because adequately designed diagnostic accuracy studies are essentially lacking.

Jegerlehner S, Suter-Riniker F, Jent P, Bittel P, Nagler M. Diagnostic accuracy of a SARS-CoV-2 rapid antigen test in real-life clinical settings. *Int J Infect Dis*. 2021;109:118–122. doi:10.1016/j.ijid.2021.07.010

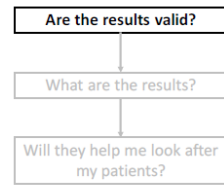
OFFICIAL

Appraising diagnostic test studies: 3 easy steps



OFFICIAL

Appraising diagnostic test studies: 3 easy steps



OFFICIAL

1. Are the results valid?

- Appropriate spectrum of patients?
 - Spectrum bias
- Do all patients have the gold standard?
 - Verification (work-up) bias
 - Incorporation bias
 - Differential reference bias
- Is there an independent, blind or objective comparison with the gold standard?
 - Observer bias

OFFICIAL

Methods

Study design, setting, and population

The Arip study was a prospective cross-sectional study conducted at a COVID-19 testing facility affiliated to a Swiss university hospital. Consecutive individuals presenting on their own between January and March 2021 were recruited. Inclusion criteria were: (a) suspected SARS-CoV-2 infection; (b) age ≥ 18 years; and (c) signed informed consent. Exclusion criteria were clinical warning signs that required emergency medical care (CDC, 2020). A flow chart of the patient selection process is given in Figure 1. The COVID-19 testing facility is one of the largest testing facilities in the greater Bern area, affiliated to a large, specialized laboratory running high-throughput RT-PCR (Hirsiger et al., 2021). During the study period, individuals were instructed by the authorities to present themselves when experiencing symptoms consistent with SARS-CoV-2. The authorities also referred patients suspected of exposure to infected individuals. Some individuals presented for other reasons (e.g. travel requirements or for shortening quarantine measures). The study protocol was approved by the appropriate ethical committee (Kantonale Ethikkommission Bern #2020-02729) and the institutional authorities. All participants signed informed consent. The study was conducted in accordance with the declaration of Helsinki.

Spectrum

Jegerlehner S, Suter-Riniker F, Jent P, Bittel F, Nagler M. Diagnostic accuracy of a SARS-CoV-2 rapid antigen test in real-life clinical settings. *Int J Infect Dis.* 2021;109:118-122. doi:10.1016/j.ijid.2021.07.010

OFFICIAL

1. Are the results valid?

- Appropriate spectrum of patients?
 - Spectrum bias
- Do all patients have the gold standard?
 - Verification (work-up) bias
 - Incorporation bias
 - Differential reference bias
- Is there an independent, blind or objective comparison with the gold standard?
 - Observer bias

OFFICIAL

Sample collection

supermarket during the first few days of practice. Swabs were collected using iClean Specimen Collection Pouches (iClean Technology Co., Shenzhen, China) and iCollecture Viral Transport Medium (Italy). Sample material was stored at 4°C and processed within 6 hours (samples test) or 12 hours (RT-PCR). Collected clinical data and laboratory test results were stored in separate databases and merged before analysis.

Index test

Determination of the rapid antigen test
Using the same sample material, the RocheSD Biosensor SARS-CoV-2 rapid antigen test was conducted. It is assisted by a trained medical laboratory technician (unaware of the RT-PCR results). Quality control was performed daily, and the manufacturer's instructions were strictly followed (package leaflet, Roche Diagnostics, Mannheim, Germany). In brief, three drops of the extracted sample were applied to the specimen well of the test device and the test result was recorded after 15-30 minutes. The result was only considered valid if the control line was visible. Even faint test lines were considered positive.

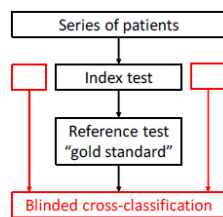
Gold standard

Determination of real-time PCR
As a reference standard test, confirming the presence of COVID-19, two real-time PCR (RT-PCR) assays were conducted, as previously described (Roche cobas® SARS-CoV-2; Seegene Allplex 2019-nCoV) (Hirsiger et al., 2021). Analyses were performed according to the manufacturers' instructions on a 3 thermal cycler system or a LightCycler 480 system. RT-PCR was carried out in line with clinical practice, with laboratory technicians unaware of the index test results. Detectable SARS-CoV-2 below or at a cycle threshold of 40 were considered positive. Commercially available quality control was conducted with each test run.

Jegerlehner S, Suter-Riniker F, Jent P, Bittel F, Nagler M. Diagnostic accuracy of a SARS-CoV-2 rapid antigen test in real-life clinical settings. *Int J Infect Dis.* 2021;109:118-122. doi:10.1016/j.ijid.2021.07.010

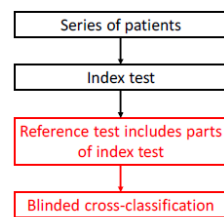
OFFICIAL

Verification (work-up) bias



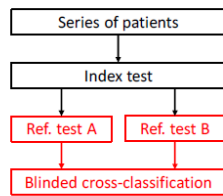
OFFICIAL

Incorporation bias



OFFICIAL

Differential Reference Bias



OFFICIAL

1. Are the results valid?

- Appropriate spectrum of patients?
 - Spectrum bias
- Do all patients have the gold standard?
 - Verification (work-up) bias
 - Incorporation bias
 - Differential reference bias
- Is there an independent, blind or objective comparison with the gold standard?
 - Observer bias

OFFICIAL

Sample collection

Index test

Gold standard

supervised during the first few days of practice. Swabs were collected using (Class Specimen Collection Packet) Swabs (Crisp) Technology Co., Shenzhen, China) and Löffkern Viral Transport Medium (Italy). Sample material was stored at 4°C and processed within 6 hours (antigen test) or 12 hours (RT-PCR). Coded clinical data and laboratory test results were stored in separate databases and merged before analysis.

