From Drug Resistance to Donuts: Applied Epidemiology in the Australian Capital Territory

A thesis submitted for the degree of Master of Philosophy (Applied Epidemiology)

Keeley Allen
Communicable Diseases Branch
ACT Health Directorate
2021–2022

ACT Government | ACT Health

Australian National University

Field supervisor:
Alexandra Marmor

Academic supervisor:
Dr Davoud Pourmarzi

ORIGINALITY STATEMENT

I hereby declare that this submission is my own work and to the best of my knowledge it contains no materials previously published or written by another person, or substantial proportions of material which have been accepted for the award of any other degree or diploma at ANU or any other educational institution, except where due acknowledgement is made in the text. Any contribution made to the research by others, with whom I have worked with at ACT Health, ANU, or elsewhere, is explicitly acknowledged in the thesis. I also declare that the intellectual content of this thesis is the product of my own work, except to the extent that assistance from others in the project's design and conception or in style, presentation, or linguistic expression is acknowledged.

Keeley Allen

25 October 2022

ACKNOWLEDGEMENTS

Firstly, I would like to acknowledge my field placement, studies, and preparation of this thesis were conducted on the lands of the Ngunnawal people, with considerable periods of writing on the lands of the Gadigal and Wangal people of the Eora Nation and the lands of the Kaurna people. I would like to acknowledge and pay my respect to these traditional custodians and recognise their continuing unbroken connection to Country for over 60,000 years. I am deeply humbled by the opportunity to live, work, and learn on these lands. Always was, always will be.

I have been blessed with the greatest of MAE supervisors, Alexandra Marmor and Dr Davoud Pourmarzi. I am so grateful to have the opportunity to learn from both of you. Thank you for your teachings, kindness, and patience over the past 20 months. Thank you for always having time for me. I am in awe of your expertise, wisdom, and passion. I am so grateful that you shared some of it with me.

I would like to acknowledge the legends of the Disease Surveillance Unit at ACT Health Communicable Disease Control, an absolute powerhouse team of women whose work and successes so often fly under the radar. Thank you to Alison Kingsbury, Dr Nevada Pingault, Alexandra Marmor, Julia Smythe, Rachael Crane, Jenny Post, Milica Stefanovic, Felicity Greenville, and Evelyn Pappas for taking the time to teach me your ways, assisting on projects, and for all your efforts protecting the health of our communities. Special thanks as well to Dr Philippa Binns for your guidance and your advocacy.

Thank you to the 2021 cohort, forged on Zoom and bonded for life. We've constantly been told we are lucky to be undertaking the MAE during a pandemic, but what has been truly fortunate is being able to learn alongside you. Special thanks to Justine Marshall for your joy and your friendship, Kirsty Nicholls for standing with me in the fight for our education, Aidan Yuen for your calm diligence through our shared projects, and Leonie Williamson for your sage wisdom and high fashion. Most of all, this thesis would not have been possible without the High Risk Hype Queens, Aruna Phabmixay and Yasmin Lisson. Thank you both for support, care, and friendship as we raise each other up and celebrate our successes. It has been my privilege to reign alongside you as we power through the MAE program together.

Thank you to my husband, Matthew Hirsh, for all your support while I pursue my applied epidemiology dreams. Thank you for always listening, travelling up and down to Canberra for weekends together, keeping us sane during quarantine and lockdowns, and keeping the cups of tea flowing. Thank you as well for your understanding when I had to miss Thanksgiving dinner due to an outbreak investigation. With you, every day is Turkey Day.

To every person who picked up the phone when I called for a case interview or for contact tracing, thank you for your trust.

Finally, this thesis is dedicated to my granddad, Jack McKendrick, the richest man in the world without any money.

ABSTRACT

This volume presents four projects and additional public health experiences satisfying the competencies of my Master of Philosophy (Applied Epidemiology) conducted through my field placement at ACT Health's Communicable Disease Control Branch.

These projects comprise of two outbreak investigations, an outbreak of the B.1.617.2 (Delta) variant of SARS-CoV-2 in a high school setting and a food-borne gastroenteritis outbreak associated with donuts from a single bakery; an epidemiological investigation into factors associated with a willingness to receive a COVID-19 booster vaccine among migrants in Australia born in the World Health Organization's Eastern Mediterranean Region; design of a surveillance system to add the multidrug-resistant organisms carbapenemase-producing *Enterobacterales* (CPE) as a notifiable condition in the ACT; and a descriptive and spatial analysis of hepatitis C notifications in the ACT over a ten-year period.

The two final chapters of this thesis describe my experiences teaching epidemiology and other key public health activities of my field placement, including a secondment to ACT Health COVID-19 Operations branch, establishment of a surveillance and case management system for monkeypox virus, evaluating a letter program for GPs diagnosing hepatitis C in their patients, development of interactive dashboards for notifiable conditions, and introducing applied epidemiology to a high school class.

The findings from my projects and the outputs of these additional experiences contribute to the body of knowledge for applied epidemiology and inform public health decision making and action.

TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION

“How many people can safely isolate in a yurt?”

This was not a question I was expecting to answer during my time as a Master of Philosophy (Applied Epidemiology) Scholar.

I was asked this question during my secondment to ACT Health’s COVID-19 Operations Branch during the territory’s local outbreak of the Delta variant. This secondment provided a unique opportunity to work directly in an acute public health response with other members of my cohort and with our teachers at the ANU.

The question came from a case investigator after they had just finished a COVID-19 case interview. I was six weeks into this secondment and feeling pretty comfortable with the processes of case investigation and management. I had rapidly developed skills in case interviewing, managing the welfare of a case, identifying chains of transmission, and interpreting whole genome sequencing data. However, I was not prepared to talk about yurts.

This question has been a good reminder throughout my study that no matter how knowledgeable or comfortable we may feel as field epidemiologists, there is always a new public health question to consider and a new problem to solve. It has also been a good test of my adaptability and flexibility, being prepared to put aside the work I am doing to deal with the acute problem of the yurt. Finally, it has been a reminder that it is fundamental to know the communities you are working with. It was a surprise to all of us in COVID-19 Operations that the ACT even had yurts, and if we don’t regularly engage with our population we would never have known.

This chapter outlines the field placements and projects meeting the degree requirements where I have applied these lessons.

If you are wondering, the answer is that one person can safely isolate in a yurt provided they have their own bathroom arrangements.

Field placement overview

Communicable Disease Control Branch

My field placement was undertaken in the Communicable Disease Control Branch (CDC) at ACT Health. CDC is responsible for the surveillance of and response to notifiable conditions in the ACT, assessing infection control procedures in ACT businesses, and administering the ACT component of the National Immunisation Program. CDC operates as both the local public health unit and the strategic arm of the Territory's public health response. I was involved in the daily activities of the Disease Surveillance team; interviewing cases for a variety of notifiable conditions, cleaning, analysing and reporting surveillance data, joining outbreak investigation teams, and building new surveillance systems. I was directly involved in the second largest foodborne gastroenteritis outbreak the ACT had ever experienced (Chapter 2) and established the territory's first surveillance system for a multidrug-resistant organism (Chapter 4). Throughout my time at CDC, I was involved in the investigation of five foodborne outbreaks, developed REDCap projects for the follow up of a wide range of notifiable conditions, designed and implemented two additional surveillance systems, evaluated a letter program for the management of hepatitis C cases, and produced interactive dashboards combining routine and enhanced surveillance data for notifiable conditions. My field placement at CDC has been a busy, productive, and deeply rewarding experience.

As part of my field placement, I had the opportunity to complete my epidemiological study through the ANU. I was part of a wider research team exploring the information needs, information seeking behaviours, and barriers faced by migrants living in Australia accessing information about COVID-19 vaccines. I lead a cross-sectional study assessing factors associated with a willingness to receive a booster dose of COVID-19 vaccine and highlight the importance of the news we see to our decision to receive a vaccine (Chapter 3). As part of this research team, I had the privilege to work closely with an interstate MAE colleague and contribute to qualitative research and explore aspects of health promotion and risk communication I may not have had the opportunity to investigate otherwise.

COVID-19 Operations Branch

With the arrival of local transmission of COVID-19 in the ACT, members of the CDC were seconded in COVID-19 Operations. My secondment was for three months from August-October 2021 in the Case Investigation and Epidemiology. I was directly involved in the investigation of 20 clusters, analysis and reporting of COVID-19 surveillance data, refining COVID-19 case investigation questionnaires, and interviewing cases. The first COVID-19 cluster I investigated was an outbreak in a local high school prior to knowledge of local transmission and in the absence of public health measures in educational settings (Chapter 2).

Summary of degree requirements

A summary of my projects and activities against the competencies of the MAE program are shown below.

Competency	Chapter 2	Chapter 3	Chapter 4	Chapter 5	Chapter 6
Investigation of an acute public health problem or threat	X				
Analysis of a public health dataset				X	
Establish or evaluate a surveillance system or other health information system			X		
Design and conduct an epidemiological study		X			
Literature review				X	
Lay summary	X		X	X	X
Conference presentation	X	X			
Peer-reviewed publication	X	X			
Teaching field epidemiology					X

Investigate an acute public health event

Chapter 2 includes two outbreak investigations I led during my field placement.

I investigated an outbreak of the B.1.617.2 (Delta) variant of SARS-CoV-2 in a local secondary school. This outbreak occurred at a time when local transmission was not known, and few public health and social measures were in place. As part of this outbreak, I liaised with the Education Directorate and developed a standard questionnaire to re-interview student cases to detail movements on the school site and understand chains of transmission. I also reviewed the vaccination status of cases and household contacts to understand household transmission dynamics. We found that active classes where students move around the room and mingle, such as drama and personal development, health and physical education, saw more transmission compared with passive classes. Further, we found that household contacts who were effectively vaccinated before the first case in their household became infectious were less likely to become cases compared with those who were not effectively vaccinated. These findings were shared with the Education Directorate and formed part of the evidence base to introduce mask wearing in ACT secondary schools.

I also investigated the second largest foodborne gastroenteritis outbreak ever recorded in the ACT. As part of this investigation, I conducted a hypothesis generating interview with initial complainants and developed a standard questionnaire for case and non-case interviews used for a total of 301 phone and self-administered online responses. I also attended the initial food safety inspection to interview the proprietor and collect environmental samples and coordinated the collection of stool samples from ill participants. I led the collation, cleaning, and analysis of epidemiological data; preparing the internal outbreak investigation report; and preparation of a summary of findings to participants. We found that donuts contaminated with norovirus from a single bakery were the vehicle of transmission. The suspected source of contamination was an ill food handler who attended work over a five-day period. The findings of this outbreak resulted in the redesign of the food poisoning surveillance and complaints system and highlight the need to consider novel food products as the potential source of a foodborne outbreak.

Plan and conduct an epidemiological study

Chapter 3 details my epidemiological study as a final draft manuscript.

My epidemiological study was conducted through the Australian National University assessing factors associated with a willingness to receive a COVID-19 booster vaccine among migrants born in the World Health Organization's Eastern Mediterranean region currently living in Australia. As part of a larger research project led by my academic supervisor, Dr Davoud Pourmarzi, we designed a cross-sectional study assessing the association between willingness to receive a booster dose with sociodemographic factors, information sources, and perceptions of COVID-19 vaccines at a time when booster vaccines were not a reality for the majority of Australian residents. This analysis assessed these associations using univariate and multivariate logistic regression. We found the majority of study participants had received two doses of COVID-19 vaccine, but this did not guarantee willingness to receive a booster dose. Increasing age and no exposure to concerning news about COVID-19 vaccines were associated with COVID-19 booster vaccine willingness. These results reinforce that addressing vaccine concerns and transparent communication about uncertainty should be a priority in the current and future pandemics.

Establishment of a surveillance system

Chapter 4 describes my design of a surveillance system for carbapenemase-producing *Enterobacterales* (CPE) in the ACT.

CPE is a significant public health threat as a group of multidrug-resistant organisms that carry genes conferring resistance to carbapenems. The ACT does not have oversight of CPE and no mechanisms in place to identify local transmission and outbreaks. I led the development of a new surveillance system under the guidance of my field supervisor, Alexandra Marmor, to identify and follow up CPE cases in the ACT. The surveillance system was designed with the intention of adding CPE as a notifiable condition in the ACT, coordinating notifications from

laboratories, enhanced surveillance data collection, and whole genome sequencing to identify the source of acquisition, detect local transmission, and follow up contacts to stop further spread. I identified key internal and external stakeholders required for the successful implementation and operation of the surveillance system, consulting on their needs and potential barriers for the system. I designed bespoke information flows based on the location of the case at the time of testing and the enhanced surveillance data collection tool and data fields required to meet the objectives of the system. I prepared the business case to make CPE a notifiable condition in the ACT, including a case assessment against the national criteria endorsed by Communicable Disease Network Australia (CDNA), a protocol for notification and follow up, and communications strategy.

At the time of submission, the case to add CPE to the list of notifiable conditions in the ACT was under assessment by the Chief Health Officer. If CPE is made notifiable, the surveillance system will be used for the follow up of cases and contacts to understand the burden of CPE on the ACT population and respond to indications of local transmission. If CPE is not made notifiable in the short term, the relationships built between ACT Health and colleagues in public and private hospitals through this project provide a solid foundation for collaborative public health action in the future.

Analysis of a public health data set

Chapter 5 details an analysis of hepatitis C notification data in the ACT between 2012 and 2021.

The World Health Organization has set a target to eliminate hepatitis C by 2030. ACT Health is working towards this elimination goal through public health follow up of cases and collecting enhanced surveillance data on the sociodemographic and behavioural risk factors associated with individual cases of hepatitis C. I prepared a descriptive and spatial analysis of this notification and enhanced surveillance data to describe hepatitis C notifications by person, place and time. I found that hepatitis C notifications have been declining since 2017 alongside the availability of direct-acting antivirals. Males, people in correctional centres, and people living in relatively disadvantaged areas of the ACT were overrepresented among hepatitis C notifications compared with the overall ACT population. Spatial cluster hepatitis C notifications were also evident in relatively disadvantaged areas of the ACT. The findings of this analysis have established a baseline for understanding the epidemiology of hepatitis C in the ACT and informed directions for public health actions to eliminate the condition in the Territory.

Literature review

I conducted a review of existing literature examining the epidemiology of hepatitis C in Australia, including the prevalence, known risk factors, and characteristics associated with re-infections (Chapter 5).

Prepare a scientific manuscript for a peer-reviewed journal

I prepared the following manuscripts as the first author:

- Factors associated with COVID-19 booster vaccine willingness among migrants from the Eastern Mediterranean living in Australia: a cross-sectional study, under peer review at *BMC Public Health*
- Pens down: An outbreak of the B. 1.617.2 SARS-CoV-2 variant in an Australian high school, August 2021, published in *Communicable Diseases Intelligence*
- Donuts for weight loss? A foodborne norovirus outbreak associated with a bakery in the Australian Capital Territory, published in *Communicable Diseases Intelligence*

I also assisted in the preparation of the following manuscripts as a co-author:

- A mixed-methods systematic review on the prevalence of, and reasons for, COVID-19 vaccine hesitancy among racial and ethnic minorities in high-income English-speaking countries, under peer review at *Globalization and Health*
- "They said we're all in it together, but we were kind of separated": Barriers to access, and suggestions for improving access to official information about COVID-19 vaccines for migrants in Australia, under peer review at *BMC Public Health*

Communication to a lay audience

I prepared the following documents for lay audiences :

- A one-page letter to communicate the findings of the norovirus outbreak to all participants (Chapter 2)
- Development of a new factsheet for CPE intended to be sent to clinicians and cases, and available on the ACT Health website (Chapter 4)
- Development of a new factsheet for contacts of CPE cases to be sent during contact tracing (Chapter 4)
- An update to the ACT Health factsheet for Hepatitis C sent to clinicians and cases, and available on the ACT Health website (Chapter 5)

In addition, I delivered a presentation on applied epidemiology to a high school audience of year 10 students.

Conference presentations

I delivered the following oral presentations at the Communicable Diseases and Immunisation Conference, Sydney, Australia, 20-22 June 2022:

- Donuts for weight loss? A norovirus outbreak in the Australian Capital Territory
- Factors affecting COVID-19 vaccine booster willingness among migrants in Australia

I also co-chaired the 6D - Outbreak Response and Investigation session at the Communicable Diseases and Immunisation Conference, Sydney, Australia, 20-22 June 2022.

Teaching epidemiology

I prepared and delivered a practical teaching exercise introducing geographic information software (GIS) and its uses for applied epidemiology for my Lesson from the Field. I also attended the sessions prepared by my MAE colleagues (Chapter 6).

As part of a group of five, I prepared and delivered a teaching session entitled “Forget COVID-19: Why you should be afraid of AMR and what to do about it” for the 2022 MAE cohort (Chapter 6).

CHAPTER 2: INVESTIGATION OF TWO OUTBREAKS IN THE ACT

TABLE OF CONTENTS

Prologue

This chapter details two outbreak investigations I led during my field placement at ACT Health:

- A COVID-19 outbreak of the B.1.617.2 variant in a high school setting
- A foodborne norovirus outbreak associated with a bakery

This chapter addresses the following competencies:

- Investigation of an acute public health problem or threat
- Lay summary
- Conference presentation
- Peer-reviewed publication

This chapter consists of the two manuscripts I prepared during my field placement detailing these two outbreaks that have been published in *Communicable Diseases Intelligence*. This chapter also includes a conference presentation delivered at the Communicable Disease and Immunisation conference in June 2022 (Appendix C) and a lay summary of the foodborne norovirus outbreak findings sent to all respondents who participated in the investigation (Appendix D).

My role

I have chosen to include two outbreaks in this chapter where I led the epidemiological investigation. For both outbreaks, I designed and conducted the field investigation, including the development of a case definition, design of a data collection tool for case interviews, conducted case interviews and collated data to characterise the outbreak, by person, place, and time, and conducted an analytical study to test hypotheses. However, each outbreak required a different response and engagement of different teams and organisations to successfully investigate the event and produce public health advice.

The COVID-19 outbreak took place at the beginning of a local outbreak of the B.1.617.2 variant when local transmission was not known and limited public health and social measures in this case. This outbreak was one of 20 COVID-19 cluster investigations I conducted during my secondment to ACT Health COVID-19 Operations. This outbreak focused on investigation rather than control primarily for the purpose of informing the ACT's COVID-19 response. I developed a standardised data collection tool and interviewed all student cases with a parent or guardian present to understand potential transmission chains on site. I liaised with the Education Directorate to access timetables and understand any public health measures in place. I designed the cohort study under the guidance of my academic and field supervisors and conducted the analysis. I also prepared the internal outbreak report including recommendations for safe face-to-face learning in the context of the Delta variant.

The foodborne norovirus outbreak took place in the absence of an OzFoodNet epidemiologist at ACT Health and was one of five foodborne outbreaks I participated in during my field placement. This outbreak included investigation and control elements to identify the source of illness and provide food safety education to the bakery proprietors. I led the epidemiological analysis of this investigation which also included environmental health and laboratory analyses. Under the guidance of the Director of Disease Surveillance, I adapted the ACT's standard food poisoning questionnaire to the menu of the bakery, rapidly pivoted our paper-based investigation into a REDCap database to collate phone and online responses from cases and non-cases, attended a food safety inspection and prepared briefings for the outbreak investigation team meetings. I designed the case-control study to investigate the source of infection, analysed the investigation's epidemiological data, prepared an internal report detailing the investigation, and a lay summary letter to all respondents summarising the findings. I also contributed to a Freedom of Information Request requesting information on this investigation. One of the roles I hadn't anticipated having in this investigation was driving collection kits to cases and stool specimens to pathology collection centres for testing.

Key reflections

Prior to the COVID-19 outbreak, I had limited exposure to genomic analysis and how to interpret findings for an epidemiological analysis. This outbreak provided a solid foundation for interpreting genomic analysis findings that I was able to apply and build on in the 19 other COVID-19 clusters I investigated. The high media interest in this outbreak investigation and the significant proportion of cases who were children reinforced the importance of maintaining the confidentiality of cases and the information they share to protect their privacy.

During the investigation of the COVID-19 outbreak, all students and staff of the school, and their entire households, were required to quarantine for 14 days. My interactions with the outbreak cases and their households during this period increased my awareness of the challenges our public health measures can have on our communities and the importance of adequate wellbeing and resources support to make compliance with public health measures as easy and safe as possible.

The foodborne norovirus outbreak enabled me to apply my course block learnings in a real, imperfect investigation. We were unable to conduct active case finding in this investigation and I learnt firsthand the impact of selection biases on the strength of epidemiological analyses and the uncertainty of their results. The findings of the epidemiological investigation taught me the value and how to interpret analyses that are not statistically significant in the context of a foodborne outbreak. I also learnt the importance of adaptability in an outbreak investigation and the importance of the flexibility to rapidly scale up investigations to respond to surges in reports of illness. The rapid development of a REDCap database and training team members from other areas of ACT Health Communicable Disease Control to conduct case interviews to meet the volume of responses was an urgent challenge and a tremendous opportunity to lead a wider team.

The most valuable learning from the foodborne norovirus outbreak was the importance and fragility of trust. Outbreak investigations and applied epidemiology more broadly rely on members of the public feeling safe, respected and confident enough to share information about their illness and actions for us to be able to collate, analyse and interpret data for public health action. The inability to conduct active case finding as part of this investigation was unfortunately interpreted as silence due to inaction or a lack of care or interest, particularly in light of the strength and volume of messaging for COVID-19. The most challenging and rewarding case interviews in this investigation were focused on working with community members who had not felt seen or valued, listening to their concerns, answering their questions, and explaining the investigation process. These long phone interviews reminded me how fragile trust in public health and governments can be, and the significance of communication for maintaining and improving our relationships with the populations we serve.

Public health impact

The COVID-19 outbreak investigation provided early evidence that children and adolescents infected with the B.1.617.2 variant could develop symptoms, transmit their infection to adults, and transmit their infection to each other. This was not common knowledge in August 2021 and informed the requirements for mask wearing, cohorting, and physical distancing measures in ACT schools after the lifting of stay-at-home orders in November 2021. The findings of this investigation supported the efficacy of COVID-19 vaccines against the B.1.617.2 variant and added to the body of evidence that transmission of SARS-CoV-2 relies more on droplets and airborne transmission compared with contamination of surfaces.

The foodborne norovirus outbreak has led to significant changes in the way food poisoning complaints are reported, recorded, and investigated in the ACT. I adapted the outbreak investigation REDCap project in consultation with the Environmental Health team to develop an online form for members of the public to report a food poisoning complaint (Chapter 7). I reviewed and refined the questions asked for food poisoning complaints to only include data that would impact the way ACT Health investigates and respond. I also conducted training for all Environmental Health Officers to familiarise them with the REDCap form for online responses and phone interviews. The food poisoning complaint REDCap project has been in use since July 2022. The legal framework of the *ACT Food Act 2001* and the ability to approach and request third-party food delivery applications for order history for active case finding is currently under review in the ACT.

Acknowledgements

COVID-19 outbreak

Thank you to my supervisors Dr Davoud Pourmarzi and Alexandra Marmor for your guidance and feedback in this outbreak investigation. It was a pleasure working with both of you in the same office as we were all on secondment to ACT Health COVID-19 Operations. Thank you to every case investigator who conducted the initial case interviews and the case management

team who supported cases and their families through isolation and quarantine. I would also like to thank Dr Sally Singleton and Dr Nevada Pingault for your rapid review and feedback on the bespoke questionnaire for this outbreak investigation. Thank you to the school and the ACT Education Directorate for your collaboration on this outbreak. Finally, thank you to every case and their parents/guardians for your honesty and trust when answering all of my questions.

Foodborne norovirus outbreak

I would like to acknowledge my supervisors Alexandra Marmor and Dr Davoud Pourmarzi for supporting me to include this outbreak in my bound volume and for letting me keep the title of the manuscript. The timely investigation of this outbreak would not have been possible without the generosity of the wider team at ACT Health Communicable Disease Control who were willing to assist in case interviews and the delivery of stool specimen kits. Thank you to Alexandra Marmor, Felicity Greenville, Milica Stefanovic, Fotis Sgouros, Raleigh Evans, Connor Goldrick, and Aleksander Surdonjic for answering the call for help. Special thanks to Dr Nevada Pingault for your supervision, your input into this investigation, and your advocacy. Thank you to every person who took the time to reach out to ACT Health to report your suspected food poisoning and to speak with us. I am deeply humbled by your trust.

APPENDIX A: PENS DOWN: AN OUTBREAK OF THE B.1.617.2 SARS-COV-2 VARIANT IN AN AUSTRALIAN HIGH SCHOOL, AUGUST 2021

PUBLISHED IN *COMMUNICABLE DISEASES INTELLIGENCE* VOLUME 46

Original article

Pens down: An outbreak of the B.1.617.2 SARS-CoV-2 variant in an Australian high school, August 2021

Keeley Allen, Alexandra Marmor, Davoud Pourmarzi

Abstract

Background

Little is known about the transmission dynamics of the B.1.617.2 (Delta) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) among children and young adolescents. We investigated an outbreak in an Australian high school, with limited public health mitigation measures in place, to understand the school activities associated with transmission, and the role of young adolescents in spreading SARS-CoV-2.

Methods

All 1,164 school attendees were monitored for SARS-CoV-2 infection through their mandated 14-day quarantine period. A cohort study design was used to investigate the effect of contact with the index case in different classes on the transmission of SARS-CoV-2, and the effect of vaccination among household contacts on becoming infected by SARS-CoV-2.

Results

There were 48 outbreak cases, including 14 students and one teacher who likely acquired their infection at the school. Attack rates among students in the index case's classes ranged from 0% to 45%. The greatest risk of infection for students in the same grade attending a class with the index case were from the drama class (risk ratio, RR: 111.6; 95% confidence interval (95% CI): 14.88–837.19) and the personal development, health, and physical education class (RR: 7.45: 95% CI: 2.27–24.44). The overall household attack rate was 57%, and household contacts who were not fully vaccinated were 2.9 times more likely (95% CI: 1.07–7.87) to become cases than were effectively-vaccinated household contacts.

Conclusion

Children can play an important role in the transmission of the Delta variant of SARS-CoV-2 within schools and at home. Transmission in this outbreak was largely associated with active, practical lessons that had close contact between students. This study demonstrates that the absence of public health and social measures in a low-incidence context resulted in the rapid spread of coronavirus disease 2019 (COVID-19) within an educational setting. These findings reinforce the role of public health and social measures and vaccinations to reduce airborne transmission and to enable a safe face-to-face learning environment.

Keywords: COVID-19; SARS-CoV-2; schools; risk factors; outbreak; contact tracing; adolescent; child; transmission; classroom

Introduction

After 16 months of no known local transmission in the Australian Capital Territory (ACT), the first locally-acquired coronavirus disease 2019 (COVID-19) case of 2021 was notified to the ACT Health Directorate (ACT Health) on 12 August 2021. This prompted a territory-wide stay-at-home order and the closure of the ACT's schools. A mask mandate was introduced for all persons aged 12 years and over; non-essential services were closed; schools were closed; and home-based learning was introduced for ACT students.[1] On 15 August 2021, ACT Health was notified of a high school student with a positive reverse transcription polymerase chain reaction (RT-PCR) test result for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

While infectious, the student attended a local public high school serving 1,079 students aged 12–16 years (grades 7–10), with 114 staff. Students were grouped into different classes for each subject and attended multiple classrooms through the school day. The school had been operating face-to-face learning for the 2021 school year and masks were not required for staff or students. Public health and social measures across ACT schools focused on hand hygiene promotion and on increased frequency of cleaning services. At the time of this outbreak, people aged 29 years and younger were not eligible for a COVID-19 vaccination.[2]

The index case became symptomatic on 12 August 2021 with a sore throat and fever, undertook a RT-PCR test on 14 August 2021 and was notified to ACT Health on 15 August 2021. The student was considered infectious while symptomatic and for three days before symptom onset. From Monday 9 August to Thursday 12 August 2021 during this infectious period they had attended school, which was considered a high-risk setting.[3] Genomic sequencing on 17 August 2021 confirmed that the student case was infected with the B.1.617.2 (Delta) variant. This outbreak investigation documents the transmission of the B.1.617.2 variant of SARS-CoV-2 from a single student to others in a classroom setting. In this report, we describe the investigation, the epidemiological characteristics of the outbreak, and the risk factors associated with transmission at the high school.

Methods

A school-associated case was defined as a person with a positive RT-PCR test for SARS-CoV-2 who attended the high school between 9 August 2021 and 12 August 2021. A household-associated case was defined as a person who received a positive RT-PCR test for SARS-CoV-2 and who was a household contact of an outbreak case. All people who attended the school campus any day between 9 August 2021 and 12 August 2021 were considered close contacts of the index case and were required to quarantine for 14 days after their exposure date, and to be tested immediately and on days 5 and 13 of quarantine, or upon the development of symptoms. The household contacts of the close contact attendees were considered secondary contacts and were required to quarantine for 14 days and to get tested if they developed symptoms of COVID-19.[4] A household close contact was defined as a person residing in the same dwelling as an outbreak case during their infectious period.

All cases in this outbreak were interviewed to ascertain their symptomology, potential exposures, and vaccination status. A breakthrough infection was defined as a confirmed case who had received two doses of COVID-19 vaccine at least 14 days prior to symptom onset.

A cohort study design was used to investigate the effect of contact with the index case in different classes on the transmission of SARS-CoV-2. The cohort included all students in the same grade as the index case who attended the high school between Monday 9 August and Thursday 12 August 2021. Only students in the same grade as the index case were included, as students from other year groups could not be enrolled in the index case's classes. Exposure was defined as attending a class with the index case for any length of time. The outcome was defined as

having a positive RT-PCR test. Data on exposure were collected through interviews using a standard questionnaire, with the case and their legal guardian, to ascertain movements and activities at school, and through reviewing school timetables. All attendees were followed up until 14 days after their last exposure date at the school. Data was collected and managed using REDCap electronic data capture tools hosted at ACT Health.[5,6]

Attack rates were calculated for attendees and non-attendees for each class attended by the index case. Relative risk (RR) and associated 95% confidence intervals (95% CI) were calculated for students in the same grade as the index case, to examine the association between attending different classes and becoming a confirmed COVID-19 case. Staff members were excluded from these analyses. The effect of being fully vaccinated on becoming infected by SARS-CoV-2 was examined by calculating attack rates and relative risk for household contacts of outbreak cases. For the purposes of the relative risk calculations, fully vaccinated was defined as receiving two doses at least 14 days before the start of the infectious period for the first case in the household. Results of hypothesis testing were considered statistically significant where confidence intervals did not include 1 and *p* values were less than 0.05. Statistical analysis was conducted in *R* version 4.1.1.

Whole genomic sequencing was conducted by the Australian National University on behalf of ACT Health, with lineage assigned using Phylogenetic Assignment of Named Global Outbreak Lineages (PANGOLIN) nomenclature.[i]

The investigation formed part of a public health emergency response under the *ACT Public Health Act 2010;* therefore, ethics approval was not required. This investigation is covered by the Australian National University Human Research Ethics Committee (Protocol 2017/909) standing approval for outbreak investigations involving staff and students.

Results

Outbreak associated cases

Fifteen students who had not attended the school campus between 9 August and 12 August 2021 were excluded. A total of 110 out of 114 (96.5%) staff members and 1,054 out of 1,064 (99.1%) included students were tested for SARS-CoV-2 during the quarantine period.

Overall, there were 48 outbreak cases. Sixteen cases were school-associated and were likely to have acquired their infection from the index case at the school, including one staff member and fifteen students. A further five students who attended the school were assessed as likely to have acquired their infection as a household close contact of an infectious sibling who also attended the high school, based on their time of symptom onset. A further 27 household contacts were notified as confirmed COVID-19 cases. The key characteristics of the cases are summarised in Table 1. The median age of the cases was 15 years (IQR: 13–40 years) and 63% of cases (30/48) were female. There were no hospitalisations or deaths.

Forty-two samples from this outbreak were sequenced, and six were unable to be sequenced. All sequenced samples were the B.1.617.2 (Delta) variant and were within two single nucleotide polymorphisms (SNPs) of the index case's sequence.

An epidemic curve of the outbreak by symptom onset date is shown in Figure 1. One school-associated case reported the same symptom onset date as the index case. The genomic analysis indicated that this secondary case was closely related, but not identical and suggests the transmission event may have occurred earlier in the index case's infectious period. Further, this second student did not share their genomic

i https://cov-lineages.org/.

Table 1: Characteristics of cases associated with the B.1.617.2 high school outbreak (n = 48), Australian Capital Territory, August 2021

Characteristic	School associated[a]	Household associated	Total
Total	**16**	**32**	**48**
Sex			
Male	4	14	18
Female	12	18	30
Age group (years)			
0–9	—	3	3
10–19	15	13	28
20–29	1	—	1
30–39	—	3	3
40–49	—	9	9
50+	—	4	4
Indigenous status			
Aboriginal and Torres Strait Islander people	1	—	1
Non-Indigenous people	15	31	46
Not stated	—	1	1
Country of birth			
Australia	15	22	38
Overseas	1	9	10
Vaccination status			
Not age eligible	16	16	31
Unvaccinated	—	6	6
1 dose	—	5	5
2 doses	—	5	5
2 doses > 14 days before onset	—	3	3

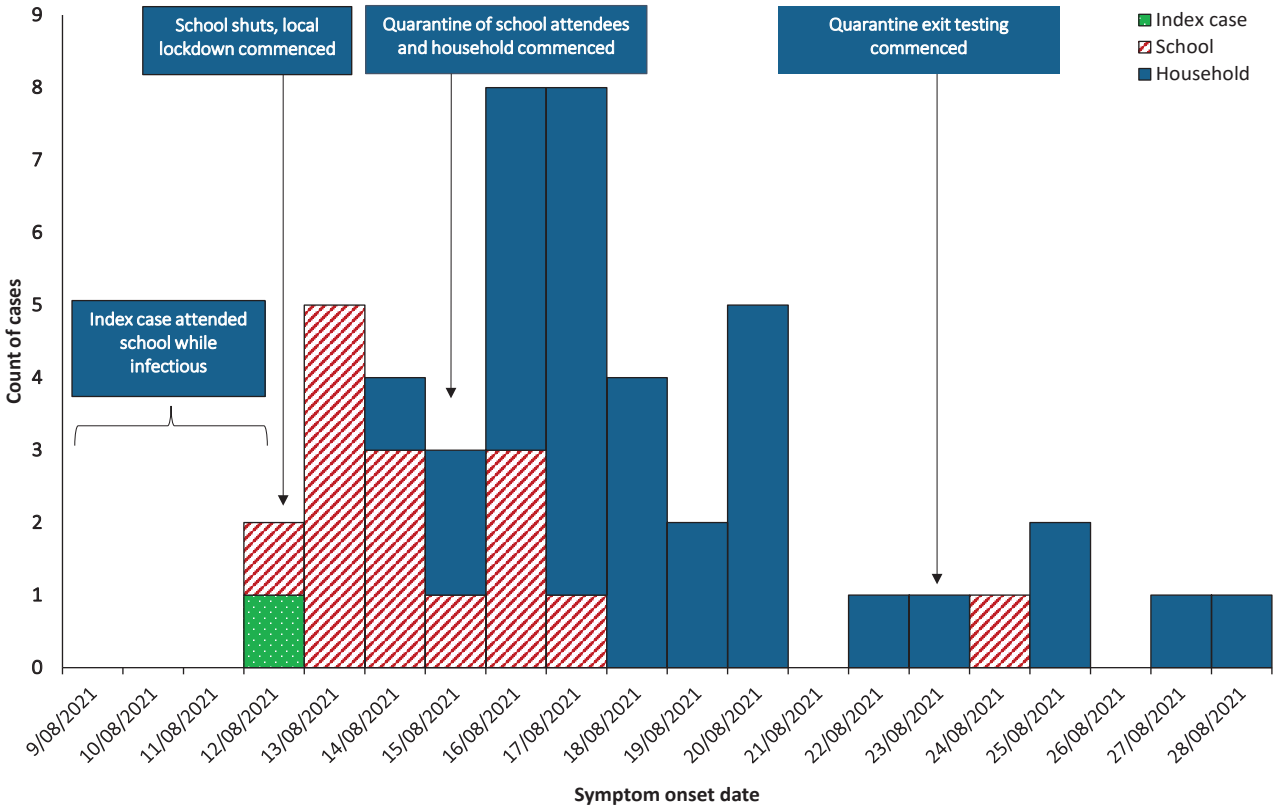
a Includes the index case, students who likely acquired their infection at school, and the staff member case.

sequence with any other school-associated cases, suggesting only one index case was present in this outbreak.

Among the 14 age-eligible cases, six were unvaccinated, three had received one dose, and five cases had received two doses. Three of the latter were breakthrough infections.

All but one case reported at least one COVID-19 symptom throughout their infection. The remaining case was asymptomatic through their infection. The most commonly-reported symptoms among child and adult cases were cough (83%; 40/48), runny or blocked nose (81%; 39/48), and headache (79%; 38/48) (Figure 2). A greater proportion of adult cases than child cases reported alteration of taste or smell; muscle or joint pain; diarrhoea; shortness of breath; or chest pain.

Figure 1: Epidemic curve of COVID-19 cases associated with the B.1.617.2 outbreak (n = 48), by symptom onset date,[a] Australian Capital Territory, August 2021



a Specimen collection date was used for cases that remained asymptomatic throughout their infection.

Transmission events

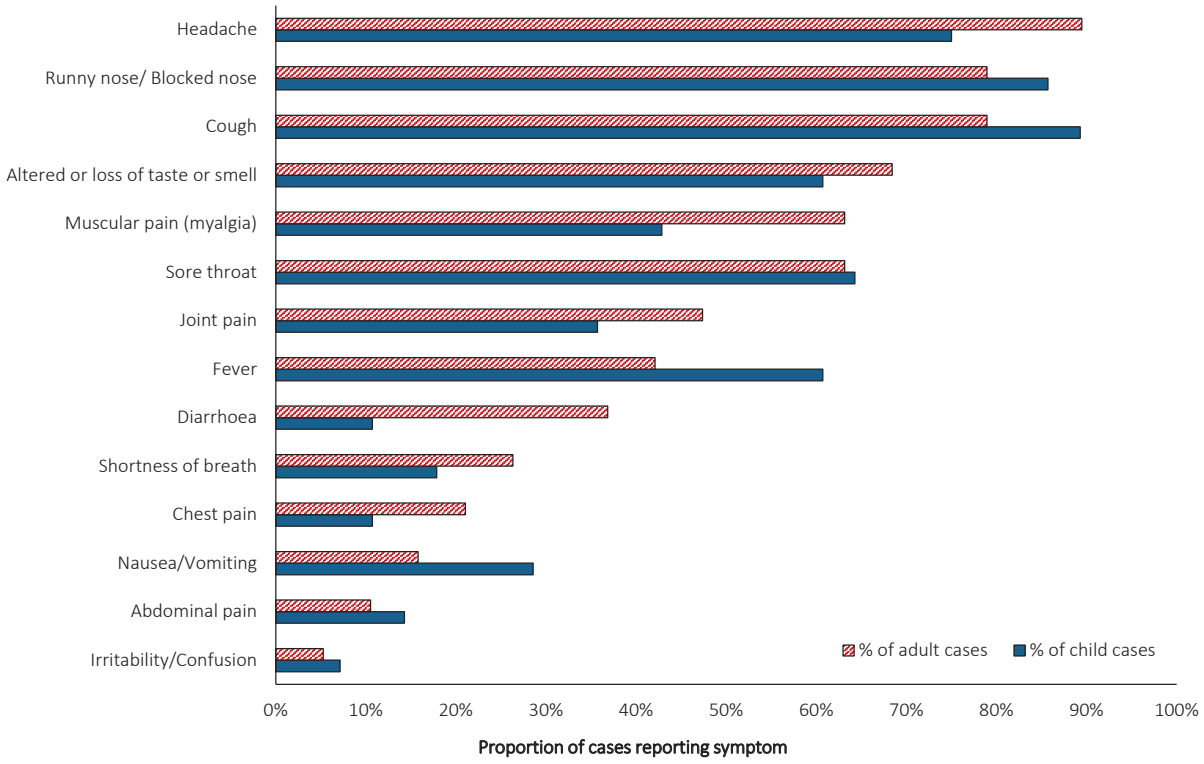
Based on the findings of the case interview and genomic analysis, the source of the index case's infection was identified as a theatre group rehearsal at a community hall the weekend before onset.

School transmission

The in-school transmission events associated with this outbreak are shown in Figure 3. Ten of the 14 school-acquired cases (71%) were in the same grade as the index case and had attended at least one class together. Four of these students attended multiple classes with the index case. The attack rates for the eight classes that the index case attended ranged between 0% and 45% (median: 3.2%) (Table 2). All lessons were indoors.

The highest attack rate was seen in the drama class, where nine of the 20 classmates of the index case were confirmed outbreak cases. This practical class had three timetabled indoor lessons during 9–12 August 2021 and involved small groups in close contact preparing short performances and the class sitting together as an audience. Risk of infection for students attending drama class was over one hundred times the risk for students in the same grade who did not attend this class (95% CI: 14.88–837.19; $p < 0.001$). Three student cases attended a personal development, health, and physical education (PDHPE) class with the index case for three lessons during 9–12 August 2021. All three practical lessons involved indoor physical activity, social mixing and close contact between students, and using the change rooms before and after class. Students in the PDHPE class were seven times more likely to be cases (RR 7.45; 95% CI: 2.27–24.44; $p < 0.001$) than were students who did not attend the class. The teacher of this class was also a confirmed outbreak case.

Figure 2: Symptom profile of child and adult COVID-19 cases associated with the B.1.617.2 high school outbreak (n = 48),[a] Australian Capital Territory, August 2021



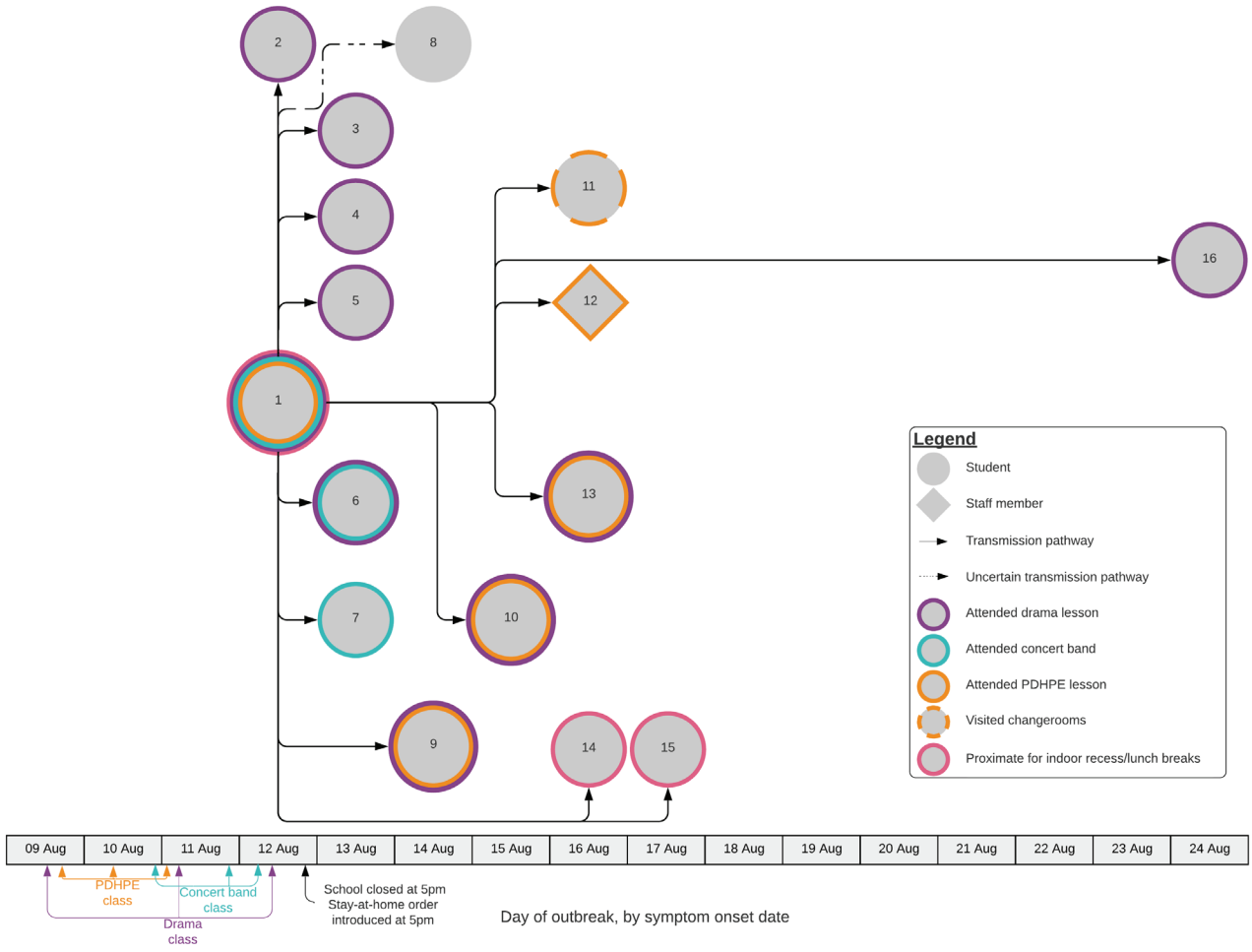
a One case reported remaining asymptomatic through their infection.

Two student cases attended a concert band rehearsal with the index case for two lessons during 9–12 August 2021. These lessons involved students playing brass and woodwind instruments and were conducted indoors in a dedicated music performance space. The risk of transmission in this class was not statistically significant (RR: 0.54; 95% CI: 0.12–2.48; p = 0.418). Two student cases also attended home group and a science class with the index case; however, these cases also attended the drama class.

Four school-associated cases were in a different grade to the index case. None of these four cases reported social interactions or timetabled classes with the index case, or with each other, and no likely sources of infection outside the educational setting were identified. Genomic analysis confirmed these four cases shared the same sequence as the index case. One of these four cases reported three timetabled practical PDHPE lessons with a different teacher at the same time as the index case, and both cases reported using the change rooms before and after each lesson. Although the lessons were conducted in different areas of the school, the repeated use of the change rooms may have provided an opportunity for transmission between the index case and this student.

Two additional students reported sitting near the index case for recess and lunch periods during 9–12 August 2021. The seating area was indoors and an informal setting enabled students to move freely. There was potential for the virus to have been transmitted to students during the lunch and recess periods in this shared space. One student case had an unclear source of exposure. This student had practical PDHPE lessons timetabled directly after the index case on three days; however, they reported using different change rooms and a different PDHPE teacher.

Figure 3: Likely transmission tree of school-associated COVID-19 cases associated with the B.1.617.2 high school outbreak (n = 16), by symptom onset date,[a] Australian Capital Territory, August 2021[b]



a Specimen collection date used for cases that remained asymptomatic throughout their infection.

b Note: This figure only includes school-associated cases. Household associated cases have been excluded.

c PDHPE: Personal development, health, and physical education.

Household transmission

Household size ranged from three to six people with a median of four residents. Twelve school-associated cases led to onward transmission within their household. Household attack rates ranged from 33% to 100% of household contacts and the overall attack rate among household contacts was 57% (30/56). Three school-associated cases did not lead to onward transmission at home. The median household size was the same for households with transmission (four residents) and households with no transmission (four residents).

The relative risk of a household contact becoming a COVID-19 case was 2.9 times higher (95% CI: 1.07–7.87; $p = 0.003$) among household contacts who were not fully vaccinated than among those who had received two doses of COVID-19 vaccine at least 14 days before the infectious period of the outbreak case (Table 3).

The outbreak was declared over on 12 September 2021, fourteen days after the notification of the final household-associated case.

Table 2: Attack rates and relative risk of COVID-19 among students in different classes, B.1.617.2 high school outbreak, Australian Capital Territory, August 2021 (n = 258)

Class	Student cases who attended the class	Student non-cases who attended the class	AR	Student cases who did not attend the class	Student non-cases who did attend the class	RR	*p* value	95% CI
Home group	2	18	10%	8	240	3.10	0.124	0.70–13.63
PDHPE[a]	4	18	18%	6	240	7.45	< 0.001	2.27–24.44
History and social sciences	0	24	0%	10	234	—	—	—
Science	1	24	4%	9	234	1.08	0.941	0.14–8.18
Drama	9	11	45%	1	247	111.6	<0.001	14.88–837.19
English	0	21	0%	10	237	—	—	—
Concert band	2	83	2.4%	8	175	0.54	0.417	0.12–2.48
Maths	0	25	0%	10	233	—	—	—

a PDHPE: Personal development, health, and physical education.

Table 3: The risk of transmission to household contacts (n = 52) by vaccination status among cases associated with the B.1.617.2 high school outbreak, Australian Capital Territory, August 2021

Vaccination status[a]	Case	Negative contact	Total	AR	RR
Fully vaccinated	3	9	12	25%	2.9[b]
Not fully vaccinated	29	11	40	73%	
Total	**32**	**20**	**52**		

a For this analysis, fully vaccinated was defined as receiving 2 doses > 14 days before the start of the infectious period for of the first case in the household.

b 95% CI: 1.07–7.87; $p = 0.003$.

Discussion

This high school outbreak demonstrates the transmission of the Delta variant of COVID-19, in an education setting with limited mitigation measures in place, during a period of low incidence. Masks were not worn during indoor lessons and public health and social measures in place had focused on surface cleaning and hand hygiene. These conditions promoted transmission among young adolescents in class and have been associated with in-school transmission in other COVID-19 outbreaks.[7–14]

Transmission in this outbreak was largely associated with active, practical lessons that had close contact between students. The drama, PDHPE and concert band classes all involved activities—including students mingling throughout the room, raised voices, physical activity, and playing musical instruments—with greater aerosol-generating potential than did quietly sitting at a desk. Transmission of SARS-CoV-2 has been documented in PDHPE classes in other jurisdictions,[8,9,15,16] and in classes and extracurricular activities with raised voices from teachers and students.[7,11,17,18] These activities may explain why transmission occurred in these classes and not during didactic lessons, where students are more often passive listeners as a teacher gives a lecture. Practical lessons are core components to student learning and safe

face-to-face learning will require adherence to public health and social measures, such as mask wearing among staff and students, and conducting practical lessons outdoors where feasible.

Although schools and students were previously considered to play limited roles in transmission for ancestral strains of SARS-CoV-2 in Australia and internationally,[19–22] this investigation suggests that new variants may have greater potential for transmission within educational settings. Investigations of outbreak of the B.1.617.2, B.1.1.57 (Alpha), and B.1.1.159 (Omicron) variants within schools have found higher attack rates compared to ancestral strains, and more frequent student-to-student and student-to-staff transmission.[7,11,21,23–26] The introduction of mask wearing in high schools and of vaccinations for children have been shown to reduce attack rates of the B.1.617.2 variant compared to ancestral SARS-CoV-2 in schools elsewhere in Australia,[21] demonstrating the value of public health and social measures to reduce transmission.

It is evident from this outbreak investigation that children experience symptoms and can play an important role in the transmission of the B.1.617.2 variant of COVID-19, particularly when limited public health mitigation measures are in place. Only one child case (2%) in this outbreak reported no symptoms. This is a lower proportion of asymptomatic cases than in previously-reported symptom profiles among children with B.1.617.2 infection.[27–32] The household attack rate in this outbreak indicates the potential for increased transmissibility of the Delta variant compared with other variants.[33–38]

The findings of this outbreak investigation are subject to some limitations. Firstly, not every student and staff member was recorded in ACT Health's quarantine database or had testing records identified. This may have resulted in under-ascertainment of cases. Further, the exact number of household contacts of staff and students is unknown, limiting our understanding of the extent of those impacted by the outbreak. Secondly, while all cases were able to be interviewed, the school-specific interviews took place up to two weeks after last attending the school campus. Recall bias may have affected the quality of data collected; the recall was particularly low for the use of toilets and attending non-timetabled areas of the school such as the library or the office. Thirdly, six cases were unable to have their samples sequenced to confirm their lineage and relatedness to other outbreak associated cases. Despite these limitations, these findings demonstrate transmission between young adolescents in an educational setting.

The transmission events in this outbreak demonstrate that the absence of public health and social measures in a low prevalence setting resulted in rapid spread in an educational setting. Promoting vaccination among eligible populations; mask wearing during class; improving indoor ventilation; encouraging outdoor rest periods and lessons (especially for practical classes); physical distancing of students; and staying home when symptomatic all remain crucial components to limit transmission and to enable a safe face-to-face learning environment for children and school staff.

Acknowledgements

The authors would like to thank the following case investigators for their efforts conducting initial case interviews: Charissa Hayward, Regan Bartholomew, Kari Tveit, Margaret Curran, Brody Bamford, Algreg Gomez, Gabrielle Robens, Leonie Williamson, Yasmin Lisson, Mary Brunton, Aruna Phabmixay, Christopher Harris, Rebekah Bowman, Pallavi Venkatesh. We also thank Dr Nevada Pingault and Timothy Sloan-Gardner for their review of the manuscript and subsequent suggestions. We would also like to thank the school, the ACT Education Directorate, and Dr Sally Singleton for their collaboration and collation of data. The Master of Philosophy (Applied Epidemiology) (MAE Program) is funded by Australian federal and state and territory health departments.

Author details

Keeley Allen[1,2]
Alexandra Marmor[2]
Dr Davoud Pourmarzi[1]

1. National Centre for Epidemiology and Population Health, Australian National University, Acton, ACT, Australia.

2. Communicable Disease Control, ACT Health, Holder, ACT, Australia.

Corresponding author

Keeley Allen

National Centre for Epidemiology and Population Health, Australian National University, Acton, ACT

Phone: (02) 5124 6215

Email address: keeley.allen@anu.edu.au

References

1. Australian Capital Territory Government (ACT Government), ACT Legislation Register. *Public Health (Lockdown Restrictions) Emergency Direction 2021 (No 1)*. ((ACT) NI2021-480). [Legislation.] Canberra: ACT Government; 12 August 2021. Available from: https://www.legislation.act.gov.au/ni/2021-480/.

2. ACT Government. COVID-19 vaccine bookings open for 16–29 year old Canberrans. [Internet.] Canberra: ACT Government; 1 September 2021. Available from: https://www.covid19.act.gov.au/news-articles/covid-19-vaccine-bookings-open-for-16-29-year-old-canberrans.

3. Australian Government Department of Health. Coronavirus Disease 2019 (COVID-19). CDNA National guidelines for public health units. Version 4.7. [Internet.] Canberra: Australian Government Department of Health; 2021. Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-novel-coronavirus.htm.

4. ACT Government, ACT Legislation Register. *Public Health (Diagnosed People and Close Contacts) Emergency Direction 2021 (No 1)*. ((ACT) NI2021–421). [Legislation.] Canberra: ACT Government; 9 July 2021. Available from: https://www.legislation.act.gov.au/ni/2021-421/.

5. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform*. 2019;95:103208. doi: https://doi.org/10.1016/j.jbi.2019.103208.

6. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377–81. doi: https//doi.org/10.1016/j.jbi.2008.08.010.

7. Baumgarte S, Hartkopf F, Hölzer M, von Kleist M, Neitz S, Kriegel M et al. Investigation of a limited but explosive COVID-19 outbreak in a German secondary school. *Viruses*. 2022;14(1):87. doi: https://doi.org/10.3390/v14010087.

8. Gettings JR, Gold JAW, Kimball A, Forsberg K, Scott C, Uehara A et al. SARS-CoV-2 transmission in a Georgia school district – United States, December 2020–January 2021. *Clin Infect Dis*. 2022;74(2):319–26. doi: https://doi.org/10.1093/cid/ciab332.

9. Gold JAW, Gettings JR, Kimball A, Franklin R, Rivera G, Morris E et al. Clusters of SARS-CoV-2 infection among elementary school educators and students in one school district – Georgia, December 2020–January 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70(8):289–92. doi: https://doi.org/10.15585/mmwr.mm7008e4.

10. Jehn M, McCullough JM, Dale AP, Gue M, Eller B, Cullen T et al. Association between K–12 school mask policies and school-associated COVID-19 outbreaks – Maricopa and Pima Counties, Arizona, July–August 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70(39):1372–3. doi: https://doi.org/10.15585/mmwr.mm7039e1.

11. Lam-Hine T, McCurdy SA, Santora L, Duncan L, Corbett-Detig R, Kapusinszky B et al. Outbreak associated with SARS-CoV-2 B.1.617.2 (Delta) variant in an elementary school – Marin

County, California, May–June 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70(35):1214–9. doi: https://doi.org/10.15585/mmwr.mm7035e2.

12. Schoeps A, Hoffmann D, Tamm C, Vollmer B, Haag S, Kaffenberger T et al. Surveillance of SARS-CoV-2 transmission in educational institutions, August to December 2020, Germany. *Epidemiol Infect*. 2021;149:e213. doi: https://doi.org/10.1017/S0950268821002077.

13. Stein-Zamir C, Abramson N, Shoob H, Libal E, Bitan M, Cardash T et al. A large COVID-19 outbreak in a high school 10 days after schools' reopening, Israel, May 2020. *Euro Surveill*. 2020;25(29):2001352. doi: https://doi.org/10.2807/1560-7917.ES.2020.25.29.2001352.

14. Torres JP, Piñera C, De La Maza V, Lagomarcino AJ, Simian D, Torres B et al. Severe acute respiratory syndrome coronavirus 2 antibody prevalence in blood in a large school community subject to a coronavirus disease 2019 outbreak: a cross-sectional study. *Clin Infect Dis*. 2021;73(2):e458–65. doi: https://doi.org/10.1093/cid/ciaa955.

15. Atherstone C, Siegel M, Schmitt-Matzen E, Sjoblom S, Jackson J, Blackmore C et al. SARS-CoV-2 transmission associated with high school wrestling tournaments – Florida, December 2020–January 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70(4):141–3. doi: https://doi.org/10.15585/mmwr.mm7004e4.

16. Zimmerman KO, Brookhart MA, Kalu IC, Boutzoukas AE, McGann KA, Smith MJ et al. Community SARS-CoV-2 surge and within-school transmission. *Pediatrics*. 2021;148(4). doi: https://doi.org/10.1542/peds.2021-052686.

17. Pray IW, Gibbons-Burgener SN, Rosenberg AZ, Cole D, Borenstein S, Bateman A et al. COVID-19 outbreak at an overnight summer school retreat – Wisconsin, July-August 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(43):1600–4. doi: https://doi.org/10.15585/mmwr.mm6943a4.

18. Vishnu Prasad S, Mukherjee G, Bobdey S, Kaushik SK, Yadav AK, Teli P et al. Epidemiological analysis of SARS-COV-2 B.1.617.2 (delta variant) transmission in an educational institute. *Med J Armed Forces India*. 2022. doi: https://doi.org/10.1016/j.mjafi.2022.02.008.

19. Brandal LT, Ofitserova TS, Meijerink H, Rykkvin R, Lund HM, Hungnes O et al. Minimal transmission of SARS-CoV-2 from paediatric COVID-19 cases in primary schools, Norway, August to November 2020. *Euro Surveill*. 2021;26(1):2002011. doi: https://doi.org/10.2807/1560-7917.ES.2020.26.1.2002011.

20. Macartney K, Quinn HE, Pillsbury AJ, Koirala A, Deng L, Winkler N et al. Transmission of SARS-CoV-2 in Australian educational settings: a prospective cohort study. *Lancet Child Adolesc Health*. 2020;4(11):807–16. doi: https://doi.org/10.1016/S2352-4642(20)30251-0.

21. National Centre for Immunisation Research and Surveillance (NCIRS), New South Wales Government Department of Health (NSW Health). *COVID-19 in schools – the experience in NSW: 18 October 2021 to 17 December 2021*. Sydney: NCIRS, NSW Health; 18 February 2022. Available from: https://www.ncirs.org.au/sites/default/files/2022-02/NCIRS_NSW_Schools_COVID_Summary_Term_4_2021_Report%20-%2024-02-2022_Final.pdf.

22. Otte Im Kampe E, Lehfeld AS, Buda S, Buchholz U, Haas W. Surveillance of COVID-19 school

outbreaks, Germany, March to August 2020. *Euro Surveill*. 2020;25(38):2001645. doi: https://doi.org/10.2807/1560-7917.ES.2020.25.38.2001645.

23. Hwang H, Lim JS, Song SA, Achangwa C, Sim W, Kim G et al. Transmission dynamics of the Delta variant of SARS-CoV-2 infections in South Korea. *J Infect Dis*. 2021;225(5):793–9. doi: https://doi.org/10.1093/infdis/jiab586.

24. Li YF, Fan W, Wang WH et al. A school cluster outbreak of COVID-19 caused by SARS-CoV-2 Omicron variant. *Chin J Public Health*. 2022;38(5):614–8. doi: https://doi.org/10.11847/zgggws1138512.

25. Lorthe E, Bellon M, Berthelot J, Michielin G, L'Huillier AG, Posfay-Barbe KM et al. A SARS-CoV-2 omicron (B.1.1.529) variant outbreak in a primary school in Geneva, Switzerland. *Lancet Infect Dis*. 2022;S1473-3099(22)00267-5. doi: https://doi.org/10.1016/S1473-3099(22)00267-5.

26. Grant R, Charmet T, Schaeffer L, Galmiche S, Madec Y, Von Platen C et al. Impact of SARS-CoV-2 Delta variant on incubation, transmission settings and vaccine effectiveness: results from a nationwide case-control study in France. *Lancet Reg Health Eur*. 2022;13:100278. doi: https://doi.org/10.1016/j.lanepe.2021.100278.

27. Assaker R, Colas AE, Julien-Marsollier F, Bruneau B, Marsac L, Greff B et al. Presenting symptoms of COVID-19 in children: a meta-analysis of published studies. *Br J Anaesth*. 2020;125(3):e330–2. doi: https://doi.org/10.1016/j.bja.2020.05.026.

28. Forrest CB, Burrows EK, Mejias A, Razzaghi H, Christakis D, Jhaveri R et al. Severity of acute COVID-19 in children <18 years old March 2020 to December 2021. *Pediatrics*. 2022;149(4):e2021055765. doi: https://doi.org/10.1542/peds.2021-055765.

29. Meuris C, Kremer C, Geerinck A, Locquet M, Bruyère O, Defêche J et al. Transmission of SARS-CoV-2 after COVID-19 screening and mitigation measures for primary school children attending school in Liège, Belgium. *JAMA Netw Open*. 2021;4(10):e2128757. doi: https://doi.org/10.1001/jamanetworkopen.2021.28757.

