Applied Epidemiology of Infectious Diseases in Australia

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

Malinda Vibol Chea

BHSc MPH GradDipIDI

November 2020

Health Emergency Management

Office of Health Protection

Australian Government Department of Health

Academic supervisor

Martyn Kirk

Field supervisor

Rhonda Owen

Australian National University

Australian Government

Department of Health

Declaration of work

I certify that this work contains no material which has been accepted for the award of any other degree or diploma, in any university or other tertiary institution and, to the best of my knowledge, contains no material previously published or written by another person, except where due reference has been made in the text.

Malinda Vibol Chea

November 2020

Abstract

This thesis is a body of work that was completed whilst undertaking the Master of Applied Epidemiology (MAE) program at the Australian National University from February 2019 to November 2020. During this time, I was placed at the Department of Health, Office of Health Protection, in the Health Emergency Management Branch (HEMB). I also spent 8 weeks with the Victorian Government Department of Health and Human Services (DHHS) to fulfil the outbreak investigation requirement. I discuss my experiences as a MAE Scholar and my involvement in the day-to-day activities in the work placements.

I completed four key projects to meet the core competencies of field epidemiology:

- **Data analysis:** Cholera risk in Australian returned travellers: An analysis of notifications to the National Notifiable Diseases Surveillance System (NNDSS) from 1991– 2018
- **Outbreak investigation:** Measles outbreak in seasonal horticultural workers in regional Victoria, Australia, 2019
- **Public health surveillance:** Establishing a 2019 novel coronavirus (2019-nCoV) surveillance system in Victoria for travellers returning from Wuhan, Hubei Province in China, 2020
- **Epidemiological study:** Do symptoms predict COVID-19 infection? A case-control study, Australia, 2020

I presented findings for the cholera data analysis study at the Communicable Diseases Control conference in 2019, and prepared a manuscript for the measles outbreak chapter intended for submission to a scientific journal.

As part of the MAE teaching requirements, I prepared a lessons from the field exercise on accessing publicly available data sources and data visualisation, and conducted a group teaching session for the 2020 MAE cohort on introduction to data linkage.

In summary, this thesis describes my experiences in the MAE program and the projects I completed during my placement with HEMB and secondment to DHHS, all of which demonstrates the core competencies in field epidemiology.

Acknowledgements

The MAE journey was challenging yet highly valuable for both my professional and personal development. I would like to thank the National Centre for Epidemiology & Population Health, the Research School of Population Health, and the Australian National University for the opportunity to be a part of this rewarding program. I also wish to thank the Victorian Department of Health and Human Services for enabling my short-term involvement, and the Australian Government Department of Health, Office of Health Protection for supporting and funding my placement.

This final product would not be possible without the following persons who provided support and advice. Thank you to my academic and field supervisors Martyn Kirk and Rhonda Owen. A further thanks to Luis Furuya-Kanamori, Lucinda Franklin, Janet Strachan, Charles Alpren, Steph Davis and Katie Glass.

I am glad to have been part of a diverse group of passionate epidemiologists who supported each other throughout the program. In particular Liz and Gen for their moral support and all the laughs, coffees, snacks, rants, gym sessions, and life advice. It was comforting to have each other throughout these two years. You have truly kept me sane in these crazy times. To the LDC family for all the wonderful friendships made and for providing an outlet away from all the chaos. Thanks for all the great memories of my time in Canberra.

Finally but most importantly, to my parents and family and friends back home in Melbourne, in Canberra and around the world. You have been with me every step of the way. To Amanda, Asja, Nimo, Phuong and Zane, I am grateful for your continued love and support and for keeping me motivated, especially in times where I was uncertain of my place in the program.

Abbreviations

ABARES	Australian Bureau of Agricultural and Resource Economics and Sciences
ABS	Australian Bureau of Statistics
AHPPC	Australian Health Protection Principal Committee
AIHW	Australian Institute of Health and Welfare
AIR	Australian Immunisation Register
ANU	Australian National University
ARDS	Acute Respiratory Distress Syndrome
CDES	Communicable Diseases Epidemiology and Surveillance
CDC	Communicable Diseases Control
CDI	Communicable Diseases Intelligence
CDGN	Communicable Diseases Genomics Network
CDNA	Communicable Diseases Network Australia
CFR	Case Fatality Rate
CHO	Chief Health Officer
CMO	Chief Medical Officer
COVID-19	Coronavirus Disease 2019
DAP	Data Analysis Plan
DAWR	Department of Agriculture and Water Resources
DHHS	Department of Health and Human Services
DO	Duty Officer
DoH	Department of Health
ED	Emergency Department
ERP	Estimated Resident Population
ETEC	Enterotoxigenic escherichia coli

GP	General Practitioner
GPRCs	General Practice Respiratory Clinics
HEMB	Health Emergency Management Branch
HIV	Human Immunodeficiency Virus
HPB	Health Protection Branch
HPG	Health Protection Group
HREC	Human Rights Ethics Committee
ICD-10-AM	International Classification of Diseases
IHR	International Health Regulations
IMM	Incident Monitoring Meeting
IMT	Incident Management Team
IR	Incidence Rate
LFF	Lessons from the field
LHD	Listed Human Disease
MAE	Master of Applied Epidemiology
MERS-CoV	Middle-Eastern Respiratory Syndrome Coronavirus
MCV1	Measles-containing-vaccine-first-dose
MCV2	Measles-containing-vaccine-second-dose
MMR	Measles, Mumps and Rubella
NFP	National Focal Point
NHS Act	National Health Security Act 2007
NIR	National Incident Room
NMS	National Medical Stockpile
NNDSS	National Notifiable Diseases Surveillance System
OAD	Overseas Arrivals and Departures
OHP	Office of Health Protection
PCR	Polymerase Chain Reaction

PHEIC	Public Health Emergency of International Concern
PHESS	Public Health Events Surveillance System
PHLN	Public Health Laboratory Network
PHN	Public Health Network
PHOs	Public Health Officer
PNG	Papua New Guinea
PPE	Personal Protective Equipment
PUI	Person Under Investigation
RB	Responsible Bodies
SACC	Standard Australian Classification of Countries
SARS-CoV	Severe Acute Respiratory Syndrome
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SoNG	Series of National Guidelines
SSBA	Security Sensitive Biological Agents
SSBARS	Sensitive Biological Agents Regulatory Scheme
STRR	Short-term Resident Returns
STVA	Short-term Visitor Arrivals
VIDRL	Victorian Infectious Diseases Reference Laboratory
WHO	World Health Organization
WO	Watch Officer
2019-nCoV	2019 Novel Coronavirus

Table of contents

1 Introduction: Master of Applied Epidemiology (MAE)

Overview of the MAE experience

1.1 Introduction

From March 2019 to November 2020, I undertook field placement at the Australian Government Department of Health (DoH) in Canberra as part of the Master of Philosophy in Applied Epidemiology (MAE) program at the Australian National University (ANU). I was placed within the Office of Health Protection (OHP), Health Emergency Management Branch (HEMB). The operational nature of the branch enabled my involvement at the national level for health emergency preparedness and response activities. My work also aligned with the requirements of the International Health Regulations (IHR) under the World Health Organization (WHO).

I also spent 8 weeks with the Communicable Diseases Epidemiology and Surveillance (CDES) unit at the Victorian Department of Health and Human Services (DHHS) at the end of my first year to meet the requirements for the outbreak investigation competency.

This bound volume comprises of the day to day activities and projects undertaken during my placement at HEMB and DHHS which demonstrates the skills and knowledge developed to meet the following MAE core competencies:

- Analysis of a public health data set
- Investigation of an acute public health problem
- Establish a public health surveillance system
- Design and conduct an epidemiological study

During my time at HEMB, the National Incident Room (NIR) was activated for various incidents including the measles outbreak in the pacific and the COVID-19 pandemic in which I was a part of the COVID-19 National Incident Room Epidemiology and Surveillance Team and provided support across the working streams. In addition to working on core MAE projects, I also participated in various daily activities and attended workshops and conferences relevant to the work of the placements summarised in the table below.

Table 1. Activities undertaken during MAE placement at HEMB and DHHS, February 2019 to November 2020

Activities undertaken	Description
Health Emergency Management Branch (HEMB)	
Laboratory visits	• Clinical microbiology • Food and water microbiology • Security Sensitive Biological Agents (SSBA)
Watch Officer (WO) duty	• Managing incidents for the National Incident Room (NIR) and providing correspondence to National Focal Points (NFP) and Responsible Bodies (RB) • Reporting events to the World Health Organization (WHO) under the International Health Regulations (IHR) • Writing and distributing debriefs to HEMB and relevant stakeholders
COVID-19 National Incident Room Epidemiology and Surveillance Team	• Writing the national coronavirus epidemiology report for CDI and presenting to CDNA • Literature reviews for CDNA • Data cleaning and analysis for surveillance output activities • Writing daily situation reports and government talking points • Supporting data collection for the COVID-19 modelling study • Assisting with contact tracing activities for Victorian cases
Training and workshops	• One Health Priority Zoonotic Diseases – Department of Agriculture and Water Resources (DAWR) • EmergenSea Detour for managing outbreaks on cruise ships – Border Health and DAWR • Core Concepts of Public Health – half-day course • WO/Duty Officer (DO) training – human remains, national medical stockpile (NMS), notifiable disease incidents
Conferences	• Presenting at the Communicable Diseases Control (CDC) conference in Canberra
Initial Call Exercise	• Emerging disease incidents • Mass casualty incidents
Weekly, fortnightly and monthly meetings and teleconferences	• Weekly data quality meetings with the Primary Care Division COVID-19 response team on data from the Commonwealth-funded GP respiratory clinics (GPRC)

	• Incident Monitoring Meeting (IMM) • Communicable Diseases Genomics Network (CDGN) • Public Health Laboratory Network (PHLN) • Disease briefings (measles, legionella, influenza, polio)
OHP Public Lectures and presentations	• Geospatial Analysis and Visualisation of Health Data • Bug breakfast – measles • OHP fortnightly stand up
Victorian Department of Health and Human Services (DHHS)	
Incident Management Team (IMT)	• Participating in weekly IMT meetings for various incidents including measles, Q fever, bushfires and 2019-nCoV • Developing a COVID-19 case definition and questionnaire form
Case and contact management	• Conducting case follow-up interviews for measles and salmonella
Planning function – intelligence	• Developing and updating measles exposure timeline
Preparedness and response	• Supporting the development and modification of the 2019-nCoV case definition in Victoria • Developing a COVID-19 case questionnaire and updating relevant fields as the case definition changes
Public Health Events Surveillance System (PHESS)	• Data cleaning for disease notifications and updating relevant fields as new information is recorded by public health officers

1.2 Overview of the field placement

The Health Emergency Management Branch is a specialised branch that sits under the Office of Health Protection (OHP) within the Health Protection Group (HPG). The HPG leads the department's public health role for the Commonwealth, in particular in surveillance of, and protection measures against, infectious disease and preparation and response to health disasters. The OHP works in partnership with key stakeholders to protect the health of the Australian community through effective national leadership and coordination, and building of appropriate capacity and capability to detect, prevent, and respond to threats to public health and safety.

The HEMB is one of four branches under the OHP and is responsible for prevention, preparedness and response activities related to national health emergencies and risks. This encompasses mass casualty incidents, communicable disease outbreaks, acts of terrorism, and the health impacts of natural disasters.

The National Incident Room (NIR) is located within HEMB and is responsible for ensuring a nationally consistent and coordinated response to a national health emergency. Some of the main activities conducted in the NIR include: providing technical advice to committees and government, implementing health aspects of Commonwealth disaster plans, coordinating medical response teams nationally and internationally, and coordination of the National Medical Stockpile (NMS). Emergencies that lead to the activation of the NIR include: significant infectious disease outbreaks, mass casualty incidents, and chemical biological or radiological incidents that are either accidental or criminal.
Since its establishment, the NIR has responded to numerous emergencies including: 2003 SARS outbreak, 2005 Bali Bombings, 2009 H1N1 Pandemic and 2011 Christchurch Earthquake.

During my placement, the NIR was activated for various incidents including:

- Ebola in the Democratic Republic of Congo
- Measles outbreak in the pacific
- White Island volcano eruption in New Zealand
- Bushfire crisis in Australia
- COVID-19 pandemic

1.3 Summary of MAE requirements

The MAE is a two-year master's degree by research involving coursework conducted over three course blocks. The field placement component enables MAE scholars to apply their learning in a practical, real world scenario. During this time, MAE scholars complete four research projects and other requirements which demonstrate the competencies in field epidemiology.

Analysis of a public health data set (Chapter 2)

This project described cholera risk in Australian returned travellers through the analysis of notifications to the National Notifiable Diseases Surveillance System (NNDSS) from 1991 to 2018. The analysis summarised yearly trends of cholera notifications and identified the most common regions and countries of overseas acquired cholera infections. The results informed traveller risk to cholera endemic countries and the overall risk of cholera in Australia from returned travellers. Findings from the study was presented at the Communicable Diseases Control conference in 2019.

Investigation of an acute public health problem (Chapter 3)

I was involved in an investigation of a measles outbreak in seasonal horticultural workers in regional Victoria as part of my 8 weeks placement with DHHS. The cluster included 8 confirmed and 4 suspected cases who had been workplace or accommodation contacts with two primary cases who had arrived from Samoa for short-term seasonal work. DHHS worked with local councils to conduct on-site vaccination to prevent ongoing transmission and subsequent vaccination outreach programs targeted at seasonal workers from the Pacific and other backgrounds.

Establishing a public health surveillance system (Chapter 4)

My time at DHHS enabled my involvement with planning and response to the (at the time known as) 2019-nCoV outbreak in Wuhan, Hubei Province, China. In the early stages I supported the establishment of a 2019-nCoV surveillance system in Victoria for identifying at risk travellers returning from outbreak affected areas. I provided input to developing the case definition and case questionnaire for identification of suspected cases and persons under investigation (PUI) to assist with further follow up of notifications made to DHHS.

Design and conduct an epidemiological study (chapter 5)

I conducted a case-control study comparing differences in reported symptoms between COVID-19 cases notified to NNDSS and people who tested negative to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at Commonwealth funded GP respiratory clinics (GPRC). I worked closely with the COVID-19 response team in the Primary Care Division and developed coding for data cleaning and analysis. Results from the study supported national guidelines for early detection of cases, and to identify potential symptoms that may indicate COVID-19 infection across different age groups.

Literature review (Chapters 2–5)

I conducted literature reviews for all of the major projects undertaken to develop a better understanding of the context and scope of each project prior to commencement. I also conducted literature reviews for CDNA and the COVID-19 weekly epidemiology reports published in CDI during my time in the NIR as part of the COVID-19 Epidemiology and Surveillance team for the national response.

Report to a non-scientific audience

I provided epidemiological input in the daily situation reports and government talking points as part of the COVID-19 Epidemiology and Surveillance team for the national response. As these are internal documents, they have not been included in this thesis.

Scientific manuscript for a peer-reviewed journal (Chapter 3 appendix)

- Measles outbreak among seasonal horticultural workers—Victoria Australia, November–December 2019. Intended for submission in Communicable Diseases Intelligence.

Conference presentation (Chapter 2)

- 2019 Communicable Diseases Conference (CDC), 19-21 November 2019, Canberra, Australia. “Cholera risk in Australian travellers, 1991-2018.”

Teaching requirements (Chapter 6)

- Lessons from the field (LFF): Accessing public data sets and data visualisation
- Group teaching exercise for the 2020 MAE cohort: Introduction to data linkage

Other publications (Chapter 7)

- COVID-19, Australia: Epidemiology Report 7. Reporting week ending 19:00 AEDT 14 March 2020. Communicable Diseases Intelligence (Appendix 1)
- COVID-19, Australia: Epidemiology Report 3. Reporting week ending 19:00 AEDT 15 February 2020. Communicable Diseases Intelligence

1.5 Course work

POPH8917	Public Health Surveillance	Semester 1 2019
POPH8916	Outbreak Investigation	Semester 1 2019
POPH8913	Analysis of Public Health Data	Semester 1 2019
POPH8915	Research Design and Methods	Semester 1 2019
POPH8920F	Applied Epidemiology Thesis	Semester 1&2 2019–2020

Table 2. Summary of core MAE competencies completed within chapters

MAE competency	Chapter					
	1: Field placement and summary of core activities	2: Cholera risk in Australian travellers	3: Establishing nCoV-2019 surveillance	4: Measles outbreak in Victoria	5: COVID-19 symptom profile case-control study	6: Lessons from the field and teaching
Analysis of a public health dataset		✓			✓	
Outbreak investigation				✓		
Establishing a surveillance system			✓			
Epidemiological study					✓	
Literature review		✓	✓	✓	✓	
Lay summary for non-scientific audience	✓					
Manuscript for scientific journal				✓		
Conference presentation		✓				
Teaching requirements						✓

2 Data analysis

Cholera risk in Australian returned travellers: An analysis of notifications to the National Notifiable Diseases Surveillance System (NNDSS), 1991–2018

Table of contents

2.1 Prologue

2.1.1 My role

I undertook an analysis of cholera notifications to describe the risk of cholera in Australian return travellers using data from the National Notifiable Diseases Surveillance System (NNDSS). I submitted an ethics application to the Human Research Ethics Committee (HREC) at ANU and developed the data analysis plan to calculate cholera notification rates by country and/or region of travel. I searched through previous reports published in national and state bulletins and journals, and contacted OzFoodNet epidemiologists in states and territories to validate existing cholera data in NNDSS and obtain additional data. I was responsible for organising ongoing meetings with my field and academic supervisors for this project. I presented the findings from this study at the Communicable Diseases Control (CDC) conference in 2019.

2.1.2 Lessons learnt

Missing or incomplete data was a challenge for this analysis, particularly in trying to categorise serotype and country of acquisition for notifications dating back 10 years and earlier. I searched through past infectious disease reports and bulletins across different states to find missing information. I also contacted epidemiologists in all states and territories to verify the notifications in which all but one state were able to verify. This process recovered some missing data on serogroup and place of acquisition, but there was still a large amount of missing information for older notification data. I initially thought working with such a small dataset would be simpler and more straightforward but soon realised that was not the case with missing data being such a big issue and limiting the types of analyses I could undertake. This project challenged me to think about ways to present data and finding suitable denominator data from publicly available government data sources.

2.1.3 Acknowledgements

Martyn Kirk, Luis Furuya-Kanamori, Rhonda Owen, Tsheten Tsheten, OzFoodNet epidemiologists in all states and territories.

2.2 Abstract

2.2.1 Background

Cholera has been reported to the National Notifiable Diseases Surveillance System (NNDSS) in Australia since 1991. The vast majority of cases in Australia are travel-associated. I describe cholera risk importation from return travellers to Australia, and provide risk estimates by country/region of travel.

2.2.2 Methods

I used cholera notifications from NNDSS from 1991-2018. I excluded cases of cholera acquired in Australia in travel-related analyses. I used descriptive analysis to summarise the data and calculated rates of infection using Australian population and returned traveller data from the Australian Bureau of Statistics as the denominator.

2.2.3 Results

There were 84 cholera notifications in the 27-year period, with a median of 3 (range 2-6) cases reported per year. Six were locally acquired and were excluded from further analysis. Of the 78 travel-related cases, 50% were male, 49% female and 1% unknown, with a median age of 42 years (IQR = 28-53). Isolates were reported as O1 (77%) or O139 (1%) serogroups, with 21% untyped. 73% (61/84) of all notifications had information on country/region of acquisition. The highest rate of cholera cases was 1.52 per million travellers from Southern and Central Asia, 0.46 per million travellers from South-East Asia, and 0.40 per million travellers from Sub-Saharan Africa. Bangladesh had the highest rate of infection with 99.5 cases per million travellers from 1991-2018.

2.2.4 Conclusion

The risk of cholera importation to Australia is very low. Most infections were acquired from travel to Asia and Papua New Guinea (PNG) Despite the low risk, travellers should take general precautions to prevent enteric infections while travelling to cholera endemic areas. There is a need to improve data quality within NNDSS, particularly for earlier years.

2.3 Background

Cholera is an acute bacterial enteric disease associated with poor access to clean water and sanitation facilities.[1] Most infections are asymptomatic with mild cases of diarrhoea, particularly among children. Cholera causes prolific diarrhoea that can lead to severe dehydration and potentially fatal outcomes if left untreated.[2] With timely and adequate treatment, the case fatality rate (CFR) is less than 1%, however, many countries report a much higher CFR which may reflect poor health systems, limited access to healthcare and limited capacity of surveillance systems to detect outbreaks and trigger timely response.[3]

Cholera is caused by the infectious agent *Vibrio cholerae*, with Serogroup O1 (biotypes classical and El Tor) the most commonly occurring.[2] The classical biotype O1 was associated with earlier pandemics but in the past 20 years has been replaced by El Tor. Serogroup O139 first emerged in 1992 and also causes typical cholera with a similar clinical illness. Although cholera outbreaks in the 1990s were caused by the O139 serogroup, El Tor remains the current dominant strain globally.[4] Of more than 200 O-antigen serogroups of *V. cholerae* identified, only toxigenic serogroups O1 and O139 are known to cause cholera epidemics or pandemics.[5] Non-toxigenic strains within these serogroups also exist in the environment and may cause sporadic cases and rare outbreaks of diarrhoeal diseases, but are not associated with large cholera epidemics.[2]

Transmission occurs through consumption of food or water contaminated with faeces or vomitus of infected persons, where *V. cholerae* O1 and O139 can persist in water for long periods of time. Direct person-to-person transmission may also occur through close contact but is less common. Humans are the main reservoirs, however, environmental reservoirs of *V. cholerae* have also been observed and are associated with copepods and other zooplankton in brackish water or estuaries.[2] The incubation period of cholera ranges from a few hours up to 5 days, with an average of 2-3 days.[4] The concentration of vibrios per gram shed in stool is 10^3 –10^8 organisms and vary for asymptomatic, mild and severe infection. Symptomatic patients may shed vibrios before the onset of illness and up to 7-14 days. Patients who are asymptomatic generally shed vibrios in their stool for only 1 day.[4] The infectious dose in humans varies depending on bacterial strain and host factors. A study in healthy volunteers found that doses of 10^8 –10^{11} are required to establish infection. This dosage drops to 10^4 –10^8 when stomach acids are neutralised through consumption of food or a bicarbonate buffer.[6,7]

For treatment purposes, it is not necessary to obtain a laboratory confirmed diagnosis of typical cases of cholera. However, laboratory confirmed diagnosis is necessary for implementing control measures in response to large scale outbreaks.[8] Diagnosis is confirmed by isolating *V. cholerae* from the Serogroup O1 or O139 by culture of a stool specimen. Stool samples or rectal swabs should be collected early in the course of disease and before administration of antimicrobial drugs. For identification and characterisation of suspected colonies, tests should be carried out with appropriate dilution of standard anti-cholera O-Group 1 serum.[9] For identification and characterisation, slide agglutination should be used with group and type-specific antisera and demonstration of characteristic biochemical reactions.[9] In non-endemic areas, suspected cases should be confirmed by biochemical and serological reactions. The organism should be tested for cholera toxin production or for the presence of cholera toxin genes.[2] In areas with limited laboratory testing capacity, rapid testing kits such as the dipstick rapid test can provide an early warning to public health authorities on the occurrence of an outbreak.[10] In epidemics, testing for all cases is not required once laboratory confirmation and antibiotic sensitivity has been established.[2]

Risk factors for cholera infection range from environmental and socioeconomic, to individual patient characteristics. The main risk factors for infection are related to water, sanitation and hygiene.[1] Higher cholera risk is associated with poor access to safe drinking water, method of water storage (in a bucket or open container), lack of access to latrines and flush toilets, inadequate sewage systems, and low levels of sanitation and hygiene including handwashing before food preparation and eating, and after defecation.[11] Broader socio-economic factors also influence risk of cholera infection including education, health literacy and income which influence level of access to health care and improved living conditions.[11] Patient characteristics including blood type and genetic features are also factors for cholera risk. Patients with gastric achlorhydria (inability to produce gastric acid) decreases the required infectious dose of cholera, thereby increasing the risk of infection.[2] People with blood group O have a lower risk of initial colonisation by *V. cholera* but a higher risk of symptomatic cholera.[11] People who are immunocompromised are also at an increased risk of cholera infection. Large cholera outbreaks may also occur in humanitarian crises where populations are in overcrowded camps and lack access to clean water and latrines.[1]

Studies have shown that people travelling to endemic areas may also be at an increased risk if they don't take precautionary measures against enteric infections.[12] Traveller's diarrhoea is the most common health issue among visitors to tropical and sub-tropical regions.[12] It is estimated that over 60% of travellers visiting these regions will acquire a gastrointestinal infection.[13] Morbidity associated with enteric infections in

travellers is broader and include serious or prolonged cases of diarrhoea which have not been well characterised.[13] Incidence of diarrhoea associated with cholera in travellers is believed to be underestimated as approximately 90% of cholera episodes are of mild to moderate severity and often indistinguishable from other causes of traveller's diarrhoea.[14]

An orally administered vaccine against Serogroup O1 is available and is recommended for children over 2 years old and adults travelling to cholera endemic areas who are at higher risk of developing cholera and other travel associated diarrhoeal infections.[15] Studies have shown that this vaccine may also provide cross-protection against other common causes of traveller's diarrhoea including enterotoxigenic *Escherichia coli* (ETEC).[16] Currently there are no mandatory requirements for vaccination against cholera before entry to any countries, and routine vaccination is not recommended for travellers. As the risk to most travellers is very low, greater emphasis should be on accessing clean food and water to prevent cholera infection overseas.

Cholera in Australia

Cholera was included in the National Notifiable Diseases Surveillance System (NNDSS) in 1991 to detect and monitor cases in Australia.[17] Since standardised reporting of cholera to NNDSS, notification rates have been low across Australia. Approximately 0-6 cases are reported annually.[17] New South Wales (NSW) state accounts for over a third of all notifications during the 27-year period.[17]

In Australia, cholera is not endemic with the majority of all cases acquired from overseas travel to endemic areas. Cholera was listed as a quarantinable disease up until 2015 when it was removed. Cholera was classed as one of the security sensitive biological agents (SSBA) in Australia under the Security Sensitive Biological Agents Regulatory Scheme (SSBARS) until its removal on 14 March 2016.[18] The scheme operates under the National Health Security Act 2007 (NHS Act) which provides for the establishment of a list of biological agents that the Minister of Health considers to be of security concerns to Australia and regulates the handling of SSBAs.[19]

Although NNDSS notifications have remained stable over time, there have been no analyses looking at epidemiological trends in time, age, sex, serogroup/serotype/biotype, and country/region of acquisition. The number of Australians travelling overseas and visitors arriving have almost doubled in the past decade and continued on an increasing trajectory.[20] The top three destinations for returning residents and visitors arriving were countries in Oceania, South-East Asia

and North-East Asia. Cholera is endemic in many countries in these regions, which increases the risk of infection among people travelling to these areas. Therefore, it is important to estimate the risk cholera importation by country/region of travel to inform and update current travel advice and provide information for people travelling to these areas. This analysis will highlight areas to improve national cholera surveillance and reduce the risk of infection for people travelling to cholera endemic countries.

2.4 Aims

The aim of this study was to describe cholera risk importation from return travellers to Australia, and estimate risks by country and region of travel. The study had the following objectives:

1. To summarise and describe the yearly trend of cholera notifications from 1991 to 2018;
2. To describe the distribution of cholera notifications by age, sex and serogroup and place of acquisition; and
3. To identify the most common countries or regions where cholera infections were acquired and estimate risk for travelling to different countries.

2.5 Methods

2.5.1 Data Source

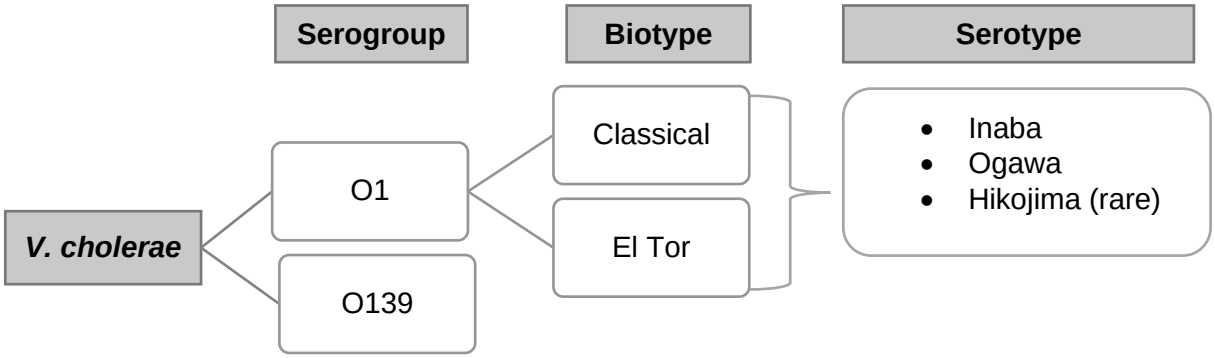
Cholera is nationally notifiable in Australia with all states and territories reporting de-identified data on confirmed cases to the NNDSS.[21] The Australian Government Department of Health (DoH) is the data custodian of the NNDSS and manages the national data on behalf of the Communicable Diseases Network Australia (CDNA). The core data fields collected for all cases of cholera include: state, age, sex, diagnosis date, Serogroup and subtype, indigenous status and country of acquisition. Overseas arrivals and departures (OAD) data was publicly available from the ABS website and was used as the denominator.[22] To calculate rates by state and territory I used a midpoint population estimate for the 27-year time period in 2006 and divided it by 27 to get an average annual rate.

National Notifiable Diseases Surveillance System (NNDSS)

The current case definition used for national surveillance of cholera requires notification of only confirmed cases. A confirmed case requires laboratory definitive evidence only for isolation of toxigenic *V. cholerae* O1 or O1319.[21]

I extracted all notified cases of cholera from the NNDSS where diagnosis date was from 1991 to 2018. The NNDSS core dataset field specifications defines the diagnosis date as "the true onset date if known, otherwise it will be the earliest of the specimen date, the notification date, or the notification received date".[23] I included both overseas-acquired and locally-acquired cases in the descriptive analysis of the cases and then excluded locally-acquired cases from the travel-related analyses. I categorised serogroup/biotype into a consistent format across all notifications (Figure 1). I created a new category for region of acquisition for notifications where country-specific denominator data was unavailable. A significant proportion of the dataset contained missing values on serogroup and place of acquisition, where the majority of missing data were for earlier notifications made before 2010. I conducted a search through past CDI quarterly and yearly NNDSS reports from 1994 to 2015, and state-wide communicable disease bulletins. The search provided information on country of acquisition and mapped serogroup and biotype that was missing for some notifications. I contacted OzFoodNet epidemiologists across Australia to validate notification details in their jurisdiction.

Figure 1. Mapped Serogroup/Biotype/Serotype for *V. cholerae*



Overseas arrivals and departures data

The study used Overseas Arrival and Departure (OAD) data from 1991 to 2018 from the ABS for the denominator. The OAD dataset contains monthly data on short-term (less than one year) visitor arrivals (STVA) and short-term resident returns (STRR). The population coverage included all international travellers who crossed Australia's international border. Exclusions were made for: movements of operational air and ships' crew, transit passengers who pass through Australia but not cleared for entry (including some defence force personnel), passengers on pleasure cruises commencing and finishing in Australia, and undocumented arrivals or departures.[22]

Monthly OAD data was combined for each year from 1991 to 2018 for both STVA and STRR. Both STVA and STRR data in the 27-year period were combined for the denominator. Country specific OAD data that was available for the identified countries of acquisition was combined for the same time period and across both STVA and STRR. At the time of analysis, the Standard Australian Classification of Countries, 2011, Version 2.3 (SACC) was the most current classification used for country of stay/residence with different versions also used for previous years (Table 1).

Table 1. Standard Australian Classification of Countries (SACC) 2011, Version 2.3, country of stay/residence, visitor arrivals and resident returns, ABS

Country of stay/residence	
Oceania and Antarctica	New Zealand, New Caledonia, Papua New Guinea, Vanuatu, Cook Islands, Fiji, French Polynesia, Samoa, Tonga, Other Oceania and Antarctica
North-West Europe	UK CIs and IOM, Ireland, Austria, France, Germany, Netherlands, Switzerland, Sweden, Other North-West Europe
Southern and Eastern Europe	Italy, Spain, Croatia, Greece, Poland, Other Southern and Eastern Europe
North Africa and the Middle East	Egypt, Israel, Lebanon, Turkey, United Arab Emirates, Other North Africa and the Middle East
South-East Asia	Cambodia, Thailand, Vietnam, Indonesia, Malaysia, Philippines, Singapore, Timor-Leste, Other South-East Asia
North-East Asia	China, Hong Kong, Taiwan, Japan, Korea South, Other North-East Asia
Southern and Central Asia	Bangladesh, India, Nepal, Pakistan, Sri Lanka, Other Southern and Central Asia
Americas	Canada, United States of America, Argentina, Brazil, Chile, Peru, Mexico, Other Americas
Sub-Saharan Africa	Mauritius, South Africa, Other Sub-Saharan Africa

ABS country-specific overseas arrivals data was available for only Bangladesh, India, Thailand, Indonesia, Philippines, Pakistan and Papua New Guinea (PNG). Incidence rates were calculated per million travellers by country of travel over the 27-year period. Differences in the volume of return travellers impacted the incidence rates for each country of travel.

2.5.2 Analysis

I conducted descriptive analysis of cholera notifications over the study period by year, age group, sex, state, serotype/biotype/serotype, and country/region of acquisition. I calculated total rates of infection for cholera notifications by country and/or region of acquisition, dependent on available OAD denominator data from the ABS for the entire 27 years of the surveillance period. I used a chi-square test to investigate the relationship between 10-year age groups and sex on cholera notifications. I performed all of the analyses using StateSE 13 and Microsoft Excel 2016.

2.5.3 Ethics

Ethics approval was obtained from the Australian National University Human Research Ethics Committee (HREC). Permission to access NNDSS data was granted through the Office of Health Protection at the Department of Health.

2.6 Results

A significant proportion of the dataset contained missing values including 26% missing data on serogroup and 57% on place of acquisition. The majority of missing data were for earlier notifications made before 2010. Searches conducted through CDI quarterly and yearly NNDSS reports from 1994 to 2015, and state-wide communicable disease bulletins recovered 8% of missing information on serogroup/biotype and 37% on country of acquisition.

2.6.1 Characteristics of cholera notifications

From 1991 to 2018, there was a total of 84 cholera notifications in Australia. 93% (78/84) of all notifications were acquired overseas, representing a rate of 0.26 per million return travellers for the 27-year period. 7% (6/84) of the cases were locally acquired, three were through laboratory exposure, and the remaining three cases were acquired through consumption of imported whitebait.[24] The majority of notifications were from New South Wales (36%), followed by Queensland (23%), Victoria (18%), Western Australia (12%), South Australia (10%) and the Australian Capital Territory (2%). No notifications were reported in Tasmania or the Northern Territory (Table 2).

Over the 27-year period the number of notifications per year ranged from 0 to 6, with a median of 3. There were 6 notifications each year in 1993, 1995 and 2011. There were no notifications in 2003 and 2018 (Figure 2).

The sex distribution for cholera notifications was similar among males (50%) and females (49%). Sex was unknown for 1% of all notifications. Data on age was available for 98% (82/84) of all notifications. The median age of cases was 42 years old, with a range of 0 to 84 years (IQR = 28-53 years). The highest notification rates were reported in the 40-49 age group with 6.7 per million population, followed by those in the 70-79 age group with 3.9 per million population, and the 30-39 year age group with 3.8 per million population (Figure 3). There was no difference in cholera notifications between 10 year age groups when comparing to sex (p=0.70).

Table 2. Number of cholera notifications by state, and the average annual rate per million population, Australia, 1991-2018

State	Total	%	Australian population (2006)	Average annual rate per million population
NSW	30	36%	6,827,700	0.16
QLD	19	23%	4,053,400	0.17
VIC	15	18%	5,091,700	0.11
WA	10	12%	2,050,900	0.18
SA	8	10%	1,554,700	0.19
ACT	2	2%	328,800	0.23
Australian total	84	100%	20,602,800	0.15

Figure 2. Number of cholera notifications and incidence rate per million population, by year, Australia, 1991-2018

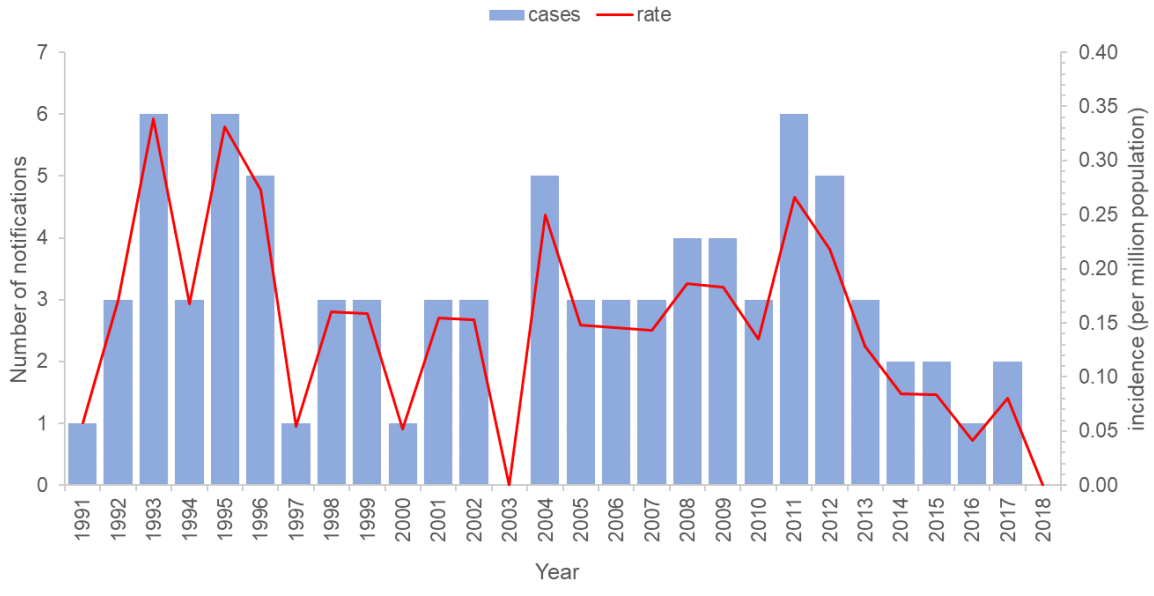
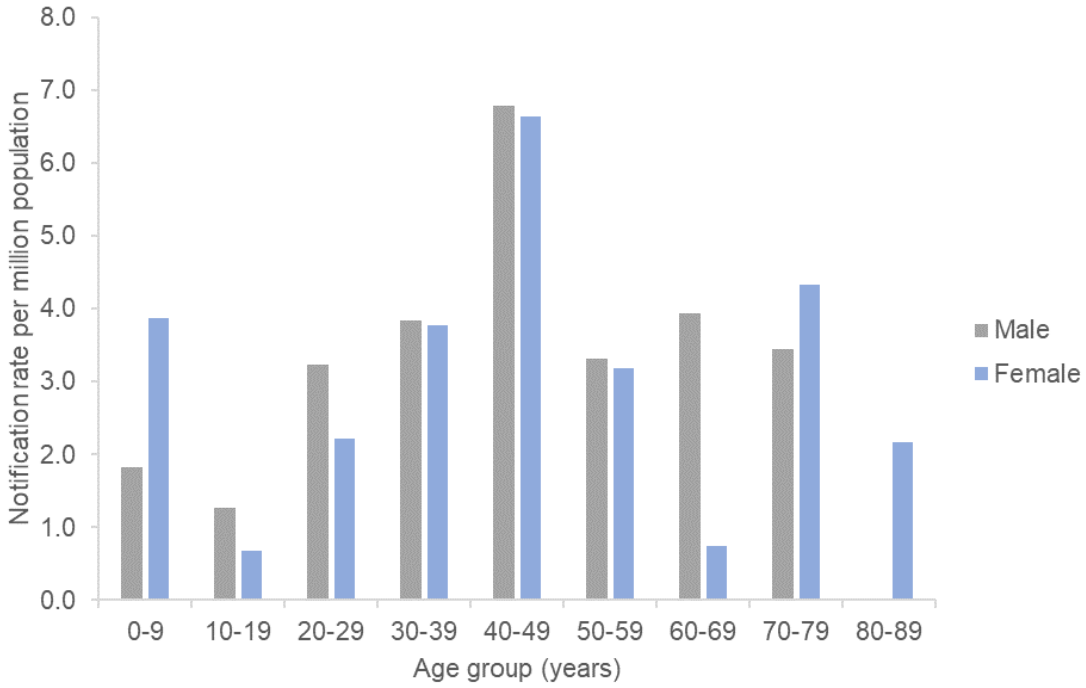


Figure 3. Cholera notification rates per million population, by 10-year age groups and sex, Australia, 1991-2018.