Determination of the rapid antigen test

Using the same sample material, the Roche/SD Biosensor SARS-CoV-2 rapid antigen test was conducted in parallel by a trained medical laboratory technician (consequence of the RT-PCR results). Every patient was performed only one test (independence). Instructions were strictly followed (package leaflet: Roche Diagnostics, Mannheim, Germany). In brief, three drops of the extracted sample were applied to the specimen well of the test device and the test result was recorded after 15–30 minutes. The result was only considered valid if the control line was visible. Even faint test lines were considered positive.

Determination of real-time PCR

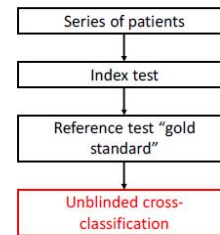
As a reference standard test confirming the presence of COVID-19, two real-time PCR (RT-PCR) assays were conducted, as previously described (Roche cobas SARS-CoV-2; Sanger et al., 2020; uCoV) (Bogner et al., 2021). Analyses were performed according to the manufacturer's instructions (cobas SARS-CoV-2; Sanger et al., 2020; uCoV) system. RT-PCR was carried out in line with clinical practice with laboratory technician (consequence of the index test results). The Roche cobas SARS-CoV-2 assay is a fully licensed test and was considered positive. Commercially available quality control was conducted with each test run.

Jägerlehner S, Suter-Riniker F, Jent P, Bittel P, Nagler M. Diagnostic accuracy of a SARS-CoV-2 rapid antigen test in real-life clinical settings. Int J Infect Dis. 2021;109:118–122. doi:10.1016/j.ijid.2021.07.010

OFFICIAL

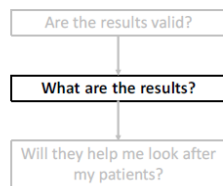
Blinding

Observer bias



OFFICIAL

Appraising diagnostic test studies: 3 easy steps



OFFICIAL

Roche/SD Biosensor rapid antigen test for SARS-CoV-2 infection

The overall sensitivity of the Roche/SD Biosensor rapid antigen test was 65.3% (95% confidence interval [CI] 56.8–73.1); the specificity was 99.9 (95% CI 99.5–100.0). The number of false-negative test results was 49, and the number of false-positives was 2 ($n = 92$ true positives; $n = 1319$ true negatives). The sensitivity of the rapid antigen test was higher in patients with any symptom (69.8%), acute respiratory syndrome (69.2%), and fever (73.9%). The sensitivity was lower in asymptomatic individuals (44%) and other subgroups. Details of sensitivities and specificities according to age group, presence of symptoms, or billing mode are presented in Figure 2.

Jägerlehner S, Suter-Riniker F, Jent P, Bittel P, Nagler M. Diagnostic accuracy of a SARS-CoV-2 rapid antigen test in real-life clinical settings. Int J Infect Dis. 2021;109:118–122. doi:10.1016/j.ijid.2021.07.010

OFFICIAL

2 X 2 tables

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a)	False positive (b)
	Test negative	False negative (c)	True negative (d)

OFFICIAL

Measures of test validity

- Sensitivity = Proportion of people **WITH** the disease who have a **POSITIVE** test result

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a)	False positive (b)
	Test negative	False negative (c)	True negative (d)

$$\text{Sensitivity} = \frac{a}{a + c}$$

OFFICIAL

Measures of test validity

- **Specificity** = Proportion of people **WITHOUT** the disease who have a **NEGATIVE** test result

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a) 92	False positive (b) 2
	Test negative	False negative (c) 49	True negative (d) 1319

$$\text{Specificity} = d / (b + d)$$

Roche/SD Biosensor rapid antigen test for SARS-CoV-2 infection

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a) 92	False positive (b) 2
	Test negative	False negative (c) 49	True negative (d) 1319

$$\text{Sensitivity} = a / (a + c)$$

$$\text{Specificity} = d / (b + d)$$

Roche/SD Biosensor rapid antigen test for SARS-CoV-2 infection

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a) 92	False positive (b) 2
	Test negative	False negative (c) 49	True negative (d) 1319

$$\text{Sensitivity} = 92 / (92 + 49)$$

$$\text{Specificity} = 2 / (2 + 1319)$$

Roche/SD Biosensor rapid antigen test for SARS-CoV-2 infection

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a) 92	False positive (b) 2
	Test negative	False negative (c) 49	True negative (d) 1319

$$\text{Sensitivity} = 65\%$$

$$\text{Specificity} = 100\%$$

Roche/SD Biosensor rapid antigen test for SARS-CoV-2 infection

The overall **sensitivity** of the Roche/SD Biosensor rapid antigen test was **65.3%** (95% confidence interval [CI] 56.8–73.1); the **specificity** was **99.9%** (95% CI 99.5–100.0). The number of false-negative test results was 49, and the number of false-positives was 2 ($n = 92$ true positives; $n = 1319$ true negatives). The sensitivity of the rapid antigen test was higher in patients with any symptom (69.8%), acute respiratory syndrome (69.2%), and fever (73.9%). The sensitivity was lower in asymptomatic individuals (44%) and other subgroups. Details of sensitivities and specificities according to age group, presence of symptoms, or billing mode are presented in Figure 2.