30. Shoji K, Akiyama T, Tsuzuki S, Matsunaga N, Asai Y, Suzuki S et al. Comparison of the clinical characteristics and outcomes of COVID-19 in children before and after the emergence of Delta variant of concern in Japan. *J Infect Chemother*. 2022;28(4):591–4. doi: https://doi.org/10.1016/j.jiac.2022.01.009.

31. Viner RM, Ward JL, Hudson LD, Ashe M, Patel SV, Hargreaves D et al. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents. *Arch Dis Child*. 2020. doi: https://doi.org/10.1136/archdischild-2020-320972.

32. Yasuhara J, Kuno T, Takagi H, Sumitomo N. Clinical characteristics of COVID-19 in children: a systematic review. *Pediatr Pulmonol*. 2020;55(10):2565–75. doi: https://doi.org/10.1002/ppul.24991.

33. Chudasama DY, Tessier E, Flannagan J, Leeman D, Webster H, Demirjian A et al. Surge in SARS-CoV-2 transmission in school-aged children and household contacts, England, August to October 2021. *Euro Surveill*. 2021;26(48):2101019. doi: https://doi.org/10.2807/1560-7917.

ES.2021.26.48.2101019.

34. Dougherty K, Mannell M, Naqvi O, Matson D, Stone J. SARS-CoV-2 B. 1.617. 2 (Delta) variant COVID-19 outbreak associated with a gymnastics facility—Oklahoma, April–May 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70(28):1004. doi: https://doi.org/10.15585/mmwr.mm7028e2.

35. Goldstein E, Lipsitch M, Cevik M. On the effect of age on the transmission of SARS-CoV-2 in households, schools, and the community. *J Infect Dis*. 2020;223(3):362–9. doi: https://doi.org/10.1093/infdis/jiaa691.

36. Madewell ZJ, Yang Y, Longini IM, Halloran ME, Dean NE. Household transmission of SARS-CoV-2: a systematic review and meta-analysis. *JAMA Netw Open*. 2020;3(12):e2031756. doi: https://doi.org/10.1001/jamanetworkopen.2020.31756.

37. Peng J, Liu J, Mann SA, Mitchell AM, Laurie MT, Sunshine S et al. Estimation of secondary household attack rates for emergent spike L452R SARS-CoV-2 variants detected by genomic surveillance at a community-based testing site in San Francisco. *Clin Infect Dis*. 2022;74(1):32–9. doi: https://doi.org/10.1093/cid/ciab283.

38. Tanaka H, Hirayama A, Nagai H, Shirai C, Takahashi Y, Shinomiya H et al. Increased transmissibility of the SARS-CoV-2 Alpha variant in a Japanese population. *Int J Environ Res Public Health*. 2021;18(15):7752. doi: https://doi.org/10.3390/ijerph18157752.

APPENDIX B: DONUTS FOR WEIGHT LOSS? A FOODBORNE NOROVIRUS OUTBREAK ASSOCIATED WITH A BAKERY IN THE AUSTRALIAN CAPITAL TERRITORY

PUBLISHED IN *COMMUNICABLE DISEASES INTELLIGENCE* VOLUME 46

Original article

Donuts for weight loss? A norovirus outbreak associated with a bakery in the Australian Capital Territory

Keeley Allen, Felicity Greenville, Alexandra Marmor, Natasha Waters, Victoria Wansink, Lyndell Hudson, Nevada Pingault

Abstract

Background

An outbreak of gastroenteritis was investigated following complaints of illness after eating donuts from a food premises in the Australian Capital Territory (ACT).

Methods

Food poisoning complainants and contacts were surveyed using a standard gastroenteritis questionnaire including menu items from the food premises. Descriptive analyses were performed on data collected for all responses. A case-control study was conducted for a group of 140 people at a catered function. Food safety inspections were conducted with food and environmental samples tested at the ACT Government Analytical Laboratory. Stool specimens were collected from cases who were ill at the time of interview. Neither active case finding, nor viral testing of food or environmental samples, could be conducted.

Results

Three hundred and one people were surveyed, and 215 individuals (71.4%) reported vomiting and/or diarrhoea following consumption of a donut purchased from the business over a five-day period. All ill respondents reported eating a donut. The medians of incubation period and illness duration were 34 hours (interquartile range, IQR: 29–42 hours) and 48 hours (IQR: 29–72 hours) respectively. Diarrhoea, vomiting and abdominal pain were the most commonly reported symptoms. Eight out of 11 specimens collected from ill individuals were positive for norovirus.

For the case-control study, data from 59 attendees were collected, with an attack rate of 46% (27/59). Eating any kind of filled donut was associated with a person becoming ill (odds ratio: 10.4; 95% confidence interval: 1.18–478.13). No single flavour was identified as the likely source of infection.

Elevated levels of coliforms were present in two samples of donut filling obtained during the food safety inspection.

Conclusion

Donuts are a novel vehicle for norovirus infection. This implicated pathogen, plus evidence collected at the food premises suggestive of faecal contamination, indicates the source of this outbreak was likely an ill food handler. The findings of this outbreak highlight the importance of excluding food

handlers from work while ill. While this was one of the largest foodborne outbreaks investigated in the ACT, the true extent of illness remains unknown. Active case finding should be pursued to determine the magnitude of outbreaks.

Keywords: outbreak; foodborne disease; gastroenteritis; norovirus; food handling; case-control study; donuts

Introduction

Foodborne gastrointestinal illness places a significant burden on the health of Australians, with an estimated 4.1 million cases occurring each year.[1] Norovirus is estimated to be the most common cause of gastroenteritis illness in Australia.[1] This highly infectious pathogen often transmits person-to-person but can also spread through contact with contaminated surfaces and foods. This report describes an outbreak of norovirus infection associated with consumption of donuts, a novel vehicle for foodborne illness in Australia.

On 25 November 2021, the Australian Capital Territory Department of Health (ACT Health) received notice from the proprietor of a food premises that they had received a report from a patron of illness occurring among eleven people following consumption of donuts. The food premises primarily sold donuts made onsite, with additional baked good products, including tarts and flans which were sold at the premises, purchased wholesale and made offsite. Separately, ACT Health received two additional reports of illness on the same day for the same food premises. Initial interviews with complainants and their contacts found that they had all eaten donuts from the food premises 24 to 48 hours before becoming unwell. An outbreak investigation was initiated to identify the cause of illness and to apply appropriate public health actions to prevent further cases.

Methods

Epidemiological investigation

Active case finding was not able to be conducted for this outbreak as most orders were reportedly from walk-in customers; the food premises denied keeping records of orders; and no public alerts were issued by ACT Health. This investigation therefore relied on passive case finding from complainants contacting ACT Health and identifying contacts who shared meals with them.

A case was defined as a person who reported diarrhoea and/or vomiting to ACT Health following the consumption of a donut purchased from the food premises from 20 November to 24 November 2021 inclusive.

Complainants and their contacts were sent an online questionnaire, developed in REDCap[2,3] using a standard gastrointestinal outbreak questionnaire, adapted to the menu of the food premises. Complainants and contacts who required translation services, or who could not otherwise complete the online questionnaire, were interviewed via phone using the same REDCap questionnaire. Non-respondents were contacted up to three times before being considered lost to follow up.

Interview data was stored in REDCap and analysis was performed in R version 4.04.[4]

A descriptive analysis was conducted for all respondents. An analytical study could not be conducted for the overall community-wide outbreak, as sufficient controls could not be recruited through passive case finding. A case-control study was conducted for the largest cohort identified among respondents, a catered function at an ACT workplace held on 24 November 2021. The REDCap questionnaire was distributed by the workplace, on behalf of ACT Health, to all attendees of this function. A case-control study was conducted rather than a cohort study as it was unclear if respondents were representative of the event attendees.

Univariate analysis included calculating odds ratios (OR) for donuts consumed, by filling type and by flavour.

This investigation is covered by the Australian National University Human Research Ethics Committee standing approval for outbreak investigations involving staff and students (Protocol 2017/909) and formed part of a public health response under the ACT *Public Health Act 1997.*

Environmental investigation

Environmental health officers from ACT Health attended the food premises on 25 November 2021 to conduct a food inspection, to interview the proprietor of the food premises and to collect food and environmental samples under the ACT *Food Act 2001*. An additional interview with the proprietor was conducted on 6 December 2021 to discuss laboratory results and food preparation procedures.

Laboratory investigation

Eleven stool specimens were collected from cases. Stool specimens were tested at private or public hospital laboratories for common bacterial and viral pathogens by polymerase chain reaction (PCR) and/or by culture. Three clinical laboratories tested stool specimens for viral pathogens. Antigen tests were performed using the R-Biopharm® RIDA®QUICK assay. PCR testing was conducted using the Cepheid® GeneXpert® or the Seegene Allplex TM GI-Virus assay.

Food and environmental samples were tested at the ACT Government Analytical Laboratory (ACTGAL). Six samples of various donut fillings were tested for *Salmonella* spp., *Listeria monocytogenes*, *Escherichia coli*, standard plate count (SPC), *Clostridium perfringens*, coagulase-positive *Staphylococcus* spp., *Bacillus cereus,* and coliforms. Results were interpreted following best practice guidance from the Food Standards Australia New Zealand (FSANZ).[5]

Seventeen environmental samples collected included a piping bag and swabs from kitchen surfaces and mixing equipment. Seven swabs and the piping bag were tested for *L. monocytogenes* detection and ten swabs were tested for *Salmonella* spp. detection. The method used for environmental sample analysis requires the whole item to be submerged in culture media specific to the target organism. As a result, only one organism may be tested from each swab/item.

No viral testing was conducted for food or environmental samples as ACTGAL does not have the capabilities to test for viral pathogens in food and environmental samples.

Results

Epidemiological investigation

Descriptive analysis

The total number of patrons who consumed donuts in the study period was unknown. A total of 301 individuals were interviewed or surveyed as part of this outbreak; 71% of respondents (215/301) met the case definition. A further 16 individuals (5%; 16/301) reported a milder illness without vomiting and/or diarrhoea and did not meet the case definition.

The median age of respondents was 33 years (range: 3–91 years; interquartile range, IQR: 27–41 years) and 53% (159/301) were female. The median age (32 years for ill respondents, 34 for non-ill respondents) and sex (52% female for ill respondents, 55% female for non-ill respondents) of respondents were similar between ill and non-ill respondents.

The most commonly reported symptoms were diarrhoea (89%; 191/215); vomiting (85%; 182/215); nausea (74%; 159/215) and abdominal pain (72%; 155/215). Eight cases (4%; 8/215) reported the presence of blood in stool. Two cases were hospitalised for their illness.

The median incubation period for all ill respondents was 34 hours (range: 9–112 hours; IQR: 29–42 hours) and the median illness duration was 48 hours (range: 4–150 hours; IQR: 29–72 hours).

All interviewed or surveyed patrons ate food purchased from the premises between 20 November and 24 November 2021 inclusive. All 215 cases reported eating a donut from the food premises. Most cases became unwell between the late hours of 21 November and 22 November 2021 (Figure 1).

One case had an illness onset on 20 November 2021, which was the same day as consumption. This case was hospitalised for their illness and had previously received gastric sleeve surgery. This medical history was considered to be a potential characteristic increasing a person's susceptibility to infection, and the case was included in this analysis.

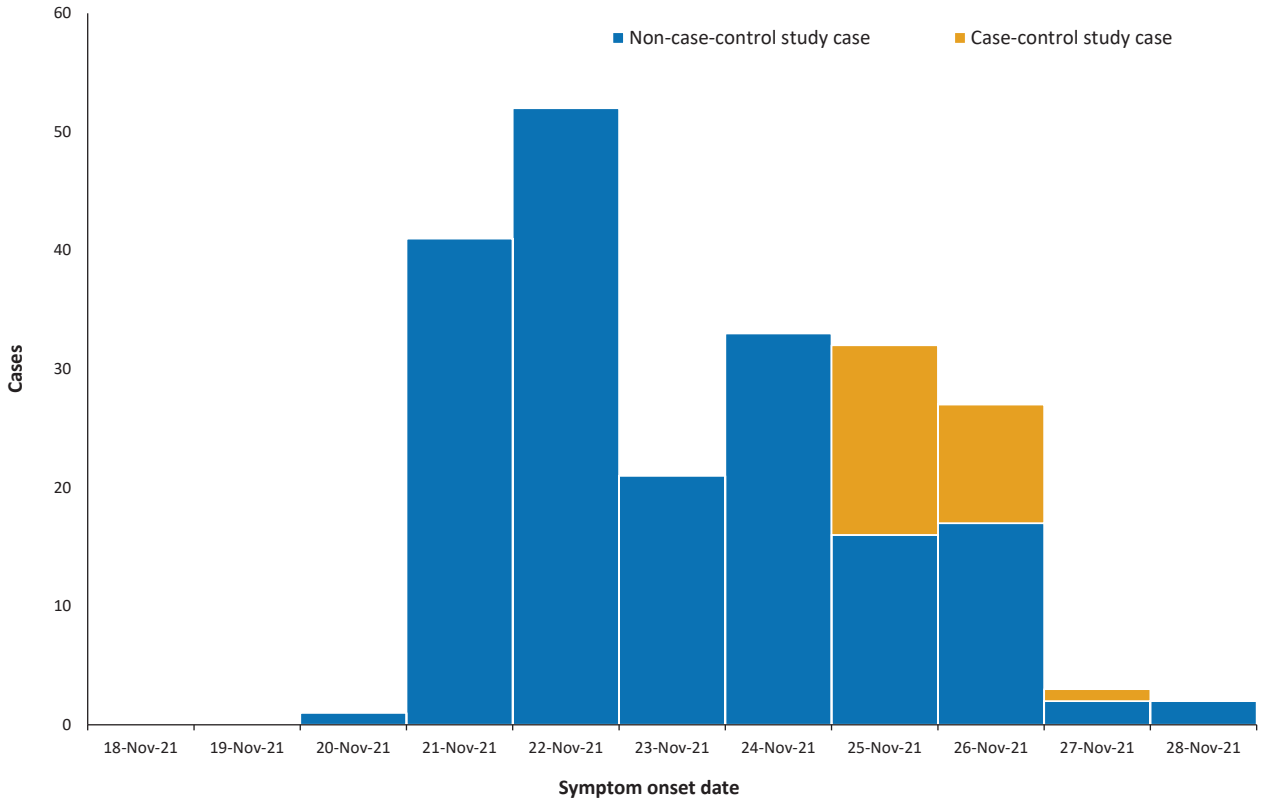
Eight cases had an incubation period of 96 hours or more. All eight of these cases had at least one other member of their household who was a case and had an earlier illness onset. These cases were likely infected by secondary transmission from a household contact, rather than from a food source.

Case-control study

The catered function included 192 donuts prepared the day of the function and included a mix of filled and unfilled donuts. The event was attended by 140 people who had not shared a meal in the week prior, and no other food products were served.

Of the 140 attendees at the workplace function, 59 individuals (42%) completed the questionnaire. Almost half of respondents (46%; 27/59) met the case definition, and a further four individuals reported a milder illness without vomiting and/or diarrhoea and were not considered as cases in this analysis. These four cases were excluded in this analysis. The remaining sample of 55 respondents were included.

Figure 1: Epidemic curve of symptom onset date of cases, by general investigation and case-control study, norovirus outbreak, Australian Capital Territory, November 2021



The median age of study participants was 37 years (range: 28–50 years; IQR: 34–39 years) and 35% of participants were female. There were no statistically significant differences in age (test $t = 1.25$; p-value = 0.22) or sex (test chi-squared = 1.74; p-value = 0.19) between cases and controls in the study.

The median incubation period for cases in the case-control study was 35 hours (range: 13–71 hours; IQR: 31–46 hours) and the median illness duration was 39 hours (range: 4–87 hours; IQR: 22–66 hours).

Attendees ate a wide variety of donut flavours at the catered function (Table 1). No single flavour was statistically associated with illness. The only statistically significant association was found between eating any kind of filled donut and a person becoming unwell; however, the confidence interval (CI) for this association was wide (OR:10.40; 95% CI: 1.18–478.73).

Table 1: Summary of attack rates and odds ratios for donuts, by filling type and the most commonly eaten flavours at a catered function,[a] 24 November 2021

Exposures	Cases			Controls			OR	95% CI
	Number	Total	%	Number	Total	%		
Donut filling type								
Any filled donut	26	27	96.3%	20	28	71.4%	10.40	1.18–478.73
Any cream/custard filled donut	15	27	55.6%	12	28	42.9%	1.67	0.51–5.53
Any caramel/jam/Nutella filled donut	7	27	25.9%	8	28	28.6%	0.86	0.22–3.38
Any unfilled donut	5	27	18.5%	3	28	10.7%	1.89	0.32–13.46
Most frequently consumed donut flavours								
Nutella[b]	4	27	14.8%	5	28	17.9%	0.80	0.14–4.27
Vanilla custard[c]	4	27	14.8%	3	28	10.7%	2.26	0.29–26.80
Dark chocolate mousse[c]	0	27	0.0%	3	28	10.7%	N/A[d]	N/A
Crème Brûlée[c]	1	27	3.7%	3	28	10.7%	0.32	0.01–4.38
Salted caramel[b]	3	27	11.1%	1	28	3.6%	3.38	0.25–183.59
Cookies and cream[c]	2	27	7.4%	1	28	3.6%	2.16	0.10–132.06
Cream and jam[b,c]	2	27	7.4%	1	28	3.6%	2.16	0.10–132.06
Jam[b]	1	27	3.7%	2	28	7.1%	0.50	0.01–10.28
Biscoff milky bar gold[c]	2	27	7.4%	1	28	3.6%	2.16	0.10–132.06
Tiramisu custard[c]	2	27	7.4%	0	28	0.0%	N/A	N/A
Oreo cheesecake[c]	1	27	3.7%	1	28	3.6%	1.04	0.13–84.49
Cotton candy custard[c]	1	27	3.7%	1	28	3.6%	1.04	0.13–84.49
Boston cream[c]	1	27	3.7%	1	28	3.6%	1.04	0.13–84.49
Pistachio[c]	1	27	3.7%	1	28	3.6%	1.04	0.13–84.49

a Only flavours reported to have been eaten by two or more participants are included.

b Donut has a pre-bought Nutella, salted caramel, or jam filling.

c Donut has a cream/custard filling made at the food premises.

d N/A: not applicable.

Environmental investigation

Environmental health officers collected six food samples during their inspection on 25 November 2021, including custard fillings, cream filling, and icing. No ready-for-sale donuts, filled or otherwise, were available for sampling. No food was being prepared at the time of the inspection, so hand hygiene and food preparation techniques could not be observed. Seventeen environmental samples were collected, including a reusable piping bag and swabs of surfaces.

Food handlers had designated activities during preparation, with separate staff for baking steps such as dough preparation and frying, and one staff member for decorating, including custard or filling preparation, piping fillings, and icing donuts. Dough making was kept separate from other activities in the premises, in separate mixing bowls. Proving and cooking of donuts were automated. All donut flavours had the same dough base, and different fillings and icings were applied to create unique flavours.

Cream and custard were prepared onsite. Cream fillings were made by whipping heavy cream. Custard fillings were made in batches using sugar, milk, and custard powder, with purchased flavourings added for different donut flavours. Flavourings were stored in tubs and reportedly used until empty, a general duration of approximately two days. Compliance with storage times could not be confirmed, because date labels were missing from some storage containers. The food premises used reusable piping bags for cream and custard fillings, which were cleaned with soap in a sink. Nutella, salted caramel, and jam fillings were purchased and injected into donuts using designated nozzles. Unsold donuts were reportedly disposed of each evening.

The proprietor initially reported only two staff members onsite during the study period; however, this was later revised to two staff in the kitchen and two who served customers. Donuts were reportedly served by staff wearing gloves and using tongs and were kept refrigerated before sale. Gloves were not worn during food preparation and hand washing facilities were available in the kitchen.

The food premises primarily conducted sales through walk-in customers and through fulfilment of pre-booked orders. Orders were taken over the phone; the proprietor reported disposing of order records immediately after fulfilment. An unknown number of orders were also fulfilled through third-party food delivery applications. The proprietor was not able to access order information through third-party food delivery applications, and ACT Health did not pursue these order lists further for active case finding.

The proprietor denied any reports of staff illness during the study period and reported no incidences of vomiting or diarrhoea on site among staff or patrons.

Following the outbreak investigation, staff at the food premises were advised on the transmission routes for gastrointestinal illness and were provided education on proper food handling, cleaning and sanitising techniques.

Laboratory investigation

Food and environmental samples

No targeted pathogens were detected in the six food samples, the seventeen environmental swabs, or the piping bag. Two food samples returned results above detectable limits for coliforms; both samples were fillings made at the premises. The sample of tiramisu custard filling returned a coliform most probable number (MPN) of 4.5 per gram and the cream filling sample returned a coliform MPN of 920 per gram. The cream filling sample also had a SPC of 920,000 colony-forming units (CFU) per gram.

The sample of white chocolate icing recorded a SPC result of 33,000 CFU per gram, which was an unusual result for an icing product. The interview with the proprietor found that

the same scoop had repeatedly been used for the white chocolate buds. The scoops were also stored within the product and may have provided a vehicle for contamination.

Human samples

Of the eleven specimens collected, eight were positive for norovirus. This included two specimens that returned negative norovirus antigen results when initially tested but were PCR-positive when sent to a second laboratory for confirmatory testing.

Two specimens were negative for norovirus, and for all other pathogens screened for in the laboratory tests. One specimen was not tested for norovirus and was negative for all the pathogens included in the laboratory testing.

Discussion

The epidemiological investigation was suggestive of a very large norovirus outbreak associated with donuts from a food premises in the ACT. The symptom profile, incubation period, and illness duration satisfied Lively's criteria for norovirus infection.[6] The epidemiological investigation was supported by eight stool samples positive for norovirus.

This investigation highlights the potential for a foodborne illness outbreak with donuts as a vehicle for infection. Foodborne norovirus outbreaks have historically been associated with foods which do not have a kill step in preparation or which are subject to significant handling, such as salads and sauces.[7–12] Norovirus is a highly contagious pathogen that has the potential to cause large-scale foodborne outbreaks with ready-to-eat foods generally, as only a low dose is required to cause illness; the pathogen does not need to multiply to reach infectious dose levels.[13,14] While two recent norovirus outbreaks have been associated with donuts in the United States of America in grey literature,[15,16] to the best of our knowledge, this is the first Australian foodborne norovirus outbreak associated with donuts. This investigation highlights the potential for a foodborne illness outbreak in a food product not previously considered as a vehicle for norovirus.

While the source of contamination was not confirmed, it is suspected that a food handler worked while infectious and contaminated the donuts. The only statistically significant association with illness found in this study was consumption of any filled donut, the preparation of which involved close handling of each donut after cooking. The elevated coliforms and SPC results in one sample may indicate improper food handling practices, although these results were not consistent across all laboratory-tested samples. Elevated coliforms were present in two filling samples results found through the laboratory investigation. Illness in a food handler has previously been reported as the source of norovirus foodborne outbreaks,[8,9,11,12,17–21] and of foodborne outbreaks associated with bakeries.[22–26] There were no reports of vomiting or diarrhoeal episodes among patrons onsite, making it unlikely that environmental contamination from a patron was the source of infection. The food handlers at the food premises did not provide stool specimens for testing. These factors together suggest that an ill food handler engaging in food preparation was the most likely source of infection. There is the potential for a food handler to have worked with an asymptomatic norovirus infection;[27–29] however, the scale of illness associated with this outbreak suggests there was a lapse in hand hygiene and proper food handling procedures regardless. While national food standards require exclusion from food handling of employees with a gastrointestinal illness,[30] the lack of leave entitlements for casual employees may be a disincentive to remain away from work. This outbreak reinforces the importance of safe food handling practices and of exclusion of ill staff to prevent further spread of illness.

A major limitation of the investigation was the inability to conduct active case finding. The food premises reported that most donuts were purchased by walk-in customers and there were limited records of orders. In addition, no

public health alerts were released regarding the outbreak or an alert indicating an increase of gastroenteritis in the community, and case finding through food delivery applications was not pursued. The true extent of this outbreak remains unknown. Relying on passive case finding biases the epidemiological findings towards ill patrons who may be more motivated to contact public health units and to complete an interview. A lack of responses from well patrons limited our capacity to conduct an analytical study for the whole outbreak. Measurement bias was minimised by using a standard questionnaire based on the menu of the food premises; however, recall of specific flavours from participants may have been limited when several days had passed since the event, when the food premises could not provide accurate records of what donuts were sold on each day, or when the participant was not the person who purchased the donuts. Finally, while stool samples were able to identify the cause of the illness, no food or environmental samples were able to be tested for viral pathogens.

This outbreak investigation was one of the largest foodborne illness outbreaks ever investigated in the ACT. It is essential that food premises and food regulators promote and enforce exclusion of ill food handlers from work to prevent further illness. The rise of third-party food delivery services is an emerging challenge for the pursuit of active case findings, and the role of such delivery services in outbreak investigations should be explored further. Future foodborne illness outbreaks should employ active case finding, where possible, to provide greater certainty in the investigation and its findings.

Acknowledgements

The authors would like to thank the team at Health Protection Services, ACT Health, for their tireless support during this outbreak investigation. The authors would particularly like to acknowledge the work of Mr Arif Mirza in this outbreak investigation. The authors also thank Dr Davoud Pourmarzi for his review of this manuscript and his invaluable feedback. The corresponding author would like to thank Mr Matthew Hirsh for his understanding as this outbreak evolved and cancelled Thanksgiving dinner.

Author details

Keeley Allen[1,2]
Felicity Greenville[2]
Alexandra Marmor[2]
Dr Natasha Waters[3]
Dr Victoria Wansink[3]
Lyndell Hudson[4]
Dr Nevada Pingault[2]

1. National Centre for Epidemiology and Population Health, Australian National University, Acton, Australia.

2. Communicable Disease Control Section, Health Protection Service, Public Health Protection and Regulation, ACT Health

3. ACT Government Analytical Laboratory, Health Protection Service, Public Health Protection and Regulation, ACT Health

4. Environmental Health Section, Health Protection Service, Public Health Protection and Regulation, ACT Health

Corresponding author

Keeley Allen

National Centre for Epidemiology and Population Health, Australian National University, Acton, ACT
Phone: (02) 5124 6215
Email address: keeley.allen@anu.edu.au

References

1. Kirk M, Ford L, Glass K, Hall G. Foodborne illness, Australia, circa 2000 and circa 2010. *Emerg Infect Dis*. 2014;20(11):1857–64. doi: https://doi.org/10.3201/eid2011.131315.

2. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform*. 2019;95:103208. doi: https://doi.org/10.1016/j.jbi.2019.103208.

3. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377–81. doi: https://doi.org/10.1016/j.jbi.2008.08.010.

4. R Core Team. R: A language and environment for statistical computing. [Software.] Vienna: R Foundation for Statistical Computing; 2018. Available from: https://www.R-project.org/.

5. Food Standards Australia and New Zealand (FSANZ). *Compendium of Microbiological Criteria for Food*. Canberra: FSANZ; March 2022. Available from: https://www.foodstandards.gov.au/publications/pages/compendium-of-microbiological-criteria-for-food.aspx.

6. Lively JY, Johnson SD, Wikswo M, Gu W, Leon J, Hall AJ. Clinical and epidemiologic profiles for identifying norovirus in acute gastroenteritis outbreak investigations. *Open Forum Infect Dis*. 2018;5(4):ofy049. doi: https://doi.org/10.1093/ofid/ofy049.

7. Barclay L, Davis T, Vinjé J. Rare norovirus GIV foodborne outbreak, Wisconsin, USA. *Emerg Infect Dis*. 2021;27(4):1151–4. doi: https://doi.org/10.3201/eid2704.204521.

8. Coutts SP, Sturge K, Lalor K, Marshall JA, Bruggink LD, Subasinghe N et al. An outbreak of foodborne norovirus gastroenteritis linked to a restaurant in Melbourne, Australia, 2014. *Western Pac Surveill Response J*. 2017;8(2):12–6. doi: https://doi.org/10.5365/WPSAR.2017.8.1.008.

9. Hall AJ, Eisenbart VG, Etingüe AL, Gould LH, Lopman BA, Parashar UD. Epidemiology of foodborne norovirus outbreaks, United States, 2001–2008. *Emerg Infect Dis*. 2012;18(10):1566–73. doi: https://doi.org/10.3201/eid1810.120833.

10. Kendall ME, Mody RK, Mahon BE, Doyle MP, Herman KM, Tauxe RV. Emergence of salsa and guacamole as frequent vehicles of foodborne disease outbreaks in the United States, 1973–2008. *Foodborne Pathog Dis*. 2013;10(4):316–22. doi: https://doi.org/10.1089/fpd.2012.1328.

11. Mayet A, Andreo V, Bedubourg G, Victorion S, Plantec J, Soullie B et al. Food-borne outbreak of norovirus infection in a French military parachuting unit, April 2011. *Euro Surveill*. 2011;16(30):19930. doi: https://doi.org/10.2807/ese.16.30.19930-en.

12. Yu JH, Kim NY, Koh YJ, Lee HJ. Epidemiology of foodborne norovirus outbreak in Incheon, Korea. *J Korean Med Sci*. 2010;25(8):1128–33. doi: https://doi.org/10.3346/jkms.2010.25.8.1128.

13. Bányai K, Estes MK, Martella V, Parashar UD. Viral gastroenteritis. *Lancet*. 2018;392(10142):175–86. doi: https://doi.org/10.1016/S0140-6736(18)31128-0.

14. Teunis PF, Moe CL, Liu P, E. Miller S, Lindesmith L, Baric RS et al. Norwalk virus: how infectious is it? *J Med Virol*. 2008;80(8):1468–76. doi: https://doi.org/10.1002/jmv.21237.

15. Boyette C. Ohio doughnut shop closes during norovirus investigation. [Internet.] Atlanta: Cable News Network (CNN), CNN Health; 11 August 2017. Available from: https://edition.cnn.com/2017/08/10/health/ohio-doughnuts-norovirus-outbreak/index.html.

16. Statement from DPH on the Recent Norovirus Outbreak Involving a Food Service Establishment in Ellington. [Press release.] Hartford: Connecticut Department of Public Health, North Central District Health Department; 19 May 2021. Available from: http://www.ncdhd.org/newsItem/statement-from-dph-on-the-recent-norovirus-outbreak-involving-a-food-service-establishment-in-ellington.

17. Kuo HW, Schmid D, Jelovcan S, Pichler AM, Magnet E, Reichart S et al. A foodborne outbreak due to norovirus in Austria, 2007. *J Food Prot*. 2009;72(1):193–6. doi: https://doi.org/10.4315/0362-028x-72.1.193.

18. Maritschnik S, Kanitz EE, Simons E, Höhne M, Neumann H, Allerberger F et al. A food handler-associated, foodborne norovirus GII.4 Sydney 2012-outbreak following a wedding dinner, Austria, October 2012. *Food Environ Virol*. 2013;5(4):220–5. doi: https://doi.org/10.1007/s12560-013-9127-z.

19. Smith KC, Inns T, Decraene V, Fox A, Allen DJ, Shah A. An outbreak of norovirus GI-6 infection following a wedding in North West England. *Epidemiol Infect*. 2017;145(6):1239–45. doi: https://doi.org/10.1017/S0950268816003368.

20. Somura Y, Mizukoshi F, Nagasawa K, Kimoto K, Oda M, Shinkai T et al. A food poisoning outbreak due to food handler-associated contamination with the human norovirus GII.P16-GII.2 variant strain in Italian cuisine in Tokyo during the 2016/17 winter season. *Jpn J Infect Dis*. 2018;71(2):172–3. doi: https://doi.org/10.7883/yoken.JJID.2017.264.

21. Vo TH, Okasha O, Al-Hello H, Polkowska A, Räsänen S, Bojang M et al. An outbreak of norovirus infections among lunch customers at a restaurant, Tampere, Finland, 2015. *Food Environ Virol*. 2016;8(3):174–9. doi: https://doi.org/10.1007/s12560-016-9236-6.

22. Evans MR, Tromans JP, Dexter ELS, Ribeiro CD, Gardner D. Consecutive salmonella outbreaks traced to the same bakery. *Epidemiol Infect*. 1996;116(2):161–7. doi: https://doi.org/10.1017/s0950268800052390.

23. Frank C, Buchholz U, Maass M, Schröder A, Bracht KH, Domke PG et al. Protracted outbreak of *S*. Enteritidis PT 21c in a large Hamburg nursing home. *BMC Public Health*. 2007;7:243. doi: https://doi.org/10.1186/1471-2458-7-243.

24. Guo Z, Huang J, Shi G, Su CH, Niu JJ. A food-borne outbreak of gastroenteritis caused by norovirus GII in a university located in Xiamen City, China. *Int J Infect Dis*. 2014;28:101–6. doi: https://doi.org/10.1016/j.ijid.2014.06.022.

25. Harries M, Monazahian M, Wenzel J, Jilg W, Weber M, Ehlers J et al. Foodborne hepatitis A outbreak associated with bakery products in northern Germany, 2012. *Euro Surveill*.

2014;19(50):20992. doi: https://doi.org/10.2807/1560-7917.es2014.19.50.20992.

26. Kuritsky JN, Osterholm MT, Greenberg HB, Korlath JA, Godes JR, Hedberg CW et al. Norwalk gastroenteritis: a community outbreak associated with bakery product consumption. *Ann Intern Med*. 1984;100(4):519–21. doi: https://doi.org/10.7326/0003-4819-100-4-519.

27. Jeong AY, Jeong HS, Lee JS, Park YC, Lee SH, Hwang IG et al. Occurrence of norovirus infections in asymptomatic food handlers in South Korea. *J Clin Microbiol*. 2013;51(2):598-600. doi: https://doi.org/10.1128/JCM.01856-12.

28. Nicolay N, McDermott R, Kelly M, Gorby M, Prendergast T, Tuite G et al. Potential role of asymptomatic kitchen food handlers during a food-borne outbreak of norovirus infection, Dublin, Ireland, March 2009. *Euro Surveill*. 2011;16(30):19931. doi: https://doi.org/10.2807/ese.16.30.19931-en.

29. Okabayashi T, Yokota S, Ohkoshi Y, Ohuchi H, Yoshida Y, Kikuchi M et al. Occurrence of norovirus infections unrelated to norovirus outbreaks in an asymptomatic food handler population. *J Clin Microbiol*. 2008;46(6):1985–8. doi: https://doi.org/10.1128/JCM.00305-08.

30. FSANZ. *Australia New Zealand Food Standards Code – Standard 3.2.2 – Food Safety Practices and General Requirements*. Canberra: FSANZ; November 2021. Available from: https://www.foodstandards.gov.au/industry/safetystandards/safetypractices/pages/default.aspx.

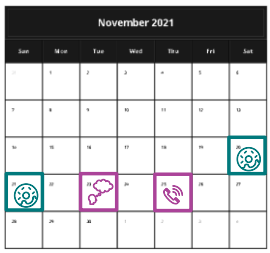
APPENDIX C: CONFERENCE PRESENTATION: DONUTS FOR WEIGHT LOSS? A NOROVIRUS OUTBREAK IN THE AUSTRALIAN CAPITAL TERRITORY

PRESENTED AT THE COMMUNICABLE DISEASES AND IMMUNISATION CONFERENCE, JUNE 2022

Donuts for weight loss? A norovirus outbreak in the Australian Capital Territory

Keeley Allen, Felicity Greenville, Alexandra Marmor, Lyndell Hudson, Dr Natasha Waters, Dr Victoria Wansink, Dr Nevada Pingault

Introduction



- Call from proprietor regarding food poisoning complaint
- Two separate direct food poisoning complaints
- Further two indirect food poisoning complaints initially suspecting other food businesses

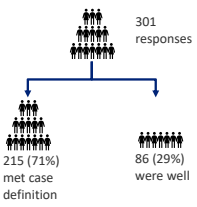
Methods

- No active case finding could be undertaken
- Online and phone case questionnaire
  - Online questionnaires for identified catered functions
- Case control study for largest catered function
- Environmental health investigations
- Laboratory investigations

Outbreak case definition

A person who reported diarrhoea and/or vomiting to ACT Health following the consumption of food purchased from the food premises from Saturday 20 November 2021 to Thursday 25 November 2021, inclusive.

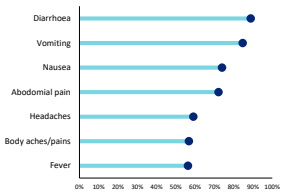
Results – epidemiological investigation



- Median age of 35 years (range 3-91 years, IQR 27-41 years)
- 53% female
- 100% of cases ate a donut

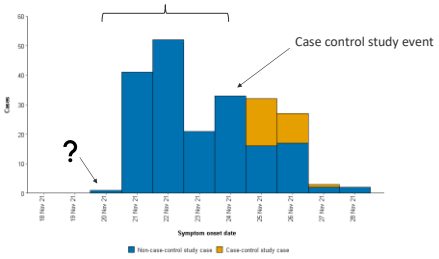
Results – epidemiological investigation

- Median incubation period = 33.5 hours
- Median illness duration = 48 hours



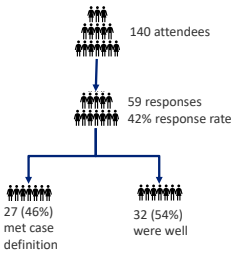
Results – epidemiological investigation

Donuts were eaten by cases over a five day period



Results – case-control study

A catered function was held at a workplace on Wednesday 24 November



Donut eaten	Odds ratio	95% CI
Donut filling type		
Any filled donut	7.56	1.22-200.61
Any cream/custard filled donut	1.24	0.44-3.56
Any caramel/jam/Nutella filled donut	1.05	0.31-3.50
Any unfilled donut	2.13	0.45-12.07
Most frequently consumed donut flavours		
Nutella	0.95	0.20-4.13
Vanilla custard	1.65	0.31-9.73
Crème Brule	0.4	0.13-3.76
Salted caramel	3.5	0.38-105-01
Cookies and cream	1.2	0.12-12.18

Results – environmental investigation

- Business closed at time of inspections
- Designated activities for food handlers
- Cream and custard fillings stored 'until empty'
- No reports of illness on site
- Limited record keeping
  - Quantity or flavours sold
  - Past orders, and difficulty accessing food delivery app orders
  - Illness register

Results – laboratory investigation (environmental)

Tests

- Environmental swabs, and a piping bag tested for *Salmonella* spp. and *Listeria monocytogenes*
- Food samples tested for panel of bacterial pathogens, standard plate count, and coliforms
- Unable to test for viral pathogens

Results

- All pathogens tested not detected
- Two filling samples returned results above detectable limits for coliforms
- One icing sample recorded an elevated standard plate count

Results – laboratory investigation (human)

- 10 stool samples collected, 9 by ACT Health

8 positive for norovirus

2 negative for all pathogens screened

Discussion

- Donuts contaminated with norovirus suspected vehicle for the outbreak
- An ill food handler was the suspected source of contamination

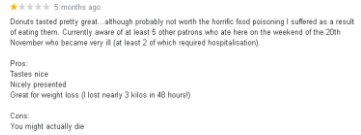
- Investigation subject to some significant limitations
  - Selection bias in case finding towards ill patrons
  - Limited/no record keeping
  - Capability for viral testing of food and environmental samples

Recommendations and follow up actions

- Letter to clinicians reinforcing importance of sample collection
- Review of legislation with rise of food delivery apps
- New online food poisoning complaint register

Conclusions

- Donuts are a novel vehicle for foodborne outbreaks
- Electronic surveys are a viable case finding tool
- Rise of food delivery apps can change outbreak investigation
- Future foodborne outbreaks should employ active case finding



★☆☆☆☆ 5 months ago

Donuts tasted pretty great...although probably not worth the horrific food poisoning I suffered as a result of eating them. Currently aware of at least 5 other patrons who ate here on the weekend of the 20th November who became very ill (at least 2 of which required hospitalisation).

Pros:
Tastes nice
Nicely presented
Great for weight loss (I lost nearly 3 kilos in 48 hours!)

Cons:
You might actually die

Acknowledgements

CDC
Fotis Sgouros
Raleigh Evans
Milicia Stefanvoic
Connor Goldrick
Dr Phillipa Binns

Environmental Health
Arif Mirza
Keith Rogers
Nicki Norbert

COVID-19 Operations
Algreg Gomez

ACT Government | ACT Health

Australian National University

Thank you for your time!

Get in touch:

@Keeley__Allen
Keeley Allen
keeley.allen@anu.edu.au/keeley.allen@act.gov.au

APPENDIX D: SUMMARY LETTER OF FOODBORNE NOROVIRUS OUTBREAK INVESTIGATION

ACT Government | ACT Health

Foodborne Illness Outbreak Investigation - November 2021

Epidemiologists and Public Health Officers at ACT Health investigated a foodborne illness outbreak linked to consumption of food purchased from a Canberra food business. Thank you for your assistance with this investigation.

ACT Health interviewed or surveyed 301 individuals. A total of 231 people reported illness after consuming food purchased from the business. All people reporting illness purchased food from the business between Saturday 20 November and Wednesday 24 November 2021.

The median incubation period, which is the time from consuming the food to becoming ill, was 33 hours; with a median symptom duration of 48 hours. Diarrhoea, vomiting and/or abdominal pain were the most common symptoms reported. The incubation period, symptoms and duration of illness was consistent with infection with norovirus. Specimens collected from affected individuals were positive for norovirus.

Norovirus is a common virus that causes gastroenteritis (inflammation of the stomach and intestines). Norovirus is highly infectious and is spread from the vomit or faeces of an infected person. Infection can occur from close person-to-person contact, consuming contaminated food or drink (often contaminated as a result of poor food handling or poor hand washing), or contact with contaminated objects or surfaces (such as door and tap handles).

As part of its regulatory responsibilities, Public Health Officers conduct onsite inspections in response to reports of illness linked to a food business. In this case, the business assisted officers with their investigation. These inspections normally include interviews with owners and staff, review of food preparation, storage and hygiene practices. Officers also collect samples of food and take swabs from food preparation areas for analysis. No further action in relation to the business is proposed at this time.

Thank you again for your assistance.

Dr Kerryn Coleman
Chief Health Officer
ACT Health Directorate
21 December 2021

GPO Box 825 Canberra ACT 2601 | phone: 132281 | www.act.gov.au

CHAPTER 3: FACTORS ASSOCIATED WITH COVID-19 BOOSTER VACCINE WILLINGNESS AMONG MIGRANTS FROM THE EASTERN MEDITERRANEAN LIVING IN AUSTRALIA

TABLE OF CONTENTS

Prologue

This chapter details my epidemiological study, a cross-sectional analysis of factors associated with willingness to receive a COVID-19 booster vaccine among migrants living in Australia who were born in the Eastern Mediterranean region. This chapter addresses the following competencies:

- Design and conduct an epidemiological study
- Lay summary
- Conference presentation
- Peer-reviewed publication

Rationale

Vaccination is a key tool in our response to the COVID-19 pandemic. The need for booster vaccines has become increasingly clear with the realities of waning immunity and new variants of SARS-CoV-2. However, as we continue to live through the pandemic, the acceptability of vaccines and our willingness to receive additional doses may change. We need to have adequate information available to make informed decisions and be comfortable with a choice to receive a booster dose.

One population in Australia where the need for information about COVID-19 booster vaccines has been recognised is migrants. The need to understand the information needs and willingness to receive COVID-19 vaccines of migrants living in Australia who were born in the Eastern Mediterranean region was recognised by the National Centre for Epidemiology and Population Health in light of a disproportionate burden of illness, severity and death on this population during COVID-19 outbreaks in 2020 and early 2021.

My study is a component of a larger project investigating the information needs of migrants born in the Eastern Mediterranean region currently living in Australia. My cross-sectional study aimed to answer the following questions:

- What information do migrants from the Eastern Mediterranean region living in Australia need to know about COVID-19 vaccines?
- What is the level of vaccine acceptance and booster willingness among migrants from the Eastern Mediterranean region living in Australia?
- What factors are associated with willingness to receive a booster vaccine among migrants from the Eastern Mediterranean region living in Australia?

My role

I joined the project after the initial submission of the ethics application and contributed to addressing the comments and concerns of the initial assessment by the Australian National University Human Ethics Research Committee (ANU HREC). I designed a process for a raffle to encourage participation in the study that did not violate the privacy of participants, clearly

outlined the terms and conditions of the draw, and did not compromise the ethical rigour of the study.

I worked closely with the project lead to design and refine the questionnaire for data collection, develop a communications strategy to reach potential study participants, develop flyers to advertise the study, and disseminate the flyers for the larger project. I identified a specific question for my study component to meet the competencies and timeframes of this degree, electing to focus on willingness to receive a booster vaccine. I designed a cross-sectional study to answer my study questions and contribute to the body of work from the larger project.

I collated and cleaned the raw dataset with invaluable translation support from the project lead who reviewed responses in Arabic and Farsi. I conducted the data analysis in Stata and interpreted the findings in light of the limitations of the dataset and its collection.

I prepared a manuscript detailing this study, which is under peer review at *BMC Public Health* at the time of writing. The manuscript forms the body of this chapter (Appendix A). I also prepared a conference presentation to disseminate these findings at the Communicable Disease and Immunisation Conference in June 2022 (Appendix B).

I had the opportunity to contribute to other studies in the wider project that were outside of the scope of the epidemiological study presented in this chapter. I contributed to a systematic review of quantitative and qualitative studies assessing COVID-19 vaccine hesitancy among ethnic and racial minorities, and a qualitative study detailing the barriers and potential solutions for communicating COVID-19 vaccine information for migrants born in the Eastern Mediterranean region living in Australia. Both studies have been submitted to peer-reviewed journals for publication.

Key reflections

One of the key lessons I learnt in this project is the value and challenges of using social media platforms to recruit study participants. The study team were able to disseminate the flyers in our networks (including the overall project lead, who, for better or worse, I taught how to make a post on Facebook), however, it became evident that this would not result in a sufficient sample size. I learnt the value of paid advertising in addition to targeting community-specific groups and pages to recruit potential study participants, and for sharing the study among a wider network. At the same time, the link for the study was repeatedly completed by respondents with IP addresses outside of Australia, with over 1000 responses received from IP addresses in the United States. The cleaning of this dataset was a significant feat but necessary to ensure a valid epidemiological study and prompted the addition of a geographic filter to prevent people outside of Australia from accessing the questionnaire.

I learnt the advantages and disadvantages of a cross-sectional study design, and the limits we face when interpreting the results. The study team discussed the potential for conducting a time series of administering the same surveys over time as booster vaccines became more available

and new variants emerged limiting the efficacy of vaccines against infection. While this would be a valuable endeavour, I learnt that this study and our epidemiological investigations more broadly need to be designed with the confides on what is achievable with the available resources, timeframes and personnel.

The preparation of a questionnaire and lay summary in multiple languages has been a tremendous opportunity. As someone who only reads and speaks one language, I was humbled by the process to prepare clear concise questions and statements in English to enable the meaning, tone, and content to be effectively translated into Arabic and Farsi. This process has reinforced my awareness of the importance of listening to our communities' concerns and being transparent about our intentions.

Finally, I learnt that the ethics application and approval processes require us to think about a wide range of issues and study design elements. While I was comfortable with the data management, confidentiality, and analysis processes, the comments from the ANU HREC were exceedingly valuable to consider other important ethical issues. I learnt valuable skills in using simple, concise language for participant information sheets to better inform potential participants and gain consent and considered the ethical conditions where incentives may be offered.

Public health implications

This study contributes to a wider body of evidence examining the acceptance, willingness, and hesitancy to receive COVID-19 vaccines. While most research to date focused on willingness to receive initial vaccinations, by focusing on booster vaccines we have recognised every vaccination is a new choice. Recognising this choice shifts our discussions in health promotion and communication about vaccines from a mass, English-only, one-off campaign to a constant, iterative, two-way conversation. The findings of this study were presented at the Communicable Disease and Immunisation Conference in June 2022 to disseminate its findings to a wide audience of nurse practitioners, epidemiologists and public health professionals and encourage this reframing of health communications. The findings of this study were part of a report to the Australian Partnership for Preparedness Research on Infectious Disease Emergencies (APPRISE) as a funder of the project. This report was also communicated with the leaders of some of the migrant communities targeted for this study.

Acknowledgements

Thank you to the project lead, Dr Davoud Pourmarzi, for all your guidance and contributions to this study. Thank you to the study team, my fellow MAE Scholar Aidan Yuen for your diligent review of the statistical methods and results of this study and Associate Professor Stephen Lambert for your guidance in the design of the study and interpretation of the findings. I would like to acknowledge the support of Alexandra Marmor and Alison Kingsbury for allowing me to pursue a project outside of my field placement. Thank you to every person, social media group, and organisation who distributed the study flyer on our behalf so we could recruit participants.

Finally, thank you to every person who chose to participate in this study, gave us the privilege of reviewing your honest responses, and has assisted us in improving our communications about COVID-19 vaccines.

APPENDIX A: FINAL DRAFT MANUSCRIPT

UNDER PEER REVIEW ASSESSMENT AT TIME OF SUBMISSION

Abstract

Background: Migrants have been disproportionally affected by COVID-19 in Australia. Vaccination against COVID-19 is a key pillar of Australia's public health response, but little is known about the willingness to receive booster vaccinations among migrants. This study aimed to assess the factors associated with a willingness to receive a COVID-19 booster vaccine among migrants living in Australia born in the World Health Organization's Eastern Mediterranean Region (EMRO).

Methods: A cross-sectional survey was conducted from September to November 2021 (n=300). Participants were questioned on booster vaccine willingness, sociodemographic characteristics, COVID-19 vaccine information needs and sources, and perceptions of COVID-19 vaccines. Univariate and multivariate logistic regression were used to assess factors associated with booster willingness.

Results: Most respondents (87%) had received two doses of COVID-19 vaccine, of which 81% were willing to receive a booster dose. About half of the participants reported high or very high needs for receiving information about "COVID-19 vaccines' safety monitoring in Australia", "COVID-19 vaccines protection against illness", "Safety of COVID-19 vaccines used in Australia", and "The Australian COVID-19 vaccination program". People who were willing to receive a boost dose had significantly higher self-estimated knowledge of COVID-19 vaccines, confidence in COVID-19 vaccines and trust in the Australian government's vaccine recommendations, and perceived COVID-19 as a greater risk compared to those who were unsure/hesitant. Both groups reported similar perceptions of their personal risks from COVID-19 but diverged on their views of COVID-19 as a broader health problem. There were no statistically significant differences between the two groups in terms of channels used to find information about COVID-19 vaccines. Factors associated with willingness to receive a COVID-19 booster vaccine in the multivariate logistic regression were age (OR:1.07, 95%CI:1.02–1.12), and no exposure to concerning news about COVID-19 vaccines (OR:3.71, 95%CI:1.51–9.08).

Conclusion: Vaccine acceptance and reported booster willingness was high. The results suggest the news and information seen may impact willingness to receive booster doses, even among those who have already received doses of COVID-19 vaccine. Addressing vaccine concerns and transparent communication about uncertainty should be a priority in the current and in future pandemics.

Key words: Migrant health, COVID-19, vaccine, booster, hesitancy, health behaviour

Authors: Keeley Allen, Stephen Lambert, Aidan Yuen, Davoud Pourmarzi

Background

Vaccinations are fundamental to controlling the spread of COVID-19 and protecting populations. Australia has seen significant uptake of primary vaccine doses with over 76% of the population having received at least two doses of COVID-19 vaccines.[1] High vaccine uptake has stemmed from widespread community acceptance, targeted vaccine mandates to engage in aspects of public life until a threshold of adult vaccinations was met, and vaccination mandate for specific industries' workforce.[2] Waning immunity from vaccines and the emergence of new variants have seen booster doses become a pillar of public health responses worldwide. In Australia, people who were severely immunocompromised were recommended to receive a third dose (considered part of the primary course) of a COVID-19 vaccine in early October 2021.[3] A third (booster) dose of COVID-19 vaccine was recommended from 8 November 2021 for the general population aged 18 years and older who received their primary doses at least six months prior.[4] However, a recent Australian survey showed that the availability of booster vaccines and receiving primary doses of COVID-19 vaccines are not indicative of a willingness to receive a COVID-19 booster vaccine for all populations.[5]

Worldwide, migrants have been disproportionately affected by the COVID-19 pandemic, amplifying existing health and social disparities.[6-9] Several factors make migrants more vulnerable to COVID-19 and less engaged in public health measures, compared with locally born populations. Migrants have had a higher risk of exposure to the pathogen as this population generally fills roles in essential services more likely to require face-to-face contact with the public.[7-9] Migrants generally face additional accessibility barriers to health care that have been exacerbated by the COVID-19 pandemic, such as unmet language requirements, limited access to culturally appropriate services, and limited entitlement to subsidised health care.[7, 10-13] In addition, migrant communities have had limited input and engagement in the development of public health messages to promote COVID-19 vaccinations, contributing to lower vaccination coverage against COVID-19.[10] As a result, migrants have higher hospitalisation and death rates than locally born populations.[7, 14, 15] Recent analysis of COVID-19 death data in Australia revealed that migrants had an age-standardised death rate over 2.5 times higher than locally born populations, and migrants born in Middle Eastern countries have been subject to the highest age-standardised death rate at 29.3 deaths per 100,000 population per year in Australia.[16] An estimated 7.6 million Australian residents were born overseas, accounting for approximately 30% of the total population.[17] Migrants have the right to health and for them to successfully contribute to the society, it is fundamental that their health is protected and that they are included in health system responses.[18]

Understanding migrants' willingness to receive a booster dose and factors affecting their decision can help inform interventions to prevent COVID-19 and promote health equity. Knowledge about the acceptance of COVID-19 booster vaccines among migrant populations in Australia is currently lacking. With this study we aimed to understand willingness to receive a

COVID-19 booster and associated factors among migrants from the World Health Organization's Eastern Mediterranean (EMRO) region living in Australia.

Methods

Research Design and Sampling

We conducted a cross-sectional study using an anonymous online questionnaire available to participants between 27 September 2021 and 30 November 2021. During this period, the primary doses of COVID-19 vaccines were becoming available to the adult population of Australia. Various restrictions and vaccine mandates were in place, with Victoria, New South Wales, and the Australian Capital Territory subject to stay-at-home orders for some part of the study period.[2] Although booster doses became available during the study period on 8 November 2021, discussion among health authorities and the public about the need for a booster dose had started months before data collection for this project, as some countries had started offering booster does to their population.[3, 4]

Individuals were eligible to participate if they were aged 18 years and older, currently residing in Australia, and born in one of the following countries which make up the EMRO region: Afghanistan, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, United Arab Emirates, or Yemen.

Recruitment of participants relied on convenience (non-random) sampling. The researchers disseminated the study flyer through social media platforms (primarily Facebook, Twitter, and Instagram), approaching community leaders and social media community groups supporting migrants from the targeted countries in Australia. The flyer was also distributed electronically through non-government organisations that provide support for migrant populations in Australia.

Data collection

The questionnaire was developed based on a review of literature and using the Risk Information Seeking and Processing model,[19] and the three Cs model of vaccine hesitancy: confidence, complacency, and convenience.[20] The questionnaire was designed and administered using Qualtrics software (Qualtrics, Provo, UT, USA, version November 2021) hosted by the Australian National University. The questionnaire was developed in English and translated into Arabic and Persian (Farsi), and participants could select which language to view. Prior to release, the online questionnaire was reviewed by five individuals from the targeted communities to ensure its clarity and simplicity.

The questionnaire consisted of six domains. The first domain collected sociodemographic data, including age, gender, jurisdiction of residence, country of birth, years lived in Australia, highest level of educational attainment, and health profession status. Health profession status was

defined as employment or studying a clinical (nursing, medical, or allied health) or public health profession. Participants were asked to describe their occupation or area of study. Participants were also asked about their current COVID-19 vaccination status.

The second domain asked participants to subjectively assess their level of knowledge of COVID-19 vaccines and the Australian COVID-19 vaccination program on a 0–100 continuous scale. The third domain asked participants to indicate their level of need for information across five different aspects of COVID-19 vaccines, and the Australian COVID-19 vaccination program on a 5-point scale (very low need, low need, moderate need, high need, very high need).

The fourth domain measured a participant's confidence in COVID-19 vaccines (two items), trust in the Australian government's decision making around COVID-19 vaccines (one item) and risk perception of COVID-19 (four items). Each question was asked on a 5-point Likert scale (strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree).

The fifth domain focused on information channels participants used to collect information on COVID-19 vaccines. Participants were able to select multiple options, including official sources (such as government and health care professionals) in Australia, official sources in their home country, and unofficial sources such as mass media or friends and family.

The final domain measured a participant's willingness to receive a COVID-19 booster vaccine. This domain formed the outcome variable for this study and was only available to participants who indicated they either had already received two COVID-19 vaccine doses or had received one dose and planned to receive a second dose. Participants were asked on a 5-point Likert scale "If it is recommended, how likely are you to get a COVID-19 vaccine again next year?". Responses were combined into a binary variable, with participants responding, "extremely likely" or "likely" considered willing, and participants responding, "neither likely nor unlikely", "unlikely", or "extremely unlikely" considered unsure/hesitant.

Data analysis

Descriptive analyses were conducted to describe study participants. Frequencies and proportions were calculated for categorical variables, and continuous variables were summarised by mean and standard deviation. Median values and ranges were also calculated for age and years lived in Australia; in anticipation the data would follow a non-normal distribution. Ten-year age groups were created for descriptive analyses and age was entered as a continuous variable for univariate and multivariate analyses. Those who identified as non-binary or preferred not to disclose their gender were excluded from cross-tabulations, univariate, and multivariate analyses due to low numbers. Jurisdiction of residence was grouped based on stay-at-home order experiences. New South Wales and the Australian Capital Territory residents were combined as respondents who experienced extended stay-at-home orders in 2021, Victorian residents experienced extended stay-at-home orders in 2020 and 2021, and all other jurisdictions were combined as regions of Australia experiencing relatively minimal periods of stay-at-home orders. Cross-tabulation analyses were prepared to assess the

association of categorical variables with willingness to receive a booster vaccine using the chi-squared test. Continuous variables were analysed using the Wilcoxon rank sum test. Univariate analyses were conducted to calculate unadjusted odds ratios (ORs). Variables that returned a p-value ≤ 0.2 were included in the multivariate logistic regression as risk factors/exposures and potential confounders. Age and gender were included as a priori confounders in the multivariate logistic regression regardless of statistical significance found in the univariate analysis. Statistical significance for adjusted ORs in the multivariate logistic regression was set at a p-value <0.05 and where the 95% confidence interval (CI) did not contain 1. All data were analysed in Stata (version 17.0).

Ethical considerations

The protocol for this study was approved by the Australian National University Human Research Ethics Committee (2021/224). Participation was voluntary and informed consent was obtained at the start of the questionnaire. Only questions that related to the inclusion criteria (i.e., age and country of birth) and health professional status were compulsory. Participants had the option to enter a prize draw to win one of ten $100 grocery vouchers. Contact details of participants who elected to enter the draw were collected and kept in a separate online form from questionnaire responses.

Results

The questionnaire was attempted by 302 participants. One respondent was younger than 18 years of age and one respondent did not complete all questions regarding inclusion criteria. Inclusion criteria were met by 300 respondents and 216 responded to the outcome variable (i.e., willingness to receive a COVID-19 booster vaccine). Approximately half of the participants were male (52.0%), the median age of respondents was 39 years (range: 18–74 years, IQR: 34–48 years) and the median time lived in Australia was seven years (range: 0.2–40 years, IQR: 4.3–11 years) (Table 1). Most respondents (71%) were university-educated and were not studying or working in a health profession (87%) (Table 1). Responses were received from migrants born in all EMRO countries except for Djibouti and Qatar.

Table 1: Sociodemographic characteristics of study participants

Characteristics		Number	Percentage
Gender	Man or male	156	52.0%
	Woman or female	138	46.0%
	Non-binary	1	0.3%
	Prefer not to say	5	1.7%
Age group (years)	18–24 years	17	5.7%
	25–34 years	67	22.3%
	35–44 years	122	40.7%
	45–54 years	47	15.7%
	55–64 years	30	10.0%
	65+ years	17	5.7%
Jurisdiction of residence	Australian Capital Territory	55	18.3%
	New South Wales	86	28.7%
	Northern Territory	1	0.3%
	Queensland	51	17.0%
	South Australia	9	3.0%
	Tasmania	5	1.7%
	Victoria	73	24.3%
	Western Australia	20	6.7%
Years lived in Australia	0–4 years	98	32.7%
	5–9 years	111	37.0%
	10+ years	91	30.3%
Educational attainment	Have not completed high school	27	9.0%
	Completed high school	34	11.3%
	Vocational certificate	27	9.0%
	Associate degree	33	11.0%
	Bachelor degree	84	28.0%
	Master or Doctoral degree	95	31.7%
Health profession status	Yes	38	12.7%
	No	262	87.3%
Vaccination status at time of questionnaire	Have not received a COVID-19 vaccine	10	3.9%
	Had received one vaccine, and not intending to have a second	4	1.6%
	Had received one vaccine, and intending to have a second	19	7.4%
	Had received two doses	224	87.2%
Country of birth	Iran	84	28.0%
	Iraq	37	12.3%
	Pakistan	30	10.0%
	Syria	30	10.0%
	Afghanistan	24	8.0%
	Other EMRO country	95	31.7%

Most respondents (87%) reported receiving two doses of a COVID-19 vaccine at the time they completed the questionnaire. Of the 10 respondents who had not received a COVID-19 vaccine, four were extremely likely or somewhat likely to receive a COVID-19 vaccine, four were neither

likely nor unlikely, and two were somewhat unlikely or extremely unlikely to receive a COVID-19 vaccine.

On the scale from 0 to 100, the mean self-estimated knowledge of COVID-19 vaccines was 71.3 out of 100 (± 24.6) and the mean self-estimated knowledge of the Australian COVID-19 vaccination program was 70.3 ± 27.1. About half of participants reported high or very high needs for receiving information about "COVID-19 vaccines safety monitoring in Australia", "COVID-19 vaccines protection against illness", "Safety of COVID-19 vaccines used in Australia", and "The Australian COVID-19 vaccination program" (Table 2).