2.6.2 Serogroup/Biotype/Serotype

Only 79% (66/84) of all notifications in the study period contained Serogroup information (Table 3). Of known Serogroup, 98% (65/66) were from serogroup O1, and 2% (1/66) were from serogroup O139. Biotype information was only available for 50% (42/84) of notifications which were all under Serogroup O1. Of known biotype, 95% (40/42) were El Tor and 5% (2/42) Classical. Serotype information was only available for 57% (48/84) of all notifications. Of known Serotype, 85% (41/48) were Ogawa and 15% (7/48) were Inaba.

Table 3. Number of cholera notifications by Serogroup, Biotype and Serotype, Australia, 1991-2018

		Total	**%**
Serogroup	O1	65	77%
	O139	1	1%
	Untyped	18	22%
	Total	**84**	**100%**
Biotype	Classical	2	2%
	El Tor	40	48%
	Unknown	42	50%
	Total	**84**	**100%**
Serotype	Inaba	7	8%
	Ogawa	41	49%
	Unknown	36	43%
	Total	**84**	**100%**

2.6.3 Place of acquisition

Seventy three per cent (61/84) of all notifications had information on place of acquisition. Of known cholera regions of acquisition, the top 3 regions with the highest proportion were South-East Asia (46%), Southern and Central Asia (26%) and Oceania and Antarctica (21%). The cumulative incidence of overseas arrivals in Australia over the 27 year period per million travellers was 0.46 in South-East Asia, 1.52 in Southern and Central Asia, and 0.10 in Oceania and Antarctica (Table 5).

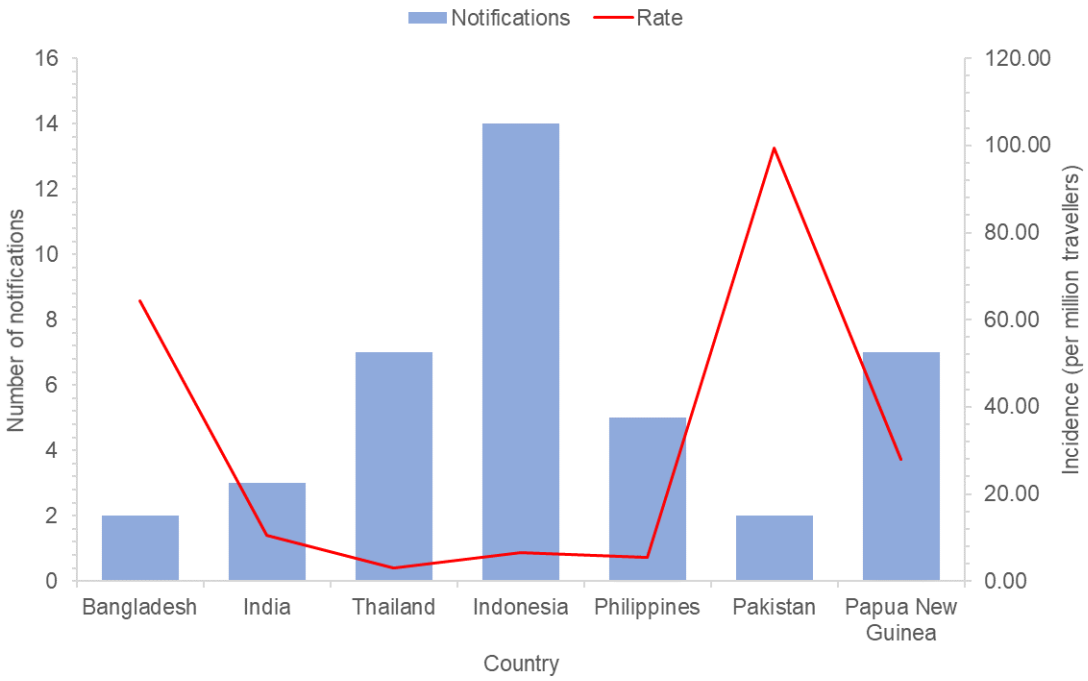
Table 4. Count, proportion, and rate of overseas acquired cholera cases in Australia by region of suspected acquisition, 1991-2018.

Region	Total	%	Rate per million returned travellers
South-East Asia	28	36%	0.46
Southern and Central Asia	16	21%	1.52
Oceania and Antarctica	7	9%	0.10
Sub-Saharan Africa	2	3%	0.40
North-East Asia	2	3%	0.04
Unknown	23	28%	-
Total	78	100%	0.26

2.6.4 Cholera incidence by country of travel

The cumulative incidence for overseas arrivals in Australia over the 27-year period per million travellers was 99.5 for Pakistan, 64.4 in Bangladesh, 28. in Papua New Guinea (PNG), 10.5 in India, 6.64 in Indonesia, 5.55 in Philippines and 3.06 in Thailand.

Figure 5. Number of cholera notifications and incidence rate for overseas arrivals in Australia by country of travel, 1991-2018



2.7 Discussion

Over the 27-year period, despite a steady increase in international travel across all regions, cholera notification rates in Australia have remained extremely low with 0-6 notifications per year. The majority of cases are overseas acquired, which is reflected in the low ratio of local to imported cases observed in the data. Travel volume was highest in countries in Oceania, South-East Asia, and Southern and Central Asia, which was reflected in the higher number of notifications coming from countries in these regions. New South Wales, Queensland and Victoria reported the highest number of cases which is reflective of the higher volume of inbound travellers arriving in these states.

The results from this study suggest a very low risk of cholera introduction in Australia with notification rates remaining well below 0.5 per million population of overseas arrivals each year over the 27-year period. Cholera notifications have remained stable with no significant increases in any of the observed years given the increase in the number of travellers over the study period. Of the locally acquired cases, infection occurred through non-travel related means, highlighting a very low risk of travel-related importation of cases into the country. Despite cholera being endemic to many neighbouring countries in regions with the highest volume of travellers from Australia[22], infection rates have remained low and there has been no evidence of ongoing local transmission from return travellers. This is shown by the low cholera incidence rates for

overseas arrivals from PNG, Thailand, Indonesia, and the Philippines. Despite the removal of cholera from the quarantinable disease list and SSBA list in 2015 and 2016, notification rates have remained at approximately 0.1 per million population.

Findings from this analysis support the advice given from the Australian Immunization Handbook guidelines for cholera vaccination. Due to the very low risk and small number of cases over the 27-year period of surveillance, routine cholera vaccination for travellers is not recommended despite cholera being endemic in some of the countries with high volumes of Australian travellers.[15] However, vaccination is recommended for travellers who have a higher risk of exposure to cholera, including humanitarian aid workers deployed to cholera endemic or outbreak active regions.[15] Vaccination is also recommended for those travelling to cholera endemic areas with medical conditions, such as achlorhydria, that may increase their risk of acquiring diarrhoeal diseases. People with pre-existing co-morbidities including inflammatory bowel disease, significant cardiovascular disease, and human immunodeficiency virus (HIV) or other immunocompromised conditions which may result in more severe outcomes should also get vaccinated.[15] Currently, there are three WHO pre-qualified oral cholera vaccines available all of which require a minimum of two doses for full protection.[25] In Australia, Dukoral is the only cholera vaccine available and provides protection against Serogroup O1.[15] Various studies conducted among different population groups across a range of settings have shown the vaccine to be effective with minimal adverse effects.[26-32] There is also some evidence that suggests the cholera vaccine may provide cross-protection against other common enteric diseases associated with travellers' diarrhoea.[16] The proportion of cholera vaccine uptake among Australian travellers is unknown. However, an assumption can be made that this number is low as no countries require mandatory vaccination before entry, and there is no recommendation made for routine vaccination against cholera.

There are some limitations in this study that should be considered when interpreting the results. Missing data was the main limitation and was addressed by extracting additional information through searches, cross-checking data, and contacting state and territory epidemiologists to validate existing data. Data completeness across all fields was available only for notifications made within the last 10 years. Information on serogroup/serotype/biotype and country of acquisition was missing for many notifications made prior to 2010. Notifications reported before 2010 also had differing places of acquisition reported in the national database when cross-checked with state databases for validation. All but one state were able to provide validation on cholera notifications in NNDSS and those recorded in their database. This may have had an impact on the results as a high number of notifications were made in this state. A large

proportion of older notifications, in particular those from Queensland, were diagnosed in private laboratories where place of acquisition was different to that reported in the national database. Upon further investigation and follow up, it was confirmed that no further typing was done in most of the notifications prior to 2000 that were diagnosed through private laboratories, therefore, additional serotyping and biotyping information remains unknown. The quality of the data was also affected by changes and upgrades across several state databases where full data completeness was not transferred across to newer systems. There is also no national standard reporting form for cholera, resulting in varying levels of information being collected by each jurisdiction and differences in data completeness captured in the national database. It is highly likely that there is underreporting of cholera cases due to the variability of symptoms of enteric infections, where mild cases may be less likely to seek medical care, and therefore are undetected and no notifications made to State health departments and to NNDSS.

Since my work on this chapter, it is likely that NNDSS has been updated with the cleaned data on cholera notifications, as this required State health departments to send through routine updates to NNDSS. I imagine that there is greater data accuracy in the State databases, as most of the States have rectified their data from the NNDSS extracts that I sent through for validation.

2.8 Conclusion

The risk of cholera importation into Australia from overseas travellers remains very low despite the steady increase in travellers each year who are either returning residents or visitors arriving. The highest risk regions for cholera acquisition are South-East Asia, Oceania and Southern and Central Asia. Among these regions, the highest risk countries are Indonesia, India, Thailand, PNG and the Philippines. These countries are among the destinations with the highest yearly rate of Australian travellers. The current travel advice provided by the Australian Immunization Handbook is appropriate given the very low level of risk for cholera acquisition abroad. It is recommended for travellers to take general precautions to reduce their risk of cholera and other enteric infections abroad. This includes maintaining personal hygiene and hand washing, avoiding drinking contaminated and untreated water sources, and making wise food choices. Vaccination has shown to be effective and should be considered for high-risk travellers including humanitarian aid works deployed to cholera outbreak settings, people who are immunocompromised, and those with existing medical conditions that could increase their risk of acquiring diarrhoeal diseases which may result in severe

outcomes. Although nationwide surveillance data has improved over the last 10 years, there is still some variability in data quality reported across jurisdictions. A nationwide standard reporting form for cholera notifications with enhanced data fields including place of acquisition and traveller type (return resident or visitor arrival) can improve data quality and completeness in NNDSS and improve routine surveillance and reporting.

2.9 References

1. World Health Organization. Cholera [Internet]. Geneva: WHO; 2019 [updated 2019 Jan 17; cited 2019 Jul 8]. Available from: https://www.who.int/news-room/fact-sheets/detail/cholera
2. Chin J, Ascher MS, editors. Control of Communicable Diseases Manual. 17th ed. Washington DC: American Public Health Association; 2000. 623 p.
3. World Health Organization. Global Health Observatory (GHO): Cholera case fatality ratio (%) [Internet]. Geneva: WHO; 2020 [cited 2020 Jul 1]. Available from: https://www.who.int/gho/epidemic_diseases/cholera/situation_trends_case_fatality_ratio/en/
4. Nelson EJ, Harris JB, Morris JG Jr, Calderwood SB, Camilli A. Cholera transmission: the host, pathogen and bacteriophage dynamic. Nat Rev Microbiol. 2009;7(10):693-702. doi:10.1038/nrmicro2204
5. Pang B, Yan M, Cui Z, Ye X, Diao B, Ren Y, et al. Genetic diversity of toxigenic and nontoxigenic *Vibrio cholerae* Serogroups O1 and O139 revealed by array-based comparative genomic hybridization. J Bacteriol. 2007 Jul;189(13):1837-4849. doi:10.1128/JB.01959-06
6. Kaper JB, Morris JG & Levine MM. Cholera. Clin Microbiol Rev. 1995 Jan;8(1):48-86. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC172849/
7. Cash RA, Music SI, Libonati JP, Craig JP, Pierce NF & Hornick RB. Response of man to infection with *Vibrio cholerae.* II. Protection from illness afforded by previous disease and vaccine. J Infect Dis. Oct 1974;130(4):325-333. Available from: https://academic.oup.com/jid/article-abstract/130/4/325/899606?redirectedFrom=fulltext
8. Joaquin A, Barua D, Burrows W, Carpenter CCJ, Cash RA, et al. Principles and practice of cholera control. (1970). Geneva: WHO; 2020 [cited 2020 Jul 1]. Available from: https://apps.who.int/iris/handle/10665/39753
9. Carpenter CC. Cholera: diagnosis and treatment. Bull N Y Acad Med. 1971 Oct;47(10):1192-203. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1749964/
10. Centers for Disease Control and Prevention. Cholera – *Vibrio cholerae* infection: diagnosis and detection [internet]. Atlanta: CDC; 2020 [updated 2018 Jul 20; cited 2020 Jul 2]. Available from: https://www.cdc.gov/cholera/diagnosis.html
11. Richterman A, Sainvilien DR, Eberly L & Ivers LC. Individual and household risk factors for symptomatic cholera infection: A systematic review and meta-analysis. J Infect Dis. 2018 Oct 15;218(suppl_3):S154-164. doi:10.1093/infdis/jiy444

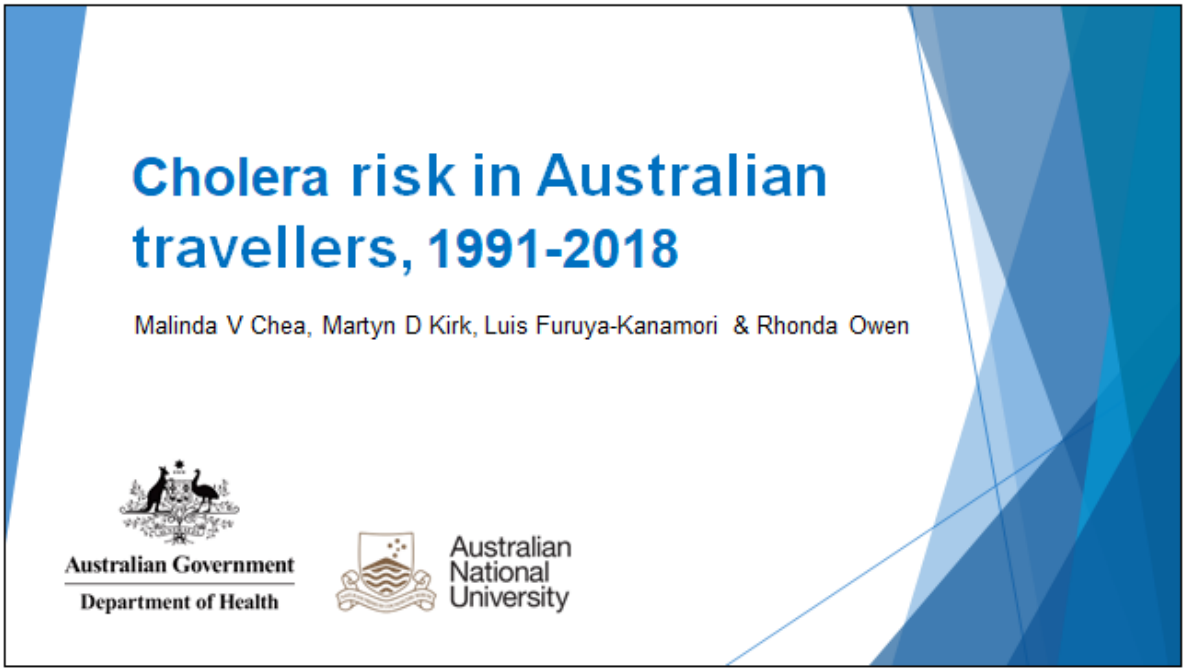
12. Steffen R, Epidemiological studies of travelers' diarrhea, severe gastrointestinal infections, and cholera. Rev Infect Dis. 1986 May 1;8(suppl_2):S122-30. doi:10.1093/clinids/8.supplement_2.s122
13. Greenwood Z, Black J, Weld L, Leder K, Von Sonnenburg F, Schwartz E, et al. Gastrointestinal infection among international travelers globally. J Travel Med. 2008 Jul 1;15(4):221-228. Available from: https://academic.oup.com/jtm/article/15/4/221/1901117
14. Torrell JMR, Aumatell CM, Ramos SM, Mestre LG & Salas CM. Reduction of travellers' diarrhoea by WC/rBS oral cholera vaccine in young, high-risk travellers. 2009 Jun 19;27(30):4074-7. doi:10.1016/j.vaccine.2009.04.025
15. Australian Government Department of Health. Australian Immunisation Handbook: Cholera [Internet]. Canberra ACT: Australian Government Department of Health; 2019 [updated 2018 Jun 1; cited 2019 Jul 8]. Available from: https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/cholera
16. Clemens JD, Sack DA, Harris JR, Chakraborty J, Neogy PK, Stanton B, et al. Cross-protection by B subunit-whole cell cholera vaccine against diarrhea associated with heat-labile toxin-producing enterotoxigenic Escherichia coli: results of a large-scale field trial. J Infect Dis. 1988 Aug;158(2):372-7. doi:10.1093/infdis/158.2.372.
17. Australian Government Department of Health. National Notifiable Diseases Surveillance System [Internet]. Canberra ACT: Australian Government Department of Health; 2019 [updated 2019 Jul 8; cited 2019 Jul 8]. Available from: http://www9.health.gov.au/cda/source/rpt_3.cfm
18. Australian Government Department of Health. SSBA Reporting Forms: Removal of Salmonella Typhi and Vibrio Cholerae [Internet]. Canberra ACT: Australian Government Department of Health; 2019 [updated 2016 Mar 17; cited 2019 Jul 8]. Available from: https://www.health.gov.au/internet/main/publishing.nsf/Content/ssba-forms-removal-samonella-typhi-vibro-cholerae
19. Australian Government Department of Health. Security Sensitive Biological Agents [Internet]. Canberra ACT: Australian Government Department of Health; 2019 [updated 2019 Feb 27; cited 2019 Jul 8]. Available from: https://www.health.gov.au/internet/main/publishing.nsf/Content/ssba.htm
20. Australian Bureau of Statistics. ABS.Stat: Visitor arrivals and resident returns by country [Internet]. Canberra ACT: Australian Bureau of Statistics; 2019 [updated 2019 Jun 18; cited 2019 Jul 8]. Available from: http://stat.data.abs.gov.au/Index.aspx?DataSetCode=ABS_OAD_COUNTRY#

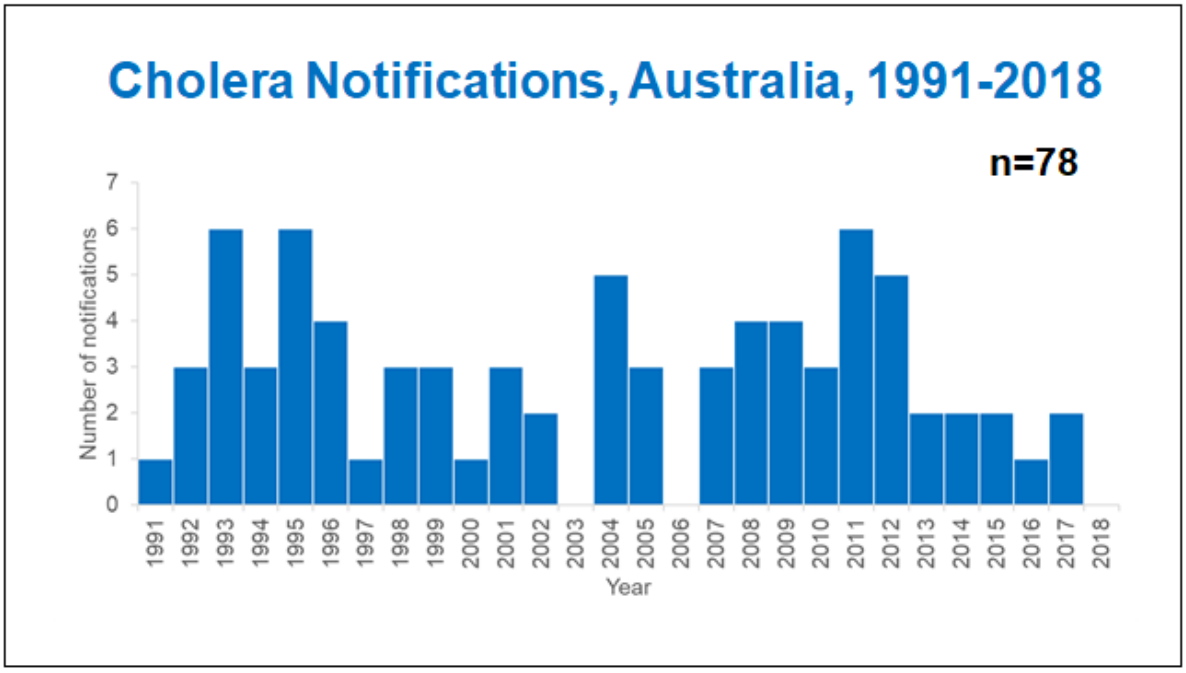
21. Australian Government Department of Health. Cholera case definition [Internet]. Canberra ACT: Australian Government Department of Health; 2019 [updated 2008 Nov 6; cited 2019 Jun 18]. Available from: https://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-nndss-casedefs-cd_cholra.htm
22. Australian Bureau of Statistics. Overseas arrivals and departures, Australia, Mar 2020 [Internet]. Canberra ACT: Australian Bureau of Statistics; 2020 [updated 2020 Jul 25; cited 2020 Aug 3]. Available from: https://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/3401.0Main+Features1Mar%202020?OpenDocument
23. Australian Government Department of Health. NNDSS Core Dataset: Dataset Field Specifications – version 10. Canberra ACT: Australian Government Department of Health; 2016. 14p.
24. Forssman B, Mannes T, Musto J, Gottlieb T, Robertson G, Natoli JD, et al. Vibrio cholerae O1 El Tor cluster in Sydney linked to imported whitebait. Med J Aust. 2007 Sep 17;187(6):345-7. Available from: https://onlinelibrary.wiley.com/doi/full/10.5694/j.1326-5377.2007.tb01278.x?sid=nlm%3Apubmed
25. World Health Organization. Immunizations, vaccines and biologicals: Cholera [Internet]. Geneva: WHO; 2020 [updated 2018 Feb 6; cited 2020 Mar 25]. Available from: https://www.who.int/immunization/diseases/cholera/en/
26. Taylor DN, Cardenas V, Sanchez JL, et al. Two-year study of the protective efficacy of the oral whole cell plus recombinant B subunit cholera vaccine in Peru. J Infect Dis. 2000;181:1667-73. Available from: https://academic.oup.com/jid/article/181/5/1667/2191435
27. Peltola H, Siitonen A, Kyronseppa H, et al. Prevention of travellers' diarrhoea by oral B-subunit/whole-cell cholera vaccine. The Lancet. 1991;338:1285-9. Available from: https://www.sciencedirect.com/science/article/pii/014067369192590X
28. Clemens JD, Sack DA, Harris JR, et al. Field trial of oral cholera vaccines in Bangladesh. The Lancet. 1986;2:124-7. Available from: https://pubmed.ncbi.nlm.nih.gov/2873397/
29. Clemens JD, Harris JR, Sack DA, et al. Field trial of oral cholera vaccines in Bangladesh: results of one year of follow-up. J Infect Dis. 1988;158:60-9. Available from: https://pubmed.ncbi.nlm.nih.gov/3392421/
30. Clemens JD, Sack DA, Harris JR, et al. Field trial of oral cholera vaccines in Bangladesh: results from three-year follow-up. The Lancet. 1990;335:270-3. Available from: https://pubmed.ncbi.nlm.nih.gov/1967730/

31. van Loon FP, Clemens JD, Chakraborty J, et al. Field trial of inactivated oral cholera vaccines in Bangladesh: results from 5 years of follow-up. Vaccine. 1996;14:162-6. Available from: https://pubmed.ncbi.nlm.nih.gov/8852414/
32. Sanchez JL, Vasquez B, Begue RE, et al. Protective efficacy of oral whole-cell/recombinant-B-subunit cholera vaccine in Peruvian military recruits. The Lancet. 1994;344:1273-6. Available from: https://pubmed.ncbi.nlm.nih.gov/7967990/
33. Lucas ME, Deen JL, von Seidlein L, et al. Effectiveness of mass oral cholera vaccination in Beira, Mozambique. N Engl J Med. 2005;352:757-67. Available from: https://pubmed.ncbi.nlm.nih.gov/15728808/

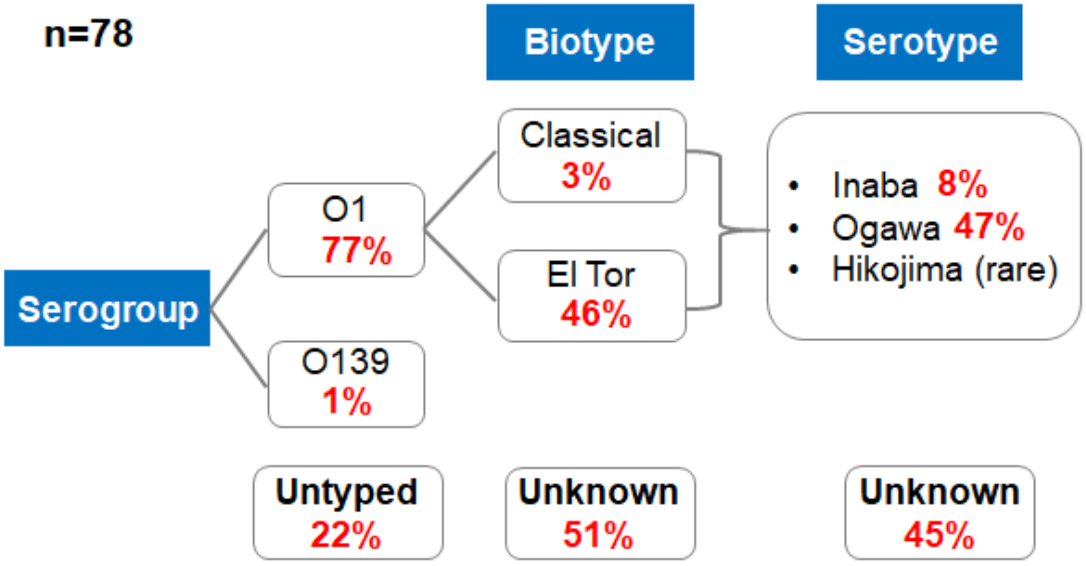
2.10 Appendix

Appendix 1. Conference presentation at the Communicable Diseases Control Conference (21 November, 2019, Canberra).

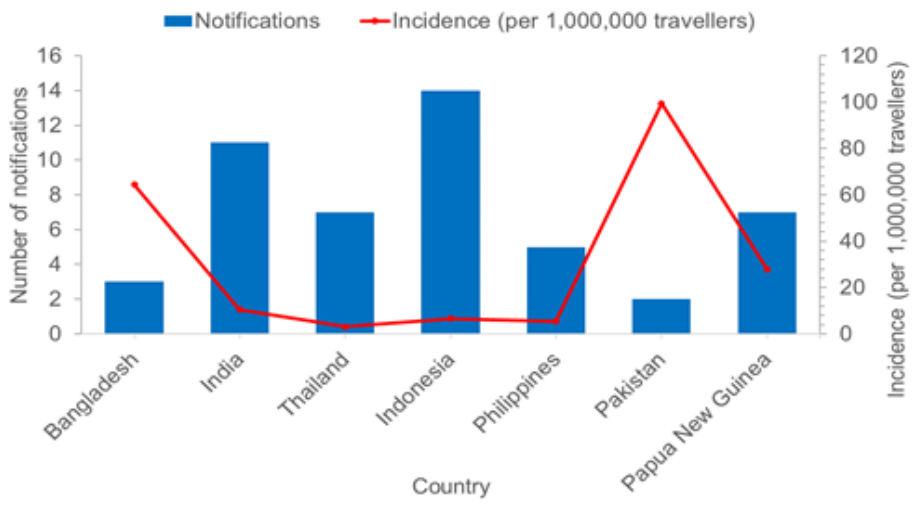




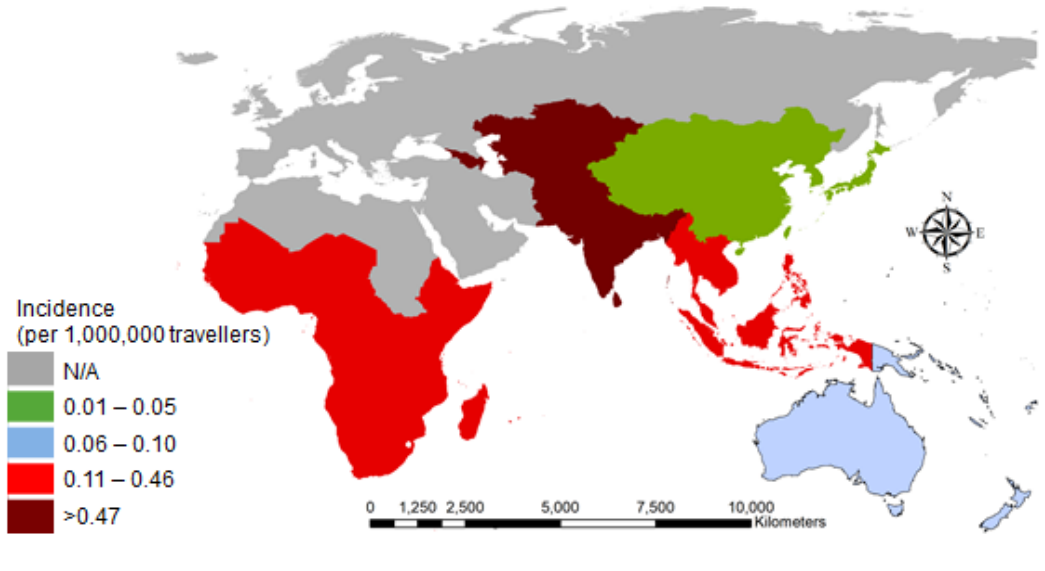
Cholera Notifications, By State, 1991-2018



Cholera In Travellers, Australia, 1991-2018



Cholera Incidence, By Region Of Travel, 1991-2018



Appendix 2. Overseas arrivals and departures (OAD) data

Overseas arrivals and departures data from the ABS show a steady increasing trend in travel to all regions over the 27-year period (Figure 4). The majority of overseas arrivals in Australia were from Oceania and Antarctica (22%), followed by South-East Asia (20%), North-East Asia (19%), North-West Europe (16%) and Americas (12%) (Table 4). The most frequently visited region among returning resident returns and visitor arrivals was South-East Asia and North-East Asia.

Figure 4. Total number of overseas arrivals to Australia (combined resident returns and visitor arrivals) from 1991-2018, by year and top 5 regions of travel.

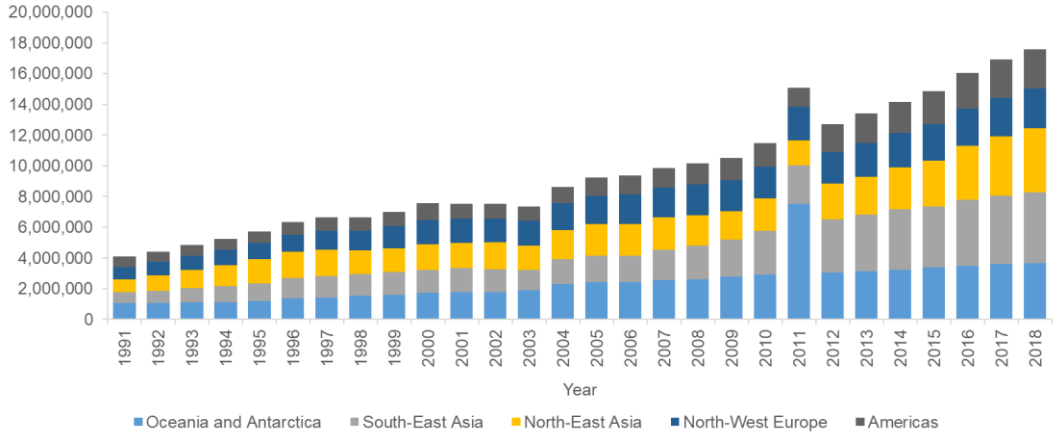


Table 4. Total number of overseas arrivals to Australia (combined resident returns and visitor arrivals) by region of travel from 1991 to 2018

Region	**Total**	**%**
Oceania and Antarctica	67,904,000	22.2%
South-East Asia	61,329,500	20.1%
North-East Asia	56,918,700	18.6%
North-West Europe	48,218,200	15.8%
Americas	36,572,400	12.0%
Southern and Eastern Europe	12,830,800	4.2%
Southern and Central Asia	10,549,300	3.5%
North Africa and the Middle East	5,577,400	1.8%
Sub-Saharan Africa	5,018,300	1.6%
Not stated/Inadequately described	462,700	0.2%
Total	305,381,300	100%

3 Outbreak investigation

Measles outbreak among seasonal horticultural workers in Victoria, Australia, November – December 2019.

Table of contents

3.1 Prologue

3.1.1 My role

Towards the end of my first year of the MAE I had the opportunity to spend 8 weeks with the Victorian Department of Health and Human Services (DHHS) in the Communicable Disease Epidemiology and Surveillance (CDES) team to assist with investigating a measles outbreak. This outbreak occurred at the same time as the measles epidemic that affected many countries in the Pacific, with Samoa being the most affected. At the time, the National Incident Room (NIR) in the Department of Health was activated in response to the outbreak in the Pacific. I worked closely with the lead epidemiologist on compiling intelligence updates for the daily Incident Management Team (IMT) meetings. This included updating the measles contact tree and chain of transmission timeline (Appendix 1) to keep track of the outbreak and identify exposure sites and at risk contacts. I assisted with planning the vaccination outreach programs and contacted employers and employment agencies to obtain an estimate of seasonal worker numbers to inform vaccine stockpile. I liaised with other government agencies to obtain additional information on estimated numbers of short term migrant workers arriving and their countries of arrival to support planning for a vaccination program delivered by local government. I worked closely with the department staff who were part of the IMT and other epidemiologists in CDES to draft a summary of the outbreak intended for submission to a journal. I also had the opportunity to conduct interviews with contacts of measles cases unrelated to this outbreak.

3.1.2 Lessons Learnt

This outbreak highlighted several issues that impacted public health planning and response capacity. The main challenges included navigating political and cultural sensitivities, especially with short term workers from migrant backgrounds. We experienced the most difficulty in trying to obtain an accurate list of the number of workers employed in farms across regional Victoria to inform planning for the vaccination outreach programs. We called directly to employers and employment contractors, most of whom were reluctant to speak to us or give out any information regarding their employees. We specified that we were not concerned about what visas or working schemes their employees were under, but instead were seeking the number of current and expected future seasonal worker arrivals in order to support planning for sufficient vaccine coverage. We also experienced difficulties with obtaining this

information at the national level from responsible government agencies through which many of the short-term seasonal worker programs were managed. Working with cultural and linguistically diverse groups presented additional challenges around communication, including provision of fact sheets and other information in appropriate languages and delivered in a culturally appropriate way. A communications advisor was part of the outbreak team worked closely with translators to develop appropriate materials. The team also contacted the local church in one of the regional areas which was identified as a common place of community gathering for the seasonal workers to distribute measles fact sheets and information on the importance of the vaccination in controlling the outbreak. This was found to be an effective means of conducting community outreach by partnering with the local leaders to communicate health messaging.

3.1.3 Public health implications

Since my involvement in the outbreak response, over 500 seasonal workers from the Pacific and other migrant backgrounds have received one dose of the measles, mumps and rubella (MMR) vaccine. The swift public health response and on-site vaccination of workplace and accommodation contacts limited further transmission in the cluster and the outbreak was contained. Information on the existing measles outbreak in the Pacific informed the planning of additional vaccination outreach programs for short-term seasonal workers, most of whom were arriving from these outbreak affected areas. This response was highly effective at reducing the risk of infection among this group and preventing further outbreak clusters and risk of transmission to the broader community.

3.1.4 Acknowledgements

Lucinda Franklin, Janet Strachan, Charles Alpren, Martyn Kirk, Thomas Tran, Katie Cronin, Carrie Barnes, Annaliese van Diemen, Mihaela Ivan, Helen Pitcher, Jay Healey, Aicha Brahmi, Miriam O’Hara & Jessica List.

3.2 Abstract

3.2.1 Background

Measles is a highly infectious disease that is notifiable in all Australian states and territories. In late 2019, a large measles epidemic affected many countries in the Pacific, in particular Samoa. Since November 2019, several measles clusters have emerged in Victoria, the largest involving seasonal workers in the horticultural industry arriving from countries in the Pacific.

3.2.2 Methods

We developed a case definition specific to this outbreak with guidance from the series of national guidelines (SoNG) for the measles confirmed case definition, and laboratory case definition. We followed standard case and contact management protocols in the SoNG. A confirmed case included clinical evidence of fever, rash and cough/coryza/conjunctivitis/Koplik spots, laboratory confirmed evidence, and an epidemiological link of contact with an infectious case on the farm or workplace accommodation.

3.2.3 Results

A cluster of 8 confirmed cases was identified among seasonal horticultural workers on short-term working visa schemes on a farm in regional Victoria. The two index cases had just arrived from Samoa for the seasonal worker program and further investigation found that the cases had been working and staying in on-site shared dormitory accommodation on the farm with approximately 40 others while they were infectious. A further 6 cases were identified as workplace and accommodation contacts linked to the same cluster.

The department liaised with public health authorities from two other states bordering the farm to deliver vaccinations for approximately 70 workplace and accommodation contacts. Further vaccination outreach programs were developed with local councils to deliver MMR vaccines for seasonal workers across other regional areas in Victoria. Additional response measures included risk communication, media alerts, and infection control of exposure sites.

3.2.4 Conclusion

The outbreak was contained with no further transmission to other workplace and accommodation contacts on the farm or within the broader community associated with this cluster. Victoria is currently exploring options for future routine vaccination for short-term seasonal workers.

3.3 Background

Measles is a highly infectious disease caused by the measles virus belonging to the Morbillivirus genus in the family of *Paramyxoviridae.*[1] The incubation period ranges from 8 to 12 days where cases present with increasing fever (up to 39°C to 40.5°C) and cough, coryza, and conjunctivitis.[2] Symptoms usually intensify over the 2 to 4 days before onset of rash and peak on the first day of rash. Measles is typically characterised by a non-blanching rash that usually appears on the face and neck before spreading to other parts of the body.[2] The rash lasts for 3 to 7 days, and fever may persist for 2 to 3 days after the onset of rash. Cough may persist for up to 10 days. Measles is transmitted through airborne respiratory droplets when an infected person breathes, coughs or sneezes. Measles infectivity is greatest in the 3 days before rash onset.[2]

Measles is notifiable in all Australian states and territories and routinely reported to the National Notifiable Diseases Surveillance System (NNDSS). The World Health Organization has certified Australia as having eliminated measles since 2014.[3] In 2019, the Victorian Department of Health and Human Services (the department) recorded 54 confirmed measles cases. The majority of infections were in people who were not fully immunised and have either travelled or been in contact with overseas travellers.