Jegerlehner S, Suter-Riniker F, Jent P, Bittel P, Nagler M. Diagnostic accuracy of a SARS-CoV-2 rapid antigen test in real-life clinical settings. *Int J Infect Dis.* 2021;109:118–122. doi:10.1016/j.ijid.2021.07.010

COVID-19SEROspeed IgM/IgG rapid test for SARS-CoV-2 infection

large cross-European investigation. The clinical specificity was assessed on 215 pre-pandemic sera (including some from patients with viral infections or autoimmune disorders). The clinical sensitivity was evaluated on 710 sera from 564 patients whose SARS-CoV-2 infection was confirmed by quantitative reverse transcription-PCR (qRT-PCR) and whose antibody response was compared to that measured by five other commercial tests. The kinetics of the antibody response were also analyzed in seven symptomatic patients. The **specificity** of the test (BioS) on pre-pandemic specimens was **98.1%** (95% confidence interval [CI], 96.2% to 99.4%). When tested on the 710 pandemic specimens, BioS showed an overall clinical **sensitivity** of **86.0%** (95% CI, 0.83 to 0.89), with good concordance with the Euroimmun assay (overall concordance of 0.91; Cohen's kappa coefficient of 0.62). Due in part to simultaneous detection of IgM

Plebani M, Parčina M, Bechri I, et al. Performance of the COVID19SEROspeed IgM/IgG Rapid Test, an Immunochromatographic Assay for the Diagnosis of SARS-CoV-2 Infection: a Multicenter European Study. *J Clin Microbiol.* 2021;59(2):e02240-20. Published 2021 Jan 21. doi:10.1128/JCM.02240-20

Top tips!

- Sensitivity is useful!
 - Of those **WITH** the disease, 86% people will test **POSITIVE**
 - Specificity seems a bit confusing!
 - Of those **WITHOUT** the disease, 98% people will test **NEGATIVE**
- False positive rate = 1 - specificity
- Of those **WITHOUT** the disease, 2% people will be **FALSE POSITIVE**
- **SpPIN SnNOUT**
 - Specific test is Positive → rules the disease **IN**
 - Sensitive test is Negative → rules the disease **OUT**

Measures of test validity

- **Positive predictive value (PPV)** = Proportion of people with a **POSITIVE TEST** who **HAVE** the disease

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a)	False positive (b)
	Test negative	False negative (c)	True negative (d)

$$\text{PPV} = a / (a + b)$$

Chapter 6

Measures of test validity

- Negative predictive value (NPV) = Proportion of people with a **NEGATIVE TEST** who **DO NOT HAVE** the disease

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a) 92	False positive (b) 2
	Test negative	False negative (c) 49	True negative (d) 1319

NPV = $d / (c + d)$

Roche/SD Biosensor rapid antigen test for SARS-CoV-2 infection

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a) 92	False positive (b) 2
	Test negative	False negative (c) 49	True negative (d) 1319

PPV = $a / (a + b)$
NPV = $d / (c + d)$

Roche/SD Biosensor rapid antigen test for SARS-CoV-2 infection

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a) 92	False positive (b) 2
	Test negative	False negative (c) 49	True negative (d) 1319

PPV = $92 / (2 + 92)$
NPV = $1319 / (49 + 1319)$

Roche/SD Biosensor rapid antigen test for SARS-CoV-2 infection

		Status based on 'gold standard'	
		Disease	No disease
'Index test' result	Test positive	True positive (a) 92	False positive (b) 2
	Test negative	False negative (c) 49	True negative (d) 1319

PPV = 98%
NPV = 96%

Top tips!

- PPV and NPV vary with disease prevalence!
- Use if the ratio of people in the disease group and the people in the healthy control group is equivalent to the prevalence of the disease in the studied population
- Otherwise, use Likelihood Ratio – does not depend on prevalence

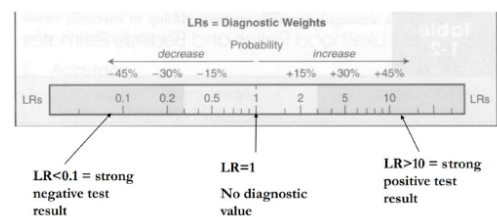
Likelihood ratios

Likelihood ratio = $\frac{\text{Probability of clinical finding in patients with disease}}{\text{Probability of same finding in patients without disease}}$

Likelihood ratios

- Positive likelihood ratio (LR+)
- If a patient tests **POSITIVE** with this test, how much does it **INCREASE** the probability that they have the condition?
- LR+ = $\text{sensitivity} / (1 - \text{specificity})$
- Negative likelihood ratio (LR-)
- If a patient tests **NEGATIVE**, how much does it **DECREASE** the probability that they have the condition?
- LR- = $(1 - \text{sensitivity}) / \text{specificity}$

What do likelihood ratios mean?



Pluddemann, A. "Teaching Tips for Diagnostic Studies". Nuffield Department of Primary Care Health Sciences Centre for Evidence-Based Medicine, University of Oxford.

Likelihood ratios for screening of pancreatic cancer

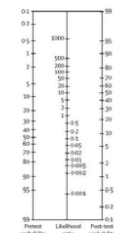
Table 5 Likelihood ratios for independent predictors of PC and variables relevant to PC diagnosis

Variables	LR+	LR-
TI	1.21	0.84
Jaundice	1.92	0.69
Glycemic disturbance	3.40	0.81
CA 19-9	5.36	0.29
Ultrasound	3.77	0.21
Computed tomography	4.15	0.26
ERCP	5.00	0.40

ERCP, endoscopic retrograde cholangiopancreatography; LR, likelihood ratio; PC, pancreatic cancer; TI, tobacco index.

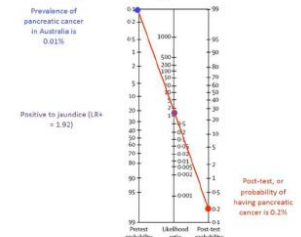
de Icaza E, López-Cervantes M, Arredondo A, Robles-Díaz G. Likelihood ratios of clinical, laboratory and image data of pancreatic cancer: Bayesian approach. *Journal of Evaluation in Clinical Practice*. 2009;15(1):62-68. doi:https://doi.org/10.1111/j.1365-2753.2008.00955.x

Understanding nomograms



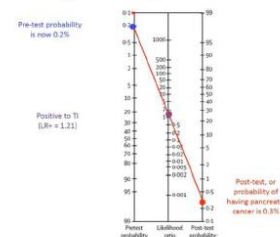
Ilic, D. "Evidence Based Clinical Practice – Likelihood ratios". School of Public Health and Preventive Medicine, Monash University.