Table 2: Level of information need of study participants regarding COVID-19 vaccines and the Australian vaccination program

Area of information need	Very low n (%)	Low n (%)	Moderate n (%)	High n (%)	Very high n (%)
Safety of COVID-19 vaccines used in Australia	10.8%	11.5%	28.2%	27.9%	21.6%
COVID-19 vaccines protection against illness	7.7%	12.9%	29.0%	32.5%	17.8%
Ingredients of the COVID-19 vaccines used in Australia	13.0%	18.0%	29.2%	27.8%	12.0%
The way that COVID-19 vaccines work	10.3%	14.6%	30.3%	31.7%	13.2%
COVID-19 vaccines' safety monitoring in Australia	7.5%	17.1%	23.9%	32.9%	18.6%
The Australian COVID-19 vaccination program	8.6%	11.9%	30.6%	32.4%	16.6%

Among participants who either had received two COVID-19 vaccine doses or had received one dose and planned to receive a second dose, 176/216 (81.4%) indicated they were willing to receive a COVID-19 booster vaccine. Two thirds (66.1%, 143/216) of respondents indicated they were "extremely likely" to receive a COVID-19 booster vaccine. Among those who were unsure/hesitant, most respondents were "neither likely nor unlikely" to receive a booster dose (87.5% of unsure/hesitant respondents, 16.2% of all respondents).

Table 3 shows aspects of information seeking behaviours by willingness to receive a COVID-19 booster dose. Respondents who were willing to receive a COVID-19 booster vaccine had a higher mean self-estimated knowledge of COVID-19 vaccines (75.04 ± 22.54) compared to respondents who were unsure/hesitant (60.50 ± 28.70) ($P < 0.01$). Overall, respondents who were willing to receive a COVID-19 booster had greater scores in confidence in COVID-19 vaccines and trust in the Australian government's vaccine recommendations domain, and perceived COVID-19 as a greater risk, compared with those who were unsure/hesitant about receive a booster dose. Both groups reported similar perceptions of their personal risks from COVID-19 but diverged on their views of COVID-19 as a broader health problem. There were no

statistically significant differences between the two groups in terms of channels used to find information about COVID-19 vaccines. A greater proportion of respondents who were willing to receiving a COVID-19 booster vaccine reported they had no recent exposure to concerning COVID-19 vaccine news and did have exposure to news about COVID-19 vaccines that made them feel confident.

Table 3: Information seeking behaviours and willingness to receive a COVID-19 booster vaccine among study participants

Domains		COVID-19 booster willingness		Total (SD)	Test statistic	p-value
		Willing Mean ± SD / N (%)	Unsure/hesitant Mean ± SD / N (%)			
Estimated knowledge	Estimated knowledge of COVID-19 vaccines (0-100)	75.04 ± 22.54	60.50 ± 28.70	72.35 ± 24.39	-2.901*	<0.01
Confidence score	The COVID-19 vaccines used in Australia are effective in protecting us	4.35 ± 0.73	3.65 ± 1.00	4.22 (0.83)	-4.308*	<0.01
	The COVID-19 vaccines used in Australia are safe	4.22 ± 0.82	3.60 ± 1.01	4.10 ± 0.89	-3.757*	<0.01
	Total	4.28 ± 0.70	3.63 ± 0.90	4.16 ± 0.78	-4.390*	<0.01
Risk perception score	COVID-19 is a serious health problem around the world	4.56 ± 0.75	4.03 ± 1.00	4.46 ± 0.83	-3.516*	<0.01
	COVID-19 is a serious health problem in Australia	4.36 ± 0.83	4.08 ± 0.87	4.31 ± 0.84	-2.090*	0.04
	I'm at risk of getting COVID-19	3.59 ± 1.09	3.49 ± 1.25	3.57 ± 1.12	-0.395*	0.69
	If I get COVID-19 I could be seriously ill	3.81 ± 1.01	3.74 ± 0.94	3.80 ± 1.00	-0.534*	0.59
	Total	4.08 ± 0.66	3.84 ± 0.60	4.03 ± 0.83	-2.394*	0.02
Trust	I trust the Australian government recommendations for COVID-19 vaccines	4.29 ± 0.83	3.73 ± 1.04	4.18 ± 0.89	-3.560*	<0.01
Used official Australian information channel	Yes	147 (83.1%)	34 (82.9%)	181 (83.0%)	<0.001^	0.99
	No	30 (16.9%)	7 (17.1%)	37 (17.0%)		
Used official home country information channel	Yes	33 (18.6%)	11 (26.8%)	44 (20.2%)	1.384^	0.24
	No	144 (81.4%)	30 (73.1%)	174 (79.8%)		
Used unofficial information channel	Yes	145 (81.9%)	31 (75.6%)	176 (80.7%)	0.852^	0.36
	No	32 (18.1%)	10 (24.4%)	42 (19.3%)		
In recent months, I have heard some news about COVID-19 vaccines that made me confident	True	137 (78.7%)	21 (51.2%)	158 (73.5%)	12.895^	<0.01
	False	37 (21.3%)	20 (49.8%)	57 (27.5%)		
In recent months, I have heard some news about COVID-19 vaccines that made me concerned	True	65 (36.9%)	28 (68.3%)	93 (43.9%)	13.355^	<0.01
	False	111 (63.1%)	13 (31.7%)	124 (57.1%)		

* Wilcoxon rank sum test statistic

^ Chi-squared test statistic

The results of the univariate and multivariate analyses are shown in Table 4. Exposure to confidence-inducing news about COVID-19 vaccines (OR 3.68 95% CI: 1.79-7.54), no exposure to concerning news about COVID-19 vaccines (OR 3.51 95% CI: 1.70-7.29), higher educational attainment (OR 2.34 95% CI: 1.13-4.84), greater confidence in COVID-19 vaccines (OR 2.76 95% CI: 1.75-4.34), perceiving COVID-19 as a risk (OR 1.74 95% CI:1.02-2.97), trust in the Australian government's approach to vaccines (OR 1.85 95% CI: 1.30-2.65), increasing age in years (OR 1.07 95% CI: 1.03-1.11), and higher mean self-estimated knowledge of COVID-19 vaccines (OR 1.02 95% CI: 1.01-1.04) were univariately associated with willingness to receive a COVID-19 booster vaccine. The strongest associations were evident regarding the news or subject of information a respondent was exposed to regarding COVID-19 vaccines. No significant differences between the groups were seen by gender, health profession status, years lived in Australia, or information channel used.

Table 4: Univariate and multivariate logistic regression analysis of factors associated with COVID-19 booster willingness

Characteristic		Unadjusted odds ratio (OR)	95% CI	p-value	Adjusted odds ratio (aOR)	95% CI	p-value
Age	Age (years)	1.07	1.03-1.11	<0.01	1.07	1.01-1.12	0.01
Gender	Man or male	REF	-	-	REF	-	-
	Woman or female	1.15	0.58-2.31	0.69	1.35	0.58-3.12	0.47
Jurisdiction of residence	NSW/ACT	REF	-	-	REF		
	Victoria	0.41	0.17-0.95	0.04	0.52	0.19-1.44	0.21
	Other	0.59	0.25-1.36	0.22	0.60	0.22-1.81	0.41
Educational attainment	Non-university	REF	-	-	REF	-	-
	University	2.34	1.13-4.84	0.02	2.35	0.96-5.75	0.06
Health profession status	No	REF	-	-	-	-	-
	Yes	6.76	0.89-51.38	0.07	-	-	-
Years lived in Australia	0–9 years	REF	-	-	REF		
	10 years +	1.77	0.77-4.09	0.18	0.82	0.29-2.33	0.71
Estimated knowledge	Estimated knowledge of COVID-19 vaccines	1.02	1.01-1.04	<0.01	1.01	0.99-1.03	0.23
Confidence	Confidence score	2.76	1.75-4.34	<0.01	1.92	0.95-3.87	0.07
Risk perception	Risk perception score	1.74	1.02-2.97	0.04	1.50	0.77-2.90	0.23
Trust	Trust score	1.85	1.30-2.65	<0.01	1.00	0.58-1.70	0.99
Used official Australian information channel	No	REF	-	-	-	-	-
	Yes	1.03	0.42-2.55	0.95	-	-	-
Used official home country information channel	No	REF	-	-	-	-	-
	Yes	0.61	0.28-1.34	0.22	-	-	-
Used unofficial information channel	No	REF	-	-	-	-	-
	Yes	1.50	0.67-3.38	0.33	-	-	-
In recent months, I have heard some news about COVID-19 vaccines that made me confident	No	REF	-	-	REF	-	-
	Yes	3.68	1.79-7.54	<0.01	1.50	0.57-3.98	0.82
In recent months, I have heard some news about COVID-19 vaccines that made me concerned	Yes	REF	-	-	REF	-	-
	No	3.51	1.70-7.29	<0.01	3.71	1.51-9.09	<0.01

A total of 209 respondents were included in the multivariate logistic regression analysis. After multivariate logistic regression analysis, only no exposure to concerning news about COVID-19 vaccines (aOR 3.71 95% CI: 1.52-9.09) and age (aOR 1.07 95% CI: 1.02-1.12) were significantly associated with willingness to receive a COVID-19 booster vaccine.

Discussion

Overall, this study found high COVID-19 vaccine uptake and a high willingness to receive a booster vaccine amongst EMRO migrants in Australia. Willingness was greatest among older respondents and those respondents who had not been exposed to concerning news about COVID-19 vaccines recently. While participants reported moderate knowledge of COVID-19 vaccines and the Australian vaccination program, the highest levels of information need were related to the safety and effectiveness of the COVID-19 vaccine.

Safety was a key domain of information need among study participants. Concerns regarding the safety of new vaccines and the structures in place to monitor these new vaccines have been found to be significant factors affecting COVID-19 booster vaccine acceptance elsewhere.[10, 21-23]

Willingness to receive a COVID-19 booster vaccine among the study population was high. These findings are similar to studies assessing willingness for booster vaccines in Europe and North America.[21-26] This is a reassuring finding for public health authorities, as the success of a vaccination program relies in part on the willingness of a population to accept available vaccines. The high primary dose uptake and willingness to receive a booster dose among our study population may be attributed to community engagement programs, which improved accessibility for different communities by providing information in several languages in written and oral formats and outreach vaccination clinics for specific communities.[27, 28]

The high vaccine uptake and willingness to receive a booster vaccine, alongside the elevated need for information on vaccine safety and effectiveness, may be in part due to the presence of vaccine mandates across Australian states and territories at the time of the study.[2] The practical considerations of interacting in public life may have outweighed safety concerns for some participants.[29, 30] Further, the emergence of new variants, increase in breakthrough infections, and waning immunity may have affected willingness to receive a booster vaccine and potentially generated concerns about effectiveness in the time since this study was conducted.

This study found older age was positively associated with willingness to receive a COVID-19 booster vaccine. Older individuals may have higher rates of vaccine willingness due to their increased risk of severe illness, hospitalised and mortality from COVID-19. However, the perceived risk of COVID-19 was not associated with the willingness of receiving a booster dose in this study. Age is a significant factor across other studies, with younger populations more likely to be hesitant or unsure.[21, 23, 31-33] If a further booster dose is recommended for all people aged 18 and older as a public health measure to control COVID-19, public health authorities

should consider providing targeted messages to younger populations to increase willingness and uptake of COVID-19 booster vaccines.

It is evident from this study that exposure to negative or concerning news can have a significant impact on willingness to receive a COVID-19 vaccine booster. This impact persists regardless of level of educational attainment, trust in government, and type of information channel used. Previous studies reported that information need, subjective norms, perceived risk, and information channels can affect COVID-19 vaccine willingness, but they did not ask participants explicitly about exposure to the concerning news.[12, 21, 22, 24, 25, 29, 30, 33-36] The effect of exposure to concerning news on willingness to receive a booster dose is an area that needs further research especially with the introduction of new vaccines. Our finding may be related to explicitly asking respondents about the news they had consumed in recent months. Exposure to news appears to affect willingness to receive COVID-19 vaccines and highlights the importance of developing and promoting meaningful, trustworthy messages to build acceptance of COVID-19 vaccines and combat misinformation.

Uncertainty about new vaccines, the COVID-19 pandemic, and the perception of changing information and advice, can affect how individuals interpret and trust information and public health expertise over time.[29, 30, 37, 38] Ambiguity around an issue such as COVID-19 vaccines is an important issue for the general public and can facilitate the spread of misinformation and rumour.[39] In the time of uncertainty about effectiveness and safety of a vaccine it is important that the health authorities are equipped with the knowledge and skills of uncertainty communication. Designing communications in a way that help people to understand what is known, what is not known, and what actions are underway can be helpful to build trust and help people to make an informed decision. Reactions to health recommendations are dependent on the trustworthiness of the source which is defined by the expertise, honesty, and good intentions of the communicator.[38, 40] Identifying, acknowledging, and understanding people's concerns about vaccines, explaining why vaccination is recommended rather than solely focusing on what an individual should do, and acknowledging information may change as new research is conducted may improve booster uptake.

Strengths and limitations

This work makes an important contribution to understanding the information needs of migrants residing in Australia and their intentions to receive a COVID-19 booster dose. The Risk Information Seeking and Processing model and the three Cs model of vaccine hesitancy were used in developing the questionnaire which helped develop a comprehensive understanding of factors affecting willingness to receive COVID-19 vaccine booster dose and information seeking behaviours. The questionnaire was available in two mainly spoken languages in the EMRO region and in English, and participants had the option to select the language they preferred. This removed some potential language barriers to participation. However, the questionnaire was not available in all languages spoken in the region, such as Urdu, Pashto and Somali. This study relied on non-random sampling, the questionnaire was only available online and largely relied

on social media dissemination, potentially limiting participation from members of the target population who do not regularly use the internet or social media. Combined, these factors may introduce selection bias and limit the generalisability of the findings to populations outside this study, including all migrants from the EMRO region living in Australia. Social desirability may have affected responses to some of questions, including question about willingness to receive a booster dose. This was minimised by anonymising the questionnaire. Finally, the cross-sectional nature of this study limits the causal relationship interpretation of findings. At the time of data collection, restrictions were in place to control the spread of the Delta variant which may have affected an individual's willingness to receive booster vaccines.

Conclusion

Migrants in Australia are from a myriad of cultural, religious, ethnic, and linguistic backgrounds and represent a wide range of experiences in the COVID-19 pandemic. This diversity needs to be considered and incorporated into vaccination education programs. Interventions and information targeting younger adults and improving information sufficiency in COVID-19 vaccines should be used to encourage booster vaccine uptake. Further qualitative research can help to explore the nuances behind the effects of concerning news and available information on willingness to receive a COVID-19 booster vaccine and other new vaccines. It is crucial that public health practitioners are open about what is known and unknown and communicate frequently to alleviate uncertainty. Addressing vaccine concerns should be a priority in the current and in future pandemics.

Declarations

Ethics approval and consent to participate

The protocol for this study was approved by the Australian National University Human Research Ethics Committee (2021/224). Participation was voluntary and informed consent was obtained at the start of the questionnaire.

Consent for publication

Not applicable

Availability of data and materials

Data is available from the corresponding author under reasonable request.

Competing interests

None.

Funding

This research was funded through a research grant from the Australian Partnership for Preparedness Research on Infectious Disease Emergencies (APPRISE). This grant was awarded for the data collection to inform this study. APPRISE had no role in the design of the study and collection, analysis, and interpretation of data and in writing.

Author contributions

DP, SL and KA designed the study, DP, SL and KA designed the questionnaire, KA collated and analysed the study data, DP and AY reviewed the analysis. DP translated the questionnaire and responses in Arabic and Farsi. AY prepared the literature review. KA and DP wrote the main manuscript, with AY and SL providing detailed review and feedback. All authors read and approved the final manuscript.

Acknowledgements

We acknowledge the financial support received for this study from Australian Partnership for Preparedness Research on Infectious Disease Emergencies (APPRISE). The research team thanks participants in this study and also organisations, community groups, and individuals who helped with the distribution of research flyer especially Ethnic Communities' Council of NSW, ACT Office for Multicultural Affairs, Multicultural Communities Council of Western Australia, MARSS Australia Inc, Canberra Multicultural Community Forum, Ethnic Communities' Council of Victoria, Multicultural Communities Council of SA, and CORE Community Services Team. The research team also thank Alexandra Marmor for her review of the manuscript and for valuable feedback and suggestions.

Reference list

1. Australian Government Operation COVID Shield. *COVID-19 Vaccine Roll-out - Monday 9 May 2022*. Canberra; 2022.
2. COVID-19 National Incident Room Surveillance Team. COVID-19 Australia: Epidemiology Report 56: Reporting period ending 5 December 2021. *Communicable Diseases Intelligence*. 2021;45.
3. *Booster shot for severely immunocompromised Australians* [press release]. Canberra: Australian Government Department of Health, 8 October 2021.
4. *Start of COVID-19 booster vaccination program* [press release]. Canberra: Australian Government Department of Health, 8 November 2021.
5. Biddle N, Sollis K. Who wants to get boosted? COVID-19 vaccine uptake in Australia in January 2022 ANU Centre for Social Research and Methods. 2022.
6. Greenaway C, Hargreaves S, Barkati S, Coyle CM, Gobbi F, Veizis A, et al. COVID-19: Exposing and addressing health disparities among ethnic minorities and migrants. *J Travel Med*. 2020;27(7):taaa113.
7. Hayward SE, Deal A, Cheng C, Crawshaw A, Orcutt M, Vandrevala 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. Jaljaa A, Caminada S, Tosti ME, D'Angelo F, Angelozzi A, Isonne C, et al. Risk of SARS-CoV-2 infection in migrants and ethnic minorities compared with the general population in the European WHO region during the first year of the pandemic: a systematic review. *BMC Public Health*. 2022;22(1):143.
9. Wright L, Steptoe A, Fancourt D. Are we all in this together? Longitudinal assessment of cumulative adversities by socioeconomic position in the first 3 weeks of lockdown in the UK. *J Epidemiol Community Health*. 2020;74(9):683-8.
10. Crawshaw AF, Farah Y, Deal A, Rustage K, Hayward SE, Carter J, et al. Defining the determinants of vaccine uptake and undervaccination in migrant populations in Europe to improve routine and COVID-19 vaccine uptake: a systematic review. *The Lancet Infectious Diseases*. 2022.
11. 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;71(709):e583-e95.
12. Lin S. COVID-19 Pandemic and Im/migrants' Elevated Health Concerns in Canada: Vaccine Hesitancy, Anticipated Stigma, and Risk Perception of Accessing Care. *Journal of Immigrant and Minority Health*. 2022.
13. Ross J, Diaz CM, Starrels JL. The Disproportionate Burden of COVID-19 for Immigrants in the Bronx, New York. *JAMA Internal Medicine*. 2020;180(8):1043-4.
14. Drefahl S, Wallace M, Mussino E, Aradhya S, Kolk M, Brandén M, et al. A population-based cohort study of socio-demographic risk factors for COVID-19 deaths in Sweden. *Nat Commun*. 2020;11(1):5097.
15. Vanthomme K, Gadeyne S, Lusyne P, Vandenheede H. A population-based study on mortality among Belgian immigrants during the first COVID-19 wave in Belgium. Can demographic and socioeconomic indicators explain differential mortality? *SSM - Population Health*. 2021;14:100797.
16. Australian Bureau of Statistics. *COVID-19 Mortality in Australia* Canberra: Australian Bureau of Statistics; 2022 [Available from: https://www.abs.gov.au/articles/covid-19-mortality-australia#death-due-to-covid-19-country-of-birth.
17. Australian Bureau of Statistics. *Migration, Australia* Canberra2022 [Available from: https://www.abs.gov.au/statistics/people/population/migration-australia/2019-20.
18. International Organization for Migration. *Migration Health in the Sustainable Development Goals: Leave No One Behind' in an increasingly mobile society*2020 1 June 2022. Available from: https://www.iom.int/resources/migration-health-sustainable-development-goals-1.
19. Yang ZJ, Aloe AM, Feeley TH. Risk information seeking and processing model: A meta-analysis. *Journal of Communication*. 2014;64(1):20-41.
20. MacDonald NE. Vaccine hesitancy: Definition, scope and determinants. *Vaccine*. 2015;33(34):4161-4.
21. Folcarelli L, Miraglia Del Giudice G, Corea F, Angelillo IF. Intention to Receive the COVID-19 Vaccine Booster Dose in a University Community in Italy. *Vaccines (Basel)*. 2022;10(2).
22. Kheil MH, Jain D, Jomaa J, Askar B, Alcodray Y, Wahbi S, et al. COVID-19 Vaccine Hesitancy among Arab Americans. *Vaccines (Basel)*. 2022;10(4).
23. Rzymski P, Poniedziałek B, Fal A. Willingness to Receive the Booster COVID-19 Vaccine Dose in Poland. *Vaccines*. 2021;9(11).

24. De Giorgio A, Kuvačić G, Maleš D, Vecchio I, Tornali C, Ishac W, et al. Willingness to Receive COVID-19 Booster Vaccine: Associations between Green-Pass, Social Media Information, Anti-Vax Beliefs, and Emotional Balance. *Vaccines*. 2022;10(3):481.
25. Jørgensen FJ, Nielsen LH, Petersen MB. Willingness to Take the Booster Vaccine in a Nationally Representative Sample of Danes. *Vaccines (Basel)*. 2022;10(3).
26. Paul E, Fancourt D. Predictors of uncertainty and unwillingness to receive the COVID-19 booster vaccine: An observational study of 22,139 fully vaccinated adults in the UK. *The Lancet Regional Health – Europe*. 2022;14.
27. Migration Council Australia. Supporting COVID-19 Vaccination Program rollout to migrant and refugee communities in Australia. Canberra; 2022.
28. Wild A, Kunstler B, Goodwin D, Onyala S, Zhang L, Kufi M, et al. Communicating COVID-19 health information to culturally and linguistically diverse communities: insights from a participatory research collaboration. *Public Health Research & Practice*. 2021;31(1):e3112105.
29. Kaufman J, Bagot KL, Tuckerman J, Biezen R, Oliver J, Jos C, et al. Qualitative exploration of intentions, concerns and information needs of vaccine-hesitant adults initially prioritised to receive COVID-19 vaccines in Australia. *Australian and New Zealand Journal of Public Health*. 2022;46(1):16-24.
30. Mahimbo A, Kang M, Sestakova L, Smith M, Dawson A. Factors influencing refugees' willingness to accept COVID-19 vaccines in Greater Sydney: a qualitative study. *Australian and New Zealand Journal of Public Health*. 2022.
31. Alabdulla M, Reagu SM, Al-Khal A, Elzain M, Jones RM. COVID-19 vaccine hesitancy and attitudes in Qatar: A national cross-sectional survey of a migrant-majority population. *Influenza Other Respir Viruses*. 2021;15(3):361-70.
32. Sønderskov KM, Vistisen HT, Dinesen PT, Østergaard SD. COVID-19 booster vaccine willingness. *Danish Medical Journal*. 2022;69(1):A10210765.
33. Trent M, Seale H, Chughtai AA, Salmon D, MacIntyre CR. Trust in government, intention to vaccinate and COVID-19 vaccine hesitancy: A comparative survey of five large cities in the United States, United Kingdom, and Australia. *Vaccine*. 2021.
34. Dodd RH, Cvejic E, Bonner C, Pickles K, McCaffery KJ. Willingness to vaccinate against COVID-19 in Australia. *Lancet Infect Dis*. 2021;21(3):318-9.
35. Hagger MS, Hamilton K. Predicting COVID-19 booster vaccine intentions. *Applied Psychology: Health and Well-Being*. 2022;n/a(n/a).
36. Yadete T, Batra K, Netski DM, Antonio S, Patros MJ, Bester JC. Assessing Acceptability of COVID-19 Vaccine Booster Dose among Adult Americans: A Cross-Sectional Study. *Vaccines*. 2021;9(12):1424.
37. Noar SM, Austin L. (Mis)communicating about COVID-19: Insights from Health and Crisis Communication. *Health Communication*. 2020;35(14):1735-9.
38. Paek HJ, Hove T. Communicating Uncertainties during the COVID-19 Outbreak. *Health Commun*. 2020;35(14):1729-31.
39. Chorus A. The basic law of rumor. *The Journal of abnormal and social psychology*. 1953;48(2):313.
40. Blastland M, Freeman ALJ, van der Linden S, Marteau TM, Spiegelhalter D. Five rules for evidence communication. *Nature*. 2020;587(7834):362-4.

APPENDIX B: CONFERENCE PRESENTATION: FACTORS AFFECTING COVID-19 VACCINE BOOSTER WILLINGNESS AMONG MIGRANTS IN AUSTRALIA

PRESENTED AT THE COMMUNICABLE DISEASES AND IMMUNISATION CONFERENCE, JUNE 2022

Factors affecting COVID-19 vaccine booster willingness among migrants in Australia

Keeley Allen
A/Prof Stephen Lambert
Dr Davoud Pourmarzi

Australian National University

Background

COVID-19 booster vaccines are one of our main tools to control spread and protect populations.

Vaccination programs are only as effective as their acceptability.

One key population to include in vaccination programs are migrants.

Research questions

01	What information do migrants from the Eastern Mediterranean region (EMRO) need to know?
02	What is the level of vaccine acceptance and booster willingness among EMRO migrants?
03	What factors are associated with willingness to receive a booster vaccine?

Methods

Cross-sectional online questionnaire from September to November 2021

Asked socio-demographic factors, beliefs about COVID-19 and vaccines, information seeking behaviours, COVID-19 vaccination status, and willingness to receive a booster dose

Open to all adults living in Australia born in an Eastern Mediterranean Region (EMRO) country

Study population

300 eligible responses received

52% male

71%

7 years

35-44 yrs

41%

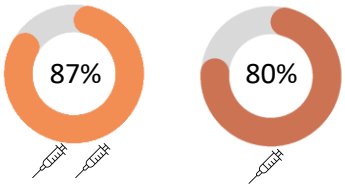
68%

1. What information do EMRO migrants need to know?

Safety was the key priority for information

2. What is the level of vaccine acceptance and booster willingness among EMRO migrants?

Vaccine acceptance was high



3. What factors are associated with willingness to receive a booster vaccine?

Booster willingness was associated with many factors in the univariate analysis…

Characteristic	Unadjusted odds ratio	95% CI
Age	**1.07**	**1.03-1.11**
Female	1.15	0.58-2.31
University education	**2.34**	**1.13-4.84**
Health professional	6.76	0.89-51.38
10+ years lived in Australia	1.77	0.77-4.09
Estimated knowledge of COVID-19 vaccines	**1.02**	**1.01-1.04**
Confidence score	**2.76**	**1.75-4.34**
Risk perception	**1.74**	**1.02-2.97**
Trust in Australian government's vaccine program	**1.85**	**1.30-2.65**
Used official Australian information channel	1.03	0.42-2.55
Used official home country information channel	0.61	0.28-1.34
Used unofficial Australian information channel	1.50	0.67-3.38
In recent months, I have heard some news about COVID-19 vaccines that made me confident	**3.68**	**1.79-7.54**
In recent months, I have NOT heard some news about COVID-19 vaccines that made me concerned	**3.51**	**1.70-7.29**

3. What factors are associated with willingness to receive a booster vaccine?

… but only the association with age and the news we see remained in the multivariate analysis

Characteristic	Adjusted odds ratio	95% CI
Age	**1.07**	**1.02-1.12**
University education	2.35	0.96-5.75
Estimated knowledge of COVID-19 vaccines	1.01	0.99-1.03
Confidence score	1.92	0.95-3.87
Risk perception	1.50	0.77-2.90
Trust in Australian government's vaccine program	1.00	0.58-1.70
In recent months, I have heard some news about COVID-19 vaccines that made me confident	1.50	0.57-3.98
In recent months, I have NOT heard some news about COVID-19 vaccines that made me concerned	**3.71**	**1.51-9.09**

Source: Shutterstock

Conclusions

The news we see and the messages we send matter.

Communicating uncertainty and communicating early is key.

We need to work with all communities to prepare and deliver clear, meaningful messages.

THANK YOU

Acknowledgements

This research received funding from Australian Partnership for Preparedness Research on Infectious Disease Emergencies (APPRISE).

Contact Us

Keeley Allen
keeley.allen@anu.edu.au
Keeley__Allen
Keeley Allen

Australian National University

CHAPTER 4: DESIGN OF A SURVEILLANCE SYSTEM FOR CARBAPENEMASE-PRODUCING *ENTEROBACTERALES*

TABLE OF CONTENTS

Prologue

This chapter details my involvement in the design and establishment of a surveillance system for carbapenemase-producing *Enterobacterales* (CPE) in the ACT. This chapter addresses the following competencies:

- Establish or evaluate a surveillance system or other health information system
- Lay summary

My role

I was involved in the design and establishment of the CPE surveillance system throughout my 20-month MAE field placement. The need for a surveillance system for CPE was identified by the Committee for Infectious Threat Surveillance and Control in the ACT in November 2019 and was a priority for the Disease Surveillance unit at ACT Health Communicable Disease Control.

I reviewed the structure, roles, and lessons learnt from other jurisdictions through a desktop review and led semi-structured interviews. I mapped out the key internal and external stakeholders for the surveillance system with the Surveillance Coordinator. We collaborated with these stakeholders to identify needs and barriers to a CPE surveillance system and to gain feedback on the draft system. I developed definitions for cases, contacts, and outbreaks in consultation with these stakeholders, and designed and developed an enhanced surveillance data collection tool in REDCap. With the support of the Surveillance Coordinator, I developed the flow of information based on a case's location of testing and the information required to successfully identify a case's source of acquisition.

I also conducted a targeted literature review to describe the public health issue and importance of CPE against the criteria for national notification endorsed by the Communicable Disease Network of Australia. This literature review was designed to summarise the clinical manifestation and severity of CPE, populations at greatest risk, outbreak potential, and preventability using peer-reviewed literature available on PubMed. The literature review also included peer-reviewed research conducted for carbapenemase-producing *Enterobacteriaceae*, a family of bacteria that form part of the order *Enterobacterales*, and carbapenemase-resistant *Enterobacteriaceae* or *Enterobacterales*, which may have acquired their resistance through of carbapenemase genes or other means. The limits of this review were necessary to include important research that can inform ACT Health's response and accommodate changing definitions of these multidrug organisms over time and across jurisdictions globally.

I drafted documents outlining the need for CPE to be included as a notifiable condition in the ACT, including a briefing note for the Chief Health Officer, a briefing note for the Minister of Health, a case assessment of CPE against the CDNA criteria, and an internal protocol for the ACT Health Communicable Disease Control response to a notification or an outbreak. I also drafted factsheets for CPE cases and contacts, letters for GP where cases and contacts consent to share this information, a communications strategy in the event CPE is made notifiable, and a guideline

for residential aged care facilities to manage and support resident CPE cases and contacts. The package of documents was submitted for the Chief Health Officer's assessment following review from the Surveillance Coordinator and Public Health Physician team.

Key reflections

I have learnt several valuable lessons through this project. The design of a CPE surveillance system was my longest running, most complex project. It was also my most rewarding project, developing a surveillance system to prepare the ACT for an emerging public health threat and serving as a potential template for future surveillance of additional multidrug-resistant organisms.

Throughout this project, I have learnt the importance of flexibility and advocating for your needs in an emergency context. The timelines and milestones for this project were affected by several public health emergencies and acute responses, including a local outbreak of the B.1.617.2 variant with stay-at-home orders, waves of several Omicron variants, the emergence of Japanese encephalitis virus in Australia, and the emergence of monkeypox virus in Australia, among other events. As a small jurisdiction, I had the opportunity to be involved in responses to these public health threats. While these were valuable experiences for my training as a field epidemiologist, I was required to adapt my project plan and timeframes to fit around these reactive acute public health threats. These events have also limited the availability of internal and external stakeholders to devote their time and expertise to this project and provide timely feedback. Through these challenges, I learnt valuable skills in advocacy and persuading internal and external stakeholders to give some of their time for this project and reinforcing the need for public health response to be proactive and prepared.

This project has reinforced the importance of stakeholder engagement and relationship building. The design of this surveillance system has been strengthened by the sustained engagement and communications with hospital infection prevention and control units and the ACT Infection Prevention and Control Network which may not have been achieved with standard, one-off consultation. Ongoing discussions have been essential to the acceptance and usefulness of this surveillance system and building relationships between ACT Health Communicable Disease Control and local hospitals more broadly.

This project has also given me technical knowledge and skills. I have gained a thorough appreciation for the threat of antimicrobial resistance to public health. While I have also learned a lot about the natural history, microbiology, and clinical management of CPE, I recognise there is more to learn and many questions about CPE worldwide remain unanswered at this time. Because of this uncertainty and the need to keep learning, it is crucial that we adapt our surveillance strategies as new information becomes available. I have also developed skills in designing a REDCap database and online data entry tool for a wide range of stakeholders to enter data in a simple, useful format.

Public health impact

At the time of submission, the decision to make CPE a notifiable condition was under review by the ACT Chief Health Officer. Prior to this project, surveillance of CPE in the ACT relied on voluntary deidentified data inadequate to inform public health action. If CPE is approved as a notifiable condition, this surveillance system will provide useful information to assess the burden of CPE on the ACT population, identify sources of acquisitions, and respond to indications of local transmission. The design of this surveillance system and the variables for enhanced surveillance may inform the design of a potential future national surveillance system for CPE.

This project has positively impacted public health in the ACT regardless of the notifiable condition decision. The engagement and networking from this project have prompted meetings and collaboration with public hospitals in the ACT for a wider range of infection control matters. The guidelines and factsheets I prepared for this surveillance system have already been used to advise residential facilities and members of the general public about the condition and the tools and processes for effective case and contact management. Finally, the development of a surveillance system for CPE has increased the general awareness of antimicrobial resistance within ACT Health and serves as a potential template for future multidrug-resistant organisms that may be made notifiable conditions in the future, such as *Candida aurus*.

Acknowledgements

My deepest thanks and gratitude to Alexandra Marmor for your invaluable insight and input for this surveillance system. Thank you to the members of the ACT Infection Prevention and Control Network for your engagement and feedback, and special thanks to Catherine Trevorrow for steering the Network. Thank you also to Dr Philippa Binns, Dr Bushra Maqsood, and Dr Sally Singleton for your review of the clinical aspects of this project. Special thanks to Dr Philippa Binns and Alison Kingsbury for your advocacy and support of this project.

Abstract

Background: Carbapenemase-producing *Enterobacterales* (CPE) are an order of gram-negative bacteria that acquired genes that confer resistance to carbapenems, rendering these 'last resort' antibiotics ineffective. A CPE infection can be difficult to treat and most commonly affect people who require repeat or long term hospitalisation. While CPE is a relatively rare condition in Australia, local outbreaks associated with healthcare facilities have been reported across the country, including the ACT. Current surveillance mechanisms are inadequate to identify and respond to cases in the ACT.

Methods: A surveillance system was designed to detect cases and identify potential local transmission. The case to make CPE a notifiable condition in the ACT was assessed against the national notification criteria endorsed by the Communicable Disease Network of Australia (CDNA). Hospital infection prevention and control teams were consulted throughout the design as the primary external stakeholders for the success of the system. The case definitions, information flow and variables for enhanced surveillance were developed with consideration of existing resources and personnel at ACT Health.

Results: The case for making CPE a notifiable condition scored 24 out of 48, warranting further consideration for notifications. The surveillance system was designed to operate as a notifiable condition with ACT Health's Communicable Disease Control branch identified as the most appropriate organisation to oversee the system. Overall, hospital infection prevention and control teams were supportive of the surveillance system, stressing the importance of information flowing back to healthcare facilities to inform their practices. A gene-based case definition was adopted as the most appropriate level of information to identify local transmission. Additional definitions were prepared for outbreaks and contacts to support a public health response. While the variables for enhanced surveillance were standardised for all cases, the process to collect this information and outbreak management was adapted for different clinical settings.

Discussion: It is anticipated that this surveillance system will be useful as it is designed to provide public health information not currently available in the ACT. The design of this surveillance system is intended to be sensitive enough to detect cases and outbreaks promptly while remaining flexible to changing epidemiology or reporting requirements. CPE is a complex condition, and the design of the system has utilised existing structures and standardised processes to improve its simplicity. The surveillance system is intended to be well accepted by key stakeholders following their involvement and the integration of their feedback into the design.

At the time of writing, the case to make CPE a notifiable condition in the ACT is currently under assessment. I recommend that CPE is made notifiable and that the effectiveness and appropriateness of the system be formally evaluated three years after implementation.

Introduction

Carbapenemase-producing *Enterobacterales* (CPE) is an order of gram-negative bacteria that have acquired genes conferring resistance to carbapenems. CPE carry genes that enable bacteria to produce carbapenemase enzymes that hydrolyse carbapenems and render them ineffective.[1-3] Carbapenems are a 'last resort' class of antibiotics that have been used to treat serious bacterial infections. Carbapenemase enzymes also hydrolyse the majority of β-lactam antibiotics, further limiting available treatment options.[4] Resistance to these treatments poses a serious threat to the clinical care and management of people with CPE and public health.

The condition

Microbiological details of the condition

The order *Enterobacterales* includes a wide range of bacteria normally found in the gastrointestinal tract including *Escherichia coli, Klebsiella pneumoniae*, and *Citrobacter spp*. The order also includes a number of pathogenic bacteria, such as *Salmonella spp*., *Yersinia enterocolitica*, and *Shigella spp*. *Enterobacterales* can acquire carbapenemase genes spontaneously from repeated exposure to antibiotics or via horizontal gene transfer between organisms. Bacteria in this order can transfer genes through the transfer of plasmids or mobile genetic elements.[4-6] This ability to easily share and acquire carbapenemase genes enables the rapid spread of antimicrobial resistance (AMR) across organisms and populations.

Five main groups of carbapenemase genes confer resistance to carbapenems. These genes have historically become endemic in specific regions of the world. For example, *Klebsiella pneumoniae* carbapenemase (KPC) is endemic in the Americas and Europe; New-Delhi metallo-β-lactamase (NDM) in the Indian subcontinent, oxacillinases (OXA-48-like) in the Mediterranean and Middle East regions; imipenemase (IMP) in the Asia-Pacific region; and Verona integron-encoded metallo-β-lactamase (VIM) in Europe and the Mediterranean.[4, 7] While these carbapenemase genes have historically clustered regionally, a variety of locally acquired CPE genes have been reported in single countries and regions, complicating the identification of the source of acquisition for cases.[7, 8] In Australia, the majority of locally acquired CPE carry the IMP gene.[9, 10]

Clinical details of the condition

There is no single disease or collection of signs or symptoms associated with CPE. CPE can asymptomatically colonise the gastrointestinal tract or urinary tract. Colonisation with CPE does not cause harm to the person; however, they remain infectious. There is limited evidence of clearance of CPE colonisation, with between 18% and 39% of people remaining colonised 12 months after an initial positive result.[11-14] CPE infection can occur when the bacteria enter other body sites such as the lungs, blood and wounds, potentially causing severe illness with limited treatment options.[15-18]

Patients with CPE infection generally spend longer in hospital and experience higher mortality compared with patients who have carbapenem-susceptible infections with the same organisms.[19-22] The crude mortality for CPE infection can range from 20% to 72% of cases depending on the setting.[16, 17, 19, 20, 23-30] Increased risk of mortality is associated with hospital patients with ICU admission, longer stay in hospital, inappropriate initial antimicrobial therapy, and older age.[16, 19, 23, 26] Individuals infected with multiple types of CPE have higher mortality compared with those infected by a single type of CPE.[25]

Treatment and prevention

The resistance of CPE to several classes of antibiotics limits treatment options. People colonised with CPE are not usually treated due to the presence of AMR and the absence of immediate risk to the person.[1] Management of CPE infection requires isolation in hospital and combination antibiotic therapies.[1]

There is no vaccine available for CPE. The *Enterobacterales* order includes bacteria normally found in the gastrointestinal tract, limiting the ability to target any potential vaccine.

Prevention of CPE spread relies on the implementation of infection prevention and control measures and antimicrobial stewardship. The implementation of infection prevention and control measures, including isolation or cohorting of positive patients in rooms with their own bathroom, hand hygiene and whole genome sequencing (WGS) of human and environmental isolates, have been successful in limiting spread in overseas and Australian healthcare facilities and ending outbreaks.[31-33] Implementing simple measures within the home, such as hand hygiene and avoiding sharing personal items such as towels and razors, may also limit transmission among household members.[34] Antimicrobial stewardship has also been associated with a reduced incidence of CPE in hospital settings.[35-37]

Epidemiology of CPE

Transmission

CPE can be transmitted through direct contact with an infected person, or indirectly through a contaminated surface, such as sinks, basins, other bathroom hardware or shared equipment.[38-40] People who are colonised with CPE and people with a CPE infection can both transmit CPE to others.[31, 41-43]

Those at greatest risk of CPE acquisition are people who frequently require hospitalisation and who are living with complex health conditions.[15, 43-45] Known risk factors for CPE acquisition in Australia include receiving medical or dental treatment overseas, prolonged periods of hospitalisation, prolonged use of antibiotics, admission to an intensive care unit, receiving an organ or stem cell transplant, dialysis, or chemotherapy, and having an indwelling medical device.[1, 4, 15, 41, 46]

People who share rooms or bathrooms with a CPE case in a healthcare facility have an increased risk of acquiring CPE. Transmission can also occur if patients use the same bathrooms without any overlap in hospital admissions, with the sinks, basins or other plumbing fixtures acting as potential reservoirs for CPE.[38, 40, 47] Transmission of CPE has also been reported in residential aged care facilities (RACFs) in Europe and North America, requiring infection prevention and control measures and contact tracing to limit spread.[42, 45, 48-50]

Household contacts are also at increased risk of CPE acquisition. Household transmission of CPE has been reported in the Americas, Asia, New Zealand, and Australia.[34, 51-54] The estimated risk of onward transmission among household contacts is approximately 10%, with increased risk among people who shared bedroom or bathroom facilities.[34, 54]

Global epidemiology of CPE

It is difficult to ascertain the global burden of CPE as there is no one set of signs or symptoms to identify the condition, and a lack of consistent definitions, testing, and reporting worldwide. To date, no estimates of the global incidence of CPE or the global prevalence of people living with the condition have been published.

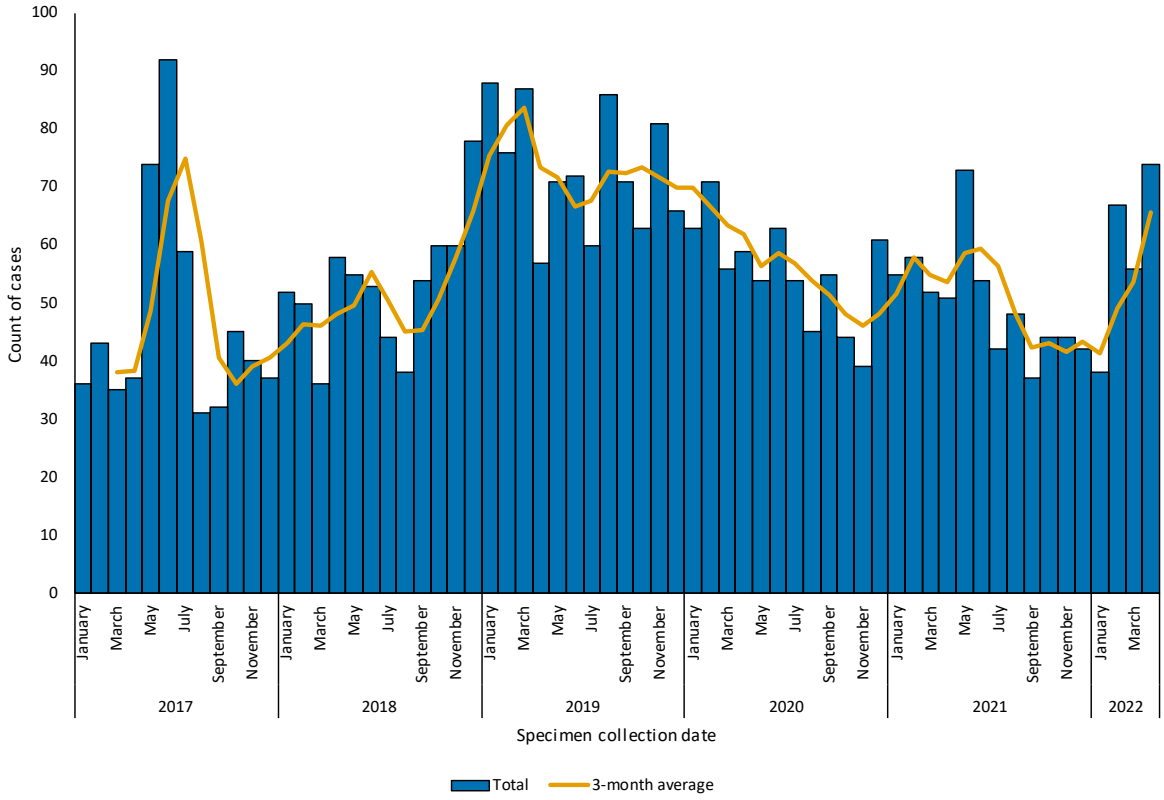
In endemic regions such as Southern Europe, Israel, and India, the prevalence of CPE in hospitalised patients ranges from 4% to 30%.[18, 55-58] Prevalence in healthy community members in India and Pakistan has been reported between 6% and 14%.[59, 60] Globally, cases are most often aged 65 years and over, with a relatively even distribution between male and female cases.[61]

Epidemiology of CPE in Australia

CPE remains a relatively rare condition in Australia. Before 2012, CPE was largely considered to be a sporadic condition with the majority of cases acquired overseas. However, over the past decade, locally acquired cases have been increasing. These local cases to date have largely been associated with healthcare facilities and large, protracted outbreaks have occurred across Australia.[9, 41, 46]

CPE cases are voluntarily reported by some laboratories to the Australian Government through the National Alert System for Critical Antimicrobial Resistances (CARAlert). Cases of CPE have fluctuated in Australia in recent years (Figure 1). Voluntary reporting of CPE cases to CARAlert shows peaks of CPE notifications approximately every second year. Notifications in recent months have increased nationwide.[9] However, it is unclear what proportion of the true incidence of CPE is voluntarily reported to CARAlert.

Figure 1: CPE notifications to CARAlert and three-month rolling average by month, Australia, 2017-April 2022



Source: CARAlert, data extracted on 18 August 2022.

One Health and CPE

In addition to the threat to human health, CPE also has the potential to significantly impact environmental and animal health. CPE has been isolated in natural waterways and soil in all inhabited continents except Australia.[62-67] CPE have been isolated in livestock and aquaculture, including transmission within European, South East Asian and North American farms.[68-73] Companion animals may also be colonised with CPE, with reports of isolates from cats and dogs in Australia, North America and Europe.[74-77] In Australia, CPE colonisation has been identified in silver gulls in Greater Sydney and Illawarra.[78] Environmental and animal sources may act as reservoirs for CPE and a potential source of acquisition for humans, and human colonisations and infections may in turn impact the health of environments and animal populations.

Outbreaks

Outbreaks of CPE largely occur in healthcare facilities through direct contact between patients and environmental contamination. Outbreaks can be protracted and require a sustained response over years to limit spread.[6, 47, 49] In other regions, outbreaks of CPE have also been reported in RACFs, with WGS and epidemiological investigations demonstrating some outbreaks can occur across multiple healthcare facilities and RACFs over several years.[6, 61, 79-82]

To date in Australia, outbreaks of CPE have largely occurred in healthcare facilities.[41, 46, 80, 83, 84] However, without national or local notification requirements, healthcare associated outbreaks and outbreaks in RACFs in the ACT are likely to be underreported and, in some cases, undetected.

Rationale for developing a surveillance system for CPE

The rationale for designing a surveillance system for CPE combines the recognition of the potential threat to public health, the limited usefulness of existing systems, and an increased political will to respond to AMR at a Territory and national level.

CPE is an emerging threat to public health in the ACT

The threat of CPE to public health was recognised by the ACT Health Directorate. A retrospective outbreak investigation at The Canberra Hospital from 2012-2016 found 72 cases among 63 people.[80] Whole genome sequencing found two separate outbreaks each occurred over three years across multiple wards affecting 17 patients.[80] This is well in excess of the five to 10 cases reported voluntarily to CARAlert each year, indicating the potential burden of CPE may be greater than what is currently known.

The Committee for Infectious Threat Surveillance and Control in the ACT recognised the need to establish the burden of CPE in the ACT and monitor new cases at their November 2019 meeting. The Committee recommended the development of a business case to consider adding CPE to the list of notifiable conditions in the ACT.

Existing surveillance systems have limited public health utility

There is limited knowledge of the ongoing burden and epidemiology of CPE in the ACT. CPE is not currently nationally notifiable. The condition is one of several multidrug-resistant organisms (MROs) monitored by CARAlert. CARAlert is currently the only surveillance system for CPE available to ACT Health. Reporting to CARAlert is voluntarily conducted by some public health laboratories in Australia. State and territory health departments receive weekly reports of de-identified data summarising CPE detections. However, the available data has limited utility for informing a public health response. The details of the person and location of the person at the time of testing limit the ability to follow up CPE detections. No information is recorded about exposure history or known risk factors, preventing detection of local transmission. Finally, not all laboratories report CPE detections to CARAlert, limiting case ascertainment.

Surveillance is in place in other Australian jurisdictions

Following local outbreaks in their jurisdictions, CPE has become a notifiable condition in Victoria, New South Wales, Western Australia, South Australia, and Tasmania. Although CPE is not currently nationally notifiable, the Australian Government Department of Health is working in collaboration with Communicable Diseases Network Australia (CDNA) and the Public Health Laboratory Network (PHLN) to develop a framework for the implementation of a National AMR Outbreak Response Network (the Network). If implemented, the Network would seek to reduce

the impact of AMR, including priority MROs, on human health in Australia through a public health approach.

Organisation of this chapter

This chapter details the design of a surveillance system for CPE in the ACT. The methods section outlines the processes and procedures for designing the surveillance system. The design of the surveillance system is detailed in the results section. Finally, the discussion section assesses the design of the CPE surveillance system against the attributes outlines in the United States Center for Disease Control and Prevention's *Updated guidelines for evaluating public health surveillance systems*[85] and includes a proposed strategy for evaluating the usefulness of the system into the future.

Aims and objectives

The aim of this project was to develop a CPE surveillance system to limit the transmission of CPE in the ACT.

The secondary objectives are to:

- Detect all cases of CPE in the ACT
- Report trends and patterns in the person, place, and time of CPE cases in the ACT
- Detect local transmission of CPE in the ACT
- Identify and inform contacts of CPE cases

Methods

Scoping and design

The absence of appropriate oversight of CPE in the ACT necessitated the establishment of a surveillance system for the territory. The need to describe local epidemiology of the condition and to detect outbreaks directed the model and design of this surveillance system.

I conducted interviews with jurisdictions where CPE is a notifiable condition to assist in the scoping and design of the system. Interviews used non-standardised questionnaires to understand existing case definitions, information flows, and lessons learnt that may be applied in the ACT.

Stakeholders

We mapped out stakeholders who have an interest in the establishment of a surveillance system for CPE in the ACT (Table 1).

Table 1: Key stakeholders and roles in the surveillance of CPE

Stakeholders	Roles
Communicable Disease Control (CDC) Branch	Surveillance and response to notifiable conditions in the ACT
Quality and Safety Unit	Oversight of policy for clinical care, safety and quality
ACT Pathology	Testing of suspected CPE isolates
Other public health laboratories servicing the ACT (in the ACT and interstate)	Testing of suspected CPE isolates
Healthcare Infection Prevention and Control (IPC) teams	Infection prevention and control response to CPE cases within a healthcare facility
Clinicians in healthcare facilities	Clinical management of CPE cases
Residential aged care facilities (RACFs)	Infection prevention and control response and clinical management of CPE cases within a residential aged care facility
General practitioners and other primary health care clinicians	Clinical management of CPE cases
Office of the Chief Veterinary Officer	Oversight of policy for CPE surveillance and response in animals

Interviews and meetings with hospital teams were conducted to gain an understanding of current practices for CPE surveillance and outbreak management, the needs of and barriers to data collection for CPE, and to discuss proposed methods for information flow between the hospital and CDC.

Regular updates and feedback were sought on the proposed design and features of the CPE surveillance system through the quarterly ACT Infection Prevention and Control Networking (ACT IPC Network) meetings. These meetings bring IPC teams from ACT hospitals together with ACT Health to share updates on policies and practices for clinical care and innovations in IPC matters. Direct feedback was also sought via email on a draft information flow process and an enhanced surveillance data collection instrument for those who could not attend ACT IPC Network meetings.

Legal authority for surveillance

The surveillance system was designed with consideration of the *ACT Public Health Act 1997*. Part 6 outlines the powers and responsibilities for data collection and public health actions for notifiable conditions in the ACT. Notifiable conditions are listed in a disallowable instrument that can be enacted by the Minister of Health. Notifiable conditions in the ACT are listed in the *Public Health (Reporting of Notifiable Conditions) Code of Practice 2022*.

There are no local criteria for the assessment of notifiable conditions in the ACT. In the absence of local criteria, we assessed the suitability for CPE to be made a notifiable condition against the national criteria established by the Communicable Disease Network of Australia (CDNA). The 12 criteria assess the public health importance and feasibility of data collection and public health response to conditions (Table 2). A maximum score of 48 can be achieved, with scores of 26 and over recommending national notification, scores between 15 and 25 recommending national notification be considered further, and scores of less than 15 not recommended for national notifications. Scoring was undertaken by representatives of the Disease Surveillance and Medical Officer teams at CDC.

Table 2: CDNA endorsed criteria for assessment of national notification

Criterion	Minimum score	Maximum score
1. Necessity for public health response	0	4
2. Utility and significance of notification for prevention programs	0	4
3. Vaccine preventability	0	4
4. Importance for Indigenous health	0	4
5. Emerging or re-emerging disease	0	4
6. Communicability and potential for outbreaks	0	4
7. Severity and socioeconomic impacts	1	4
8. Preventability	0	4
9. Level of public concern and/or political interest	1	4
10. A case is definable	0	4
11. Data completeness is likely to be acceptable	1	4
12. Alternative surveillance mechanisms	0	4

Definitions

We reviewed case definitions for CPE currently in use in other Australian jurisdictions. Consideration was made for the level of granularity required to achieve the project's objectives, availability and timeliness of laboratory information, and known transmission dynamics of the condition. We also considered the potential for a single person to have multiple simultaneous cases of CPE and the implications for reinfections and reporting.

Definitions were also developed for CPE contacts and outbreaks following a review of existing definitions in other Australian jurisdictions and a review of CPE transmission literature.

Flow of information through the system

We reviewed the existing structures for information flows for notifiable conditions in the ACT as a foundation for a CPE surveillance system. Stakeholders were also consulted to determine data specifications and information required to achieve the project objectives.

Resource requirements

We reviewed the resources, infrastructure, and personnel required to support the surveillance system. Consideration was given to these requirements internally at CDC, and the additional requirements that may be placed on external stakeholders.

As one of 71 notifiable conditions in the ACT, the surveillance system for CPE will need to function within the existing resourcing, personnel, and funding arrangements for the CDC.

Role of setting and place of testing

The majority of CPE cases in Australia to date have occurred in healthcare facilities. Most surveillance systems in Australia, therefore, have focussed on the management of cases and contacts in these settings, and the flow of information from hospitals to public health units. However, CPE outbreaks have been reported in RACFs, and cases have been identified through

primary care settings. All three settings have different systems in place for patient data collection and different capabilities to respond.

In recognition of increasing reports of transmission in other settings, we considered the flow of information and resources required based on where the case was at the time of testing.

Evaluation

An evaluation of this system was not conducted. The determination to make CPE a notifiable condition was still in progress at the time of submission and therefore no cases had been reported to ACT Health. An evaluation plan has been prepared to guide future review of the system, including consideration of its aims and objectives, desired attributes, and key indicators for performance.

Ethical considerations

This project was conducted under the *ACT Public Health Act 1997*, with particular consideration for the principles of notifiable conditions under Section 99, and Ministerial determination under Section 100. Protocol 2017/909 approved by the Australian National University Human Research Ethics Committee provides a waiver of consent for surveillance projects conducted by Master of Philosophy (Applied Epidemiology) students.

Results

Scoping and design

Lessons from other jurisdictions

We conducted interviews with disease surveillance and IPC teams responsible for the surveillance of CPE in New South Wales, Victoria, South Australia, Western Australia, and Tasmania. All five jurisdictions thought the addition of CPE to their local list of notifiable conditions was worthwhile and supported our efforts in the ACT.

All jurisdictions reported using their existing notifiable disease management system as a foundation for CPE surveillance, with additional processes to collect enhanced surveillance information from clinicians and infection control practitioners in healthcare facilities. Interviewees emphasised the importance of timely, accurate enhanced surveillance information to identify the source of acquisition for cases and detect local transmission. They recommended the use of simple data collection tools and collecting only the information required for public health action to improve the timeliness and acceptability of the system by healthcare facility staff.

Needs of ACT stakeholders

Infection prevention and control units in ACT hospitals were identified as the primary external stakeholder for the surveillance of CPE as most cases are expected to be detected within healthcare facilities. These teams would also be the primary data collectors and implementers of clinical and public health actions.

Six meetings with ACT IPC Network were conducted with a mean of five attendees and four people who were not able to attend provided feedback via emails. Responses indicated in-principle support for the addition of CPE to the ACT's list of notifiable conditions from IPC units in ACT hospitals. The level of information currently collected about patients with CPE varied between healthcare facilities, and the introduction of a standard instrument for data collection was supported. The ACT IPC Network stressed the importance of information flowing back to healthcare facilities to inform the immediate response to cases and longer term protocols for IPC and antimicrobial stewardship.

The design of the surveillance system and protocol were also presented at The Canberra Hospital's Infection Prevention & Control Clinical Response Committee in October 2022. The Committee included representatives from hospital IPC practitioners, infectious disease physicians, and ACT Pathology. Overall, the surveillance system was supported, noting the requirements for follow up and contact tracing were consistent with national guidelines[1] and the benefit of two-way information flow built into the system.

Governance, roles and responsibilities

The Communicable Control Branch at ACT Health would have oversight and responsibility for the CPE surveillance system. This is consistent with other notifiable conditions in the ACT. The responsibilities of internal and external stakeholders are intended to integrate within their existing remit and practice (Table 3).

Table 3: Roles and responsibilities of stakeholder in the CPE surveillance system

Stakeholders	Roles	Responsibilities
Communicable Disease Control (CDC) Branch	Surveillance and response to notifiable conditions in the ACT	Receipt of notification Follow up of CPE cases and contacts Management of data systems Analysis, interpretation, and reporting of data IPC advice to RACFs
Quality and Safety Unit	Oversight of policy for clinical care, safety and quality	Collaboration and information sharing between healthcare facilities in Networking Forum
ACT Pathology	Testing of suspected CPE isolates	Confirmatory testing of isolates Notification of cases
Other public health laboratories servicing the ACT, (in the ACT and interstate)	Testing of suspected CPE isolates	Notification of cases
Healthcare Infection Prevention and Control teams	Infection prevention and control response to CPE cases within a healthcare facility	Follow up of cases and contacts among patients Enhanced surveillance data collection
Clinicians in healthcare facilities	Clinical management of CPE cases	Provide clinical care for hospitalised CPE cases Notification and enhanced surveillance data collection
Residential aged care facilities (RACFs)	Infection prevention and control response and clinical management of CPE cases within a residential aged care facility	Case and contact management among residents
General practitioners and other primary health care clinicians	Clinical management of CPE cases	Provide clinical care for CPE cases in community Notification and enhanced surveillance data collection
Office of the Chief Veterinary Officer	Oversight of policy for CPE surveillance and response in animals	Potential future surveillance or requirements for notification of CPE in animals

Legal authority for surveillance

The condition CPE scored 24 out of 48 against the CDNA criteria, indicating that it should be considered further for notification (Appendix A). In addition to the CDNA criteria, the potential impact on animal and environmental health was also considered. On balance, we recommended that CPE be made a notifiable condition in the ACT.

Section 100 of the *ACT Public Health Act 1997* allows for the Chief Health Officer to make a condition notifiable if it is deemed necessary to protect public health. Listing CPE as a notifiable

condition was considered the most appropriate mechanism to conduct surveillance for CPE. The existing alternate surveillance system, CARAlert, was not considered detailed enough to enable public health action, and voluntary reporting potentially limits case ascertainment. An active surveillance system such as screening in healthcare facilities falls outside the remit of the Communicable Disease Control (CDC) branch and each healthcare facility, including private hospitals, set their own CPE screening protocols under national guidelines.[1]

Listing CPE as a notifiable condition would make it mandatory for laboratories and clinicians to report cases to ACT Health and requires public health follow up and action.

We prepared a Ministerial brief outlining the case for listing CPE as a notifiable condition, including drafting a revised *Public Health (Reporting of Notifiable Conditions) Code of Practice 2022* disallowable instrument.

Definitions

Case definitions

All jurisdictions use suspected and confirmed laboratory-based definitions to identify cases.

However, case definitions for CPE vary between jurisdictions, using either the carbapenemase gene or the species of bacteria to define a single case. In all jurisdictions, case definitions allowed for one person to have several cases of CPE, depending on the types of genes or bacteria present. Interviewees advised us to choose a case definition that would best inform public health action and identify potential clusters of cases.

In the ACT, we recommend a case definition based on the gene/s detected. The use of a gene-based definition enables the use of WGS information to identify related cases and detect local transmission. The ability of *Enterobacterales* to transfer genes between species and genera limits the potential utility of a species-based definition for the objectives of this surveillance system.

We also recommend using both a suspected and confirmed case definition, and require that suspected and confirmed cases should be notified to ACT Health. This approach enables ACT Health to advise on contact precautions and infection prevention and control measures in residential facilities while the transport of isolates from suspected cases to reference laboratories and confirmatory testing is underway. This approach also follows the practices of other Australian jurisdictions.

Box 1: Case definitions for carbapenemase-producing *Enterobacterales* (CPE) in the ACT

Confirmed case
Detection of a carbapenemase gene[1, 2] in an isolate of a species of *Enterobacterales*.

1 Irrespective of phenotypic susceptibility
2 Each CPE gene in an organism and/or person represents a new confirmed case (e.g., the presence of NDM-4 and NDM-1 represents two separate cases)

Suspect case
Isolation of a species of *Enterobacterales* with reduced susceptibility to a carbapenem.

A reduced susceptibility to a carbapenem is defined by any of the following:

- Disc diffusion (EUCAST/CLSI) – meropenem 10ug <28mm zone diameter, or
- Disc diffusion (CDS) – meropenem 5ug <6mm annular radius, or
- MIC – meropenem >0.25mg/L

In addition to defining a case, we also developed definitions for outbreaks and contacts to limit further transmission of CPE.