Since November 2019, several measles clusters have emerged in Victoria. The largest involved seasonal workers in the horticultural industry who were recruited from various countries in the Pacific Region, particularly from Samoa. Concurrently, several Pacific countries and territories had also experienced major measles outbreaks. In particular, Samoa experienced a largescale outbreak with approximately 5,000 cases and over 70 deaths to date, many of whom are children under 5 years of age. In response to the outbreak, Samoa declared a state of emergency and instigated a period of government shutdown to direct efforts towards mass vaccination campaigns throughout the country.[4]

This report details the public health response to a measles outbreak among Samoan seasonal horticultural workers on short-term visa schemes in regional Victoria. The dynamic nature of these working programs presents unique challenges for disease control efforts through shared living conditions and high turnover of employees. Linguistic diversities and political sensitivities around undocumented workers presented further challenges for measles control.

3.4 Methods

The outbreak investigation followed standard case and contact management protocols established through the series of national guidelines (SoNG) for state health departments' public health units (PHUs). The SoNG was established in consultation with the Communicable Diseases Network Australia (CDNA) which is comprised of communicable disease representatives from each of the state and territory health departments, and other infectious disease experts and advisors. [5] The purpose of the SoNG is to provide nationally consistent advice and guidance to state health department public health units in responding to measles and other notifiable disease events.[5]

A case definition for this outbreak was developed in alignment with the measles case definition in the SoNG.[6] A confirmed case was defined as any overseas arrival working as a short-term horticultural worker in regional Victoria from 31 October who met the laboratory, clinical or epidemiological evidence as defined in the CDNA case definition outlined below.

<u>Laboratory definitive evidence requires either:</u>

1. isolation of measles virus

OR

2. Detection of measles virus by nucleic acid testing

OR

3. Detection of measles virus antigen

OR

4. IgG seroconversion or a significant increase in antibody level.

<u>Clinical evidence requires:</u>

1. Generalised maculopapular rash lasting three or more days

AND

2. fever (at least 38°C if measured) at the time of rash onset

AND

3. Cough OR coryza OR conjunctivitis OR Koplik spots.

Epidemiological evidence requires:

1. Contact between two people on the farm or workplace accommodation at a time when:
    a. one of them is likely to be infectious (from 24 hours before onset of prodromal symptoms or four days before rash onset to four days after rash onset)

AND

    b. The other has an illness that starts within seven to 18 days after this contact

AND

2. At least one case in the chain of epidemiologically linked cases (which may involve many cases) has laboratory confirmed measles

Case and contact management

As part of routine surveillance, PHUs are required to commence case follow-up on the same day of receiving a notification for a suspected, probable, or confirmed case using the measles case investigation form. The case investigation is typically undertaken by an authorised officer (usually a Public Health Officer), which often involves an initial interview with the treating clinician who diagnosed the patient, followed by an interview with the patient or their carer. I worked with public health officers to conduct case investigations via phone interviews to obtain detailed information on exposure history, establish and epidemiological link and determine a plausible chain of transmission. This information enabled to the team to identify the dates for incubation period, symptom onset, infectious period, and investigate potential close contacts. The interviews conducted with the two primary cases traced their travel history and movements during their infectious periods and identified potential exposure sites including the hospital they presented to, shared cabin accommodation on the farm, local shopping centre, and the workplace bus. This information enabled the team to respond in a timely manner to conduct further active case finding.

Contact management for cases of measles involves conducting contact tracing to identify all potential contacts, and targeting those who are at a higher risk of infection for intervention, thereby minimising the risk of transmission to others. PHUs are required to identify contacts of measles cases to determine those who may have been exposed to an infectious case and assess their infection risk in order to provide advice and implement post-exposure prophylaxis where appropriate. As the route of transmission for measles is primarily air-borne, a contact is defined as anyone who has

or may have shared the same air-space or been in an enclosed area for any length of time with an infectious case.[5] Information obtained from the initial case interviews enabled risk communication to identified exposure sites and a media alert sent out to the broader community to raise awareness of measles risk in the area. This was aimed at increasing testing activity and to trace and isolate other potential cases in the community who may have visited one of the exposure sites while the two confirmed cases were infectious. For exposure sites with a contained population such as the shared cabin accommodation and workplace bus, contact details were obtained from the employer and all contacts were asked to restrict movement and isolate to limit further transmission in the community. As measles is highly infectious, the public health team also provided on-site workplace vaccination of contacts and staff as timely intervention to reduce transmission.

I conducted a descriptive epidemiological analysis using excel and stata to describe the spread of infection from person-to-person.

3.5 Results

Outbreak

On 21 November 2019, two recently arrived overseas seasonal workers presented to a rural Victorian hospital with cough, conjunctivitis, fever and non-blanching rash. Medical staff suspected measles infection, leading to isolation of both cases in a negative pressure room in the emergency department and the cases were reported to the department.

In the days prior to presenting at the hospital, both cases reported fever, cough, conjunctivitis, coryza, and rash starting on the face and neck and subsequently spreading downwards. Public Health Officers (PHOs) conducted phone interviews with the cases and discovered that the two individuals had recently travelled together from Samoa on the 15 or 16 November for seasonal horticultural work in regional Victoria. On interview, it was discovered that the younger brother of one of the cases had been diagnosed with measles in the weeks prior to the two cases departing from Samoa. The vaccination history of both cases was unknown, however, one case stated they had received “an injection” prior to leaving Samoa but could not confirm whether it was a measles-containing vaccine. The treating clinician requested serology testing and nasopharyngeal swabs and measles virus was detected for both cases by polymerase chain reaction (PCR).

The case interviews identified several risk factors associated with the movements of both cases during their infectious periods. Both cases had been picking fruit on a farm in regional Victoria and had stayed in shared accommodation on-site with approximately 40 other workers, most of whom were overseas-born. Both cases also reported visiting the local shopping centre during their infectious period and had taken the workplace-provided bus from their accommodation to work and to hospital. The department identified a further six confirmed cases epidemiologically linked to the two primary cases via shared cabin accommodation on a farm (Figure 1).

The farm where the outbreak occurred had a total of 67 employees; 40 who were living in shared dormitory accommodation on-site, 23 others who worked on the farm but lived offsite, and four ground staff. Epidemiological investigation identified eight confirmed cases with symptom onsets ranging between 18 November to 1 December 2019. The median age of cases was 29 years (range 21 to 36 years); all were Samoan-born; and seven of the eight cases were male (Table 1). All cases presented with fever at rash onset, seven (88%) with a cough, and three (38%) with coryza. Only the two primary cases presented with conjunctivitis. Subsequent to diagnosis by PCR, the Victorian Infectious Diseases Reference Laboratory (VIDRL) detected measles genotype B3 for five cases, but insufficient viral RNA hindered genotyping of the remaining cases in the cluster (Table 1). Cell culture failed to grow virus. The genotype detected matched the strain circulating in Samoa at the time. Exposure and infectious periods suggest that the two primary cases infected a further 6 cases, all of whom developed symptom onset within the expected time frame of 7–18 days (Figure 2). It is plausible that case 3 and case 7 acquired their infection from case 1 who had the earliest onset date on 18 November, as their acquisition period was consistent with the infectious period of case 1 (Appendix 1). Cases 4, 5, 6 and 8 may have contracted measles from either of the two index cases as all of their acquisition periods were consistent with the infectious periods of both index cases (Appendix 1). The last case presented on 1 December 2019 and no further cases were identified in the cluster.

Table 1. Demographic characteristics of measles cases associated with the farm (n=8)

Age	Range	21–36 years
	Median	29 years
Sex	Male	7 (88%)
	Female	1 (12%)
Country of residence	Samoa	8 (100%)
Genotype	B3	5 (63%)

	Unknown	3 (37%)

Figure 1. Date of symptom onset of confirmed measles cases associated with Samoan seasonal horticultural workers, Victoria Australia, 18 November – 1 December, 2019 (n=8)

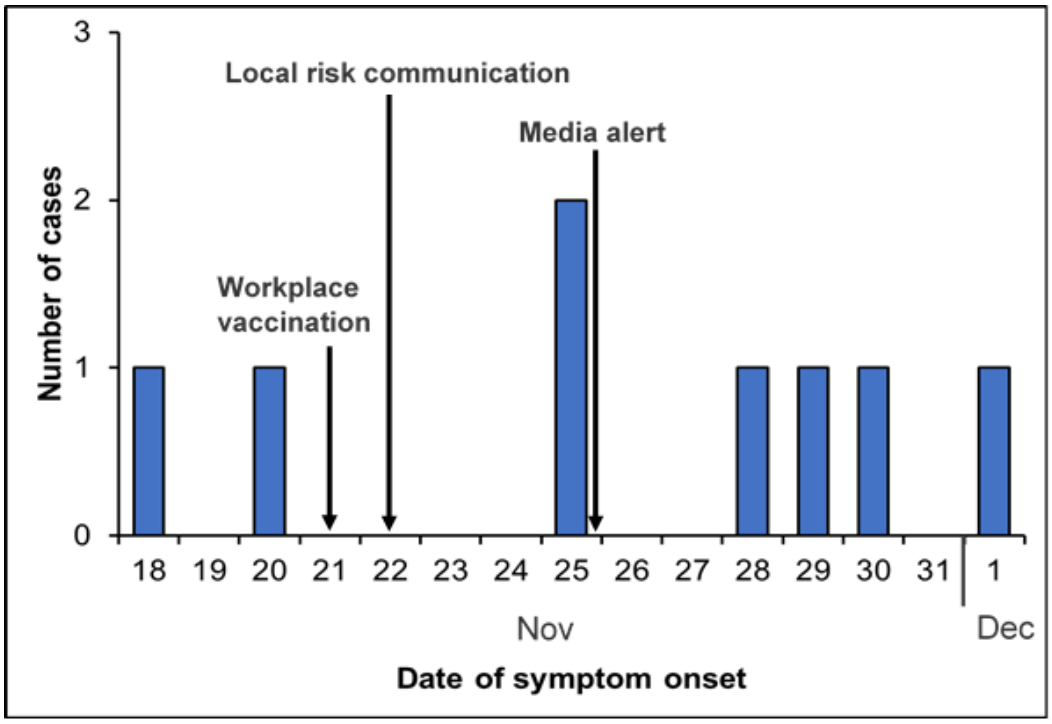
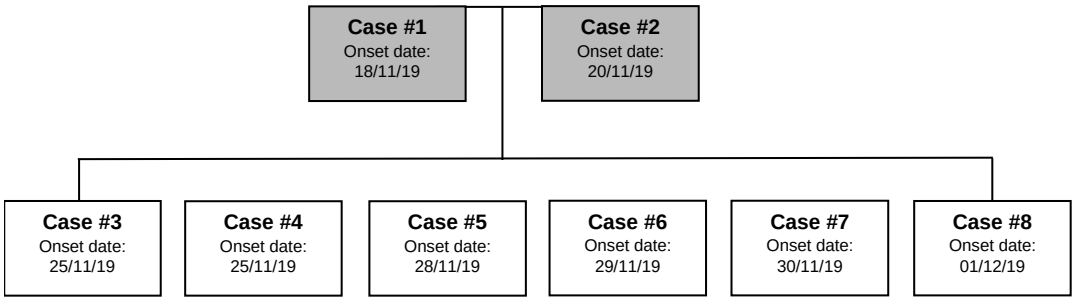


Figure 2. Contact tree of measles cases associated with seasonal horticultural workers, Victoria, 18 November to 1 December (n=8)



Response

The department convened an Incident Management Team to respond to the outbreak and implemented strategies to reduce the risk of transmitting measles into the broader

community. In liaison with health authorities from two other states bordering the farm, initial outbreak management included vaccination of workplace and accommodation contacts, risk communication for employers and at-risk workers regarding measles and measles vaccination, and media alerts regarding possible exposure sites. On 21 November approximately 70 accommodation and workplace contacts were vaccinated, followed by infection control of the emergency department where cases initially presented. All six secondary cases received one dose of MMR vaccine on 21 November, which ranged from 7-14 days prior to symptom onset, suggesting they were likely exposed before mounting sufficient immunity. The following day on 22 November, the department commenced local risk communication activities by advising the local council of the measles risk and sent letters to employers advising that individuals should remain on site until further notice to reduce the risk of transmission into the community. On 25 November, the department issued a media alert of public exposure sites that may have posed a risk to others not fully vaccinated for measles.

The department notified the Australian National Focal Point (NFP) of the potential for more cases among seasonal workers arriving from countries currently experiencing measles outbreaks. The NFP coordinated information sharing between government departments to ascertain workforce numbers and their intended destinations upon entering Australia under national governmental seasonal-work schemes. The department also contacted local employment agencies to obtain further estimates of workforce numbers to ensure there were sufficient vaccine stocks available should a broader community vaccination campaign be required.

On 12 December, local authorities provided free measles vaccine to approximately 120 seasonal workers from the Pacific Islands, as well as other seasonal workers in the local area regardless of citizenship and visa status. Communication materials including posters, fact sheets, a pre-vaccination checklist and vaccination consent forms were developed by the department and translated to the relevant languages. All vaccinations provided under the campaign were recorded on the Australian Immunisation Register (AIR). The department also collaborated with other local councils across the state to schedule additional vaccination programs over December and January across other parts of regional Victoria to target high-risk groups including Pacific Island seasonal workers and other migrant workers in the horticultural industry. As of mid-December 2019, a total of 464 seasonal workers originating from Asia-Pacific regions who were working across various areas in regional Victoria (including the workplace and accommodation contacts on the farm where the outbreak occurred) had received a single dose of MMR vaccine.

In addition to the routine surveillance and case and contact management for measles conducted in Victoria, a number of enhanced surveillance activities were implemented. A Chief Health Officer (CHO) alert was issued along with a media release which was translated into various languages for the wider Victorian community. The department also provided further targeted communications to clinicians to ensure broader awareness of measles risk (to increase testing activity) and to promote the availability of a Victorian government funded dose of Measles Mumps and Rubella (MMR) vaccine for at risk groups. Further information and advice included testing women who were planning to become pregnant for measles, in addition to the standard conditions for which they were routinely screened prior to pregnancy.

3.6 Discussion

Measles is highly infectious particularly in susceptible populations as observed in this outbreak. Measles outbreaks which were occurring globally and in the Pacific at the time, presented a greater risk of importation of measles cases to Australia. In particular, the large outbreak in Samoa with approximately 5,000 cases and over 70 deaths to date, many of whom are children under 5 years of age.[4] The global resurgence in measles at the time prompted discussions on declaring measles a Public Health Emergency of International Concern (PHEIC).[7] Some experts believed that declaring measles a PHEIC could have multiple advantages including encouraging the global community to strengthen health systems to ensure that every child born receives the recommended two doses of measles-containing vaccine.[7] They also believed that a PHEIC presented opportunities for communication outreach high risk populations such as migrants and travellers on the risks and benefits of measles vaccination.[7] This may subsequently have an associated effect of increasing donor and other stakeholder engagements in continued measles elimination efforts, thereby reducing the burden on emergency funding from global bodies such as the World Health Organization (WHO) and the World Bank Group.[8]

Since November 2019, several clusters emerged throughout Victoria with a large proportion of affected individuals being Samoan-born nationals who either visited friends and relatives or entered the country on a seasonal work visa. This outbreak highlights challenges with controlling measles transmission in short-term dynamic occupational environments that rely on transient workers, including those from migrant groups on short-term visas or informal employment. Short-term international work is

common in Australia, particularly in the horticultural industry where crop harvesting and fruit picking is increasingly reliant on migrant workers. According to the Australian Bureau of Agricultural and Resource Economics and Sciences (ABARES) in 2016, approximately one third of the workforce employed in this industry are filled by overseas workers.[9] Approximately 75% of all agricultural workers in 2016 were employed across New South Wales, Victoria and Queensland.[9] The median age of workers was 49 years, however the proportion aged less than 35 years increased from 21% in 2011 to 24% in 2016.[9] Statistics on this workforce may not be entirely accurate as data is based on a single month and fruit picking work is seasonal with fewer workers employed in winter. Furthermore, workers are highly mobile and may move between regions and states for work resulting in duplication of numbers. Another factor to consider is that labour hire companies are not included in labour force surveys, despite a growing number of workers being contracted through these agencies. To address the high demands for seasonal workers, the Australian Government Department of Education, Skills and Employment introduced the Seasonal Worker Programme aimed at assisting employers in the agriculture and accommodation sectors to fill employment gaps unable to be met by the Australian workforce.[10] This program is open to workers from nine participating countries from the Pacific Islands and Timor-Leste. In 2018-19, there were approximately 12,000 workers on six month visas under this scheme.[11]

This growing number of short-term migrant workers increases the risk of imported infections such as measles into Australia. According to the WHO, measles vaccination coverage varies widely across these countries. As of 2018, routine vaccination coverage for measles-containing-vaccine-first-dose (MCV1) and measles-containing-vaccine-second-dose (MCV2) in Fiji was estimated to be 94%. However, MCV1 and MCV2 coverage in Samoa was 31% and 13%, which is well below the 95% vaccination coverage required for herd immunity.[12] Information on vaccination status and immunity in this cohort may not be reliable, as evidenced by this outbreak.

Concurrent with this outbreak, five other measles cases not linked to this cluster were also reported in Victoria, all of whom had acquired their infection in the Asia-Pacific region. In the setting of a major outbreak in Samoa[4], the Victorian outbreak provides an example of the risk of international spread in highly mobile populations. Our response to this outbreak ensured local containment of infected travellers exposed to an area where there was a major international outbreak of measles occurring at the time and

effectively prevented reintroduction of measles to the community surrounding the outbreak-affected areas.

The public health response to this outbreak was coordinated and timely. Within less than a week of the primary cases arriving from Samoa, DHHS worked closely with the local Council to implement appropriate prevention and control measures to reduce the risk of further transmission. This included case and contact management, identification of exposure sites and at risk populations, advising both the council and the employers of the measles risk, vaccination of workplace and accommodation contacts, and infection control of exposure sites. Effective laboratory capacity also supported timely testing and availability of results.

The department identified further possible measles risks among Pacific Island seasonal workers and other migrant workers in the horticultural industry and developed targeted vaccination outreach programs. Strategic planning ensured high vaccination coverage among seasonal workers, particularly those arriving from outbreak active countries, with an expected increase in worker and visitor volume over the Christmas and New Year period. Further targeted messaging aimed at clinicians and the broader community was disseminated through updates and media alerts to increase awareness on measles risk and further promote vaccination.

Similar outbreaks in other settings and countries have also been reported including an outbreak among Thai and other migrant workers in two factories located in one province in Thailand involving 56 cases.[13] Another outbreak involved mainly seasonal workers at a ski station in France where the majority of cases were either unvaccinated or had only one dose of the MMR vaccine.[14] The investigation team in both outbreaks outlined the unique challenges, situations which were similar to the setting for this outbreak in Victoria. Firstly, seasonal work presents a dynamic environment with incoming workers on various visa programs, sponsored by different agencies under different visa arrangements with varying levels of support, arriving in both small and large groups on both organised and ad-hoc bases, for a particular season but for varying durations of time. This meant there was an increased risk of disease transmission with the potential of a multi-jurisdictional outbreak requiring timely public health co-ordination and response. The status of workers also varied, with some arriving on government approved visa schemes and others who were undocumented or informal workers. This posed challenges in communication with employers to obtain access reliable data on worker numbers, and to understand recruitment processes.

Language barriers also required appropriate messaging and translation of communication materials.

The contact management protocol in the SoNG briefly addresses workplace settings with shared communal facilities and settings where vaccination histories and immunity is uncertain for a large number of individuals. Implications from this outbreak highlight the need for more detailed information unique to transient working populations, particularly from migrant backgrounds, to prevent the risk of measles importation and widespread community transmission.

a. Conclusion

This outbreak highlights the global resurgence of measles, particularly in the Asia-Pacific region, and the implications it has on imported measles risk to Australia. This outbreak occurred due to the spill over event from the largescale outbreak in Samoa which demonstrates the imported measles risk to Australia. As seasonal horticultural work is largely dependent on short-term workers arriving from countries with a high measles incidence, timely intervention is imperative to limit widespread transmission in the community. The co-ordinated public health response to this outbreak demonstrated the urgency of implementing prevention and control measures through case and contact management, risk communication, isolation, testing and vaccination. A broader public health response was also established via targeted vaccination outreach programs for other seasonal workers arriving from the Asia-Pacific region to limit the risk of measles outbreaks in similar high-risk settings. Victoria continues to explore options for preventing further measles outbreaks including vaccination upon arrival for short-term workers with no documented evidence of measles immunity. Strengthening partnerships and communications across government sectors, including health, employment and immigration, is critical to improving access to the information required to ensure timely and effective public health responses at local, state, national and international levels.

3.8 References

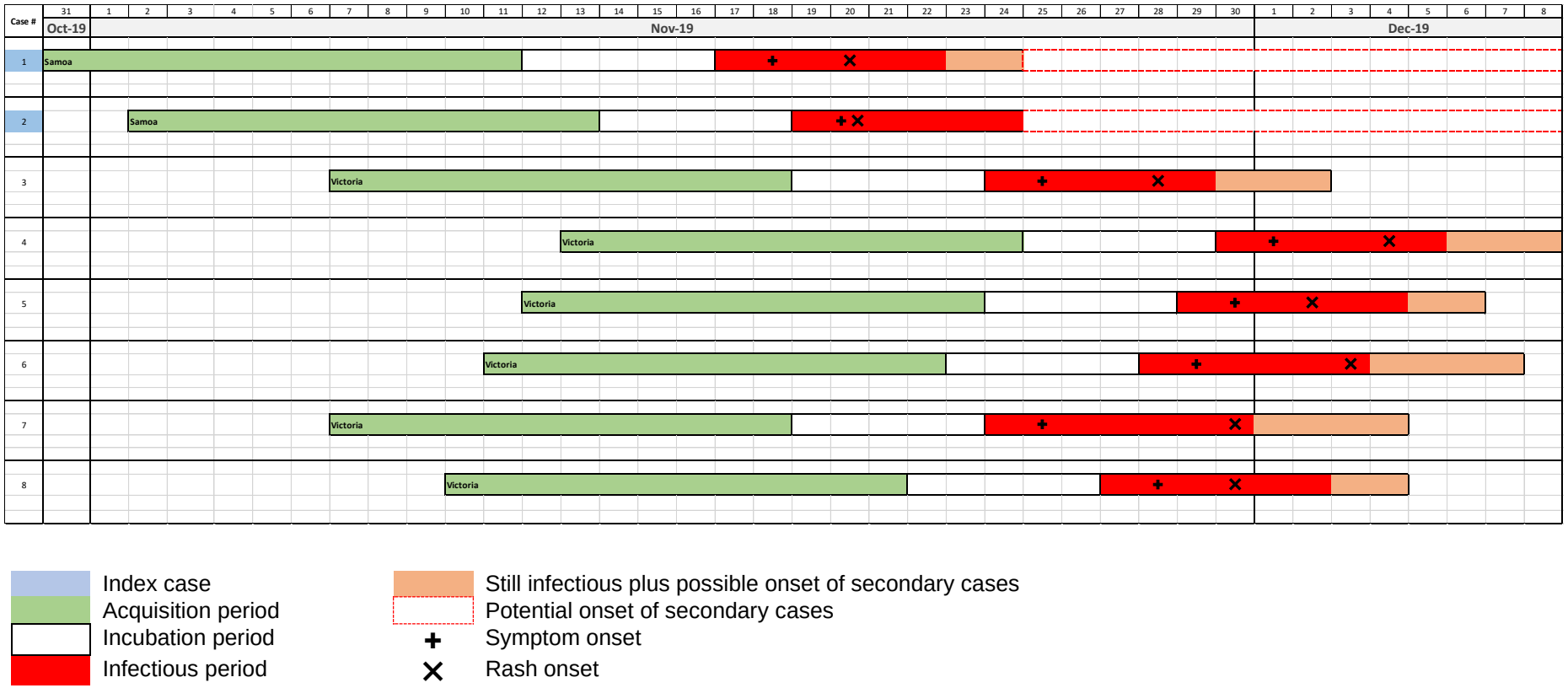
1. Moss WJ & Griffith DE. Global measles elimination. Nat Rev Microbiol. 2006 Dec;4(12):900-9. doi:10.1038/nrmicro1550.
2. Perry RT & Halsey NA. The clinical significance of measles: a review. J Infect Dis. 2004 May 1;189 Suppl 1:S4-16. doi: 10.1086/377712.

3. MacIntyre CR, Kpozehouen E, Kunasekaran M, et al. Measles control in Australia - threats, opportunities and future needs. Vaccine [Internet]. 2018 Jul;36(30):4393-4398. doi:10.1016/j.vaccine.2018.06.022
4. Dyer O. Measles: Samoa declares emergency as cases continue to spike worldwide. BMJ [Internet]. 2019 Nov;367:l6767. doi:10.1136/bmj.l6767
5. Australian Government Department of Health. Series of National Guidelines (SoNG) – Measles [Internet]. Canberra ACT: Australian Government Department of Health, 2020. Updated 2019 May 9 [cited 2020 Oct 6]. Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-measles.htm
6. Australian Government Department of Health. Australian national notifiable diseases case definitions – Measles case definition [Internet]. Canberra ACT: Australian Government Department of Health, 2020. Updated 2019 May 29 [cited 2020 Oct 6]. Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-nndss-casedefs-cd_measl.htm
7. Durrheim DN, Crowcroft NS, Blumberg LH. Is the global measles resurgence a "public health emergency of international concern"? Int J Infect Dis [Internet]. 2019 Jun;83:95-97. doi:10.1016/j.ijid.2019.04.016
8. Gostin LO, Katz R. The International Health Regulations: The Governing Framework for Global Health Security. Milbank Q [Internet]. 2016 Jun;94(2):264-313. doi:10.1111/1468-0009.12186
9. Australian Bureau of Agricultural and Resource Economics and Sciences (ABARES). Snapshot of Australia's agricultural workforce [Internet]. Canberra ACT: Australian Government Department of Agriculture, Water and the Environment, 2020. Updated 2020 Jul 27 [cited 2020 Oct 6]. Available from: https://www.agriculture.gov.au/abares/publications/insights/snapshot-of-australias-agricultural-workforce#people-from-cald-backgrounds-in-the-agriculture-industry
10. Australian Government Department of Education, Skills and Employment. Seasonal Worker Programme. Canberra ACT: Australian Government Department of Education, Skills and Employment, 2020. Updated 2020 Jul 7 [cited 2020 Oct 6]. Available from: https://www.employment.gov.au/seasonal-worker-programme
11. Development Policy Centre. Australia's seasonal worker program now bigger than NZ's [Internet]. Australian National University, 2020. Updated 2019 Jul 25 [cited 2020 Oct 6]. Available from: https://devpolicy.org/australias-seasonal-worker-program-now-bigger-than-nzs-20190725/

12. World Health Organization. Measles – Pacific Island countries and areas [Internet]. Geneva, WHO, 2020. Updated 2019 Dec 15 [cited 2020 Oct 6]. Available from: https://www.who.int/csr/don/15-december-2019-measles-pacific-island-countries-and-areas/en/
13. Wongsanuphat S, Thitichai P, Jaiyong R, Plernprom P, Thintip K, Jitpeera C, et al. Investigation of measles outbreak among Thai and other migrant workers in two factories in Nakhon Pathom, Thailand, 2019. Int J Environ Res Public Health. 2020 Jul;17(13):1627. doi:10.3390/ijerph17134627
14. Brottet E, Ronnaux-Baron AS, Grangeret N, DEher M, Andrivot B & Fougere E. Measles outbreak at the Val Thorens ski station, France, 2019. Eur J Public Health. 2019 Nov 4;29(4):185-459. Available from: https://academic.oup.com/eurpub/article-abstract/29/Supplement_4/ckz185.459/562459

3.8 Appendix

Appendix 1. Periods of transmission of measles cases associated with seasonal horticultural workers, Victoria, 18 November to 1 December (n=8)



Appendix 2. Late draft paper developed for submission to MMWR

Notes from the field: Measles outbreak among seasonal horticultural workers—Victoria Australia, November–December 2019

Malinda Chea[1]; Charles Alpren[2]; Janet Strachan[2]; Lucinda Franklin[2]; Martyn Kirk[1]; Katie Cronin[2]; Carrie Barnes[2]; Helen Pitcher[2]; Thomas Tran[3]; Mihaela Ivan[2]

On 21 November 2019, two recently arrived overseas seasonal workers presented to a rural Victorian hospital with cough, conjunctivitis, fever and non-blanching rash. Measles infection was confirmed by polymerase chain reaction (PCR). The Victorian Department of Health and Human Services (DHHS) identified a further six confirmed cases epidemiologically linked to the primary cases via shared cabin accommodation on a farm (Figure 1).

The farm where the outbreak occurred had 40 employees in shared dormitory accommodation on-site, 23 others who worked on the farm but lived offsite, and four ground staff. Epidemiological investigation identified eight confirmed cases with reports of symptom onset from 18 November to 1 December. Median age was 29 years (range 21 to 36 years); all were Samoan; seven were male. All had fever at rash onset, seven (88%) reported cough and three (38%) coryza. Only the two primary cases reported conjunctivitis. Subsequent to diagnosis by PCR, the Victorian Infectious Diseases Reference Laboratory detected measles genotype B3 for five cases, but insufficient viral RNA hindered genotyping of remaining cases. Cell culture failed to grow virus. The genotype detected matched the strain circulating in Samoa at the time.

In liaison with health authorities from two other states bordering the farm, initial outbreak management included vaccination of workplace and accommodation contacts, risk communication for employers and at-risk workers regarding measles and measles vaccination, and media alerts regarding possible exposure sites. All six secondary cases received one MMR vaccine dose on 21 November, which was 7-14 days before symptom onset, suggesting they were likely exposed before mounting sufficient immunity. DHHS notified the Australian National Focal Point (NFP) of the potential for more cases among seasonal workers arriving from countries currently experiencing measles outbreaks. The NFP coordinated information sharing between government departments to ascertain workforce numbers and their intended destinations upon entering Australia under national governmental seasonal-work schemes. DHHS contacted local employment agencies to obtain further estimates of workforce numbers to ensure sufficient vaccine stocks.

On 12 December, local authorities provided free measles vaccine to approximately 120 seasonal workers from the Pacific Islands, and other seasonal workers in the local area regardless of citizenship and visa status. Fact sheets, consent forms and posters in relevant languages were provided. DHHS and local councils scheduled additional vaccination programs over December and January across other parts of regional Victoria targeting high-risk groups including Pacific Island seasonal workers and other migrant workers in the horticultural industry. To date, a total of 464 seasonal workers from the Asia-Pacific (including the workplace and accommodation contacts on the farm) have received one MMR vaccine dose in regional Victoria.

This outbreak highlights challenges with controlling measles transmission in short-term dynamic occupational environments that rely on transient workers, including those from migrant groups on short-term visas or informal employment. Concurrent with this outbreak, five other measles cases not linked to this cluster were reported in Victoria, all of which were acquired in the Asia-Pacific region. In the setting of a major outbreak in Samoa[1], the Victorian outbreak provides an example of international spread in highly

mobile populations. Our response to this outbreak ensured local containment and prevented reintroduction of measles to outbreak affected areas from returning travellers.

Victoria is currently exploring options to prevent further measles outbreaks including vaccination upon arrival for short-term workers with no documented evidence of immunity. Strengthening partnerships and communications across government sectors, including health, employment and immigration, is critical to improving access to information required to ensure timely and effective public health responses at local and national levels.

Acknowledgements

The authors acknowledge all who contributed to this response including Jay Healy, Aicha Brahmi, Miriam O'Hara, and Jessica List.

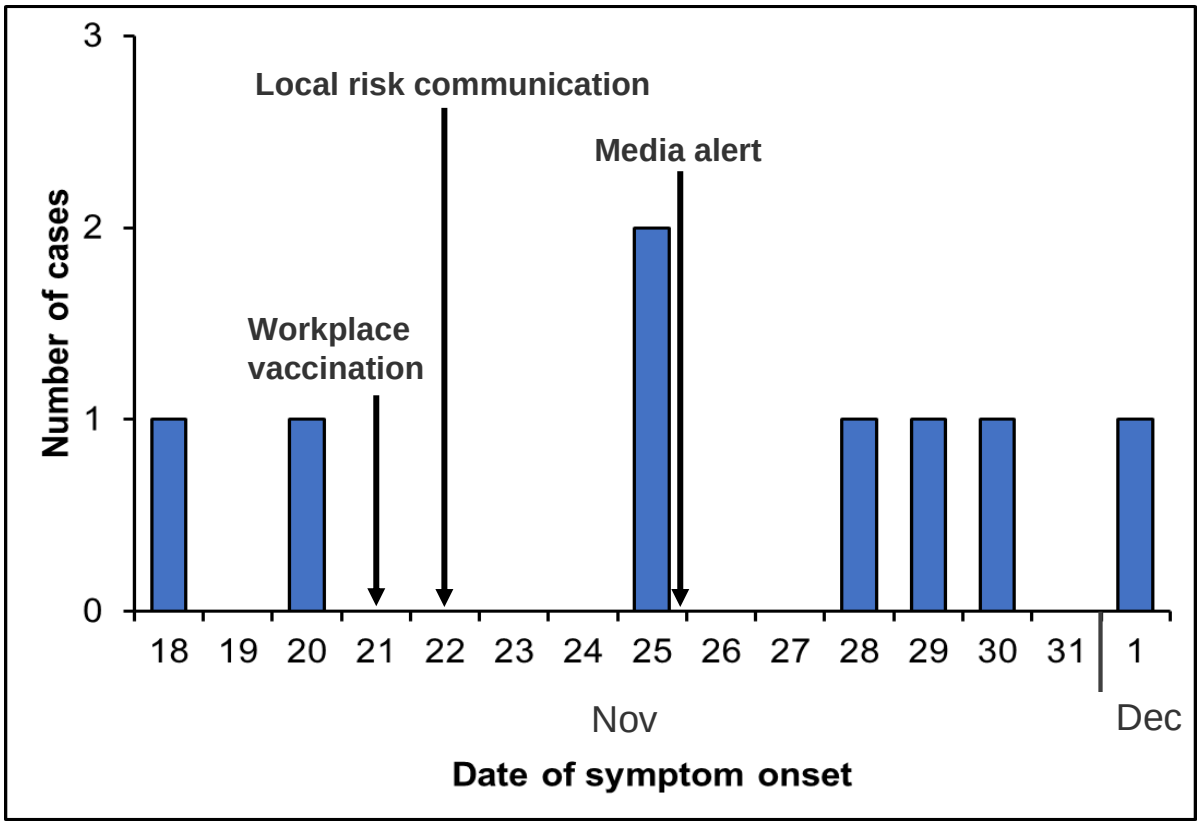
---

[1]Research School of Population Health, National Centre for Epidemiology and Population Health, Australian National University; [2]Health Protection Branch, Health Protection and Emergency Management Division, Department of Health and Human Services, [3]Victorian Infectious Diseases Reference Laboratory

References

1. Dyer O. Measles: Samoa declares emergency as cases continue to spike worldwide. BMJ [Internet]. 2019 Nov [cited 2019 Dec 16];367:l6767. doi:10.1136/bmj.l6767

Figure 1. Date of symptom onset of confirmed measles cases associated with Samoan seasonal horticultural workers, Victoria Australia, 18 November – 1 December, 2019 (n=8)



4 Establishing a public health surveillance system

Establishing a 2019 novel coronavirus (2019-nCoV) surveillance system in Victoria for travellers returning from Wuhan, Hubei Province in China, 2020

Table of Contents

4.1 Prologue

4.1.1 My role

From 20 January to 3 February 2020 during my placement with the Victorian Department of Health and Human Services (DHHS), I was involved with the Victorian preparedness and response activities for the 2019 novel coronavirus (2019-nCoV) outbreak. My daily tasks included supporting the Communicable Disease Epidemiology and Surveillance (CDES) team with gathering intelligence on the evolving nature of the outbreak and gaining a better understanding of the clinical and epidemiological features. This included me conducting a routine review on the WHO and CDC websites to updated information on presenting symptoms and newly identified cases in other countries. I used this information to inform the evolving development of the Victorian case definition and case questionnaire which determined the eligibility for testing of return travellers with presenting symptoms of interest and a travel history to outbreak affected areas. I attended the initial Incident Management Team (IMT) meetings to support the response and undertook regular data cleaning and management of notifications reported to the Public Health Events Surveillance System (PHESS).

During the time of my involvement, there were a total of 4 confirmed cases notified to the department, and the official name of 2019-nCoV was changed to coronavirus disease 2019 (COVID-19). Both these two acronyms are used throughout this chapter to describe the novel coronavirus.

4.1.2 Lessons learnt

There were many challenges in responding to an outbreak of a novel disease where there were still many unknowns about the pathogen and the rapidly evolving situation globally. Having a direct involvement in this process enabled me to gain a better understanding of the processes behind establishing a surveillance system for a new, emerging disease. While Australia was preparing its state and national surveillance systems and capacity for detection, the first case to be confirmed in Australia was notified in Melbourne, Victoria. The virus was isolated from a traveller who had recently returned from Wuhan, China where the pathogen was currently causing a major outbreak. I worked with the Victorian team to develop the initial case definition that was specific to the existing infection risk, which at the time was focused on a history of travel to Wuhan, China and identifying close contacts of any confirmed cases in order to prevent the risk of local transmission. Victoria had been monitoring the situation for

some time and were expecting cases in Australia since there were no travel restrictions or border closures in place at the time. The case definition was based on guidelines issued by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC). As this was a newly identified novel coronavirus, information on disease characteristics were limited and as a result, the case definition and case questionnaire were based on the best available information at the time which were WHO, CDC and the existing literature on the Middle-Eastern respiratory syndrome coronavirus (MERS-CoV). I was initially tasked with reviewing the scientific literature on MERS-CoV and the current MERS-CoV case questionnaire in order to extract information that could be used for the new coronavirus. I developed a list of questions that would be important to collect for the initial cases to help with the case and contact management and understanding of the new virus. I found this process challenging but was able to extract questions on routes of transmission and signs and symptoms. There were constant changes made to the case definition and case questionnaire as new, credible information became available from the international scientific community. This was an ongoing process and highlighted the importance and challenges of gathering intelligence in a dynamic scenario, as well as ensuring information was credible to inform best practice.

There were other challenges identified during the early days of this response including language barriers which made it more challenging to interview some of the first few suspected cases and their contacts. Although I was not directly involved in interviewing cases and contacts, the issue of language barriers was discussed at IMT meetings and noted by public health officers (PHOs) when updating case details in PHESS. Managing the media during such a highly publicised event was also a challenge, further highlighting the importance of providing sound information and advice to the public, whilst taking into consideration general concerns. The main lesson learnt from this event was the importance of preparedness: the readiness of resources, laboratory and staff capacity, guidelines and communication materials for clinicians and hospital and health-care services, and the general public all take time to develop. The team at DHHS were preparing for a pandemic scenario weeks before the first case was identified in Australia using the best available information at the time. It was a highly valuable experience for me to have had an insight into the processes involved in establishing surveillance for a new disease and integrating it into an existing surveillance system.