Understanding nomograms



Ilic, D. "Evidence Based Clinical Practice – Likelihood ratios". School of Public Health and Preventive Medicine, Monash University.

Understanding nomograms



Ilic, D. "Evidence Based Clinical Practice – Likelihood ratios". School of Public Health and Preventive Medicine, Monash University.

Bayesian reasoning

Stage	Probability of pancreatic cancer
Initial presentation	0.01%
1 st test positive (jaundice)	0.2%
2 nd test positive (TI)	0.3%
3 rd test positive (glycemic disturbance)	0.7%
4 th test positive (CA 19-9)	4.0%
5 th test positive (ultrasound)	10%
6 th test positive (CT)	30%
7 th test positive (ERCP)	70%

Ilic, D. "Evidence Based Clinical Practice – Likelihood ratios". School of Public Health and Preventive Medicine, Monash University.

Roche/SD Biosensor rapid antigen test for SARS-CoV-2 infection

The overall sensitivity of the Roche/SD Biosensor rapid antigen test was 65.3% (95% confidence interval [CI] 56.8–73.1%); the specificity was 99.9% (95% CI 99.5–100.0%). The number of false-negative test results was 48, and the number of false-positives was 2 ($n = 92$ true positives; $n = 1319$ true negatives). The sensitivity of the rapid antigen test was higher in patients with any symptom (69.8%), acute respiratory syndrome (69.2%), and fever (73.9%). The sensitivity was lower in asymptomatic individuals (44%) and other subgroups. Details of sensitivities and specificities according to age group, presence of symptoms, or billing mode are presented in Figure 2.

Jägerlehner S, Suter-Riniker F, Jent P, Bittel P, Nagler M. Diagnostic accuracy of a SARS-CoV-2 rapid antigen test in real-life clinical settings. *Int J Infect Dis*. 2021;109:118-122. doi:10.1016/j.ijid.2021.07.010

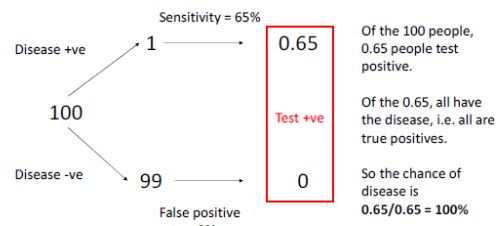
Natural Frequencies

"If I had this test and it was positive, what's the chance that I'm infected with SARS-CoV-2?"

- Suppose SARS-CoV-2 infection has a prevalence of 1%
- The test has sensitivity of 65% and specificity of 100%

100% Always
50% Maybe
0% Never

Prevalence 1%, sensitivity of 65%, specificity of 100%



Appendix D. 11th TEPHINET Global Scientific Conference: Beyond principles: How do we use learning theories to facilitate learning experiences for FETP trainees?

BEYOND PRINCIPLES: HOW DO WE USE LEARNING THEORIES TO FACILITATE LEARNING EXPERIENCES FOR FETP TRAINEES? Panama 4 September 2022 Australian National University Master of Applied Epidemiology & Field Epidemiology in Action	WORKSHOP GOAL Explore learning theories to improve training experiences
WHAT, WHO, WHAT, WHY – ICEBREAKER ● Spend some time getting to know your colleagues. ● Assign facilitator duties to the person who lives closest to this room and note-taker duties to the one who lives furthest. ● Discuss the following: ● What are you? Work roles and previous experience. ● Who are you? Something unique about you as a human, something that makes you different from everyone in the room. ● What resources do you bring? Any special resources (knowledge, skills, experiences) from past experience or study that might be useful for others to know about in this workshop. ● Why are you here? What questions, problems, and concerns are you hoping to deal with in this training? ● Write a group summary on flip-chart	LEARNING CONTRACTS ● Effective way to help learners structure their learning ● Not a 'contract' but an agreement on a plan ● Prepared jointly between facilitator and learner or mentor and mentee ● Links learning objectives/outcomes to learning resources and strategies and assessments
WORKSHOP AGENDA	PARKING LOT ● Topics come up that the group cannot address because of time or discussion ● Facilitators write on the "Parking Lot"—set aside to be discussed later ● Review the Parking Lot at the end of each day ● Group discusses whether to address or include in agenda
WORKSHOP ROLES Facilitate—to make easier We are here to facilitate you finding solutions to your own questions and challenges Ask and answer questions, facilitate discussions and activities, provide resources, keep everyone on task, maintain an encouraging learning environment, and (TtT) model effective training facilitation skills.	GROUP NORMS ● Guidelines that the group agrees to follow for how we will work together. ● We learn best when we feel comfortable—when we do not have to worry about our environment or our peers, we can focus, share, and take risks. ● Group norms help us achieve comfort, create an encouraging and respectful learning environment, and enable us to complete tasks efficiently.

WORKSHOP EVALUATION

- ⦿ On-going feedback
- ⦿ Discussions and activities
- ⦿ Facilitator debriefs
- ⦿ Final group evaluation

HOUSEKEEPING

- ⦿ Bathrooms
- ⦿ Breaks & lunch
- ⦿ Wifi is not necessary unless we are on break
- ⦿ Paper, pens, toys, etc. on the table are for you but please don't distract others

BREAK

DEMONSTRATION OF TRAINING APPROACH



Participate in this activity as a trainee and a reflective observer of training.



Take notes of your thoughts, reactions, feelings, and those of others.



Introduction to Epidemiology

Note: This slide set has been modified for educational purposes.



Epidemiology — Defined

Study of the distribution and determinants of health-related states among specified populations and the application of that study to the control of health problems

Adapted from: Last JM, ed. A dictionary of epidemiology. 2nd ed. Toronto, Canada: Oxford University Press; 1988.