Outbreak definition

As CPE remains a relatively rare condition across Australia, two genomically and epidemiologically linked cases are considered an outbreak in jurisdictions where CPE is notifiable. We developed a similar definition in the ACT as, in light of what we currently understand to be a low incidence environment, any local transmission would be considered to be an outbreak.

Box 2: Outbreak definition for carbapenemase-producing *Enterobacterales* (CPE) in the ACT

Two or more confirmed cases of genetically related CPE identified in two or more people and a plausible epidemiological connection between the two people, either through geographic proximity or shared staff, equipment or other exposures.

OR

Where acquisition from an environmental source is hypothesised, clustering in time and place without a direct person-to-person epidemiological link.

Contact definition

The definition of a contact of a CPE case in other jurisdictions is generally limited to hospitalised patients who share a room or bathroom facilities.

In the ACT, we chose to expand our contact definition to include household contacts based on the emerging importance of household transmission in other countries, and to include follow up

of contacts who have been discharged from hospital. This expansion requires greater follow up workload but also provides an opportunity to further detect cases and limit spread in what is believed to be a low incidence environment.

Box 3: Contact definition for carbapenemase-producing *Enterobacterales* (CPE) in the ACT

A person who:

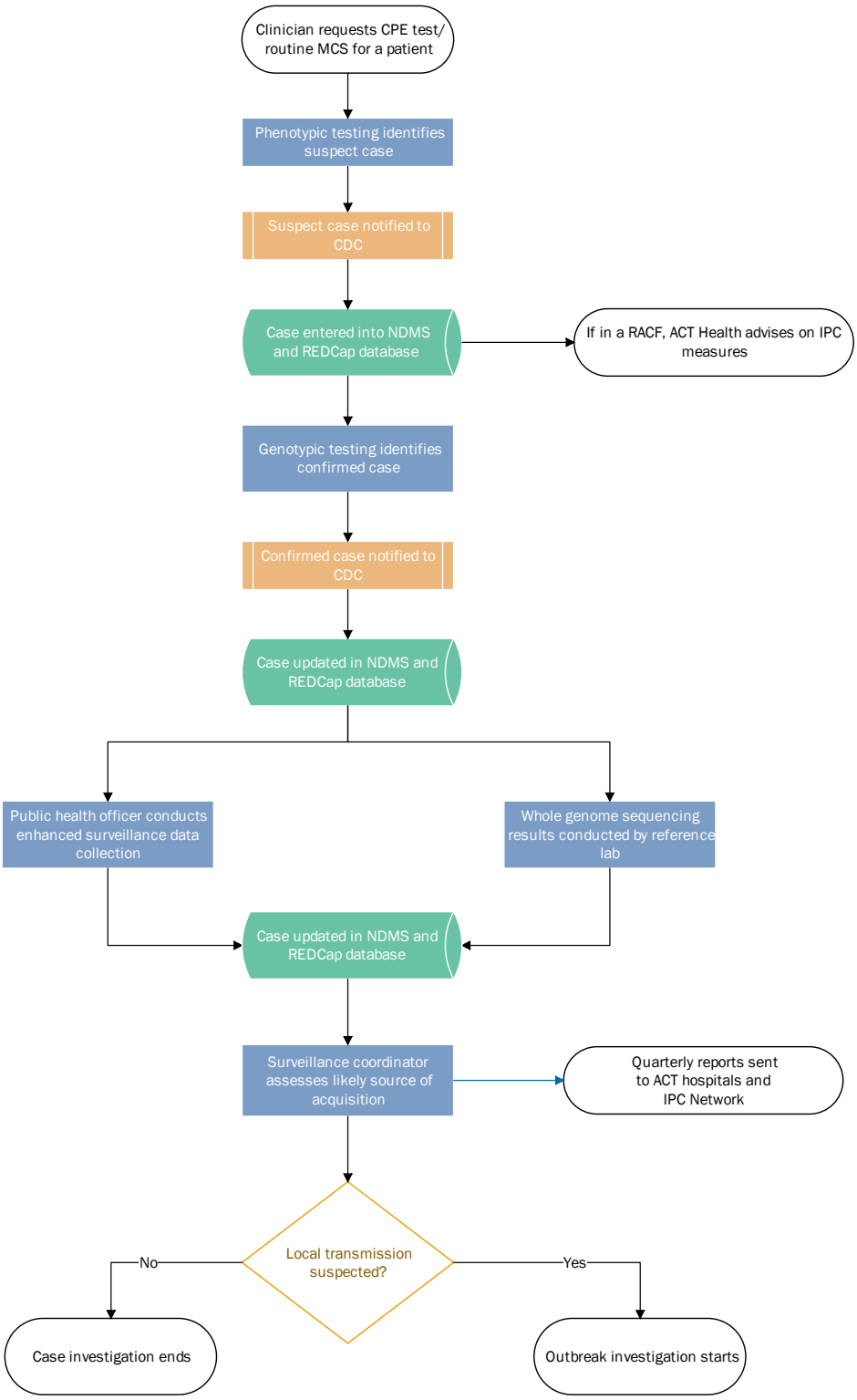
- shared a room for 24 hours or more with a confirmed CPE case at a healthcare facility or residential aged care facility
  OR
- shared a bathroom for 24 hours or more with a confirmed CPE case at a healthcare facility or residential aged care facility
  OR
- lived in the same household as a confirmed CPE case within 12 months of the case's date of acquisition.

Flow of information through the system

Several stakeholders need to be engaged in the CPE surveillance given the variety and complexity of information required to identify local transmission of CPE.

A high-level overview of the CPE surveillance system is shown in Figure 2. The flow of information follows a similar path to other notifiable conditions in the ACT, with notification received from laboratories and clinicians, entered into the ACT notifiable disease management system (NDMS) and public health follow up conducted by the CDC branch. Whole genome sequencing information is sent from laboratories to CDC at a later date and taken with enhanced surveillance data to determine the likely source of acquisition and identify potential local transmission.

Figure 2: High-level overview of information flow in the CPE surveillance system



The current NDMS database has limited fields and no capacity to record enhanced surveillance data in a systematic format. Further, the CDC branch was transitioning to a new NDMS at the

same time as this surveillance system was being designed. Therefore, a REDCap project was built to ensure the variables for enhanced surveillance and laboratory information can be recorded, electronic notifications and reminders can be sent, and to enable rapid changes to be made as new variables may need to be included.

The REDCap project contains three instruments:

- an initial form completed by the Surveillance Officer containing demographic details of the person and laboratory results,
- a case investigation form to be completed by a Public Health Officer at ACT Health and Infection Prevention and Control Practitioner at an ACT hospital, recording the clinical details, exposure history, and details of contacts, and
- an epidemiological assessment completed by a CDC epidemiologist to record the likely place of acquisition, exposure setting, and link to an outbreak, if applicable.

The case investigation form includes standard variables for all CPE cases, regardless of the location of testing. However, the terminology to refer to the person with CPE automatically varies depending on the location of the case (patient for cases identified in a hospital or primary care, resident for cases identified in RACFs).

We selected variables for enhanced surveillance with consideration of the known risk factors of CPE and the experiences of other Australian jurisdictions (Appendix B). The case investigation form prompts for information to be collected on:

- reason for testing (clinical suspicion, screening, contact tracing)
- classification (colonisation/infection)
- death status at the time of follow up and date of death, if applicable
- overseas travel
- previous hospitalisations in Australia and/or overseas
- antibiotic therapy history
- residency at a residential aged care facility
- medical procedures associated with CPE exposure, including ICU admission, dialysis, and endoscopy
- in-dwelling device history
- known contact with a CPE case

The exposure history, clinical status, and laboratory information are standard for all cases. However, the processes to collect that information have been adapted for different clinical settings based on the location of the case at the time of testing.

A fact sheet will be provided to all CPE cases or their Power of Attorney/Guardian with information about the condition, what it may mean for their health care in the future, advice on how to limit spread to others, and where to find further information (Appendix C).

Flow of information for CPE cases in ACT hospitals

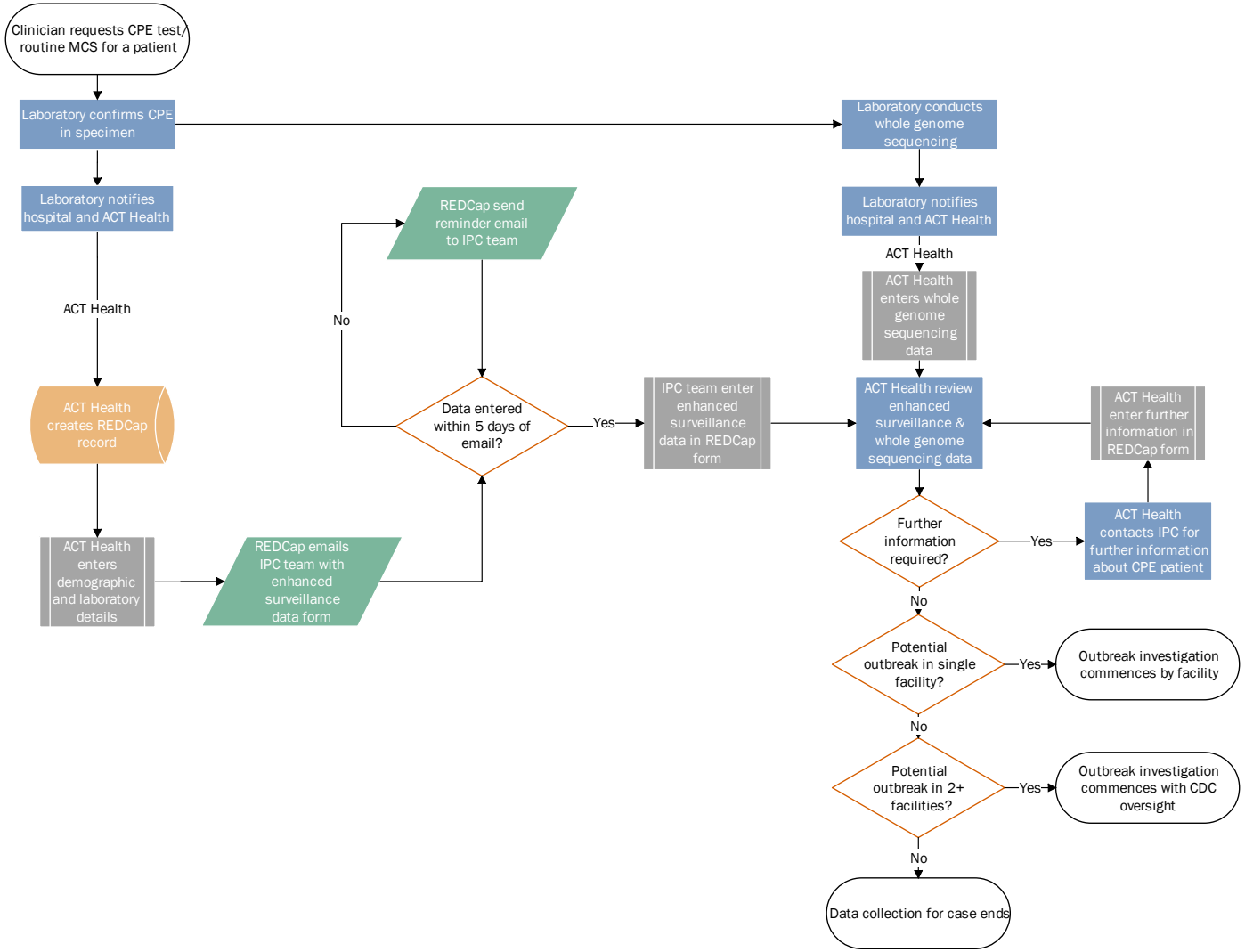
We developed an electronic system through REDCap in consultation with IPC teams in ACT hospitals (Figure 3). In the event a CPE case in an ACT hospital is notified, the hospital IPC team are responsible for enhanced surveillance data collection with review and potential follow up and clarification by the Surveillance Coordinator at the CDC branch.

An email will be automatically generated with a link to the case investigation form for that notification and sent to the hospital's IPC team. This allows for the team to collect enhanced surveillance information from clinical records and interview with the case and/or their Power of Attorney/Guardian within their day-to-day tasks, rather than rely on their availability for a phone interview. Alerts have been built into REDCap to prompt the IPC team to complete the case investigation form five and 10 days after the initial email is sent. After ten days, a public health officer will call the IPC team and the case to conduct a phone interview.

Quarterly reports will be prepared summarising each healthcare facility's own cases to provide data back to ACT hospitals, and an aggregated summary excluding facility names will be reported at the IPC Network to share information and lessons across IPC teams.

It is anticipated that the majority of CPE cases will flow through this process.

Figure 3: Notification and follow up process for CPE cases in ACT hospitals

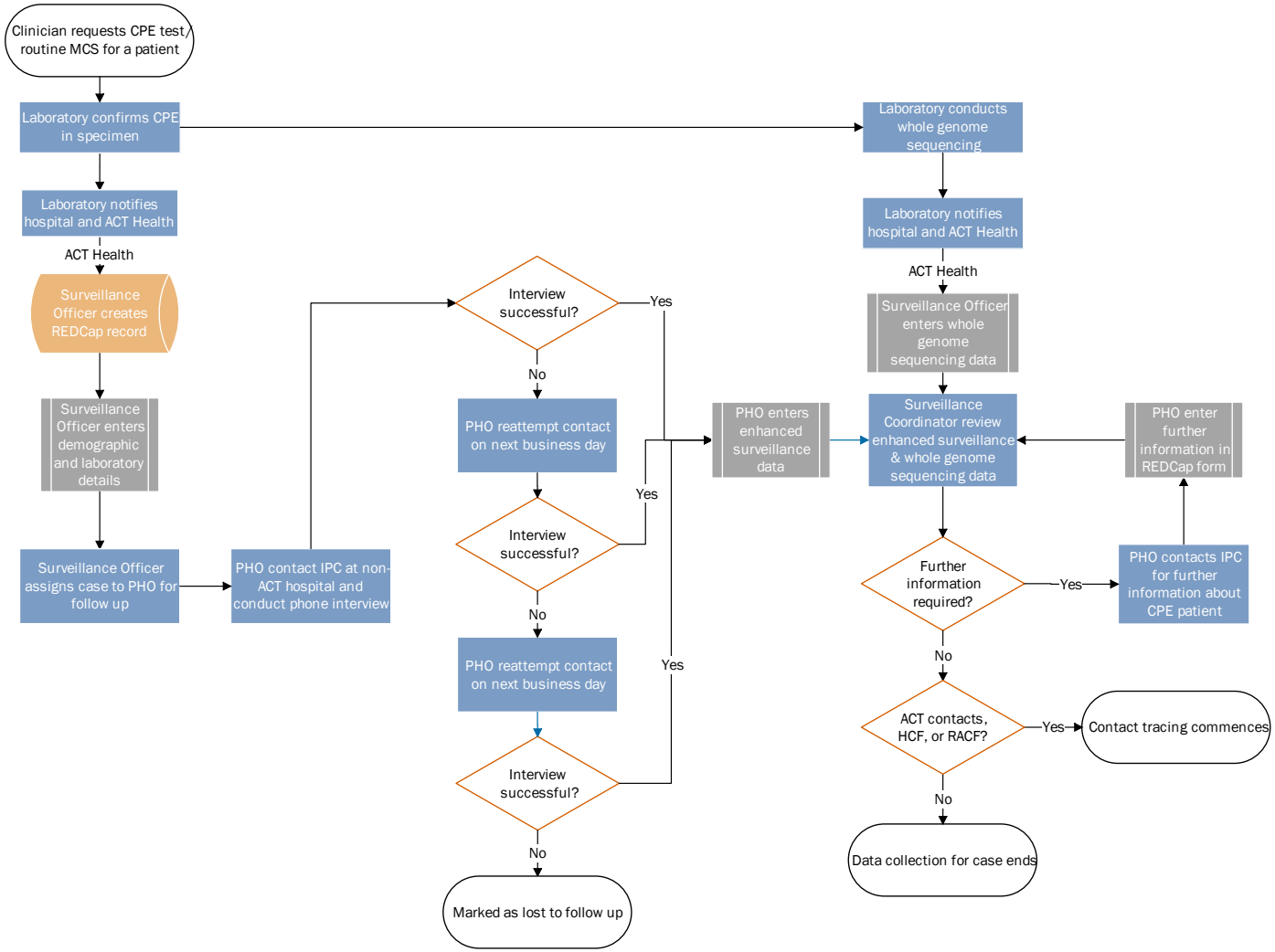


Flow of information for CPE cases in an interstate hospital

The reporting of notifiable conditions in Australia is based on the jurisdiction of residence and based upon what is known from CARAlert data, there will certainly be ACT residents diagnosed with CPE in hospitals in other states or territories. In this event, follow up and enhanced surveillance data collection will be the responsibility of the public health officers at the CDC Branch (Figure 4).

An electronic process is not recommended for cases in interstate hospitals as ACT Health does not have existing connections with these healthcare facilities or an appropriate email address for all hospitals. We chose to introduce a mechanism to integrate a standard practice for cases to be lost to follow up after three unsuccessful attempts to contact the interstate hospital, the case, and/or their Power of Attorney/Guardian.

Figure 4: Notification and follow up process for CPE cases in interstate hospitals

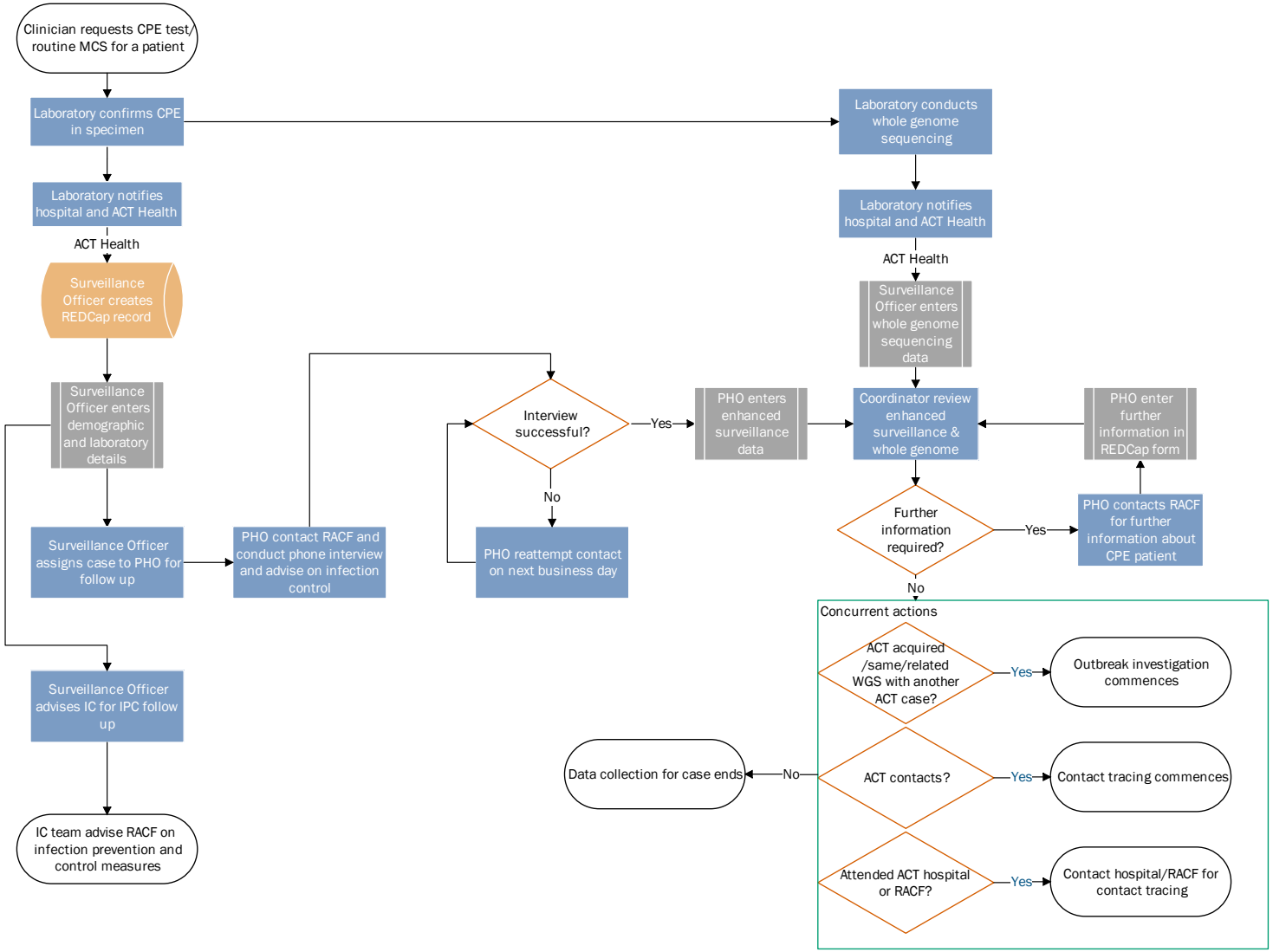


Flow of information for CPE cases in a residential aged care facility (RACF)

In the event that a CPE case is notified in a resident in a RACF, follow up and enhanced surveillance data collection will be the responsibility of the public health officers at the CDC Branch (Figure 5).

In addition to this follow up, the Infection Control team at the CDC Branch will also contact the RACF to provide advice on infection prevention measures to limit transmission to other residents and staff. The Infection Control team currently provides similar advice for outbreaks of respiratory illness and gastroenteritis in RACFs, and it is intended to utilise these existing relationships to support public health action.

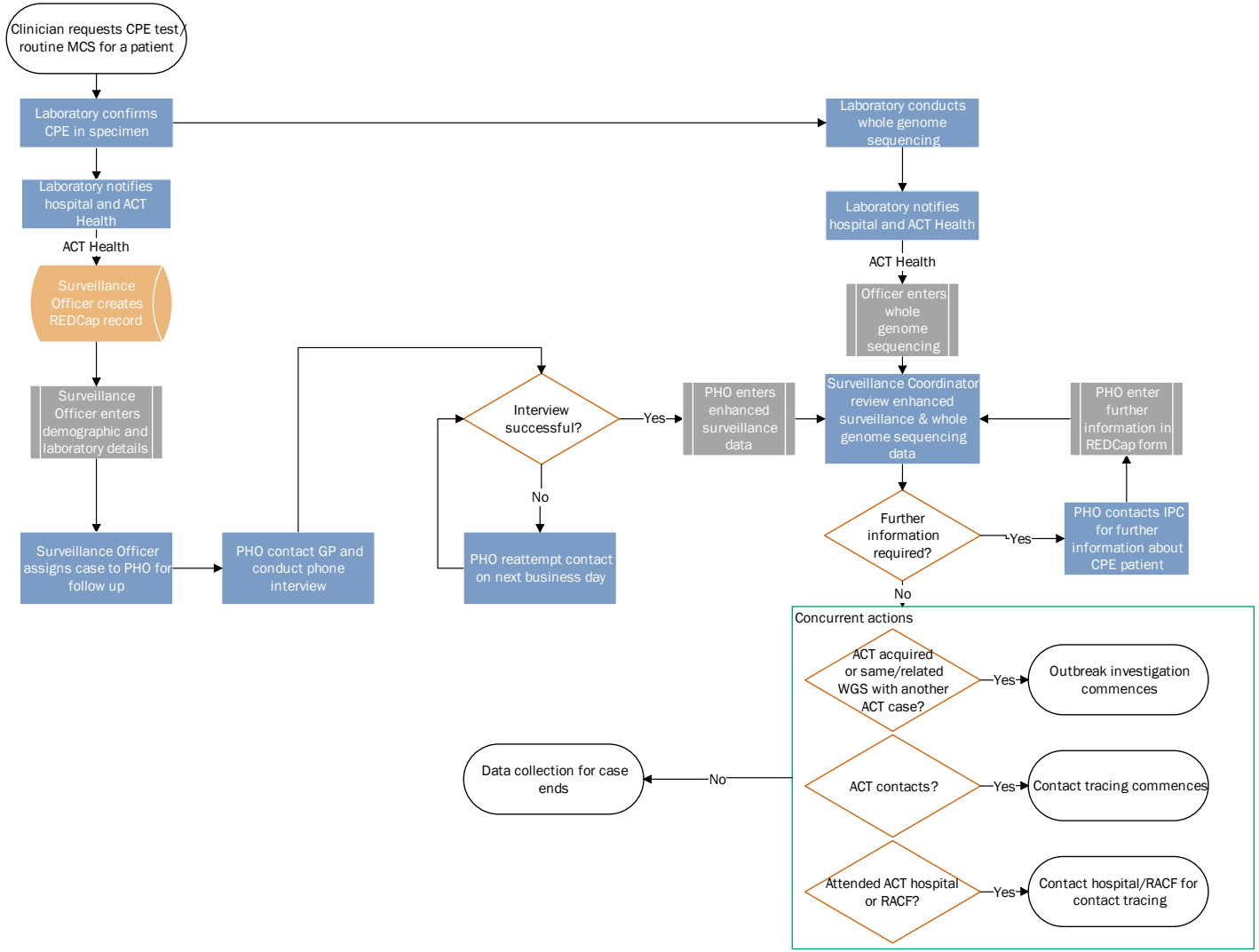
Figure 5: Notification and follow up process for CPE cases in a residential aged care facility (RACF)



Flow of information for CPE cases in a primary health care or community setting

The process for following up a CPE case in a primary health care or community setting will follow a similar process to RACFs (Figure 6). Public health officers at CDC Branch will conduct a phone interview with the clinician, case, and/or their Power of Attorney/Guardian to collect enhanced surveillance information.

Figure 6: Notification and follow up process for CPE cases in a primary health care or community setting



Follow up for multiple cases in a single individual

The case definition for CPE allows for a single individual to have acquired multiple cases of CPE if there are multiple carbapenemase genes present. In the ACT's NDMS, each case requires their own disease incident to be created. It is recognised, however, that the exposure history and clinical details may be the same across cases in a single individual.

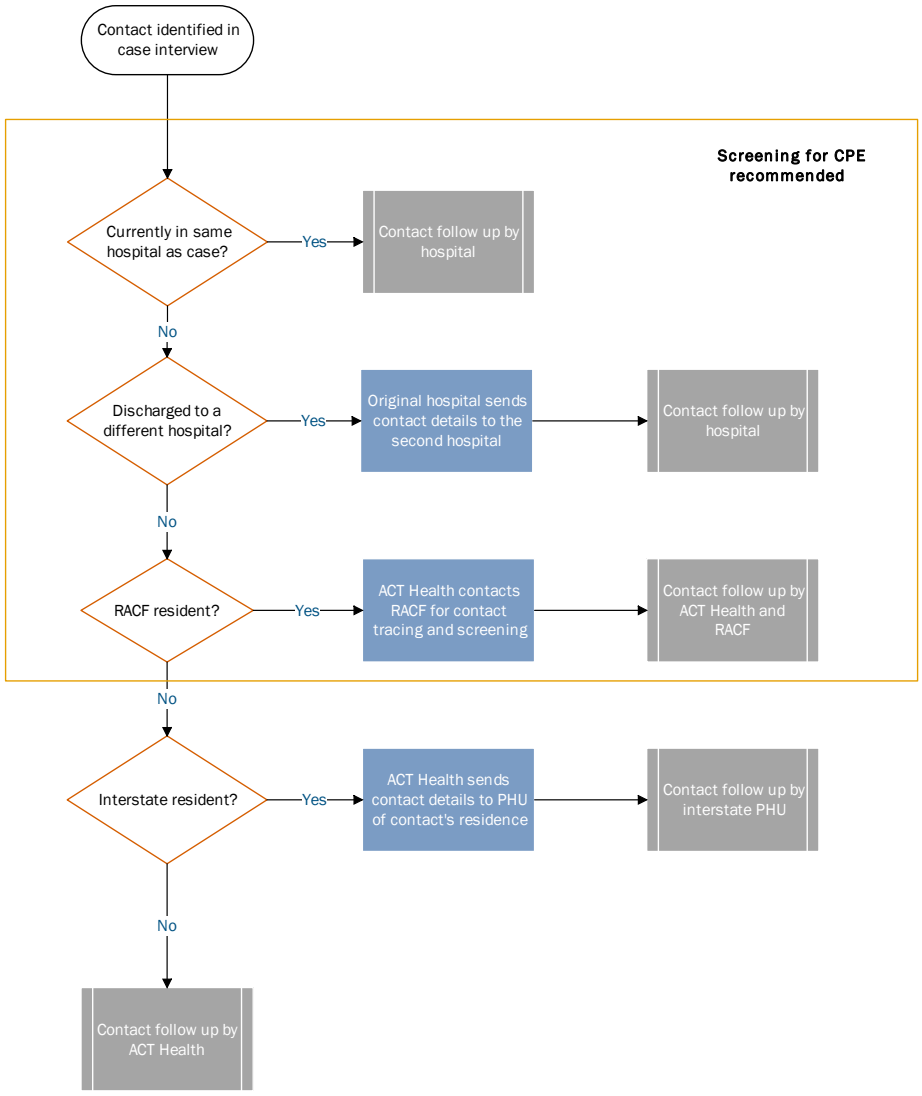
We decided to limit enhanced surveillance data collection to one instance per individual within 14 days of the first notification, regardless of the number of genes detected. If new carbapenemase genes are detected after 14 days, the follow up process for collecting updated exposure history and clinical details will be triggered.

Contact management

A key component of the surveillance system is the identification of and communication with contacts of a CPE case to limit further spread. All contacts of CPE cases will be contacted, informed of their status, and be provided with a short fact sheet providing information about the condition, what actions they may need to take, and where to find further information (Appendix C).

The responsibilities for the follow up of CPE contacts will be dependent on the location of the contact when they are identified (Figure 7). Screening for CPE is recommended for CPE contacts in a hospital or a RACF. This is consistent with national guidelines[1] for the clinical management of CPE contacts and enables the timely detection of any local transmission in the ACT.

Figure 7: Responsibility for the follow up of CPE contacts in the ACT



We do not recommend screening for CPE contacts outside of a hospital and RACF settings as current evidence suggests that transmission in community settings is limited.

Outbreak investigation processes

A summary of the proposed processes and governance for outbreak investigations of CPE is shown in Table 4. A healthcare facility remains responsible for the investigation if only their facility is affected. In the event that an outbreak involves more than one healthcare facility or a RACF, CDC Branch takes oversight of the investigation.

It is proposed that the oversight and roles in outbreak investigation are established on an outbreak-by-outbreak basis in the event of local transmission is suspected in other residential facilities in the ACT (such as a correctional centre, barracks, or group home), or where no epidemiological link to an exposure setting has been identified.

Table 4: Governance and role of ACT Health in outbreak investigation of CPE by location/s of the outbreak

Location/s of outbreak	Organisation leading investigation	Role/s of ACT Health	Other organisations involvement
Single health care facility	The health care facility	Data collection, analysis and reporting	N/A
Multiple healthcare facilities	ACT Health	Oversee outbreak investigation Facilitate communication between affected facilities Data collection, analysis and reporting	Each health care facility affected
Single residential facility	ACT Health	Oversee outbreak investigation Advise of infection control measures Data collection, analysis and reporting	Residential aged care facility
One or more health care facility AND one or more residential aged care facility	ACT Health	Oversee outbreak investigation Facilitate communication between affected facilities Advise of infection control measures in residential aged care facility/ies Data collection, analysis and reporting	Each health care facility affected Each residential aged care facility affected
Other residential facility	Determined on an outbreak-by-outbreak basis	Facilitate communication between affected facility/ies Advise of infection control measures in residential facility Data collection, analysis and reporting	Determined on an outbreak-by-outbreak basis
No exposure setting identified	ACT Health	Oversee outbreak investigation Determine source of acquisition Data collection, analysis and reporting	Determined on an outbreak-by-outbreak basis

Discussion

I used the United States Center for Disease Control and Prevention guideline[85] for developing a discussion around usefulness of the proposed surveillance system for CPE. In this discussion, I have provided information on how the attributes of simplicity, data quality, acceptability, sensitivity, representativeness, flexibility, timeliness, and stability were considered in the development of the system and how the surveillance system is anticipated to perform.

Attributes of the CPE surveillance system

Simplicity

> *'refers to both its structure and ease of operation. Surveillance systems should be as simple as possible while still meeting their objectives'.*[85]

CPE is a complex condition, and the surveillance of the condition involves multiple stakeholders working together to limit transmission in the ACT. The surveillance system has been designed to utilise familiar processes as much as possible to reduce complexity and integrate into existing ACT health processes.

The case definition is easy to apply, relying only on laboratory definitive evidence using established phenotypic and genotypic susceptibility. However, CPE is a complex condition that requires the integration of laboratory testing, WGS, and epidemiological investigation to establish the likely source of acquisition. Multiple internal and external stakeholders are needed to input enhanced surveillance information depending on the location of the case at diagnosis. This is not a unique issue and is experienced across the surveillance of notifiable conditions in the ACT. The CPE surveillance system has been designed to minimise some of the complexity through simple data collection instruments and protocols.

The use of a single REDCap instrument is intended to keep data in a single location while also remaining responsive to different contexts where CPE cases are detected. Variables for enhanced surveillance were kept to those needed to achieve the objectives of the system and undertake public health action. The standardised methods for data collection across ACT healthcare facilities, primary care, and other community settings provide the opportunity for simpler collation and analysis of trends and patterns in the ACT

There is a potentially complex administrative burden placed on ACT Health staff to follow up cases and process multiple sources of information. While these processes are part of the day-to-day work for notifiable conditions, the complexity of the condition may place a further burden on public health officers. Some of these complexities have been addressed through the development of a protocol for CPE notifications (Appendix B), however, the manual entry of information and duplicate entry of exposure history for individuals with multiple CPE cases remain limitations of the system. As cases are notified to ACT Health over time, the system should be reviewed and adjusted to improve information flows and update internal protocols.

Data quality

> *'The completeness and validity of the data recorded in the public health surveillance system.'*[85]

We have focused on increasing the acceptability of the surveillance system to provide the best conditions for high data quality and engagement. As a notifiable condition, reporting of CPE would be mandatory and the information included in pathology reports provides a strong foundation for understanding the specimens and reasons for testing. Feedback on the draft enhanced surveillance data collection form was positive overall and informed changes to improve the usefulness and ease of data entry.

Enhanced surveillance for CPE relies on data entry from external stakeholders in ACT hospitals. The use of simple language and explanation of key terms aims to minimise misinterpretation and standardise responses across facilities. The separation of 'unknown' and 'information not asked' has been included to assist in a future evaluation to determine the reasons behind incomplete data.

Acceptability

> *'The willingness of persons and organizations to participate in the surveillance system.'*[85]

This surveillance system is anticipated to be well accepted by key stakeholders and decision makers. The public health importance and design of this surveillance system have been communicated to key stakeholders and their feedback has been integrated to improve utility and meet their needs. The dissemination of data back to healthcare facilities and aggregate reporting of findings to the ACT IPC Network is anticipated to demonstrate the use of information collected and increase engagement with the system among healthcare facilities.

However, the acceptability of the CPE surveillance system among general practitioners is not clear. Many general practitioners and other primary care providers will have had no experience diagnosing and managing CPE. The preparation of a communications strategy to engage with clinicians in the ACT if CPE is made notifiable would be a key component to raise awareness and increase the acceptability of the surveillance system among primary care clinicians.

Within ACT Health, it is recognised that the introduction of a new, complex notifiable condition may place an additional burden on surveillance officers and public health officers in the Disease Surveillance Unit. This surveillance system has been designed using existing familiar tools and resources for the follow up of other notifiable conditions to support the workflow for surveillance officers and public health officers.

Sensitivity

Case reporting

> *'at the level of case reporting, sensitivity refers to the proportion of cases of a disease (or other health-related event) detected by the surveillance system.'*[85]

First, at the level of case reporting, sensitivity refers to the proportion of cases of a disease (or other health-related event) detected by the surveillance system.

The system relies on passive surveillance, with the notification of CPE cases relying on clinical or screening tests by clinicians. The detection of CPE cases is therefore dependent on the level of testing for the condition. This is a potential limitation of the surveillance system resulting in under-reporting as the detection of cases is subject to the presentation of a person with CPE to a healthcare facility, the screening and testing protocols for that facility, the clinician thinking to test for CPE, and the test being undertaken. While the testing procedures are outside the control of ACT Health, the availability of diagnostic tests for CPE and the mandatory requirement to report all detected cases as a notifiable condition increases some aspects of case ascertainment.

Changes to screening protocols for CPE at ACT hospitals also represent a potential challenge to the system's sensitivity for case reporting. The introduction of screening procedures or changes to criteria may introduce artefactual increases or decreases to case reporting as case ascertainment shifts. Collecting the reason for testing and regular communications with the IPC Network may assist future evaluations to measure the potential presence and effects of these artefacts.

Detect outbreaks

> *'Second, sensitivity can refer to the ability to detect outbreaks, including the ability to monitor changes in the number of cases over time.'*[85]

We anticipate high sensitivity to detect local outbreaks of CPE in this surveillance system. The combination of epidemiological review of enhanced surveillance information and WGS can provide information about the source of acquisition and potential local transmission, particularly within a healthcare facility or involving an environmental source. Similar approaches in other Australian jurisdictions have resulted in the timely identification and response to CPE outbreaks.[41] It is noted that the detection of outbreaks relies on the sensitivity of case reporting. The identification of local transmission may in turn change testing practices and potentially increase case ascertainment.

Representativeness

> *'Accurately describes the occurrence of a health-related event over time and its distribution in the population by place and person'*[85]

A public health surveillance system that is representative accurately describes the occurrence of a health-related event over time and its distribution in the population by place and person.

It may be difficult to accurately assess the representativeness of this surveillance system in the absence of estimates of the true prevalence and incidence of CPE in Australia. This creates a

potential selection bias towards individuals who are more likely to be hospitalised repeatedly and who have severe illness, compared with those who have asymptomatic colonisation of CPE.

The surveillance system has been designed to include processes for cases identified in hospitals, where the majority of cases in Australia are currently diagnosed. Further, we developed processes for cases identified in RACFs and the community in anticipation of cases identified outside of our currently understood risk factors and will collect appropriate surveillance information for all cases.

The collection of sociodemographic data, such as age and residential aged care residency status, and clinical details, such as hospitalisations, enables the comparison of characteristics with those reported by other Australian jurisdictions and current literature.

Flexibility

> *'can adapt to changing information needs or operating conditions with little additional time, personnel, or allocated funds... In addition, systems that use standard data formats (e.g., in electronic data interchange) can be easily integrated with other systems and thus might be considered flexible'*[85]

The variables for enhanced surveillance data collection have been developed using the findings of current literature and CPE surveillance in other Australian jurisdictions. However, once cases are notified to ACT Health, the information needed to meet the objectives of the surveillance system may change. The surveillance system has been designed using a REDCap database, which enables changes to variables to be made quickly and within the resources of the Disease Surveillance Unit. This flexibility in enhanced surveillance data collection is a key attribute for this system to rapidly adapt ACT Health's public health response and to accommodate specifications from the Commonwealth Department of Health if CPE becomes nationally notifiable.

Timeliness

> *'the speed between steps in a public health surveillance system'*[85]

For this surveillance system, timeliness is focused on the speed of reporting to ACT Health, collection of enhanced surveillance data, and speed of follow up of CPE contacts. As CPE can occur without symptoms, there is limited utility and practicality in assessing the timeliness of detection at occurrence. However, the timely collection and reporting of data and follow up of contacts is a key measure of the success of this surveillance system and limiting local transmission.

Delays in these processes are a potential threat to the surveillance system. Listing CPE as a Group B notifiable condition requires reporting within five working days, minimising delays in initial notification. The reporting of suspected cases enables the rapid implementation of

infection prevention and control measures in healthcare facilities and RACFs while confirmatory testing and enhanced surveillance data collection are underway.

We have addressed potential delays in data collection through the establishment of automatic reminders for ACT hospitals for enhanced surveillance data collection and protocols for the follow up by public health officers. The delineation of responsibilities for contact tracing adds some complexity to the system but enables ACT Health and healthcare facilities to simultaneously follow up CPE contacts and provide public health advice. Future reviews of this system should review the time between receipt of notification and completion of enhanced surveillance data collection to determine timeliness and identify potential improvements to information flows.

Stability

> *'refers to the reliability (i.e., the ability to collect, manage, and provide data properly without failure) and availability (the ability to be operational when it is needed) of the public health surveillance system.'*[85]

The follow up, data collection and reporting for this surveillance system has been designed with consideration of the existing resources, personnel and funding of the Disease Surveillance Unit. The CPE surveillance system uses existing information and communications technology (ICT) tools and infrastructure for notifiable conditions in the ACT. Therefore, the stability of the CPE surveillance system is not anticipated to be any more or less than for the existing surveillance of other notifiable conditions in the ACT.

Level of usefulness and evaluation

It is anticipated that this surveillance system will be useful as it is designed to provide public health information not currently available in the ACT. Current oversight of CPE is limited and the voluntary, deidentified information available through CARAlert does not allow for the detection and response to local transmission. The surveillance system has been designed to contribute to the control and prevention of CPE in the ACT by collating sufficient laboratory and epidemiological data to inform public health action.

The usefulness of the CPE surveillance system is supported by:

- mechanisms to promptly detect disease using a standard laboratory-based definition,
- estimating morbidity of illness through the categorisation of colonisation/isolation status,
- detecting trends and patterns in the occurrence of CPE
- establishing definitions for outbreaks of CPE and collating laboratory and epidemiological data to detect local transmission, and
- collating enhanced surveillance data to inform public health response and potential research or evaluation of infection control and outbreak response

However, the level of usefulness cannot truly be determined until the CPE surveillance system has been implemented for some time. We prepared an evaluation plan to inform a future review of the surveillance system against its objectives. We developed key indicators to measure the timeliness, acceptability and data quality of the surveillance system:

- time taken from notification received date to completion of case investigation form
- completeness of case investigation variables (including the proportion of 'unknown' and 'information not asked')
- time taken from identification of contacts to completion of follow up interview

Conclusion

CPE poses a significant threat to public health. Public health authorities need to have oversight of CPE to monitor trends and identify local transmission to prevent further cases. This surveillance system intends to collate epidemiological and laboratory data within existing resources to follow up cases and contacts identified in healthcare facilities, RACFs, and the general community.

Recommendations

At the time of submission, the decision to make CPE a notifiable condition was under review by the ACT Chief Health Officer. I recommend adding CPE to the ACT's notifiable condition and the adoption of the surveillance system in this chapter. I also recommend a formal evaluation of the surveillance system three years after adoption to ensure the system is efficiently and effectively detecting CPE cases, identifying local transmission, and limiting transmission in the ACT.

Reference list

1. Australian Commission on Safety and Quality in Health Care. *Recommendations for the control of carbapenemase-producing Enterobacterales (CPE). A guide for acute care health service organisations*. Sydney: Australian Commission on Safety and Quality in Health Care; 2021.
2. Bradford PA, Bratu S, Urban C. Emergence of carbapenem-resistant Klebsiella species possessing the class A carbapenem-hydrolyzing KPC-2 and inhibitor-resistant TEM-30 β-lactamases in New York City. *Clin Infect Dis*. 2004;39(1):55-60.
3. Yigit H, Queenan AM, Anderson GJ. Novel carbapenem-hydrolyzing β-lactamase, KPC-1, from a carbapenem-resistant strain of Klebsiella pneumoniae. *Antimicrob Agents Chemother*. 2001;45(4):1151-61.
4. van Duin D, Doi Y. The global epidemiology of carbapenemase-producing Enterobacteriaceae. *Virulence*. 2017;8(4):460-9.
5. Redondo-Salvo S, Fernández-López R, Ruiz R, Vielva L, de Toro M, Rocha EPC, et al. Pathways for horizontal gene transfer in bacteria revealed by a global map of their plasmids. *Nature Communications*. 2020;11(1):3602.
6. Yamagishi T, Matsui M, Sekizuka T, Ito H, Fukusumi M, Uehira T, et al. A prolonged multispecies outbreak of IMP-6 carbapenemase-producing Enterobacterales due to horizontal transmission of the IncN plasmid. *Scientific Reports*. 2020;10(1):4139.
7. Kazmierczak KM, de Jonge BLM, Stone GG, Sahm DF. Longitudinal analysis of ESBL and carbapenemase carriage among Enterobacterales and Pseudomonas aeruginosa isolates collected in Europe as part of the International Network for Optimal Resistance Monitoring (INFORM) global surveillance programme, 2013–17. *Journal of Antimicrobial Chemotherapy*. 2020;75(5):1165-73.
8. Hussein K, Geffen Y, Eluk O, Warman S, Aboalheja W, Alon T, et al. The Changing Epidemiology of Carbapenemase-Producing Enterobacterales. *Rambam Maimonides Med J*. 2022;13(1).
9. Australian Commission on Safety and Quality in Health Care. *CARAlert annual report: 2021*. Sydney: Australian Commission on Safety and Quality in Health Care; 2022.
10. Sidjabat HE, Townell N, Nimmo GR, George NM, Robson J, Vohra R, et al. Dominance of IMP-4-producing enterobacter cloacae among carbapenemase-producing Enterobacteriaceae in Australia. *Antimicrob Agents Chemother*. 2015;59(7):4059-66.
11. Bar-Yoseph H, Hussein K, Braun E, Paul M. Natural history and decolonization strategies for ESBL/carbapenem-resistant Enterobacteriaceae carriage: systematic review and meta-analysis. *J Antimicrob Chemother*. 2016;71(10):2729-39.
12. Lübbert C, Lippmann N, Busch T, Kaisers UX, Ducomble T, Eckmanns T, et al. Long-term carriage of Klebsiella pneumoniae carbapenemase–2-producing K pneumoniae after a large single-center outbreak in Germany. *American Journal of Infection Control*. 2014;42(4):376-80.
13. Mo Y, Hernandez-Koutoucheva A, Musicha P, Bertrand D, Lye D, Ng OT, et al. Duration of Carbapenemase-Producing Enterobacteriaceae Carriage in Hospital Patients. *Emerg Infect Dis*. 2020;26(9):2182-5.
14. Zimmerman FS, Assous MV, Bdolah-Abram T, Lachish T, Yinnon AM, Wiener-Well Y. Duration of carriage of carbapenem-resistant Enterobacteriaceae following hospital discharge. *Am J Infect Control*. 2013;41(3):190-4.
15. Nicolas-Chanoine M-H, Vigan M, Laouenan C, Robert J. Risk factors for carbapenem-resistant Enterobacteriaceae infections: a French case-control-control study. *European Journal of Clinical Microbiology & Infectious Diseases*. 2019;38(2):383-93.
16. Tumbarello M, Viale P, Viscoli C, Trecarichi EM, Tumietto F, Marchese A, et al. Predictors of Mortality in Bloodstream Infections Caused by Klebsiella pneumoniae Carbapenemase–Producing K. pneumoniae: Importance of Combination Therapy. *Clinical Infectious Diseases*. 2012;55(7):943-50.
17. Hovan MR, Narayanan N, Cedarbaum V, Bhowmick T, Kirn TJ. Comparing mortality in patients with carbapenemase-producing carbapenem resistant Enterobacterales and non-carbapenemase-producing carbapenem resistant Enterobacterales bacteremia. *Diagn Microbiol Infect Dis*. 2021;101(4):115505.
18. Souli M, Galani I, Antoniadou A, Papadomichelakis E, Poulakou G, Panagea T, et al. An outbreak of infection due to beta-Lactamase Klebsiella pneumoniae Carbapenemase 2-producing K. pneumoniae in a Greek University Hospital: molecular characterization, epidemiology, and outcomes. *Clin Infect Dis*. 2010;50(3):364-73.
19. Dautzenberg MJ, Wekesa AN, Gniadkowski M, Antoniadou A, Giamarellou H, Petrikkos GL, et al. The association between colonization with carbapenemase-producing enterobacteriaceae and overall ICU mortality: an observational cohort study. *Crit Care Med*. 2015;43(6):1170-7.

20. Tamma PD, Goodman KE, Harris AD, Tekle T, Roberts A, Taiwo A, et al. Comparing the Outcomes of Patients With Carbapenemase-Producing and Non-Carbapenemase-Producing Carbapenem-Resistant Enterobacteriaceae Bacteremia. *Clin Infect Dis*. 2017;64(3):257-64.
21. Lee XJ, Stewardson AJ, Worth LJ, Graves N, Wozniak TM. Attributable Length of Stay, Mortality Risk, and Costs of Bacterial Health Care-Associated Infections in Australia: A Retrospective Case-cohort Study. *Clin Infect Dis*. 2021;72(10):e506-e14.
22. Rodriguez-Acevedo AJ, Lee XJ, Elliott TM, Gordon LG. Hospitalization costs for patients colonized with carbapenemase-producing Enterobacterales during an Australian outbreak. *J Hosp Infect*. 2020;105(2):146-53.
23. Biehle LR, Cottreau JM, Thompson DJ, Filipek RL, O'Donnell JN, Lasco TM, et al. Outcomes and Risk Factors for Mortality among Patients Treated with Carbapenems for Klebsiella spp. Bacteremia. *PLOS ONE*. 2015;10(11):e0143845.
24. Brescini L, Morroni G, Valeriani C, Castelletti S, Mingoia M, Simoni S, et al. Clinical and epidemiological characteristics of KPC-producing Klebsiella pneumoniae from bloodstream infections in a tertiary referral center in Italy. *BMC Infectious Diseases*. 2019;19(1):611.
25. Chen WK, Yang Y, Tan BH. Increased Mortality Among Carbapenemase-Producing Carbapenem-Resistant Enterobacteriaceae Carriers Who Developed Clinical Isolates of Another Genotype. *Open Forum Infect Dis*. 2019;6(2):ofz006.
26. Lim FK, Liew YX, Cai Y, Lee W, Teo JQM, Lay WQ, et al. Treatment and Outcomes of Infections Caused by Diverse Carbapenemase-Producing Carbapenem-Resistant Enterobacterales. *Front Cell Infect Microbiol*. 2020;10:579462.
27. Xu L, Sun X, Ma X. Systematic review and meta-analysis of mortality of patients infected with carbapenem-resistant Klebsiella pneumoniae. *Annals of Clinical Microbiology and Antimicrobials*. 2017;16(1):18.
28. Zhao S, Kennedy S, Perry MR, Wilson J, Chase-Topping M, Anderson E, et al. Epidemiology of and risk factors for mortality due to carbapenemase-producing organisms (CPO) in healthcare facilities. *J Hosp Infect*. 2021;110:184-93.
29. Borer A, Saidel-Odes L, Riesenberg K, Eskira S, Peled N, Nativ R, et al. Attributable mortality rate for carbapenem-resistant Klebsiella pneumoniae bacteremia. *Infect Control Hosp Epidemiol*. 2009;30(10):972-6.
30. Daikos GL, Tsaousi S, Tzouvelekis LS, Anyfantis I, Psichogiou M, Argyropoulou A, et al. Carbapenemase-producing Klebsiella pneumoniae bloodstream infections: lowering mortality by antibiotic combination schemes and the role of carbapenems. *Antimicrob Agents Chemother*. 2014;58(4):2322-8.
31. O'Connor C, Cormican M, Boo TW, McGrath E, Slevin B, O'Gorman A, et al. An Irish outbreak of New Delhi metallo-β-lactamase (NDM)-1 carbapenemase-producing Enterobacteriaceae: increasing but unrecognized prevalence. *Journal of Hospital Infection*. 2016;94(4):351-7.
32. Marchaim D, Chopra T, Pogue JM, Perez F, Hujer AM, Rudin S, et al. Outbreak of Colistin-Resistant, Carbapenem-Resistant Klebsiella pneumoniae in Metropolitan Detroit, Michigan. *Antimicrobial Agents and Chemotherapy*. 2011;55(2):593-9.
33. Martin J, Phan HTT, Findlay J, Stoesser N, Pankhurst L, Navickaite I, et al. Covert dissemination of carbapenemase-producing Klebsiella pneumoniae (KPC) in a successfully controlled outbreak: long- and short-read whole-genome sequencing demonstrate multiple genetic modes of transmission. *J Antimicrob Chemother*. 2017;72(11):3025-34.
34. Jamal AJ, Faheem A, Farooqi L, Zhong XZ, Armstrong I, Boyd DA, et al. Household Transmission of Carbapenemase-producing Enterobacterales in Ontario, Canada. *Clinical Infectious Diseases*. 2020;73(11):e4607-e15.
35. Cipko K, Cuenca J, Wales E, Harris J, Bond S, Newton P, et al. Implementation of an antimicrobial stewardship programme and reduction in carbapenemase-producing Enterobacterales in an Australian local health district. *JAC Antimicrob Resist*. 2020;2(3):dlaa041.
36. Viale P, Giannella M, Bartoletti M, Tedeschi S, Lewis R. Considerations About Antimicrobial Stewardship in Settings with Epidemic Extended-Spectrum β-Lactamase-Producing or Carbapenem-Resistant Enterobacteriaceae. *Infect Dis Ther*. 2015;4(Suppl 1):65-83.
37. Giacobbe DR, Del Bono V, Mikulska M, Gustinetti G, Marchese A, Mina F, et al. Impact of a mixed educational and semi-restrictive antimicrobial stewardship project in a large teaching hospital in Northern Italy. *Infection*. 2017;45(6):849-56.
38. Lemarié C, Legeay C, Mahieu R, Moal F, Ramont C, Kouatchet A, et al. Long-term contamination of sink drains by carbapenemase-producing Enterobacterales in three intensive care units: characteristics and transmission to patients. *J Hosp Infect*. 2021;112:16-20.

39. Marimuthu K, Venkatachalam I, Koh V, Harbarth S, Perencevich E, Cherng BPZ, et al. Whole genome sequencing reveals hidden transmission of carbapenemase-producing Enterobacterales. *Nat Commun*. 2022;13(1):3052.
40. Turner C, Mosby D, Partridge D, Mason C, Parsons H. A patient sink tap facilitating carbapenemase-producing enterobacterales transmission. *J Hosp Infect*. 2020;104(4):511-2.
41. Lane CR, Brett J, Schultz M, Gorrie CL, Stevens K, Cameron DRM, et al. Search and Contain: Impact of an Integrated Genomic and Epidemiological Surveillance and Response Program for Control of Carbapenemase-producing Enterobacterales. *Clin Infect Dis*. 2021;73(11):e3912-e20.
42. Bruins MJ, Koning Ter Heege AH, van den Bos-Kromhout MI, Bettenbroek R, van der Lubben M, Debast SB. VIM-carbapenemase-producing Escherichia coli in a residential care home in The Netherlands. *J Hosp Infect*. 2020;104(1):20-6.
43. Kim YA, Lee SJ, Park YS, Lee YJ, Yeon JH, Seo YH, et al. Risk Factors for Carbapenemase-Producing Enterobacterales Infection or Colonization in a Korean Intensive Care Unit: A Case-Control Study. *Antibiotics (Basel)*. 2020;9(10).
44. Trepanier P, Mallard K, Meunier D, Pike R, Brown D, Ashby JP, et al. Carbapenemase-producing Enterobacteriaceae in the UK: a national study (EuSCAPE-UK) on prevalence, incidence, laboratory detection methods and infection control measures. *Journal of Antimicrobial Chemotherapy*. 2016;72(2):596-603.
45. Segagni Lusignani L, Presterl E, Zatorska B, Van den Nest M, Diab-Elschahawi M. Infection control and risk factors for acquisition of carbapenemase-producing enterobacteriaceae. A 5 year (2011–2016) case-control study. *Antimicrobial Resistance & Infection Control*. 2020;9(1):18.
46. Kwong JC, Lane CR, Romanes F, Gonçalves da Silva A, Easton M, Cronin K, et al. Translating genomics into practice for real-time surveillance and response to carbapenemase-producing Enterobacteriaceae: evidence from a complex multi-institutional KPC outbreak. *PeerJ*. 2018;6:e4210.
47. Jolivet S, Couturier J, Vuillemin X, Gouot C, Nesa D, Adam M, et al. Outbreak of OXA-48-producing Enterobacterales in a haematological ward associated with an uncommon environmental reservoir, France, 2016 to 2019. *Eurosurveillance*. 2021;26(21):2000118.
48. Chen HY, Jean SS, Lee YL, Lu MC, Ko WC, Liu PY, et al. Carbapenem-Resistant Enterobacterales in Long-Term Care Facilities: A Global and Narrative Review. *Front Cell Infect Microbiol*. 2021;11:601968.
49. French CE, Coope C, Conway L, Higgins JPT, McCulloch J, Okoli G, et al. Control of carbapenemase-producing Enterobacteriaceae outbreaks in acute settings: an evidence review. *Journal of Hospital Infection*. 2017;95(1):3-45.
50. Legeay C, Hue R, Berton C, Cormier H, Chenouard R, Corvec S, et al. Control strategy for carbapenemase-producing Enterobacteriaceae in nursing homes: perspectives inspired from three outbreaks. *Journal of Hospital Infection*. 2019;101(2):183-7.
51. Blakiston MR, Heffernan H, Roberts SA, Freeman JT. Household transmission of NDM-producing E. coli in New Zealand. *The New Zealand Medical Journal (Online)*. 2017;130(1452):63-5.
52. Blyth CC, Pereira L, Goire N. New Delhi metallo-beta-lactamase-producing enterobacteriaceae in an Australian child who had not travelled overseas. *Medical Journal of Australia*. 2014;200(7):386-.
53. Howard JC, Anderson T, Creighton J, Freeman JT. Geographical and temporal clustering of OXA-48-producing Escherichia coli ST410 causing community-onset urinary tract infection in Christchurch, New Zealand. *Journal of Antimicrobial Chemotherapy*. 2018;73(10):2900-1.
54. Marimuthu K, Mo Y, Ling ML, Hernandez-Koutoucheva A, Fenlon SN, Bertrand D, et al. Household transmission of carbapenemase-producing Enterobacteriaceae: a prospective cohort study. *Journal of Antimicrobial Chemotherapy*. 2021;76(5):1299-302.
55. Touati A, Mairi A. Epidemiology of carbapenemase-producing Enterobacterales in the Middle East: a systematic review. *Expert Review of Anti-infective Therapy*. 2020;18(3):241-50.
56. Ben-David D, Masarwa S, Adler A, Mishali H, Carmeli Y, Schwaber MJ. A national intervention to prevent the spread of carbapenem-resistant Enterobacteriaceae in Israeli post-acute care hospitals. *Infect Control Hosp Epidemiol*. 2014;35(7):802-9.
57. Galani I, Karaiskos I, Karantani I, Papoutsaki V, Maraki S, Papaioannou V, et al. Epidemiology and resistance phenotypes of carbapenemase-producing Klebsiella pneumoniae in Greece, 2014 to 2016. *Eurosurveillance*. 2018;23(31):1700775.
58. Albiger B, Glasner C, Struelens MJ, Grundmann H, Monnet DL. Carbapenemase-producing Enterobacteriaceae in Europe: assessment by national experts from 38 countries, May 2015. *Eurosurveillance*. 2015;20(45):30062.

59. Arum N, Ghafur A, Kazi M, Rao R, Rodrigues C, Ratnamani M, et al. Prevalence of faecal carriage of Carbapenemase Producing Enterobacteriaceae in healthy Indian subjects from the community. *Indian Journal of Medical Microbiology*. 2022.
60. Habib A, Lo S, Villageois-Tran K, Petitjean M, Malik SA, Armand-Lefèvre L, et al. Dissemination of carbapenemase-producing Enterobacterales in the community of Rawalpindi, Pakistan. *PloS one*. 2022;17(7):e0270707.
61. van Duin D, Arias CA, Komarow L, Chen L, Hanson BM, Weston G, et al. Molecular and clinical epidemiology of carbapenem-resistant Enterobacterales in the USA (CRACKLE-2): a prospective cohort study. *Lancet Infect Dis*. 2020;20(6):731-41.
62. Djenadi K, Zhang L, Murray AK, Gaze WH. Carbapenem resistance in bacteria isolated from soil and water environments in Algeria. *Journal of Global Antimicrobial Resistance*. 2018;15:262-7.
63. Fernando DM, Tun HM, Poole J, Patidar R, Li R, Mi R, et al. Detection of Antibiotic Resistance Genes in Source and Drinking Water Samples from a First Nations Community in Canada. *Appl Environ Microbiol*. 2016;82(15):4767-75.
64. Hooban B, Fitzhenry K, O'Connor L, Miliotis G, Joyce A, Chueiri A, et al. A Longitudinal Survey of Antibiotic-Resistant Enterobacterales in the Irish Environment, 2019–2020. *Science of The Total Environment*. 2022;828:154488.
65. Laurens C, Jean-Pierre H, Licznar-Fajardo P, Hantova S, Godreuil S, Martinez O, et al. Transmission of IMI-2 carbapenemase-producing Enterobacteriaceae from river water to human. *Journal of Global Antimicrobial Resistance*. 2018;15:88-92.
66. Proia L, Anzil A, Subirats J, Borrego C, Farrè M, Llorca M, et al. Antibiotic resistance along an urban river impacted by treated wastewaters. *Sci Total Environ*. 2018;628-629:453-66.
67. Walsh TR, Weeks J, Livermore DM, Toleman MA. Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study. *The Lancet infectious diseases*. 2011;11(5):355-62.
68. Effelsberg N, Kobusch I, Linnemann S, Hofmann F, Schollenbruch H, Mellmann A, et al. Prevalence and zoonotic transmission of colistin-resistant and carbapenemase-producing Enterobacterales on German pig farms. *One Health*. 2021;13:100354.
69. Guo X, Akram S, Stedtfeld R, Johnson M, Chabrelie A, Yin D, et al. Distribution of antimicrobial resistance across the overall environment of dairy farms – A case study. *Science of The Total Environment*. 2021;788:147489.
70. Janecko N, Martz SL, Avery BP, Daignault D, Desruisseau A, Boyd D, et al. Carbapenem-Resistant Enterobacter spp. in Retail Seafood Imported from Southeast Asia to Canada. *Emerg Infect Dis*. 2016;22(9):1675-7.
71. Mollenkopf DF, Mathys DA, Feicht SM, Stull JW, Bowman AS, Daniels JB, et al. Maintenance of Carbapenemase-Producing Enterobacteriaceae in a Farrow-to-Finish Swine Production System. *Foodborne Pathog Dis*. 2018;15(6):372-6.
72. Mollenkopf DF, Stull JW, Mathys DA, Bowman AS, Feicht SM, Grooters SV, et al. Carbapenemase-Producing Enterobacteriaceae Recovered from the Environment of a Swine Farrow-to-Finish Operation in the United States. *Antimicrob Agents Chemother*. 2017;61(2).
73. Atterby C, Osbjer K, Tepper V, Rajala E, Hernandez J, Seng S, et al. Carriage of carbapenemase- and extended-spectrum cephalosporinase-producing Escherichia coli and Klebsiella pneumoniae in humans and livestock in rural Cambodia; gender and age differences and detection of bla(OXA-48) in humans. *Zoonoses Public Health*. 2019;66(6):603-17.
74. Cole SD, Rankin SC. Characterization of 2 Klebsiella pneumoniae carbapenemase–producing Enterobacterales isolated from canine rectal swabs. *Journal of Veterinary Diagnostic Investigation*. 2022;34(2):306-9.
75. Abraham S, O'Dea M, Trott DJ, Abraham RJ, Hughes D, Pang S, et al. Isolation and plasmid characterization of carbapenemase (IMP-4) producing Salmonella enterica Typhimurium from cats. *Scientific Reports*. 2016;6(1):35527.
76. Schmitt K, Biggel M, Stephan R, Willi B. Massive Spread of OXA-48 Carbapenemase-Producing Enterobacteriaceae in the Environment of a Swiss Companion Animal Clinic. *Antibiotics (Basel)*. 2022;11(2).
77. Sellera FP, Da Silva LCBA, Lincopan N. Rapid spread of critical priority carbapenemase-producing pathogens in companion animals: a One Health challenge for a post-pandemic world. *Journal of Antimicrobial Chemotherapy*. 2021;76(9):2225-9.