4.1.3 Public health implications

On 30 January 2020, one month after the first case was identified in Wuhan, China, 2019-nCoV was declared a public health emergency of international concern (PHEIC) by the World Health Organization (WHO). In the weeks following that declaration, WHO officially named the disease COVID-19. At the time of writing, this pandemic continues to be a significant public health event impacting many countries globally with economic and social implications resulting from the implementation of strict nationwide lockdown measures and international travel restrictions. The first Australian case was identified in Melbourne, Victoria with further cases reported over the following weeks across the country. Establishing a surveillance system for COVID-19 is essential for monitoring infection rates, identifying at risk groups and settings, and providing an overall picture of both the short term and long term disease trends. During my involvement, details on public exposure sites such as restaurants were documented through case interviews which were then recorded in the notifiable disease surveillance system. Some of these fields required setting up but were largely based on existing fields already in the system for other notifiable diseases. This enabled public health authorities to develop an informative media release which was used to alert the general public on specific dates and times when the case was infectious and may have come into contact with other members of the public. This information was important to ensure that patrons who may have been exposed were able to be directed to self-isolate, monitor themselves for symptoms and seek further medical attention and testing if they became unwell. Data collected in the surveillance system were also used in modelling disease trends, and possible progression of the outbreak, as well as the impact potential impact of various control measures on case numbers and health system capacity. Since my involvement in the early days of the Victorian outbreak, the COVID-19 surveillance objectives and data fields have continued to evolve and are expected to do so as the pandemic progresses.

4.1.4 Acknowledgements

The Victorian Department of Health and Human Services (DHHS), Lucinda Franklin, Charles Alpren, Janet Strachan, Martyn Kirk.

4.2 Abstract

4.2.1 Background

A new novel coronavirus known as COVID-19 (previously 2019-nCoV) was identified in Wuhan, China in late December 2019 and declared a public health emergency of international concern (PHEIC) by the World Health Organization (WHO). COVID-19 has had a large-scale global impact with over 30 million confirmed cases and almost one million deaths. This chapter describes the establishment of a surveillance system in Victoria to assess the risk of nCoV-2019 infection and support early identification of suspected cases in travellers returning from Wuhan, Hubei Province in response to the 2019-nCoV epidemic in Mainland China. This public health incident was ongoing at the time this chapter was written. This chapter details the surveillance system at the point in time of my involvement, acknowledging that there may have been many changes to the system as the epidemic progressed and as more information became available. At the time of writing this chapter, the disease was known as 2019-nCoV and was later officially renamed COVID-19. Both terms are used interchangeably throughout this chapter.

4.2.2 Methods

An incident management team was convened by DHHS to coordinate the public health response to 2019-nCoV in Victoria. We established a new surveillance system that was integrated into the existing state notifiable diseases database, the Public Health Events and Surveillance System (PHESS). As part of the IMT, I helped develop a case definition using the existing published scientific literature on Middle-Eastern Respiratory Syndrome Coronavirus (MERS-CoV), and resources from the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC). A case questionnaire was developed based on an existing MERS-CoV surveillance case form and additional fields were developed based on the current knowledge of 2019-nCoV. We also developed a protocol for investigation to guide the public health response which included all available information on the disease, clinical presentation, laboratory and testing method, case and contact management, and current exclusion, restriction and isolation requirements. We updated this protocol regularly as new information became available.

4.2.3 Results and discussion

The establishment of the 2019-nCoV surveillance system in Victoria identified a total of 4 confirmed cases between 25 January to 8 February 2020. Two were female and two were male aged between 25 – 66 years (median - 53 years). All were overseas acquired infections. Minimal resources were used as the system was integrated into the existing state-based notifiable diseases dataset, the Public Health Events Surveillance System (PHESS) and a case report form and questionnaire was adapted using existing locally-developed MERS-CoV resources. Other countries including France and Singapore took a similar approach to establishing surveillance for COVID-19, although Singapore adopted additional measures early on to include surveillance not only of those with a history of travel from Wuhan, China, but also introduced measures to help identify local cases. The process for establishment of this surveillance system is also similar to that of previous enhanced surveillance for emerging infectious diseases such as SARS and MERS-CoV in the United States and England. There were some challenges in the establishment and operation of the system. As further data fields were added to the case report forms and questionnaires, contact tracing became more labour and time intensive, especially when completed through paper-based reporting, which required manual data entry into the surveillance database.

4.2.4 Conclusion and reflections

The pandemic has had a significant impact on the health system and economies of countries globally. My involvement in the initial establishment of a surveillance system for 2019-nCoV in Victoria has been an insightful experience with valuable reflections. There is no one size fits all approach to preparedness efforts, and what has worked effectively for one country may differ to another due to various factors that should be considered. An important next step is to conduct a formal evaluation of this surveillance system and its attributes to highlight the functional components of the system, and identify additional areas needing improvement in order to inform changes made in the future. Challenges remain given the limited public health resources for pandemic preparedness and planning. However, the lessons learnt from this preliminary response to establishing a state level surveillance system for COVID-19 are valuable not only for future pandemics and similar large-scale outbreaks, but also for improving the surveillance and response to current infectious diseases.

4.3 Introduction

This chapter details the establishment of a surveillance system in Victoria to assess the risk of 2019-nCoV infection and support the early identification of suspected cases for travellers returning from Wuhan, Hubei Province in China. This was the main location of initial cases of the 2019 novel coronavirus (2019-nCoV) at the time. The epidemiological features of 2019-nCoV is described including the clinical features and modes of transmission known at the time. This chapter also details the preventative measures, public health significance and impact, and disease prevention and control strategies in Victoria. This is followed by a description of the surveillance system established for early identification of 2019-nCoV cases in travellers returning from Wuhan, Hubei Province in China, and its integration into the existing notifiable diseases dataset used in Victoria.

4.3.1 Background

2019-nCoV in China

The first case of 2019-nCoV was reported in a cluster in Wuhan, Hubei Province, in China in late December 2019. The disease subsequently spread across mainland China and throughout the globe.[1] The index case was linked to a wholesale seafood market in Wuhan City which sold live animals including poultry, bats and other mammals both exotic and native.[2] Tens of thousands of infections have since been reported in China with evidence of human to human transmission from household contacts and in healthcare settings in Hubei Province.[3-6] There is evidence of imported cases across other parts of Asia, Europe and America from travellers returning from Wuhan or other parts of China with known active outbreaks.[7-9] On 30 January 2020, the World Health Organization declared 2019-nCoV a public health emergency of international concern (PHEIC) and subsequently named the disease COVID-19 on 11 February 2020.[10,11] Since the first case was identified, there has been multiple locations reporting high case numbers and large-scale transmission. The novel pathogen initially spread from mainland China, to cause major outbreaks in France, Spain and Italy, and subsequently the United States, Brazil and India. As of 28 September 2020, COVID-19 has spread to at least 235 countries worldwide with over 30 million confirmed cases reported and almost one million deaths.[12]

Australian context

The Australian Health Protection Principal Committee (AHPPC) is the key decision-making committee for health emergencies and takes the lead role in coordinating a national response to outbreaks.[13] AHPPC provides recommendations for reducing 2019-nCoV transmission in Australia following advice from the Communicable Diseases Network Australia (CDNA).[14] At the time of establishing this surveillance system, AHPPC released a statement on 5 February 2020 recommending self-isolation for people who have been in contact with any confirmed 2019-nCoV case for 14 days following exposure. Returned travellers who had been to Hubei Province of China were also required to self-isolate in their homes 14 days after departing Hubei Province, other than for seeking individual medical care.[15] It was acknowledged at the time that these recommendations reflected a highly precautionary approach taken to minimise the spread of disease in the community from possible asymptomatic cases.

Victoria is the second largest jurisdiction with a population of approximately six million people. The Victorian Department of Health and Human Services (DHHS) is the state government agency responsible for communicable disease surveillance and public health regulatory functions. The Health Protection Branch within the Regulation, Health Protection and Emergency Management Division is responsible for notifiable communicable disease surveillance functions including 2019-nCoV surveillance in Victoria.[16]

4.3.2 Clinical features

At the time of my involvement in establishing this surveillance system, much of the information on disease characteristics, clinical features and transmission was largely unknown and assumed to be similar to that of MERS-CoV and Severe Acute Respiratory Syndrome (SARS-CoV).

Coronaviruses are a large family of viruses known to cause illness of varying severity in humans and animals including camels, bats, cats and cattle. The 2019 novel coronavirus (2019-nCoV) is a betacoronavirus similar to the Middle Eastern Respiratory Syndrome (MERS-CoV) and viruses, both of which originated in bats.[17] The incubation period for 2019-nCoV ranges from 2 to 14 days with documented evidence of asymptomatic transmission occurring in various settings globally.[18,19] The virus causes a broad spectrum of symptoms; most are mild with the most common clinical presentations including fever, cough, sore throat, headache, diarrhoea, and joint and muscle pain.[20] Loss of taste and smell have also been reported in some cases.[21] More severe outcomes associated with COVID-19 infection include

pneumonia and acute respiratory distress syndrome (ARDS) which may result in acute respiratory failure.[22] There is also evidence of cardiovascular outcomes including arrhythmias, cardiomyopathy and heart failure associated with infection.[23] Although the majority of cases have presented with fever, or history of fever, some cases have presented with respiratory symptoms alone. The case fatality rate (CFR) can range from 0.1% to over 25%, varies between different settings and population groups, and is often underestimated due to asymptomatic cases and those with lower levels of access to healthcare.[24] In the initial stages of the pandemic in Wuhan, the CFR was reported to be 15% in a small cohort of hospitalised patients.[5] As more data emerged, the CFR decreased to between 4.3% and 11%, and later to 3.4%.[26,27] A recent study found the global CFR to be 7.05%, ranging from 3.74% in the African region and 9.48% in the European region.[28] Studies show that the CFR for COVID-19 appears to be lower than SARS but higher than H1N1 influenza with an estimated CFR of 14% and <0.1% respectively.[25-29] The CFR may be higher in older age groups and among patients who are immunocompromised or have existing comorbidities.[26]

4.3.3 Transmission

Coronaviruses are classified as zoonotic, which means that they are capable of being transmitted from animals to humans. Genetic sequencing of the virus show similarity to other bat viruses, suggesting that the virus may have originated in bats and was later acquired through an intermediary animal host prior to human transmission occurring.[17] Initial cases were business operators at the Hua Nan Seafood Wholesale Market which sold live animals such as poultry, bats and other mammals along with other wildlife parts.[4] The primary mode of transmission for SARS-CoV-2 is through respiratory droplets with possible aerosol transmission in enclosed spaces with elevated levels of aerosol concentrations.[30] Evidence of human to human transmission was confirmed by the World Health Organization (WHO) and has since been shown in multiple studies in published literature observed in various settings including healthcare facilities and among close contacts of family members.[31-33]

The true source of the outbreak is still to be determined with no confirmed single origin reservoir for the virus.[34] Preliminary investigations identified environmental samples positive for 2019-nCoV from Hua Nan Seafood Wholesale Market in Wuhan City, however, some laboratory-confirmed patients reported at the time had not visited this market.[2,4] This suggests that there were likely other sources of the outbreak not connected to the market.

4.3.4 Preventative measures

General preventative measures recommended to lower the risk of infection include maintaining good overall personal hygiene including hand and respiratory hygiene, social distancing, and avoiding crowded places.[35] The WHO recommends thorough hand washing with soap and water or using an alcohol-based hand sanitiser.[36] Good respiratory hygiene including covering your mouth and nose with your elbow or tissue when coughing or sneezing, and immediate disposal of the used tissue followed by handwashing.[36] Maintaining at least 1.5 metre distance between yourself and others reduces the risk of exposure to liquid droplets sprayed from the mouth when speaking or from coughs and sneezes.[36] Avoiding crowded places and large gatherings also reduces the risk of coming into close contact with someone who may be infected with COVID-19.[36] In line with recommendations from WHO, The Australian Government Department of Health also advises people to stay home and self-isolate if experiencing symptoms, and wearing a face mask when out in public.[37] These recommendations have changed over the course of the pandemic.

At the time of writing this chapter, specific recommendations were made for travellers visiting countries affected by 2019-nCoV (which at the time only included China). This included avoiding contact with live animals, including those in live animal markets, and avoiding contact with sick people.[31] Travellers were also recommended to follow travel advice or restrictions in place prior to travel by regularly checking credible sources such as government websites or WHO resources.

4.3.5 Public health importance

In Australia, human coronavirus with pandemic potential, which includes 2019-nCoV, is a listed human disease (LHD) under the *Biosecurity Act 2015*.[38] Among the list are other specific diseases which are contagious and can cause significant harm to human health. The Act enables officials at the border to investigate suspected cases of illness, and if required, have the authoritative right to place people under quarantine.[38] In Victoria, 2019-nCoV is a notifiable condition under the *Public Health and Wellbeing Act 2008* and the *Public Health and Wellbeing Regulations 2019* which requires medical practitioners and pathology services to notify the Department of Health and Human Services (DHHS) of suspected cases for further investigation and reporting to the Commonwealth under the National Notifiable Diseases Surveillance System (NNDSS).[39]

Novel coronaviruses continue to be a public health concern globally with previous epidemics of SARS-CoV in 2003 and MERS-CoV in 2012 evidence of the potential for

imported cases. The 2019-nCoV is a new type of coronavirus previously undetected with limited knowledge on characteristics of the disease and its epidemiological features. The outbreak has progressed to a global pandemic event since it was first detected in China in late December 2019, and has since spread to 235 countries worldwide.[12] The large-scale impact the pandemic has had so far on health systems and economies of countries globally is evidence that this event is of significant public health importance to prevent and control further waves of infection. Political sensitivities around quarantine procedures, travel bans and economic impact is an ongoing global issue that continues to be widely debated within governments. The public health importance of 2019-nCoV in the early stages is reflected in the government response to evacuations of Australian citizens from Wuhan who were initially quarantined on Christmas Island for 14 days upon re-entry into Australia.[40] This was also a highly topical issue for the cruise ship industry which has seen multiple large scale outbreaks of 2019-nCoV, such as the outbreak that occurred on a ship moored off the coast of Japan.[41] There is also growing concern and frustration among Australian citizens stranded overseas who have been unable to return home due to limited availability of international flights, closure of key travel hubs worldwide, and the ongoing implementation of travel restrictions.[42] Media interest has been high across all of these areas, as well as progress towards discovery of an effective vaccine and the advent of several vaccine trials.

National and state efforts to limit imported cases and local transmission is time consuming and resource-intensive requiring extensive contact tracing capacity. This places additional burden on health systems and local public health units who may require additional surge capacity to manage. The Victorian Department of Health and Human Services (DHHS) has established a 2019-nCoV surveillance system integrated into their existing notifiable diseases surveillance system in order to mitigate the public health risk of 2019-nCoV in Victoria. Well-established, systematic processes of the system enabled identification and monitoring of the health of people entering Victoria from recent travel to 2019-nCoV affected areas and their contacts who may also be at risk.

4.4 Victorian surveillance system for 2019-nCoV

4.4.1 Objectives of the system

The main objective of the 2019-nCoV surveillance system is to rapidly identify and isolate cases and their contacts to prevent local transmission.

4.4.2 Identification of stakeholders

The following stakeholders were identified as having responsibility for the development, monitoring and response components of the surveillance system:

- Health Protection Branch, Department of Health and Human Services: responsible for developing, updating and monitoring the 2019-nCoV surveillance system and following up with any actions required
- Victorian Infectious Diseases Reference Laboratory (VIDRL): responsible for providing laboratory capacity for diagnosis of 2019-nCoV cases
- Ambulance Victoria: responsible for patient transport of suspected 2019-nCoV cases
- Hospitals and GP clinics: responsible for early assessment and treatment of cases and notifying suspected cases to DHHS
- Commonwealth Department of Health (DoH): responsible for collecting 2019-nCoV data at a national level under the National Notifiable Diseases Surveillance System (NNDSS). Development and changes to the 2019-nCoV surveillance system were guided by advice from DoH and AHPPC in line with guidelines produced by the Communicable Diseases Network Australia (CDNA) and the Public Health Laboratory Network (PHLN).

4.4.3 Legislation for surveillance

The communicable disease surveillance system including 2019-nCoV surveillance in Victoria is supported by the following legislation:

- *Public Health and Wellbeing Act 2008* and the *Public Health and Wellbeing Regulations 2019* (VIC)
- *The Health Record Act (2001)*
- *Biosecurity Act 2015* (Commonwealth)
- *National Health Security Act 2007* (Commonwealth)

The *Public Health and Wellbeing Act 2008* and the *Public Health and Wellbeing Regulations 2019* require all medical practitioners and pathology services to notify DHHS of any suspected cases of 2019-nCoV for public health follow up and

investigation.[39] Under the *Biosecurity Act 2015,* officials at the border are authorised to take appropriate actions, including quarantining of passengers, if they are identified as being suspected or at risk of 2019-nCoV.[38] The *National Health Security Act 2007* enables the sharing of public health surveillance data by state and territory health authorities to the Commonwealth.[43]

4.5 Methods

4.5.1 Description of the surveillance system

In response to the 2019-nCoV outbreak in Hubei Province China, an Incident Management Team (IMT) was convened by DHHS to coordinate the public health response to 2019-nCoV in Victoria. As part of the roles and responsibilities within the IMT, a 2019-nCoV surveillance system was established and integrated into the existing notifiable diseases dataset, collected in the Public Health Events Surveillance System (PHESS). The 2019-nCoV surveillance system very closely followed the existing surveillance for MERS-CoV given the similar clinical and epidemiological features (from what was currently known at the time) between the two infections. As more details of the epidemic emerged, adjustments were made to the case questionnaire to capture specific details of 2019-nCoV exposures including travel to Hubei Province China, known contact with a confirmed case, or hospital or other healthcare and animal markets. The Health Protection Branch (HPB) within DHHS received information on suspected cases, as well as flight details of travellers who have recently arrived from Hubei Province, China from the National Incident Room (NIR) for contact tracing.

The surveillance process is described below and summarised in Figure 1.

1. GP or hospital presentation

1.1. A patient presents to either a GP clinic or hospital and initial assessment is conducted by the clinician or other treating staff to determine if the patient meets the 2019-nCoV case definition for a suspected case.

1.2. If diagnosis is uncertain, clinicians may consult with a public health practitioner at DHHS to discuss whether the patient meets the case definition.

1.3. Once a patient meets the suspected case definition, sample collection for testing is approved by the clinician and a notification is made to DHHS

2. Department of Health and Human Services

2.1. Case investigation for suspected cases is undertaken by a PHO for each notification received using the 2019-nCoV case questionnaire.

2.2. Actions required include:

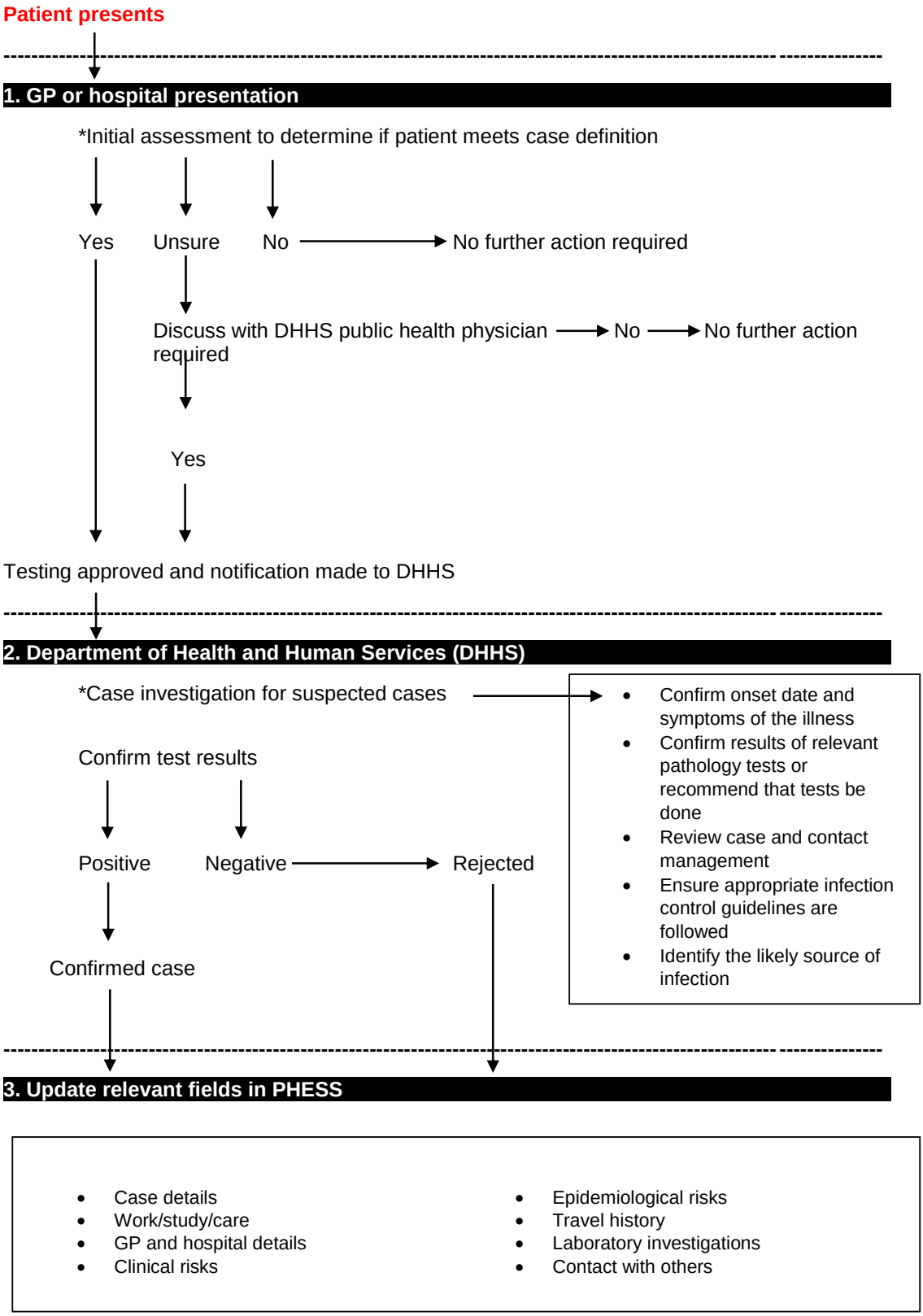
- Confirm the onset date and symptoms of illness
- Confirm the results of relevant pathology tests or recommend that tests be done
- Interview the treating doctor and determine whether the case is aware of their diagnosis, and able to be interviewed
- Review case and contact management
- Ensure appropriate infection control guidelines have been followed in caring for the case
- Identify the likely source of infection

3. Update relevant fields in the Public Health Events Surveillance System (PHESS)

3.1. Upon completion of the investigation, public health officers and/or other staff responsible for case follow-up and data collection should update all relevant fields in PHESS

3.2. Fields include: case detail, work/study/care (employment status and occupation, and details on whether a case attends childcare, school, or lives in residential aged care), General Practitioner (GP) and hospital details, clinical and epidemiological risks, travel history, laboratory investigations, and contact with others

Figure 1. 2019-nCoV surveillance system of returned travellers from Wuhan, Hubei Province China, 2020.



4.5.2 Case definitions

In the beginning of the pandemic, the 2019-nCoV case definition varied from state to state before the series of national guidelines (SoNG) was finalised by CDNA. Table 1 describes the case definition used at the time of my involvement in establishing the surveillance system. As the pandemic progressed and new information emerged, various changes and updates have been made to the case definition.

Table 1. Case definitions for 2019-nCoV surveillance in Victoria, 27 January 2020*

Confirmed case A person tested for 2019-nCoV at the Victorian Infectious Diseases Reference Laboratory (VIDRL) and found to be positive for 2019-nCoV.
Suspected case Both clinical and epidemiological criteria needed to be met for a person to be classified as a suspected case. <u>Clinical criterial:</u> Acute lower respiratory infection with a history of fever and cough (clinicians should also be alert to the possibility of atypical presentation in patients who are immunocompromised) AND <u>Epidemiological criteria:</u> A history of being in Wuhan, Hubei Province China, in the 14 days prior to symptom onset OR <u>Clinical criteria:</u> Acute respiratory illness of any severity AND <u>Epidemiological criteria:</u> Contact within 14 days of symptom onset with any of the following:

- A confirmed case of 2019-nCoV;
- A person under investigation (PUI) for 2019-nCoV;
- A live animal market in Wuhan
- A healthcare facility in a country where hospital-associated infections have been reported

Person under investigation (PUI)

People need both clinical and epidemiological criteria to be classified as a person under investigation.

Clinical criteria:

Acute respiratory illness of any severity

AND

Epidemiological criteria:

A history of travel to a location other than Wuhan, in which there is suspicion of human-to-human transmission of 2019-nCoV.

**This was the case definition used at the time of establishment of the surveillance system and may have subsequently changed.*

4.5.3 Contact management

All persons identified as a contact of a confirmed case required follow-up and monitoring for the development of symptoms for the 14 days after the last exposure to the case. Priority for contact tracing included close contacts, particularly healthcare workers and those who may be at higher risk of severe disease, including the elderly and those with pre-existing co-morbidities.

Table 2. Definitions for close and casual contacts for 2019-nCoV surveillance in Victoria*

Close contact	**Casual contact**

A close contact is defined as requiring greater than 15 minutes face-to-face contact with a symptomatic suspected or confirmed case in any setting, or the sharing of a closed space with a symptomatic suspected or confirmed case for more than 2 hours without recommended PPE. A close contact may include any person meeting the following criteria: • Living in the same household or household-like setting (for example, a boarding school or hostel) • Direct contact with the body fluids or laboratory specimens of a confirmed case without recommended Personal Protective Equipment (PPE) • A person who spent two hours or longer in the same room (such as a GP clinic or emergency department (ED) waiting room) • A person in the same hospital room when an aerosol generating procedure is undertaken on the case, without recommended PPE (airborne/droplet and contact precautions) • Aircraft passengers who were seated in the same row as the case, or in the two rows in front or two rows behind a suspected or confirmed case of 2019-nCoV	Casual contact is defined as any person having less than 15 minutes face-to-face contact with a symptomatic probable or confirmed case in any setting or sharing a closed space with a symptomatic probable or confirmed case for less than 2 hours. This will include healthcare workers, other patients or visitors who were in the same closed healthcare space as a case, but for shorter periods than those required for a close contact. Other closed settings might include schools or offices. Note that healthcare workers and other contacts who have taken recommended infection and control precautions, including the use of recommended PPE, while caring for a symptomatic probable or confirmed 2019-mCoV case are not considered to be close contacts but are considered casual contacts. For the purpose of public health contact tracing, other casual contacts may include: • Extended family groups, for example, in an Aboriginal community • Contact tracing of people who may have had close contact on long bus or train trips should also be attempted where possible, using similar seating/proximity criteria • All crew members on an aircraft who worked in the same cabin

• Face-to-face contact for more than 15 minutes with the case in any setting not listed above Contact needs to have occurred within the potential infectious period of the case, which is up to 48 hours before symptom onset.	area as a suspected or confirmed case of 2019-nCoV. If a crew member is the 2019-nCoV case, contact tracing efforts should concentrate on passengers seated in the area where the crew member was working during the flight and all of the other members of the crew. Casual contacts should be advised to self-monitor and if they develop symptoms consistent with 2019-nCoV infection they should isolate themselves and notify the department so they can be tested and managed as a suspected case of 2019-nCoV if considered necessary.

**This was the active definition for close and casual contacts used at the time of establishment of the surveillance system and may have subsequently changed since.*

4.5.4 Internal protocol for investigation

I assisted with developing a protocol for investigation to support the establishment of the 2019-nCoV surveillance system. One of my key roles was to conduct a routine review of information on presenting symptoms, and to monitor the number of newly identified cases in other countries and regions. I used this information to the evolving case definition and questionnaire to determine testing eligibility of return travellers from outbreak active areas. This document provided ongoing updates to support the public health response to rapidly identify and isolate cases and their contacts to prevent local transmission. This protocol includes information on:

- Disease description
- Clinical presentation
- Laboratory and testing
- Case and contact management
- Public health response
- Exclusion, restriction and isolation

Public Health Officers (PHO) were mainly responsible for case and contact management, with support from public health physicians. Members of the IMT provided input to the development of the protocol to ensure appropriate investigation measures were followed. In addition to training for PHOs on identification and assessment and data entry of cases, DHHS developed fact sheets and guidelines for clinicians and other healthcare workers based on standard infection prevention and control protocols. Due to the increasingly large volumes of phone calls from the public, DHHS established a dedicated 2019-nCoV hotline with support from Nurse on Call who attended the phone lines and responded to general enquiries. I provided input to developing coronavirus fact sheets with information on risk, signs and symptoms, and testing criteria were to assist with response to public enquiries.

4.6 Results

For the duration of my involvement in the establishment of the surveillance system, there were a total of four cases notified between 25 January to 8 February 2020. Of the four cases identified, two were female and two were male aged between 25 – 66 years with a median of 53 years. All were overseas acquired infections. Of the information I was able to access, the first case identified was a return traveller from Wuhan who flew to Melbourne from Guangdong on January 19 and presented with respiratory illness. The case was treated in an isolation unit at Monash hospital in accordance with infection prevention and control procedures, and close contacts were provided support and monitored closely for signs or symptoms of illness. The Department conducted interviews with the case and worked closely with the Commonwealth Government to contact passengers on the flights that the case boarded and conduct contact tracing. I supported the public health officers who conducted contact tracing and case interviews through my contribution to informing the case questionnaire by ensuring that the most up to date information was available on presenting symptoms, exposure sites, and eligibility criteria for testing.

4.7 Discussion

This chapter describes my involvement at the time of the establishment of a surveillance system in Victoria to monitor travellers returning from Wuhan, Hubei Province in China in response to the nCoV-2019 epidemic in mainland China. Early on in the pandemic the case definition in Victoria was restricted to returned travellers from high risk settings, which at the time was limited to Wuhan. The purpose of the surveillance system was to assess the risk of nCoV-2019 infection and early

identification of suspected cases for active investigation and management of cases and contacts.

The Victorian 2019-nCoV surveillance system was established using resources from WHO and CDC, including updated information on presenting symptoms and newly identified cases in other countries/regions. This informed our questionnaire to determine symptoms for testing, and to identify outbreak active regions for return travellers who were eligible for testing. We also incorporated existing MERS-CoV literature and surveillance resources as guidelines. The system was established prior to finalised 2019-nCoV recommendations issued as part of the series of national guidelines (SoNG) developed by CDNA and agreed to by Chief Health Officers (CHO) in all states and territories and the Chief Medical Officer (CMO) in Australia. Since then, the SoNG has had multiple versions and ongoing updates. Surveillance case definition and objectives continues to change based on scientific evidence and expert advice as the pandemic progresses.

The Victorian team that I was a part of developed a surveillance system that needed to be fit for the urgent nature of the emerging epidemic. The attributes that we considered in the early development of the surveillance were:

- Simplicity: The ease of operation of the system was reflected in its rapid integration within the existing State disease surveillance system. The informatics team within the Communicable Diseases and Surveillance Section at the Department integrated 2019-nCoV into the existing PHESS platform through existing pathways.
- Flexibility: The system was able to adapt to the changing information needs and operating conditions. For example, drop down field options were added when new exposure sites and symptoms were identified. This was constantly changing as new information on the disease emerged.
- Data quality: Data completeness was maintained through the standardised case questionnaire form adapted from MERS-CoV. Detailed notes entered into PHESS by public health officers through interviews with cases and medical staff also ensured information was up to date. Furthermore, contact details recorded enabled public health officers to contact cases and GPs for further information if required.
- Acceptability: There were no significant changes in reporting pathways for GPs and other medical staff to notify the Department of potential cases. The integration of the system into PHESS also enabled public health officers to

continue using the system for routine reporting on the disease as they do for other notifiable conditions.

- Timeliness: The existing structure of PHESS and integration of COVID-19 surveillance ensured minimal delay between medical presentation, case interview and contact tracing. The urgent nature of the pandemic and the public health response communicated to returning travellers and the medical community in Victoria.
- Sensitivity: The inclusion of a very sensitive suspect case definition and timely alerts to the medical community ensured that the system was able to detect cases.

A protocol for investigation was developed which provided information on the disease and detailed steps for case and contact management. This was referred to internally by DHHS to guide response activities. The establishment of the surveillance system involved minimal resources as it was integrated into the existing state-based notifiable diseases surveillance system, and a case report form and questionnaire was able to be adapted from pre-existing MERS-CoV resources. Contact tracing however proved to be quite labour intensive with the fields in the questionnaire continuing to expand as new information on disease characteristics and transmission became available. During this time, all questionnaires and laboratory reporting for test results were entered into PHESS manually from either paper forms or via email spreadsheets. This was manageable at the time as case numbers were still relatively low, however, later proved to be a time consuming and overwhelming process as cases increased. Updating individual cases also required cross-checking notes made by PHOs on paper reporting forms as additional phone interviews were made.

Preliminary establishment of a COVID-19 surveillance system followed a similar process in other comparable countries. In France, where cases were first reported on 24 January 2020, surveillance was implemented on 10 January 2020 with the objective of early identification of imported cases to prevent secondary transmission.[44] Similar to the initial case definition developed in Victoria, health authorities in France defined three categories of risk exposure and developed procedures for follow-up of identified contacts. French health authorities required physicians who suspected a COVID-19 case to contact the patient's general practitioner to evaluate whether the patient met the case definition and confirm testing. This information was then reported via a 24/7 phone line to the Regional Health Agency, which informs the hospital infection and control team responsible for managing the patient, the French Public Health Agency, and the Ministry of Health.[44] France also developed a case investigation form with enhanced information on exposure history (travel to Wuhan, or contact with a

confirmed case) and data sent to the national health database. In contrast, early surveillance in Singapore was further enhanced for their national surveillance system to identify not only people with a travel history to Wuhan, China, but also identification of local cases.[45] This proved to be effective where a local cluster was identified through surveillance for pneumonia of people with no history of travel to China. Among the first 84 confirmed cases in Singapore, ten were identified by enhanced surveillance through either patient testing in intensive care unit or at the doctor's discretion based on clinical or epidemiological evidence.[45]

Before the emergence of COVID-19, there is evidence of similar approaches to enhanced surveillance. In response to the emergence of SARS in 2003, the United States CDC established national surveillance to identify patients in the US and determine the risk of local transmission.[46] The initial surveillance definition for a suspected case of SARS was based on the first published definition by WHO.[46] National surveillance was designed to meet important surveillance objectives whilst allowing for rapid and frequent updates to case definitions and testing criteria. When the first confirmed case of MERS-CoV was reported in 2012, Public Health England implemented enhanced MERS surveillance to rapidly identify and investigate possible cases of travellers to England from the Middle East.[47] Possible and confirmed case definitions were developed based on areas of high risk, which at the time only included Kingdom of Saudi Arabia and Qatar.[47] The case definition was revised on a regular basis in response to new information and in agreement with WHO case definitions to include extensions of geographic areas of infection, testing criteria and updates on clinical features, transmission routes and the incubation period.

Since writing this chapter at the beginning of the pandemic much has changed globally, in Victoria and across Australia. Being involved in the early establishment of a surveillance system for a global pandemic was an insightful experience with valuable reflections. We have observed the progression of the outbreak from its origins as a small cluster in Wuhan, to its ultimate spread throughout mainland China and across international borders affecting almost every country globally. In a short period of time there have been various locations reporting a high number of cases and large-scale transmission. The virus has moved from mainland China to Iran, France, Italy and Spain, to currently the United States, Brazil and India, proving the pandemic potential of a highly transmissible virus with human to human transmission. COVID-19 has had a significant public health and socioeconomic impact in Australia. Social inequalities have exacerbated with an overwhelming demand placed on charities and other social

services to support those who have lost their jobs and sources of income as a result of the measures put in place and deemed necessary by states and territories in order to control transmission.[48] The pandemic has also shown the disparities in access to mental health services, highlighting the need to strengthen service provision and accessibility in this area.[48] A study investigating the impact of COVID-19 on Australia's health research workforce concluded the importance of government funding to reduce short-term and long-term repercussions on research outcomes including limited capacity to develop new products for industry, health services and the community.[49] Although case numbers and reported deaths vary across states and are much lower than other comparable countries, implications from the pandemic are evident. Despite Australia's sophisticated health system, there are still areas for improvement to ensure strong pandemic preparedness and response capacity at both state and national level.

Despite my involvement in the early days of establishment of this surveillance system and having reviewed literature on establishing surveillance of COVID-19 and other emerging infectious diseases in other countries, I am not in a position to provide detailed and informed recommendations for future improvements. I have not been as heavily involved in the Victorian response to COVID-19 to have an insight into the organisational structure and changes to funding. I have not interviewed stakeholders or conducted a formal evaluation to gain a better understanding behind some of the processes to establishing this surveillance system and challenges faced to be able to present sound recommendations. Furthermore, in the lead up to this outbreak in Victoria, there had been several public health incidents that had occurred which added additional complications to preparedness and response efforts. From October to December 2019 there was a resurgence of measles in neighbouring countries and notifications of imported cases and clusters throughout the state. Concurrent at the time, there was a major nationwide bushfire crisis which started in September 2019 and persisted through to March 2020. All of these events triggered an activation of the National Incident Room (NIR) in the Commonwealth Department of Health for urgent and ongoing response, and occupied much of the public health capacity for response across the country. I acknowledge that there is no one size fits all approach to preparedness efforts, and what has worked effectively for one country may differ to another due to various factors that should be considered.

I anticipate that had my deployment been longer, I would have been involved in the establishment of the surveillance system; largely focusing on adapting the case interview form and contact tracing protocols to the rapidly changing case definitions. This would have required monitoring the global situation and emerging literature on symptoms, periods of infection and exposure history to inform and update relevant

protocols. I may have also been required to support routine functioning of the system through assisting with case interviews and contact tracing as more cases were detected and greater resourcing was required to collect, manage, and provide up to data. The experience and insights I gained while at the Department of Health in Victoria enabled me to contribute to the response in the National Incident Room when I returned to the Commonwealth. I gained a greater understanding of the process for changing and updating the CDNA case definitions and how they impacted testing and notifications to health departments.

4.8 Conclusion

Being involved in the early establishment of a surveillance system for a novel virus was a valuable learning experience to have been a part of a major public health response from the beginning. I was able to participate in the initial planning and had a firsthand experience in understanding the time sensitive nature of such activity, which required urgent public health action in the event of limited information available. was also able to see how surveillance system attributes including simplicity, flexibility, timeliness, and sensitivity were put in the context of a real-life scenario. An important next step is to conduct a formal evaluation of this surveillance system and its attributes to highlight the functional components of the system, and identify additional areas needing improvement in order to inform changes made in the future. Challenges remain given the limited public health resources for pandemic preparedness and planning. However, the lessons learnt from this preliminary response to establishing a state level surveillance system for COVID-19 are valuable not only for future pandemics and similar large-scale outbreaks, but also for improving the surveillance and response to current infectious diseases. Being involved at the State Government level also provided a different perspective and angle of response to a pandemic scenario which differed from the national level response. I have been able to reflect on my experiences of establishing a surveillance system and use the insights that I have learnt for future scenarios.