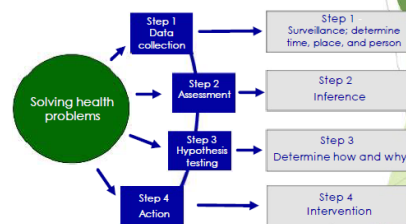
14

Epidemiology Purposes in Public Health Practice

- Discover the agent, host, and environmental factors that affect health
- Determine the relative importance of causes of illness, disability, and death
- Identify those segments of the population that have the greatest risk from specific causes of ill health
- Evaluate the effectiveness of health programs and services in improving population health

15

Solving Health Problems



16

Chapter 6

Epidemiology Key Terms

epidemic or outbreak: disease occurrence among a population that is in excess of what is expected in a given time and place.

cluster: group of cases in a specific time and place that might be more than expected.

endemic: disease or condition present among a population at all times.

pandemic: a disease or condition that spreads across regions.

rate: number of cases occurring during a specific period; always dependent on the size of the population during that period.

17

Comparing Population Characteristics



Rates help us compare health problems among different populations that include two or more groups who differ by a selected characteristic

18

Rate Formula

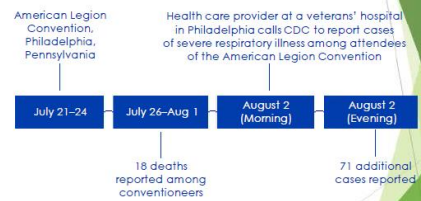
To calculate a rate, we first need to determine the frequency of disease, which includes

- the number of cases of the illness or condition
- the size of the population at risk
- the period during which we are calculating the rate

$$\text{Rate (\%)} = \frac{\text{number of cases}}{\text{population at risk}} \times 100$$

19

Scenario: Unexplained Pneumonia



Preiser DM, Tauxe T, Grentham W, et al. Legionnaires' disease: description of an epidemic of pneumonia. *New Engl J Med* 1977;297:1189-91.

20

Legionnaires' Disease, by Age Group

Hotel A Residents
Time: July 21-24, 1976

Age (yrs)	frequency		Unit size	
	Sick	Total	Percentage	
≤39	3	44	6.8	
40-49	9	160	5.6	
50-59	27	320	8.4	
60-69	12	108	11.1	
≥70	11	54	20.4	
Unknown	0	2	0	

Preiser DM, Tauxe T, Grentham W, et al. Legionnaires' disease: description of an epidemic of pneumonia. *New Engl J Med* 1977;297:1189-91.

21

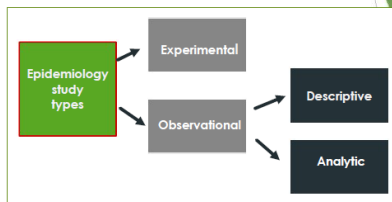
Legionnaires' Disease Rate

Hotel A Residents
Time: July 21-24, 1976

Age (yrs)	Frequency		Unit		Rate
	Sick	Total	Percentage		
≤39	3	44	6.8		
40-49	9	160	5.6		
50-59	27	320	8.4		
60-69	12	108	11.1		
≥70	11	54	20.4		
Unknown	0	2	0		

22

Epidemiology Study Types



23

Descriptive and Analytic Epidemiology

Descriptive epidemiology	Analytic epidemiology
When was the population affected?	How was the population affected?
Where was the population affected?	Why was the population affected?
Who was affected?	

24

Chapter 6

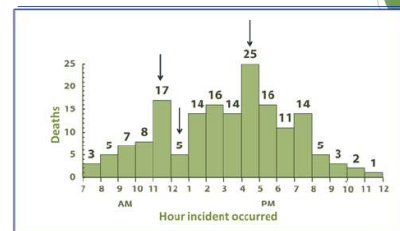
Fatalities Associated with Farm Tractors



In 1982, the number of farm tractor-associated deaths was described in terms of time, place, and person by using records from an existing surveillance system

25

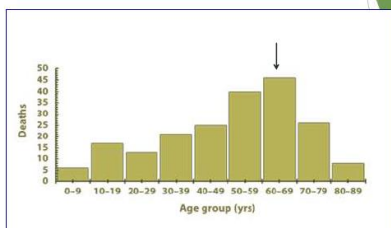
Fatalities Associated with Farm Tractors



Goodman RA, Smith JO, Sikes RC, et al. Fatalities associated with farm tractor injuries: an epidemiologic study. Public Health Rep. 1985;100:329-33.

26

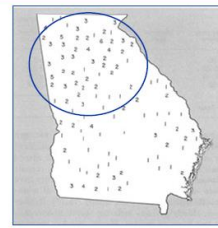
Fatalities Associated with Farm Tractors



Goodman RA, Smith JO, Sikes RC, et al. Fatalities associated with farm tractor injuries: an epidemiologic study. Public Health Rep. 1985;100:329-33.

27

Fatalities Associated with Farm Tractors



Goodman RA, Smith JO, Sikes RC, et al. Fatalities associated with farm tractor injuries: an epidemiologic study. Public Health Rep. 1985;100:329-33.

28

Data Sources and Collection Methods

Source	Method	Example
Individual persons	- Questionnaire - Survey	- Foodborne illness outbreak - CDC's National Health and Nutrition Examination Survey - Health data on U.S. residents
Environment	- Samples from the environment (river water, soil) - Sensors for environmental changes	- Collection of water from area streams — check for chemical pollutants - Air-quality ratings
Health care providers	Notifications to health department if cases of certain diseases are observed	Report cases of meningitis to health department
Nonhealth-related sources (financial, legal)	- Sales records - Court records	- Cigarette sales - Intoxicated driver arrests

29

Conducting Studies



Studies are conducted in an attempt to discover associations between an exposure or risk factor and a health outcome

30

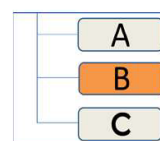
Study Design — Cross-Sectional Study



Subjects are selected because they are members of a certain population subset at a certain time