78. Dolejska M, Masarikova M, Dobiasova H, Jamborova I, Karpiskova R, Havlicek M, et al. High prevalence of Salmonella and IMP-4-producing Enterobacteriaceae in the silver gull on Five Islands, Australia. *Journal of Antimicrobial Chemotherapy*. 2015;71(1):63-70.
79. Marimuthu K, Venkatachalam I, Koh V, Harbarth S, Perencevich E, Cherng BPZ, et al. Whole genome sequencing reveals hidden transmission of carbapenemase-producing Enterobacterales. *Nature Communications*. 2022;13(1):3052.
80. Marmor A, Daveson K, Harley D, Coatsworth N, Kennedy K. Two carbapenemase-producing Enterobacteriaceae outbreaks detected retrospectively by whole-genome sequencing at an Australian tertiary hospital. *Infection, Disease & Health*. 2020;25(1):30-3.
81. Räisänen K, Lyytikäinen O, Kauranen J, Tarkka E, Forsblom-Helander B, Grönroos JO, et al. Molecular epidemiology of carbapenemase-producing Enterobacterales in Finland, 2012-2018. *Eur J Clin Microbiol Infect Dis*. 2020;39(9):1651-6.
82. Lo S, Lolom I, Goldstein V, Petitjean M, Rondinaud E, Bunel-Gourdy V, et al. Simultaneous Hospital Outbreaks of New Delhi Metallo-beta-Lactamase-Producing Enterobacterales Unraveled Using Whole-Genome Sequencing. *Microbiology Spectrum*. 2022;10(2):e02287-21.
83. Munnoch S, Deane J, Varadhan H, Givney R, Iredell J, Zakour NB, et al. An outbreak of carbapenemase-producing Enterobactericeae in a neonatal intensive care unit, NSW, Australia. *Infection, Disease & Health*. 2018;23:S15.
84. Roberts LW, Harris PN, Forde BM, Ben Zakour NL, Catchpoole E, Stanton-Cook M, et al. Integrating multiple genomic technologies to investigate an outbreak of carbapenemase-producing Enterobacter hormaechei. *Nature communications*. 2020;11(1):1-11.
85. German RR, Horan JM, Lee LM, Milstein B, Pertowski CA. Updated guidelines for evaluating public health surveillance systems; recommendations from the Guidelines Working Group. *MMWR Recomm Rep*. 2001;50(RR-13):1-35.

APPENDIX A: CASE ASSESSMENT FOR ADDING CPE AS A NOTIFIABLE CONDITION

Criterion	Scoring Guide	Score	Explanatory notes
1. Necessity for public health response	0 = Not important for public health to know about a case 1 = Case reporting important for describing trends only 2 = Case reporting important for detecting outbreaks that require investigating or contacts require routine intervention 3 = Case reporting important to detect outbreaks of cases and investigate contacts that require immediate intervention to prevent fatalities or severe outcomes 4 = A single case can be considered an outbreak or having the potential to cause an outbreak and requires immediate follow-up	2	CPE can cause life-threating infections with limited treatment options. Currently, ACT Health has limited oversight of CPE infections in the territory, and no means to monitor local transmission in community or high-risk residential settings. Making CPE a notifiable condition would enable ACT Health to follow up each case, determine the source of acquisition, and identify clusters and outbreaks. Case reporting will also enable ACT Health to identify contacts that require follow up and screening.
2. Utility and significance of notification for prevention programs	0 = No national prevention program / international or national regulation 1= Need to establish burden of illness for monitoring or research purposes / priority setting 2= Notifiable to the WHO but no regional / global targets for elimination or eradication 3 = National prevention programs in place or WHO Western Pacific Regional Office (WPRO) targets for elimination or eradication 4 = Security sensitive biological agent (SSBA) or WHO global targets for elimination or eradication / critical for monitoring prevention programs	1	Duration of colonisation with CPE is uncertain and may be prolonged. Cases have the potential to transmit CPE for the duration of their illness or colonisation. These features require healthcare facilities to undertake screening and possibly maintain contact procedures each time a previously CPE positive person presents to limit transmission. This is a resource intensive procedure but necessary to prevent further cases. There are national guidelines for clinical settings to limit transmission in healthcare facilities. In terms of public health, the Commonwealth Department of Health released a national strategy for AMR surveillance in 2020 and has commenced discussion for the development of an AMR network. As part of these preliminary discussions, the potential for CPE to become a nationally notifiable condition has been discussed. If this becomes the case, ACT Health will be required to report on case numbers and enhanced surveillance through NINDSS. Making CPE a notifiable condition in the current environment enables ACT health Directorate to pre-empt national notification and develop a surveillance system that best serves the needs of the ACT population.
3. Vaccine preventability	0 = No vaccine available 2 = Vaccine available, but no national immunisation program 4 = Vaccine available, national immunisation program in	0	CPE is not a vaccine preventable condition.

Criterion	Scoring Guide	Score	Explanatory notes
	place (including programs targeted at particular subgroups)		
4. Importance for Indigenous health	0 = Low: Disease rates in Indigenous community similar to in non-Indigenous people, not an Indigenous health priority 2 = Medium: Disease rates similar or somewhat higher in Indigenous and non-Indigenous people, but severity higher in Indigenous people e.g., influenza 3 = High: Significantly higher disease rates in Indigenous people than in non-Indigenous people e.g., shigellosis 4 = Very high: Almost exclusively occurs in Indigenous communities and/or identified as a priority for prevention e.g., trachoma	0	There have been no studies to date analysing the prevalence, incidence, or severity of CPE on Aboriginal and Torres Strait Islander communities. In the absence of data, this criterion has been scored at 0. Future surveillance would provide further information to assess this further.
5. Emerging or re-emerging disease	0 = Has been stable, absent or declined in incidence over past 5 years 2 = Slowly re-emerging or increasing incidence/prevalence disease over the past 5 years 3 = Risk of emergence in Australia due to ecological or epidemiological change or importation 4 = New, rapidly emerging disease in Australia	3	The risk of CPE in Australia has shifted over the past decade from sporadic, overseas acquired infections to increasingly common outbreaks driven by local transmission. While the majority of infections have been associated with healthcare facilities, Western Australia have reported CPE cases identified in community settings. It is difficult to ascertain the true incidence of CPE in Australia in the absence of notification data. However, voluntary reports to CARAlert have shown increasing cases of CPE in each state and territory.
6. Communicability and potential for outbreaks	0 = Not communicable or no outbreak potential 1 = Low 2 = Medium 3 = High 4 = Very high	2	CPE can be transmitted through direct contact, and through environmental sources such as shared bathrooms, sinks, and surfaces. Transmission has also been reported in cases without direct contact through sinks in adjoining rooms connected through plumbing. Outbreaks have been reported in healthcare facilities across Australia. Outbreaks of CPE are protracted and can last several years. The Canberra Hospital has experienced at least two outbreaks of CPE in recent years.
7. Severity and socioeconomic impacts	1 = Low severity and socioeconomic impacts 2 = Medium severity and socioeconomic impacts 3 = High severity and socioeconomic impacts 4 = Very high severity and socioeconomic impacts	2	CPE is a serious condition. Approximately 50% of those infected with CPE die from the condition. Patients with CPE have been found to have longer length of stay in hospital, a higher mortality rate compared with patients who have carbapenemase-susceptible *Enterobacterales* infections.

Criterion	Scoring Guide	Score	Explanatory notes
			Infection and colonisation of CPE is most commonly reported in older populations, and among populations who are seriously unwell and require significant health care. These communities are some of the most vulnerable in the ACT population. It is further noted at older age is a component characteristic of relative socioeconomic disadvantage in the socioeconomic index of areas (SEIFA) published by the Australian Bureau of Statistics. CPE also has the potential to become a serious One Health issue in Australia. There have been reports of CPE detection in food systems through Europe, North Africa, and the Middle East, including on farms and in aquaculture. If CPE establishes in the Australian food system and/or animal populations, there may be significant implications for safe food supply, further impacting more vulnerable communities in the ACT.
8. Preventability	0 = No preventive measure 1 = Preventive measure available but low efficacy and/or uptake or acceptability 2 = Preventive measure with moderate efficacy /low acceptability or uptake 3 = Preventive measure with moderate efficacy/low side effects/acceptable uptake 4 = Preventive measure with high efficacy/low side effects/high acceptability and uptake	2	As a highly resistant pathogen, there are limited treatment options available for CPE , requiring public health measures to reduce onward transmission. Contact precautions in healthcare facilities and residential long-term care facilities, such as the isolation of cases, dedication of their own bathroom facilities, and disinfecting surfaces, have been effective in the Australian context to prevent onward transmission and to stop outbreaks.
9. Level of public concern and/or political interest	1 = No to low public concern or political interest 2 = Low to medium public concern or political interest 3 = Medium to high public concern or political interest 4= High public concern/perceived “crisis” situation if cases identified	2	The current pandemic has increased public interest and concern in public health generally. Further, there have been increasing reports about AMR and the potential impact AMR has on our health care system. Alongside this increasing public interest, the Commonwealth Department of Health have shown increasing interest in AMR and surveillance of multidrug-resistant pathogens. The national strategy for AMR surveillance (*Australia’s National Antimicrobial Resistance Strategy - 2020 and Beyond*) calls for integrated surveillance and response to AMR and plans for a national AMR network have commenced.

Criterion	Scoring Guide	Score	Explanatory notes
			Making CPE a notifiable condition in the current environment enables the ACT Health Directorate to pre-empt more intensive public and/or political interest.
10. A case is definable	0 = Case is difficult to define, or agreement between stakeholders on definition cannot be reached 2 = A case is definable, but with complexities 4 = Case has an acceptable laboratory definition with or without a clinical definition	4	There are definitive molecular laboratory tests available to determine if a CPE gene is present. Clinical signs and symptoms do not need to be present to determine if a patient is a CPE case. However, defining a case has some complexities, as an individual could be infected or colonised with multiple organisms and/or with multiple CPE genes present. The proposed case definition is based on the genes present, which means one person can be multiple cases. This definition will assist with the detection of outbreaks but may result in some confusion in reporting. The proposed case definition is modelled off the Victorian surveillance system as the jurisdiction with the most experience responding to CPE.
11. Data completeness is likely to be acceptable	1 = Data likely to be incomplete, representing only a very small fraction of community cases 2 = Data represents a proportion of community cases with a known undercount 4 = Data likely to represent a high proportion of cases, or all cases	4	Incidence in Australia is currently low and while it is unlikely all cases are identified by any surveillance system; case ascertainment is believed to be high. CDC will be working with hospitals in the ACT to increase routine screening for CPE. CPE is notifiable in 5 other Australian jurisdictions, with the majority of cases reported in healthcare settings. Some community cases have been identified in WA, indicating the surveillance of CPE through notification can identify non-facility cases.
12. Alternative surveillance mechanisms	0 = Robust, comprehensive and continuing alternative national surveillance mechanism in place e.g., Human papillomavirus (HPV) 2 = Alternative surveillance mechanism in place, but not nationally coordinated, only sentinel sites or surveys, significant gaps or weaknesses e.g., rotavirus 4 = No alternative surveillance mechanisms in place	2	There is currently a voluntary surveillance system in place for monitoring AMR. CARAlert is a national surveillance system for a wide range of multidrug-resistant organisms, however this surveillance system does not have utility for public health surveillance or response: CARAlert data is deidentified. Staff at ACT Health cannot identify the case, meaning there is limited utility to respond to the presence of a CPE case in the ACT, or to detect outbreaks . CARAlert is voluntary and not all laboratories report. ACT Pathology does send through CPE detections to CARAlert, however not all private laboratories in the ACT do. CARAlert does not include the place of testing. Staff at ACT health can see that ACT Pathology has detected a CPE case, but cannot

Criterion	Scoring Guide	Score	Explanatory notes
			determine which healthcare facility conducted the test, or why the test was undertaken. There are preliminary discussions underway to add CPE to the list of nationally notifiable conditions. This may take some years to implement, and it is considered imperative that CPE is made a notifiable condition as soon as practicable in the ACT to gain oversight of any multi facility outbreaks, residential long term care facility cases, or community cases.
Total score		**24**	

APPENDIX B: FACTSHEETS FOR CPE CASES AND CONTACTS IN THE ACT

INFORMATION

ACT Government | ACT Health

Information for CPE cases

What is CPE?

CPE stands for carbapenemase-producing *Enterobacterales*.

Enterobacterales are bacteria that normally live harmlessly in the gut. If these bacteria move outside the gut, they can cause infections such as pneumonia, urinary, wound and bloodstream infections.

Carbapenems are a group of antibiotics that usually work against these bacteria. However, some of these bacteria carry genes that make them resistant to carbapenems. This means these antibiotics no longer work. Infections from CPE can be serious and very difficult to treat.

How common is CPE?

CPE is not very common in Australia. When people in Australia have CPE, they have often picked it up from having medical care overseas. It is also possible to pick up CPE in Australian hospitals. People who spend a lot of time in hospital are more likely to get CPE than other people.

What is CPE colonisation?

Some people who have CPE may not have any signs or symptoms of infection and may remain healthy. This is called colonisation. Most people with CPE are colonised. People who have CPE colonisation do not usually require treatment. If CPE moves from the gut to another part of the body, it may cause an infection and require treatment. People who have CPE colonisation are still able to spread CPE to other people.

What is CPE infection?

If CPE is causing harm and making someone unwell, this is called an infection. CPE can cause urinary tract infections, pneumonia, bloodstream infections and wound infections. A CPE infection can be serious and requires treatment.

Healthy people, including children and pregnant women, have a very low risk of CPE infection. People at higher risk of CPE infection include those who have:

- had major surgery
- a medical device inserted into their body
- received cancer treatment or an organ transplant
- received treatment in an intensive care unit

What are the signs and symptoms of CPE?

There is no specific CPE disease. People who have CPE colonisation may have no symptoms at all. For people with CPE infection, signs and symptoms may be similar to other bacterial infections, such as fever, aches and pains, tiredness, and redness, swelling or pain at a specific site.

How is CPE spread?

CPE can be spread person to person through contact with an infected or colonised person. This can be directly from another person's hands, or through contamination of shared equipment or surfaces such as sinks, toilets, and benches.

CPE is not spread through coughing or sneezing.

How is CPE treated?

People who have CPE colonisation are not normally treated.

If you have a CPE infection, there are still some antibiotics that can be used. Your doctor will work with the laboratory to identify the best antibiotic to treat you. Common antibiotics usually will not work.

There is no vaccine for CPE.

What happens in health care or hospital if I have CPE?

If you have CPE, your treating team will need to take extra precautions to prevent spread. Some of these extra precautions may include:

- You may be moved to a single room with a dedicated bathroom
- Everyone who enters and leaves your room, including you, your hospital staff and visitors, will need to clean their hands
- Hospital staff may also wear gloves and a gown or apron while caring for you
- A sign may be added to the door of your room reminding everyone of the importance of infection control. It will not disclose that you have CPE.
- An alert will be placed on your hospital record. If you have future hospital admissions to a public hospital in the ACT, this tells staff that extra precautions need to be taken.

If you go to another healthcare facility, or a healthcare provider such as a GP or a physiotherapist, or receive care services at home, you will need to tell them that you have CPE. This helps the healthcare provider organise the best care for you.

Can I have visitors in hospital if I have CPE?

Yes. Healthy people can come visit you. If your visitors are sick, they should stay home until they are healthy again.

Your visitors will need to clean their hands before entering your room, and when leaving. Your visitors should not use your bathroom.

Individual hospitals may have additional guidelines or rules in place, so check with your treating team.

What happens when I go home?

There are some simple precautions you can take at home to prevent the spread of CPE to other people:

- Wash your hands with soap and water regularly and dry them. This is especially important:
  - after using the toilet
  - before preparing or eating food
  - before and after touching any wounds or medical devices that you may have
- Use your own towels, face cloths, loofah, soap, razors, brushes and nail scissors. Do not share these items with other people
- Cover any skin wounds where possible.

You can share plates and eating utensils after they have been cleaned. You can launder your clothes along with the rest of the household laundry.

You can return to work, there are no special precautions other than washing your hands. If you work at a hospital or residential aged care facility, there may be additional guidelines for your workplace.

You can continue to be visited and go visit friends and family. You do not need to limit contact with other people, and you can continue to go wherever you want to go.

Remember to inform health or residential care providers that you have CPE so they can provide the best care. You do not need to notify non-healthcare related business or facilities.

Need more information?

For more information about CPE, contact your doctor, and if you are in hospital, speak to your treating team or someone from the hospital's infection control team.

You can also call the Health Protection Service, Communicable Disease Control Information Line during business hours on **(02) 5124 9213**.

Communicable Disease Control Section at Health Protection Service is responsible for the investigation and surveillance of notifiable or infectious conditions in the ACT in order to control or prevent their spread in the community. This includes the promotion of immunisation, education and other strategies that help to limit the spread of diseases.

CPE is a notifiable condition.

Accessibility

If you have difficulty reading a standard printed document and would like an alternative format, please phone 13 22 81.

Interpreter

If English is not your first language and you need the Translating and Interpreting Service (TIS), please call 13 14 50.

For further accessibility information, visit: www.health.act.gov.au/accessibility

www.health.act.gov.au | Phone: 132281 | Publication No XXXXX

INFORMATION

ACT Government | ACT Health

Information for people being tested for CPE

What is CPE?

CPE stands for carbapenemase-producing Enterobacterales.

Enterobacterales are bacteria that normally live harmlessly in the gut. If these bacteria move outside the gut, they can cause infections such as pneumonia, urinary, wound and bloodstream infections.

Carbapenems are a group of antibiotics that usually work against these bacteria. However, some of these bacteria carry genes that make them resistant to carbapenems. This means these antibiotics no longer work. Infections from CPE can be serious and very difficult to treat.

How common is CPE?

CPE is not very common in Australia. When people in Australia have CPE, they have often picked it up from having medical care overseas. It is also possible to pick up CPE in Australian hospitals. People who spend a lot of time in hospital are more likely to get CPE than other people.

How is CPE spread?

CPE can be spread person to person through contact with an infected or colonised person. This can be directly from another person's hands, or through contamination of shared equipment or surfaces such as sinks, toilets, and benches.

CPE is not spread through coughing or sneezing.

Why am I being tested for CPE?

People are tested for CPE in hospital if there is a possibility that they have acquired CPE.

You may be tested if you have had medical or dental care overseas, lived in a residential aged care facility overseas, or if you have had contact with a known CPE case, such as sharing a room or bathroom in a hospital ward. This may be called screening.

You may also be tested for CPE if you have symptoms of a bacterial infection.

It is important to know if you have CPE so that your treating team can organise the best care for you, and so you can take precautions when go you home to reduce the risk of spread to others in your household.

With your consent, a nurse or doctor will take samples.

How will I be tested for CPE?

The preferred way to test for CPE in people who are being screened is to take a sample of your faeces (poo). Alternatively, a nurse or doctor may take a swab from your rectum .

If your treating team suspects that you may have a CPE infection, they may take samples from other parts of the body, such as urine, wound, or a medical device (if you have one inserted in your body).

What will happen while I wait for the results?

Test results may take a few days. You may be asked to stay in a single room while your samples are being tested. Hospital staff may wear gloves and gowns or aprons when caring for you.

What happens if I test positive for CPE?

If you test positive for CPE, your treating team will talk to you about the test results, what it means for your care, and what you can do to help limit spread to other people.

Your treating team will need to take extra precautions to prevent spread within the hospital. Some of these extra precautions may include:

- You may be moved to a single room with a dedicated bathroom
- Everyone who enters and leaves your room, including you, hospital staff and visitors, will need to clean their hands
- Hospital staff may wear gloves and a gown or apron while caring for you
- A sign may be added to the door of your room reminding everyone of the importance of infection control. It will not disclose that you have CPE.
- An alert will be placed on your hospital record. If you have future hospital admissions to a public hospital in the ACT, this tells staff that extra precautions need to be taken.

How is CPE treated?

If you have CPE but remain healthy and have no symptoms, you are not normally treated for CPE.

If you have a CPE infection, there are still some antibiotics that can be used. CPE infections are usually managed with advice from an infectious disease specialist to help identify the best treatment as common antibiotics usually will not work.

There is no vaccine for CPE.

Need more information?

For more information about CPE, contact your doctor, and if you are in hospital, speak to your treating team or ask to speak to someone from the hospital's infection control team.

You can also call the Health Protection Service, Communicable Disease Control Information Line during business hours on **(02) 5124 9213**.

Communicable Disease Control Section at Health Protection Service is responsible for the investigation and surveillance of notifiable or infectious conditions in the ACT in order to control or prevent their spread in the community. This includes the promotion of immunisation, education and other strategies that help to limit the spread of diseases.

CPE is a notifiable condition.

Accessibility

If you have difficulty reading a standard printed document and would like an alternative format, please phone 13 22 81.

Interpreter

If English is not your first language and you need the Translating and Interpreting Service (TIS), please call 13 14 50.

For further accessibility information, visit: www.health.act.gov.au/accessibility

www.health.act.gov.au | Phone: 132281 | Publication No XXXXX

INFORMATION

ACT Government | ACT Health

Information for contacts of CPE cases

What is CPE?

CPE stands for carbapenemase-producing Enterobacterales.

Enterobacterales are bacteria that normally live harmlessly in the gut. If these bacteria move outside the gut, they can cause infections such as pneumonia, urinary, wound and bloodstream infections.

Carbapenems are a group of antibiotics that usually work against these bacteria. However, some of these bacteria carry genes that make them resistant to carbapenems. This means these antibiotics no longer work. Infections from CPE can be serious and very difficult to treat.

How common is CPE?

CPE is not very common in Australia. When people in Australia have CPE, they have often picked it up from having medical care overseas. It is also possible to pick up CPE in Australian hospitals. People who spend a lot of time in hospital are more likely to get CPE than other people.

How is CPE spread?

CPE can be spread person to person through contact with an infected or colonised person. This can be directly from another person's hands, or through contamination of shared equipment or surfaces such as sinks, toilets, and benches.

CPE is not spread through coughing or sneezing.

What does it mean to be a CPE contact?

ACT Health follows up all CPE cases in the ACT. During this follow up, we identify who may have had contact with a person who has CPE. This contact may have occurred if you shared a room or bathroom in a hospital, or if you live with a case. It is important for us to identify contacts to make sure you are healthy and to limit further spread of CPE.

What do I need to do as a CPE contact?

If you live in a residential aged care facility, you will be offered a test to see if you have CPE. This is called screening.

If you do not live in a residential aged care facility, you do not need to do anything straight away.

If you are admitted to a hospital or a residential aged care facility in the future, you will need to tell them that you are a CPE contact. The hospital or facility will usually do a screening test to see if you have CPE.

How will I be tested for CPE?

The preferred way to test for CPE in people who are being screened is to take a sample of your faeces (poo). A nurse or doctor may take a swab from your rectum (bottom).

If your treating team suspects that you may have a CPE infection, they may take samples from other parts of the body, such as urine, wound, or a medical device if you have one inserted in your body.

What will happen while I wait for the results?

Test results may take a few days. You may be asked to stay in a single room while your samples are being tested. Hospital staff or staff at your residential aged care facility may wear gloves and gowns or aprons when caring for you.

I live in a residential aged care facility, what happens if I test positive for CPE?

If you test positive for CPE, someone at your facility will talk to you about the test results, what it means for your care, and what you can do to help limit spread to other people.

Staff at your facility will need to take extra precautions to prevent spread. Some of these extra precautions may include:

- You may be moved to a single room with a dedicated bathroom
- Everyone who enters and leaves your room, including you, staff and visitors, will need to clean their hands
- Staff may also wear gloves and a gown or apron while caring for you

You would still be able to receive visitors, and to leave the facility [as you do now/without additional restrictions].

I don't live in a residential aged care facility, what happens if I test positive for CPE?

If you are tested in a hospital, hospital staff will take extra precautions to prevent spread within the hospital.

If you are tested by a GP, the doctor will talk to you about the test results, what it means for your care, and what you can do to help limit spread to other people.

If you are well enough to stay at home, you would continue to be able to be visited and go visit friends and family. You would not need to limit contact with people, and you could continue to go wherever you want to go.

Need more information?

For more information about CPE, contact your doctor, and if you are in hospital, speak to your treating team or ask to speak to someone from the hospital's infection control team.

You can also call the Health Protection Service, Communicable Disease Control Information Line during business hours on **(02) 5124 9213**.

Communicable Disease Control Section at Health Protection Service is responsible for the investigation and surveillance of notifiable or infectious conditions in the ACT in order to control or prevent their spread in the community. This includes the promotion of immunisation, education and other strategies that help to limit the spread of diseases.

CPE is a notifiable condition.

Accessibility

If you have difficulty reading a standard printed document and would like an alternative format, please phone 13 22 81.

If English is not your first language and you need the Translating and Interpreting Service (TIS), please call 13 14 50.

For further accessibility information, visit: www.health.act.gov.au/accessibility

www.health.act.gov.au | Phone: 132281 | Publication No XXXXX

APPENDIX C: PROTOCOL FOR NOTIFICATION AND FOLLOW UP OF CPE CASES AND CONTACTS

ACT Government | ACT Health

Protocol for control of carbapenemase-producing *Enterobacterales* in the ACT

October 2022

Contents

ACKNOWLEDGMENT OF COUNTRY

ACT Health acknowledges the Traditional Custodians of the land, the Ngunnawal people. ACT Health respects their continuing culture and connections to the land and the unique contributions they make to the life of this area. ACT Health also acknowledges and welcomes Aboriginal and Torres Strait Islander peoples who are part of the community we serve.

Glossary, acronyms and abbreviations

AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
Beta-lactam	A class of antibiotics used to treat bacterial infections. This class includes penicillin and cephalosporins
Carbapenemase	Enzymes produced by CPE that hydrolyse carbapenems
Carbapenems	A class of powerful antibiotics used to treat severe bacterial infections, including treatment of multidrug resistant bacteria
CDC	Communicable Disease Control branch, ACT Health
CPE	Carbapenemase-producing *Enterobacterales*
Enterobacterales	An order of gram-negative bacteria normally found in the gastrointestinal tract. Some of these bacteria produce enzymes, called carbapenemase, which stop antibiotics from working against the bacteria.
GP	General practitioner
MRO	Multidrug-resistant organism
WGS	Whole genome sequencing

1. Background

1.1 What are carbapenemase-producing *Enterobacterales* (CPE)?

Enterobacterales are an order of gram-negative bacteria that are normally found in the gastrointestinal tract. *Enterobacterales* can cause infections when they spread outside the gastrointestinal tract and can result in urinary tract infections, wound infection, bacteraemia, and pneumonia.

Carbapenemase-producing *Enterobacterales* (CPE) carry genes which can confer resistance to carbapenems. Carbapenems are a 'last resort' class of antibiotics used to treat severe bacterial infections. CPE can produce enzymes (carbapenemases) that hydrolyse carbapenems and other beta-lactam antibiotics. This means that CPE often have limited treatments available for infections.

There are five main types of genes carried by CPE:

- Imipenemase (IMP)
- Klebsiella pneumoniae carbapenemase (KPC)
- New-Delhi metallo-β-lactamase (NDM)
- Oxacillinases (OXA-48-like)
- Verona integron-encoded metallo-β-lactamase (VIM)

While CPE genes have historically had a geographic distribution (KPC in the Americas and Europe, NDM in the Indian subcontinent, OXA-48-like in the Mediterranean and Middle East regions, IMP in the Asia-Pacific region, VIM in Europe and the Mediterranean), the five main CPE genes are increasingly found across the world.

The majority of locally acquired CPE cases in Australia carry the IMP gene.

1.2 Public health significance of CPE

1.2.1 Epidemiology

At the time of writing, the burden of CPE in Australia is relatively low. Other regions have reported higher burdens of CPE compared with Australia, including North America, Europe, the Middle east, and Asia. Most CPE infections in Australia have been associated with overseas travel, and overseas medical treatment.

However, since 2012, the proportion of locally acquired CPE has been increasing. Outbreaks have been experienced in Victoria, NSW, and SA associated with healthcare facilities. CPE cases have been reported in every state and territory, including the ACT.

1.2.2 Implications for public health

CPE are a significant risk to public health for the following reasons:

- CPE infection can have severe clinical outcomes, including high mortality.
- Treatment options for CPE are limited as they are often resistant to carbapenems and other antibiotics.
- CPE can be spread between people and through the environment in healthcare facilities.
- CPE can persist in environment, including basins, sinks and surfaces in healthcare facilities.
- CPE genes can be transferred between organisms, including organisms of different species, enabling easier spread.
- Because of these features, CPE have caused several outbreaks in healthcare facilities across Australia with resultant morbidity and mortality.

1.3 Transmission and risk factors

CPE can be transmitted through direct contact with an infected person, or indirectly through a contaminated surface, such as sinks, basins, other bathroom hardware or shared equipment.

Risk factors for CPE acquisition include:

- Overseas travel
- Medical or dental treatment overseas
- Hospital admission overseas
- Prolonged hospitalisation in Australia
- Presence of an in-dwelling medical device
- Prolonged exposure to different antibiotics, including prolonged exposure to carbapenems, cephalosporins and fluoroquinolones
- Admission to an ICU
- Undertaking dialysis, radiotherapy, or chemotherapy.

1.4 People at higher risk of developing severe CPE infection

Severe CPE infection is most likely to occur in people who are very ill, including:

- Have a history of prolonged and/or frequent hospitalisation
- Patients admitted to an ICU
- Patients who have received organ transplants

1.5 Development of an ACT protocol for CPE

The design of the CPE surveillance system occurred in 2021-2022 and involved the input and feedback from the following organisations and teams:

- Disease Surveillance Unit, Communicable Disease Control, ACT Health Directorate
- Medical Officer Team, Office of the Chief Health Officer, ACT Health Directorate
- Quality and Safety Unit, ACT Health Directorate,
- ACT Pathology, Canberra Health Services
- Infection Prevention and Control Unit, The Canberra Hospital

- National Infection Control Coordinator, Calvary Health
- ACT Infection Prevention and Control Networking Group
- Acting Chief Veterinary Officer

This protocol for CPE has been developed through the review and adaptation of the following documents to the ACT context:

- Australian Commission on Safety and Quality in Health Care, *Recommendations for the control of carbapenemase-producing Enterobacterales (CPE). A guide for acute care health service organisations*. Sydney: ACSQHC, 2021
- Victorian Department of Health, *Victorian guideline on CPE for health services, version 2.1, Melbourne*, Department of Health, 2018
- Victorian Department of Health, *Victorian guideline on CPE for long-term residential care facilities*, Department of Health, 2018
- New South Wales Department of Health, *Surveillance & Response for Carbapenemase-Producing Enterobacterales (CPE) in NSW Health Facilities*, Department of Health, 2019
- Tasmanian Public Health Services, *Carbapenemase-producing Enterobacteriaceae (CPE) – management and surveillance protocol*, Department of Health and Human Services, 2016

Short explanations for definitions and processes in this protocol are at Appendix A (page 18).

A bibliography is available at the end of this document for further reference.

2. Governance

2.1 Roles and responsibilities

Table 1 outlines the roles and responsibilities of CPE surveillance in the ACT

Table 1: Summary of key roles and responsibilities of CPE surveillance by organisation

Organisation	Roles and responsibilities
ACT Health, Communicable Disease Control branch	Lead agency in territory-wide response to CPE. Undertake territory-wide surveillance of all CPE notifications Collate and report on enhanced surveillance data Oversee outbreak response affecting multiple health care facilities and/or a residential aged care facility Contact tracing for non-hospital CPE contacts Liaise with other Australian health agencies regarding multi-jurisdictional outbreaks
ACT healthcare facilities	Provide clinical care for hospitalised CPE cases Implement infection prevention and control measures for CPE cases Identify and trace contacts of CPE cases in the healthcare facility Collect enhanced surveillance data on cases identified in hospital to report to ACT Health Lead outbreak response in single healthcare facility outbreaks
ACT Pathology	Conduct confirmatory testing of suspect CPE isolates Notify results to ACT Health and requesting clinician Liaise with ICPMR for WGS for confirmed CPE cases
Other laboratories servicing the ACT	Conduct phenotypic testing of samples requesting CPE testing Send all suspect cases of CPE to ACT pathology for confirmatory testing Notify suspected cases to ACT Health
Residential aged care facilities	Implement infection prevention and control measures for CPE cases Collect enhanced surveillance data to report to ACT Health, for cases who are RACF residents Identify CPE contacts in RACFs and work with ACT Health to trace contacts Work with ACT Health to control local transmission and respond to outbreaks
General practitioners	Provide enhanced surveillance data to report to ACT Health Clinical care for cases in the community

2.2 Roles and responsibilities within CDC

Table 2 outlines the roles and responsibilities of CPE surveillance within the CDC team.

Table 2: Summary of key roles and responsibilities of CPE surveillance within CDC

Organisation	Roles and responsibilities
Surveillance Coordinator, Disease Surveillance	Collate and report on enhanced surveillance data Generate quarterly reports for ACT hospitals Prepare deidentified quarterly summary of CPE in the ACT for the ACT IPC Networking Group Liaise with other Australian health agencies regarding multi-jurisdictional outbreaks
Public Health Officer, Disease Surveillance	Interview CPE cases, next of kin and/or treating clinician for enhanced surveillance data collect Contact tracing for non-hospital CPE contacts Support outbreak response
Surveillance Officer, Disease Surveillance	Enter notifications of CPE into NDMS Create and enter notification data for CPE cases in REDCap Enter additional laboratory data, including whole genome sequencing data, as it becomes available
Infection Control team	Provide infection control advice to residential aged care facilities with CPE contacts or cases
Public Health Physician	Oversee outbreak response affecting multiple health care facilities and/or a residential aged care facility as Chair This role may also be fulfilled by a Health Emergency Management unit team member, or the Senior Director, CDC if a Public Health Physician is unavailable to consistently act as Chair.

3. Case and contact definitions

ACT Health has definitions for confirmed and suspect cases.

Both confirmed and suspect cases are notifiable in the ACT.

One person can have multiple cases of CPE simultaneously.

Confirmed case

Detection of a carbapenemase gene[1, 2] in an isolate of a species of *Enterobacterales*.

[1] Irrespective of phenotypic susceptibility

[2] Each CPE gene in an organism and/or person represents a new confirmed case (e.g., the presence of NDM-4 and NDM-1 represents two separate cases)

Suspect case

Isolation of a species of *Enterobacterales* with reduced susceptibility to a carbapenem.

A reduced susceptibility to a carbapenem is defined by any of the following:

- Disc diffusion (EUCAST/CLSI) – meropenem 10ug <28mm zone diameter, or
- Disc diffusion (CDS) – meropenem 5ug <6mm annular radius, or
- MIC – meropenem >0.25mg/L

Contact of a confirmed case

A person who:

- shared a room for 24 hours or more with a confirmed CPE case at a healthcare facility or residential aged care facility

  OR

- shared a bathroom for 24 hours or more with a confirmed CPE case at a healthcare facility or residential aged care facility

  OR

- lived in the same household as a confirmed CPE case within 12 months of the case's date of acquisition.

Local transmission/outbreak

Two or more confirmed cases of genetically related CPE and a plausible epidemiological connection between the two cases, either through geographic proximity or shared staff, equipment or other exposures.

OR

Where acquisition from an environmental source is hypothesised, clustering in time and place without a direct patient to patient epidemiological link.

Any local transmission of CPE is considered to be an outbreak in the ACT.

4. Laboratory testing

Laboratories should follow local in-house testing protocols.

If a suspect case has been identified, all isolates should be sent to ACT Pathology for confirmatory testing and typing.

All confirmed isolates may then be sent to Institute of Clinical Pathology and Medical Research (ICPMR) for whole genome sequencing (WGS) and bioinformatic analysis. Suspect isolates detected in ACT residents who were tested in the ACT should not be sent directly to ICPMR.

Note: the current proposed strategy for WGS is to send isolates to ICPMR. However, the WGS strategy for all notifiable conditions is currently under review and the approach for CPE may change.

CPE is a Group B notifiable condition. Laboratories must report suspect and confirmed cases of CPE to ACT Health within five business days of detection.

5. Managing notifications and follow up within CDC

5.1 Purpose of surveillance

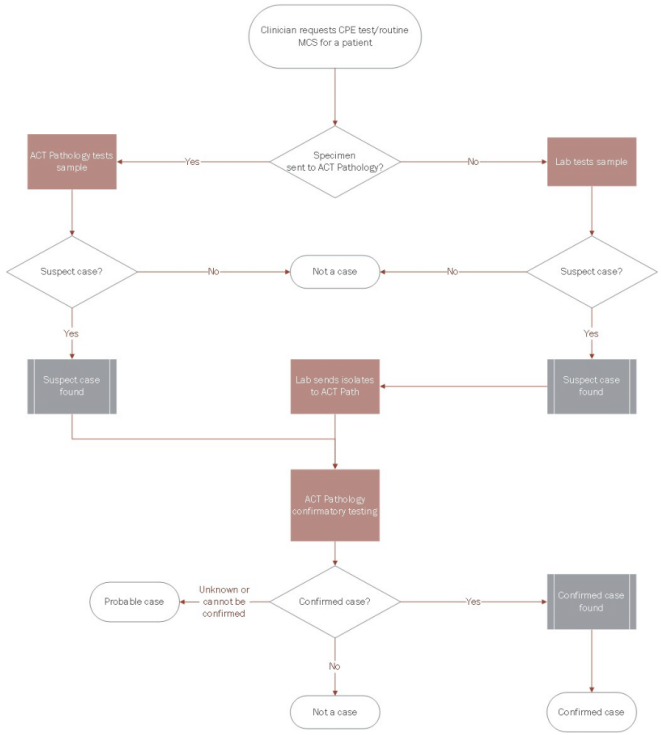
- To identify cases of CPE and their source of acquisition
- To detect local transmission and outbreaks of CPE
- To understand the local epidemiology of CPE
- To ensure appropriate IPC precautions are in place

This section outlines how ACT Health manages CPE cases. The management of cases depends on the case classification (suspect or confirmed) and the case's location at testing.

The clinical management of the case is the responsibility of the treating doctor.

Figure 1 outlines the initial steps for case classification in the ACT.

Figure 1: Flowchart for determining CPE case classification



5.2 Suspect CPE cases

1. Record details from pathology report into NDMS as a new Disease Incident, classify the Process Status as "Staging" and the Resolution Status as "Under Investigation".

2. Contact laboratory to ensure the isolate/s are sent directly to ACT Pathology for confirmatory testing and typing.

3. If the case was tested in a residential aged care facility, refer case to CDC Infection Control for follow up with the facility and advice on infection prevention and control measures.

4. If the case is in a healthcare facility or residential aged care facility, contact precautions should be implemented by the facility, until confirmatory testing is required.

CDC will consider the need for contact tracing on a case-by-case basis. Health facilities may proceed with contact tracing according to facility protocols or standards.

5.3 Not a CPE case

If ACT Pathology advises that the probable case does not have a CPE gene detected and is not a confirmed case:

1. Update NDMS Disease Incident record to classify the Process Status as "Closed "and the Resolution Status as "Not a case".

2. If the case was tested in a residential aged care facility, advise the facility of the result. As residential aged care facilities fall outside the scope of ACT Health Disease Surveillance jurisdiction, the facility will need to determine what, if any, infection prevention and control precautions are appropriate.

5.4 Confirmatory testing unable to be conducted

If ACT Pathology advises that confirmatory testing could not be conducted for the suspect case, first contact the requesting clinician to request a repeat specimen. If confirmatory testing remains unavailable:

1. Update NDMS Disease Incident record to classify the Process Status as Closed and the Resolution Status as Probable.

2. If the case was tested in a residential aged care facility, advise the facility of the result and recommend sending isolates to a different laboratory for confirmation As residential aged care facilities fall outside the scope of ACT Health Disease Surveillance jurisdiction, the facility will need to determine what, if any, infection prevention and control precautions are appropriate.

5.5 Confirmed CPE cases

Flowcharts for follow up procedures for confirmed CPE cases by testing location are shown at Appendix B (page 20). The variables for enhanced surveillance for confirmed CPE cases are shown at Appendix C (page 25).

1. Update NDMS Disease Incident record to classify the Process Status as "Under Investigation" and the Resolution Status as "Confirmed".

2. Create a REDCap form in the External CPE Investigation Project for Disease Incident.

3. Enhanced surveillance data collected. The method for case interview and responsible role will be different depending on where the case was tested. The case interview includes questions on:

- Reason for testing
- Status of the case (hospitalised, discharged, dead etc.)

- Risk factors, including overseas travel, overseas medical treatment, in-dwelling devices, hospitalisation, residency in a residential aged care facility, and past antibiotic therapy
- Contacts of the CPE case

5.5.1 ACT hospital cases

A flowchart for following up CPE cases in ACT hospitals is shown at Figure B.1 in Appendix B.

Enhanced surveillance data collection is conducted electronically through REDCap for the following hospitals:

- The Canberra Hospital
- Calvary Public Hospital
- Calvary Bruce Private Hospital
- Calvary John James Private Hospital
- National Capital Private Hospital
- University of Canberra Hospital
- Barton Private Hospital
- Canberra Private Hospital
- Canberra Eye Hospital

1. Send email through REDCap to the hospital's infection prevention and control team by selecting the 'Send email now' option and setting the CDC form status to 'Confirmed'. This email requests the ACT hospital to collect enhanced surveillance data on cases identified through their facilities with a unique link for a case's REDCap form. The CDC inbox will be notified when the enhanced surveillance form has been completed.

2. If no response has been received in 5 days, REDCap will send a reminder email.

3. If no response is received in 10 days, REDCap will send a reminder email and CDC will call hospital IPC team to discuss best process for case interview.

4. If patient is discharged, a Public Health Officer is to contact the case and/or their regular GP to collect missing enhanced surveillance information.

5.5.2 Non-ACT hospital cases

A flowchart for following up CPE cases in non-ACT hospitals is shown at Figure B.2 in Appendix B.

1. Contact the hospital IPC team and inform them that CPE is notifiable condition in the ACT and that an ACT resident case has been identified at their facility.

2. Conduct case interview. The interview process may vary between non-ACT hospitals and may involve:

- Public Health Officer calling the hospital IPC team to conduct case interview based on available clinical notes

- Public Health Officer emailing the REDCap enhanced surveillance form after an initial phone call confirming IPC team will conduct data collection
- Public Health Officer contacting the case or other next of kin directly to conduct phone interview

3. If initial attempt is unsuccessful, contact the next business day.

4. If second attempt is unsuccessful, contact the next business day.

5. If third attempt is unsuccessful, close case and add note they are as lost to follow up.

5.5.3 Residential aged care facility cases

A flowchart for following up CPE cases in residential aged care facilities is shown at Figure B.3 in Appendix B.

1. Contact the facility to advise of confirmed case and arrange for Public Health Officer to conducts case interview.

- The case interview may be conducted with the case, the case's next of kin, the case's regular GP and/or residential aged care facility staff depending on available information.
- It is recommended the initial interview is conducted with the residential aged care facility staff at the time infection prevention and control advice is provided and further phone call supplement any information gaps.

2. Provide the case and/or their next of kin with factsheet

2. If initial attempt is unsuccessful, contact the next business day. Continue until the case interview is successful.

5.5.4 GP/community cases

A flowchart for following up CPE cases identified in the community is shown at Figure A.4

1. Contact the GP practice to advise of confirmed case
2. Provide the GP with the GP factsheet.
3. Conduct case interview. Ideally this interview is conducted with the case themselves but may be conducted with a next of kin or clinician.
4. If initial attempt is unsuccessful, contact the next business day. Continue until the case interview is successful.
5. If the case is deemed to be community acquired, send a clinician alert to GPs and hospitals advising that a community acquired CPE case has been identified.

5.6 Review of enhanced surveillance data

Review of enhanced surveillance data is conducted by the Surveillance Coordinator.

Data from case interview will be combined with WGS information from ICMPR to identify source of acquisition, exposure setting, and the presence of local transmission.

Reports are to be sent to each ACT Hospital once a quarter summarising that facility's notifications and the findings of their enhanced surveillance data.

A deidentified report summarising all notifications that does not name facilities or cases is to be presented at the ACT IPC Network quarterly meetings.

5.6.1 Determining date of acquisition

The date of acquisition will be calculated as the following:

- First date of contact with a known CPE case
- First date of contact with a known environmental contaminant or transmission risk area
- First date of contact with overseas medical care

If none of these can be determined, the date of acquisition is unknown and calculated as one month prior to collection of the first positive specimen.

5.7 Multiple confirmed cases in a single person

A CPE case is defined by the presence of a specific carbapenemase gene. This means that one person may have multiple cases of CPE if multiple different carbapenemase genes are detected.

The results of WGS may indicate that a single person has multiple cases of CPE diagnosed simultaneously. If this is the case:

1. A new Disease Incident is created for the Person ID
2. Enhanced surveillance data should be duplicated in each Disease Incident record

Enhanced surveillance data collection is only collected once per person per diagnosis date.

If a new notification is received more than six months from the previous notification, and there is evidence of a new CPE gene, new enhanced surveillance data is collected.

5.8 Clearance of cases

The duration of CPE colonisation remains uncertain and may vary between individuals. Some people with CPE colonisation may have the condition for life and may remain infectious indefinitely.

Healthcare facilities can elect to undertake screening to determine clearance of CPE carriage. In accordance with national guidelines, healthcare facilities may screen cases to determine clearance of CPE carriage and cessation of contact precautions if:

- More than 12 months has passed since the last positive result
- Three negative screening swabs are taken at least 24 hours apart

It is important to note that one person may have multiple cases of CPE and may be renotified to ACT Health if a new gene is detected.

6. Managing contacts

6.1 Purpose of contact tracing

- To identify potentially infected or colonised persons
- To manage risk of onwards transmission from those persons

6.2 Identify contacts of confirmed cases of CPE

Contacts of confirmed cases should be identified through enhanced surveillance data collection. The organisation responsible for managing the contact depends on their location:

- If a contact remains in hospital at the time they are identified, the hospital's infection prevention and control team is responsible for contact management.
- If a contact has been transferred to another health care facility, the transferring hospital must notify the receiving hospital. The receiving hospital is then responsible for contact management.
- If a contact has been discharged home or resides in the community in a non-residential aged care facility setting, CDC is responsible for contact management.
- If a contact is a resident in a residential aged care facility at the time they are identified, the residential aged care facility and CDC are responsible for contact management.
- If a contact is interstate, CDC will forward their details to the relevant public health unit for follow up.

6.3 Notifying and advice for contacts

Contacts should be informed of their potential exposure within five business days.

All contacts should be sent the CPE contact fact sheet:

- Factsheet for CPE contacts in hospital
- Factsheet for CPE contacts in residential aged care facilities, or in the community

6.4 Screening/testing of contacts

Screening of contacts depends on their location:

- If the contact is an inpatient at a hospital, or still in an emergency department, the facility should test for CPE as soon as practicable
- If the contact has been discharged to a residential aged care facility, the facility should test for CPE as soon as practicable
- If the contact has been discharged home (but not to a residential aged care facility), or is a household contact, CDC will:
    - Advise the contact that if they present to a hospital or are being admitted to a residential aged care facility in the next 12 months, they must declare their CPE contact status.

    - With consent, advise the contact's regular GP of the contact's status and recommend adding a note to their patient record

It is not advised to test contacts in community settings.

7. Outbreak detection and investigation

When local transmission is suspected, action should be taken to prevent any further ongoing transmission. Confirmation of local transmission by WGS should not delay the outbreak response.

Any local transmission in the ACT is considered to be an outbreak.

If transmission has occurred in a defined geographic area, such as a ward of a healthcare facility or a residential aged care facility, that area will be designated as a transmission risk area. This designation is used to identify contacts and potential onwards transmission.

Note: the use of transmission risk areas is subject to further consultation with ACT hospitals.

7.1 Single healthcare facility outbreak

If the outbreak only involves a single healthcare facility, that healthcare facility is responsible for the outbreak response.

7.2 Multiple healthcare facility outbreak

If two or more healthcare facility are linked by the results of WGS or epidemiological investigation, an Outbreak Response team is formed. Depending on the scale, the Outbreak Response team may take the form of an Acute Response Team (ART).

The role of the Outbreak Response team is to:

- Develop an outbreak management plan
- Facilitate communication between facilities and ACT Health
- Determine communication requirements
- Investigate possible transmission routes and contamination sources
- Determine additional infection prevention and control measures to reduce ongoing transmission
- Coordinate screening of contacts, and review criteria for contact definition

The Outbreak Response team should include representation from the following:

- Disease Surveillance Unit, CDC
- Infection Control Unit, CDC
- Senior Director, CDC
- Public Health Physician, HPS
- ACT Pathology
- Infection Prevention and Control from each healthcare facility

- Infectious Disease Physician from each health care facility, if applicable
- Communications from ACT Health, and each healthcare facility

The healthcare facility remains responsible for managing their cases and contacts in clinical and infection prevention and control matters. ACT Health will oversee the co-ordination of the outbreak response and provide data analysis and reporting support.

7.3 Residential aged care facility outbreak

If local transmission is detected at a residential aged care facility, or local transmission occurred in a healthcare facility and the individual is discharged to a residential aged care facility, an Outbreak Response team is formed. Depending on the scale, the Outbreak Response team may take the form of an ART.

The role of the Outbreak Response team is to:

- Develop an outbreak management plan
- Facilitate communication between facilities and ACT Health
- Determine communication requirements
- Investigate possible transmission routes and contamination sources
- Determine additional infection prevention and control measures to reduce ongoing transmission
- Coordinate screening of contacts, and review criteria for contact definition

The Outbreak Response team should include representation from the following:

- Disease Surveillance Unit, CDC
- Infection Control Unit, CDC
- Public Health Physician, HPS
- ACT Pathology
- Infection Prevention and Control from each residential aged facility
- Infection Prevention and Control from each health care facility, if applicable
- Infectious Disease Physician from each health care facility, if applicable
- Communications from ACT Health, and each facility

The residential aged care facility remains responsible for managing cases and contacts in clinical and infection prevention and control matters.

ACT Health will oversee the outbreak response for any outbreaks that include a residential aged care facility. This includes any outbreaks that involve a single residential aged care facility, multiple residential aged care facilities, or involve a healthcare facility. ACT Health will also be responsible for the reporting and analysis associated with the outbreak response.

7.4 Other residential facility setting outbreak

While CPE remains a relatively rare condition, there is a low risk that local transmission may occur in other residential settings, such as a correctional facility, barracks, or group home.

In these events, ACT Health will work with the residential facility to oversee the outbreak response through an ART. The roles and responsibilities will be determined on a case-by-case basis.

It is recommended that a clinician alert is sent to GPs and hospitals advising that local transmission of CPE has been identified.

7.5 Community outbreak

Globally, local transmission outside of healthcare or residential facilities is rare. If local transmission occurs in the community, it largely occurs within households.

If local transmission is identified outside of a healthcare facility or a residential aged care facility, ACT Health will lead the response through an ART.

It is recommended that a clinician alert is sent to GPs and hospitals advising that local transmission of CPE has been identified.

Appendix A: Explanatory notes

Why are cases defined by genes?

CPE case definitions in Australia generally fall into two categories:

- A species-based definition
  - This is the approach in NSW
- A gene-based definition
  - This is the approach in Victoria, Tasmania, South Australia, and Western Australia

We have elected to use a gene-based definition in the ACT for a few reasons:

- *Enterobacterales* can transfer genetic material across species and genera, meaning the same carbapenemase gene may be found across multiple species
- Whole genome sequencing of carbapenemase genes can provide greater utility to identify linked cases than the sequences of the bacteria
- Outbreaks in other jurisdictions and overseas have found chains of transmission linked by carbapenemase genes across several species of bacteria.

How can one individual be counted as multiple cases?

The case definition we have chosen for the ACT is gene-based. One individual may have multiple carbapenemase genes present, which is an indication they may have had multiple exposures and/or the CPE may have come from different sources. It is important for the epidemiological investigation to identify these potential sources of acquisition to determine if local transmission has occurred.

Across Australian jurisdictions, case definitions allow for one individual to have multiple cases of CPE simultaneously.

Only one enhanced surveillance data collection is required per individual, even when multiple CPE genes are identified at the same time. The clinical management of patients of CPE does not change.

Why are there suspect and confirmed case definitions?

The option of a suspect case allows for more rapid notification to ACT Health and to advise on public health action.

- The presence of phenotypic resistance can be clinically significant and require infection prevention and control procedures.
- Private laboratories who do not have in house genotypic testing available are required to notify about the suspect case, enabling more rapid notification while the isolate travel to another lab for confirmatory testing.
- The requirement for confirmatory testing is a step for typing and whole genome sequencing.

ACT Pathology has advised that they always confirm phenotypic resistance in a potential CPE (isolates that meet the suspect case definition) with genotyping.

The reporting of suspect and confirmed cases is a standard practice in jurisdictions where CPE is notifiable (New South Wales, Victoria, South Australia, Western Australia, Tasmania).

What is the rationale behind the contact definition?

We have elected to use 24 hours as the threshold for a few reasons:

- This is the contact definition recommended in the national *Recommendations for the control of carbapenemase-producing Enterobacterales (CPE)*.
- This contact definition is also standard across Australian jurisdictions where CPE is notifiable and would potentially integrate into a national contact definition if CPE becomes nationally notifiable.

We have elected to include household contacts in the CPE contact definition due to findings in recent literature that transmission occurs within households:

- Jamal A et al, Household Transmission of Carbapenemase-producing Enterobacterales in Ontario, Canada, *Clinical Infectious Diseases*, Volume 73, Issue 11, 1 December 2021, Pages e4607–e4615, https://doi.org/10.1093/cid/ciaa1295
- Marimuthu K et al, Household transmission of carbapenemase-producing Enterobacteriaceae: a prospective cohort study, *Journal of Antimicrobial Chemotherapy*, Volume 76, Issue 5, May 2021, Pages 1299–1302, https://doi.org/10.1093/jac/dkaa561

Why is the outbreak threshold two related cases?

Currently, CPE is a rare condition in Australia. Local transmission when it does occur is largely limited to healthcare facilities. Based on available data, the ACT is believed to have a low incidence of CPE.

The objective of CPE surveillance in the ACT is to limit transmission. Responding to any indication of local transmission enables public health and clinical care to stop spread as early as possible and prevent future cases.

The two case threshold has been adopted in other jurisdictions where CPE is notifiable. Adopting a similar definition means we could potentially integrate into a national outbreak definition without disrupting our procedures.

Appendix B: Flowcharts for follow up of CPE cases.

This section includes flowcharts for following up cases identified in:

- ACT hospitals
- Non-ACT hospitals
- Residential aged care facilities
- Community setting/GP

Figure B.1: Process for follow-up of CPE cases identified in an ACT hospital

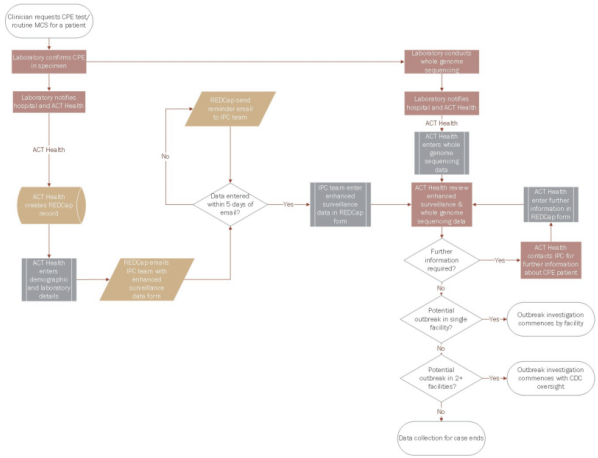


Figure B.2: Process for follow-up of CPE cases identified in a non-ACT hospital

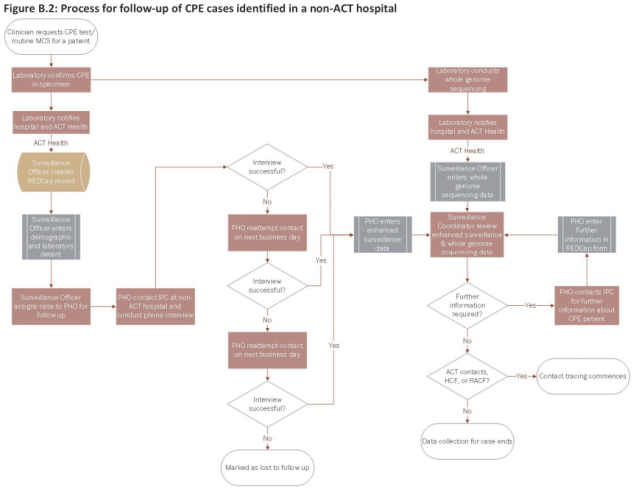


Figure B.3: Process for follow-up of CPE cases identified in an ACT residential aged care facility

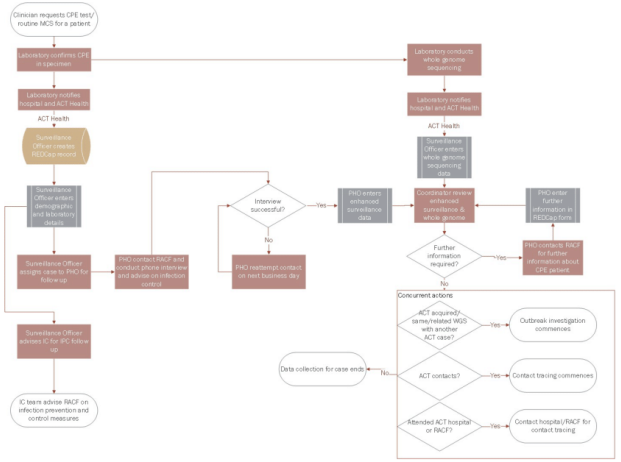
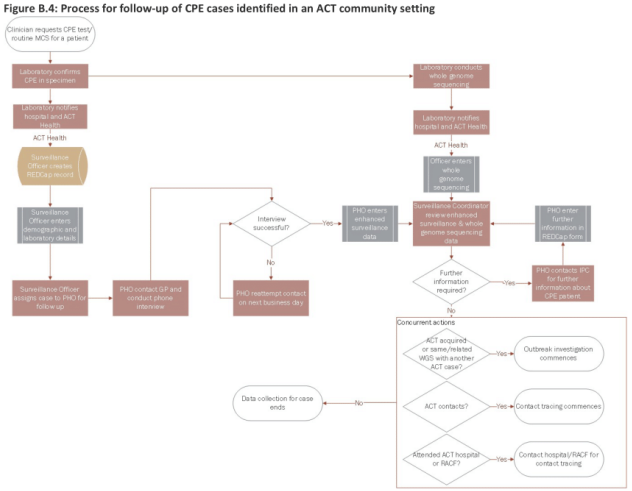


Figure B.4: Process for follow-up of CPE cases identified in an ACT community setting



Appendix C: Enhanced surveillance collection for CPE

The form below outlines the details to be collected at case interview for CPE notifications.

These questions supplement the details from the original pathology reports, and the typing and sequencing information from the confirming laboratory.

What was the reason for requesting a CPE test?
○ Clinically indicated ○ Screening ○ Contact tracing (i.e. a contact of a known CPE case) ○ Other
What was the location of the patient when they were tested?
○ Inpatient - ICU/HDU ○ Inpatient - other ward, please specify ○ Emergency department ○ Outpatient clinic ○ Primary care ○ Residential aged care facility ○ Other, please specify
Clinical details
What is the CPE status of the patient?
○ Colonisation ○ Infection ○ Unknown
Has the patient died at the time of follow-up?
○ Yes ○ No

- ○ Unknown

Please list any underlying health conditions

e.g. malignancy, diabetes, organ transplant recipient

Exposure history

Has the patient ever had contact with a known CPE case?

If we do not know if a case has been in contact with a known CPE case, please select 'No'

- ○ Yes
- ○ No
- ○ Information not asked

If yes, provide details of the case

Has the patient had any antibiotic therapy in the 12 months before the specimen collection date (_____)?

- ○ Yes
- ○ No
- ○ Unsure/information not available when asked
- ○ Information not asked/collected

If yes provide details of the antibiotic, course, and method of administration

Has the patient been a resident of an aged or long term care facility in the 2 years before the specimen collection date (_____)?

- ○ Yes
- ○ No
- ○ Unsure/information not available when asked
- ○ Information not asked/collected

If yes, provide details of the facility, ward and dates

Overseas travel

Did the patient travel or live overseas in the 2 years before the specimen collection date (_____)?

- ○ Yes
- ○ No
- ○ Unsure/information not available when asked
- ○ Information not asked/collected

If yes, list the countries, and provide details of any overseas, medical or dental care overseas

Hospitalisation in Australia

Has the patient been hospitalised (including day surgery/day admissions) IN AUSTRALIA in the 2 years before the specimen collection date (_____)?

- ○ Yes
- ○ No
- ○ Unsure/information not available when asked
- ○ Information not asked/collected

If yes, provide details of the hospital, ward, and dates

Has the patient received any of the following procedures IN AUSTRALIA in the 2 years before the specimen collection date (_____)?

Please select all that apply.