4.9 References

1. Wu P, Hao X, Lau EHY, Wong JY, Leung KSM, Wu JT et al. Real-time tentative assessment of the epidemiological characteristics of novel coronavirus infections in Wuhan, China, as at 22 January 2020. Euro Surveill. 2020 Jan;25(3):2000044. Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.3.2000044
2. Zhou P, Yang X, Wang X, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020 Mar;579(7798):270-273. doi:10.1038/s41586-020-2012-7
3. Chan JF, Yuan S, Kok K, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Nature. 2020 Feb 15;395(10223):514-523. doi:10.1016/S0140-6736(20)30154-9
4. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020 Mar 26;382(13):1199-1207. Doi:10.1056/NEJMoa2001316
5. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb:395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5
6. Nishiura H, Linton NM & Akhmetzhanov AR. Initial cluster of novel coronavirus (2019-nCoV) infections in Wuhan, China is consistent with substantial human-to-human transmission. J Clin Med. 2020 Feb 11;9(2):488. doi:10.3390/jcm9020488.
7. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. Frist case of 2019 novel coronavirus in the United States. N Engl J Med. 2020 Mar 5;382(10):929-936. doi:10.1056/NEJMoa2001191.
8. Pongpirul W, Pongpirul K, Ratnarathon AC & Prasithsirikul W. Journey of a Thai taxi driver and novel coronavirus. N Engl J Med. 2020 Mar 12;382(11):1067-1068. doi:10.1056/NEJMc2001621.
9. Backer JA, Klinkenberg D & Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20-28 January 2020. Euro Surveill. 2020 Feb;25(5):2000062. doi:10.2807/1560-7917.ES.2020.25.5.2000062.
10. World Health Organization. Novel Coronavirus (2019-nCoV) Situation Report - 22. Geneva, WHO 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22-ncov.pdf?sfvrsn=fb6d49b1_2

11. World Health Organization. COVID-19 public health emergency of international concern (PHEIC) global research innovation forum [Internet]. Geneva: WHO; 2020 [updated 2020 Feb 12; cited 2020 Feb 15]. Available from: https://www.who.int/publications/m/item/covid-19-public-health-emergency-of-international-concern-(pheic)-global-research-and-innovation-forum
12. World Health Organization. Coronavirus disease (COVID-19) weekly epidemiological update and weekly operational update – 28 September 2020. WHO 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200928-weekly-epi-update.pdf?sfvrsn=9e354665_2
13. Australian Government Department of Health. Australian Health Protection Principal Committee (AHPPC) [Internet]. Canberra ACT: Australian Government Department of Health; 2020 [updated 2020 Sep 3; cited 2020 Feb 7]. Available from: https://www.health.gov.au/committees-and-groups/australian-health-protection-principal-committee-ahppc
14. Australian Government Department of Health. Series of National Guidelines (SoNGs): Coronavirus Disease 2019 (COVID-19) [Internet]. Canberra ACT: Australian Government Department of Health; 2020 [updated 2020 Mar 15; cited 2020 Mar 15]. Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-novel-coronavirus.htm
15. Australian Government Department of Health. Australian Health Protection Principal Committee (AHPPC) novel coronavirus statement on 1 February 2020 [Internet]. Canberra ACT: Australian Government Department of Health; 2020 [updated 2020 Feb 2; cited 2020 Feb 2]. Available from: https://www.health.gov.au/news/australian-health-protection-principal-committee-ahppc-novel-coronavirus-statement-on-1-february-2020-0
16. Department of Health and Human Services, State Government of Victoria, Australia. Our organisation: Divisions [Internet]. Victoria: Department of Health and Human Services, State Government of Victoria, Australia; 2020 [updated 2020 Mar 15; cited 2020 Mar 15]. Available from: https://www.dhhs.vic.gov.au/our-organisation
17. Ji W, Wang W, Zhao X, Zai J & Li X. Cross-species transmission of the newly identified coronavirus 2019-nCoV. J Med Virol. 2020 Apr;92(4):433-440. doi:10.1002/jmv.25682.
18. Mizumoto K, Kagaya K, Zarebski A & Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-10) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill. 2020 Mar 12;25(10):2000180. Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000180/

19. Huang L, Zhang X, Zhang X, Wei Z, Zhang L & Xu J et al. Rapid asymptomatic transmission of COVID-19 during the incubation period demonstrating strong infectivity in a cluster of youngsters aged 16-23 years outside Wuhan and characteristics of young patients with COVID-19: A prospective contact-tracing study. J Infect. 2020 Jun;30(6):e1-e13. Available from: https://www.sciencedirect.com/science/article/pii/S0163445320301171
20. Zhu J, Ji P, Pang J, Zhong Z, Li H, He C et al. Clinical Characteristics of 3,062 COVID-19 Patients: A Meta-Analysis. J Med Virol. 2020 Apr 15;10.1002/jmv.25884. Available from: https://pubmed.ncbi.nlm.nih.gov/32293716/?from_term=coronavirus&from_sort=date&from_page=5&from_pos=3
21. Salmon D, Bartier S, Hautefort C, Nguyen Y, Nevoux J & Hamel A et al. Self-reported loss of smell without nasal obstruction to identify COVID-19. The multicenter CORANOSMIA cohort study. J Infect. 2020 Oct;81(4):614-620. Available from: https://www.sciencedirect.com/science/article/pii/S0163445320304631
22. Zhang MQ, Wang XH, Chen YL, Zhao KL, Cai YQ, An CL, et al. Clinical features of 2019 novel coronavirus pneumonia in the early stage from a fever clinic in Beijing. Chinese Journal of Tuberculosis and Respiratory Diseases. 2020 Feb 15;43(0):E013. Available from: https://pubmed.ncbi.nlm.nih.gov/32061066/
23. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J & Biondi-Zoccai G et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. J Am Coll Cardiol. 2020 May 12;75(18)2352-2371. Available from: https://pubmed.ncbi.nlm.nih.gov/32201335/
24. World Health Organization. Estimating mortality from COVID-19 [Internet]. Geneva, WHO 2020. Updated 2020 Aug 4 [cited 2020 Oct 6]. Available from: https://www.who.int/news-room/commentaries/detail/estimating-mortality-from-covid-19
25. Chen L, Liu HC, Liu W, Liu K, Shang J, Deng Y, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. Chinese Journal of Tuberculosis and Respiratory Diseases. 2020 Feb 6;43(0):E005. Available from: https://pubmed.ncbi.nlm.nih.gov/32026671/
26. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020 Feb 15;395(10223):507-513. doi:10.1016/S0140-6736(20)30211-7

27. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020 Mar 17;323(11):1061-1069. doi:10.1001/jama.2020.1585
28. Kazemi-Karyani A, Safari-Faramani R, Amini S, Ramezani-Doroh V, Berenjian F, Dizaj MY, et al. World one-hundred days after COVID-19 outbreak: Incidence, case fatality rate and trend. J Educ Health Promot. 2020 Aug 31;9:199. doi:10.4103/jehp.jehp_483_20.
29. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020 Feb 22;395(10224):565-574. doi:10.1016/S0140-6736(20)30251-8
30. Cascella M, Rajnik M, Cuomo A, Dulebohn SC & Di Napoli R. Features, evaluation and treatment coronavirus (COVID-19). StatPearls [Internet], 2020 Aug 10. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554776/
31. World Health Organization. Mission summary: WHO field visit to Wuhan, China 20-21 January 2020. Geneva: WHO; 2020 [updated 2020 Jan 22; cited 2020 Feb 15]. Available from: https://www.who.int/china/news/detail/22-01-2020-field-visit-wuhan-china-jan-2020
32. Chang D, Xu H, Rebaza A, Sharma L, Dela Cruz CS. Protecting health-care workers from subclinical coronavirus infection. Lancet Respir Med. 2020 Mar;8(3):e13. Available from: https://pubmed.ncbi.nlm.nih.gov/32061333/
33. Riou J & Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. Euro Surveill. 2020 Jan;25(4):2000058. doi:10.2807/1560-7917.ES.2020.25.4.2000058.
34. Rothan HA & Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Authoimmun. 2020 May;109:102433. doi:10.1016/j.jaut.2020.102433.
35. World Health Organization. Report of the WHO-China joint mission on coronavirus disease 2019 (COVID-19) [Internet]. Geneva: WHO; 2020 [updated 2020 Feb 24; cited 2020 Feb 20]. Available from: https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf
36. World Health Organization. Coronavirus disease (COVID-19) – Advice for the public [Internet]. Geneva, WHO 2020. Updated 2020 Oct 7 [cited 2020 Oct 7]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public
37. Australian Government Department of Health. Coronavirus (COVID-19) heath alert – How to protect yourself and others from coronavirus (COVID-19) [Internet]. Canberra ACT, Australian Government Department of Health 2020. Updated 2020 Sep 7 [cited 2020 Oct

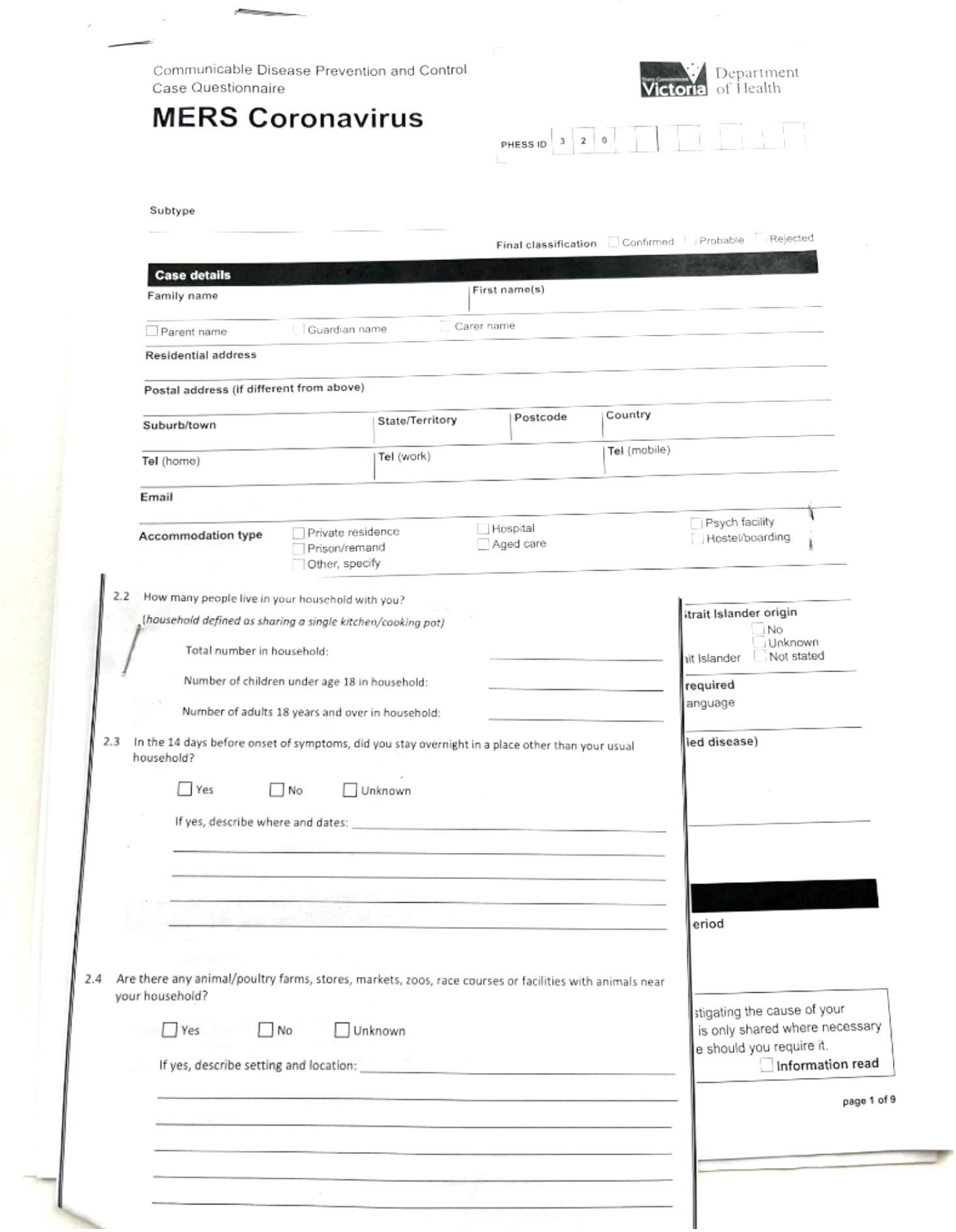
7]. Available from: https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/how-to-protect-yourself-and-others-from-coronavirus-covid-19

38. Australian Government Department of Health. Listed human diseases [Internet]. Canberra ACT: Australian Government Department of Health; 2020 [updated 2020 Jan 31; cited 2020 Feb 20]. Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/ohp-biosec-list-diseases.htm
39. State Government of Victoria. Victorian Legislation: Public Health and Wellbeing Regulations 2019 [Internet]. Victoria: State Government of Victoria; 2020 [updated 2020 Feb 5; cited 2020 Feb 20]. Available from: https://www.legislation.vic.gov.au/in-force/statutory-rules/public-health-and-wellbeing-regulations-2019/007
40. Australian Nursing & Midwifery Journal. Australians to be evacuated from Wuhan over coronavirus and quarantined on Christmas Island [Internet]. Australian Nursing & Midwifery Federation; 2020 [updated 2020 Jan 30; cited 2020 Feb 20]. Available from: https://anmj.org.au/australians-to-be-evacuated-from-wuhan-over-coronavirus-and-quarantined-on-christmas-island/
41. Australian Government Department of Health. Four more Diamond Princess passengers test positive for COVID-19 [Internet]. Canberra ACT: Australian Government Department of Health; 2020 [updated 2020 Feb 22; cited 2020 Feb 20]. Available from: https://www.health.gov.au/news/four-more-diamond-princess-passengers-test-positive-for-covid-19
42. Smartraveller. COVID-19: Trying to get home [Internet]. Canberra ACT, Australian Government Department of Foreign Affairs and Trade 2020. [Cited 2020 Oct 7]. Available from: https://www.smartraveller.gov.au/COVID-19/trying-get-home
43. Australian Government. National Health Security Act 2007 [Internet]. Canberra ACT: Australian Government; 2020 [cited 2020 Feb 21]. Available from: https://www.legislation.gov.au/Details/C2016C00847
44. Stoecklin SB, Rolland P, Silue Y, Mailles A, Campese C, Simondon A et al. Frist cases of coronavirus disease 2019 (COVID-19) in France: surveillance, investigations and control measures, January 2020. Euro Surveill. 2020 Feb;25(6):2000094. doi:10.2807/1560-7917.ES.2020.25.6.2000094.
45. Pung R, Chiew CJ, Young BW, Chin S, Chen MIC, Clapham HE et al. Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures. Lancet. 2020 Mar 28:395(10229):1039-1046. doi:10.1016/S0140-6736(20)30528-6.

46. Schrag SJ, Brooks JT, Van Beneden C, Parashar UD, Griffin PM, Anderson LJ et al. SARS surveillance during emergency public health response, United States, March-July 2003. Emerg Infect Dis. 2004 Feb;10(2):185-194. doi:10.3201/eid1002.030752
47. Thomas HL, Zhao H, Green HK, Boddington NL, Carvalho CFA, Osman HK et al. Enhanced MERS coronavirus surveillance of travellers from the Middle East to England. Emerg Infect Dis. 2014 Sep;20(0):1562-1564. doi:10.3201/eid2009.140817
48. O'Sullivan D, Rahamathulla M & Pawar M. The impact and implication of COVID-19: An Australian perspective. Int J Comm Soc Dev. 2020 Jul 1;2(2):134-151. Available from: https://doi.org/10.1177/2516602620937922
49. Peeters A, Mullins G, Becker D, Orellana L & Livingston P. COVID-19's impact on Australia's health research workforce. Lancet. 2020 Aug 15;398(10249):461. Available from: https://doi.org/10.1016/S0140-6736(20)31533-6

4.10 Appendix

Appendix 1. Early draft of MERS-CoV case questionnaire form adapted for COVID-19



Communicable Disease Prevention and Control
Case Questionnaire

Department of Health

MERS Coronavirus

PHESS ID 3 2 0

Subtype

Final classification ☐ Confirmed ☐ Probable ☐ Rejected

Case details

Family name | First name(s)

☐ Parent name ☐ Guardian name ☐ Carer name

Residential address

Postal address (if different from above)

Suburb/town | State/Territory | Postcode | Country

Tel (home) | Tel (work) | Tel (mobile)

Email

Accommodation type ☐ Private residence ☐ Hospital ☐ Psych facility
☐ Prison/remand ☐ Aged care ☐ Hostel/boarding
☐ Other, specify

2.2 How many people live in your household with you?

(household defined as sharing a single kitchen/cooking pot)

Total number in household:

Number of children under age 18 in household:

Number of adults 18 years and over in household:

2.3 In the 14 days before onset of symptoms, did you stay overnight in a place other than your usual household?

☐ Yes ☐ No ☐ Unknown

If yes, describe where and dates:

2.4 Are there any animal/poultry farms, stores, markets, zoos, race courses or facilities with animals near your household?

☐ Yes ☐ No ☐ Unknown

If yes, describe setting and location:

strait Islander origin
☐ No
☐ Unknown
ait Islander ☐ Not stated

required
anguage

ied disease)

eriod

stigating the cause of your
is only shared where necessary
e should you require it.
☐ Information read

page 1 of 9

PHESS ID 3 2 0

General Practitioner

Doctor name

Clinic address

Suburb/town

Tel (work)

Email

Work/Study/Care

- Complete as many work/school/care groups as applicable.

1

Occupation | **Employer/School/Child care centre name**

Street address

Suburb/town | **State/Territory** | **Postcode** | **Country**

Tel (work) | **Tel** (mobile) | **Tel** (fax)

Email

Normal hours of attendance | **Contact person at institution**

Date last attended before onset of illness / / | **Was this during the period of interest** ☐ Yes ☐ No

3.3 Describe your daily activities at work/school (in the morning, afternoon, and evening) during the last 14 days before onset of symptoms:

3.4 Have you attended any social gatherings (e.g. worship, sporting and other events) during the last 14 days before onset of symptoms?

☐ Yes ☐ No ☐ Unknown

If yes, describe what, when and where:

erest ☐ Yes ☐ No

3.5 Describe all other activities outside work/school with location and dates (including leisure/outdoor/ sports activities/ other hobbies) that you have participated in *during the last 14 days before onset of symptoms*.

3.6 Have you been involved in any activity that is not part of your usual routine at work/school/home during the last 14 days before onset of symptoms?

☐ Yes ☐ No ☐ Unknown

If yes, describe what, when and where:

PHESS ID 3 2 0

General Practitioner

Doctor name | Clinic name

Clinic address

Suburb/town | State/Territory | Postcode

Tel (work) | Tel (mobile) | Tel (fax)

Email

Hospital presentation

Did the case present to hospital ☐ Yes → | Date / /
☐ No

Was the case admitted to hospital ☐ Yes ☐ No

Date of admission / / | Date of discharge/death (circle appropriate) / /

Name of hospital | Ward | Tel

Address

Hospital UR number

Treating doctor name / Treating team (if not GP) | Pager No

Email

Was treating doctor informed that Department of Health will conduct a follow-up interview with the case or NOK ☐ Yes ☐ No

Infection control consultant notified ☐ Yes → Date / /
☐ No
☐ Not applicable

Name of ICC / Contact details

Laboratory investigations

Date of specimen collection / /

Specimen type

☐ Nasopharangeal swab
☐ Endotracheal aspirate
☐ Faeces
☐ Bronchoalveolar lavage
☐ Postmortem
☐ Other → Specify _____

Coronavirus test method

☐ Nucleic acid testing / PCR
☐ EIA
☐ Other antigen test→ Specify_____
☐ Electron microscopy
☐ IFA
☐ Other → Specify_____

Date specimen sent to WHO / /

Date specimen sent to VIDRL / /

Progress Notes

PHESS ID 3 2 0

Clinical summary

Date of first symptoms / /

Symptoms

Fever ___°C	☐ Yes ☐ No	Cough	☐ Yes ☐ No
Fever by self report	☐ Yes ☐ No	Diarrhoea	☐ Yes ☐ No
ARDS	☐ Yes ☐ No	Shortness of breath	☐ Yes ☐ No
Pneumonia	☐ Yes ☐ No	Other	headache, sore throat, chills

↓

☐ Clinical diagnosis

☐ Chest X-ray → Describe _____

Clinical Notes

Was the case admitted to ICU ☐ Yes ☐ No

Did the case receive oxygen therapy ☐ Yes ☐ No

Was the case intubated ☐ Yes ☐ No

Did the case receive Extracorporeal Membrane Oxygenation (ECMO) ☐ Yes ☐ No

Does the case have any of the following conditions that may place them at risk of severe complications

- ☐ Chronic respiratory conditions (inc asthma and COPD)
- ☐ Cardiac disease (not simple hypertension)
- ☐ Diabetes mellitus ☐ Type 1 ☐ Type 2
- ☐ Immunosupression (inc cancer, HIV/AIDS)
- ☐ Immunosupressive therapy
- ☐ Haemoglobinopathies
- ☐ Neurological
- ☐ Renal Failure
- ☐ Morbid obesity
- ☐ Metabolic diseases
- ☐ Pregnancy
- ☐ Other _____

Risk factors

Has the case had recent travel (within the last ? days) to Saudi Arabia, Qatar, UK, France, Jordan or UAE ☐ Yes → travel history ☐ No ☐ N/A

Has the case had contact with someone with a similar illness within 14 days of illness onset ☐ Yes → contact with others ☐ No ☐ N/A

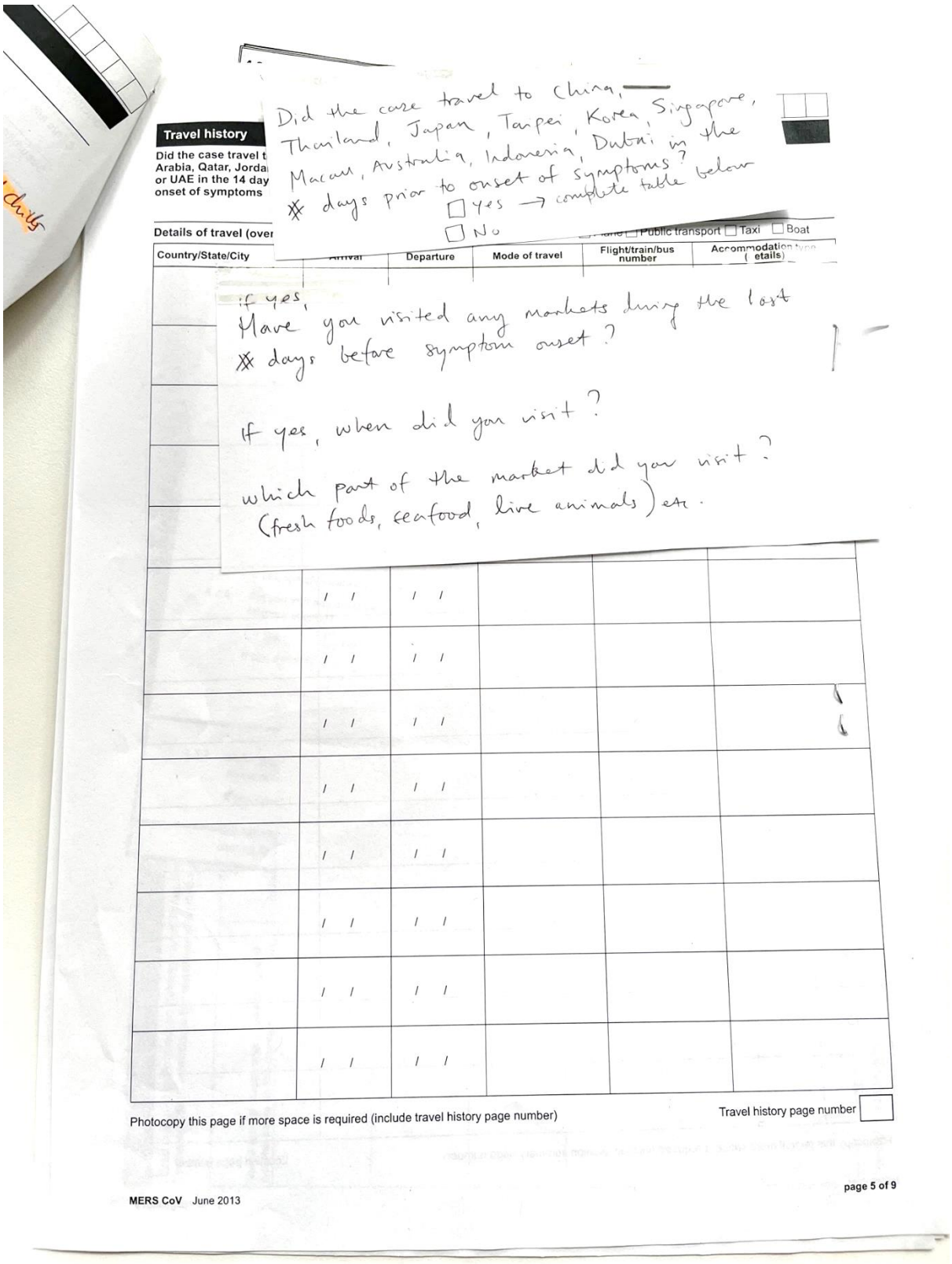
Notes

Travel history

Did the case travel Arabia, Qatar, Jord or UAE in the 14 da onset of symptoms

Details of tra

Country/s



Travel history

Did the case travel t
Arabia, Qatar, Jorda
or UAE in the 14 day
onset of symptoms

Did the case travel to China, Thailand, Japan, Taipei, Korea, Singapore, Macau, Australia, Indonesia, Dubai in the ※ days prior to onset of symptoms?
☐ Yes → complete table below
☐ No

Details of travel (over

☐ Public transport ☐ Taxi ☐ Boat

Country/State/City	Arrival	Departure	Mode of travel	Flight/train/bus number	Accommodation type (details)
	/ /	/ /			
	/ /	/ /			
	/ /	/ /			
	/ /	/ /			
	/ /	/ /			
	/ /	/ /			
	/ /	/ /			
	/ /	/ /			

if yes,
Have you visited any markets during the last ※ days before symptom onset?

If yes, when did you visit?

which part of the market did you visit? (fresh foods, seafood, live animals) etc.

Photocopy this page if more space is required (include travel history page number)

Travel history page number

PHESS ID 3 2 0

Locations visited during 14 days prior to onset of symptoms

Venue prompts ☐ Farm ☐ Zoo/Petting zoo ☐ Abbattoir ☐ Animal market ☐ River/lake ☐ Swanp marsh ☐ Camping ☐ Hunting ☐ Stockyards ☐ Agricultural show

Days prior to onset of symptoms	Day/Date (e.g. Mon 23/5)	Name/Description: use venue prompts (above)	Address
0 (Day of onset)			
1			
2			
3			
4			
5			
6			
7			

4.1.2 Have you attended any recent festivals or pilgrimages *during the last 14 days before onset of symptoms*?

☐ Yes ☐ No ☐ Unknown

If yes, describe what, when and where: _____

_____

_____

4.1.3 Did you visit any healthcare facilities *during the last 14 days before onset of symptoms*?

☐ Yes ☐ No ☐ Unknown

If yes, describe what, when and where: _____

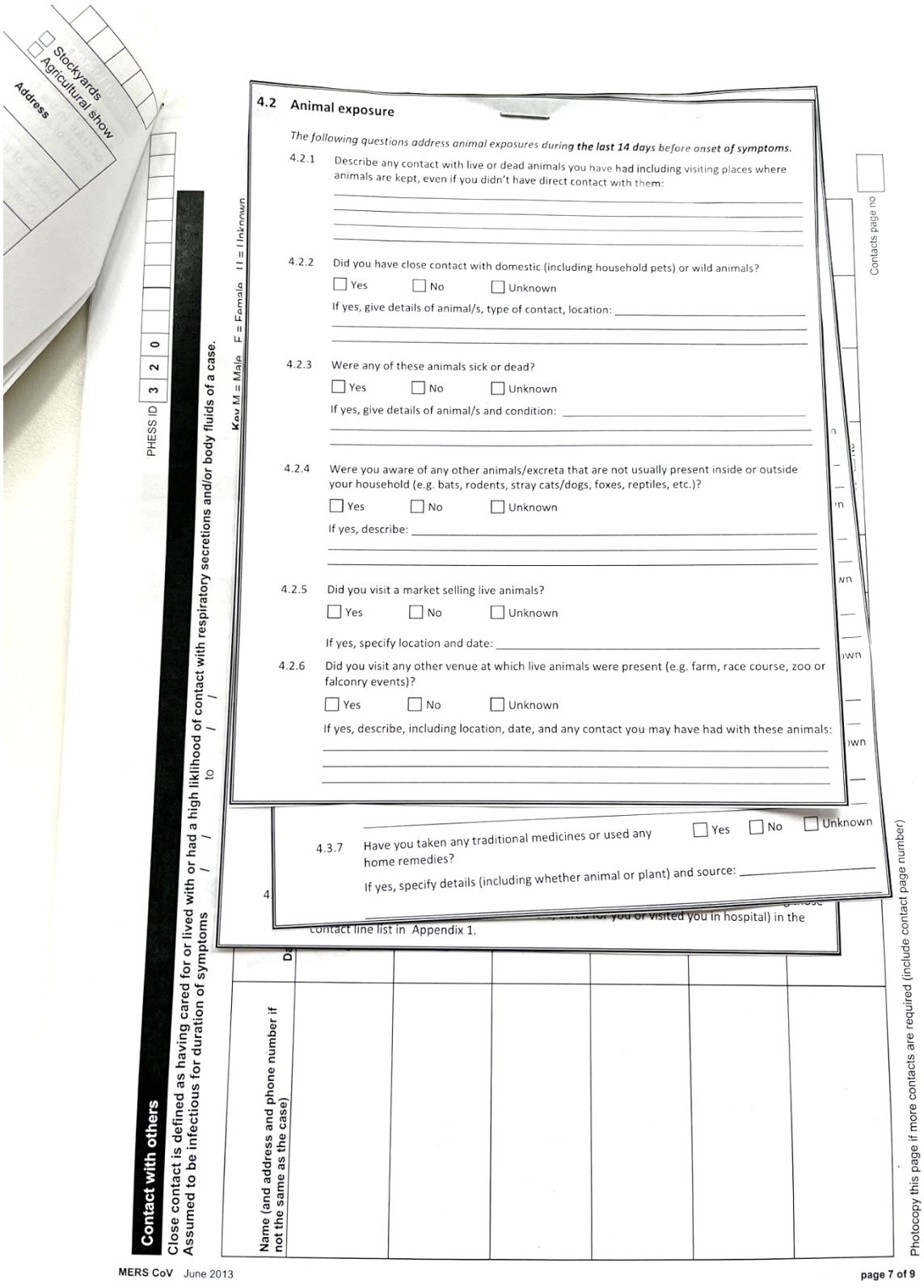
_____

_____

14			

Photocopy this page if more space is required (include location summary page number)

Location page number ☐



Stockyards
Agricultural show
Address

PHESS ID 3 2 0

Key M = Male F = Female U = Unknown

Contacts page no

4.2 Animal exposure

*The following questions address animal exposures during **the last 14 days** before onset of symptoms.*

4.2.1 Describe any contact with live or dead animals you have had including visiting places where animals are kept, even if you didn't have direct contact with them:

4.2.2 Did you have close contact with domestic (including household pets) or wild animals?
☐ Yes ☐ No ☐ Unknown
If yes, give details of animal/s, type of contact, location:

4.2.3 Were any of these animals sick or dead?
☐ Yes ☐ No ☐ Unknown
If yes, give details of animal/s and condition:

4.2.4 Were you aware of any other animals/excreta that are not usually present inside or outside your household (e.g. bats, rodents, stray cats/dogs, foxes, reptiles, etc.)?
☐ Yes ☐ No ☐ Unknown
If yes, describe:

4.2.5 Did you visit a market selling live animals?
☐ Yes ☐ No ☐ Unknown
If yes, specify location and date:

4.2.6 Did you visit any other venue at which live animals were present (e.g. farm, race course, zoo or falconry events)?
☐ Yes ☐ No ☐ Unknown
If yes, describe, including location, date, and any contact you may have had with these animals:

4.3.7 Have you taken any traditional medicines or used any home remedies? ☐ Yes ☐ No ☐ Unknown
If yes, specify details (including whether animal or plant) and source:

contact line list in Appendix 1.

Contact with others

Close contact is defined as having cared for or lived with or had a high liklihood of contact with respiratory secretions and/or body fluids of a case.
Assumed to be infectious for duration of symptoms / / to / /

Name (and address and phone number if not the same as the case)						

Photocopy this page if more contacts are required (include contact page number)

PHESS ID 3 2 0

Public health actions

Is case in a high-risk occupation such as a health care worker.

☐ Yes → Exclusion discussed with case — ☐ Yes → Date / / ☐ No

→ Exclusion letter sent by Department of Health — ☐ Yes → Date / / ☐ No

→ Infection control guidelines sent to institution — ☐ Yes → Date / / ☐ No

☐ No

Incident created/sent ☐ Yes → Date / / ☐ No ☐ Not applicable

Voluntary home quarantine commenced ☐ Yes → Date / / ☐ No ☐ Not applicable

Public Health officer to perform active surveillance of possible case daily ☐ Yes → Date commenced / / ☐ No ☐ Not applicable

Case informed to notify Doctor or Hospital if symptoms worsen. ☐ Yes → Date / / ☐ No ☐ Not applicable

Other actions → specify

Education

Preventing transmission of MERS Coronavirus discussed ☐ Yes ☐ No

Was the case provided with educational material ☐ Yes → if yes, date sent/provided / / ☐ No ☐ Not applicable

Information sent to workplace / school / childcare/ institution ☐ Yes → if yes, date sent/provided / / ☐ No ☐ Not applicable

Privacy information requested by case ☐ Yes → if yes, date sent/provided / / ☐ No ☐ Not applicable

Directed to IDEAS website ☐ Yes → if yes, date sent/provided / / ☐ No ☐ Not applicable

Case summary

Investigation type
☐ Single case
☐ Contact*
☐ Cluster investigation
☐ Outbreak investigation*
* Name + PHESS ID

Source of infection identified
☐ Yes*
☐ No
☐ Not applicable
* Name + PHESS ID

Novel Coronavirus subtype

Other cases linked to this case
☐ Yes
☐ No
☐ Not applicable

Notifying doctor informed of our intent to contact case
☐ Yes
☐ No

Person interviewed
☐ Case
☐ Parent/guardian/carer
☐ General Practitioner
☐ Treating doctor
☐ Other, specify _____

PHESS ID | 3 | 2 | 0 | | | | | | | | | |

Interview attempts	Completed	Interviewer	Notes
/ /	☐ Yes ☐ No		
/ /	☐ Yes ☐ No		
/ /	☐ Yes ☐ No		
/ /	☐ Yes ☐ No		
/ /	☐ Yes ☐ No		

PHESS

Case closed on	Case closed by (initials)	Final classification	PHESS completed	PHESS completed by (initials)
/ /		☐ Confirmed ☐ Probable ☐ Rejected	/ /	

Signature

Name of interviewer (please print clearly)

Signature | Date / /

Investigation notes

5 Epidemiological study

Do symptoms predict COVID-19 infection? A case-control study, Australia, 2020

Table of Contents

5.1 Prologue

5.1.1 My role

During my second year at the Department of Health (DoH) I was a part of the national COVID-19 response team and undertook various projects related to the pandemic. For my epidemiological project, I conducted a case-control study to identify the symptom profile of COVID-19 by comparing and analysing reported symptom data between two data sources. Cases were people with COVID-19 who were notified to the National Notifiable Diseases Surveillance System (NNDSS). Controls were people who tested negative to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) from Commonwealth-funded General Practice Respiratory Clinics (GPRCs). I worked with the Office of Health Protection and Primary Care Division who are the data custodians of each of the data sets. I attended GPRCs data quality meetings to gain a better understanding of how the data is collected, and to identify potential issues with data quality and completeness. I was the lead investigator for the project and developed the proposal and methodology, prepared an ethics application, organised team meetings, cleaned, coded and analysed the data, and wrote and disseminated the results of the study.

5.1.2 Lessons learnt

This was my first time working with not only a large dataset, but also working with data from two different sources. It was a bit overwhelming at the start but nonetheless a very valuable project to undertake. I spent a lot of time developing my skills in Stata and learning different codes to clean, merge and analyse the data. There were many lessons learnt during this whole process. Firstly, I underestimated the time it would take to get approval and access to data, and to write up the Stata code. I got involved with the project in April and didn't get access to the data until July, and even then, had to wait another 3 weeks for the final extract to come through to ensure data completeness. Secondly, although I had written a straightforward data analysis plan prior to accessing the data, there were times where I got side tracked with suggestions and ideas on ways to analyse the data and other variables to consider. These were all great suggestions, but there were challenges with the short time frame and the potential for the project to go in many directions. It was important to bring the scope back on to what the main objectives for the study were and to agree on an achievable level of analysis that would still allow me to meet the MAE requirements for this chapter. Given that this was the largest project in my MAE and one that required the most time, I also felt a lot of pressure to produce detailed analysis in such a short time

frame, with different input and changing suggestions. I was able address this by reinstating the data analysis plan and project agenda, and focus on doing a good analysis, albeit simple, rather than a complicated but rushed analysis with many uncertainties. There were also issues with both data sets. Some of the symptoms were not systematically collected across both data sets, with symptom data not collected at all in NNDSS in July, when the majority of cases were reported in Victoria. This meant that the investigation team and I had to come to a decision on the study period and ultimately decided to exclude all cases in July in the study, even if it meant losing more than 50% of cases but having better symptom data completeness. Co-morbidity data were also poorly reported in NNDSS and excluded from the main analyses. I understood that this was the reality of data collection, particularly during a pandemic and sudden increase in case numbers concentrated in one state, which meant that the priority was shifted to collecting data that was manageable for contact tracing.

5.1.3 Outcomes and potential public health impact

Although there was no definitive symptom predictor of COVID-19 in this initial analysis, there were indications of several symptoms which were more commonly reported among cases than controls. These symptoms include: respiratory symptoms including pneumonia and acute respiratory distress syndrome (ARDS), diarrhoea, joint pain, diarrhoea, fever and headache. After adjusting for age and sex, shortness of breath, sore throat, runny nose and abdominal pain had an odds ratio of less than 1 among cases compared to controls. Among the five most commonly reported symptoms, four were reported by both cases and controls including cough, fever, sore throat and runny nose. This is consistent with results from previous studies that show similar clinical symptoms between COVID-19 positive cases and COVID-19 negative patients. The study also suggests differences in COVID-19 infection by gender and age group. These results are largely consistent with existing published literature. The study also shows extensive COVID-19 surveillance in Australia with almost 300,000 tests conducted nationwide at GPRCs alone from March to July. This study serves as a good starting point for further, more complex analyses and exploration of the data. It also reinforces the need for systematic collection of symptoms and other important variables to ensure data validity and completeness to be able to examine their potential association with COVID-19 infection.

5.1.4 Acknowledgements

Martyn Kirk, Stephanie Davis, Katie Glass, Liam Gage-Brown, Elise Bickley

5.2 Abstract

5.2.1 Background

The COVID-19 pandemic has had a major global impact with over 30 million cases and almost one million deaths reported globally. There are a broad spectrum of symptoms and those commonly reported include fever, cough and sore throat. I identify symptoms associated with COVID-19 infection in Australia, and examine the differences of symptoms in COVID-19 confirmed cases and people with acute respiratory illness who tested negative to SARS-CoV-2.

5.2.2 Methods

Cases were all notified cases of COVID-19 to the NNDSS between 22 January to 30 June 2020. Controls were people who presented to GPRCs and tested negative to SARS-CoV-2 from 21 March to 31 July 2020. Positive cases in GPRCs were excluded from the analysis. I used descriptive analysis to summarise the data. I performed univariable and multivariable logistic regression to calculate odds ratios for SARS-CoV-2 infection between cases and controls, and adjusted for age group and gender on symptoms of SARS-CoV-2 infection.