31

Study Design — Cohort Study



Subjects are categorized on the basis of their exposure to one or more risk factors

32

Study Design Type — Case-Control Study



Subjects identified as having a disease or condition are compared with subjects without the same disease or condition

33

Outbreak Investigation

Ten steps are involved in outbreak investigations, including



- establishing the existence of an outbreak
- preparing for fieldwork
- verifying the diagnosis
- defining and identifying cases
- using descriptive epidemiology
- developing hypotheses
- evaluating the hypotheses
- refining the hypotheses
- implementing control and prevention measures
- communicating findings

34

Outbreak Investigation — Steps 1 and 2



Step 1 — Establishing the existence of an outbreak

- Use data from data sources

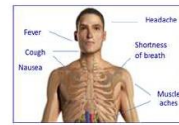
Step 2 — Preparing for field work

- Research the disease
- Gather supplies and equipment
- Arrange travel

Praser DH, Tsai T, Orenstein W, et al. Legionnaires' disease: description of an epidemic of pneumonia. New Eng J Med 1977;297:1189-97.

35

Outbreak Investigation — Steps 3 and 4



Step 3 — Verifying the diagnosis

- Speak with patients
- Review laboratory findings and clinical test results

Step 4 — Defining and identifying cases

- Establish a case definition by using a standard set of criteria

Praser DH, Tsai T, Orenstein W, et al. Legionnaires' disease: description of an epidemic of pneumonia. New Eng J Med 1977;297:1189-97.

36

Outbreak Investigation — Step 5



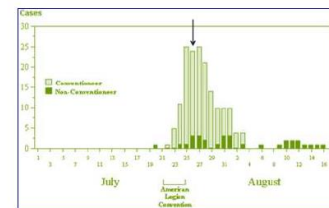
Step 5 — Using descriptive epidemiology

- Describe and orient the data

Praser DH, Tsai T, Orenstein W, et al. Legionnaires' disease: description of an epidemic of pneumonia. New Eng J Med 1977;297:1189-97.

37

Legionnaires' Disease Cases, by Day



Praser DH, Tsai T, Orenstein W, et al. Legionnaires' disease: description of an epidemic of pneumonia. New Eng J Med 1977;297:1189-97.

38

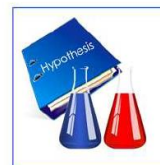
Legionnaires' Disease Attack Rates

Age Year	Hotel A			Hotel B			Hotel C		
	#	Total	Percent	#	Total	Percent	#	Total	Percent
≤39	3	44	6.8	3	116	2.6	6	160	3.7
40-49	9	161	5.6	11	202	4.7	20	392	5.1
50-59	27	320	8.4	25	323	4.8	52	643	6.2
60-69	12	106	11.1	19	247	9.1	31	315	9.8
≥70	11	54	20.4	5	76	6.5	16	130	12.3
Unknown	0	2	0	0	7	0	0	9	0
Total	62	688	9.0	63	1,161	5.4	125	1,849	6.8

Praser DH, Tsai T, Orenstein W, et al. Legionnaires' disease: description of an epidemic of pneumonia. New Eng J Med 1977;297:1189-97.

39

Outbreak Investigation — Steps 6, 7, and 8



Step 6 — Develop a focused hypothesis

Step 7 — Evaluate the hypothesis for validity

Step 8 — Refine the hypothesis as needed

Praser DH, Tsai T, Orenstein W, et al. Legionnaires' disease: description of an epidemic of pneumonia. New Eng J Med 1977;297:1189-97.

40

Chapter 6

Legionnaires' Disease Study Results



Five months after the first cases of Legionnaires' disease occurred, results of the case-control study indicated that spending time in the lobby of Hotel A was a risk factor for illness.

Legionnaires' Disease Study Results



In December 1976, a CDC laboratorian successfully located the source bacteria after continuing to test the specimens that were thought to be dead.

Outbreak Investigation — Steps 9 and 10



Step 9 — Implement control and prevention measures

- Control and prevent additional cases



Step 10 — Communicate findings

- Determine who needs to know
- Determine how information will be communicated
- Identify why the information needs to be communicated

Pringle DM, Tarr PI, O'Brien W, et al. Legionnaires' disease: description of an epidemic of pneumonia. New Engl J Med. 1977;297:1189-97.

QUESTIONS?

Knowledge Check

All of the following illustrate the purpose of epidemiology in public health, except

- identifying populations who are at risk for certain diseases.
- assessing the effectiveness of interventions.
- providing treatment for patients in clinical settings.
- determining the importance of causes of illness

Knowledge Check

Epidemiologists use a model for studying infectious disease and its spread that involves the microbe that causes the disease, the organism that harbors the disease, and the external factors that cause or allow disease transmission. This is also known as

- host, vector, and transmission.
- transmission, host, and environment.
- host, agent, and environment.
- organism, transmission, and environment.

Knowledge Check

On Day 1 of a technology conference in San Diego, 15 presenters who were setting up for their sessions in Annex X became ill with flu-like symptoms. During the course of the conference, 20 participants who attended sessions in Annex X also became ill with the same symptoms.

To begin calculating the rate of this outbreak, investigators should first determine

- the size of the conference population.
- the number of cases of illness.
- the number of days the conference was held.
- the location of the conference.

Knowledge Check

Which of the following are examples of a health-related source of data collection?

- Intoxicated driver arrests.
- Electronic health records.
- Measurement of toxins in a river.
- Medical board action against a physician.



Knowledge Check

Evaluate the approach that the epidemiologists took to investigate Legionnaires' disease in the Philadelphia outbreak.

1. What processes were effective?
2. What processes were not effective?
3. Justify your answers.
4. Recommend improved processes.