- ☐ Endoscopy
- ☐ Colonoscopy
- ☐ Admission to ICU
- ☐ Mechanical ventilation
- ☐ Chemotherapy or radiotherapy
- ☐ Dialysis
- ☐ None of the above
- ☐ Unsure/information not available when asked
- ☐ Information not asked/collected

Has the patient had any in-dwelling devices IN AUSTRALIA in the 12 months prior to the specimen collection date (_____)?

- ○ Yes
- ○ No
- ○ Unsure/information not available when asked
- ○ Information not asked/collected

If yes, please provide details

Who was the exposure history obtained from?

- ○ The patient
- ○ Another person
- ○ Clinical notes only

If from another person, provide details

Bibliography

Australian Commission on Safety and Quality in Health Care, *Recommendations for the control of carbapenemase-producing Enterobacterales (CPE). A guide for acute care health service organisations*. Sydney: ACSQHC, 2021

Jamal A et al, Household Transmission of Carbapenemase-producing Enterobacterales in Ontario, Canada, *Clinical Infectious Diseases*, Volume 73, Issue 11, 1 December 2021, Pages e4607–e4615, https://doi.org/10.1093/cid/ciaa1295

Kwong, J, (2018). Translating genomics into practice for real-time surveillance and response to carbapenemase-producing Enterobacteriaceae: evidence from a complex multi-institutional KPC outbreak. PeerJ, 6, January 2018 e4210. https://doi.org/10.7717/peerj.4210

Lane C et al, Search and Contain: Impact of an Integrated Genomic and Epidemiological Surveillance and Response Program for Control of Carbapenemase-producing Enterobacterales, Clinical Infectious Diseases, Volume 73, Issue 11, 1 December 2021, Pages e3912–e3920, https://doi.org/10.1093/cid/ciaa972

Marimuthu K et al, Household transmission of carbapenemase-producing Enterobacteriaceae: a prospective cohort study, *Journal of Antimicrobial Chemotherapy*, Volume 76, Issue 5, May 2021, Pages 1299–1302, https://doi.org/10.1093/jac/dkaa561

New South Wales Department of Health, *Surveillance & Response for Carbapenemase-Producing Enterobacterales (CPE) in NSW Health Facilities*, Department of Health, 2019

Tasmanian Public Health Services, *Carbapenemase-producing Enterobacteriaceae (CPE) – management and surveillance protocol*, Department of Health and Human Services, 2016

Victorian Department of Health, *Victorian guideline on CPE for health services, version 2.1, Melbourne*, Department of Health, 2018

Victorian Department of Health, *Victorian guideline on CPE for long-term residential care facilities*, Department of Health, 2018

CHAPTER 5: ANALYSIS OF HEPATITIS C NOTIFICATIONS IN THE ACT, 2012-2021

TABLE OF CONTENTS

Prologue

This chapter details an analysis of hepatitis C notification data in the ACT from 2012 to 2021 inclusive. This chapter addresses the following competencies:

- Analysis of a public health data set
- Literature review
- Lay summary

My role

The ACT Government has committed to the World Health Organization's goal to eliminate hepatitis C by 2030. The need to review existing trends and patterns for hepatitis C in the ACT was identified as a first step to guide public health action and achieve elimination.

I led the design, implementation and reporting for this analysis. I led the preparation and submission of an ethics application for this project, and for future analysis of hepatitis B and D by others at ACT Health. Following ethics approval, I collated and cleaned the notification and enhanced surveillance data, including a review of all original paper records. I conducted the statistical and spatial analyses for inclusion in this chapter and a short internal report to guide the decision making of ACT Health Protection Services.

In the ACT, hepatitis C cases can be classified as newly acquired (within the past 2 years), of unspecified duration, and reinfection. Reinfections of hepatitis C are not nationally defined or notifiable and public health nurses apply a local definition. In the absence of a comprehensive national picture, I conducted a targeted literature review to understand current evidence of hepatitis C reinfections in Australia. The methods are detailed in Appendix A and the findings have been synthesised into this chapter's introduction.

Key reflections

This was my first foray into the epidemiology of blood-borne viruses. I thoroughly enjoyed learning about the condition and follow up procedures from the public health nurse team in the Disease Surveillance Unit. I have gained a deeper appreciation for the complexity of the work of public health nurses and the challenges of follow up for sexually transmitted infections and blood-borne viruses.

This project also enabled me to stretch my spatial science skills. My undergraduate study was in geography and spatial sciences, and I had intended to build on my descriptive geospatial knowledge in this project through the preparation of spatial autocorrelation and hotspot analysis to establish any statistically significant spatial relationships in the distribution of hepatitis C notifications. However, the skewing in the data and the presence of significant outliers contravened the underlying assumptions of these approaches and prevented further valid statistical analysis. Performing these preliminary tests was initially disappointing but a necessary check to ensure appropriate valid data analysis and findings.

This project has reinforced the importance of language when describing and defining data. Hepatitis C can be a highly stigmatising condition for some people, potentially impacting access to and quality of testing, treatment, and care. Importantly, living with hepatitis C is just one aspect of a person's life, and may not be who they choose to be defined. Throughout this project, I have aimed to maintain a person-centred approach as a reminder that our data represent the lived experiences of others and to recognise the agency of the people whose information I have been entrusted with. Further, through this project, I've recognised the significance of how we define risk factors and the importance of focusing on where the risk actually is. For instance, the risk of blood-borne virus infection lies not solely in the act of injecting a drug, but in the act of injecting using unsterile equipment. It has been a challenge to reconcile what data is collected with our understanding of the risks of transmission, and through this chapter, I have aimed to use terminology that reflects the reality of public health follow up and recognises the agency and dignity of people living with hepatitis C identified during this study period.

Public health impact

This project was defined by ACT Health as a priority to inform public health actions in achieving the elimination of hepatitis C virus in the ACT by 2030. The findings of this project and recommendations have been provided to ACT Health and will be used to inform public health policies and programs to increase testing and access to treatment.

Further, this project has highlighted some significant gaps in the current procedures for follow up and enhanced surveillance of hepatitis C. The findings of this project will be used by ACT Health to enhance data quality and completeness, especially around risk factors including the collection of data about sharing of unsterile injecting equipment.

Finally, I used the findings of the analysis and literature review to update ACT Health's hepatitis C factsheet for lay audiences (Appendix B).

Acknowledgements

Thank you to Rachael Crane and Julia Smythe, the wonderful public health nurses who took the time to answer all my questions, sense-check my data cleaning, review drafts and provide valuable feedback. Special thanks as well to Sue Reid for your meticulous follow up notes that shed so much light on the early cases in this study period. Thank you to Dr Davoud Pourmarzi, Alexandra Marmor and Dr Philippa Binns for your supervisory support and guidance through this study.

Abstract

Background: The World Health Organization and the Australian Government have set a target to eliminate hepatitis C as a public health problem by 2030. There are effective treatments available for hepatitis C, however previous infection and treatment do not prevent future reinfections. ACT Health has been collecting data from the public health follow up of hepatitis C notifications and reinfections, however little is known about the epidemiology of the condition in the ACT.

Methods: Newly acquired infections, cases of unspecified duration and reinfections of hepatitis C notified between 2012 and 2021 were included (n=1555). Notification information, enhanced surveillance data, and original paper records were reviewed. Descriptive statistics were prepared to describe cases by person, place and time, and to compare notifications by disease classification and time period. Spatial analysis was conducted to describe the distribution of cases by socioeconomic status and residential location.

Results: Notifications of hepatitis C decreased through the study period, however, rates of newly acquired cases and reinfections were relatively stable over the 10 years. The majority of cases were of unspecified duration, male, and between 30 and 50 years old at notification. While half of the cases of unspecified duration were diagnosed in primary care, two-fifths of newly acquired cases and reinfections were detected at a correctional centre. The majority of newly acquired cases and reinfections disclosed a history of injecting drug use. One third of hepatitis C cases resided in areas of the lowest quintile of relative socioeconomic advantage, with spatial clustering evident in Canberra's east and south.

Discussion: The decline in hepatitis C notifications follows the availability of direct-acting antivirals in 2016 and is consistent with national trends. The ACT is currently the only Australian jurisdiction routinely identifying and following up reinfections. Reinfections are an important consideration for public health and warrant further follow up to treat individuals and limit transmission. While injecting drug use was the most commonly reported risk factor in this analysis, future public health follow up should collect information on unsterile injecting behaviours such as sharing needles. Hepatitis C cases in the ACT follow a social gradient, with concentrations of cases identified in correctional facilities and relatively socioeconomically disadvantaged areas of the ACT and represent an opportunity to target community education, testing and treatment to eliminate hepatitis C in the Territory.

Introduction

Hepatitis C is a significant global public health concern, estimated to affect over 150 million people worldwide.[1] Hepatitis C is caused by infection with the hepatitis C virus (HCV), which largely affects the liver. While there may be an acute phase of infection with fatigue, jaundice, and nausea, most people do not experience symptoms unless a chronic infection has developed.[2] Without treatment, chronic hepatitis C can inflame the liver and lead to significant health outcomes, such as chronic liver disease, cirrhosis, hepatocellular carcinoma, and death.[2]

HCV is largely transmitted through contact with contaminated blood. Transmission risks for hepatitis C conditions include sharing unsterile needles and injecting drug equipment, unsterile medical procedures, receipt of blood transfusions prior to screening programs being implemented, sexual exposure, and vertical transmission.[2] Transmission of hepatitis C in Australia is largely associated with unsafe and unsterile practices among people who inject drugs,[3-5] with increased cases also reported among populations with limited direct agency and access to healthcare, including people who are in correctional facilities or have experienced homelessness.[6-11] People with bleeding disorders and conditions that compromise the immune system, such as HIV infection, are potentially at greater risk of infection and severe outcomes from hepatitis C.[2]

Previous HCV infection does not prevent future infection, meaning an individual can have multiple incidences of hepatitis C over their lifetime. There is no vaccine available for hepatitis C.

Treatment and elimination targets

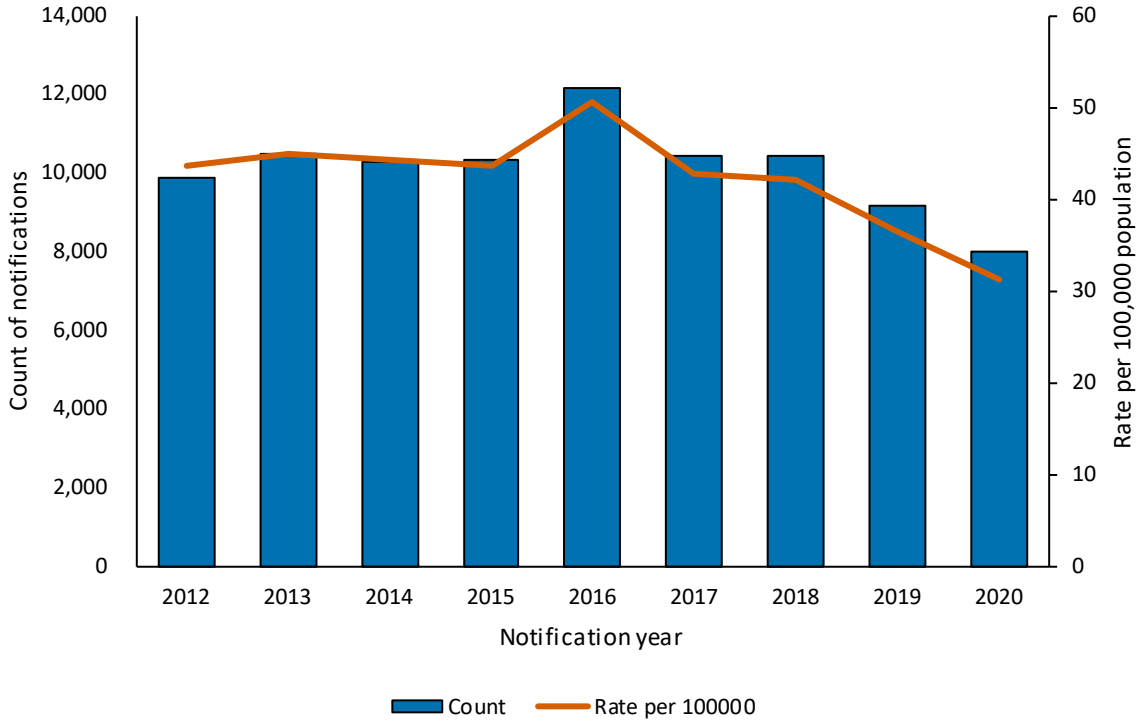
Recent pharmaceutical developments have provided an opportunity to prevent and treat different viral hepatitis conditions. Direct-acting antivirals (DAAs) are oral treatments that target the hepatitis C virus and are effective in inducing a sustained virological response, meaning virus RNA cannot be detected through nucleic acid testing 12 weeks or more after completing treatment. Treatment with DAAs has also been associated with reduced incidence of hepatocellular carcinoma, cirrhosis, and mortality.[12, 13] In Australia, subsidised DAAs were made available to treat hepatitis C through the Pharmaceutical Benefits Scheme (PBS) in March 2016.[14]

With the introduction of DAAs as a viable way to treat and potentially cure hepatitis C, the World Health Organization (WHO) set a target for the global elimination of the condition by 2030.[1] Specifically, the WHO has set targets for 80% of people living with hepatitis C to receive treatment, a 95% reduction in hepatitis C infections, and a 65% reduction in mortality associated with HCV.[1] The Australian Government and the ACT Government have both endorsed this target.[15, 16]

Hepatitis C in Australia

Hepatitis C is a nationally notifiable condition, with all jurisdictions reporting newly acquired cases and cases of unspecified duration. Approximately 9000 to 10,000 cases of hepatitis C are notified in Australia each year (Figure 1).[17] Following a peak in notifications in 2016 when DAAs became available through the PBS, the rate of notifications per 100,000 population has declined across Australia.[17]

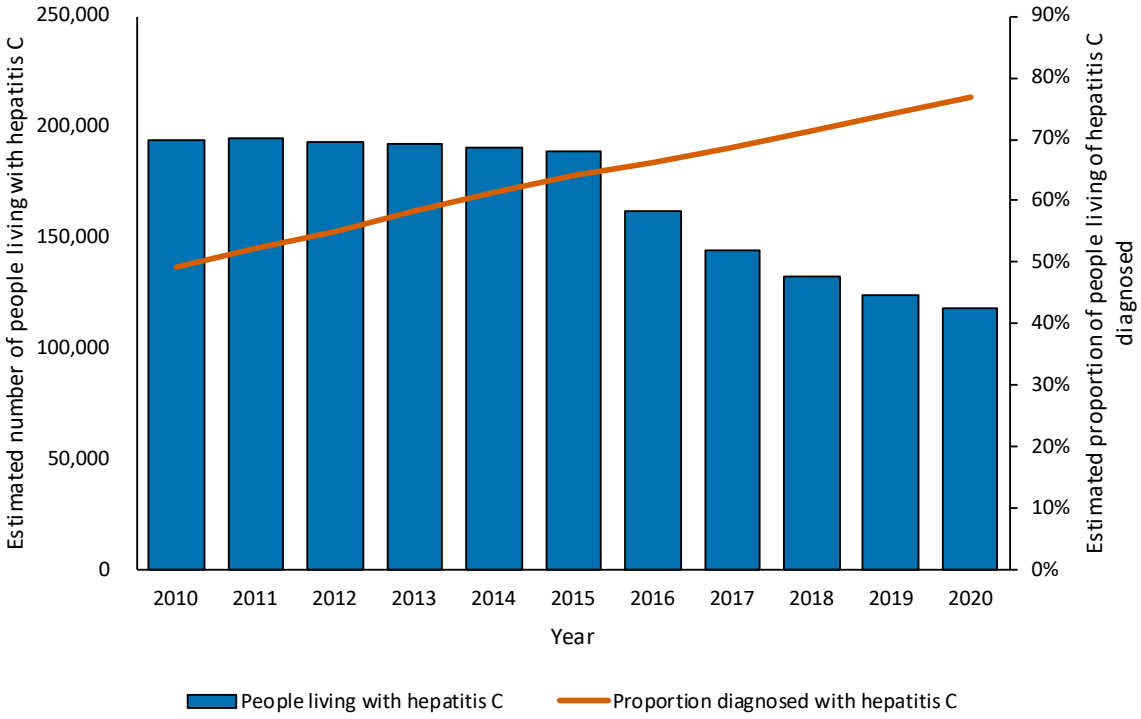
Figure 1: Number and rate per 100,000 population of hepatitis C notifications, Australia, 2012-2020



Source: Kirby Institute, 2021.[18]

The estimated prevalence of people living with hepatitis C has also decreased over time (Figure 2). The number of people estimated to be living with hepatitis C was approximately 210,000 people in 2000 or approximately 1.1% of the Australian population.[19] Since 2011, the estimated number of people living with hepatitis C has decreased annually to the most recent estimate of 117,810 people living with hepatitis C in 2020.[17] The incidence of new infections of hepatitis C has also decreased, from an estimated 1.6 per 100 person-years in 2012 to 0.6 per 100-person years among patients attending sentinel primary care facilities.[18]

Figure 2: Estimated number of people living with hepatitis C in Australia and proportion diagnosed, 2010-2020



Source: Kirby Institute, 2021.[17]

The prevalence and incidence of hepatitis C vary among different sub-populations in Australia. The highest prevalence and incidence have been estimated among people who inject drugs. Estimates of the prevalence of HCV infection among people who inject drugs in Australia range from 20% to 87%.[20-23] A higher prevalence has been estimated among people injecting drugs while in a correctional centre compared with people in community settings.[24, 25] However, the incidence of hepatitis C among people who inject drugs has been decreasing over time from a peak of 30.8 to 45.8 infections per 100 person-years in the late 1990s-early 2000s down to 7.9 to 12.8 per 100 person-years in the late 2000s-mid 2010s.[26-32]

People in correctional facilities and other closed settings also have a higher reported prevalence and incidence of hepatitis C compared with the general population. Prevalence estimates range from 5% to 58% of people in correctional facilities consenting to testing,[24, 33-35] and the incidence of newly acquired infections between 4.6 infections per 100 person-years and 34.2 infections per 100 person-years among people continuously imprisoned.[10, 11, 25, 36-38] Factors associated with hepatitis C infection among people in correctional facilities include injecting drugs while in a correctional facility, sharing needles and injecting equipment, frequency of injection, and younger age.[9, 25, 38] There have been mixed results regarding the associations between seroconversion while residing in a correctional facility and tattooing, sex, and Indigenous status.[9-11, 25, 39]

Lower prevalence and incidence have been reported among people living with HIV (between 0.8 and 1.2 infections per 100 person-years)[40-43] and among gay, bisexual, and other men who have

sex with men (GBMSM; between 0.1 and 1.0 infections per 100 person-years)[41, 42, 44, 45] compared with people who inject drugs and people in correctional facilities. There has been a decline in the incidence of hepatitis C among people living with HIV in recent years, dropping from 1.2 infections per 100 person-years in 2015 to 0.23 per 100 person-years in 2019. [45] While condomless intercourse has been reported as a potential risk factor in hepatitis C prevalence studies concerning GBMSM,[41, 44] the highest incidence rates among people who live with HIV and GBMSM have been reported among members of these populations who also inject drugs and report sharing unsterile injecting equipment (4.7 per 100 person-years).[40, 42, 43]

Since the introduction of blood and tissue donation screening in 1990, the prevalence of hepatitis C among blood donors has remained low, with the most recent estimate of one per 3,636,000 donations testing positive.[46] The prevalence of hepatitis C has also been found to be low among children, with the most frequently reported risk factor being HCV infection diagnosed in the birth mother.[47]

Public health surveillance of hepatitis C

Confirmed cases of hepatitis C are nationally notifiable and case definitions are set by the Communicable Disease Network of Australia (CDNA). A confirmed case of hepatitis C requires either a serological test detecting anti-hepatitis C antibody, or the detection of the hepatitis C virus by nucleic acid testing. Hepatitis C cases are defined as newly acquired if an individual had a negative anti-hepatitis antibody or PCR result within 24 months of the positive result. If evidence of a negative result within 24 months of the positive result is not available, the duration of hepatitis C infection cannot be determined, and the case is defined as unspecified. Case definitions for unspecified hepatitis remained the same throughout the study period. The definition for newly acquired hepatitis C in infants was amended in 2014, to include infants who test positive between 28 days and 24 months, from the previous definition of 3 months to 24 months.

In addition to the CDNA definitions, ACT Health informally adopted a definition for reinfections of hepatitis C virus in 2015 to allow local surveillance of reinfections. Confirmed hepatitis C reinfection requires evidence of two negative PCR tests for hepatitis C virus in the past 24 months or evidence of genotype change. Hepatitis C reinfections are defined as probable if only one negative PCR result is conducted. Reinfections are not reported to the Australian Government Department of Health and Ageing.

Reinfections of HCV in Australia

Reinfection with hepatitis C has increasingly become an important consideration for public health, with the availability of effective treatment and the limited protection previous infections confer. Currently, there is no national definition or notification requirement for reinfections of hepatitis C in Australia.

Studies in Australia estimated the incidence of reinfections at between 1.1 per 100 person-years among people living with HIV and 46.8 per 100 person-years among people who inject drugs.[26, 48] The incidence of reinfection per 100 person-years of follow up in correctional facilities and in the broader community have decreased following the availability of DAAs.[26, 27, 32, 38, 49, 50]

Risk factors associated with reinfection in Australia with HCV include injecting drug use after treatment, frequency of injecting drugs, injecting drugs with multiple partners, and condomless anal intercourse.[27, 48, 51-53] While injecting with unsterile needles and other injecting equipment has been a recognised risk factor for hepatitis C generally, there is mixed evidence on its association with hepatitis C reinfections in Australia.[26, 27, 38, 48, 51-54]

Age, sex, gender, type of drug injected, age at first injection, any history of imprisonment, continuous or intermittent imprisonment, educational attainment, employment status, living with HIV, or a history of depression were not associated with a risk of reinfection.[27, 49, 51-53]

Aim of this study

While there is a broad understanding of the epidemiology of hepatitis C at a national level, little is known about the trends and patterns of hepatitis C notifications in the ACT. To achieve local elimination, further study is required to better understand the current context and inform public health interventions to eliminate hepatitis C in the ACT. This project aimed to describe the epidemiology of hepatitis C notifications by person, place, and time to serve as a foundation for further public health action.

Methods

Study population

The study population included all notifications of hepatitis C in ACT residents that met national and local public health criteria between 2012 and 2021. Retests of existing cases or cases previously notified in a different state or territory were excluded. Cases notified outside of the ACT were identified by 2016 Statistical Area 2 (SA2) defined by the Australian Bureau of Statistics and were excluded from the analysis.

Data collection and cleaning

All notifications are recorded in the ACT Notifiable Diseases Management System (NDMS). Individual notifications are recorded using a unique notification identification number (ID), with variables for one diagnostic test, sex, country of birth, Indigenous status, residential address, details of the diagnosing clinician, and a free text field for the suspected source. A comments box is used to record any other relevant information for a notification, including past testing history, risk factors and reasons for testing.

In the ACT, newly acquired cases and suspected reinfections are followed up by a public health nurse and enhanced surveillance data is collected from the diagnosing clinician as per the specification set by the Australian Government Department of Health and Ageing. The case is not contacted for public health follow up. Enhanced surveillance data collected includes current or previous injecting drug use status, other risk factors for blood-borne virus transmission, and reason for testing. Blood-borne virus risk factors other than current or previous injecting drug use are only recorded if a case did not report this exposure, and if the potential exposure occurred within 24 months of the time of diagnosis.

Enhanced surveillance data for newly acquired cases are stored in separate Microsoft Excel files by calendar year and include the notification ID recorded in the NDMS. Enhanced surveillance for reinfections is stored in the comments box in the NDMS. Hepatitis C infections of unspecified duration are not routinely followed up.

New variables were generated following the review of the NDMS fields and comments to record the diagnostics tests undertaken, and the results of the tests. Paper records of all the notifications were reviewed to record diagnostic tests conducted and the residential address of the case at the time of testing. The clinical notes of pathology reports and comments field in the NDMS were reviewed under the supervision of public health nurses who routinely follow up hepatitis C cases to determine the reason for testing or potential risk factors. Following the review of all paper records, a unique study ID was generated for each notification, and the original notification ID was removed from the dataset.

Enhanced surveillance for hepatitis C allows for multiple blood-borne virus risk factors to be recorded but only one reason for testing. The original risk factor variable was separated into 23

variables, one for each potential non-injecting drug use risk factor in the Department of Health data specifications. Responses to 'other' risk factors and 'other' reasons for testing were reviewed and collated to identify potential trends that may not have been covered by national data specifications. If more than five comments for the 'other' risk factor were identified that covered the same topic, a new variable was generated. A new risk factor variable was also generated to record where the public health follow-up indicated there was known sharing of needles or injecting equipment. If more than five 'other' comments for the reason for testing covered the same reason, a new value was generated in the reason for testing variable.

A new variable was generated from the notification year to classify cases notified to ACT Health before the availability of DAAs (2012-2015 inclusive) and after DAAs became available to treat people with hepatitis C (2016-2021 inclusive).

The Australian Bureau of Statistics Correspondence for Australian Statistical Geography Standard 2016 was used to generate two new variables from the suburb of residence of cases: SA2 and Statistical Area 3 (SA3). The Australian Statistical Geography Standard is published by the Australian Bureau of Statistics to group people and communities to report official statistics and demographic data. Statistical Areas are a nested hierarchy of geographies that represent communities (SA2) and regions (SA3) of similar population sizes.

The Index of Relative Socio-economic Advantage and Disadvantage (IRSAD) decile of the Australian Bureau of Statistics Socio-Economic Indexes for Areas (SEIFA), 2016 was linked to each notification based on their SA2 of residence. Notifications with an unknown address or no fixed address at the time of diagnosis did not have an SA2 or SA3 value generated. Notifications with an SA2 that did not have an IRSAD value (due to low/no official population numbers or no permanent places of residence) were kept blank and considered missing data.

Data quality and completeness

The completeness for each variable was calculated as a proportion of all cases to understand data quality. Completeness considered blank values and unknowns.

Descriptive analysis

Analysis was conducted to describe hepatitis C notifications by person, place and time. Age-specific notification rates per 100,000 population were calculated using the mid-year estimated resident population from 2012 to 2021 published by the Australian Bureau of Statistics. Cross-tabulations were prepared to assess the association of variables with disease classification (newly acquired/unspecified/reinfection) and DAA period (2012-2015/2016-2021) using the Pearson's chi-squared test, or Fisher's exact test where any individual stratum was less than 5.

The observed values of hepatitis C notifications by age, sex, Indigenous status, place of birth, and IRSAD decile were compared with the expected distribution based on the distribution of these sociodemographic characteristics in the ACT population at the 2016 Census at the mid-point of the study period using Pearson's chi-squared test. The 2016 Census was also the most

recent IRSAD available at the time of this study. Notifications for people with hepatitis C living in a correctional facility at the time of their diagnosis were excluded from the IRSAD analysis. Values less than five were reported as '<5' to protect the confidentiality and prevent reidentification. Statistical analyses were conducted in R version 4.1.3.

Spatial analysis

Cases with a known, fixed place of residence at the time of their diagnosis were included in the spatial analysis. Choropleth maps were prepared to aggregate the count and average annual rate of notifications by SA2 and SA3 in the study period. The 2016 boundaries for SA2 and SA3 were used in this analysis as the mid-point population distribution in the study period.

There were no changes between the 2016 and 2021 SA3 boundaries, and minimal boundary changes involving one SA2 in 2016 split into 3 in the 2021 release. Spatial analysis was conducted in QGIS version 3.22.

Ethical considerations

Ethics approval was obtained through the Australian Capital Territory Human Research Ethics Committee (protocol 2022/ETH00603).

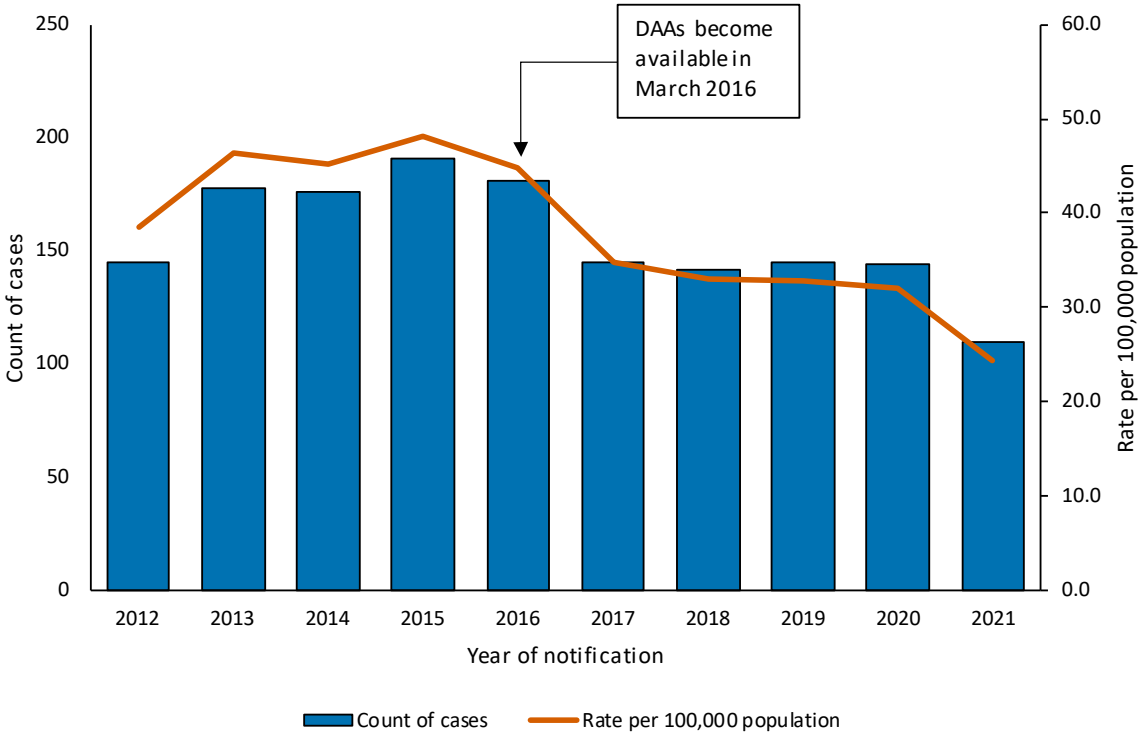
Results

There were 1,557 cases of hepatitis C notified during the study period (2012-2021). Two of these cases were excluded as residents of the Jervis Bay Territory, which is a federal territory administered by the Australian Government, not the Australian Capital Territory. A total of 1,555 notifications were included in this analysis.

Notification rates

The annual crude notification rate of hepatitis C cases per 100,000 population is shown in Figure 3. Overall, the annual crude notification rate increased in the first half of the study period to a peak in 2015 and then decreased to below the annual crude notification rate experienced in 2012. The crude notification rate in 2021 of 24.3 per 100,000 population represents a 50% decrease from the peak crude notification rate in 2015 of 48.3 per 100,000 population.

Figure 3: Number of hepatitis C notifications and crude notification rate per 100,000 population by year, 2012 to 2021, Australian Capital Territory

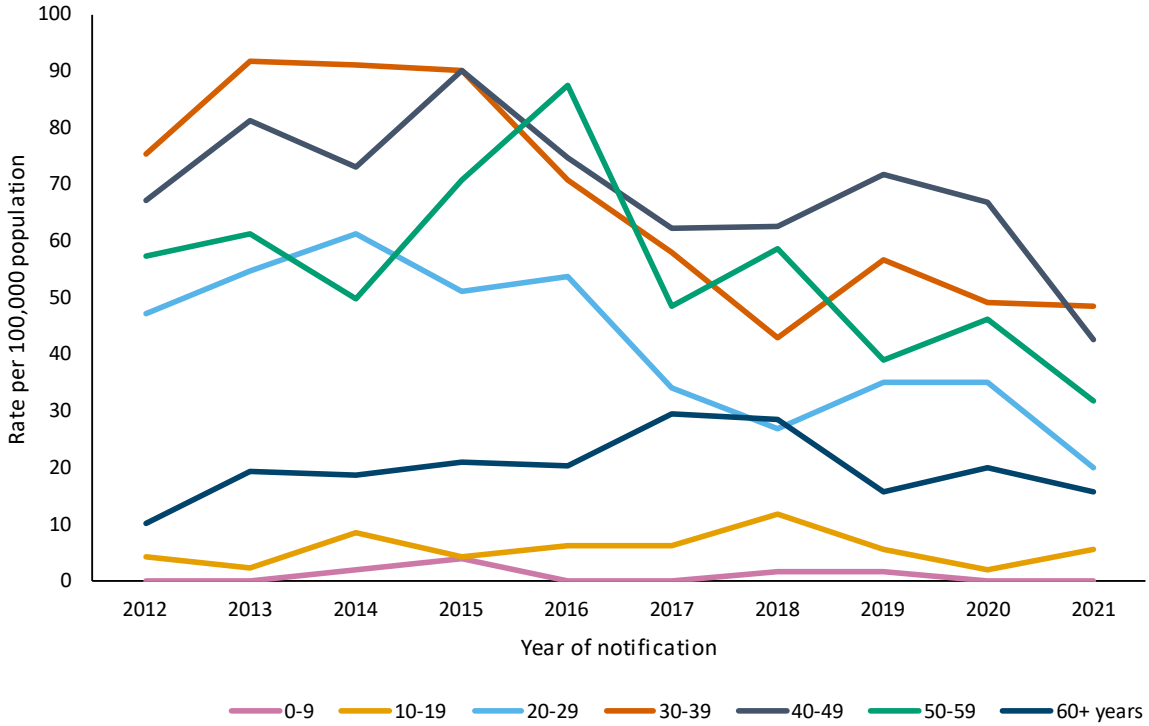


Source: ACT Health Notifiable Diseases Management System.

Age-specific notification rates per 100,000 population decreased across most age groups in the study period (Figure 4). The notification rate among ACT residents aged 60 years and over increased overall compared with the notification rate in 2012. However, a decrease in the notification rate per 100,000 population is evident from 2019 onward. The notification rate per 100,000 population for 10-19 years older remained stable through the study period, however, it remained low compared with other age groups. Notification rates per 100,000 population were

highest among ACT residents aged 30-49 years, while children had the lowest notification rates per 100,000 across the study period.

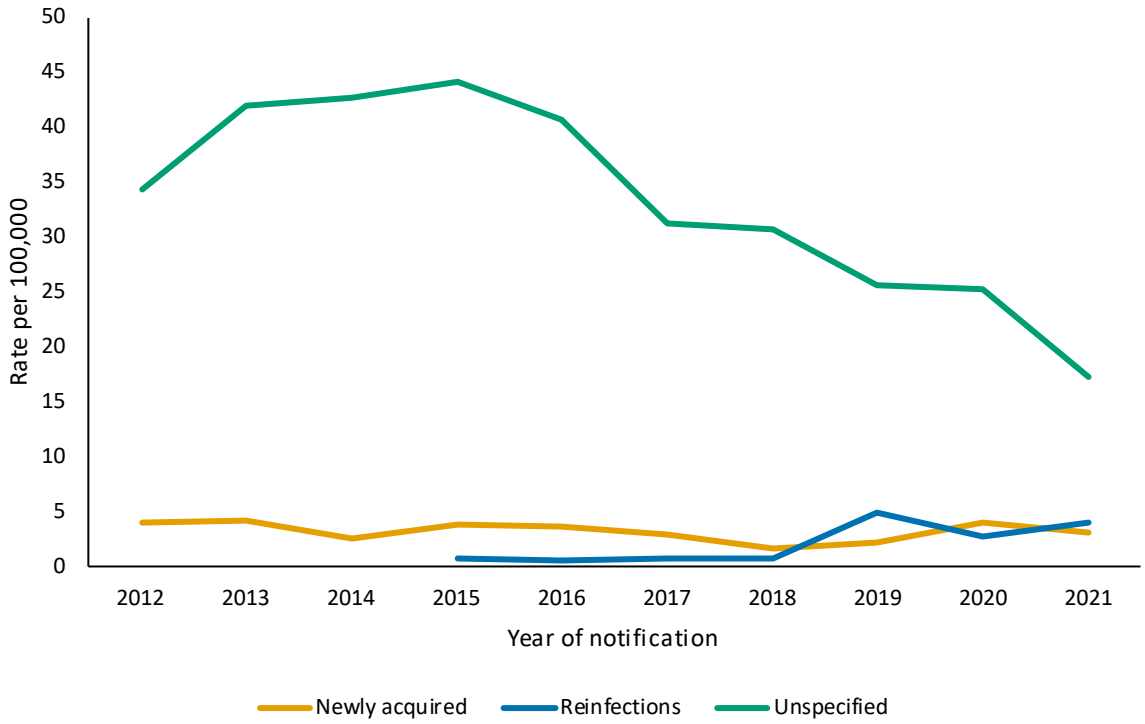
Figure 4: Age-specific notification rate per 100,000 population by year, 2012 to 2021, Australian Capital Territory



Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C.

The notification rate for hepatitis C cases of unspecified duration per 100,000 population decreased from 2016 to 2021 (Figure 5). The rate of newly acquired cases of hepatitis C remained relatively stable through the study period between 3 and 4 notifications per 100,00 population. Since the introduction of a definition and follow up of reinfections in 2015, the rate per 100,000 population has increased, with a notable increase in 2019.

Figure 5: Notification rate per 100,000 population by disease classification and by year, 2012 to 2021, Australian Capital Territory



Source: ACT Health Notifiable Diseases Management System.

Description of cases

The majority of hepatitis C notifications (87%, 1360/1555) were classified as unspecified, 64% (996/1555) of cases were male and the mean age was 41 years (range 0-90 years, IQR 31-50 years, standard deviation 13.2 years). About one fifth (22.8%, 355/1555) of cases had an unknown Indigenous status or did not have an Indigenous status recorded, and 11.2% (174/1555) of cases identified as Aboriginal and Torres Strait Islander. Most cases were born in Australia (65.2% 1012/1555) however 23.1% (359/1555) cases have an unknown country of birth (Table 1).

The most common ABS regions of birth among the 184 overseas-born cases were South-East Asia (19.0%, 35/184), Northern and Western Europe (17.9%, 33/184), Southern and Eastern Europe (14.7%, 27/184), and Southern and Central Asia (14.7%, 27/184).

Table 1: Sociodemographic characteristics of hepatitis C cases by disease classification

Characteristic		Newly acquired N (%)	Unspecified N (%)	Reinfection N (%)	Total hepatitis C cases N (%)
Total		132	1360	63	1555
Sex	Male	91 (69.0%)	857 (63.0%)	48 (76.2%)	996 (64.0%)
	Female	41 (31.0%)	503 (37.0%)	15 (23.8%)	559 (36.0%)
10-year age group	0-9 years	<5 (<3.8%)	<5 (<0.4%)	0 (0.0%)	5 (0.3%)
	10-19 years	<5 (<3.8%)	24 (1.8%)	0 (0.0%)	28 (1.8%)
	20-29 years	67 (50.8%)	216 (15.9%)	10 (15.9%)	293 (18.8%)
	30-39 years	34 (25.8%)	389 (28.6%)	19 (30.2%)	442 (28.4%)
	40-49 years	16 (12.1%)	344 (25.3%)	26 (41.3%)	386 (24.8%)
	50-59 years	6 (4.6%)	246 (18.1%)	8 (12.7%)	260 (16.7%)
	60 years +	<5 (<3.8%)	139 (10.2%)	0 (0.0%)	141 (9.1%)
Indigenous status	Aboriginal and Torres Strait Islander	25 (18.9%)	134 (9.9%)	15 (23.8%)	174 (11.2%)
	Non-Indigenous	106 (80.3%)	872 (64.1%)	48 (76.2%)	1026 (66.0%)
	Unknown	<5 (<3.8%)	354 (26.0%)	0 (0.0%)	355 (22.8%)
Country of birth	Australian born	119 (90.2%)	832 (61.2%)	61 (96.8%)	1012 (65.1%)
	Overseas born	12 (9.1%)	170 (12.5%)	<5 (<7.9%)	184 (11.83%)
	Unknown	<5 (<3.8%)	358 (26.3%)	0 (0.0%)	359 (23.1%)

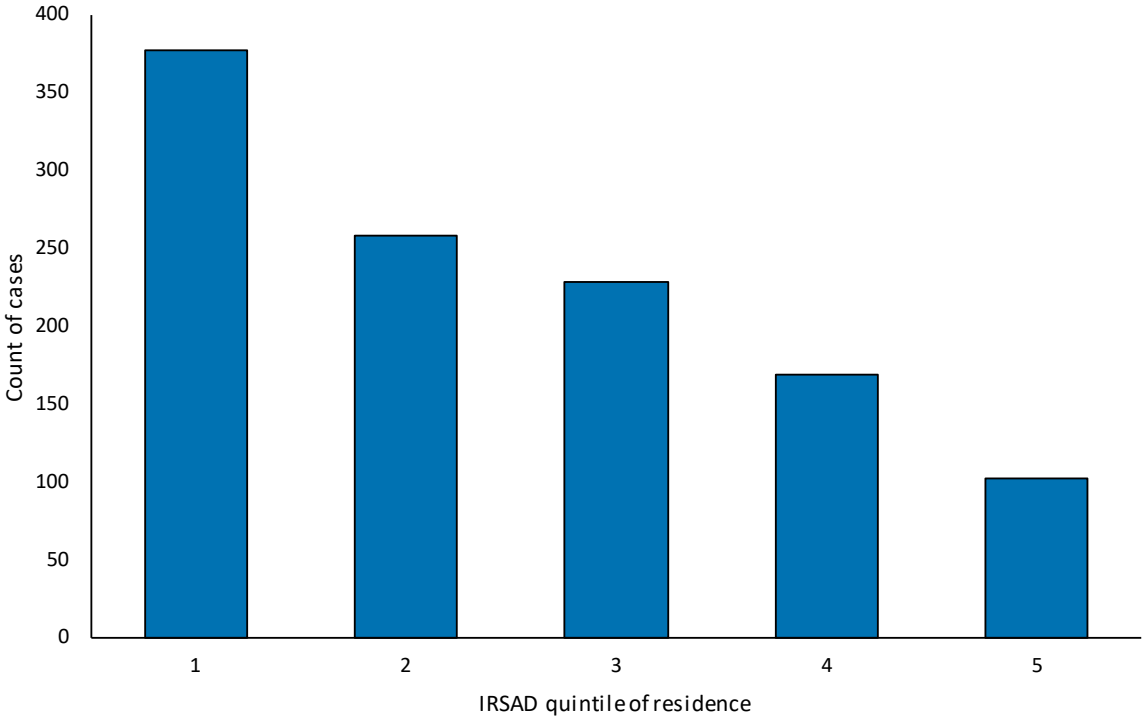
Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C
Note: Unspecified cases are not routinely followed up.

Socioeconomic status

A total of 305 cases were residing in a correctional facility at the time of diagnosis, 39 cases had no fixed address and 47 cases had an unknown address. A further 31 cases resided in an SA2 that did not have an IRSAD calculated in 2016.

The number and proportion of the remaining 1,135 hepatitis C notifications by IRSAD quintile is shown in Figure 6. One third of notifications (33.3%, 378/1135) with a known address resided in an area with the greatest relative disadvantage in the Australian Capital Territory.

Figure 6: Index of Relative Socioeconomic Advantage and Disadvantage 2016 quintile of hepatitis C cases with a known, fixed, non-correctional centre address (n=1135)



Source: ACT Health Notifiable Diseases Management System, Australian Bureau of Statistics Index for Relative Socioeconomic Advantage and Disadvantage.

Note: This chart excludes cases without a known address, no fixed address, or residing in a correction centre at time of diagnosis. Quintile 1 = lowest relative advantage, quintile 5 = highest relative advantage.

Diagnosis and testing

Diagnosing clinician

Almost half of hepatitis C notifications (48.2%, 749/1555) were diagnosed in a primary care facility (Table 2). While primary care remains the most common diagnosing facility for unspecified cases, newly acquired (40.9%, 54/132) and reinfection (40.0%, 25/63) notifications were most commonly diagnosed in a correctional facility.

Table 2: Diagnosing clinician of hepatitis C cases by disease classification

Diagnosing clinician	Newly acquired N (%)	Unspecified N (%)	Reinfection N (%)	Total hepatitis C cases N (%)
Blood and tissue donation	0 (0.0%)	14 (1.0%)	0 (0.0%)	14 (0.9%)
Correctional facility	54 (40.9%)	217 (16.0%)	25 (40.0%)	296 (19.0%)
Drug and alcohol services	9 (6.8%)	58 (4.3%)	<5 (7.9%)	71 (4.6%)
Hospital	30 (22.7%)	353 (26.0%)	13 (20.6%)	396 (25.5%)
Primary care	39 (29.6%)	689 (50.7%)	21 (33.3%)	749 (48.2%)
Other	0 (0.0%)	29 (2.1%)	0 (0.0%)	29 (1.9%)

Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C.
Note: Unspecified cases of hepatitis C are not routinely followed up.

Diagnostic tests

The majority of cases were diagnosed with both serological and nucleic acid testing (Table 3). However, only 51.8% of unspecified cases had both diagnostic tests conducted, compared with 84.9% of newly acquired cases. By definition, all notified reinfections of hepatitis C included a PCR result.

Table 3: Diagnostic tests performed for hepatitis C cases at time of notification by disease classification

Diagnostic test conducted		Newly acquired N (%)	Unspecified N (%)	Reinfection N (%)	Total hepatitis C cases N (%)
Serology	Yes	128 (97.0%)	1237 (91.0%)	26 (41.3%)	1392 (89.5%)
	No	<5 (<3.8%)	94 (6.9%)	37 (58.7%)	134 (8.6%)
	Unknown	0 (0.0%)	26 (2.1%)	0 (0.0%)	29 (1.9%)
PCR	Yes	116 (87.9%)	828 (60.9%)	63 (100.0%)	1006 (64.7%)
	No	16 (12.1%)	477 (35.1%)	0 (0.0%)	494 (31.8%)
	Unknown	0 (0.0%)	55 (4.0%%)	0 (0.0%)	55 (3.5%)
Both Serology and PCR	Yes	112 (84.9%)	705 (51.8%)	26 (41.3%)	843 (54.2%)
	No	20 (15.1%)	571 (42.0%)	37 (58.7%)	623 (40.4%)
	Unknown	0 (0.0%)	84 (6.2%)	0 (0.0%)	84 (5.4%)

Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C.
Note: Unspecified cases of hepatitis C are not routinely followed up. Testing at a separate time to the initial notification that returned a negative result were not notified to ACT Health.

Reason for testing

The reason for testing was not able to be determined for 44.8% (696/1555) of all hepatitis C cases, and over half (50.4%, 684/1360) of unspecified cases. The most common, known reasons for testing among all hepatitis C cases are screening in correctional facilities, screening for sexually transmitted infections, and abnormal liver function tests in the absence of hepatitis symptoms (Table 4). One third of all newly acquired and reinfection cases were tested as a part of a prison screen.

The most common other reasons for testing for hepatitis C not covered within the Australian Government Department of Health and Ageing enhanced surveillance data specifications were a health screening for another condition (76 notifications, 38.2% of other responses), screening for blood-borne viruses (44 cases, 22.1% of other responses), a known history of hepatitis C but the first detection in the ACT (41 cases, 20.6% of other response), and health checks for migration or visa applications (17 cases. 8.5% of other responses). The most common conditions for health screening were a general health screen or check-up, monitoring the progress of HIV infection, and cancer diagnosis (including hepatocellular carcinoma).

Table 4: Reason for testing for hepatitis C cases by disease classification

Reason for testing	Newly acquired N (%)	Unspecified N (%)	Reinfection N (%)	Followed up cases (Newly acquired & reinfections) N (%)	Total hepatitis C cases N (%)
Investigation of symptomatic hepatitis	15 (11.4%)	65 (4.8%)	<5 (<7.9%)	18 (9.3%)	83 (5.3%)
Abnormal liver function test (not symptomatic)	11 (8.3%)	68 (5.0%)	<5 (<7.9%)	13 (6.7%)	81 (5.2%)
Blood or organ donor screen	0 (0.0%)	13 (1.0%)	0 (0.0%)	0 (0.0%)	13 (0.8%)
Prison screen	45 (34.1%)	180 (13.3%)	20 (31.8%)	65 (33.5%)	245 (15.8%)
Antenatal screen	9 (6.8%)	49 (3.6%)	<5 (<7.9%)	10 (5.2%)	59 (3.8%)
Drug/alcohol screen	16 (12.1%)	22 (1.6%)	10 (15.9%)	26 (13.4%)	48 (3.1%)
STI screen	12 (9.1%)	76 (5.6%)	<5 (<7.9%)	16 (8.2%)	92 (5.9%)
Occupational exposure (exposed)	0 (0.0%)	5 (0.4%)	0 (0.0%)	0 (0.0%)	5 (0.3%)
Perioperative	0 (0.0%)	6 (0.4%)	<5 (<7.9%)	<5 (<2.6%)	8 (0.5%)
Patient request	10 (7.6%)	9 (0.7%)	<5 (<7.9%)	11 (5.7%)	20 (1.3%)
Research or study	<5 (<3.8%)	<5 (<0.4%)	0 (0.0%)	<5 (<2.6%)	<5 (<0.3%)
Other	10 (7.6%)	179 (13.2%)	10 (15.9%)	20 (10.3%)	199 (12.8%)
Unknown (not recorded)	<5 (<3.8%)	684 (50.4%)	10 (15.9%)	13 (6.7%)	697 (44.9%)

Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C.
Note: Unspecified cases of hepatitis C are not routinely followed up.

Reinfections

The majority of reinfections were diagnosed with the presence of a negative PCR result in the previous 24 months (71.4%, 45/63) compared with evidence of genotypic change (28.6%, 18/63). Reinfections were most commonly diagnosed in a correctional centre (39.6% 25/63) or in primary care (33.3%, 21/63).

Risk factors

Injecting drug use

Overall, 252 cases disclosed injecting drug use within two years of their hepatitis C diagnosis (Table 5). A further 44 cases disclosed a history of injecting drug use more than two years before their diagnosis. However, most cases (80.2%, 1246/1555) have an unknown history of injecting drug use. This is largely comprised of unspecified cases, who are not routinely followed up.

Among cases who are routinely followed up by public health nurses, 83.5 % (162/194) of newly acquired cases and reinfections disclosed injecting drug use within two years of their diagnosis. Newly acquired cases more commonly disclosed injecting drug use within two years of their diagnosis (90.9%) compared with reinfections (67.7%).

Table 5: Injecting drug use history of hepatis C cases by disease classification

Injecting drug use history	Newly acquired N (%)	Unspecified N (%)	Reinfection N (%)	Followed up cases (Newly acquired & reinfections) N (%)	Total hepatitis C cases N (%)
Injecting drug use in the previous two years	120 (90.9%)	92 (6.7%)	42 (67.7%)	162 (83.5%)	254 (16.4%)
Injecting drug use but not in the previous 2 years	<5 (<4%)	35 (2.7%)	7 (11.3%)	8 (4.1%)	44 (2.8%)
Never injected drugs	9 (6.8%)	<5 (<0.4%)	0 (0.0%)	9 (4.6%)	11 (0.8%)
Injecting drug use unknown	<5 (<4%)	1228 (90.4%)	13 (21.0%)	16 (8.2%)	1243 (80.0%)

Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C.
Note: Unspecified cases of hepatitis C are not routinely followed up.

Other risk factors

Most hepatitis C cases had no additional risk factors recorded (Table 6). The highest frequency risk factors recorded (not including injecting drug use history) were imprisonment before diagnosis, a sexual partner of the opposite sex with hepatitis C, and a household contact with hepatitis C.

In addition to the risk factors required in the Australian Government Department of Health and Ageing's enhanced data specifications, 41 cases had experienced homelessness before or at the time of their diagnosis, and 8 cases had reported a sexual partner with hepatitis C, but the sex of the partner was not recorded (Table 7). The records of 27 cases contained explicit mention of sharing needles and/or injecting equipment, and fourteen of these cases disclosed sharing unsterile needles and/or injecting equipment while in a correctional facility.

Table 6: Risk factors (excluding injecting drug use) of hepatitis C cases, Australian Government Department of Health and Ageing specifications, by disease classification

Risk factor	Newly acquired N (%)	Unspecified N (%)	Reinfection N (%)	Total hepatitis C cases N (%)
Occupational needlestick/biohazardous injury in healthcare worker	0 (0.0%)	<5 (<0.4%)	0 (0.0%)	<5 (<0.3%)
Occupational needlestick/biohazardous injury in non-healthcare worker	<5 (<3.7%)	<5 (<0.4%)	0 (0.0%)	<5 (<0.3%)
Surgical work	0 (0.0%)	<5 (<0.4%)	0 (0.0%)	<5 (<0.3%)
Tattoos	<5 (<3.7%)	<5 (<0.4%)	<5 (<7.9%)	8 (0.5%)
Perinatal transmission	0 (0.0%)	<5 (<0.4%)	0 (0.0%)	<5 (<0.3%)
Sexual partner of opposite sex with HCV	12 (9.1%)	<5 (<0.4%)	0 (0.0%)	15 (1.0%)
Imprisonment	36 (27.3%)	12 (0.9%)	35 (55.6%)	83 (5.3%)
Household contact with HCV	<5 (<3.7%)	10 (0.7%)	0 (0.0%)	12 (0.9%)
Non-occupational or unspecified needlestick/biohazardous injury	<5 (<3.7%)	<5 (<0.4%)	0 (0.0%)	<5 (<0.3%)
Sexual partner of same sex with HCV	<5 (<3.7%)	0 (0.0%)	0 (0.0%)	<5 (<0.3%)
Non-IDU remote risk (non-IDU associated risk identified, but not in the 24 months prior to diagnosis)	0 (0.0%)	<5 (<0.4%)	0 (0.0%)	<5 (<0.3%)
Other risk within the 24 months prior to diagnosis (specify in other risk details)	5 (3.8%)	<5 (<0.4%)	9 (14.3%)	15 (1.0%)
Risk unable to be determined	<5 (<3.7%)	<5 (<0.4%)	0 (0.0%)	<5 (<0.3%)
Unknown (not recorded)	11 (8.3%)	1267 (93.2%)	12 (19.0%)	1299 (83.5%)

Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C.

Note: Unspecified cases of hepatitis C are not routinely followed up. Multiple risk factors could be selected for individual cases, totals may not sum to 100%. The following risk factors had zero responses and were excluded from the table: Blood/blood products/tissues in Australia, Blood/blood products/tissues overseas, major dental surgery, Haemodialysis, Acupuncture, ear or body piercing, Health care worker with no documented exposure, Organ transplantation in Australia, Organ transplantation overseas.

Table 7: Risk factors (excluding injecting drug use) of hepatitis C cases, categorisation of 'Other' risks, by disease classification

Risk factor	Newly acquired N (%)	Unspecified N (%)	Reinfection N (%)	Total hepatitis C cases N (%)
Sexual partner with HCV, sex of partner not specified	5 (3.8%)	<5 (<0.4%)	0 (0.0%)	8 (0.5%)
Experienced homelessness	5 (3.8%)	32 (2.4%)	<5 (<7.9%)	41 (2.6%)
Known needle or injecting equipment sharing	8 (6.1%)	10 (0.7%)	9 (14.5%)	27 (1.7%)

Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C.

Note: Unspecified cases of hepatitis C are not routinely followed up. Multiple risk factors could be selected for individual cases, totals may not sum to 100%. Risk factors collated from review of text responses for 'Other' in Table 7, only risk factors with five or more total responses shown.

Comparison by disease classification

Table 8 shows sociodemographic characteristics of hepatitis C cases by disease classification. Overall, newly acquired cases and those with reinfections were more commonly males born in Australia compared with unspecified cases. Newly acquired cases were more likely to be younger and disclose injecting drug use within two years of diagnosis compared with unspecified cases and reinfections. There was no statistically significant association between disease classification and the level of relative advantage or disadvantage.

Table 8: Association between sociodemographic characteristics and disease classification

Characteristic		Newly acquired N (%)	Unspecified N (%)	Reinfection N (%)	Test statistic	p-value
Sex	Male	91 (69.0%)	857 (63.0%)	48 (76.2%)	6.04*	0.049
	Female	41 (31.0%)	503 (37.0%)	15 (23.8%)		
Age group	0-29 years	74 (56.1%)	242 (17.8%)	10 (15.9%)	122.19*	<0.01
	30-49 years	50 (37.9%)	733 (53.9%)	45 (71.4%)		
	50 years +	8 (6.1%)	385 (28.3%)	8 (12.7%)		
Indigenous status	Non-Indigenous	106 (80.9%)	872 (86.7%)	48 (76.2%)	7.75*	0.02
	Aboriginal and Torres Strait Islander	25 (19.1%)	134 (13.3%)	15 (23.8%)		
Place of birth	Australia	119 (90.8%)	832 (83.0%)	61 (96.8%)	-^	<0.01
	Overseas born	12 (9.2%)	170 (17.0%)	<5 (<7.9%)		
IRSAD quintile	1-2 – Most relatively disadvantaged	33 (45.8%)	585 (56.6%)	18 (60.0%)	-^	0.345
	3	15 (20.8%)	207 (20.0%)	6 (20.0%)		
	4-5 – Most relatively advantaged	24 (33.3%)	241 (23.3%)	6 (20.0%)		
Injecting drug use status	Injecting drug use in the previous two years	120 (92.3%)	92 (70.2%)	42 (85.7%)	N/A~	N/A~
	Injecting drug use but not in the previous 2 years	<5 (<3.8%)	36 (27.5%)	7 (14.3%)		
	Never injected drugs	9 (6.9%)	3 (2.3%)	0 (0.00%)		

Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C.
Note: Unspecified cases of hepatitis C are not routinely followed up. Unknown responses have been excluded.
* Chi-squared test. ^ Fisher's exact test. ~No appropriate statistical test conducted as one stratum is equal to zero. Fisher's exact test returned a p-value of <0.01, however this is not considered a statistical valid test.

Comparison of DAA period

Table 9 shows the characteristics of hepatitis C cases by period of DAA availability. The sex distribution was similar between the two periods. The proportion of cases with unknown Indigenous status, place of birth, and injecting drug use history was lower in the post DAA

period compared with the pre DAA period. While the proportion of total cases classified as newly acquired was similar between the two periods, an increasing proportion of cases were classified as reinfections in the post DAA period following the introduction of a local definition in 2015.

Table 9: Sociodemographic characteristics of all hepatitis C cases by period of direct-acting antiviral availability

Characteristic		Pre DAA N (%)	Post DAA N (%)
Sex	Male	447 (65.0%)	549 (63.3%)
	Female	241 (35.0%)	318 (36.7%)
Age group	0-9 years	<5 (<0.7%)	<5 (<0.6%)
	10-19 years	9 (1.3%)	19 (2.2%)
	20-29 years	144 (20.9%)	149 (17.2%)
	30-39 years	212 (30.8%)	230 (26.5%)
	40-49 years	166 (24.1%)	220 (25.4%)
	50-59 years	110 (16.0%)	150 (17.3%)
	60 years +	44 (6.4%)	97 (11.2%)
Indigenous status	Non-Indigenous	372 (54.1%)	654 (75.4%)
	Aboriginal and Torres Strait Islander	51 (7.4%)	123 (14.2%)
	Unknown	265 (38.5%)	90 (10.4%)
Place of birth	Australia	345 (50.2%)	667 (76.9%)
	Overseas	57 (8.3%)	127 (14.7%)
	Unknown	286 (41.6%)	73 (8.4%)
IRSAD quintile	1	179 (26.0%)	199 (23.0%)
	2	226 (32.8%)	142 (16.4%)
	3	104 (15.1%)	124 (14.3%)
	4	75 (10.9%)	94 (10.8%)
	5	42 (6.1%)	60 (6.9%)
	Unknown/NA	172 (25.0%)	248 (28.6%)
Disease classification	Newly acquired	56 (8.1%)	76 (8.8%)
	Unspecified	629 (91.4%)	731 (84.3%)
	Reinfection	<5 (<0.7%)	60 (6.9%)
Injecting drug use status	Injecting drug use in the previous two years	89 (12.8%)	165 (19.2%)
	Injecting drug use but not in the previous 2 years	17 (2.5%)	27 (3.1%)
	Never injected drugs	<5 (<0.7%)	8 (0.9%)
	Injecting drug use unknown	583 (84.1%)	660 (76.7%)

Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C.
Note: Unspecified cases of hepatitis C are not routinely followed up. Unknown responses have been excluded.
* Chi-squared test. ^ Fisher's exact test.

When unknown values were excluded, no statistically significant associations between DAA period and sex, Indigenous status, place of birth or socioeconomic status were evident (Table 10). Cases notified before the availability of DAAs were more likely to be younger and of unspecified duration, compared with cases notified after the availability of DAAs. There was no statistically significant difference in the proportion of cases disclosing injecting drug use history between the two periods when unknown values were excluded.