5.2.3 Results

During the study period there were 8,030 COVID-19 cases notified to NNDSS and 295,530 COVID-19 negative controls presenting at GPRCs. There were some differences in the demographic characteristics of cases and controls. The most common symptom among cases were cough (62%), fever (43%) and headache (39%). The most common symptom among controls were sore throat (65%), cough (60%) and runny nose (49%). There was a significant difference in the proportion of controls reporting all symptoms compared to cases due to the large sample size. The odds of respiratory symptoms including pneumonia and ARDS were much higher in cases compared to controls (aOR 7.13, CI 5.88–8.64). The odds of joint pain (aOR 3.83, CI 3.53–4.16), diarrhoea (aOR 3.45, CI 3.19–3.73), fever (aOR 2.50, CI 2.38–2.63) and headache (aOR 2.25, CI 2.13–2.38) were higher among cases than controls. The odds of reporting fever and cough were higher in cases and significantly increased by age group compared to controls when using the 0-9 age group as the reference category.

5.2.4 Conclusion

This study identified symptoms that were more commonly associated with cases including pneumonia and ARDS, joint pain, diarrhoea, fever and headache. Much of the findings from this study are consistent with existing literature. This study adds to the international understanding of the symptoms associated with COVID-19 and provides clinicians and the broader community information on the symptom profile of COVID-19 compared to other respiratory viruses. This can inform national guidelines, diagnosis, and early detection and isolation of cases. Further case-control studies examining symptom combinations and the association of co-morbidities and other risk factors will be useful in understanding the full symptom profile associated with COVID-19 infection.

5.3 Background

Coronaviruses are a large group of RNA viruses that mostly cause diseases in their particular host species.[1] Zoonotic transmission of coronaviruses from animals to humans pose a growing concern to public health with two major outbreaks occurring in the past: severe acute respiratory syndrome (SARS-CoV-1) in 2003,[2] and Middle Eastern respiratory syndrome (MERS-CoV) in 2012.[3] In late December 2019, a new human coronavirus that caused a severe respiratory known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was discovered and coined 2019 coronavirus (COVID-19).[4] The first case was associated with a seafood market in Wuhan, China, and was believed to have been acquired through exposure to live animals.[5] Genetic sequencing of the virus showed similarity to other bat coronaviruses, suggesting the virus originated in bats and was acquired through an intermediary animal host before transmission to humans occurred.[4] The outbreak spread quickly through other parts of China before cases emerged internationally, and subsequently declared a public health emergency of international concern (PHEIC) by the World Health Organization (WHO).[5] As of September 28, COVID-19 had spread to 235 countries worldwide with over 30 million cases and almost one million deaths reported globally.[7]

SARS-CoV-2 is transmitted primarily through respiratory droplets with possible aerosol transmission in enclosed spaces with elevated aerosol concentrations.[8] Various studies show the incubation period ranges from 2 to 14 days with evidence of asymptomatic transmission.[9,10] COVID-19 is characterised by a broad spectrum of presentations, most of which are mild. Current evidence shows cough and fever as the most prevalent symptoms associated with COVID-19 infection worldwide.[11] A meta-analysis of pooled prevalence of symptoms found that among symptomatic cases, approximately 53% reported cough and 69% reported fever.[12] Symptoms were also more common in adults compared to the paediatric population.[12] Published literature also indicate that most symptomatic cases present with common flu-like symptoms including sore throat, shortness of breath and runny nose.[13] Other common symptoms reported are enteric and musculoskeletal related including vomiting, diarrhoea, abdominal pain, muscle pain and joint pain.[13] Emerging literature has also found symptoms of loss of taste and smell commonly reported among cases.[14,15]

There is evidence of asymptomatic infection with studies showing that younger age is associated with asymptomatic and mild infections. Emerging research through seroprevalence and contact tracing studies has shown large clusters in school and household settings, suggesting children may also be drivers of transmission.[16-20]

Estimates of asymptomatic transmission vary from 18–81%, although consensus appears to be around 20–40% of all cases. .[21,22] Studies have shown that individuals with underlying health conditions are at a higher risk of severe outcomes including pneumonia and acute respiratory distress syndrome (ARDS)[23], which may result in acute respiratory failure requiring mechanical ventilation.[24] COVID-19 has also been linked to cardiovascular complications including arrhythmias, cardiomyopathy and heart failure.[24] The clinical features and severity experienced by COVID-19 patients also varies by age, with worse prognosis in older patients.[25] Studies have also shown symptoms may persist after recovery from COVID-19 with reports of one or more persisting symptoms most commonly including fatigue, shortness of breath, joint pain and chest pain.[26]

Identification of common symptoms associated with COVID-19 is essential in controlling disease transmission through case and contact management including early detection, self-isolation, and selecting patients for further diagnostic testing. This information may also be useful in providing clinical guidelines for assessment of potential cases based on early symptom presentations, particularly in resource-limited contexts with poor laboratory and testing capacity. Currently, the literature on the presence or absence of symptoms in ruling in or ruling out COVID-19 infection is inconclusive.[27] There is a need for high quality research using data collected on cases and those with acute respiratory illness to examine differences in clinical presentations that may be predictive of COVID-19 infection. This may provide further insight into COVID-19 infection by age, gender and other covariates.

National Notifiable Diseases Surveillance System (NNDSS)

The National Notifiable Diseases Surveillance System (NNDSS) was established in 1990 through the Communicable Diseases Network Australia (CDNA). The main function of CDNA is to provide national public health co-ordination and leadership, and to support best practice for the prevention and control of communicable diseases.[28] The Australian Government Department of Health (DoH) is responsible for co-ordinating the national surveillance of 65 communicable diseases or disease groups through the NNDSS and are the data custodians.[29] Notifications made to state and territory health authorities under the public health legislation in each jurisdiction are sent to NNDSS on a daily basis.[29] Data quality and completeness compiled in the NNDSS are influenced by various factors including notification practices from clinicians, diagnostic laboratories and hospitals, data fields collected across each jurisdiction, and completeness of data entry in each of the databases.[29]

COVID-19 was added to the national notifiable disease list (NNDL) shortly after the pandemic began. A CDNA working group developed a Series of National Guidelines (SoNG) for COVID-19 to provide nationally consistent advice and guidance to public health units in response to COVID-19.[30] State and territory health departments agreed on a list of core data fields for collection including date of onset, age, gender, symptoms and underlying conditions. Additional information collected varied between states. Data were collected for surveillance purposes across each state and territory with daily updates of a subset of the data required to be sent through to the national database. All notified cases of COVID-19 in Australia were reported to the NNDSS.

General Practice Respiratory Clinics (GPRCs)

As part of the Primary Care response to the COVID-19 pandemic, the Commonwealth government funded 149 General Practice Respiratory Clinics (GPRCs) around Australia. The first clinic was opened on 21 March. These clinics operated as COVID-19 testing centres to assess and treat any patients presenting with respiratory illness. GPRCs also organised COVID-19 testing where indicated by jurisdictional guidelines. GPRCs were designed to manage mild to moderate respiratory illness within the community, therefore diverting these illnesses away from other GP clinics and Emergency Departments (ED).[31]

Information from each patient encounter was entered into a bespoke app, specifically designed for use in the GPRCs, by the consulting clinician. The data collected included information on: demographic details, exposures, symptoms, COVID-19 test taken, and test status (positive/negative). Line listed data on patient encounters were made available to the Commonwealth and local Public Health Network (PHN) within 24-48 hours. Data on test results had a varying delay depending on timeliness of test results and was entered into the App by the clinic.

GPRCs data can be a useful source of surveillance data and has been incorporated into the national surveillance plan. Current uses of the data from this system include:

- Reporting purposes with summary of data provided to CDNA, individual clinics and jurisdictions
- Potential for research to be conducted at local, state and national levels using GPRCs data
- Identification of differences in levels of testing by geographic localities and changes in presentations over time

5.4 Aims and objectives

The aim of this study was to identify, describe and analyse differences in symptoms between confirmed COVID-19 cases and people with respiratory disease who tested negative to identify whether symptoms can predict COVID-19 infection. The study had the following objectives:

1. To describe and compare the symptom profile of COVID-19 cases and those with acute respiratory illness who have tested negative for COVID-19 in Australia
2. To examine the relationship between the symptom profile of COVID-19 cases and age group and gender

5.5 Methods

We conducted a case-control study to identify differences in symptom profiles and how they differed by age and sex. Variables collected in both the NNDSS and GPRCs databases included demographic data (patient ID, age, gender, state and indigenous status), and clinical data (specimen collection date, presenting symptoms, and underlying conditions and risk factors). Symptoms that were systematically collected for both NNDSS and GPRCs are presented below in Table 1.

Case definition

Cases included all notifications of COVID-19 made to the NNDSS in Australia from 22 January to 30 June 2020. Cases notified to NNDSS from 1 July 2020 onwards were excluded from the study due to incomplete symptom data. The below outlines the current case definition used for national surveillance of COVID-19 in Australia as of 23 August 2020.[30]

<u>Confirmed case</u>

A person who:

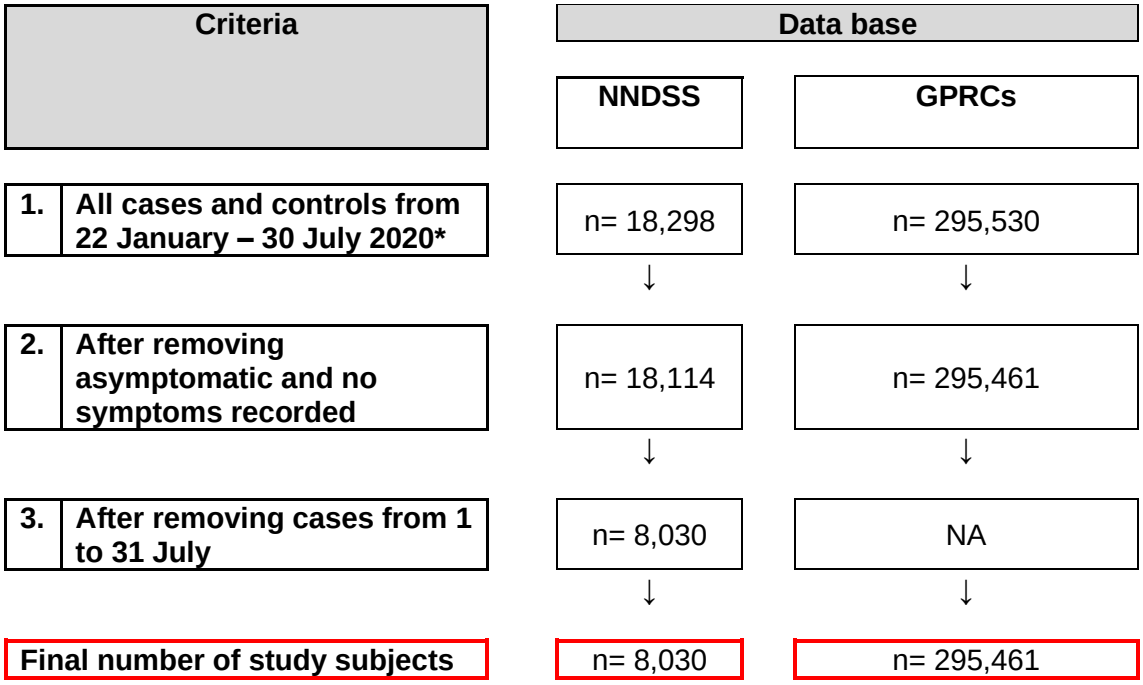
i. Tests positive to a validated specific SARS-CoV-2 nucleic acid test;
   OR
ii. Has the virus isolated in cell culture, with PCR confirmation use a validated method;
   OR

iii. Undergoes seroconversion to or has a significant rise in SARS-CoV-2 neutralising or IgG antibody level (e.g. four-fold or greater rise in titre). Antibody detection must be by a validated assay and included in an external quality assurance program.

Control definition and selection

Controls were persons who presented to GPRCs and tested negative to SARS-CoV-2 in Australia between 21 March and 31 July 2020. Before enhanced testing was approved on 24 April 2020, testing at GPRCs only included those with an epidemiological link, After the introduction of enhanced testing, anyone with respiratory symptoms were tested at GPRCs. For this study, I excluded patients at GPRCs if they had no test results (no test taken or results pending) where a COVID-19 result could not be confirmed. I considered patients with multiple presentations within 28 days as presentations for the same illness. Symptom data were captured if they were reported from any of these presentations. Patients who converted from negative to positive within this time frame were excluded from the analysis. Patients who attended GPRCs with <50% of completeness of symptoms recording were excluded from the study.

Figure 1. Selection criteria for cases and controls, January to July 2020, Australia



**Excludes GPRCs with <50% symptom completeness*

Table 1. Symptoms included in the analysis and indication of systematically collected symptoms from cases in NNDSS and patients at GPRCs

Symptoms	**Systematically collected**	
	NNDSS	GPRCs
Cough	✓	✓
Fever	✓	✓
Fatigue/tired		✓
Shortness of breath	✓	✓
Sore throat	✓	✓
Runny nose	✓	✓
Headache	✓	✓
Nausea/vomiting	✓	✓
Diarrhoea	✓	✓
Confusion	✓	✓
Respiratory/pneumonia/ARDS	✓	✓
Muscular pain	✓	✓
Joint pain	✓	✓
Chest pain	✓	✓
Abdominal pain	✓	✓
Ear pain		
Allergy like		
Sweats and chills		
Loss of smell		✓
Loss of taste		✓

The majority of symptoms across both NNDSS and GPRCs data were systematically collected. Pneumonia and ARDS are severe conditions associated respiratory illness but were reported under symptoms in this study. Ear pain, allergy like and sweats and chills symptoms were not systematically collected in either NNDSS or GPRCs data and were extracted from free-text fields. Fatigue/tired, loss of taste and smell were extracted from free-text fields in NNDSS. Loss of smell and taste were systematically collected in GPRCs data from May 2020 onwards.

5.6 Data analysis

I performed descriptive analysis to identify symptoms associated with cases and controls based on SARS-CoV-2 test result. The demographic characteristics of both cases and controls were presented in a frequency table with totals and percentages for count data, and median and range for numeric data. A chi-square test was performed to test for differences in proportions between cases and controls. I examined differences in presenting symptoms in cases based on local or overseas acquired infection, and the effect of age and gender on presenting symptoms between cases

and controls. I used univariable logistic regression to generate crude odds ratios for all symptoms. I developed a multivariable logistic regression to include only systematically reported symptoms, adjusting for age and gender. Data analysis was performed using StataSE 13.

5.7 Ethics

Ethics approval was obtained from the Australian National University (ANU) Human Research Ethics Committee (HREC) protocol: 2020/321. Permission to access NNDSS data was granted through the Office of Health Protection (OHP) and access to GPRCs data was granted through the Primary Care Division in the Australian Government Department of Health.

5.8 Results

The epidemic curve for COVID-19 cases notified to NNDSS showed two distinct peaks (Figure 2). The first peak occurred in March through to April peaking in mid to late March with the majority of cases overseas acquired. A smaller number of cases were reported over the following months with increasingly more locally acquired infections. The second peak of infections occurred in late June through to July with the majority being locally acquired. Since the first case was identified in early January, the cumulative total number of cases exceeded 18,000 by the end of July 2020.

GPRCs consultations for acute respiratory illness began in mid-March with an increase in consultations over the next few months through to July where there was a slight decrease (Figure 2). The number of GPRCs consultations peaked in late June to July, the same time where there was a second wave of COVID-19 with the majority of cases reported in Victoria.

Participants

There were a total of 8,030 COVID-19 cases notified to the NNDSS and 295,530 COVID-19 negative controls in GPRCs included in the analysis.

Age, gender and state

There were some differences observed in the distribution of demographic characteristics between cases and controls (Table 2). The median age of cases and

controls were similar (39 years and 36 years). There were more patients aged 0-19 years among those who tested negative at GPRCs. More cases were reported in the 20-29 year age group and for those aged 60 and older. The male to female ratio for COVID-19 cases in NNDSS was approximately 1:1, compared to controls where 59% (172,826/295,230) were female. The distribution of cases and controls were very similar by state.

Symptoms

Cough was the most common symptom reported among cases and second most common among controls (Table 2). Sore throat was the most common symptom reported among controls compared to cases. Almost half of all controls reported runny nose. Fever and respiratory illnesses including pneumonia and ARDS were more common in cases compared to controls. Muscular pain, joint pain, chest pain and abdominal pain were also more commonly reported among cases than controls. A higher proportion of controls reported an underlying condition and/or risk factor compared to cases. Less than 10% of all cases reported an underlying condition and/or risk factor. The most commonly reported underlying condition and/or risk factor among controls were asthma, hypertension, smoker, and high blood pressure.

Table 2. Characteristics of NNDSS cases (n=8,030), and GPRCs negative controls (n=295,530), January to July 2020, Australia

Characteristics		NNDSS		GPRC	
		n	**%**	**n**	**%**
Median age (range)		39 (0-101)		36 (0–109)	
Age group (years)	0-9	180	2%	38,639	13%
	10-19	316	4%	29,890	10%
	20-29	1,707	21%	43,606	15%
	30-39	1,343	17%	55,209	19%
	40-49	1,057	13%	43,536	15%
	50-59	1,224	15%	34,596	12%
	60-69	1,198	15%	27,867	10%
	70-79	757	9%	15,279	5%
	80-89	196	2%	4,190	1%
	90+	52	1%	430	0%
	Total	**8,030**		**293,242**	
Gender	Male	4,083	51%	122,153	41%
	Female	3,887	49%	172,826	59%
	Other	0	0%	251	0%
	Total	**7,970**		**295,230**	

Indigenous status	Aboriginal and Torres Strait Islander	63	1%	10,500	4%
	Non-Aboriginal and Torres Strait Islander	7,577	97%	252,107	85%
	Not stated	210	3%	32,536	11%
	Total		**7,850**		**295,143**
State	NSW	3,331	41%	123,142	42%
	VIC	2,287	28%	93,845	32%
	QLD	1,046	13%	42,900	15%
	SA	437	5%	16,507	6%
	WA	565	7%	6,865	2%
	ACT	107	1%	4,985	2%
	TAS	228	3%	5,513	2%
	NT	29	0%	1,773	1%
	Total		**8,030**		**295,530**
Symptoms	**Cough**	**4,966**	**62%**	**178455**	**60%**
	Fever	3,464	43%	57111	19%
	Headache	3,146	39%	54247	18%
	Sore throat	2,933	37%	193021	65%
	Runny nose	2,056	26%	146098	49%
	Muscular pain	1,643	20%	19209	7%
	Shortness of breath	1,612	20%	41930	14%
	Joint pain	1,266	16%	6319	2%
	Diarrhoea	1,235	15%	8165	3%
	Nausea/vomiting	909	11%	9859	3%
	Chest pain	422	5%	4500	2%
	Respiratory/pneumonia/ARDS	215	3%	553	0%
	Abdominal pain	194	2%	3913	1%
	Confusion	176	2%	2200	1%
	Sweats and chills	163	2%	906	0%
	Fatigue/tired	102	1%	119019	40%
	Allergy like	100	1%	4637	2%
	Loss of smell	77	1%	3605	1%
	Ear pain	24	0%	3015	1%
	Loss of taste	7	0%	3982	1%
	Total		**8,030**		**295,461**
Underlying conditions and risk factors	Cardiac disease	539	7%	10868	4%
	Diabetes	450	6%	11633	4%
	Obesity	227	3%	5778	2%
	Chronic respiratory condition	211	3%	4820	2%
	Hypertension	192	2%	29562	10%
	Immunosuppressive	179	2%	3132	1%
	Asthma	122	2%	36879	12%
	Neurological disorder	101	1%	1414	0%
	Renal disease	67	1%	1062	0%
	Liver disease	47	1%	753	0%
	Pregnant	47	1%	2772	1%
	High blood pressure	30	0%	26031	9%
	Smoker	26	0%	30949	10%
	Lung disease	19	0%	9402	3%
	Total		**8,030**		**295,530**

Figure 2. Number of COVID-19 notifications to NNDSS and consultations for acute respiratory illness, GPRCs, Australia, January to July 2020

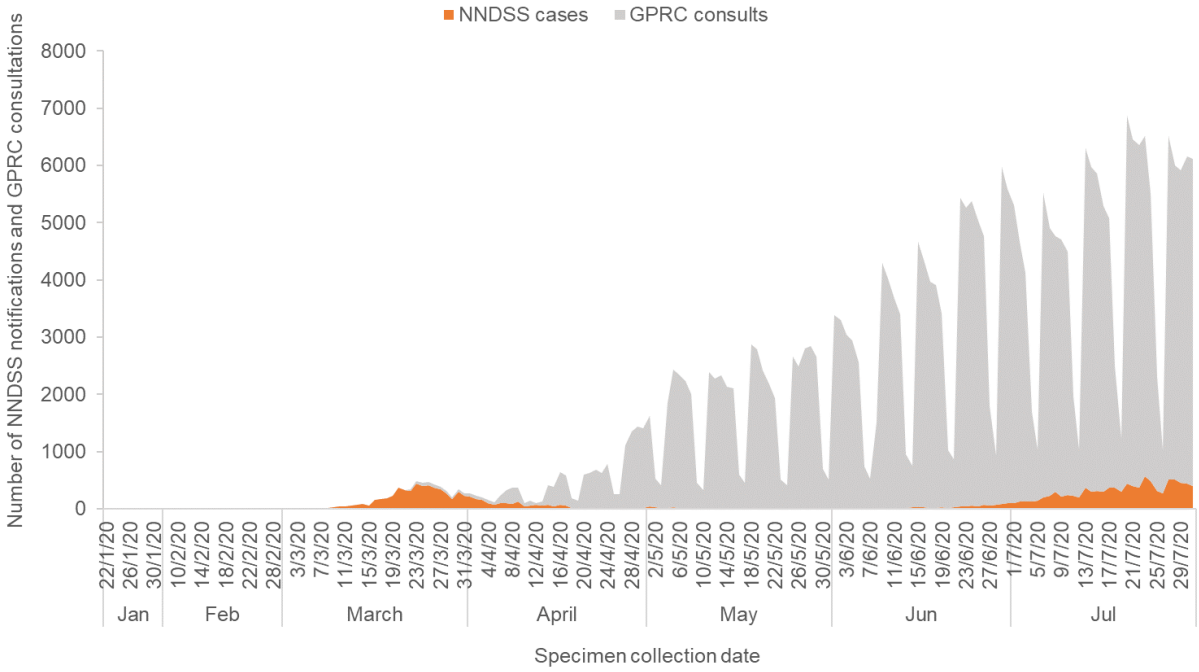
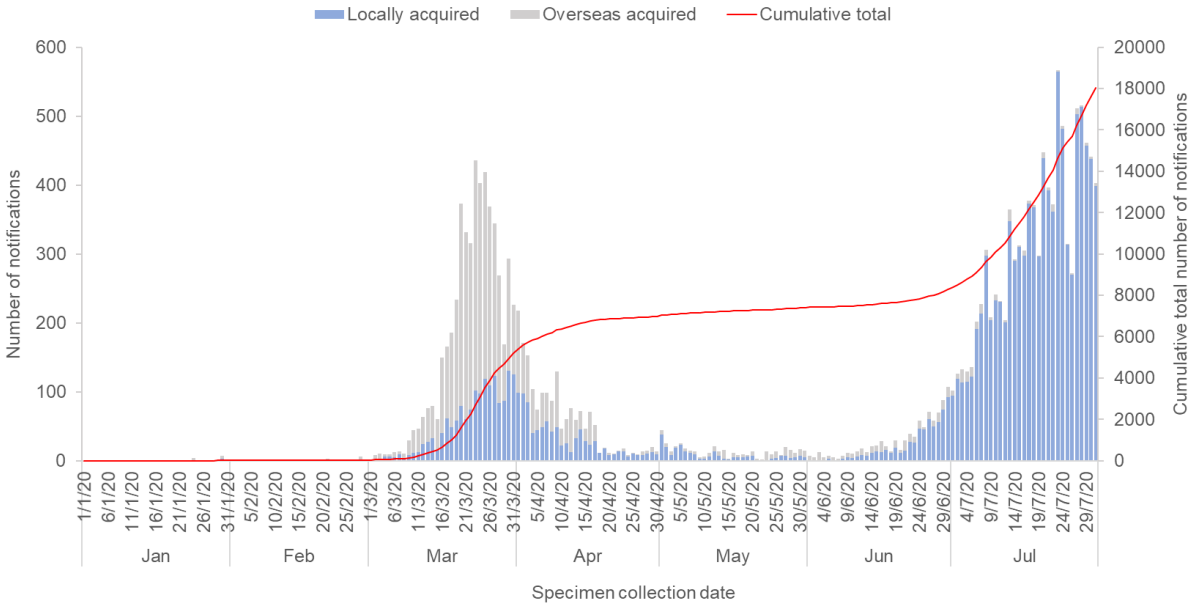
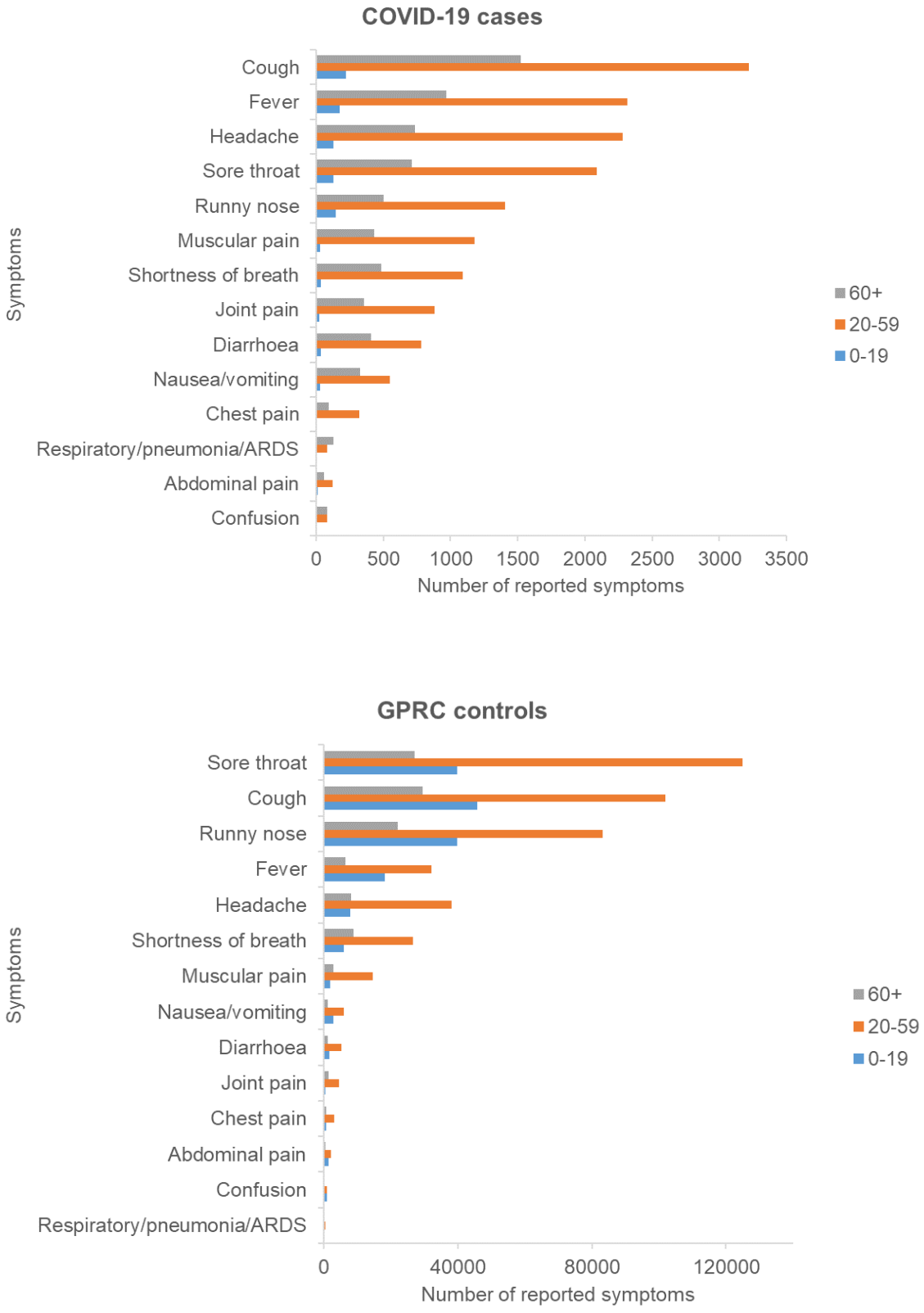


Figure 3. Number of COVID-19 cases notified to NNDSS, by place of acquisition, Australia, January to July, 2020.



There was no significant difference in presenting symptoms for cases based on local or overseas acquired COVID-19 infection (Appendix 1). Cough, fever, sore throat and runny nose were among the top 5 most commonly reported symptoms for cases and controls (Figure 4). The proportion of cases and controls who reported cough, fever, sore throat and runny nose differed significantly by age group. Generally, a higher proportion of cases in the 60+ age group reported more symptoms compared to controls in the same age group. A higher proportion of controls in the 0-19 age group reported more symptoms compared to cases in the same age group. The number of cases in the 60+ age group who reported cough, fever and headache was almost twice than controls. The number of controls in the 0-29 age group who reported sore throat, cough and runny nose was almost five times higher than among cases. Respiratory symptoms including pneumonia and ARDS were the least frequently reported symptoms among controls (0.2%) compared to 3% reported among NNDSS cases.

Figure 4. Systematically collected symptoms reported by COVID-19 cases and GPRCs controls, by age group, Australia, January to July 2020



Regression analysis

Table 3 shows the odds of respiratory symptoms including pneumonia and ARDS were much higher in cases compared to controls (aOR 7.13, CI 5.88–8.64). The odds of joint pain (aOR 3.83, CI 3.53–4.16), diarrhoea (aOR 3.45, CI 3.19–3.73), fever (aOR 2.50, CI 2.38–2.63) and headache (aOR 2.25, CI 2.13–2.38) were higher among cases than controls. Compared to controls, cases were less likely to report sore throat (aOR 0.26, CI 0.25–0.27), runny nose (aOR 0.35, CI 0.33–0.36), abdominal pain (aOR 0.37, CI 0.30–0.44) and shortness of breath (aOR 0.82, CI 0.77–0.88).

Males had a higher odds of being a COVID-19 positive case (aOR 1.48, CI 1.41–1.55). Odds ratios for COVID-19 infection generally increased with age. Those in the 80+ age group had a much higher odds of COVID-19 infection compared to controls when using the 0-9 age group as the reference category (aOR 10.64, CI 8.70–13.0). The odds of COVID-19 infection was lowest in the 10-19 age group (aOR 2.76, CI 2.29–3.33) and generally increased with age (Table 3).

The odds of reporting cough were slightly more common among cases compared to controls (aOR 1.06, CI 1.02 – 1.55) (Table 3). The odds of reporting cough increased slightly by age group for cases when compared to controls and using the 0-19 age group as the reference category (Appendix 2). The odds of reporting fever increased by age group and were highest among cases aged 60+ (OR 3.53, CI 3.20 – 3.90) when compared to controls and using the 0-19 age group as the reference category (Appendix 2). The odds of respiratory symptoms including pneumonia and ARDS, and diarrhoea also increased by age group and were higher among cases aged 60+ when compared to controls and using the 0-19 age group as the reference category (Appendix 2).

Table 3. Univariable and multivariable analysis of demographic features and symptoms for COVID-19 infection, Australia 2020*

Exposure variable		Cases (n=8,030)		Controls (n=295,461)		OR (95% CI)	P-value	aOR (95% CI)	P-value
		n	%	n	%				
Age group	0-9	180	2%	38,638	13%	Reference	-	-	-
	10-19	316	4%	29,888	10%	2.27 (1.89 - 2.73)	<0.001	2.76 (2.29 - 3.33)	<0.001
	20-39	3,050	38%	98,791	34%	6.63 (5.70 - 7.71)	<0.001	7.16 (6.14 - 8.36)	<0.001
	40-59	2,281	28%	78,115	27%	6.27 (5.38 - 7.30)	<0.001	5.92 (5.06 - 6.92)	<0.001
	60-79	1,955	24%	43,126	15%	9.73 (8.35 - 11.34)	<0.001	9.06 (7.74 - 10.59)	<0.001
	80+	248	3%	4,616	2%	11.53 (9.5 0-14.01)	<0.001	10.64 (8.70 - 13.0)	<0.001
Gender	Female	3,887	49%	172,782	59%	Reference	-	-	-
	Male	4,083	51%	122,129	41%	1.49 (1.42 - 1.55)	<0.001	1.48 (1.41 - 1.55)	<0.001
Symptoms	Cough	4,966	62%	178,455	60%	1.06 (1.02 - 1.11)	0.009	1.19 (1.13 - 1.25)	<0.001
	Fever	3,464	43%	57,111	19%	3.17 (3.03 - 3.31)	<0.001	2.50 (2.38 - 2.63)	<0.001
	Headache	3,146	39%	54,247	18%	2.86 (2.74 – 3.0)	<0.001	2.25 (2.13 - 2.38)	<0.001
	Sore throat	2,933	37%	193,021	65%	0.31 (0.29 - 0.32)	<0.001	0.26 (0.25 - 0.27)	<0.001
	Runny nose	2,056	26%	146,098	49%	0.36 (0.33 - 0.37)	<0.001	0.35 (0.33 - 0.36)	<0.001
	Muscular pain	1,643	20%	19,209	7%	3.7 (3.5 - 3.91)	<0.001	1.37 (1.27 - 1.47)	<0.001
	Shortness of breath	1,612	20%	41,930	14%	1.52 (1.43 - 1.61)	<0.001	0.82 (0.77 - 0.88)	<0.001
	Joint pain	1,266	16%	6,319	2%	8.56 (8.03 - 9.14)	<0.001	3.83 (3.53 - 4.16)	<0.001

	Diarrhoea	1,235	15%	8,165	3%	6.4 (6.0 - 6.82)	<0.001	3.45 (3.19 - 3.73)	<0.001
	Nausea/vomiting	909	11%	9,859	3%	3.7 (3.44 - 3.97)	<0.001	1.42 (1.30 - 1.55)	<0.001
	Chest pain	422	5%	4,500	2%	3.59 (3.24 - 3.97)	<0.001	1.90 (1.69 - 2.14)	<0.001
	Respiratory/pneumonia/ARDS	215	3%	553	0%	14.67 (12.51 - 17.2)	<0.001	7.13 (5.88 - 8.64)	<0.001
	Abdominal pain	194	2%	3,913	1%	1.84 (1.6 - 2.13)	<0.001	0.37 (0.30 - 0.44)	<0.001
	Confusion	176	2%	2,200	1%	2.99 (2.56 - 3.49)	<0.001	1.71 (1.40 - 2.09)	<0.001
	Sweats and chills	163	2%	906	0%	6.74 (5.63 - 7.97)	<0.001	-	-
	Fatigue/tired	102	1%	119,019	40%	0.02 (0.02 - 0.02)	<0.001	-	-
	Allergy like	100	1%	4,637	2%	0.79 (0.95 - 0.97)	0.021	-	-
	Loss of smell	77	1%	3,605	1%	0.78 (0.62 - 0.98)	0.035	-	-
	Ear pain	24	0%	3,015	1%	0.3 (0.19 - 0.43)	<0.001	-	-
	Loss of taste	7	0%	3,982	1%	0.06 (0.03 - 0.13)	<0.001	-	-

*Note: OR: unadjusted odds ratio, aOR: adjusted odds ratio, CI: confidence interval. *Missing data not included in the totals*

5.9 Discussion

This case-control study identified that people with COVID-19 were more likely to present with symptoms related to respiratory, systemic, gastrointestinal and musculoskeletal illness when compared to controls. Reporting of symptoms also varied by age between cases and controls.

Pneumonia and ARDS were more frequently reported among cases than controls, both of these conditions indicate a more severe illness and commonly require hospital admission and mechanical ventilation.[32-35] This study found that the odds of presenting with respiratory symptoms including pneumonia and ARDS were highest for people who tested positive for COVID-19, suggesting that severe respiratory illnesses were more commonly associated with COVID-19 infection. This finding is consistent with other published studies which show that the estimated incidence of ARDS from COVID-19 infection is between 5-10%.[36] Furthermore, studies have also found that COVID-19 patients with ARDS are more likely to have a pre-existing respiratory conditions as well as other co-morbidities such as obesity and hypertension.[37,38] However, this finding in our study could also be due to a difference in the severity of illness observed in cases notified to NNDSS as opposed to patients presenting to GPRCs, most of whom have mild illness.

In this study, gastrointestinal symptoms including diarrhoea were more commonly reported by cases. International literature is incongruent regarding this, a number of studies have increasingly recognised gastrointestinal symptoms with COVID-19 infection.[39] A case-control study found that among those who met the criteria for COVID-19 testing, people who presented with gastrointestinal symptoms including diarrhoea and nausea/vomiting were 70% more likely to test positive.[40] A recent prospective case-control study found that diarrhoea was commonly reported in both cases and controls, however, when combined with loss of taste/smell and fever, was 99% specific for COVID-19 infection.[41]

Cases in this study reported a higher rate of musculoskeletal symptoms including joint pain and muscle pain. This is consistent with emerging research which estimated the prevalence of these symptoms to range between 1-35% among COVID-19 patients.[42] There are also reports of musculoskeletal symptoms present from onset of symptoms through to more severe stages of illness.[43] Other studies have shown that approximately 20-50% of COVID-19 patients reported muscle pain.[44] Although these are not among the commonly reported symptoms associated with COVID-19 infection, recognising such symptoms may help in early diagnosis and preventing further transmission.

Cough and fever were the most prevalent symptoms reported by COVID-19 cases which is consistent with results from previous studies that show similar general symptoms most frequently reported.[45] Both cases and controls reported some of the same symptoms including cough, fever sore throat and runny nose. However, controls reported sore throat and runny nose at a higher rate. This could be due to how symptoms are reported based on what stage of illness patients are at. Controls may be more likely to report these symptoms which are commonly associated with cold and flu, as they generally had a milder illness when presenting to GPRCs. In contrast, cases who may be at a more severe stage of illness are less likely to report symptoms associated with a milder illness. This finding also varies in current literature with some studies showing a lower incidence of sore throat reported overall, and other studies showing that shortness of breath, sore throat and runny nose were more frequently reported among COVID-19 positive patients than in negative patients.[45-47]

Symptoms were found to vary by age group in this study. The analysis found that among cases, the proportion of overall reported symptoms were higher among those in the 20-59 and 60+ age group compared to cases aged 19 years and younger. Cases aged 60+ more commonly reported respiratory symptoms including pneumonia and ARDS. Among controls, a higher proportion of all symptoms were reported in those aged 19 years and younger. The odds of reporting respiratory symptoms including pneumonia and ARDS, fever and diarrhoea generally increased by age group.

Our study had some limitations, which may be due to the effects of confounding and bias. In particular, the way cases and controls were selected into the study may have resulted in some selection bias. Cases in NNDSS may have been more likely to be at a severe stage of illness and identified at hospital or ED, therefore less likely to present to a primary care setting. This may account for our observation of more severe respiratory symptoms including pneumonia and ARDS reported among cases compared to controls. In contrast, controls only included people who presented to a GP clinic with a mild illness for the purposes of being tested. This may have introduced selection bias towards those who were symptomatic, which may have resulted in an under-estimation of asymptomatic presentations among controls. It is also possible that there was information bias in the study due to differences in the timing of symptom assessment between cases and controls. Cases were more likely to be assessed at a later stage of their illness and symptoms data could be collected at multiple times. However, updated case information including specific days of symptom onset are not continually updated in NNDSS. Symptom assessment of controls however only occurred at the initial presentation and was captured at one point in time and potential hospitalisations would not have been captured. Improved data on severity could be

obtained by accessing data from the FluCAN surveillance system, which provides real-time sentinel hospital surveillance for acute respiratory illness requiring hospitalisation across various hospitals in Australia. The data collection form for symptoms at GPRC was based on what was collected in NNDSS which reduced differences in the types of information collected, but may have been impacted from differences in the data collection tool used. Furthemore, reported symptoms may have been impacted by recall bias where cases were more likely to recall symptoms than controls who may have had a mild illness and were less observant of their symptoms.