Resources and Additional Reading

- Bogdanich W. Panama releases report on '04 poisoning. The New York Times. February 14, 2005. <http://www.nytimes.com/2005/02/14/world/americas/14panama.html>.
- Centers for Disease Control and Prevention (CDC). CDC helps solve Panama mystery illness. Atlanta, GA: US Department of Health and Human Services; CDC News, October 7, 2005. http://www.cdc.gov/news/2005_10/panama.htm.
- Dean H. Introduction to public health, epidemiology, and surveillance. Atlanta, GA: US Department of Health and Human Services; CDC Science Ambassador Program, July 16, 2012.
- Fraser DW, Tsai T, Orenstein W, et al. Legionnaires' disease: description of an epidemic of pneumonia. New Engl J Med 1977;297:1189-97.
- Goodman RA, Smith JD, Sives RT, et al. Fatalities associated with farm tractor injuries: an epidemiologic study. Public Health Rep 1985;100:329-33.
- Centers for Disease Control and Prevention (CDC). How to investigate an outbreak. Epidemiology in the Classroom, November 17, 2004. Atlanta, GA: US Department of Health and Human Services; CDC. <http://www.cdc.gov/eic/te/ob/ob/outbreak/step.html#step1>.
- Last JM, ed. A dictionary of epidemiology, 2nd ed. Toronto, Canada: Oxford University Press; 1988.
- Rents DE, Lewis L, Mujica OJ, et al. Outbreak of acute renal failure in Panama in 2004: a case-control study. Bull World Health Organ 2008;86:749-55.
- Sakamoto R, Chino A, Nakahara T, et al. Legionella pneumophila in rainwater on roads. Emerg Infect Dis 2009;15:1295-7.
- Thacker SB, Birkhead GS. Surveillance [Chapter 3]. In: Gregg MB, ed. Field epidemiology. 3rd ed. New York, NY: Oxford University Press; 2005.

WHAT, WHO, WHAT, WHY - ICEBREAKER

- Spend some time getting to know your colleagues.
- Assign facilitator duties to the person who lives closest to this room and note-taker duties to the one who lives furthest.
- Discuss the following:
 - What are you? Work roles and previous experience.
 - Who are you? Something unique about you as a human, something that makes you different from everyone in the room.
 - What resources do you bring? Any special resources (knowledge, skills, experiences) from past experience or study that might be useful for others to know about in this workshop.
 - Why are you here? What questions, problems, and concerns are you hoping to deal with in this training?
- Write a group summary on flip-chart

THINK, PAIR, SHARE

- Think – Reflect on your own
- Pair – Discuss your reflections with your partner
- Share – Pairs will write discussion points on flipchart paper to share with the rest of the group

THINK, PAIR, SHARE – GUIDING QUESTIONS

- What are some of the things you observed in the demonstration?
- What are some of the things we or you did in the demonstration?
- What was different, unexpected, or surprising about the demo?
- If someone were watching, what would they say was happening?
- What reactions or thoughts did you have during the demo?
- Why do you think you had these reactions, thoughts, or observations?
- How would you describe the demo to someone who was not here?
- What experiences have you had that are similar to this demo?
- If you had to re-do the demo, what are some of the important points to consider?
- What questions, concerns, or problems do you have about demo that you want to address?

TEACH-BACK – LEARNING OUTCOMES

Andragogy

1. Define andragogy
2. Outline the key principles of andragogy relative to pedagogy
3. Recall how we have/haven't used these principles in this workshop
4. Consider how you would apply these principles in your own training

Experiential learning theory

1. Describe the experiential learning theory
2. Outline each phase of the experiential learning cycle, and compare these with traditional learning approaches
3. Recall how we have/haven't used this theory in this workshop
4. Consider how you would apply this theory in your training

BUZZ-GROUP EVALUATION



Get your feedback



Reflect on your own learning

BUZZ-GROUP EVALUATION

- Discuss the following questions:
 1. What progress have you observed among yourself and your colleagues in this workshop?
 2. What most contributed to that progress?
 3. What questions do you have today about mentoring (either new or still existing)?
 4. How could this workshop have addressed those questions better?
- Write group answers on a sheet of regular paper and hand in
- You have learning contracts
- Good to assign facilitator and note-taker duties

Monkeypox FAQ

What is monkeypox?

Monkeypox is a rare but potentially serious disease caused by infection with the monkeypox virus. Since mid-May 2022, monkeypox has been reported in multiple countries where it is not usually seen, including Australia. While the current outbreak has disproportionately impacted men who have sex with men, monkeypox can affect anyone who comes into close contact with someone with monkeypox. While most cases reported in Australia have acquired monkeypox overseas, the number of people acquiring their infections locally is increasing.

What are the symptoms?

Symptoms of monkeypox can include a rash, fever, chills, muscle aches, backache, swollen lymph nodes, exhaustion, and headache.

The rash can be painful and can affect any part of the body including:

- The genitals and anus (these are most common in the current outbreak);
- Inside the mouth;
- Face;
- Body;
- Palms of the hands; and
- Soles of the feet.

Rashes can vary in number, and may involve pimples, vesicles (blisters with clear fluid), pustules (blisters with pus), or ulcers (breaks in the skin). The rash may change and go through these different stages, before becoming a scab that falls off.

Some people also develop proctitis (rectal pain, bloody stools, and diarrhoea) and urethritis (swelling and irritation of the urethra, causing pain on urination).

Symptoms may resemble sexually transmitted infections (STIs), such as herpes or syphilis. Simultaneous infection with monkeypox and an STI is possible.

Symptoms may begin to develop up to 21 days—typically 7 to 14 days—following close contact with someone with monkeypox. The disease is usually mild, but severe illness can develop in a small percentage of people. Children, pregnant women, and immunocompromised individuals are at higher risk for severe disease.

How is monkeypox spread?

Monkeypox does not spread easily between people, as it usually requires very close contact. It can spread from person-to-person through:

- Contact with monkeypox skin rashes, lesions, sores, and scabs;
- Contact with contaminated surfaces and items, such as clothing, towels, or bedding; and
- Respiratory droplets (such as coughs and sneezes) from an infected person.