Table 10: Sociodemographic characteristics of hepatitis C cases (excluding those with unknown values) by period of direct-acting antiviral availability

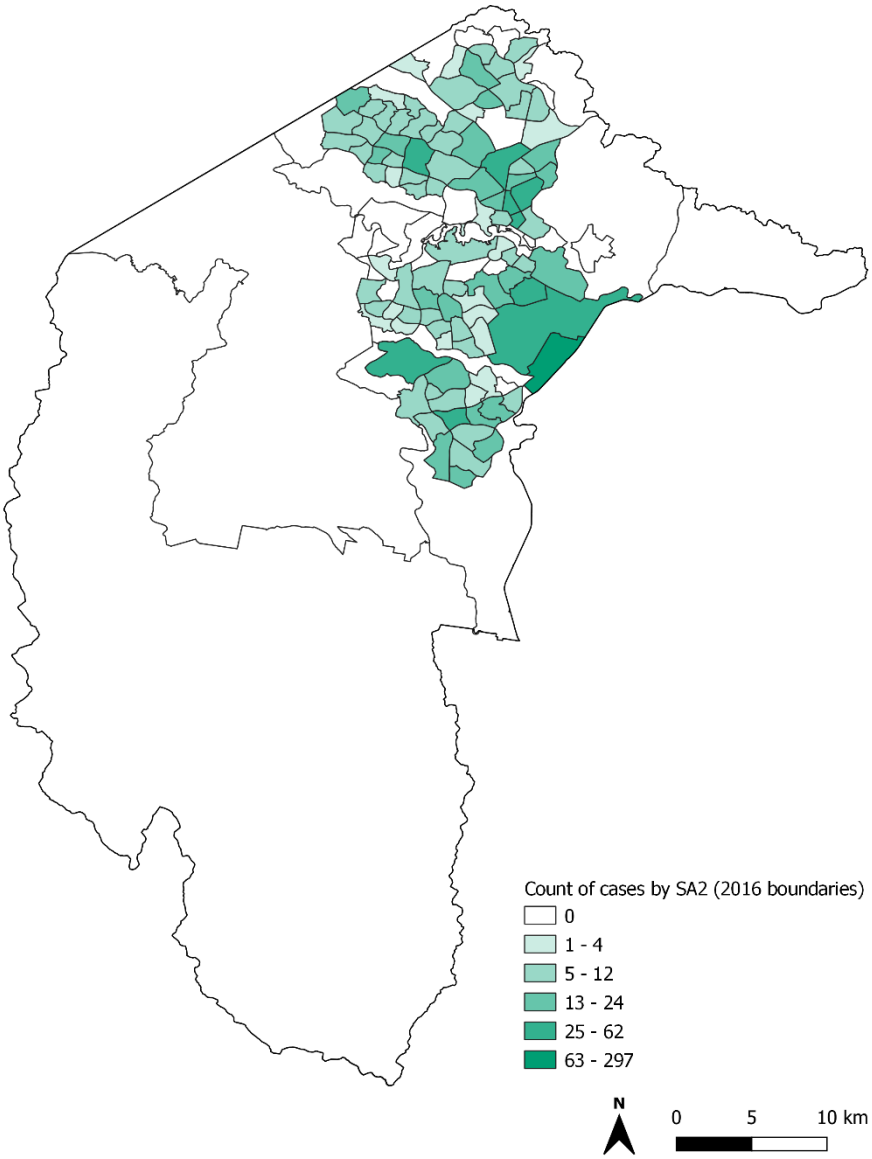
Characteristic		Pre DAA N (%)	Post DAA N (%)	Test statistic	p-value
Sex	Male	447 (65.0%)	549 (36.7%)	0.4531*	0.50
	Female	241 (35.0%)	318 (63.3%)		
Age group	0-29 years	156 (22.7%)	170 (19.6%)	7.9306*	0.02
	30-49 years	378 (54.9%)	450 (51.9%)		
	50 years +	154 (22.4%)	247 (28.5%)		
Indigenous status	Non-Indigenous	372 (87.9%)	654 (84.2%)	3.1456*	0.07
	Aboriginal and Torres Strait Islander	51 (12.1%)	123 (15.8%)		
Place of birth	Australia	345 (85.8%)	667 (84.0%)	0.6760*	0.41
	Overseas	57 (14.2%)	127 (16.0%)		
IRSAD quintile	1-2 – Most relatively disadvantaged	295 (57.2%)	341 (55.1%)	0.7925*	0.67
	3	104 (20.2%)	124 (20.0%)		
	4-5 – Most relatively advantaged	117 (22.7%)	154 (24.9%)		
Disease classification	Newly acquired	56 (8.1%)	76 (8.8%)	-^	<0.01
	Unspecified	629 (91.4%)	731 (84.3%)		
	Reinfection	<5 (<0.7%)	60 (6.9%)		
Injecting drug use status	Injecting drug use in the previous two years	89 (80.9%)	165 (82.5%)	-^	0.94
	Injecting drug use but not in the previous 2 years	17 (15.5%)	27 (13.5%)		
	Never injected drugs	<5 (<4.5%)	8 (4.0%)		

Source: ACT Health Notifiable Diseases Management System, ACT Health enhanced surveillance for hepatitis C.
Note: Unspecified cases of hepatitis C are not routinely followed up. Unknown responses have been excluded.
* Chi-squared test. ^ Fisher's exact test.

Spatial analysis

Figure 7 shows the spatial distribution of hepatitis C notifications between 2012 and 2021 by SA2. A clustering of notifications is evident in eastern Canberra, which contains the ACT's adult correctional facility, the suburb Oaks Estate (where 43% of dwellings are social housing), long-stay caravan parks, and shelters providing temporary accommodation. Additional smaller spatial clusters largely follow the population distribution of the ACT, with greater case numbers evident in the more densely populated inner north, and the most populated SA2s of Belconnen and Kambah.

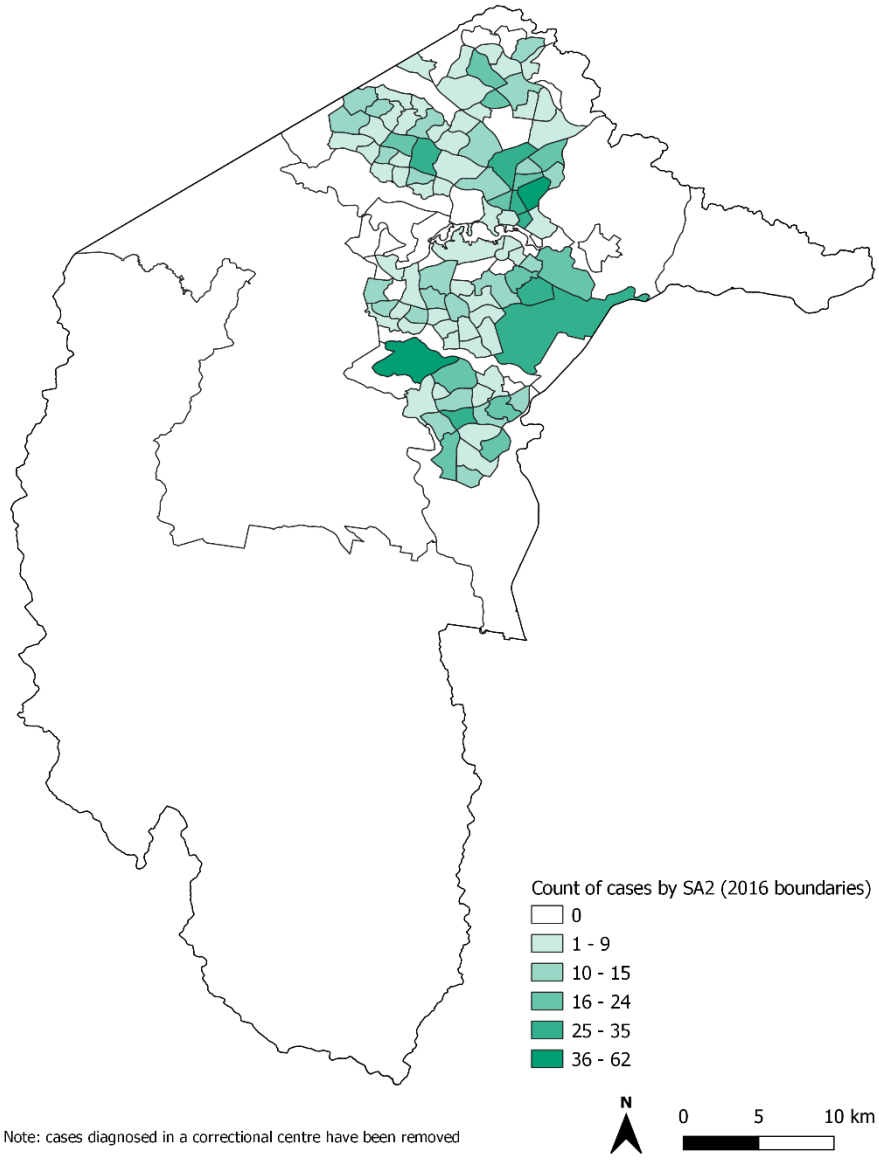
Figure 7: Count of hepatitis C cases by SA2 in the Australian Capital Territory, 2012-2021



Source: ACT Health Notifiable Diseases Management System.

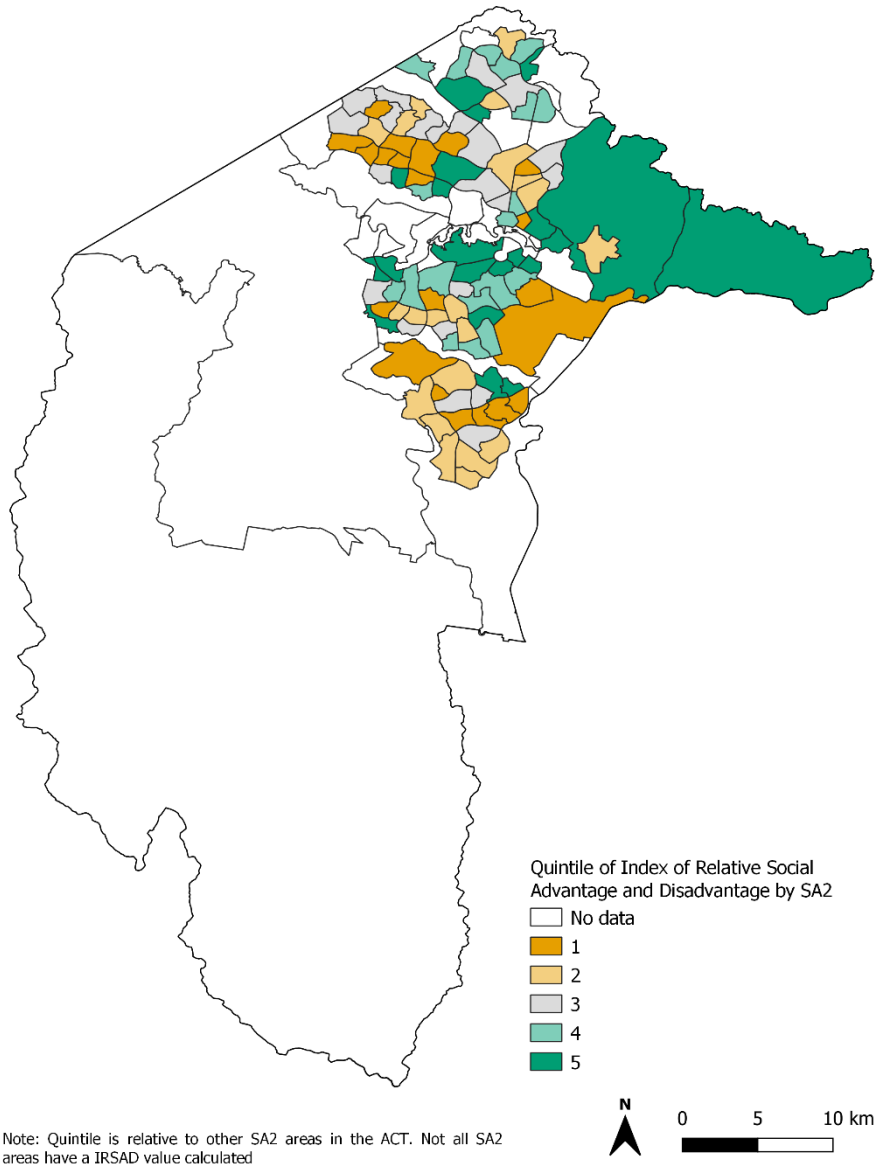
When the substantial number of cases diagnosed in a correctional facility is removed (Figure 8), smaller clusters of hepatitis C cases in SA2s experiencing greater relative socioeconomic disadvantage were evident in the western areas of Belconnen and southern suburbs of Tuggeranong. Few cases resided in relatively advantaged areas of the ACT, including Yarralumla/Deakin, and the northern suburbs of Gungahlin. The spatial distribution of cases largely reflects the locations of SA2 areas with the lowest IRSAD quintiles relative to other areas in the ACT (Figure 9).

Figure 8: Count of hepatitis C cases by SA2 in the Australian Capital Territory, excluding cases diagnosed in correctional centres, 2012-2021



Source: ACT Health Notifiable Diseases Management System.

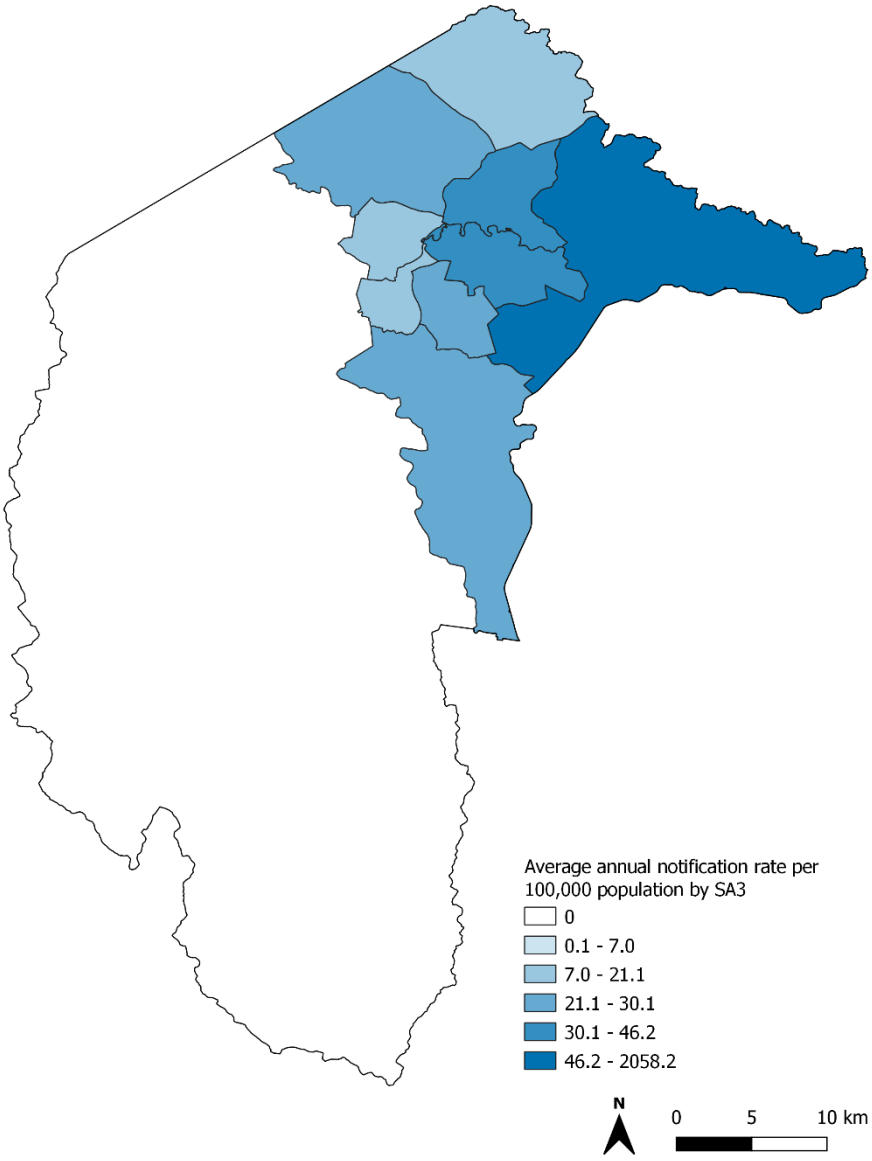
Figure 9: Quintile of Index of Relative Social Advantage and Disadvantage by SA2, 2016



Source: Australian Bureau of Statistics, SEIFA 2016.

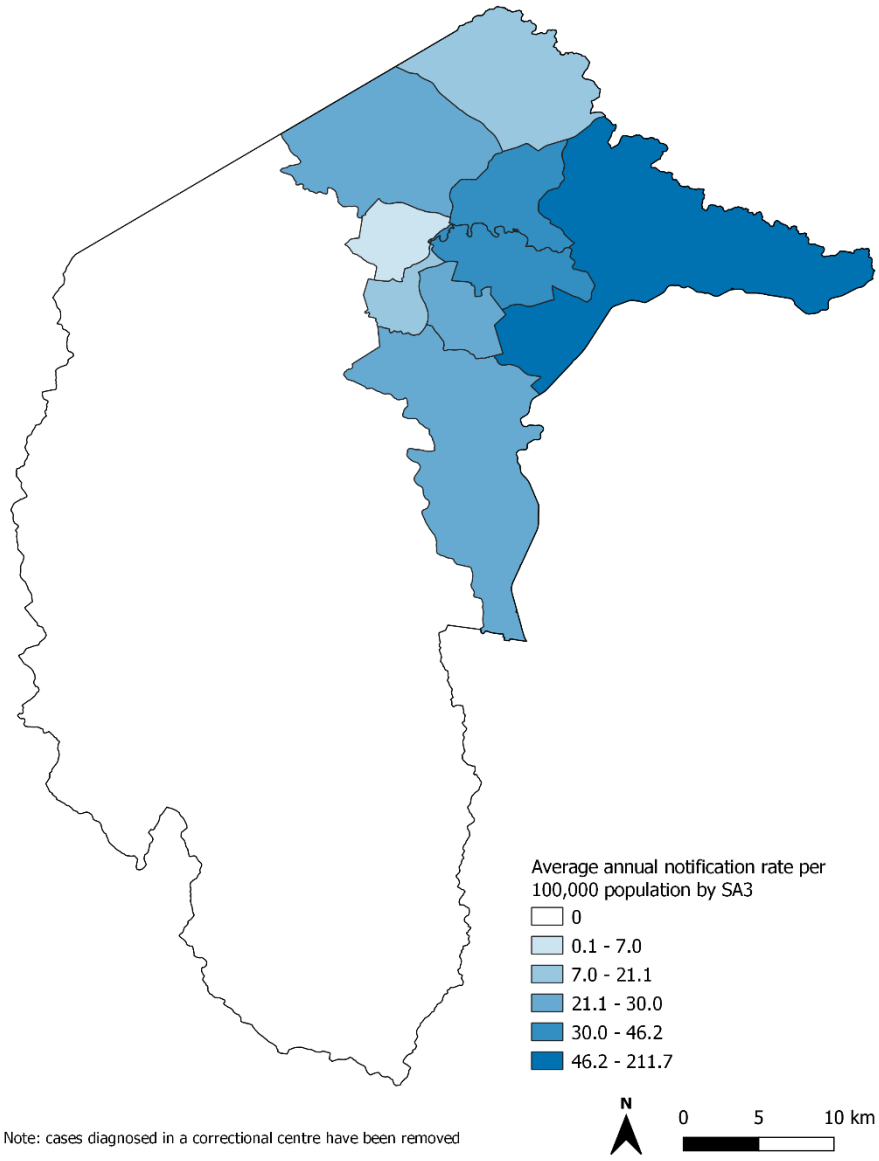
Figure 10 and Figure 11 show the rate of hepatitis C notifications per 100,000 population by SA3. Regardless of the inclusion or exclusion of cases diagnosed in a correctional facility the highest rate per 100,000 population is evident in Canberra East, followed by the Inner North and Inner South of Canberra. The Inner South SA3 contains the long-stay caravan parks of eastern Canberra. The lowest rate per 100,000 was evident in Molonglo, a residential land release area with a relatively low population throughout the study period. However, the estimated population may be underestimated for new residential areas of this SA3 and may artificially deflate the notification rate.

Figure 10: Average annual notification rate per 100,000 population of hepatitis C cases by SA3 in the Australian Capital Territory, 2012-2021



Source: ACT Health Notifiable Diseases Management System, Australian Bureau of Statistics, estimated resident population 30 June 2016.

Figure 11: Average annual notification rate per 100,000 of hepatitis C cases by SA3 in the Australian Capital Territory, excluding cases diagnosed in correctional centres, 2012-2021



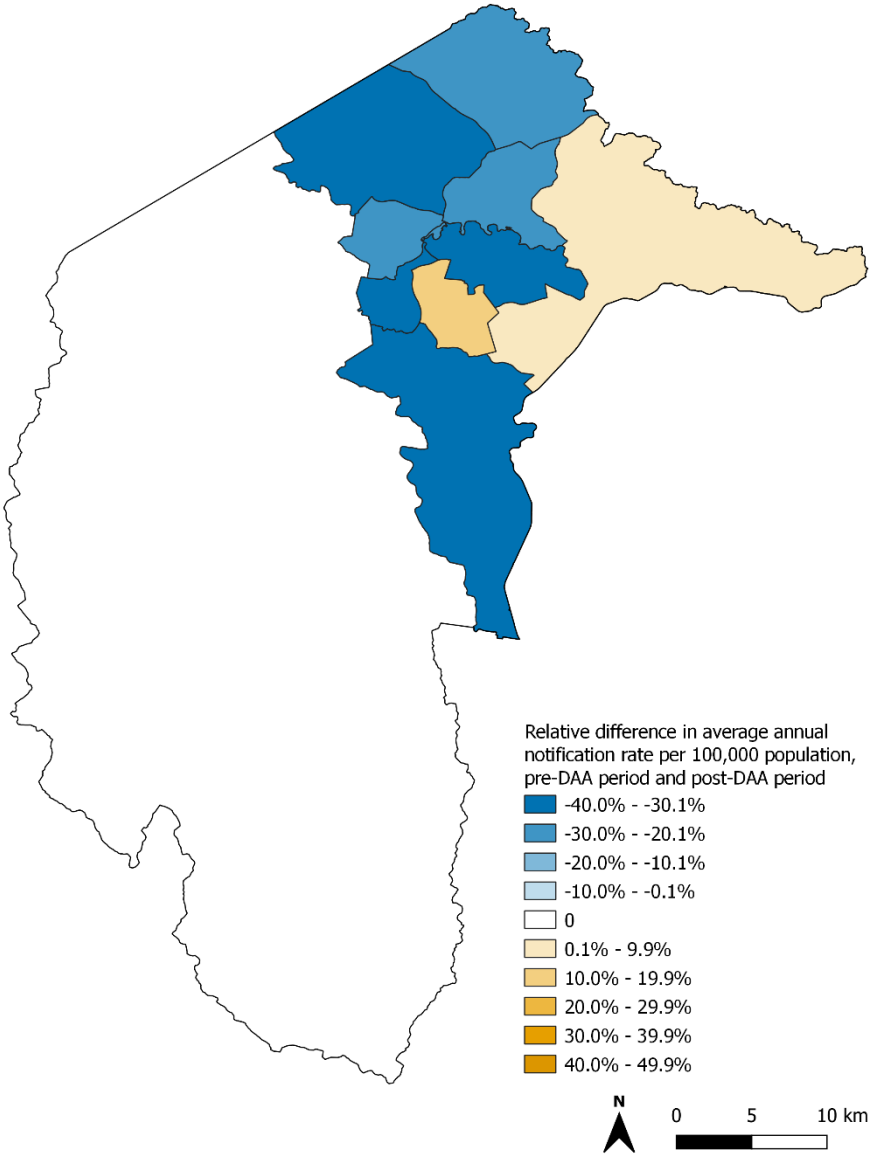
Source: ACT Health Notifiable Diseases Management System, Australian Bureau of Statistics, estimated resident population 30 June 2016.

Figure 12 and Figure 13 show the relative difference in the average annual notification rate in the period before DAA availability (2012-2015) and after the availability of DAAs (2016-2021). The average annual notification rate has decreased across the majority of SA3 regions in the ACT, with the greatest decrease evident in South Canberra, Belconnen, Weston Creek and Tuggeranong.

However, the relative difference in average annual notification rates increased in two SA3 regions, Woden Valley and Canberra East. Woden Valley recorded a total count of between five

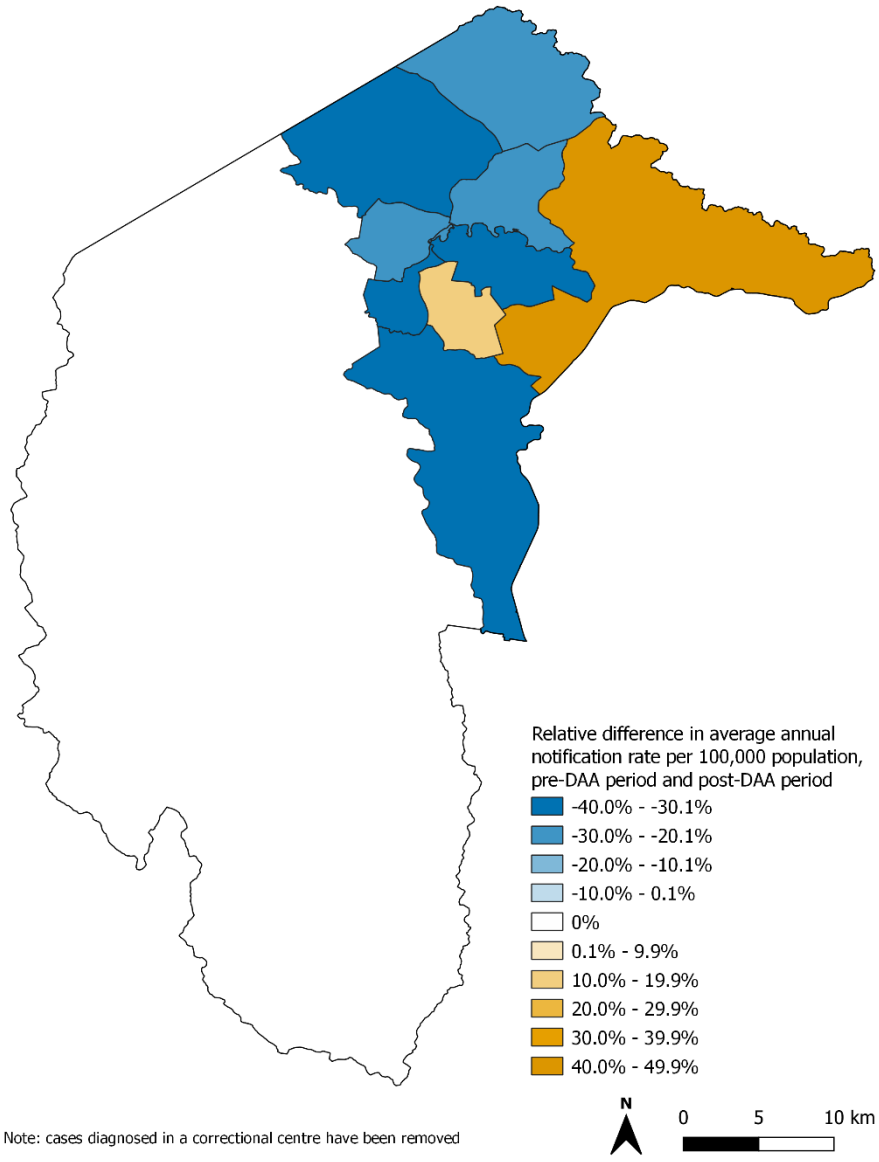
and 13 notifications per year. The relative difference increased further with the removal of notifications in the Hume SA2. While Canberra East recorded fewer than five notifications most years with the exclusion of the Hume SA2, the SA3 also contains a significantly smaller population than most other SA3s in the ACT.

Figure 12: Relative difference in the average annual notification rate of hepatitis C cases by SA3 in the pre-DAA period (2012-2015) and post-DAA period (2016-2021), Australian Capital Territory



Source: ACT Health Notifiable Diseases Management System, Australian Bureau of Statistics, estimated resident population, 2012-2021.

Figure 13: Relative difference in the average annual notification rate of hepatitis C cases by SA3 in the pre-DAA period (2012-2015) and post-DAA period (2016-2021), excluding cases diagnosed in correctional centres, Australian Capital Territory



Source: ACT Health Notifiable Diseases Management System, Australian Bureau of Statistics, estimated resident population, 2012-2021.

Discussion

Notifications have decreased over time

This descriptive cross-sectional study included hepatitis C notifications in the ACT between 2012 and 2021. Rates peaked in 2015 and declined after that. The rate in 2021 was significantly lower than in 2012. The decline observed between 2016 and 2021 is consistent with national trends.[17, 18] This decrease in notifications is likely to be driven by the access to subsidised effective treatments for hepatitis C becoming available in Australia in March 2016, reducing overall prevalence and risks of exposure.

There are other factors that may have contributed to this declining trend. The decline could in part reflect changes in the number of tests conducted in the ACT. However, national studies indicate that testing for hepatitis C has remained relatively stable between 2012 and 2019, with a recent decline in 2020.[17, 18, 55] If these trends apply to the ACT, the effect of changes may have minimal impact on the trends observed in this study.

The sharp decline in the notification rate per 100,000 population in 2020 and 2021 may in part be explained by the introduction of widespread public health measures introduced to limit the effects of the COVID-19 pandemic, including stay-at-home orders and prioritising COVID-19 management in health system resource allocation. Changes in health seeking behaviours were evident across Australia during these first two years of the COVID-19 pandemic, with individuals avoiding primary care and hospital settings due to the perceived risk of contracting COVID-19.[56-60] Simultaneously, healthcare providers moved to telehealth services and limited the number of face-to-face consultations, potentially introducing a barrier to accessing healthcare for those without telephone or internet connections thus reducing the amount of testing.[57, 60-62] There may also have been changes in risk behaviours during this period, however, there is mixed evidence of changes in the use of sterile needles, injecting drug use frequency, and access to needle and syringe programs under emergency public health measures.[63-66]

Reinfections are an important emerging area for public health action

Reinfections have emerged as an important area for the public health response to hepatitis C. While the possibility of spontaneous clearance of the virus is possible, the introduction of DAAs provides an effective treatment for existing cases but does not preclude future infection. The knowledge about the epidemiology of reinfections of hepatitis C in Australia is limited to date, and this study adds additional insight. Reinfections in the ACT were most commonly males in middle age residing in a relatively disadvantaged area of the ACT, and who were identified either while they were in a correctional facility or if they disclosed a history of imprisonment. Compared with newly acquired cases, a smaller proportion of people with a reinfection of hepatitis C disclosed a history of injecting drug use. Injecting drug use behaviour was still disclosed among the majority of reinfections, reflecting the findings of other Australian studies.[26, 27, 32, 49, 52, 53] The disclosure of injecting drug use after reinfection may be linked to different procedures for follow up, individuals feeling ashamed in being engaged in activities

that they were advised against by health professionals and stigma related to reinfection.[67-69] To date, the ACT is the only Australian jurisdiction routinely identifying and following up hepatitis C reinfections,[15, 70-75] limiting the data available to understand the epidemiology of reinfection nationally. The identification and confirmation of reinfections can be relatively resource intensive, however, future epidemiological investigations and public health surveillance should record and follow up reinfections to understand potential repeating risk behaviours and the true burden of hepatitis C.

The association with injecting drug use is evident, but the risk of unsterile injection is unknown

Injecting drug use was the most frequently reported risk factor among people notified with hepatitis C. This is consistent with studies in other jurisdictions, where injecting drug use has been associated with HCV transmission in low prevalence communities.[3, 76, 77] However, this is not necessarily the true risk for the acquisition of hepatitis C or other blood-borne viruses. The risk of transmission lies in the use and sharing of unsterile needles, syringes and other injecting equipment. However, data on sharing unsterile injecting equipment does not form part of the Australian Government Department of Health and Ageing's enhanced surveillance specifications and is not routinely collected at ACT Health. By asking directly about sharing unsterile injecting equipment, we may improve our understanding of HCV transmission in the ACT and can better inform policies and programs aiming to eliminate hepatitis C in the ACT.

The role of other risk factors is less certain

The role of other risk factors for hepatitis C infection in the ACT is less certain. In the data collection process for notified cases, when the case discloses a history of injecting drug use, information about other risk factors is not collected or recorded routinely. This results in significant incompleteness in the enhanced surveillance data and may miss additional significant risk factors and the potential likely source of acquisition. For instance, a person may only inject drugs with sterile equipment but chooses to receive a "backyard" tattoo outside of a licensed premises. Further, the data specifications from the Australian Government Department of Health and Ageing provide for a 'yes' response only for these risk factors, without options for 'no', 'unknown' or 'information not asked' options to confirm if the question was asked of the clinician and if this information is known. While it is recognised that the presence of a risk factor does not necessitate its role in a person's acquisition of HCV, systematically collecting risk factor information may provide a more complete picture of the potential risk behaviours the people with hepatitis C engage in within the ACT.

Correctional facilities are an important setting for diagnosis

Correctional facilities are an important setting for the diagnosis of hepatitis C in the ACT. Two fifths of newly acquired and reinfection notifications in the study period were identified in correctional facilities. Further, a history of imprisonment was identified as a risk factor for just over half of reinfections and over one quarter of newly acquired cases. Correctional facilities in

the ACT routinely screen people at the start of their sentence, enabling the detection of hepatitis C on entry. Blood-borne virus screening at correctional facilities also facilitates the identification of newly acquired cases and reinfections among re-entrants through a frequency of testing that is not common for other populations in the ACT. However, ongoing routine screening does not occur for the duration of an individual's sentence in the ACT, making the source of acquisition difficult to ascertain and potentially delaying treatment.

The risk of blood-borne viruses in correctional facilities and other closed residential settings can be elevated in the absence of access to sterile needles, injecting, tattooing and piercing equipment, and the sharing of available equipment. There is anecdotal evidence in a study of needle sharing within correctional centres in public health follow up reported in this analysis and from previous reviews in the ACT,[78, 79] correlating with a recent case report detailing transmission through unsterile needle sharing within an ACT correctional centre.[54] The introduction of a prison-based needle and syringe program (PNSP) has previously been discussed in the ACT and presents an opportunity to reduce transmission of hepatitis C and other blood-borne viruses by providing sterile equipment in an anonymous, dignified way.[78-80] The ACT has community-based needle and syringe programs in place and the introduction of PNSPs in other jurisdictions has been associated with a lower prevalence of hepatitis C and other blood-borne viruses, lower incidence of unsterile needle sharing, and has not been associated with increased injecting drug use or injuries among staff.[81-84] Reliance on treatment-as-prevention strategies in Australia has only had short term effects on prevalence in correctional facilities to date and may be best complemented with the primary prevention of a needle and syringe program.[85-87] Ongoing screening of people in correctional facilities with their consent may also increase case ascertainment and prompt earlier treatment, potentially reducing the risk of hepatitis C and other blood-borne viruses overall.

Notifications follow a social gradient in the ACT

Outside of correctional facilities, hepatitis C notifications in the ACT appear to follow a social gradient. One third of notifications in the study period reside in areas in the lowest quintile of socioeconomic advantage, well over-represented compared with the ACT population as a whole. This is not a unique finding to the ACT, with a higher prevalence of hepatitis C among people experiencing greater relative socioeconomic disadvantage in North America, Spain, Iran, and the Netherlands.[88-92] The prevalence of hepatitis C in these communities may compound the challenges of social stigma with barriers to access, financial costs, and demands on time, impacting testing and treatment.[90, 91] While the region has a low population and count of notifications, the increase in the average annual notification rate following the availability of DAAs in Canberra East is contrary to the experiences of most of the ACT and may indicate communities in this region have not been serviced adequately for treatment and prevention education. While areas with high overall counts of notifications are important to get the majority of cases treated, the disparities highlighted in this analysis should also be addressed. The presence of spatial clusters in Canberra East, west Belconnen, and Tuggeranong may

provide an opportunity to target hepatitis C education, testing and treatment to communities with the greatest historic notification burden and greatest relative socioeconomic disadvantage.

Limitations

The findings of this study should be considered in light of its limitations. The sociodemographic characteristics and risk factors are collected differently based on the disease classification. Hepatitis C cases of unspecified duration are not followed up due to the volume of notifications received and the personnel resources available for follow up. These practical considerations introduce differential measurement bias compared with newly acquired cases and reinfections, with unspecified cases tending towards unknown or blank responses. The review of original pathology reports identified some additional risk factor information; however, the proportion of unknown responses remains substantial and limits the appropriateness of comparing unspecified cases with newly acquired cases and reinfections.

Further, while existing public health follow up uses the same variables for newly acquired cases and reinfections, the data for reinfections are not stored in a systematic way or in a readily available database. This difference in processes further introduces differential measurement bias as not all variables may be asked or recorded in the same manner as newly acquired cases.

As a descriptive cross-sectional study, the findings represent a snapshot in time and the design of this study limits the ability to determine associations and causal relationships. The public health response to hepatitis C in the ACT relies on passive surveillance of notifications, which likely underestimates the true burden of hepatitis C in the ACT. Further, ACT Health's current notifiable disease management software does not include a person-based identification number, preventing linking initial notifications and subsequent reinfections.

The data collected for this study may be impacted by recall bias, as the majority of enhanced surveillance data are reported by clinicians rather than the person with hepatitis C. Some questions regarding enhanced surveillance may not have been asked by the clinician. Further, a patient may not be willing to disclose potentially stigmatising or incriminating information to their clinician or a public health nurse. These factors impacting recall and disclosure may introduce measurement bias and overestimate or underestimate the extent of some risk factors in the epidemiology of hepatitis C in the ACT.

The spatial analysis relies on geographies, SEIFA calculations and residential population estimates from 2016 as the midpoint of the study. This may not reflect the lived experiences of people with hepatitis C notified in the study period, particularly those diagnosed at the start or the end of the study. For instance, the ACT has undergone significant changes in the urban development of the city centre and removal of social housing, alongside the development of new greenfield suburbs which had relatively low populations in 2016, such as the Molonglo SA3 region. SEIFA calculations have been used to understand the relative socioeconomic status of people with hepatitis C in the ACT, however area-level socioeconomic status may not correlate with individual experiences and relative advantage or disadvantage. Further, the ACT generally

experiences relative socioeconomic advantage compared with other areas of Australia, and the marginal differences between relatively higher and lower areas of the ACT may be lower than in other jurisdictions.

Conclusion

Notifications of hepatitis C have declined in absolute and relative terms during the study period. This decline follows the availability of effective treatment for HCV infection, and a steep decline potentially impacted by changes in health seeking behaviours and healthcare delivery during the COVID-19 pandemic. However, the notification rate for newly acquired infections remained relatively stable throughout this study, and the rate of reinfections has risen since recording began in 2015. While these trends may in part be the result of improved case classifications, HCV reinfections pose a challenge for eliminating hepatitis C in the ACT. This study has highlighted the existing gaps and limitations to current hepatitis C surveillance data, it is evident from the available data that this condition follows a social gradient in the ACT and there are specific settings and geographic areas where communities may benefit from further public health action. With additional support for public health follow up and clinical management, the ACT may successfully reach the elimination target.

Recommendations

This analysis has highlighted the complexity of the public health response to hepatitis C. Further data collection and increased completion of existing variables may assist in further understanding the epidemiology of hepatitis C in the ACT and improving policy actions to eliminate the condition by 2030. In particular, the prevalence and extent of transmission in correctional facilities are unknown and should be a key consideration for eliminating hepatitis C in the ACT.

I suggest the following recommendations in light of the findings and limitations of this analysis:

- explore the feasibility of routinely receiving the number of tests conducted for hepatitis C in the ACT.
- advocate for the addition of a nationally consistent definition for hepatitis C reinfection.
- compile enhanced surveillance data for reinfections in a database or spreadsheet using the same format as newly acquired cases.
- commence collection of the history of sharing needles, syringes and/or injecting equipment (yes, no, unknown, information not asked) as part of routine enhanced surveillance follow up of newly acquired and reinfection cases.
- follow up on other risk factors for all newly acquired and reinfection cases (yes, no, unknown, information not asked), even if a history or current injecting drug use and sharing of unsterile equipment are disclosed.
- prepare a letter for clinicians diagnosing newly acquired cases and reinfections summarising treatment information and a short questionnaire requesting information on the reason for testing, injecting drug use, history of sharing needles, syringes and/or injecting equipment, and select other risk factors for hepatitis C (including tattooing, piercing, known contact with a person with hepatitis C)
- pilot following up newly acquired and reinfections directly with cases who are not in a correctional facility at the time of their diagnosis and who have contact information available.
- explore the feasibility of community education, testing and treatment outreach for hepatitis C in targeted geographic areas with elevated notification counts and rates, including East Canberra, Tuggeranong, and west Belconnen.
- work with ACT Justice and Community Safety Directorate to explore the feasibility of recommencing routine blood-borne virus screening for the duration of sentence/remand in correctional centres in the ACT.
- work with ACT Justice and Community Safety Directorate to explore the feasibility of a prison-based needle and syringe program to protect the health of people in correctional facilities.

Funding for an additional public health nurse at ACT Health's Communicable Disease Control Branch may be required to achieve these recommendations in the future.

Reference list

1. World Health Organization. Global health sector strategy on viral hepatitis 2016-2021: Towards ending viral hepatitis. Geneva: World Health Organization; 2016.
2. Spradling PR. Viral hepatitis. In: Heymann DL, editor. *Contorl of Communicable Diseases Manual*. 20th ed. Washington D.C.: American Public Health Association; 2015. p. 252-74.
3. Dore GJ, Law M, MacDonald M, Kaldor JM. Epidemiology of hepatitis C virus infection in Australia. *J Clin Virol*. 2003;26(2):171-84.
4. Gidding HF, Topp L, Middleton M, Robinson K, Hellard M, McCaughan G, et al. The epidemiology of hepatitis C in Australia: notifications, treatment uptake and liver transplantations, 1997-2006. *J Gastroenterol Hepatol*. 2009;24(10):1648-54.
5. Sievert W, Altraif I, Razavi HA, Abdo A, Ahmed EA, Alomair A, et al. A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt. *Liver Int*. 2011;31 Suppl 2:61-80.
6. Bajis S, Grebely J, Cooper L, Smith J, Owen G, Chudleigh A, et al. Hepatitis C virus testing, liver disease assessment and direct-acting antiviral treatment uptake and outcomes in a service for people who are homeless in Sydney, Australia: The LiveRLife homelessness study. *Journal of Viral Hepatitis*. 2019;26(8):969-79.
7. Brown MA, Gellatley W, Hoffman A, Dowdell L, Camac A, Francois R, et al. Medical complications of homelessness: a neglected side of men's health. *Internal Medicine Journal*. 2019;49(4):455-60.
8. Poulos R, Ferson M, Orr K, Lucy A, Botham S, McCarthy M, et al. Risk factors and seroprevalence of markers for hepatitis A, B and C in persons subject to homelessness in inner Sydney. *Australian and New Zealand Journal of Public Health*. 2007;31(3):247-51.
9. Butler T, Kariminia A, Levy M, Kaldor J. Prisoners are at risk for hepatitis C transmission. *European Journal of Epidemiology*. 2004;19(12):1119-22.
10. Luciani F, Bretaña NA, Teutsch S, Amin J, Topp L, Dore GJ, et al. A prospective study of hepatitis C incidence in Australian prisoners. *Addiction*. 2014;109(10):1695-706.
11. Teutsch S, Luciani F, Scheuer N, McCredie L, Hosseiny P, Rawlinson W, et al. Incidence of primary hepatitis C infection and risk factors for transmission in an Australian prisoner cohort. *BMC Public Health*. 2010;10(1):633.
12. Carrat F, Fontaine H, Dorival C, Simony M, Diallo A, Hezode C, et al. Clinical outcomes in patients with chronic hepatitis C after direct-acting antiviral treatment: a prospective cohort study. *The Lancet*. 2019;393(10179):1453-64.
13. Hajarizadeh B, Cunningham EB, Reid H, Law M, Dore GJ, Grebely J. Direct-acting antiviral treatment for hepatitis C among people who use or inject drugs: a systematic review and meta-analysis. *The Lancet Gastroenterology & Hepatology*. 2018;3(11):754-67.
14. Australian Pharmaceutical Benefits Scheme. *General Statement for Drugs for the Treatment of Hepatitis C*. Canberra: Australian Pharmaceutical Benefits Scheme; 2016.
15. Australian Government Department of Health. *Fifth National Hepatitis C Strategy 2018–2022*. Canberra: Australian Government Department of Health; 2019.
16. Australian Capital Territory Government Health Directorate. *Hepatitis B, Hepatitis C, HIV and Sexually Transmitted Infection: ACT Statement of Priorities 2016-2020*. Canberra: Australian Capital Territory Government Health Directorate; 2016.
17. Kirby Institute. Tracking the Progress 2020: National Hepatitis C Strategy. Sydney: Kirby Institute; 2021.
18. Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia Annual surveillance report 2021. Sydney: Kirby Institute; 2021.
19. Law MG, Dore GJ, Bath N, Thompson S, Crofts N, Dolan K, et al. Modelling hepatitis C virus incidence, prevalence and long-term sequelae in Australia, 2001. *Int J Epidemiol*. 2003;32(5):717-24.
20. Doyle M, Maher L, Graham S, Wand H, Iversen J. Hepatitis C virus prevalence and associated risk factors among Indigenous Australians who inject drugs. *Australian and New Zealand Journal of Public Health*. 2018;42(1):52-6.
21. Gibbs D, Grebely J, Sutherland R, Larney S, Butler K, Dietze PM, et al. Concordance between self-reported and current hepatitis C virus infection status in a sample of people who inject drugs in Sydney and Canberra, Australia. *Drug and Alcohol Review*. 2021;40(7):1349-53.
22. Graham S, Maher L, Wand H, Doyle M, Iversen J. Trends in hepatitis C antibody prevalence among Aboriginal and Torres Strait Islander people attending Australian Needle and Syringe Programs, 1996–2015. *International Journal of Drug Policy*. 2017;47:69-76.

23. Williams B, Howell J, Doyle J, Thompson AJ, Draper B, Layton C, et al. Point-of-care hepatitis C testing from needle and syringe programs: An Australian feasibility study. *Int J Drug Policy*. 2019;72:91-8.
24. Hellard M, Hocking J, Crofts N. The prevalence and the risk behaviours associated with the transmission of hepatitis C virus in Australian correctional facilities. *Epidemiology & Infection*. 2004;132(3):409-15.
25. Snow KJ, Young JT, Preen DB, Lennox NG, Kinner SA. Incidence and correlates of hepatitis C virus infection in a large cohort of prisoners who have injected drugs. *BMC Public Health*. 2014;14(1):1-7.
26. Aitken CK, Lewis J, Tracy SL, Spelman T, Bowden DS, Bharadwaj M, et al. High incidence of hepatitis C virus reinfection in a cohort of injecting drug users. *Hepatology*. 2008;48(6):1746-52.
27. Sacks-Davis R, Aitken CK, Higgs P, Spelman T, Pedrana AE, Bowden S, et al. High Rates of Hepatitis C Virus Reinfection and Spontaneous Clearance of Reinfection in People Who Inject Drugs: A Prospective Cohort Study. *PLOS ONE*. 2013;8(11):e80216.
28. White B, Dore GJ, Lloyd AR, Rawlinson WD, Maher L. Opioid substitution therapy protects against hepatitis C virus acquisition in people who inject drugs: the HITS-c study. *Medical Journal of Australia*. 2014;201(6):326-9.
29. Maher L, Li J, Jalaludin B, Chant KG, Kaldor JM. High hepatitis C incidence in new injecting drug users: a policy failure? *Aust N Z J Public Health*. 2007;31(1):30-5.
30. Maher L, Jalaludin B, Chant KG, Jayasuriya R, Sladden T, Kaldor JM, et al. Incidence and risk factors for hepatitis C seroconversion in injecting drug users in Australia. *Addiction*. 2006;101(10):1499-508.
31. Wand H, Spiegelman D, Law M, Jalaludin B, Kaldor J, Maher L. Estimating population attributable risk for hepatitis C seroconversion in injecting drug users in Australia: implications for prevention policy and planning. *Addiction*. 2009;104(12):2049-56.
32. Aitken CK, Agius PA, Higgs PG, StoovÉ MA, Bowden DS, Dietze PM. The effects of needle-sharing and opioid substitution therapy on incidence of hepatitis C virus infection and reinfection in people who inject drugs. *Epidemiology and Infection*. 2017;145(4):796-801.
33. Awofeso N, Harper SE, Levy MH. Prevalence of exposure to hepatitis C virus among prison inmates, 1999. *Medical Journal of Australia*. 2000;172(2).
34. Sullivan RP, Baird R, Freeman K, Heggie H, Davis JS, Marshall CS, et al. Viral hepatitis in correctional facilities in the Northern Territory of Australia 2003–2017. *BMC Infectious Diseases*. 2021;21(1):584.
35. Miller ER, Bi P, Ryan P. The prevalence of HCV antibody in South Australian prisoners. *Journal of Infection*. 2006;53(2):125-30.
36. Dolan K, Teutsch S, Scheuer N, Levy M, Rawlinson W, Kaldor J, et al. Incidence and risk for acute hepatitis C infection during imprisonment in Australia. *European Journal of Epidemiology*. 2010;25(2):143-8.
37. Dolan KA, Shearer J, White B, Zhou J, Kaldor J, Wodak AD. Four-year follow-up of imprisoned male heroin users and methadone treatment: mortality, re-incarceration and hepatitis C infection. *Addiction*. 2005;100(6):820-8.
38. Hajarizadeh B, Grebely J, Byrne M, Marks P, Amin J, McManus H, et al. Evaluation of hepatitis C treatment-as-prevention within Australian prisons (SToP-C): a prospective cohort study. *The Lancet Gastroenterology & Hepatology*. 2021;6(7):533-46.
39. Cunningham EB, Hajarizadeh B, Bretana NA, Amin J, Betz-Stablein B, Dore GJ, et al. Ongoing incident hepatitis C virus infection among people with a history of injecting drug use in an Australian prison setting, 2005-2014: The HITS-p study. *Journal of Viral Hepatitis*. 2017;24(9):733-41.
40. Boettiger DC, Law MG, Dore GJ, Guy R, Callander D, Donovan B, et al. Hepatitis C testing and re-testing among people attending sexual health services in Australia, and hepatitis C incidence among people with human immunodeficiency virus: analysis of national sentinel surveillance data. *BMC Infectious Diseases*. 2017;17(1):740.
41. Jin F, Prestage GP, Matthews G, Zablotska I, Rawstorne P, Kippax SC, et al. Prevalence, incidence and risk factors for hepatitis C in homosexual men: data from two cohorts of HIV-negative and HIV-positive men in Sydney, Australia. *Sexually Transmitted Infections*. 2010;86(1):25-8.
42. Gamage DG, Read TRH, Bradshaw CS, Hocking JS, Howley K, Chen MY, et al. Incidence of Hepatitis-C among HIV infected men who have sex with men (MSM) attending a sexual health service: a cohort study. *BMC Infectious Diseases*. 2011;11(1):39.
43. Doyle JS, van Santen DK, Iser D, Sasadeusz J, O'Reilly M, Harney B, et al. Microelimination of Hepatitis C Among People With Human Immunodeficiency Virus Coinfection: Declining Incidence and Prevalence Accompanying a Multicenter Treatment Scale-up Trial. *Clinical Infectious Diseases*. 2020;73(7):e2164-e72.
44. Cornelisse VJ, Traeger MW, Wright EJ, Murphy D, Stoové M, Hellard M, et al. Brief Report: Low Incidence of Hepatitis C Among a Cohort of HIV-Negative Gay and Bisexual Men Using HIV Pre-exposure

Prophylaxis (PrEP) in Melbourne, Australia, and the Contribution of Sexual Transmission. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2021;87(4):1011-5.
45. Harney BL, Sacks-Davis R, van Santen DK, Traeger M, Wilkinson AL, Asselin J, et al. The Incidence of Hepatitis C Among Gay, Bisexual, and Other Men Who Have Sex With Men in Australia, 2009–2019. *Clinical Infectious Diseases*. 2021;74(10):1804-11.
46. Seed CR, Kiely P, Keller AJ. Residual risk of transfusion transmitted human immunodeficiency virus, hepatitis B virus, hepatitis C virus and human T lymphotrophic virus. *Internal Medicine Journal*. 2005;35(10):592-8.
47. Reid S, Day CA, Bowen DG, Minnis J, Ludlow J, Jacobs S, et al. Vertical transmission of hepatitis C: Testing and health-care engagement. *Journal of Paediatrics and Child Health*. 2018;54(6):647-52.
48. Hosseini-Hooshyar S, Martinello M, Yee J, Read P, Baker D, Post JJ, et al. Low hepatitis C virus reinfection rate despite ongoing risk following universal access to direct-acting antiviral therapy among people living with HIV. *AIDS*. 2020;34(9):1347-58.
49. Micallef JM, Macdonald V, Jauncey M, Amin J, Rawlinson W, van Beek I, et al. High incidence of hepatitis C virus reinfection within a cohort of injecting drug users. *J Viral Hepat*. 2007;14(6):413-8.
50. Pham ST, Bull RA, Bennett JM, Rawlinson WD, Dore GJ, Lloyd AR, et al. Frequent multiple hepatitis C virus infections among injection drug users in a prison setting. *Hepatology*. 2010;52(5):1564-72.
51. Grebely J, Pham ST, Matthews GV, Petoumenos K, Bull RA, Yeung B, et al. Hepatitis C virus reinfection and superinfection among treated and untreated participants with recent infection. *Hepatology*. 2012;55(4):1058-69.
52. Martinello M, Grebely J, Petoumenos K, Gane E, Hellard M, Shaw D, et al. HCV reinfection incidence among individuals treated for recent infection. *J Viral Hepat*. 2017;24(5):359-70.
53. Carson JM, Dore GJ, Lloyd AR, Grebely J, Byrne M, Cunningham E, et al. Hepatitis C Virus Reinfection Following Direct-Acting Antiviral Treatment in the Prison Setting: The SToP-C Study. *Clinical Infectious Diseases*. 2022.
54. Harkness B, Levy M, Evans R, Wenke J. Why is there still hepatitis C transmission in Australian prisons? A case report. *Harm Reduction Journal*. 2017;14(1):75.
55. Scott N, Sacks-Davis R, Wade AJ, Stoove M, Pedrana A, Doyle JS, et al. Australia needs to increase testing to achieve hepatitis C elimination. *Medical Journal of Australia*. 2020;212(8):365-70.
56. Collyer TA, Athanasopoulos G, Srikanth V, Tiruvoipati R, Matthews C, Mcinnes N, et al. Impact of COVID-19 lockdowns on hospital presentations and admissions in the context of low community transmission: evidence from time series analysis in Melbourne, Australia. *Journal of Epidemiology and Community Health*. 2022;76(4):341-9.
57. Efunnuga H, Higgs P, Walker S, O'Keefe D. Health service utilisation and access for people who inject drugs during COVID-19. *Drug and Alcohol Review*. 2022;41(6):1304-10.
58. Siette J, Seaman K, Dodds L, Ludlow K, Johnco C, Wuthrich V, et al. A national survey on COVID-19 second-wave lockdowns on older adults' mental wellbeing, health-seeking behaviours and social outcomes across Australia. *BMC Geriatrics*. 2021;21(1):400.
59. Sutherland K, Chessman J, Zhao J, Sara G, Shetty A, Smith S, et al. Impact of COVID-19 on healthcare activity in NSW, Australia. *Public Health Research & Practice*.
60. White J, Cavenagh D, Byles J, Mishra G, Tooth L, Loxton D. The experience of delayed health care access during the COVID 19 pandemic in Australian women: A mixed methods exploration. *Health & Social Care in the Community*. 2022;30(4):e1384-e95.
61. De Guzman KR, Snoswell CL, Smith AC. The impact of telehealth policy changes on general practitioner consultation activity in Australia: a time-series analysis. *Australian Health Review*. 2022;46(5):605-12.
62. Sotomayor-Castillo C, Nahidi S, Li C, Hespe C, Burns PL, Shaban RZ. General practitioners' knowledge, preparedness, and experiences of managing COVID-19 in Australia. *Infection, Disease & Health*. 2021;26(3):166-72.
63. Baillie G, Peacock A, Hammoud M, Memedovic S, Barratt M, Bruno R, et al. *Key findings from the 'Australians' Drug Use: Adapting to Pandemic Threats (ADAPT)' Study Wave 4*. Sydney: National Drug and Alcohol Research Centre,; 2021 August.
64. Grau-López L, Daigre C, Palma-Alvarez RF, Sorribes-Puertas M, Serrano-Pérez P, Quesada-Franco M, et al. COVID-19 Lockdown and Consumption Patterns among Substance Use Disorder Outpatients: A Multicentre Study. *European Addiction Research*. 2022;28(4):243-54.
65. Otiashvili D, Mgebrishvili T, Beselia A, Vardanashvili I, Dumchev K, Kiriazova T, et al. The impact of the COVID-19 pandemic on illicit drug supply, drug-related behaviour of people who use drugs and provision of

drug related services in Georgia: results of a mixed methods prospective cohort study. *Harm Reduction Journal*. 2022;19(1):25.
66. Zolopa C, Hoj S, Bruneau J, Meeson J-S, Minoyan N, Raynault M-F, et al. A rapid review of the impacts of "Big Events " on risks, harms, and service delivery among people who use drugs: Implications for responding to COVID-19. *International Journal of Drug Policy*. 2021;92:103127.
67. Goodyear T, Brown H, Browne AJ, Hoong P, Ti L, Knight R. "Stigma is where the harm comes from": Exploring expectations and lived experiences of hepatitis C virus post-treatment trajectories among people who inject drugs. *International Journal of Drug Policy*. 2021;96:103238.
68. Lafferty L, Rance J, Grebely J, Dore GJ, Lloyd AR, Treloar C. Perceptions and concerns of hepatitis C reinfection following prison-wide treatment scale-up: Counterpublic health amid hepatitis C treatment as prevention efforts in the prison setting. *International Journal of Drug Policy*. 2020;77:102693.
69. Pourmarzi D, Smirnov A, Hall L, FitzGerald G, Rahman T. 'I'm over the moon!': patient-perceived outcomes of hepatitis C treatment. *Australian Journal of Primary Health*. 2020;26(4):319-24.
70. State of Queensland (Queensland Health). *Queensland Hepatitis C Action Plan 2019–2022*. Brisbane: Queensland Health; 2019.
71. New South Wales Department of Health. *NSW Hepatitis C Strategy 2022-2025*. Sydney: New South Wales Department of Health; 2022.
72. Northern Territory Department of Health. *Sexually Transmissible Infections and Blood Borne Viruses Strategic and Operational Plan 2019-2023*. Darwin: Northern Territory Department of Health; 2019.
73. South Australian Department of Health and Wellbeing. *South Australian Hepatitis C Implementation Plan 2019-2023*. Adelaide: South Australian Department of Health and Wellbeing; 2020.
74. Victorian Department of Health and Human Services. *Victorian hepatitis C strategy 2016-2020*. Melbourne: Victorian Department of Health and Human Services; 2016.
75. Western Australian Department of Health. *Western Australian Hepatitis C Strategy 2019-2023*. Perth: Western Australian Department of Health; 2019.
76. Han R, Zhou J, François C, Toumi M. Prevalence of hepatitis C infection among the general population and high-risk groups in the EU/EEA: a systematic review update. *BMC Infectious Diseases*. 2019;19(1):655.
77. Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. *The Lancet Infectious Diseases*. 2005;5(9):558-67.
78. Australian Capital Territory Inspector of Correctional Services. *Report of a healthy prison review of the Alexander Maconochie Centre*. Canberra: ACT Inspector of Correctional Services; 2019.
79. Australian Capital Territory Human Rights Commission. *Review of the opioid replacement treatment program at the Alexander Maconochie Centre*. Canberra: ACT Human Rights Commission; 2018.
80. Public Health Association of Australia. Balancing access and safety meeting the challenge of blood-borne viruses in prison: Report for the ACT Government into implementation of a Needle and Syringe Program at the Alexander Maconochie Centre. Canberra: Public Health Association of Australia; 2011.
81. Dolan K, Rutter S, Wodak AD. Prison-based syringe exchange programmes: a review of international research and development. *Addiction*. 2003;98(2):153-8.
82. Lazarus JV, Safreed-Harmon K, Hetherington KL, Bromberg DJ, Ocampo D, Graf N, et al. Health Outcomes for Clients of Needle and Syringe Programs in Prisons. *Epidemiologic Reviews*. 2018;40(1):96-104.
83. Moazen B, Dolan K, Saeedi Moghaddam S, Lotfizadeh M, Duke K, Neuhann F, et al. Availability, Accessibility, and Coverage of Needle and Syringe Programs in Prisons in the European Union. *Epidemiologic Reviews*. 2020;42(1):19-26.
84. Stöver H, Nelles J. Ten years of experience with needle and syringe exchange programmes in European prisons. *International Journal of Drug Policy*. 2003;14(5):437-44.
85. Bartlett SR, Fox P, Cabatingan H, Jaros A, Gorton C, Lewis R, et al. Demonstration of Near-Elimination of Hepatitis C Virus Among a Prison Population: The Lotus Glen Correctional Centre Hepatitis C Treatment Project. *Clinical Infectious Diseases*. 2018;67(3):460-3.
86. Merone L, Ashton S, Harris A, Edwards WS, Preston-Thomas A, Gair R, et al. A complex increase in hepatitis C virus in a correctional facility: bumps in the road. *Australian and New Zealand Journal of Public Health*. 2022;46(3):377-81.
87. Rance J, Lafferty L, Treloar C, Group TS-CS. Expert stakeholder perspectives on the acceptability of treatment-as-prevention in prison: a qualitative substudy of the 'Surveillance and Treatment of Prisoners with Hepatitis C' project (SToP-C). *Addiction*. 2021;116(10):2761-9.
88. Kauhl B, Heil J, Hoebe CJ, Schweikart J, Krafft T, Dukers-Muijrers NH. The Spatial Distribution of Hepatitis C Virus Infections and Associated Determinants--An Application of a Geographically Weighted Poisson Regression for Evidence-Based Screening Interventions in Hotspots. *PLoS One*. 2015;10(9):e0135656.

89. García Comas L, Ordobás Gavín M, Sanz Moreno JC, Ramos Blázquez B, Gutiérrez Rodríguez A, Astray Mochales J, et al. Prevalence of hepatitis C antibodies in the population aged 16–80 years in the Community of Madrid 2008–2009. *Journal of Medical Virology*. 2015;87(10):1697-701.
90. Rezaei F, Noroozi A, Armoon B, Farhoudian A, Massah O, Sharifi H, et al. Social determinants and hepatitis C among people who inject drugs in Kermanshah, Iran: Socioeconomic status, homelessness, and sufficient syringe coverage. *Journal of Substance Use*. 2017;22(5):474-8.
91. Rourke SB, Sobota M, Tucker R, Bekele T, Gibson K, Greene S, et al. Social determinants of health associated with hepatitis C co-infection among people living with HIV: results from the Positive Spaces, Healthy Places study. *Open Med*. 2011;5(3):e120-31.
92. Stopka TJ, Goulart MA, Meyers DJ, Hutcheson M, Barton K, Onofrey S, et al. Identifying and characterizing hepatitis C virus hotspots in Massachusetts: a spatial epidemiological approach. *BMC Infect Dis*. 2017;17(1):294.

APPENDIX A: TARGETED LITERATURE REVIEW METHODS

Abbreviations

aHR	Adjusted hazard ratio
aIRR	Adjusted incidence rate ratio
aOR	Adjusted odds ratio
CI	Confidence interval
DAA	Direct-acting antivirals
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HR	Hazard ratio
IRR	Incidence rate ratio
IQR	Interquartile range
OR	Odds ratio
PY	Person-year

Aim and research questions

The literature review aimed to better understand the epidemiology of reinfection in different Australian populations. I conducted a targeted literature review to answer the following question:

> What is the current evidence for the reinfection of hepatitis C in Australia?