Due to limited resources, time constraints in the study and a large sample size, particularly in the control group, it was more feasible to conduct an unmatched case-control study. Potential confounders including age and gender were controlled for in the analysis of the study rather than the design to limit confounding bias.

The NNDSS is a dynamic dataset; the data presented in this study represents a point-in-time analysis of the symptoms of COVID-19 cases in Australia and may differ from other reports or other studies covering the same time period. Data on COVID-19 cases notified to NNDSS only includes a proportion of the total cases occurring in the community known as the notified fraction, which includes only those that sought health care, were tested and had a diagnosis made. It is likely that ascertainment of cases were high due to enhanced testing that was introduced in late April. Data for this study were collected for public health surveillance purposes and data completeness may vary by jurisdiction. There may be differences in the type of data that is collected, how it is collected, how definitions in NNDSS are interpreted by each jurisdiction, and what they report to NNDSS.

There were no symptoms data collected for NNDSS cases in July where the majority of cases identified during that time were largely from Victoria during the second wave of the outbreak. This is unlikely, as we do not suspect any major differences in presenting symptoms due to no changes in the testing criteria, seasonality or place of acquisition. Changes in testing may have had a greater impact on the proportion of people who presented with generalised cold and flu symptoms such as sore throat and runny nose.

Data quality may have affected the results and scope of this study where data completeness varied between cases and controls. Particularly in the NNDSS, symptoms including fatigue, loss of taste and loss of smell were not systematically collected, therefore we could not examine the true relationship between these symptoms and COVID-19 infection. There is increasing evidence of loss of taste and loss of smell symptoms associated with COVID-19 infection reported in studies in in Europe, the Middle East, Asia and the United States.[48-52] Systematic collection of these

symptoms could be useful in better understanding their association with COVID-19 infection in the Australian population. Furthermore, poor recording of data on co-morbidities in NNDSS meant that we were unable to explore these pre-existing conditions as potential confounders. Co-morbidities and risk factors including asthma and smoking may be potential confounders for presenting symptoms such as shortness of breath, sore throat and runny nose and COVID-19 infection. The co-morbidity data captured in this study was inconsistent between cases and controls and were largely incomplete in NNDSS. The overall prevalence of underlying conditions were much lower in this study compared to data published in AIHW reports. The estimated prevalence of hypertension and asthma in Australia is approximately 21% and 34% across all ages.[53] This figure is more than double the proportion of hypertension and asthma captured in this study. However, the proportion of smokers reported in this study (10%) is similar to the estimated prevalence of 11.6% among adults in Australia in 2019.[54]

There were multiple strengths in this study including the large sample size and largely consistent data that was collected for both cases and controls using the same reporting forms and data collection tools. Results from this study of symptoms by age group can be used to inform potential early diagnosis for clinicians to identify specific presenting symptoms that are more commonly reported by age. Broader implications from this study can also inform national guidelines and management and control measures including advice on self-isolation and testing to ensure early identification of cases to prevent further transmission.

5.10 Conclusion

The results from this large case-control study is consistent with existing literature on the symptoms most commonly associated with COVID-19 infection. A broad spectrum of symptom presentations were captured in this study and support the current knowledge on symptoms associated with respiratory, systemic, gastrointestinal and musculoskeletal illness. These included fever, cough, diarrhoea, pneumonia and ARDS, joint pain and muscle pain. Although cough is one of the most common presenting symptoms, it is not a strong descriptor of COVID-19 infection alone. This study adds to the international understanding of the symptoms associated with COVID-19 and provides public health units, clinicians and the broader community information on the symptom profile of COVID-19 compared to other respiratory viruses. This study identified some candidate symptoms that are worth exploring further by identifying symptom combinations that may be more predictive of COVID-19 infection. Other

similar studies have shown that combinations of symptoms are more specific in predicting COVID-19 infection and have identified symptom severity relating to pre-existing co-morbidities. Further research should aim to identify symptom constellations and examine whether they can provide a more definitive prediction of COVID-19 infection. Improvements in data collection to ensure completeness of fields for all symptoms and co-morbidities can enable additional analysis on other factors that may influence COVID-19 infection. Identification of common symptoms associated with COVID-19 can inform disease control efforts through case and contact management, early detection, self-isolation, and selection of patients for further diagnostic testing. The initial results from this study supports the current case definition and national guidelines for identification and detection of cases and contact tracing.

5.11 References

1. Shi Z & Hu Z. A review of studies on animal reservoirs of the SARS coronavirus. Virus Res. 2008 Apr (cited 2020 Aug 11). Available from: https://pubmed.ncbi.nlm.nih.gov/17451830/
2. Yang Y, Peng F, W Runsheng, Guan K, Jiang T, Xu G et al. The deadly coronaviruses: The 2003 SARS pandemic and the 2020 novel coronavirus epidemic in China. J Autoimmun. 2020 May (cited 2020 Aug 11). Available from: https://pubmed.ncbi.nlm.nih.gov/32143990/
3. Khan S, El Morabet R, Kahn RA, Bindajam A, Alqadhi S Alsubih M et al. Where we missed? Middle Eastern Respiratory Syndrome (MERS-CoV) epidemiology in Saudi Arabia; 2012-2019. Science Direct. 2019 Dec 10 (cited 2020 Aug 11). Available from: https://www.sciencedirect.com/science/article/pii/S0048969720348981
4. Wolfel R, Corman VM, Guggemos W, Selmaier M, Zange S, Muller MA et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020 May (cited 2020 Aug 11). Available from: https://www.nature.com/articles/s41586-020-2196-x
5. Wu P, Hao X, Lau EHY, Wong JY, Leung KSM, Wu JT et al. Real-time tentative assessment of the epidemiological characteristics of novel coronavirus infections in Wuhan, China, as at 22 January 2020. Euro Surveill. 2020 Jan (cited 2020 Aug 11). Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.3.2000044
6. World Health Organization. COVID-19 public health emergency of international concern (PHEIC) global research and innovation forum. WHO 2020. Available from: https://www.who.int/publications/m/item/covid-19-public-health-emergency-of-international-concern-(pheic)-global-research-and-innovation-forum
7. World Health Organization. Coronavirus disease (COVID-19) weekly epidemiological update and weekly operational update – 28 September 2020. WHO 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200928-weekly-epi-update.pdf?sfvrsn=9e354665_2
8. Cascella M, Rajnik M, Cuomo A, Dulebohn SC & Di Napoli R. Features, evaluation and treatment coronavirus (COVID-19). StatPearls [Internet], 2020

Jul 4 (cited 2020 Aug 12). Available from: https://www.ncbi.nlm.nih.gov/books/NBK554776/

9. Mizumoto K, Kagaya K, Zarebski A & Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-10) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill. 2020 Mar 12 (cited 2020 Aug 12). Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000180/
10. Huang L, Zhang X, Zhang X, Wei Z, Zhang L & Xu J et al. Rapid asymptomatic transmission of COVID-19 during the incubation period demonstrating strong infectivity in a cluster of youngsters aged 16-23 years outside Wuhan and characteristics of young patients with COVID-19: A prospective contact-tracing study. J Infect. 2020 Jun (cited 2020 Aug 12). Available from: https://www.sciencedirect.com/science/article/pii/S0163445320301171
11. Mair M, Singhavi H, Pai A, Singhavi J, Gandhi P, Conboy P et al. A meta-analysis of 67 studies with presenting symptoms & laboratory tests of COVID-19 patients. Laryngoscope. 2020 Oct 17. doi:10.1002/lary.29207.
12. Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL et al. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. PLoS One. 2020;15(6): e0234765. doi:10.1371/journal.pone.0234765
13. J et al. Clinical Characteristics of 3,062 COVID-19 Patients: A Meta-Analysis. J Med Virol. 2020 Apr 15 (cited 2020 Apr 15). Available from: https://pubmed.ncbi.nlm.nih.gov/32293716/?from_term=coronavirus&from_sort=date&from_page=5&from_pos=3
14. Mohindra R, Sainath KG, Kanta P, Singh MP, Goyal K, Lakshmi PVM et al. Anosmia and ageusia as presenting complaints of coronavirus disease (COVID-19) infection. J Family Med Prim Care. 2020 Aug 25;9(8):4406-4408. doi:10.4103/jfmpc.jfmpc_685_20
15. Salmon D, Bartier S, Hautefort C, Nguyen Y, Nevoux J & Hamel A et al. Self-reported loss of smell without nasal obstruction to identify COVID-19. The multicenter CORANOSMIA cohort study. J Infect. 2020 Jul 7 (cited 2020 Aug 13). Available from: https://www.sciencedirect.com/science/article/pii/S0163445320304631
16. Hyde Z. COVID-19, children and schools: overlooked and at risk. Med J Aust. 2020 Oct 25. doi:10.5694/mja2.50823

17. Pollan M, Perez-Gomez B, Pastor-Barriuso R, Oteo J, Hernana MA, Perez-Olmeda M et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet 2020 Aug 22;396(10250):535-544. doi:10.1016/S0140-6736(20)31483-5
18. Song R, Han B, Song M, Wang L, Conlon CP, Dong T et al. Clinical and epidemiological features of COVID-19 family clusters in Beijing, China. J Infect 2020 Aug;81(2):e26-e30. doi:10.1016/j.jinf.2020.04.018
19. Park YJ, Choe YJ, Park O, Park SY, Kim Y, Kim J et al. Contact tracing during coronavirus disease outbreak, South Korea, 2020. Emerg Infect Dis 2020 Oct;26(10):2465-2468. doi:10.3201/eid2610.201315.
20. 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 Jul;25(29):2001352. doi:10.2807/1560-7917.ES.2020.25.29.2001352.
21. Nikolai LA, Meyer CG, Kremsner PG & Velavan TP. Asymptomatic SARS Coronavirus 2 infection: Invisible yet invincible. Int J Infect Dis. 2020 Sep 3;100:112-116. doi:10.1016/j.ijid.2020.08.076.
22. Oran DP & Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: A narrative reiew. Ann Intern Med. 2020 Sep 1;173(5):362-367. doi:10.7326/M20-3012
23. Clark A, Jit M, Warren-Gash C, Guthrie B, Wang HHX & Mercer SW. Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020; a modelling study. Lancet. 2020 June 15;8(8):e1003-e1017. doi:10.1016/S2214-109X(20)30264-3
24. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J & Biondi-Zoccai G et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. J Am Coll Cardiol. 2020 May (cited 2020 Aug 13). Available from: https://pubmed.ncbi.nlm.nih.gov/32201335/
25. Liu Y, Mao B, Liang S, Yang J, Lu H & Chai Y et al. Association between age and clinical characteristics and outcomes of COVID-19. Euro Respir J. 2020 May (cited 2020 Aug 14). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7173682/
26. Carfi A, Bernabei R & Landi R. Persistent symptoms in patients after acute COVID-19. JAMA. 2020 Jul 9 (cited 2020 Sep 28). Available from: https://jamanetwork.com/journals/jama/article-abstract/2768351
27. Struyf T, Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Leeflang MMG et al. Signs and symptoms to determine if a patient presenting in primary care or

hospital outpatient settings has COVID-19 disease. Cochrane Database Sys Rev. 2020 Jul 7 (cited 2020 Sep 28). doi:10.1002/14651858.CD013665.

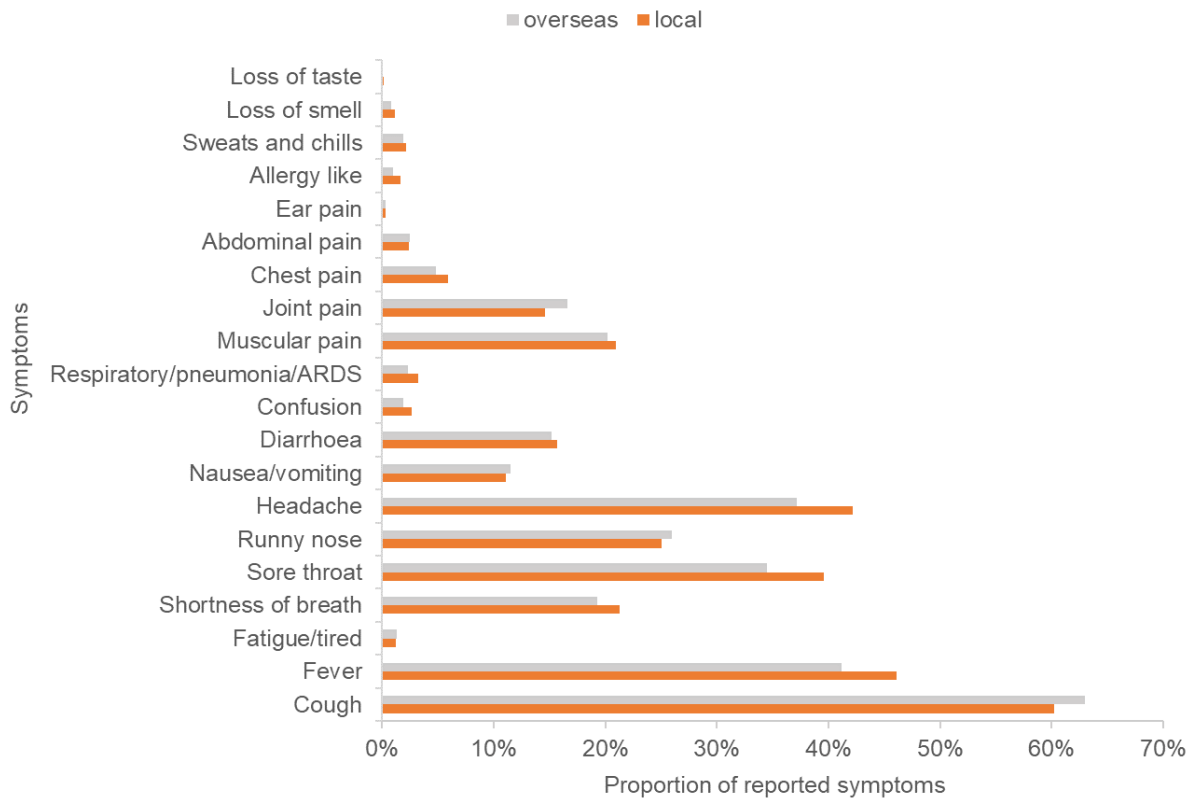
28. Australian Government Department of Health. Communicable Diseases Network Australia (CDNA) [Internet]. Canberra ACT: Australian Government Department of Health, 2020. Available from: https://www1.health.gov.au/internet/main/publishing.nsf/content/cda-cdna-cdna.htm
29. Australian Government Department of Health. National Notifiable Diseases Surveillance System (NNDSS) [Internet]. Canberra ACT: Australian Government Department of Health, 2020. Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-nndss-nndssintro.htm
30. Australian Government Department of Health. Series of National Guidelines (SoNGs) – Coronavirus Disease 2019 (COVID-19) [Internet]. Canberra ACT: Australian Government Department of Health, 2020. Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-novel-coronavirus.htm
31. The Royal Australian College of General Practitioners (RACGP). Guiding principles for the establishment and ongoing management of GP-led COVID-19 respiratory clinics [Internet]. RACGP, 2020. Available from: https://www.racgp.org.au/clinical-resources/covid-19-resources/other-health-issues/guiding-principles-for-covid19-respiratory-clinics
32. Fan E, Beitler JR, Brochard L, Calfee CS, Ferguson ND & Slutsky AS. COVID-19-associated acute respiratory distress syndrome: is a different approach to management warranted? Lancet. 2020 Jul 6;8(8):816-821. doi:10.1016/S2213-2600(20)30304-0
33. Dreher M, Kersten A, Bickenbach J, Balfanz P, Hartmann B, Cornelissen C et al. The characteristics of 50 hospitalized COVID-19 patients with and without ARDS. Dtsch Arzebl Int. 2020 Apr;117(16):271-278. doi:10.3238/arztebl.2020.0271
34. Tzotzos SJ, Fischer B, Fischer H & Zeitlinger M. Incidence of ARDS and outcomes in hospitalized patients with COVID-19: a global literature survey. Critical Care. 2020 Aug 21;24. doi:10.1186/s13054-020-03240-7
35. Ferrando C, Suarez-Sipmann F, Mellado-Artigas R, Hernandez M, Gea A, Arruti E, et al. Clinical features, ventilator management, and outcome of ARDS caused by COVID-19 are similar to other causes of ARDS. Intensive Care Med. 2020 Jul 29;1-12. doi:10.1007/s00134-020-06192-2

36. Hu Y, Sun J, Dai Z, Deng H, Li X, Huang Q et al. Prevalence and severity of corona virus disease 2019 (COVID-19): A systematic review and meta-analysis. J Clin Virol. 2020 Jun;127:104371. doi:10.1016/j.jcv.2020.104371.
37. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J et al. Clinical characteristics of coronavirus disease 2019 in China. NEJM. 2020 Feb 28;382:1708-1720. doi:10.1056/NEJMoa2002032
38. Zangrillo A, Beretta L, Scandroglio AM, Monti G, Fominskiy E, Colombo S et al. Characteristics, treatment, outcomes and cause of death of invasively ventilated patients with COVID-19 ARDS in Milan, Italy. Crit Care Resusc. 2020 Apr 23. Available from: https://pubmed.ncbi.nlm.nih.gov/32353223/
39. Mao R, Qui Y, He J, Tan J, Li X, Liang J et al. Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis. Lancet. 2020 Jul;5(7):667-678. doi:10.1016/S2468-1253(20)30126-6
40. Nobel YR, Phipps M, Zucker J, Lebwohl B, Wang TC, Sobieszczyk ME et al. Gastrointestinal symptoms and coronavirus disease 2019: A case-control study from the United States. Gastroenterology. 2020 Jul;159(1):373-375. doi:10.1053/j.gastro.2020.04.017.
41. Chen A, Agarwal A, Ravindran N, To C, Zhang T & Thuluvath PJ. Are Gastrointestinal Symptoms Specific for Coronavirus 2019 Infection? A Prospective Case-Control Study From the United States. Gastroenterology. 2020 Sep;159(3):1161-1163. doi:10.1053/j.gastro.2020.05.036.
42. Abdullahi A, Candan SA, Abba MA, Bello AH, Alshehri MA, Victor EA et al. Neurological and Musculoskeletal Features of COVID-19: A Systematic Review and Meta-Analysis. Front Neurol. 2020;11:687. doi:10.3389/fneur.2020.00687
43. Cipollaro L, Giordano L, Padulo J, Oliva F & Maffulli N. Musculoskeletal symptoms in SARS-CoV-2 (COVID-19) patients. J Orthop Surg Res. 2020 May 18;15(1):178. doi:10.1186/s13018-020-01702-w
44. Disser NP, De Micheli AJ, Schonk MM, Konnaris MA, Piacentini AN, Edon DL et al. Musculoskeletal consequences of COVID-19. J Bone Joint Surg Am. 2020 Jul 15;102(14):1197-1204. doi:10.2106/JBJS.20.00847
45. Mair M, Singhavi H, Pai A, Singhavi J, Gandhi P, Conboy P et al. A meta-analysis of 67 studies with presenting symptoms & laboratory tests of COVID-19 patients. Laryngoscope. 2020 Oct 17. doi:10.1002/lary.29207
46. George B, McGee J, Giangrasso E, Finkelstein S, Wu S & Glatt AE. What is the predictive value of a single nasopharyngeal SARS-CoV-2 PCR swab test in a patient with COVID-like symptoms and/or significant COVID-19 exposure? Open Forum Infect Dis. 2020 Sep 1;7(10):ofaa399. doi:10.1093/ofid/ofaa399.

47. Brendish NJ, Poole S, Naidu VV, Mansbridge CT, Norton N, Borca F et al. Clinical characteristics, symptoms and outcomes of 1054 adults presenting to hospital with suspected COVID-19: A comparison of patients with and without SARS-CoV-2 infection. J Infect. 2020 Sep 28;S0163-4453(20)30638-1. doi:10.1016/j.jinf.2020.09.033
48. Heidari F, Karimi E, Firouzifar M, Khamushian P, Ansari R & Mohammadi Ardehali M et al. Anosmia as a prominent symptom of COVID-19 infection. Rhinology. 2020 Jun 1 (cited 2020 Sep 29). doi:10.4193/Rhin20.140.
49. Karimi-Galougahi M, Raad N & Mikaniki N. Anosmia and the need for COVID-19 screening during the pandemic. Otolaryngol Head Neck Surg. 2020 Jul (cited 2020 Sep 29). doi:10.1177/0194599820925056.
50. Sedaghat AR, Gengler I & Speth MM. Olfactory dysfunction: A highly prevalent symptom of COVID-19 with public health significance. Otolaryngol Head Neck Surg. 2020 Jul (cited 2020 Sep 29). doi:10.1177/0194599820926464.
51. Gilani S, Roditi R & Naraghi M. COVID-19 and anosmia in Tehran, Iran. Med Hypotheses. 2020 Aug (cited 2020 Sep 30). doi:10.1016/j.mehy.2020.109757.
52. Meg X, Deng Y, Dai Z & Meng Z. COVID-19 and anosmia: A review based on up-to-date knowledge. Am J Otolaryngol. Sep-Oct 2020 (cited 2020 Sep 30). doi:10.1016/j.amjoto.2020.102581.
53. Australian Institute of Health and Welfare. Australian burden of disease study: impact and causes of illness and death in Australia 2015 [Internet]. Canberra ACT: AIHW, 2015. Available from: https://www.aihw.gov.au/reports/burden-of-disease/burden-disease-study-illness-death-2015/contents/table-of-contents
54. Australian Institute of Health and Welfare. Australia's Health: Determinants of health – tobacco smoking [Internet]. Canberra ACT: AIHW, 2020. Available from: https://www.aihw.gov.au/reports/australias-health/tobacco-smoking

5.12 Appendix

Appendix 1. Symptoms reported by COVID-19 cases notified to NNDSS, by local or overseas acquired, Australia, from January to June 2020



Appendix 2. Analysis of systematically reported symptoms for COVID-19 infection between cases and controls, by age group (0-19 years, 20-59 years and 60+ years), Australia 2020

Age group	**Cases (n=8,030)**		**Controls (n=293,174)**					
	n	**%**	**n**	**%**				
0-19 years	496	6%	68,526	23%				
Symptoms					**OR**	**95% CI**		**p-value**
Cough	225	45%	45717	67%	0.51	0.42	- 0.61	<0.001
Fever	4	1%	18258	27%	1.11	0.92	- 1.35	0.28
Shortness of breath	35	7%	6010	9%	0.86	0.60	- 1.24	0.43
Sore throat	132	27%	39663	58%	0.21	0.17	- 0.25	<0.001
Runny nose	146	29%	39664	58%	0.31	0.25	- 0.37	<0.001
Headache	131	26%	7776	11%	3.41	2.72	- 4.29	<0.001
Nausea/vomiting	30	6%	2710	4%	0.82	0.55	- 1.22	0.34
Diarrhoea	39	8%	1538	2%	2.83	1.98	- 4.04	<0.001
Confusion	8	2%	857	1%	1.20	0.58	- 2.47	0.63
Respiratory/pneumonia/ARDS	1	0%	79	0%	1.23	0.16	- 9.45	0.84
Muscular pain	32	6%	1749	3%	1.24	0.79	- 1.94	0.35
Joint pain	25	5%	498	1%	4.91	2.96	- 8.14	<0.001
Chest pain	9	2%	571	1%	1.80	0.88	- 3.68	0.11
Abdominal pain	11	2%	1358	2%	0.53	0.28	- 1.01	0.06

Age group	Cases (n=8,030)		Controls (n=293,174)					
	n	%	n	%				
20-59 years	5,331	66%	176,906	60%				
Symptoms					**OR**	**95% CI**		**p-value**
Cough	225	45%	45717	67%	0.51	0.42	0.61	<0.001
Runny nose	146	29%	39664	58%	0.31	0.25	0.37	<0.001
Sore throat	132	27%	39663	58%	0.21	0.17	0.25	<0.001
Headache	131	26%	7776	11%	3.41	2.72	4.29	<0.001
Diarrhoea	39	8%	1538	2%	2.83	1.98	4.04	<0.001
Shortness of breath	35	7%	6010	9%	0.86	0.6	1.24	0.43
Muscular pain	32	6%	1749	3%	1.24	0.79	1.94	0.35
Nausea/vomiting	30	6%	2710	4%	0.82	0.55	1.22	0.34
Joint pain	25	5%	498	1%	4.91	2.96	8.14	<0.001
Abdominal pain	11	2%	1358	2%	0.53	0.28	1.01	0.06
Chest pain	9	2%	571	1%	1.8	0.88	3.68	0.11
Confusion	8	2%	857	1%	1.2	0.58	2.47	0.63
Fever	4	1%	18258	27%	1.11	0.92	1.35	0.28
Respiratory/pneumonia/ARDS	1	0%	79	0%	1.23	0.16	9.45	0.84

Age group	Cases (n=8,030)		Controls (n=293,174)					
	n	%	n	%				
60+	2,203	27%	47,742	16%				
Symptoms					**OR**	**95% CI**		**p-value**
Cough	1525	69%	29433	62%	1.43	1.29	- 1.58	<0.001
Headache	736	33%	8032	17%	1.86	1.66	- 2.08	<0.001
Sore throat	712	32%	27024	57%	0.31	0.28	- 0.34	<0.001
Runny nose	503	23%	22111	46%	0.3	0.27	- 0.34	<0.001
Shortness of breath	483	22%	8901	19%	0.65	0.57	- 0.73	<0.001
Muscular pain	432	20%	2793	6%	1.46	1.26	- 1.7	<0.001
Diarrhoea	411	19%	1245	3%	4.18	3.59	- 4.86	<0.001
Joint pain	358	16%	1315	3%	3.09	2.62	- 3.65	<0.001
Nausea/vomiting	328	15%	1125	2%	2.4	2.03	- 2.84	<0.001
Respiratory/pneumonia/ARDS	129	6%	147	0%	11.79	8.77	- 15.86	<0.001
Chest pain	93	4%	748	2%	1.39	1.06	- 1.82	0.02
Confusion	82	4%	299	1%	3	2.13	- 4.23	<0.001
Abdominal pain	59	3%	497	1%	0.35	0.24	- 0.51	<0.001
Fever	23	1%	6315	13%	3.53	3.2	- 3.9	<0.001

6 Teaching Experience

Lessons from the field and group teaching session

6.1 Lessons from the field (LFF)

Lessons from the field (LFF)

Accessing data from the Australian Institute of Health and Welfare (AIHW) and data visualisation in Excel: Creating a bar graph with two Y-axis

Introduction

This Lesson from the field (LFF) aims to develop your skills in accessing publicly available datasets, and visualisation of data. The exercise is comprised of two parts:

1. Accessing, navigating and downloading data cubes from the Australian Institute of Health and Welfare (AIHW)
2. Using Excel graph function to create a bar graph with two Y-axis

Instructions are provided with a series of corresponding questions for your consideration.

Prepared by Malinda Vibol Chea, November 2019

Part 1: Accessing AIHW data cubes

Learning objectives

By the end of this session you should be able to:

1. Understand the purpose and use of the AIHW data cubes
2. Be able to find and access data cubes from the appropriate website/link
3. Once accessed, navigate through the data cubes
4. Download the dataset into the appropriate excel format

Background

The National Medical Stockpile (NMS) contains essential medicines stored around Australia. There are 11 anti-venoms listed in the NMS for envenomation from various insects, reptiles and marine animals. As part of the budgeting and procurement process, you have been asked to provide information on the hospitalisation trend from envenomation in Australia over the last 10 years*. This will provide insight on changes in the incidence of envenomation over time, and help inform policy and decision making on whether current procurement of current anti-venoms should be revised.

The AIHW is an independent statutory agency that produces authoritative and accessible information and statistics to inform and support better policy and service delivery decisions, leading to better health and wellbeing for all Australians.[1]

You decide to visit the AIHW website to find hospitalisation data for envenomation.

*in consideration of time for this exercise, we will only look at 2013-2015 data instead of the past 10 years.

Part 1.1 Instructions for accessing AIHW website and finding the data cubes

1. Follow the link to the AIHW website: https://www.aihw.gov.au/
2. Click on the first tab at the top of the page "**Reports & data**"
3. On the right hand side under *A-Z topics* click "**H**" and scroll down and open "**Hospitals**"
4. In the drop down tab on the left, click on "**Data sources**" and scroll down and open "**Principal diagnosis data cubes**" found under *Online hospital data*

Question 1. What is principal diagnosis? How can this information be useful for understanding hospitalisation trends for envenomation over time?

Part 1.2 Instructions for finding hospitalisation data for envenomation using the International Classification of Diseases (ICD-10-AM 8th edition)

1. Open the fourth data cube titled "**Separation statistics by principal diagnosis (ICD−10−AM 8th edition), Australia, 2013–14 to 2014–15**"
2. Go to chapter 19 **"Injury, poisoning and certain other consequences of external causes (S00–T98)**" and click the ↓ button to open the sub-chapter
3. Scroll down and find "**Toxic effects of substances chiefly nonmedicinal as to source (T51–T65)**" and click the **+** button to expand selection to view the 3 digit diagnosis
4. Scroll down and find "**T63 Toxic effect of contact with venomous animals**" and click the **+** button to view the 4 digit diagnosis

Question 2. How many 4 digit diagnosis categories are under "T63 Toxic effect of contact with venomous animals"?

Question 3. How many hospital separations were there for "T63.0 Snake venom" in 2013-2014? How many for "T63.4 Venom of other arthropods" in 2014-15?

Part 1.3 Instructions for exporting data to excel

1. Right click anywhere on the data table and select "**Export table …"**
2. Leave all fields as is and click "**OK"**
3. Open your downloaded file in excel

Your file should now look something like this:

Year	2013-14	2014-15
	Separations	Separations
4 digit diagnosis		
T63.0 Snake venom	246	229
T63.3 Venom of spider	607	644
T63.4 Venom of other arthropods	1,177	1,433
T63.5 Toxic effect of contact with fish	46	43
T63.6 Toxic effect of contact with other marine animals	98	127
T63.8 Toxic effect of contact with other venomous animals	51	52
T63.9 Toxic effect of contact with unspecified venomous animal	40	58

Feel free to customise the table as desired.

Part 2: Data visualisation using Stata graph builder and interpretation of incidence rates

Learning objectives

By the end of this session you should be able to:

1. Use the graph function to develop a bar graph with two Y-axis (count and incidence rate)
2. Understand the various options to customise the graph
3. Interpret the graph

Background

You have been asked to calculate yearly rates for envenomation by each category from the 4 Digit Diagnosis as identified in the previous exercise. You access the Australian Bureau of Statistics to find appropriate denominator data to calculate rates per 100,000 population. The Australian Demographic Statistics[2, 3] for population size are shown in the table below.

Australian Demographic Statistics – Estimated Resident Population (ERP)	
Year	**Population at end Dec qtr**
2013	23,319,400
2014	23,625,600

Part 2.1 Instructions for calculating rates for 2013 and 2014

1. Create two new columns and title them “2013 IR” and “2014 IR”
2. Calculate the incidence rates (IR) per 100,000 population for both years for each of the 4 Digit Diagnosis for using the population data in the table above as the denominator

Your table should now look something like this:

4 digit diagnosis	2013 separations	2014 separations	2013 IR	2014 IR
T63.0 Snake venom	246	229	1.05	0.97
T63.3 Venom of spider	607	644	2.60	2.73
T63.4 Venom of other arthropods	1177	1433	5.05	6.07
T63.5 Toxic effect of contact with fish	46	43	0.20	0.97
T63.6 Toxic effect of contact with other marine animals	98	127	0.42	0.54
T63.8 Toxic effect of contact with other venomous animals	51	52	0.22	0.22
T63.9 Toxic effect of contact with unspecified venomous animal	40	58	0.17	0.25

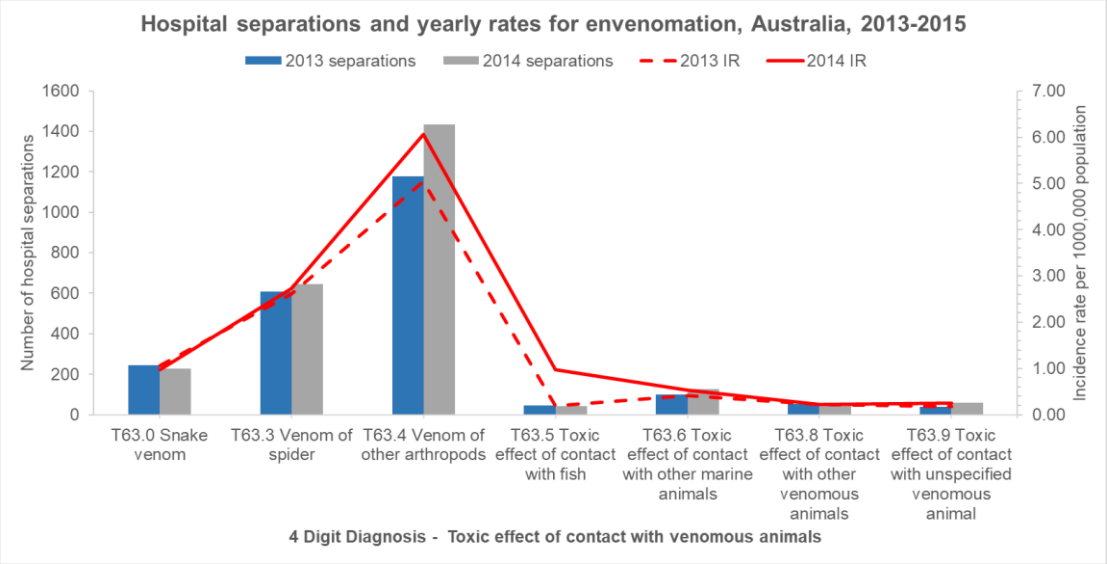
Q1. What category had the highest incidence rate per 100,000 population in both years?

Q2. In 2013, what was the incidence rate per 100,000 population for T63.5 Toxic effect of contact with fish?

Part 2.2 Instructions for creating bar graph with two Y-axis

1. Select all fields in the table and select the **"Insert"** tab up the top
2. Click "**Recommended charts**" and click the second tab "**All charts**"
3. In the drop down list on the left scroll to the bottom and select "**Combo**"
4. Select the second option up the top **"Clustered Column – Line on Secondary Axis**"
5. Click "**Ok**" and resize the graph to desired size
6. Add appropriate axis labels and tick marks, and customise the colour scheme and font size as desired

Your graph should now look something like this:



Q3. Interpret the overall trend of hospital separations for envenomation from 2013-2015.

Q4. How has the incident rate changed from 2013 to 2014? What might be some of the reasons for this?

6.2 Group teaching session to the 2020 MAE cohort

Background

As part of the MAE teaching competency we were required to develop a teaching session to deliver to the 2020 MAE cohort. My group (Alvaro and Kirsten) and I prepared a 30 minute presentation adapted from Kirsten's LFF on data linkage into a PowerPoint and delivered it via Zoom during course block 3 in August 2020. We incorporated interactive methods of participation through using live polls and a Q&A session into our presentation via Slido. We conducted an evaluation at the end of the session. The teaching session had the following learning objectives:

- Understand what is linked data and its use in epidemiological studies
- Describe dataset that can be used for linked data research
- Understand deterministic and probabilistic linkage
- Consider what we do after data linkage is complete

Delivery

The session was delivered via Zoom with a total of 16 attendees from the first year cohort. Kirsten introduced the session followed by a 2-minute video on data linkage and short introduction to deterministic and probabilistic linkage. I followed through with a series of questions based on the video and to gage the audience's existing knowledge on data linkage and to facilitate discussions. Alvaro finished up the session with a 10-minute presentation on algorithms and what we do after data linkage is complete. Our group ended with a Q&A session and a short evaluation poll delivered through Zoom.

Evaluation

The evaluation had a response rate of 88% (14/16) with an overall high rating for satisfaction of the session. 79% agreed that the session met its objectives, 57% found the content to be mostly useful, and 86% agreed that the presentation style was useful. More than half (57%) indicated that the deterministic and probabilistic linkage component was the most useful. The results are presented in Table 1 below.

Table 1. Evaluation of group teaching session

1. The teaching session met its objectives	
Strongly disagree	0% (0)
Disagree	0% (0)
Neither agree or disagree	7% (1)
Agree	79% (11)
Strongly agree	14% (2)
2. Was the content useful?	
Not at all	0% (0)
A little bit	7% (1)
Neutral	7% (1)
Mostly	57% (8)
Very	29% (4)
3. Which component of the session did you find most useful?	
Intro to data linkage video	0% (0)
Deterministic and probabilistic linkage	57% (8)
What we do after data linkage and algorithms	43% (6)
Quiz and poll questions	0% (0)
4. The complexity of the session was appropriate for the session duration	
No, too complex	0% (0)
No, too basic	14% (2)
It was adequate	29% (4)
Yes, mostly	21% (3)
Yes, definitely	36% (5)
5. The presentation style and PowerPoint was useful	
Strongly disagree	0% (0)
Disagree	0% (0)
Neither agree or disagree	0% (0)
Agree	86% (12)
Strongly agree	14% (2)

Reflection

The LFF enabled me to share a select skill that I learnt during my MAE with my peers. One of the early tasks at my placement was to access publicly available data sets to obtain incidence data on changes in envenomation in Australia over time and present a summary of this information. I wanted to do an LFF on this particular task as it was a

practical skill that could be shared with my peers. I also found the group teaching session to be a useful exercise for us to come together and prepare a presentation to share one of our learnings with the next cohort of students. It was also great to see reflected in the evaluation that the majority of the students agreed that the presentation met its objectives and found it useful.

7 Appendix

Appendix 1.

COVID-19, Australia: Epidemiology Report 7:

Reporting week ending 19:00 AEDT 14 March 2020

COVID-19 National Incident Room Surveillance Team

Summary

This is the seventh epidemiological report for coronavirus disease 2019 (COVID-19), reported in Australia as at 19:00 Australian Eastern Daylight Time [AEDT] 14 March 2020. It includes data on COVID-19 cases diagnosed in Australia, the international situation and a review of current evidence.

Keywords: SARS-CoV-2; novel coronavirus; 2019-nCoV; coronavirus disease 2019; COVID-19; acute respiratory disease; case definition; epidemiology; Australia

The following epidemiological data are subject to change both domestically and internationally due to the rapidly evolving situation. Australian cases are still under active investigation. While every effort has been made to standardise the investigation of cases nationally, there may be some differences between jurisdictions.

In Australia:

- 295 COVID-19 cases, including three deaths, were notified up until 19:00 AEDT 14 March 2020;
    - In the National Notifiable Diseases Surveillance System (NNDSS), 86% (n = 253) of all cases have a reported place of acquisition and 14% (n = 42) remain under investigation;
    - Of reported places of acquisition, 66% (n = 166) had a recent overseas travel history and 34% (n = 87) were locally acquired. 14% (n = 42) are pending investigation;
    - Of reported recent overseas travel history:
        - 22% (n = 36) have a direct link to USA;
        - 11% (n = 18) have a direct link to Italy;
        - 9% (n = 15) have a direct link to Iran;
        - 8% (n = 13) have a direct link to the UK;
        - 8% (n = 13) have a direct to China;
        - 6% (n = 10) are associated with the 'Diamond Princess' cruise ship passengers repatriated from Japan;
        - 37% (n = 61) have a recent travel history to other countries;
- Of the three reported deaths, one was associated with the 'Diamond Princess' cruise ship, and two were part of the same aged care facility cluster; and
- Since the last report, AHPPC have provided further recommendations on public events, travel restrictions, work restrictions for health and aged care workers, and public gatherings and testing.