People with monkeypox are infectious from the time they develop their first symptoms (often a fever or a rash) and until the rashes crust, dry or fall off.

Who is at risk?

In the current outbreak, anyone who has been in direct, and often intimate, contact with someone with monkeypox is at risk. The current outbreak has disproportionately impacted men who have sex with men. People who have recently returned from overseas, who were sexually active whilst travelling and/or have attended large parties are advised to watch for symptoms. People who have not travelled should also be aware of the symptoms, as some people have acquired their infections locally in Australia.

Am I at greater risk if I'm HIV-positive?

There is very limited evidence on monkeypox in people living with HIV, and most is based on research in countries where access to HIV treatment is limited. In these countries, patients with untreated HIV experience more negative health outcomes than in Australia. There is however no indication that HIV-positive people with good control of their disease would be at greater risk than the general population. People living with HIV should follow the same advice as the general population and discuss with their doctor if they have any concerns.

What do I do if I develop monkeypox symptoms?

You should isolate from others and seek immediate medical attention. Call your GP clinic, Melbourne Sexual Health Centre, or your nearest sexual health service to let them know you will be attending. Wear a mask and cover your rash or blisters if you have any and inform the reception staff and wait to be isolated until seen.

What do I need to do if I am diagnosed with monkeypox?

You should isolate from others until your symptoms are resolved and you receive clearance from your treating doctor. Victorian Public Health Officers are contacting all people

diagnosed with monkeypox and providing specific advice regarding isolation requirements and preventative measures, including how to keep people in your household protected.

How is monkeypox treated?

Most people with monkeypox have a mild illness and recover within a few weeks without specific treatment. In severe cases—and for people who are at high-risk of severe disease—treatments are available.

How can I prevent monkeypox?

You can reduce your risk of contracting monkeypox by:

- Getting vaccinated;
- Avoiding close contact—including intimate or sexual contact—with people who are unwell or have compatible symptoms;
- Avoiding skin-to-skin contact, particularly with any rashes or lesions;
- Avoiding contact with surfaces and items—including clothing, towels, and bedding used by people who are unwell or have compatible symptoms, and
- Staying vigilant with hygiene measures including wearing masks and washing hands with soap and water or alcohol-based sanitiser.

Who can get the monkeypox vaccine?

Monkeypox vaccine appointments are now available in Victoria. The vaccine is currently available free-of-charge for the following priority groups:

- Post-exposure prophylaxis for high-risk close contacts of monkeypox cases (within 4 days);
- Laboratory workers who analyse specimens from monkeypox cases;
- Sexually active men, trans people or non-binary people assigned male at birth who have sex with men (including cis and trans men)
 - with an STI in the last 12 months, or
 - intending to engage in sexual practices during overseas travel to Europe or North America before 31 October, or
 - who attend sex-on-premises venues, or
 - who are homeless, or have significant drug use or psychiatric illness; and
- Sex workers who engage in sex with the sexually active groups listed above.

Eligibility criteria are subject to change as more vaccines become available.

A person will start to build protection in the days after their first dose. It is advised that people allow for at least two weeks between getting the vaccine and engaging in behaviours that may expose them to monkeypox.

Where can I get the vaccine?

For now, vaccine enquiries can be made at the following locations:

- Thorne Harbour Health - PRONTO Clinic, 200 Hoddle Street, Abbotsford, VIC, 3067, (03) 9416 2889;
- Thorne Harbour Health - Centre Clinic, 3A/79-81 Fitzroy Street, St Kilda, VIC, 3182, (03) 9525 5866;
- Collins Street Medical Centre, Level 7/267 Collins Street, Melbourne, VIC, 3000, (03) 8575 6900;
- Prahran Market Clinic, Prahran Central Shopping Centre Mezzanine Level, 325 Chapel Street, Prahran, VIC, 3181, (03) 9514 0888;
- Northside Clinic, 370 St Georges Road, Fitzroy North, VIC, 3068, (03) 9485 7700; and
- Melbourne Sexual Health Centre, 580 Swanston Street, Carlton, VIC, (03) 9341 6200.

For people who fulfil the criteria for vaccination and live in regional Victoria, please contact your closest regional Local Public Health Unit:

- Ovens Murray—phu@awh.org.au;
- Barwon Southwest—phu@barwonhealth.org.au;
- Gippsland/La Trobe—phu@lrh.com.au;
- Goulburn Valley—phu@gvhealth.org.au;
- Ballarat/Grampians—phu@bhs.org.au; and
- Loddon Mallee—phu@bendigohealth.org.au.

Clinics may not always be able to accept new patients. More clinics and access points will be able to provide the vaccine as additional stock becomes available.

What if I am not eligible to receive the vaccine?

If you do not fit the current eligibility criteria, there is no need to book an appointment. More vaccines are on the way. We expect vaccine eligibility criteria to change once more vaccines are available.

If the vaccine is free, why do I have to pay?

While the vaccine is free of charge, consultations may not be. Please speak to the relevant clinic to verify consultation-related fees.

I can't get an appointment at any clinic to get a vaccine, even though I meet the criteria.

What should I do?

Noting the current limited supply of vaccines, we are aware that not everyone will be able to get a jab. We're making efforts to provide the vaccine to those who need it the most, until we receive additional supply. We are expecting additional vaccines sometime in September 2022. In the meantime, we recommend that you consider other preventive measures, such as avoiding close contact with people who are unwell or have compatible symptoms and staying vigilant with hygiene measures (including wearing masks and washing hands with soap and water or alcohol-based sanitiser).

If I have had contact with someone with monkeypox, should I go and get vaccinated?

Public Health Officers will contact people who are known to be at high risk of acquiring monkeypox after an exposure. Vaccination within 4 days after an exposure may prevent people developing monkeypox.

If I develop monkeypox, should I get vaccinated afterwards?

No, people who have had monkeypox do not need to be vaccinated.