Methods

I searched the PubMed database for peer-reviewed papers. The search was conducted on 27 July 2022 and included all studies published up to that date. The search was conducted using the following Medical Subject Headings (MeSH) terms:

> (Hepatitis C/transmission OR Hepatitis C/epidemiology OR Hepatitis C/diagnosis OR Hepatitis C/classification OR Hepatitis C/complications OR Hepatitis C/ethnology OR Hepatitis C/eitology) AND Australia

The inclusion and exclusion criteria are shown in Table A.1. No limits were placed on the date of publication or the study period to understand changes in prevalence and incidence in sub-populations over time. Pre-prints and grey literature were excluded from this targeted review. All observational study designs were included, including case series, cross-sectional, case-control, and cohort studies.

Table A.1: Inclusion and exclusion criteria for targeted literature review

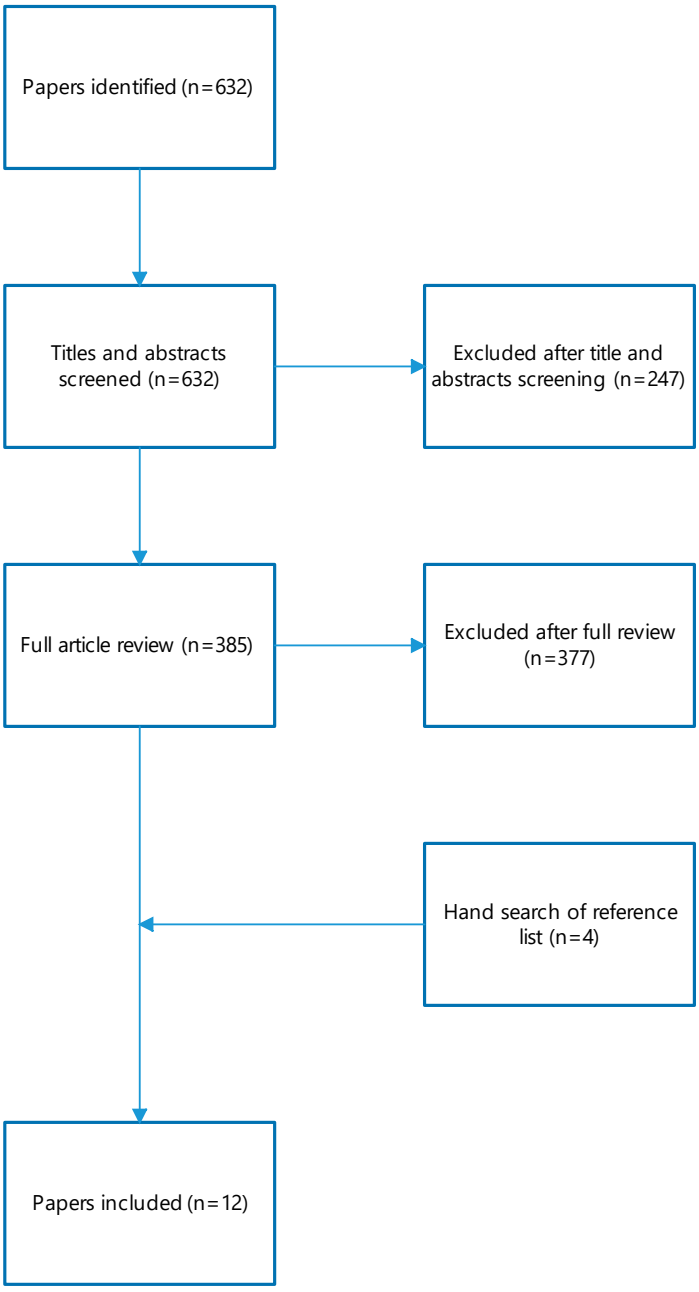
Criterion	Inclusion	Exclusion
Condition	Hepatitis C	All other viral hepatitis All other hepatitis conditions
Location	Australia	All other countries
Language of study	English	All other languages
Year	All	N/A
Study population	All	N/A
Methodology	All observational study designs Clinical trials and randomised control trials	Opinion/comment articles Reviews Modelling
Publication status	Peer-reviewed	Pre-prints Grey literature
Endpoints	Reinfection incidence estimate Transmission chain for reinfection Risk and protective factors for reinfection	Study does not include any of the listed endpoints

I developed a data collection tool in Excel to consistently collate the findings of included studies against the research question, including estimates of the incidence of reinfections, risk and protective factors for reinfection, and transmission chains. Diagnostic methods to identify infection or reinfection, study population, sample size and study period were recorded for all included studies.

Search results

The search returned 632 results (Figure A.1). After the titles and abstracts were reviewed, 247 studies were excluded. Of the remaining 385 articles, 377 were excluded after full text evaluation as they did not meet the inclusion criteria. A hand search of the reference lists of eligible articles identified 4 further studies that met the inclusion criteria. A total of 12 studies were included in the literature review.

Figure A.1: Summary of literature review search



Findings

A summary of the study findings is shown in Table A.2 and Table A.3.

Overall, studies have used a variety of diagnostic tests and treatments over time to define reinfections as new technologies have become available. The majority of studies rely on small samples, particularly older studies, in part reflecting the complexity of treatment and clearance before the availability of direct-acting antivirals (DAAs). Studies have focused on populations historically at greatest risk of hepatitis C; people who inject drugs,[1-6] people imprisoned,[7-10] and people living with HIV,[11, 12] which may impact the generalisability to the general population of the ACT.

Studies in Australia estimated the incidence of reinfections at between 1.1 per 100 person-years among people living with HIV and 46.8 per 100 person-years among people who inject drugs.[2, 11]

The incidence of reinfection was estimated to be highest among people who inject drugs, both in the community and in people who inject drugs while imprisoned.[2, 5] The lowest incidence of reinfection was reported in a study focused on people living with HIV.[11] However, another study comparing people living with HIV and people who were HIV negative found the lowest incidence of reinfection in the latter.[12] Importantly, the incidence of reinfection with hepatitis C virus declined over time within studies, and across studies.[1-5, 9]

Risk factors associated with reinfections explored in these studies include injecting drug use after treatment, frequency of injecting drugs, multiple injecting partners, and condomless anal intercourse.[4, 6, 8, 11, 12] There were mixed findings regarding the association with poorer social functioning and reinfection with hepatitis C virus.[6, 12]

A case series report detailed a transmission event involving needle sharing for injecting drug use within a correctional facility after treatment completion.[10] Sharing needles, syringes and/or injecting equipment was explored in five cohort studies with mixed findings. Four studies found no association,[1, 3-5] however the authors of one of these studies indicated that their findings may be sample-specific,[1] while one study did report a statistically significant adjusted hazard ratio among people who injected drugs while imprisoned.[8]

Age, sex, gender, type of drug injected, age at first injection, any history of imprisonment, continuous or intermittent imprisonment, educational attainment, employment status, living with HIV, or a history of depression were not associated with a risk of reinfection.[3, 4, 6, 8, 12]

The findings of this literature review were synthesised and presented in the Introduction section of this Chapter.

Table A.2: Summary of literature review of hepatitis C reinfections in Australia – cohort studies

Reference	Study period	Study design	Study population	Sample size	Definition of reinfection	Reinfections	Reinfection incidence	Risk factors	Protective factors
Aitken et al High incidence of hepatitis C virus reinfection in a cohort of injecting drug users, *Hepatology*, 2008, 48: 1762-1752	2005-2007	Prospective cohort	People who inject drugs	196 Total follow up in PY not reported	People with a previous HCV infection who had at least one negative PCR test prior to a positive PCR test result in the study period, regardless of treatment.	23 (11.7%)	46.8 per 100 PY (95% CI 31.1–70.3 per 100 PY)	Compared with naïve infections, increased frequency of injection per month associated with reinfection (HR 1.01 (95% CI 1.01-1.02)	-
Aitken et al The effects of needle-sharing and opioid substitution therapy on incidence of hepatitis C virus infection and reinfection in people who inject drugs, *Epidemiology and Infection*, 2017, 145(4), 796-801	2008-2015	Prospective cohort	People who inject drugs	139 Total follow up in PY not reported	People with a previous HCV infection who had at least one negative PCR test prior to a positive PCR test result in the study period, regardless of treatment.	39 (28.1%)	12·4 per 100 PY (95% CI 9.1–17.0 per 100 PY)	None identified. Needle sharing not associated with reinfection (HR 1.85, 95% CI 0.79–4.3), however cross model comparison with naïve infections indicates this may be sample specific (Wald χ 2(1) = 1.46, P = 0.228).	None identified. Accessing opioid substitution therapy not associated with reduced reinfection (HR 0.9, 95% CI 0.45–1.79)
Bate et al High prevalence of late relapse and reinfection in prisoners treated for chronic	2008	Retrospective cohort	People in a correctional facility	74 Total follow up in PY not reported	People who had a positive PCR result after previously treated with standard and	5 (6.8%)	-	-	-

Reference	Study period	Study design	Study population	Sample size	Definition of reinfection	Reinfections	Reinfection incidence	Risk factors	Protective factors
hepatitis C, *Journal of Gastroenterology and Hepatology*, 2010, 25: 1276-1280					pegylated interferon therapy and who had a negative PCR result 6 months following treatment completion				
Carson et al Hepatitis C Virus Reinfection Following Direct-Acting Antiviral Treatment in the Prison Setting: The SToP-C Study, *Clinical Infectious Diseases*, 2022, ciac246,	2014-2019	Prospective cohort	People in a correctional facility	161 Total follow up of 145 PY (range 2-14 months, median 9 months)	People with a previous HCV infection who had a positive PCR result with a strain distinct from their original infection following treatment and a negative PCR result. Treatment varies across the study period.	18	12.5 per 100 PY (95% CI: 7.9–19.8 per 100 PY) Those with recent injecting drug use - 24.6 per 100 PY (95% CI: 14.6–41.5 per 100 PY) Those who had recent injecting drug use and reported sharing needles or injecting equipment - 28.7 per 100 PY (95% CI: 16.3–50.6 per 100 PY)	Factors associated with reinfection were recent IDU with needle/syringe sharing (aHR, 4.74 95% CI: 1.33–16.80), adjusting for level of security at facility, gender, age, continuously/ intermittently imprisoned, frequency of injecting drug use, type of drug, opioid agonist therapy, piercing or tattooing in prison, interpersonal violence in prison, and testing intervals.	No protective factors identified. Adjusting for level of security at facility, gender, age, continuously/ intermittently imprisoned, frequency of injecting drug use, type of drug, opioid agonist therapy, piercing or tattooing in prison, interpersonal violence in prison, and sharing needles or syringes.
Grebely et al Hepatitis C virus reinfection and superinfection among treated	2004-2007	Prospective cohort	General population with previous infection and treated	67 Total follow up in PY not	People who had a positive PCR result with a strain distinct from their	7 (10.4%)	5.0 per 100 PY (95%CI 2.4-10.5 per 100 PY)	Multivariate analysis found greater odds of reinfections among those with poorer social functioning (aOR	None identified

Reference	Study period	Study design	Study population	Sample size	Definition of reinfection	Reinfections	Reinfection incidence	Risk factors	Protective factors
and untreated participants with recent infection, *Hepatology*, 2012, 55(4), 1058-1069				reported, median 1.2 years, no range reported.	original infection following treatment, or a negative PCR result. Treatment was either pegylated interferon or combination pegylated interferon and ribavirin therapy		Among those treated - 4.7 cases per 100 PY (95% CI; 1.9-11.2 per 100 PY) Among those with spontaneous clearance - 6.1 per 100 PY (95% CI; 1.5-24.6 per 100 PY)	6.05, 95% CI, 1.19-30.87) and injecting drug use during follow up (aOR 4.35, 95% CI, 1.09-17.45). Adjusted for sex, age, depression status, HIV infection, injecting drug use prior to enrolment.	
Hajarizadeh et al Evaluation of hepatitis C treatment-as-prevention within Australian prisons (SToP-C): a prospective cohort study, *The Lancet Gastroenterology and Hepatology*, 2021, 6(7): 533-546	2014-2017, 2018-2019	Prospective cohort	People in a correctional facility	725 Total follow up in PY – 579. Range and median not reported.	People who had a previous HCV infection and returned a positive PCR result following a negative result.	54 (7.4%)	9·34 per 100 PY (95% CI 7·15–12·19 per 100 PY) 2014-2017 - 12·36 per 100 PY (95% CI 8·59–17·79 per 100 PY) 2018-2019 – 7.27 per 100 PY (95% CI 4·92–10·76 per 100 PY) Among people who injected drugs at current imprisonment, 2014-2017 – 15.26	Risk factors were not reported separately for naïve infections and reinfections.	Risk factors were not reported separately for naïve infections and reinfections.

Reference	Study period	Study design	Study population	Sample size	Definition of reinfection	Reinfections	Reinfection incidence	Risk factors	Protective factors
							per 100 PY (95% CI 10.23–22.76 per 100 PY) Among people who injected drugs at current imprisonment, 2018-2019 – 9.34 per 100 PY (95% CI 6.15–14.19 per 100 PY)		
Hosseini-Hooshyar et al Low hepatitis C virus reinfection rate despite ongoing risk following universal access to direct-acting antiviral therapy among people living with HIV, *AIDS*, 2020, 34(9): 1347-1358	2014-2018	Prospective cohort	People living with HIV	254 Total follow up of 762 PY (median 2.91 years, IQR 2.23-3.45 years)	The presence of quantifiable HCV RNA after SVR12 or confirmed spontaneous clearance, or the presence of quantifiable HCV RNA between end of treatment and posttreatment week 12 with an HCV genotype or subtype distinct from the primary strain	5 (2.0%)	1.05 per 100 PY overall (95% CI, 0.44–2.53 per 100 PY) Incidence rate decreased over time. Pre DAA availability (2014-2016) - 2.20 per 100 PY (95% CI, 0.71–6.82 per 100 PY) Post DAA availability (2017-2018) - 0.60 per 100 PY (95% CI, 0.15–2.40 per 100 PY)	0.64 per 100 PY (95% CI, 0.09–4.53 per 100 PY) among those reporting injecting drug used <6 months prior 1.57 per 100 PY(95% CI, 0.50–4.86 per 100 PY) among gay, bisexual and other men who have sex with men who reported condomless anal intercourse	DAA availability described as a potential factor may reducing prevalence in population by the authors, however the confidence intervals overlap limiting the strength of any association.

Reference	Study period	Study design	Study population	Sample size	Definition of reinfection	Reinfections	Reinfection incidence	Risk factors	Protective factors
Martinello et al HCV reinfection incidence among individuals treated for recent infection, *Journal of Viral Hepatitis*, 2017, 24(5): 359-370	2004-2015	Cohort	General population with previous infection and treated	120 Total follow up of 135 PY (median 1.08 years, range 0.17, 2.53 years)	Person who had a positive PCR result with a strain distinctive from their original infecting strain after previously treated and negative PCR result after treatment completion. Treatments available vary across study period.	10	7.4 per 100 PY (95% CI 4.0-13.8 per 100 PY) Among those who were HIV negative - 4.5 per 100 PY (95% CI 1.4-13.9 per 100 PY) Among those living with HIV - 10.3 per 100 PY (95% CI 4.9-21.7 per 100 PY) Injecting drug use history - 8.5 per 100 PY (95% CI 4.2-16.9 per 100 PY) Never injected drugs - 4.9 per 100 PY (95% CI 1.2-19.8 per 100 PY) (not significantly different to those who had). Injected drugs at the end/after treatment - 15.5 per 100 PY (95% CI	Injecting drug use after treatment (aIRR 7.86 (95% CI 1.54-76.79) and age over 36 years (aIRR 5.42 95% CI 1.06-52.93), adjusted for HIV infection, mode of transmission, educational attainment, employment status, social function score, sex	None identified

Reference	Study period	Study design	Study population	Sample size	Definition of reinfection	Reinfections	Reinfection incidence	Risk factors	Protective factors
							7.8-31.1 per 100 PY) Did not inject drugs at the end/ after treatment – 2.6 per 100 PY (95% CI 0.6-10.3 per 100 PY)		
Micallef et al High incidence of hepatitis C virus reinfection within a cohort of injecting drug users, *Journal of Viral Hepatitis*, 2006, 14: 413-418	1993-2002	Retrospective cohort	People who inject drugs	18 Total follow up of 29 PY (range 0.3-3.6 years), median not reported	People who had at least one negative PCR test prior to a positive PCR test result in the study period, regardless of treatment. Retrospective testing of existing serological samples	13 (72%)	42 per 100 PY (95% CI, 25–61 per 100 PY)	None identified. No significant association with age, age at first injection, type of drug, gender, sharing of injecting equipment, history of imprisonment.	None identified. No significant association with age, age at first injection, type of drug, gender, sharing of injecting equipment, history of imprisonment.
Pham et al Frequent multiple hepatitis C virus infections among injection drug users in a prison setting. *Hepatology*,	2005-2007	Prospective cohort	People in a correctional facility	87	People who had a positive PCR result with a strain distinctive from their original infecting strain. No requirement for negative	15	40 per 100 PY (95% CI, 33-44 per 100 PY)	-	-

Reference	Study period	Study design	Study population	Sample size	Definition of reinfection	Reinfections	Reinfection incidence	Risk factors	Protective factors
2010, 52: 1564-1572					PCR result or treatment.				
Sacks-Davis et al High Rates of Hepatitis C Virus Reinfection and Spontaneous Clearance of Reinfection in People Who Inject Drugs: A Prospective Cohort Study, *PLOS ONE*, 2013, 8(11): e80216	2005-2010	Prospective cohort	People who inject drugs	118 Total follow up in PY not reported	Confirmed - People with a previous HCV infection who had a positive PCR result with a strain distinct from their original infection following a negative PCR result. Possible – sequence data for HCV infection/s not available and two consecutive negative PCR results at least 4 weeks apart prior to next positive detection	9	28.8 per 100 PY, (95%CI: 15.0-55.4 per 100 PY) – confirmed cases only 24.6 per 100 PY (95%CI: 16.8-36.1 per 100 PY) – confirmed and possible cases	In the multivariate analysis, multiple injecting partners, (HR: 3.12; 95%CI: 1.08-9.00, p=0.035) was associated with a confirmed or possible reinfection. Adjusted for age, frequency of injecting, gender, receptive needle sharing in past 12 months, history of injection	In the multivariate analysis, shorter duration of injecting drugs 0.91 (0.83-0.98) was associated with a confirmed or possible reinfection. Adjusted for age, frequency of injecting, gender, receptive needle sharing in past 12 months, number of injecting partners

Table A.3: Summary of literature review of hepatitis C reinfections in Australia – case report

Reference	Study period	Study design	Study population	Sample size	Definition of reinfections	Reinfections	Transmission chain
Harkness et al Why is there still hepatitis C transmission in Australian prisons? A case report, *Harm Reduction Journal*, 2017, 14:75	2016	Case report	People in a correctional facility	1	Person who had a positive PCR result after previously treated with ledipasvir and sofosbuvir and who had a negative PCR 4 weeks after treatment completion	1	A single episode of shared injecting with a known HCV-positive contact in the correctional centre. Injecting equipment had been flushed with diluted bleach between sharing.

Reference list

1. Aitken CK, Agius PA, Higgs PG, StoovÉ MA, Bowden DS, Dietze PM. The effects of needle-sharing and opioid substitution therapy on incidence of hepatitis C virus infection and reinfection in people who inject drugs. *Epidemiology and Infection*. 2017;145(4):796-801.
2. Aitken CK, Lewis J, Tracy SL, Spelman T, Bowden DS, Bharadwaj M, et al. High incidence of hepatitis C virus reinfection in a cohort of injecting drug users. *Hepatology*. 2008;48(6):1746-52.
3. Micallef JM, Macdonald V, Jauncey M, Amin J, Rawlinson W, van Beek I, et al. High incidence of hepatitis C virus reinfection within a cohort of injecting drug users. *J Viral Hepat*. 2007;14(6):413-8.
4. Sacks-Davis R, Aitken CK, Higgs P, Spelman T, Pedrana AE, Bowden S, et al. High Rates of Hepatitis C Virus Reinfection and Spontaneous Clearance of Reinfection in People Who Inject Drugs: A Prospective Cohort Study. *PLOS ONE*. 2013;8(11):e80216.
5. Pham ST, Bull RA, Bennett JM, Rawlinson WD, Dore GJ, Lloyd AR, et al. Frequent multiple hepatitis C virus infections among injection drug users in a prison setting. *Hepatology*. 2010;52(5):1564-72.
6. Grebely J, Pham ST, Matthews GV, Petoumenos K, Bull RA, Yeung B, et al. Hepatitis C virus reinfection and superinfection among treated and untreated participants with recent infection. *Hepatology*. 2012;55(4):1058-69.
7. Bate JP, Colman AJ, Frost PJ, Shaw DR, Harley HA. High prevalence of late relapse and reinfection in prisoners treated for chronic hepatitis C. *Journal of Gastroenterology and Hepatology*. 2010;25(7):1276-80.
8. Carson JM, Dore GJ, Lloyd AR, Grebely J, Byrne M, Cunningham E, et al. Hepatitis C Virus Reinfection Following Direct-Acting Antiviral Treatment in the Prison Setting: The SToP-C Study. *Clinical Infectious Diseases*. 2022.
9. Hajarizadeh B, Grebely J, Byrne M, Marks P, Amin J, McManus H, et al. Evaluation of hepatitis C treatment-as-prevention within Australian prisons (SToP-C): a prospective cohort study. *The Lancet Gastroenterology & Hepatology*. 2021;6(7):533-46.
10. Harkness B, Levy M, Evans R, Wenke J. Why is there still hepatitis C transmission in Australian prisons? A case report. *Harm Reduction Journal*. 2017;14(1):75.
11. Hosseini-Hooshyar S, Martinello M, Yee J, Read P, Baker D, Post JJ, et al. Low hepatitis C virus reinfection rate despite ongoing risk following universal access to direct-acting antiviral therapy among people living with HIV. *AIDS*. 2020;34(9):1347-58.
12. Martinello M, Grebely J, Petoumenos K, Gane E, Hellard M, Shaw D, et al. HCV reinfection incidence among individuals treated for recent infection. *J Viral Hepat*. 2017;24(5):359-70.

APPENDIX B: FACTSHEET FOR HEPATITIS C CASES IN THE ACT

Hepatitis C

What is hepatitis C?

Hepatitis C is a viral infection of the liver caused by the hepatitis C virus. Hepatitis means inflammation of the liver. If the liver is not working properly, it can cause serious illness. There are other viruses that cause inflammation of the liver including hepatitis A, B, D and E.

What are the symptoms?

Most people have no symptoms at all when they are first infected with hepatitis C.

If there are symptoms, they usually develop within two weeks to six months of exposure to the virus and can include:

- not feeling hungry/loss of appetite
- nausea or vomiting
- tiredness or fatigue
- abdominal pain
- yellowing of the skin and eyes (jaundice)
- dark urine

These initial symptoms usually only last a few weeks.

How long does the infection last?

Hepatitis C can be acute or chronic. A small number of people with hepatitis C infection have an acute illness and will clear the virus naturally within the first six months without treatment. These people are no longer infectious and cannot pass the virus on to others.

However, most people with hepatitis C will develop a chronic (long-term) infection and need treatment to clear the virus. Symptoms of chronic hepatitis C include:

- tiredness or fatigue
- increased moodiness and depression
- abdominal pain
- dry/itchy skin and eyes
- “brain fog” and generally feeling unwell

Without treatment, chronic hepatitis C can be a lifelong condition and may result in permanent liver damage or liver cancer. People with chronic hepatitis C usually appear well for many years but may develop symptoms as their liver damage progresses.

People can become reinfected after treatment or after clearing the virus naturally.

How is it diagnosed?

Hepatitis C infection can be diagnosed from blood tests which are available from your doctor. It may take a few weeks from the time of exposure before the test can determine whether you have the infection.

How is hepatitis C transmitted?

Hepatitis C is spread through blood-to-blood contact when blood from a person with hepatitis C enters another person's bloodstream. It only takes a very small amount of infected blood that may not be visible to the naked eye to pass the virus on.

Hepatitis C virus is most commonly passed on in Australia through sharing equipment used to inject drugs, including needles, syringes, spoons and tourniquets.

The virus may also be passed on by:

- unsterile tattooing or body piercing (including DIY)
- needle-stick injury or blood splash e.g., in the health care setting
- sharing personal items which have blood on them such as toothbrushes or razors
- direct contact with blood on an open wound or cut
- from mother to baby during pregnancy or at the time of birth

Hepatitis C is rarely transmitted through sexual contact. However, it may be passed on during sex without a condom, particularly in people living with HIV infection.

Breastfeeding is safe. However, if nipples are cracked or bleeding, cease breastfeeding until they have healed.

Hepatitis C cannot be transmitted by saliva, coughing, sneezing, casual contact like hugging, or sharing food.

Who is at risk?

Those most at risk of hepatitis C infection include:

- people who share unsterile needles, syringes, or other injecting equipment
- people who inject drugs, or have injected drugs in the past
- people who are exposed to non-sterile tattooing, piercing or acupuncture equipment
- people who have been in prison
- people who were born in, or have received a blood/tissue donation or undergone a medical procedure in countries with a high prevalence of hepatitis C
- people who have received a blood/tissue donation in Australia prior to February 1990

Hepatitis C virus testing of blood donations was introduced by Australian blood banks in February 1990. The risk of acquiring hepatitis C through blood transfusions in Australia is now extremely low.

How can hepatitis C be prevented?

There is no vaccine for hepatitis C. The only way to prevent acquiring hepatitis C is to avoid exposure to infected blood.

Hepatitis C can be prevented by:

- never sharing injecting equipment
- only using sterile injecting equipment once and dispose of it safely after use
- ensuring that practitioners performing tattoos, piercing and acupuncture use sterile equipment and are licensed
- not sharing razors, toothbrushes or other personal items which can transfer blood
- always wearing gloves and protective clothing when dealing with blood or body fluids to ensure that blood does not come in contact with the skin
- always using condoms with new or casual sexual partners ,or for sex that might involve blood-to-blood contact

How is hepatitis C treated?

There are new anti-viral medications available to people living with chronic hepatitis C with a Medicare card. The new medications are more effective, easier to take, and have fewer side-effects than the older medications. The Australian Government has listed these new medicines on the Pharmaceutical Benefits Scheme to make them accessible and affordable to people with hepatitis C. The new medications result in a cure for 90-95% of people.

If you have been diagnosed with hepatitis C you should:

- have a liver health assessment and discuss treatment options with your doctor as soon as possible
- have regular medical/specialist follow up appointments
- limit or avoid alcohol and maintain a healthy lifestyle
- consider getting vaccinated against hepatitis A and hepatitis B to minimise damage to the liver and
- contact Hepatitis ACT for further information and support on (02) 6230 6344 or go to https://hepatitisact.com.au/

INFORMATION

Need more information?

For more information about hepatitis C contact your doctor, Hepatitis ACT or call the Health Protection Service, Communicable Disease Control Information Line during business hours on **(02) 5124 9213**.

Communicable Disease Control Section at Health Protection Service is responsible for the investigation and surveillance of notifiable or infectious conditions in the ACT in order to control or prevent their spread in the community. This includes the promotion of immunisation, education and other strategies that help to limit the spread of diseases.

Hepatitis C is a notifiable disease.

Acknowledgement

Heymann DL. *Control of Communicable Diseases Manual*. 20th edn. Washington: American Public Health Association, USA; 2015.

Accessibility

If you have difficulty reading a standard printed document and would like an alternative format, please phone 13 22 81.

If English is not your first language and you need the Translating and Interpreting Service (TIS), please call 13 14 50.

For further accessibility information, visit: www.health.act.gov.au/accessibility

www.health.act.gov.au

CHAPTER 6: TEACHING APPLIED EPIDEMIOLOGY

Teaching first year scholars – an introduction to antimicrobial resistance

Our cohort of 17 was divided into four groups to prepare short teaching sessions. Our group of five developed an introductory session on antimicrobial resistance (AMR) surveillance in Australia. Our teaching session provided an opportunity to share our learnings from a broad range of areas, including surveillance in a jurisdiction, laboratory testing, and outbreak investigation. The teaching session aimed to provide an interesting, helpful introduction to the 2022 cohort.

The learning outcome of the session was for scholars to be able to describe why AMR is a public health issue and describe the components of the Australian AMR surveillance system.

Each teaching scholar was responsible for preparing a 10-minute session on a component of AMR surveillance in Australia. The session included five sections, including three introductions to different aspects of AMR, and two sections that applied these introductions to outbreak investigation and surveillance data. The introduction sections included:

- an introduction to AMR,
- an introduction to AMR surveillance in Australian and carbapenemase-producing *Enterobacterales* (CPE), and
- an introduction to phylogenomic analysis

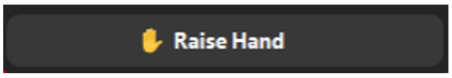
The applied sections included a summary of an outbreak investigation of CPE in South Australia and a summary of surveillance data for CPE in Victoria.

We adopted a formative learning approach. Formative learning includes regular informal assessments of students' learning during a lesson. These assessments help teachers understand comprehension and adapt their teaching approach. We used the following informal assessment tools:

- low-stakes quizzes: short quiz questions were included in the outbreak investigation and surveillance system evaluation sessions. These quizzes were not part of my section, but I reviewed these quizzes with other teaching scholars to provide feedback.
- section objectives: each teaching group member prepared short learning objectives for their session that build up to the overall learning outcomes. These section objectives provide natural breaks to check in with scholars.
- scholar self-evaluation: we checked in with scholars after introducing new concepts in each section to confirm their progress towards the learning outcome, and to refine our teaching. Scholars were asked to evaluate their progress against each section's objectives and the final learning outcomes. Scholar self-evaluation was conducted using the reactions function in Zoom. Figure 1 below shows the scholars' three options for evaluating their learning.

Figure 1: Formative assessment scholar self-evaluation reactions

I got this



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

I don't got this

My component was the first session explaining the structure of the session and introducing 2022 scholars to AMR. I designed a short presentation defining some of the key terms in this topic and outlining some key reasons why AMR is an important issue for field epidemiologists. It was important to define key terms up front to ensure all scholars had the same understanding of the content from the start of the session. I highlighted key reasons why AMR is a public health issue to engage scholars with the issue and set the context for the following sections.

Scholars' prior knowledge was established using a short free text poll asking them to respond to the prompt "why should field epidemiologists care about antimicrobial resistance?". I reviewed scholars' answers during the session to adjust my teaching approach based on the class's knowledge. I developed my slides to rely on images and infographics with a single key written message to reinforce the content of my presentation The slides for my section are shown in Appendix A.

Student feedback

In session feedback

There were 22 scholars online for our session. Each section objective was evaluated by the 2022 scholars using the reactions in Zoom. Overall, scholars reported good comprehension of the content presented (Table 1). The self-evaluation results for my section are shown in bold. However, we saw fewer scholars respond as the session went on.

Table 1: Results of scholar self-evaluation for each section

Section	Heart	Raised hand	Shocked face	Abstained (no emoji selected)
1: AMR in public health	**22**	**0**	**0**	**0**
2: AMR surveillance in Australia	21	1	0	0
3: AMR and genomics	17	0	0	5
4: CPE surveillance in SA	20	0	0	2
5: Epidemiology in Vic	19	0	0	3

Session evaluation

The 2022 scholars were asked to complete an online short evaluation of the session using a Qualtrics questionnaire. Scholars were asked about their opinions on the interest and utility of

the session, and their satisfaction on a 5-point Likert scale (1=strongly disagree, 5 = strongly agree). Overall, the session was positively received by the 16 respondents. Scholars generally reported finding the session interesting and useful to their field epidemiology studies (Table 2).

Table 2: Results of scholar feedback questionnaire

Question	Average	Range
The facilitators were well prepared for the session	4.6	4-5
I learnt something interesting today	4.6	4-5
The content was useful for my learning as a field epidemiologist	4.3	4-5
I am motivated to learn more about antimicrobial resistance after this session	4.3	3-5
Overall, I am satisfied with the session	4.3	3-5

Reflections

My reflections on our teaching session largely aligned with the free-text responses we received from 2022 scholars in their evaluation.

Time management

Our teaching session ran over time. Unfortunately, one teaching scholar presented for longer than their allocated time, causing the final two scholars to have to rapidly condense their sections. Time management was also the key area of feedback we received from the 2022 scholars in their evaluation.

We conducted a group rehearsal of the teaching session to time each section and to provide feedback on areas that could be excluded or could be improved. We had also run over time in this rehearsal, and I had provided feedback suggesting we all trim our sections to ensure equitable teaching time. Our session could have benefitted from more assertive feedback during development, and more active time management on the day.

Matching content to the audience

The other primary area of feedback received from 2022 scholars was that the depth of content was challenging. This is partially the nature of the technical content we were presenting, as well as the volume of content covered. Our session could have benefitted from reducing the amount of content covered and focussing our time on explaining more technical concepts in greater detail.

Lessons from the Field – an introduction to spatial epidemiology

I developed my lesson from the field following a data request my field placement had received that utilised my background as a spatial scientist. We had received an urgent request to identify a neighbourhood to target for hepatitis C testing and treatment as part of a nationwide initiative to eliminate the condition by 2030. One of the challenges I faced during this data request that I thought would be useful to discuss with my cohort was the selection of an appropriate geography that both protected the confidentiality of cases and provided a useful standalone figure for decision makers.

I adapted this request into a teaching session by creating a dummy data set and documenting the steps I went through to create maps in a worksheet. This worksheet was designed to be self-administered for scholars to return to after the session and included step-by-step instructions with screenshots and a glossary of key spatial science terms.

The learning objective of the sessions was for scholars to have the skills to use QGIS to make point maps and filled maps to visualise spatial data. This session built on the introduction to GIS in Course Block 3 and included:

- an introduction to coordinate reference systems
- how to add a base map
- converting an excel file into a point layer using latitude and longitude coordinates
- making a point layer map, and a discussion on the importance of confidentiality when mapping data
- converting a point layer map into a filled map
- a discussion on different geographies we can use to create a filled map, and the advantages and disadvantages of these geographies
- designing a map, including checking the accessibility of the map, adding legends and scale bars
- exporting a map

While it was designed to be an interactive session, scholars were given the option to observe only if this best suited their learning. All six scholars elected to observe the session.

Student feedback

Scholars were asked to complete a short evaluation of the interest and utility of the session through four questions on a 5-point Likert scale (1=strongly disagree, 5 = strongly agree) (Table 3). Overall, feedback was positive and there was interest in learning more about the topic. The success of this session can also be seen in the three one-on-one sessions I delivered with members of my cohort to work through mapping data for one or more of their projects.

Table 3: Evaluation of Lesson from the Field (n=6)

Question	Average	Range
This session was presented clearly	5	5-5
I learnt something interesting today	5	5-5
I learnt something useful today	5	5-5
I am interested in learning more about GIS for applied epidemiology	4.8	4-5

Reflections

It is always a challenge to learn new software in a classroom setting and to learn in a virtual environment. Combining the two was a challenge for this session. I had not fully appreciated the substantive amount of time developing the teaching resources for this session would take. However, I was well satisfied with the way the session ran and the subsequent engagement of my cohort with GIS and spatial sciences has been deeply rewarding.

Excel skills for public health nurses and CDC staff

As part of my field placement, I designed and implemented three practical sessions to build the Excel skills of the public health nurses at the ACT Health Communicable Disease Control Branch (CDC). Public health nurses at ACT Health are regularly required to enter data in Excel spreadsheets but did not necessarily have the confidence to analyse the data they have entered.

These teaching sessions came about after a team meeting where several public health nurses indicated that they would like to improve their Excel skills but found formal education sessions challenging as the content did not relate to their work.

I prepared a lesson plan, worksheet, dummy data set, and a two-page cheat sheet with helpful mathematical operations, keyboard shortcuts, and Excel functions. For these sessions, I prepared a dummy data set using the structure of NDMS outputs as a format familiar to ACT Health public health nurses. All data were fictitious.

The learning objective of these sessions was to introduce Excel to public health nurses as a data cleaning and analysis tool.

There was no assumed knowledge of Excel in this session. The Excel skills covered in this session included:

- data cleaning – sorting and filtering data, formatting as dates and numbers, true/false checks
- matching data sets – using the INDEX and MATCH functions to join data.
- summarising data – using COUNTIF, AVERAGE, MEDIAN, MIN, and MAX functions to describe data, using mathematical operations to add data and to calculate proportions
- PivotTable – using PivotTable to summarise data, create age groups, and calculate proportions
- PivotChart – using PivotChart to simultaneous create a summary table and chart
- excel charts – creating a chart of a regular Excel dataset, how to pick the best chart for the different types of data, formatting a chart, creating a combination chart

These teaching sessions were interactive with public health nurses asked to bring their laptops along to work through the worksheet. My screen was also projected to enable public health nurses to follow along and clarify steps. The sessions were designed to run for three hours to enable time for troubleshooting, accommodate learning at different paces, and allow time for breaks.

While originally designed for public health nurses, the Excel sessions were opened up to other staff at CDC who regularly enter and review Excel data. A total of 8 staff at ACT Health attended these sessions.

A short evaluation questionnaire was sent out at the end of each session asking attendees to rate the utility of the session and provide an opportunity to suggest improvements through five closed-response questions on a 5-point Likert scale (1=strongly disagree, 5 = strongly agree) and open free text responses. Responses were reviewed before the delivery of the next session to improve the content and teaching approach. A total of five evaluation responses were received.

Student feedback

Overall, the sessions were well received by CDC staff (Table 4). CDC staff indicated that they found the sessions useful and were interested in learning more about Excel (Box 1).

However, some CDC staff verbally reported finding the pace of the session to be too fast or too slow depending on their prior knowledge of Excel. This is one of the challenges I had anticipated for these sessions. At the beginning of the final two sessions, I stressed that it was encouraged for individuals to work ahead or to leave the room if the session was too slow for their learning so that additional time could be dedicated to staff requesting more support.

Table 4: Evaluation of Excel teaching sessions (n=5)

Question	Average	Range
The session was relevant to my work in disease surveillance	4.6	3-5
The facilitator was clear and explained concepts well	4.8	4-5
I feel more confident in Excel than I did prior to the session	5	5-5
I am motivated to use Excel following this session	5	5-5
Overall, I am satisfied with the Excel session	5	5-5

Box 1: Free text responses on the Excel session from CDC staff

"Awesome session"

"I would like to consolidate my understanding of the course content by putting into practice."

"All of the learning in the session was tailored to my work. The data set used in the session was relevant and meaningful. I have a better understanding of Excel and increased confidence to apply this knowledge in my workplace. The Tips and Tricks sheet that Keeley provided will be very useful. The shortcuts, maths calculation methods and pivot tables will all be very good to put into practice."

"great session, thank you!"

"The session was designed specific to my role and every aspect of the course was bespoke to my needs. It was also perfectly pitched considering my level of previous experience with the content. Keeley was able to adjust the pace of her teaching as required and I found her approach to be reassuring and confidence building. She was able to adapt throughout the session to answer questions and provide further explanation where needed. I can't thank Keeley enough for her time and her patience. I would love to attend another Excel session with Keeley. Thank you!"

Further, the section on matching data received mixed feedback, with some public health nurses indicating it was challenging. Upon reflection, I would not have introduced the INDEX and MATCH functions in the middle of the session as, while these functions are useful, they can be

tricky to structure. The INDEX and MATCH functions were included as an optional extra component of the third teaching session in light of this feedback.

Reflections

I found the design and delivery of these sessions deeply rewarding. While there is always a challenge teaching a cohort with different levels of experience, I enjoyed working with the public health nurses to improve their Excel skills and their confidence in reviewing the data they have collected. My teaching benefitted from the feedback in earlier sessions and helped me focus on what was most useful for the public health nurses and their work.

APPENDIX A: SLIDES FOR TEACHING AN INTRODUCTION TO ANTIMICROBIAL RESISTANCE

PRESENTED AS PART OF TEACHING SESSION FOR THE 2022 COHORT

FORGET COVID!

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

1

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 carbapenamese-producing enterobacteriales (CPE) as an example

2

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

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 session's learning objective

3

4

01. AMR in public health

5

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

6

TIME FOR SOME DEFINITIONS!

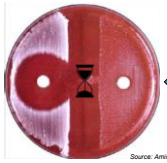
Antimicrobial resistance (AMR): **process** when a microorganism that once responded to a drug changes over time and no longer responds to that drug.

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

Susceptible to drug



Resistant to drug (an MRO)

Source: Amirreza Talaiekhozani

7

SO WHAT?

Why should field epidemiologists care about antimicrobial resistance?

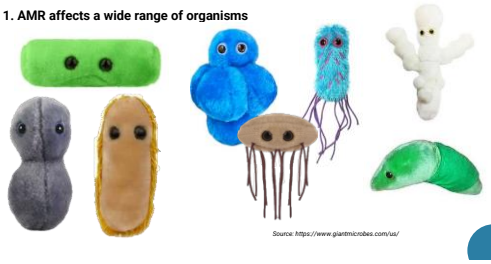
https://pollev.com/forgetcovid813

Because who doesn't love a poll??

8

SO WHAT?

1. AMR affects a wide range of organisms

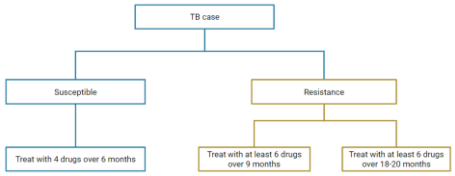


Source: https://www.giantmicrobes.com/us/

9

SO WHAT?

2. AMR makes infections harder to treat

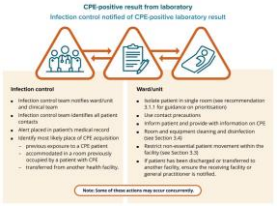


Tuberculosis CDNA national guidelines for public health units

10

SO WHAT?

3. AMR makes infections harder to control



Australian Commission on Safety and Quality in Health Care. Recommendations for the control of carbapenemase-producing Enterobacterales (CPE). A guide for acute care health service organisations. Sydney: ACSQHC, 2021

11

SO WHAT?

4. AMR is expensive

Each year, Australian patients with AMR present:

Stay in hospital for	Cost hospitals an additional	Have elevated odds of dying of
717 more days	**$1.6 million USD**	**1.39-5.01 times greater**

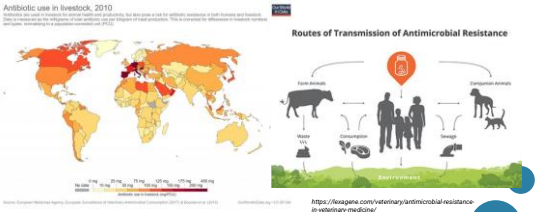
Compared to Australian hospital patients with the same infections without AMR present

Lee et al, Attributable Length of Stay, Mortality Risk, and Costs of Bacterial Health Care–Associated Infections in Australia: A Retrospective Case-cohort Study, Clinical Infectious Diseases, Volume 72, Issue 10, 15 May 2021, Pages e506–e514, https://doi.org/10.1093/cid/ciaa1228

12

SO WHAT?

5. It's not just about people



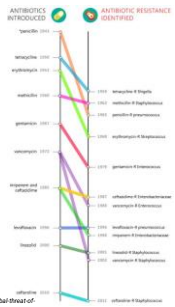
https://lexagene.com/veterinary/antimicrobial-resistance-in-veterinary-medicine/

13

SO WHAT?

6. We are running out of effective treatments

Nearly as quickly as we discover new antibiotics, bacteria build up new resistance



Source: Christopher Graham https://www.joghr.org/article/11913-the-global-threat-of-antibiotic-resistance-what-can-be-done

14

SO WHAT?

7. AMR can be deadly

Current estimated deaths from AMR = 700,000 - 1.2 million

● = 100,000 deaths

Estimated deaths from AMR in 2050 = 10 million

15

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

16

CHAPTER 7: ADDITIONAL PUBLIC HEALTH EXPERIENCES

My field placement has been a busy time.

The years 2021 and 2022 have seen major public health challenges in Australia with the COVID-19 pandemic, new emerging conditions, and great public engagement and interest in our responses. These have all come at a time when ACT Health Communicable Disease Control was transitioning to a new notifiable disease management system and were understaffed. I have had the opportunity to be involved in a wide range of operational activities, responses to acute public health problems, and spreading the word on applied epidemiology in a range of spheres.

The remaining pages of this volume outline a selection of some of the additional applied epidemiology experiences from my field placement.

Establishment of a food poisoning surveillance system

Background

In the ACT, food poisoning complaints are actioned by the Environmental Health team. Under the previous system, food poisoning complainants who contacted ACT Health were either required to conduct a phone interview or were emailed a Word document to complete and send back in their own time. The Word document had limited capabilities on mobile devices, potentially acting as a barrier to the timely receipt of complaints and public health response. Food poisoning complaints were not stored together, and no alerts were in place to assist in prioritising responses.

The scale of my foodborne norovirus outbreak investigation highlighted some gaps in the existing food poisoning surveillance system. The volume of complaints and contacts requiring interviews was well in excess of personnel resources for phone interviews, necessitating a move to a REDCap database with the ability to receive phone or online questionnaire responses.

The utility of a REDCap project for food poisoning complaints was identified as part of the after-action review of this outbreak. I volunteered to develop a food poisoning complaint register to build on the work from my outbreak investigation.

My role

I was responsible for the design and implementation of a new food poisoning surveillance system. The aim of the system was the timely reporting of food poisoning complaints and response to potential outbreaks. My role included:

- identifying key internal stakeholders for scoping, designing and implementing the system
- review of existing processes and data required for a food poisoning investigation
- design of a REDCap project for phone and online questionnaire responses
- integrating automated alerts to the Environmental Health team for priority complaints
- design of reports to collate responses
- preparation of standard email and interview scripts
- training Environmental Health Officers in the use of REDCap

Lessons learnt

This project was a great opportunity to reinforce my understanding of the attributes of a successful surveillance system. I learnt a great deal about the routine surveillance of food poisoning complaints and the many demands on and responsibilities of Environmental Health Officers.

Public health impact

The new REDCap based system has been well received by the Environmental Health team and went live on 1 July 2022. Anecdotally, responses from complainants have been received in a timelier manner and have enabled Environmental Health Officers to devote more time to following up on complaints and performing routine food safety inspections.

Establishment of a surveillance system for notification, follow up and management of monkeypox virus cases

Background

Monkeypox virus (MPXV) is a member of the Orthopoxvirus genus and is related to the smallpox virus. The MPXV causes monkeypox disease, resulting in a rash or lesions, headaches, fatigue, fever, and swollen lymph nodes.

Before 2022, MPXV was believed to primarily transmit from animal to person, have limited potential for person-to-person transmission and was only believed to be endemic in areas of Central and West Africa. In these endemic areas prior to 2022, the case fatality rate was estimated between 1% and 6%, with a higher case fatality rate in children.

In May 2022, an outbreak of monkeypox cases not linked to endemic countries was reported in Europe transmitted primarily from close skin-to-skin contact. Monkeypox was made a nationally notifiable condition in Australia on 1 June 2022 following further spread in Europe, North America, and the Middle East, however national guidance on the information required for successful follow up was not available. The need to rapidly develop an enhanced surveillance system for monkeypox in the ACT before the detection of local cases was identified. In the ACT, we developed a surveillance system for cases and contacts ahead of the availability of national guidance following notifications of cases in Victoria and NSW.

My role

I was part of a wider team designing and implementing a response to monkeypox in the ACT. I was tasked with the development of a system to collate information on suspect, probable and confirmed cases of monkeypox. My role included:

- working with public health nurses and public health physicians to identify variables required for laboratory, clinical, exposure history and contact tracing information
- developing a case investigation project in REDCap to collate information about monkeypox cases for use during case and clinician interviews, epidemiological assessment and clinical review.
- integrating automatic alerts to public health clinical and wellbeing teams based on the responses in the case investigation project.
- developing an initial screening questionnaire for potential monkeypox cases to assess their context against the suspect case definition

Further, I identified the need for a case management system to support cases in up to 21 days of isolation. The early drafts of the Monkeypox Series of National Guidelines had not included advice on how a case should be monitored or supported, however, the response to the COVID-19 pandemic had taught me that isolation requirements can be a significant challenge for some

individuals, compounding for monkeypox by the length of the isolation period and a potentially stigmatising condition. I adapted the wellbeing processes used for COVID-19 isolation. This involved the introduction of automated text messages including a short, validated wellbeing survey and working with the COVID-19 Operations Wellbeing team to provide an appropriate response to support a case. The case management system was integrated into the existing REDCap project, collating all the information about a case in one database.

Lessons learnt

Like most public health professionals in June 2022, I rapidly gained an understanding of the epidemiology, testing and changing clinical presentations of monkeypox and continue to keep learning about the condition to this day. I had the opportunity to broaden my skills in REDCap and develop a flexible surveillance system able to adapt to the introduction of national guidelines and data specifications. I also had to consider the implications for One Health and the information and response required to manage companion animals of cases. This project also reinforced the importance of only collecting information for action and the importance of speaking up to question the utility of variables if they will not alter the public health response and may further stigmatise or shame a person with the condition.

Public health impact

The monkeypox case surveillance system was almost immediately tested with the advent of suspect cases in the ACT in June 2022 and confirmed cases in July 2022. The case investigation project has been a useful tool to manage notifications and support cases during their illness and is part of a suite of REDCap projects used to manage contact tracing and MPXV vaccination appointments.

Identification of a *Salmonella Infantis* outbreak associated with a food business

Background

ACT Health Communicable Disease Control did not have an OzFoodNet epidemiologist for the first year of my field placement. I conducted over 40 salmonella case interviews to support team operations in 2021. In April 2021, two cases I interviewed reported eating the same meal from a Canberra café on the same date. This finding prompted my first outbreak investigation at ACT Health.

My role

I attended the site inspection with two environmental health officers to interview kitchen staff and collect samples of food, cloths, and environmental swabs of surfaces. I continued to interview salmonella cases to identify any other notifications that may also be linked to the outbreak and assessed the typing and phylogenomic analysis of human and environmental samples. I also attended outbreak response meetings with the Environmental Health and Australian Capital Territory Government Analytical Laboratory (ACTGAL) to provide updates on the epidemiological investigation.

Lessons learnt

This was my first site inspection, and I gained a deep appreciation for the complexity and technical detail required for the work of environmental health officers and microbiologists. This outbreak investigation was an excellent opportunity to apply my learnings from Course Block 1 to the complications of a real-world scenario and the challenge of using non-cultured results for outbreak investigation. I had a steep introduction to phylogenomic analysis and interpreting the findings which was a solid foundation for further outbreak investigations. Finally, I also learnt that sponges and tea towels can host a wide range of pathogens, helping me improve my personal food handling practices and launder frequently.

Public health impact

This outbreak remained at two cases and is an example of how a potential outbreak can be halted with early intervention. The environmental health investigation found some minor food handling issues, including inappropriate use of tea towels and cloths. *Salmonella spp*. were isolated from a sponge and a cleaning cloth, and the food business was instructed to amend their practices.

Interactive dashboard for sexually transmitted infections surveillance

Background

Notifiable sexually transmitted infections data are kept in two separate locations at ACT Health:

- The notifiable disease management system (NDMS) includes pathology information with limited variables for public health follow up
- Enhanced surveillance case and clinician interviews stored in two REDCap projects

The separation of data due to practical limitations of existing ICT systems limits the ability of public health staff to review trends and patterns quickly and simply. For staff with limited data manipulation and analytical skills, the need to match cases between the two data sources was limiting their ability to review the aggregated results for the data they were collecting. I identified this barrier in May 2021 and designed an interactive dashboard to collate these data sources and simplify aggregated reporting.

My role

My role in this project included cleaning and matching records from the three data sources in Power BI, designing the dashboard to show the most relevant variables for public health follow up, and developing interactive filters to enable individual staff members to interrogate data

Lessons learnt

This project ended up far larger than I had initially anticipated and required significant cleaning and recoding of data in the REDCap projects before integration into Power BI. This was an important learning on the importance of scoping projects and defining what is and is not included from the outset. I enjoyed learning to create calculated fields and prepare basic DAX code to improve the functioning of the dashboard. Finally, the inability to implement this dashboard was an important reminder that our projects and plans can be derailed by events outside of our control.

Public health impact

The draft dashboards were well received within Communicable Disease Control and were presented at a meeting with the Canberra Sexual Health Centre to illustrate trends in chlamydia, gonorrhoea and syphilis notifications over the previous five years. The dashboards were ready for publication in early August 2021. However, the implementation of this work was disrupted and ultimately ceased due to the detection of local transmission of COVID-19 in the ACT and the subsequent acute public health problems of the detection of Japanese encephalitis virus monkeypox virus.

Finding 50,000 Project

Background

In December 2021, ACT Health was approached by Hepatitis Australia to seek advice on a geographically targeted campaign to reduce the prevalence of hepatitis across Australia through the Finding 50,000 campaign. The campaign aims to increase awareness about testing and treatment for hepatitis C in targeted communities and identify 50,000 people living with hepatitis C who are currently unaware of their status. ACT Health was asked to identify one postcode or suburb for targeted activities that:

- have limited embedded hepatitis C services, and
- have relatively lower treatment uptake compared with other regions in the state/territory, and
- not already targeted by an existing hepatitis C campaign

A response was needed in two weeks. I volunteered to lead this project to apply my background in geography and spatial sciences and use a systematic approach to identify an appropriate location.

My role

The required outcome for this project was to identify one preferred geographic area for nomination to Hepatitis Australia. In the absence of any information on testing for hepatitis C to establish positivity rates or any data on the prevalence of known risk factors for hepatitis C in the ACT population, I designed an analysis using existing notification data over the previous five years and aggregated treatment uptake data from ASHM. My role included:

- designing the study and preparing a data analysis plan
- cleaning and geocoding addresses of hepatitis C cases
- mapping hepatitis C cases and the average annual rate per 100,000 population
- overlaying maps with existing hepatitis C services in the ACT and treatment services
- preparation of a short report and recommendations for an appropriate area to target for the campaign

Lessons learnt

I learnt the value of standardised data entry and the difficulties of cleaning free text data. My time was mostly spent cleaning data before geocoding and correcting incorrect addresses. This project reinforced the importance of time management and building contingencies into project management. This project also highlighted the difficulty of working with low numbers and small populations and the impact small changes in counts can have on the calculation of rates. I learnt some important strategies to display point data on maps while protecting the confidentiality of cases, including aggregating points and jiggling points away from the exact addresses. Finally,

this project reinforced the importance of understanding our population, its distribution, and how people live in cities and towns to identify a meaningful geographic recommendation.

Public health impact

Rather than a postcode or suburb, I recommended a region of the ACT for the Finding 50,000 campaign. I made this recommendation based on the criteria for the program, distribution of past cases and treatment uptake, and recognition of existing urban structures and communities in the ACT. This recommendation was supported by ACT Health and has been adopted by Hepatitis Australia as one of the 16 targeted areas of the Finding 50,000 campaign. This project is also the inspiration for my Lesson from the Field and for teaching my MAE colleagues some of the techniques we can use to characterise our epidemiological data by place.

Evaluation of letter to GPs diagnosing hepatitis C cases

Background

Active hepatitis C infections are diagnosed with a polymerase chain reaction (PCR) test. Active infections need to be identified to ensure appropriate clinical management of hepatitis C virus (HCV) infections. All people diagnosed with an active HCV infection should be considered for treatment with direct-acting antivirals in primary care. While a positive serological test detecting HCV antibodies meet the case definition, the test does not indicate an active infection. Even after a person clears the HCV, the antibodies will remain, and the person will continue to return positive serological tests throughout their life.

Anecdotally, ACT Health was aware of patients with serology positive results (and no PCR result) being inappropriately referred to The Liver Clinic and Hepatitis ACT from general practitioners (GPs) without first confirming an active infection. A letter for GPs was prepared to outline the importance of PCR testing for diagnosing an active HCV infection, and the pathways for treatment including referral of a hepatitis C case. The letter was sent to GPs who had not requested a PCR test for a serology positive patient and the notification was not a retest.

However, no plan was in place to evaluate the appropriateness or effectiveness of this letter. I volunteered to evaluate the GP letter project in consultation with the public health nurses at Communicable Disease Control.

My role

My role in this project included:

- defining the scope of the evaluation and aims of the project with the public health nurses
- developing an evaluation plan, including a logic model, outcome measures, and measures of success defined before the start of the project
- preparing and implementing a data analysis plan in line with the evaluation plan
- preparing a short report and recommendations for the continuation of the project

Lessons learnt

This was my first introduction to hepatitis C notifications and follow up and was an excellent opportunity to learn about the condition. I was also faced with the challenge of evaluating a program with a small number of letters sent and reinforcing the limits of relying on small numbers when I was reporting the findings. The design of this evaluation was also a challenge, as the evaluation needed to use existing resources and information and partners at The Liver Clinic and Hepatitis ACT were unable to contribute to the evaluation. Overall, I found this project was a good example of the realities of conducting an evaluation in a limited resource environment.

Public health impact

The findings of this evaluation should be interpreted with the recognition that a low number of letters were sent (n=12), however, there was an increase in the proportion of hepatitis C cases notified from GPs that included a request for a PCR test. Four GPs requested a PCR test on a date after the letter was sent to their practice. While these low numbers, some testing behaviour change was noted potentially improving the clinical management for these cases. This project also was the impetus to review the notification data for all hepatitis C cases in more detail and inspired my data analysis project in Chapter 5.

Presentation on applied epidemiology to a Year 10 class

Background

I was approached alongside the other Canberra-based scholars by the MAE team in July 2022 seeking interest in presenting on applied epidemiology to year 10 students at a local high school. The request from the school was part of a seminar series where professionals in different science, technology, engineering and mathematics (STEM) fields were invited to discuss their work and experiences.

I volunteered to present, alongside my cohort colleague Yasmin Lisson and Anna Glynn-Robinson from the MAE staff.

My role

I prepared a five minute presentation on my academic and professional background prior to the MAE, my experiences in my field placement at ACT Health, and why I have chosen a career in applied epidemiology. Yasmin, Anna and I presented at the high school's STEM seminar in August 2022 and answered questions about applied epidemiology from a very engaged class of year 10 students.

Lessons learnt

I had anticipated that an audience of 15 to 16 year-olds would have been an intimidating audience that may be hard to engage during a presentation. This was absolutely not the case. The students were polite, asking detailed questions and critically engaged with our presentations. I thoroughly enjoyed presenting and answering their questions, and this experience was a reminder to avoid assumptions about your audience. I was able to explain complex concepts in simple components for a non-expert audience. This experience was also a valuable opportunity to reflect on why I want to be a field epidemiologist and reassured me I have made the right choice.

Public health impact

While the public health impact of this project is difficult to judge, the immediate feedback we received from the students and teacher were positive. The success of our combined efforts was evident when the teacher asked who was best to contact to present again next year.

Presentation to the Japan Field Epidemiology Training Program

Background

As Australia's accredited field epidemiology training program (FETP), the MAE arranged a meeting with the Japan FETP program in May 2022. The purpose of this meeting was to introduce the two programs and to set a dialogue for future potential collaboration. The meeting included short presentations from current trainees from both the Australian and Japan FETPs about their training and experiences. I was asked to present alongside my MAE colleague Aidan Yuen.

My role

I was asked to prepare a 2 minute presentation summarising my field placement in the context of the Australian public health system, my projects addressing the major competencies of the Australian FETP, and a short summary of my experiences. Aidan and I attended the meeting and presented as a combined agenda item.

Lessons learnt

This experience was a great opportunity to meet international applied epidemiology colleagues during the active management of the COVID-19 pandemic. I was interested in hearing from the Japanese trainees about the structure of their program and learning from their experiences. This was also a valuable experience to practice succinctly summarising information to an audience in a short amount of time.

Student representative of the Australasian Epidemiological Association

Background

The Australasian Epidemiological Association (AEA) is a professional organisation that aims to promote excellence and innovation in epidemiology and connect students, academic and applied epidemiologists. The AEA advertised for a new Student Representative to sit on the AEA Council shortly after I was accepted into the Master of Philosophy (Applied Epidemiology). I nominated myself for the role and was the Student Representative throughout my Master of Philosophy (Applied Epidemiology) study.

My role

Aside from the regular duties of the Student Representative, I organised webinars for AEA student members and my MAE colleagues to assist in our professional development. In these sessions, I invited epidemiologists from different applied and academic fields to discuss their studies and professional experiences and summarise the work in their field. I also worked with the AEA Policy and Engagement Officer to prepare student profiles of current MAE scholars to promote World Field Epidemiology Day in 2022. Finally, I assisted in the organisation and operation of AEA events at the Population Health Congress in September 2022.

Lessons learnt

My time as the Student Representative on the AEA Council was a great experience to complement my field placement. I gained a deep appreciation of the challenges and time commitments required to host professional development events and the value of these events for sharing knowledge with peers. This role also enabled me to raise the profile of applied epidemiology with my academic Council colleagues and to share knowledge and practices between different fields of epidemiology.

Secondment to COVID-19 Operations to respond to a local B.1.617.2 (Delta) variant outbreak

Background

I was seconded to COVID-19 Operations Branch from August to October 2021, along with my field supervisor and the Director of Disease Surveillance. Three other MAEs from my cohort, Leonie Williamson, Yasmin Lisson, and Aruna Phabmixay (Figure 1), and applied epidemiology staff from the Australian National University also joined the Case Investigation and Epidemiology team.

My role

My role included the following:

- identification and investigation of COVID-19 clusters to identify transmission chains, source of acquisition and advise on public health interventions
- COVID-19 case interviews to determine clinical status, source of acquisition and contact tracing
- reviewing case interview data completeness for reporting requirements
- reviewing and updating whole genome sequencing results for cases
- refining case investigation questionnaires to respond to the changing epidemiology of local transmission
- preparation of automated reports describing the sociodemographic characteristics of cases

Lessons learnt

Working with members of my cohort and my teachers to respond to an acute public health event was a truly unique experience. This was a valuable learning opportunity to be in the room together to detangle clusters and interpret findings. The epidemiology of the ACT's Delta outbreak was shifting throughout my secondment, and I learnt the importance of maintaining flexibility and adapting the questions we ask and the data we collect to meet new challenges. It was difficult to step away from COVID-19 Operations in November 2021 and returning to my field placement was an important experience in defining my role and knowing when to return to business as usual.

Figure 1: Four MAE scholars and their emotional support soft toys