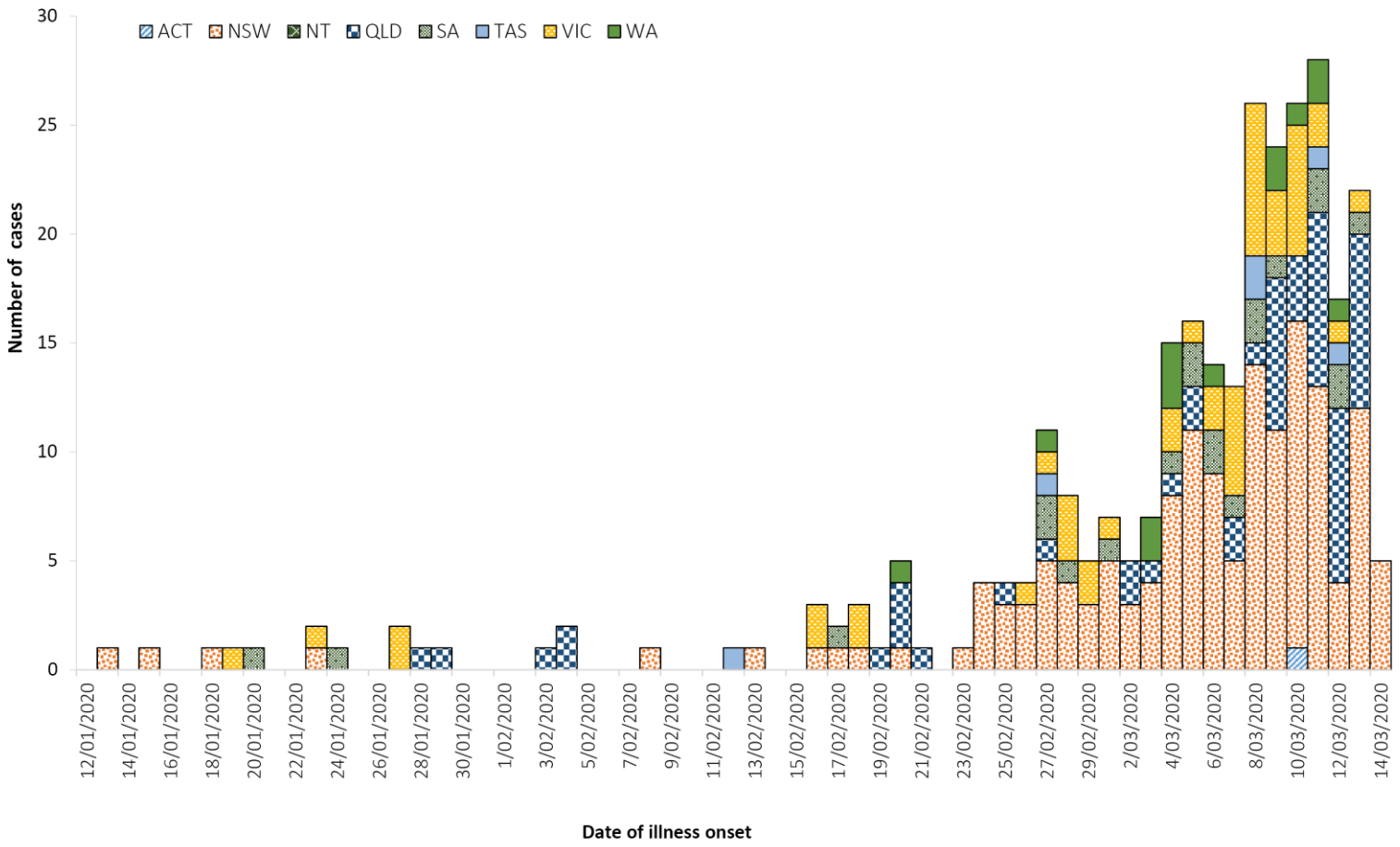
Internationally:

- 142,539 infections have been confirmed globally, with 5,393 deaths;
- The majority of confirmed infections (57%; n = 81,021) and deaths (59%; n = 3,194) have been reported in mainland China;
- Outside of mainland China, cases (n = 61,518) have been reported in 134 countries, territories and areas, with approximately 60% of those cases reported from three countries: Italy, the Islamic Republic of Iran and Republic of Korea;
- Outside of mainland China, 2,199 deaths were reported by 35 countries, territories and areas; and
- The number of daily new cases reported in mainland China has continued to decrease as cases increase in other countries, territories and areas globally.

Domestic cases

There were 295 confirmed cases, including three deaths, reported in Australia as at 19:00 AEDT 14 March 2020 (Table 1). Of the 295 confirmed cases, 51.5% (n = 152) were reported in NSW, 18.6% (n = 55) from Qld, 15.6% (n = 46) from Vic, 7.1% (n = 21) from SA, 4.7% (n = 14) from WA, 2% (n = 6) from Tas, and 0.3% (n = 1) from ACT (Figure 1).

Figure 1: Confirmed cases of COVID-19 infection by date of illness onset, Australia, 2020 (n = 295)[a,b]



a Diagnosis date used for eight cases where date of illness onset is unavailable.

b Cases associated with the Diamond Princess repatriation are included with their respective jurisdictions.

Table 1: Cumulative notified cases of confirmed COVID-19 by jurisdiction, Australia, 2020 (n = 295)

Jurisdiction[a]	This week[b] (19:00 AEDT 7 March to 14 March 2020) No. of new cases	Total cases[b] (to 19:00 AEDT 14 March 2020)
NSW	74	152
Vic	20	46
Qld	35	55
WA	6	14
SA	8	21
Tas	4	6
NT	0	0
ACT	1	1
Total cases	**148**	**295**

a NSW = New South Wales, Vic = Victoria, Qld = Queensland, WA = Western Australia, SA = South Australia, Tas = Tasmania, NT = Northern Territory, ACT = Australian Capital Territory.

b Case totals for this report, and ongoing, use data in the NNDSS to ensure systematic management of information. There may be differences in case numbers from last week due to changes in reporting methods for this report and future reports.

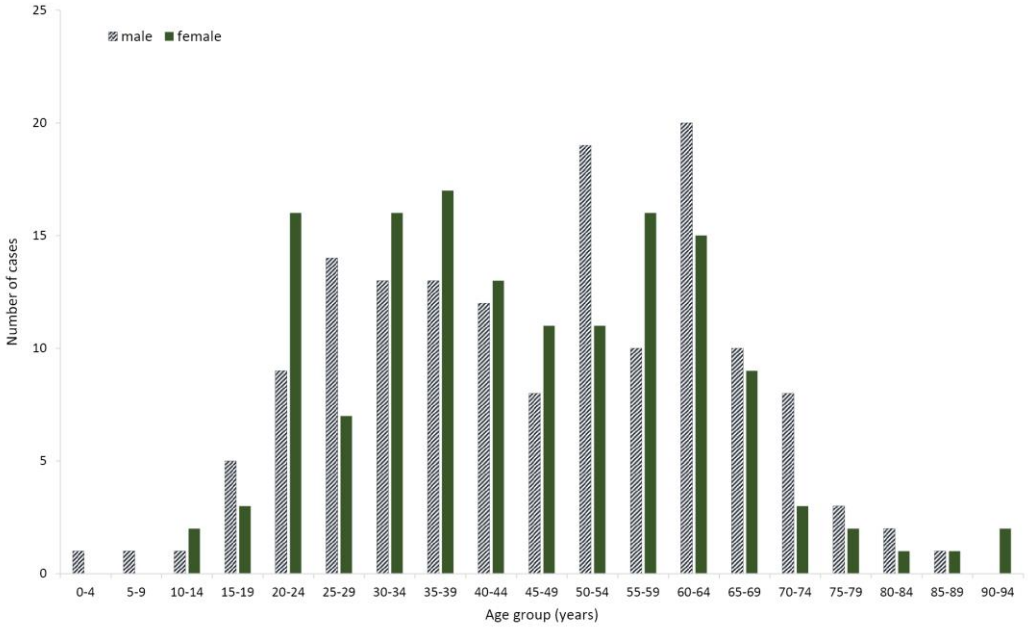
Of the 295 confirmed cases reported in the National Notifiable Diseases Surveillance System (NNDSS), 86% (n = 253) reported a place of acquisition and 14% (n = 42) remain under investigation. Of reported place of acquisition, 66% (n = 166) had a recent travel history and 34% (n = 87) were locally acquired. Of cases that reported recent travel history, 22% (n = 36) have a direct link to USA, 11% (n = 18) have a direct link to Italy, 9% (n = 15) have a direct link to Iran, 8% (n = 13) have a direct link to the UK, 8% (n = 13) have a direct link to China, 6% (n = 10) were passengers on the 'Diamond Princess' cruise ship repatriated from Japan, and 37% (n = 61) have a recent travel history to other countries.

Of the 34% (n = 87) of cases that were locally acquired, 75% (n = 65) were from NSW, 9% (n = 8) from Qld, 9% (n = 8) from SA, 2% (n = 2) from WA, 2% (n = 2) from Vic, 1% (n = 1) from ACT and 1% (n = 1) from Tas.

There were three reported deaths as of 14 March 2020, one associated with the 'Diamond Princess' cruise ship, and two who were part of the same aged care facility cluster in NSW.

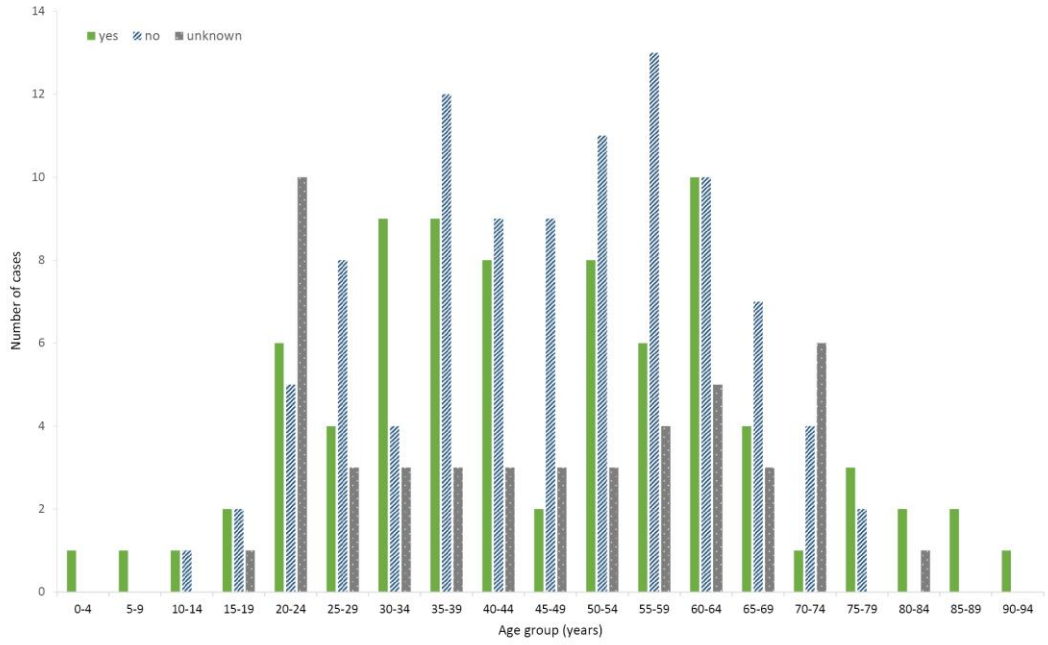
The median age of all 295 reported Australian cases was 47 years (range 0–94 years), with the highest proportion of cases aged 50–59 and 60–69 years (Figure 2). The male-to-female ratio was approximately 1:1. All three cases that were reported to have died were aged over 70 years.

Figure 2: Age distribution of COVID-19 cases, by sex, Australia, 2020 (n = 295)



Of the 295 confirmed cases, 76% (n = 225) had hospitalisation data reported (Figure 3). Of those cases, 36% (n = 80) were hospitalised, 43% (n = 97) were not hospitalised, and hospitalisation status for 21% (n = 48) was unknown. The 60–64 age group reported the highest proportion of hospitalisation at 13% (n = 10), followed by the 30–34 and 35–39 age groups both reporting 11% (n = 9), and the 40–44 and 50–54 age groups both reporting 10% (n = 8).

Figure 3: Age distribution of hospitalisation status of COVID-19 cases, Australia, 2020 (n = 225)[a]



a Hospitalisation data was missing for 26% (n = 70) of all cases

Of the 295 confirmed cases, 53% (n = 156) reported symptoms (Table 2). A total of fifteen symptoms were reported with fever being the most commonly reported by 69% of cases (n = 108). Fifty-four percent (n = 84) reported cough, 46% (n = 72) reported sore throat, 35% (n = 55) reported shortness of breath, and 31% (n = 48) reported diarrhoea. Only 1% of all cases reported either joint pain, pneumonia or acute respiratory disease (ARD).

Table 2: COVID-19 symptoms in confirmed cases in Australia, 2020 (n = 156)

Symptom	n	%
Fever	108	69%
Cough	84	54%
Sore throat	72	46%
Runny nose	62	40%
Shortness of breath	55	35%
Diarrhoea	48	31%
Nausea/vomiting	34	22%
Headache	31	20%
Irritability/confusion	27	17%
Muscular pain	22	14%
Chest pain	9	6%
Abdominal pain	6	4%
Joint pain	1	1%
Pneumonia	1	1%
Acute respiratory disease (ARD)	1	1%

Of the 295 confirmed cases, 14% (n = 42) did not report place of acquisition and 2% (n = 5) reported overseas acquisition but with country unknown. Of the 248 cases with reported place of acquisition and country level data, 65% (n = 161) were overseas acquired. Table 3 shows the most common places of acquisition for returned travellers were from countries in the European Region (n = 54), Region of the Americas (n = 39) and Western Pacific Region (n = 33). No place of acquisition was reported from the African Region. 4% of cases were acquired from the 'Diamond Princess' cruise ship under international conveyance.

Eighty-seven cases in Australia (35%) were locally acquired.

Table 3: Place of acquisition of confirmed COVID-19 cases in Australia, by WHO regions, international conveyance, and local acquisition, 2020 (n = 248)[a]

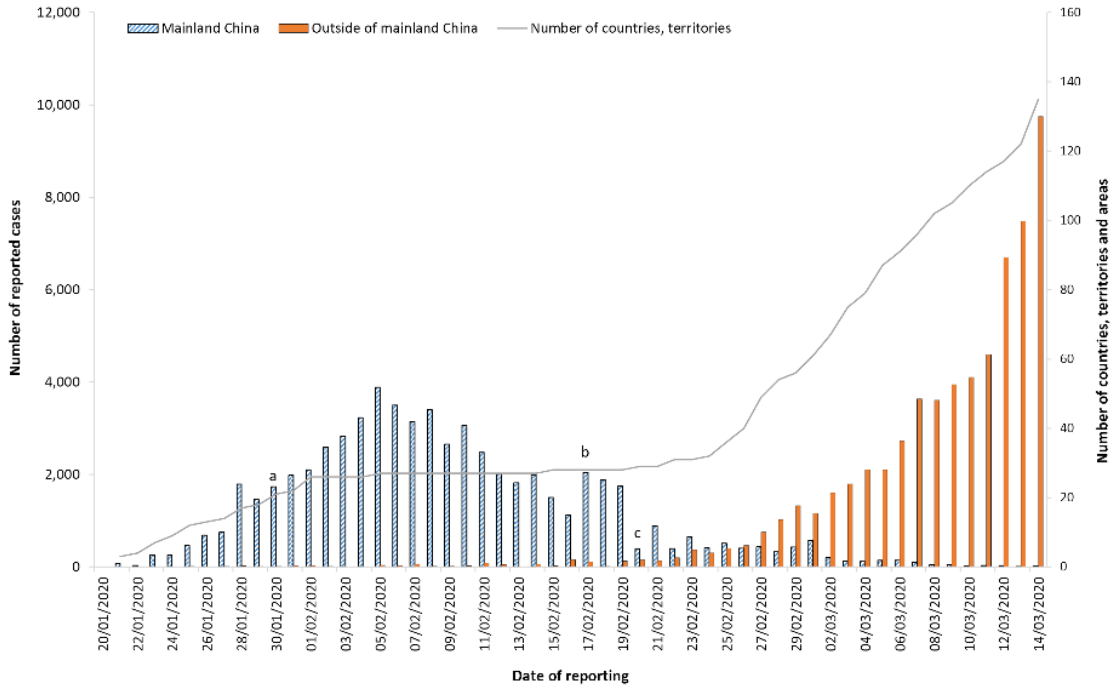
WHO regions	%	n
European Region (EURO)	22%	54
Region of the Americas (PAHO)	16%	39
Western Pacific Region (WPRO)	13%	33
Eastern Mediterranean Region (EMRO)	6%	16
South-East Asia Region (SEARO)	4%	9
International conveyance	4%	10
African Region (AFRO)	0%	0
Locally acquired	35%	87
Total	**100%**	**248**

a Five cases that reported overseas travel to an unknown country are included as under investigation.

International cases

As at 19:00 AEDT 14 March 2020, the number of confirmed COVID-19 cases reported to the World Health Organization (WHO) was 142,539 globally.[1] The proportion of total cases reported from mainland China has continued to decrease, from 79% on 7 March 2020 to 57% (n = 81,021) on 14 March 2020.[1,2] On 26 February 2020, the number of new cases reported outside of mainland China (n = 459) exceeded the number reported from mainland China (n = 412) for the first time and this trend has continued to date (Figure 4). The total number of confirmed COVID-19 cases reported by 134 countries, territories and areas outside of mainland China in the current reporting week has increased almost threefold (n = 61,518) compared to the preceding week (n = 21,110).[1,3] Italy reported 29% (n = 17,660) of all cases outside of mainland China; the Islamic Republic of Iran reported 18% (n = 11,364); the Republic of Korea reported 13% (n = 8,086) and Spain reported 7% (n = 4,231). Thirty-eight countries, territories and areas reported cases of COVID-19 for the first time in the past seven days. Of all the countries, territories and areas outside of mainland China with known transmission classification (n = 134), fifty-eight percent (n = 78) have reported local transmission of COVID-19.

Figure 4. Cases of COVID-19 reported to WHO; and number of countries, territories and areas from 21 January to 14 March 2020[1]



a WHO declares the outbreak of COVID-19 a Public Health Emergency of International Concern (30/01/2020)

b WHO start reporting both laboratory confirmed and clinically diagnosed cases from Hubei Province (17/02/2020)

c Hubei Province cease reporting clinically diagnosed cases (20/02/2020)

Globally, 5,393 deaths have been reported, with 57% (n = 3,075) reported from Hubei Province, China and 119 deaths reported from elsewhere within mainland China. The remaining 2,199 deaths were reported by 35 countries, territories and areas outside of mainland China.[1]

The current estimates on epidemiological parameters including severity, transmissibility and incubation period are uncertain. Estimates are likely to change as more information becomes available.

Country in focus: Italy

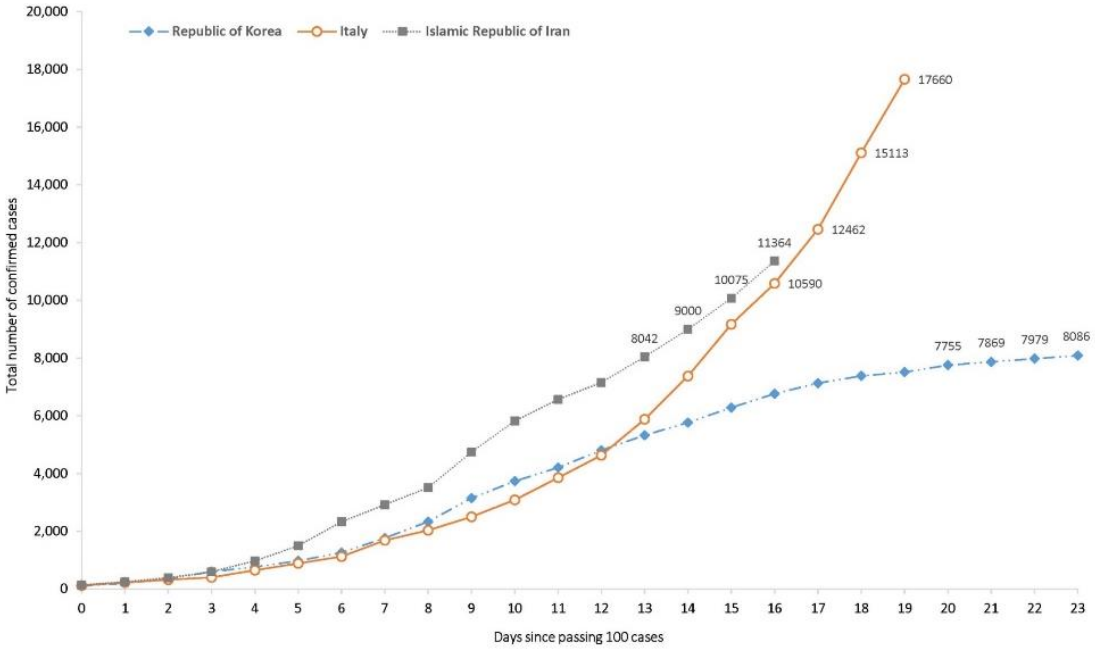
Data on confirmed cases of COVID-19 in Italy have not been made publicly available. The following is therefore a brief summary based on information obtained from WHO situation reports and the Italian Ministry of Health.

Italy reported its first two confirmed cases of COVID-19 on 31 January 2020.[4] Cases increased rapidly with 6 new cases reported on 22 February 2020 up to 17,660 cases on 14 March 2020. Reported deaths increased more than sixfold (n = 197) on 7 March to 1268 on 14 March 2020.[1,2] Among the cases reported as at 14 March 2020, 51% (n = 9,059) were reported in Lombardia, 13% (n = 2,349) in Emilia Romagna and 10% (n = 1,775) in Veneto.[5] Italy is now the epicentre outside of mainland China with the most rapid growth of COVID-19 cases, surpassing the Republic of Korea and the Islamic Republic of Iran (Figure 5).

Based on confirmed cases up to 14 March 2020, the case fatality rate (CFR) for Italy has been calculated at 7.8%. As the outbreak continues, the confirmed CFR may change. The current calculated CFR does not include the number of cases with mild infections that may be missed from current surveillance, nor does it account for the recently confirmed cases that may subsequently develop severe disease and die.

On 9 March 2020, Italy became the first European country to place a nationwide travel ban from all travel unless certified as justified on professional or health grounds.[6] The nationwide restrictions will be in effect until 3 April 2020. On 11 March 2020, the Italian Prime Minister imposed new restrictions by closing non-essential commercial activities in the country, with the exception of basic necessities and pharmacies. The new restrictions will be valid for two weeks.[7]

Figure 5: Number of COVID-19 cases by country and days since passing 100 cases, up to 14 March 2020



Transmission

Human-to-human transmission of SARS-CoV-2 is via droplets and fomites from an infected person to a close contact.[8] A study of cases and their close contacts in China supports this. Household contacts and those who travelled with a confirmed COVID-19 case were strongly associated with an increased risk of infection.[9] The study also examined the average time from symptom onset to disease confirmation among cases who were identified through symptom-based surveillance (i.e. symptomatic screening at airports, community fever monitoring and testing of hospital patients) and contact-based surveillance (i.e. monitoring and testing of close contacts of confirmed COVID-19 cases). Compared to cases identified through symptom-based surveillance, cases identified through contact-based surveillance were associated with a 2.3 day decrease from symptom onset to disease confirmation, and a 1.9 day decrease from symptom onset to isolation. Based on modelling, researchers have found that effective contact tracing increases the probability of control.[9] A virological analysis of nine hospitalised cases found proof of active virus replication in upper respiratory tract tissues, with pharyngeal virus shedding very high during the first week of symptoms.[10] COVID-19 can often present as a common cold-like illness where the virus is shed for a prolonged time after symptoms end, including in stools.[10] This may have implications for current case definitions and re-evaluation of the prospects of outbreak containment.[10]

Current evidence does not support airborne or faecal-oral spread as major factors in transmission.[8]

Incubation period

Estimates of median incubation period, based on seven published studies, are 5 to 6 days (ranging from 0 to 14 days).[11] Patients with long incubation periods do occasionally occur and have been reported, however medical experts have described these patients as 'outliers' who should be studied further and do not represent a significant shift in thinking about the virus.[11]

Clinical features

Ongoing evidence, including a recently published meta-analysis, supports previous research that COVID-19 presents as mild illness in the majority of cases with fever and cough being the most commonly reported symptoms. Severe or fatal outcomes tend to occur in the elderly or those with comorbid conditions.[8,12] Some COVID-19 patients show neurological signs such as headache, nausea and vomiting. A study identified increasing evidence that coronaviruses are not always confined to the respiratory tract and may also invade the central nervous system inducing neurological symptoms.[13] As such, it is likely that the potential invasion of SARS-CoV2 to the central nervous system is partially responsible for the acute respiratory failure of COVID-19 patients.[13] Examination of cases and their close contacts in China found a positive association between age and time from symptom onset to recovery. Median time to recovery was estimated to be 27 days in 20–29 year olds, 32 days in 50–59 year olds, and 36 days in those aged over 70 years. The study also found an association between clinical severity and time from symptom onset to time to recovery. Compared to people with mild disease, those with moderate and severe disease were associated with a 19% and 58% increase in time to recovery, respectively.[9] A retrospective cohort study looking at risk factors for mortality among

patients with COVID-19 who have experienced a definite outcome found an increase in the odds of in-hospital death associated with older age, higher sequential organ failure assessment score and elevated blood d-dimer levels on admission.[14] Detectable SARS-CoV-2 RNA persisted for a median of 20 days in survivors and sustained until death in non-survivors.[14]

Molecular epidemiology

Based on modelling, researchers estimated that initial human SARS-CoV-2 infection was in November to early December 2019.[15] An analysis based on 86 genomic sequences of SARS-CoV-2, obtained from the Global Initiative on Sharing All Influenza Data (GISAID), found many mutations.[16] This suggests that SARS-CoV-2 will continue to evolve as the outbreak occurs. Ongoing surveillance of sequences and shared mutations will assist with understanding the spread of the virus globally and within Australia.

Treatment

Current clinical management of COVID-19 cases focuses on early recognition, isolation, appropriate infection control measures and provision of supportive care.[17] Whilst there is no specific antiviral treatment currently recommended for patients with suspected or confirmed SARS-CoV-2 infection, multiple clinical trials are underway to evaluate a number of therapeutic agents, including remdesivir, lopinavir/ritonavir, and chloroquine.[18]

Comparison between COVID-19, SARS and MERS

Coronaviruses are a group of viruses that can cause upper respiratory tract infections in humans. Coronaviruses can occasionally cause severe diseases such as Middle East Respiratory Syndrome (MERS), Severe Acute Respiratory Syndrome (SARS) and more recently COVID-19. Similar to MERS-CoV and SARS-CoV, SARS-CoV-2 is thought to have originated from bats, and to have been transmitted to humans via an intermediate animal host. The intermediate animal host responsible for COVID-19 is currently unknown.[19] Table 4 provides an overview of characteristics of COVID-19, MERS and SARS.

Table 4: Characteristics of COVID-19, MERS and SARS[20–22]

	COVID-19	MERS	SARS
Median incubation period	5–6 days	5 days	4–5 days
Mode of transmission	Respiratory droplet, close contact, fomites	Respiratory droplet, close contact	Respiratory droplet, close contact, fomites
Symptoms	Fever, cough, fatigue and difficulty with breathing (dyspnoea)	Fever, cough and shortness of breath	Fever, malaise, myalgia, headache, diarrhoea and shivering (rigors)

	COVID-19	MERS	SARS
Number of countries and regions affected	134	27	29
Regions severely affected	Mainland China, Republic of Korea, Italy and Islamic Republic of Iran	Saudi Arabia	Mainland China, Hong Kong SAR, Taiwan, Canada, Singapore
Number of cases globally	142,539	2,519	8,422
Number of deaths globally	5,393	866	916
Global case fatality rate	3.8%	34.3%	10.9%
Prophylaxis available	No	No	No

Public health response

The Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) describes some of the key aspects associated with the evolving outbreak in mainland China, including transmission dynamics, disease progression and severity, mainland China's response and knowledge gaps. As part of the report, the following major recommendations were made for countries with imported cases and/or outbreaks of COVID-19:[8]

1. Immediately activate the highest level of national Response Management protocols to ensure the all-of-government and all-of-society approach needed to contain COVID-19 with non-pharmaceutical public health measures;
2. Prioritise active, exhaustive case finding and immediate testing and isolation, painstaking contact tracing and rigorous quarantine of close contacts;
3. Fully educate the general public on the seriousness of COVID-19 and their role in preventing its spread;

Background

On 31 December 2019, the World Health Organization (WHO) was notified about a large number of cases of pneumonia of unknown origin in Wuhan City, Hubei Province, China. Chinese authorities isolated and identified a novel coronavirus on 7 January 2020.[23] WHO declared the outbreak of COVID-19 a Public Health Emergency of International Concern (PHEIC) on 30 January 2020.[8]

From 1 February 2020, Australia denied entry to anyone who had left or transited through mainland China, with the exception of Australian citizens, permanent residents and their immediate family and air crew who have been using appropriate personal protective equipment (Figure 4).[24] The Australian Health Protection Principal Committee (AHPPC) have reviewed these restrictions weekly, and on 4 March 2020, they released a statement recommending current travel restrictions for mainland China and the Islamic Republic of Iran remain in place for a further seven days.[25] On 5 March 2020, the Prime Minister announced new travel restrictions for travellers coming from the Republic of Korea, and implementation of enhanced health screening for arrivals from Italy. From 5 March 2020, foreign nationals (excluding permanent residents of Australia) will be prevented from coming to Australia until 14 days after leaving the Republic of Korea.[26] On 8 March 2020, AHPPC recommended that people who have been a close contact of a confirmed COVID-19 case, or who returned from or

transited through a listed higher risk country*, must not attend public gatherings until 14 days after leaving the country or having contact with a confirmed case even if they are completely symptom free.[27] Those undergoing COVID-19 testing also must not attend public gatherings until they have received their result.[27] On March 11, AHPPC recommended that the government continue to direct primary focus toward domestic containment and preparedness of COVID-19, and that enhanced border measures and travel restrictions be maintained for a further 7 days.[28] On March 12, AHPPC provided recommendations on testing and work restriction for health and aged care workers. In addition to the other suspect case criteria, AHPPC recommended testing for any health care worker (HCW) who provides direct care AND who has a fever (> 37.5 °C) AND an acute respiratory infection (e.g. shortness of breath, cough, coryza, and/or sore throat), are classified as a suspect case and should be tested for COVID-19. Recommendations for exclusion from work for HCW were also provided.[29] On 13 March, AHPPC provided recommendations for public gatherings and testing by putting in place social distancing measures to mitigate spread.[30] This includes:

- Limiting non-essential organised gatherings to fewer than 500 people;
- Limiting non-essential meetings or conferences of critical workforce e.g. healthcare professionals and emergency services;
- Encouraging all Australians to exercise personal responsibility for social distancing measures; and
- Initiating measures to protect vulnerable populations, such as reducing visitors to all residential care facilities and remote Aboriginal and Torres Strait Islander communities.

AHPPC acknowledges that diagnostic testing issues are related to an emerging global shortage and are reviewing the case definition. The current situation emphasises the need for testing to be limited to the current recommendations.[30]

AHPPC acknowledged that Australia's border measures may no longer be able to prevent the importation of COVID-19, and the primary focus should now be directed at domestic containment and preparedness.[24] Local transmission of COVID-19 has occurred in Australia, highlighting the need of effective containment measures to limit spread. Early isolation of identified cases and quarantine of suspected cases and close contacts is a key measure to minimise transmission of COVID-19 in the community. However, as COVID-19 presents as mild illness in the majority of cases, early identification and isolation of cases may be difficult to achieve.

Methods

Data for this report were current as at 19:00 hours AEDT, 14 March 2020.

This report outlines what is known epidemiologically on COVID-19 in Australia and from publicly available data from WHO Situation Reports, other countries' official updates and the scientific literature. Data on domestic cases in this report were collected from the National Notifiable Diseases Surveillance System (NNDSS) and jurisdictional health department media releases. The Communicable Diseases Network Australia (CDNA) developed the case definition for suspect and confirmed cases, which was modified at different time points during the

outbreak (Table 5). Data were analysed using Stata to describe the epidemiology of COVID-19 in Australia and the progress of the epidemic.

Table 5: Australian COVID-19 case definition as of 14 March 2020[31]

Version	Date of development	Suspect Case	Confirmed Case
1.18	13 March 2020	A. If the patient satisfies epidemiological and clinical criteria, they are classified as a suspect case. Epidemiological criteria • International travel in the 14 days before illness onset. OR • Close contact in 14 days before illness onset with a confirmed case of COVID-19. Clinical criteria • Fever OR • Acute respiratory infection (e.g. shortness of breath, cough, sore throat) with or without fever. B. If the patient has severe community-acquired pneumonia (critically ill) and no other cause is identified, with or without recent international travel, they are classified as a suspect case. C. If any healthcare worker with direct patient contact has a fever (≥ 37.5°C) AND an acute respiratory infection (e.g. shortness of breath, cough, sore throat), they are classified as a suspect case.	A person who tests positive to a validated specific SARS-CoV-2 nucleic acid test or has the virus identified by electron microscopy or viral culture.

Data for the international cases of COVID-19 by country were compiled from the latest WHO Situation Report. Case definitions may vary by country making comparisons difficult. Rapid reviews of the current state of knowledge on COVID-19 were conducted from the literature using PubMed.

Acknowledgements

This report represents surveillance data reported through CDNA as part of the nationally-coordinated response to COVID-19. We thank public health staff from incident emergency operations centres in state and territory health departments, and the Australian Government Department of Health, along with state and territory public health laboratories.

Author details

Corresponding author

Malinda V Chea

NIR Surveillance Team, Communicable Disease Epidemiology and Surveillance Section, Health Protection Policy Branch, Australian Government Department of Health, GPO Box 9484, MDP 14, Canberra, ACT 2601.

Email: epi.coronavirus@health.gov.au

References

1. World Health Organization (WHO). Coronavirus disease 2019 (COVID-19) situation report – 54: 14 March 2020. Geneva: WHO; 2020. [Accessed on 15 March 2020.] Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200314-sitrep-54-covid-19.pdf.
2. WHO. Coronavirus disease 2019 (COVID-19) situation report – 47: 07 March 2020. Geneva: WHO; 2020. [Accessed on 15 March 2020.] Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200307-sitrep-47-covid-19.pdf.
3. WHO. Coronavirus disease 2019 (COVID-19) situation report – 40: 29 February 2020. Geneva: WHO; 2020. [Accessed on 15 March 2020.] Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200229-sitrep-40-covid-19.pdf.
4. WHO. Novel Coronavirus (2019-nCoV) situation report – 11: 31 January 2020. Geneva: WHO; 2020. [Accessed on 15 March 2020.] Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200131-sitrep-11-ncov.pdf.
5. Ministry of Health. COVID-19 cases in Italy at 6 pm on March 14th. [Internet.] Rome: Italian Government Ministry of Health; 2020. [Accessed on 15 March 2020.] Available from: http://www.salute.gov.it/imgs/C_17_pagineAree_5351_12_file.pdf.
6. Ministry of Health. COVID-19 COVID-19, closed cinemas, pubs, discos throughout Italy. [Internet.] Rome: Italian Government Ministry of Health; 2020. [Accessed on 12 March 2020.] Available from: http://www.salute.gov.it/portale/news/p3_2_1_1_1.jsp?lingua=italiano&menu=notizie&p=dalministero&id=4175.
7. Ministry of Health. COVID-19, close non-essential commercial activities. [Internet.] Rome: Italian Government Ministry of Health; 2020. [Accessed on 12 March 2020.] Available from:

http://www.salute.gov.it/portale/news/p3_2_1_1_1.jsp?lingua=italiano&menu=notizie&p=dalministero&id=4212.
8. WHO. Report of the WHO-China joint mission on coronavirus disease 2019 (COVID-19). Geneva: WHO; 2020. [Accessed on 1 March 2020.] Available from: https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf.
9. Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z et al. Epidemiology and transmission of COVID-19 in Shenzhen China: analysis of 391 cases and 1286 of their close contacts. *medRxiv*. 2020. doi: https://doi.org/10.1101/2020.03.03.20028423.
10. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020. doi: https://doi.org/10.1016/S0140-6736(20)30566-3.
11. WHO. Coronavirus disease 2019 (COVID-19) situation report – 29: 18 February 2020. Geneva: WHO; 2020. [Accessed on 15 March 2020.] Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200218-sitrep-29-covid-19.pdf.
12. Sun P, Qie S, Liu Z, Ren J, Xi JJ. Clinical characteristics of 50466 patients with 2019-nCoV infection. *medRxiv*. 2020. doi: https://doi.org/10.1101/2020.02.18.20024539.
13. Li Y, Bai W, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may be at least partially responsible for the respiratory failure of COVID-19 patients. *J. Med. Virol.* 2020. doi: https://doi.org/10.1002/jmv.25728.
14. Woelfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Mueller MA et al. Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster. *medRxiv.* 2020. doi: https://doi.org/10.1101/2020.03.05.20030502.
15. Bedford T, Neher R, Hadfield J, Hodcroft E, Ilcisin M, Müller N. Genomic analysis of nCOV spread. Situation report 2020-01-30. [Internet.] 2020. Available from: https://nextstrain.org/narratives/ncov/sit-rep/2020-01-30.
16. Phan T. Genetic diversity and evolution of SARS-CoV-2. *Infect Genet Evol*. 2020. doi: https://doi.org/10.1016/j.meegid.2020.104260.
17. WHO. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. [Internet.] Geneva: WHO; 2020. [Accessed on 23 February 2020.] Available from: https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected.
18. Harrison, C. Coronavirus puts drug repurposing on the fast track. *Nat Biotechnol*. 2020. doi: https://doi.org/10.1038/d41587-020-00003-1.
19. WHO. Novel coronavirus (2019-nCoV) situation report – 22: 11 February 2020. Geneva: WHO; 2020. [Accessed on 12 February 2020.] Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22-ncov.pdf.
20. World Health Organization Regional Office for the Eastern Mediterranean. MERS situation update, January 2020. [Internet.] Egypt: World Health Organization Regional Office for the Eastern Mediterranean; 2020. [Accessed on 7 March 2020.] Available from: http://www.emro.who.int/pandemic-epidemic-diseases/mers-cov/mers-situation-update-january-2020.html.
21. Centers for Disease Control and Prevention (CDC). MERS clinical features. [Internet.] Atlanta: United States Department of Health and Human Services, CDC; 2019. [Accessed on 7 March 2020.] Available from: https://www.cdc.gov/coronavirus/mers/clinical-features.html.
22. WHO. Consensus document on the epidemiology of severe acute respiratory syndrome (SARS). [Internet.] Geneva: WHO; 2003. [Accessed on 7 March 2020.] Available from: https://www.who.int/csr/sars/WHOconsensus.pdf.

23. WHO. Novel coronavirus (2019-nCoV) situation report – 1: 21 January 2020. Geneva: WHO; 2020. [Accessed on 22 January 2020.] Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf.
24. Australian Government Department of Health. Australian Health Protection Principal Committee (AHPPC) novel coronavirus statement on 1 February 2020. [Internet.] Canberra: Australian Government Department of Health; 2020. [Accessed on 7 February 2020.] Available from: https://www.health.gov.au/news/australian-health-protection-principal-committee-ahppc-novel-coronavirus-statement-on-1-february-2020.
25. Australian Government Department of Health. Australian Health Protection Principal Committee (AHPPC) coronavirus (COVID-19) statement on 4 March 2020. [Internet.] Canberra: Australian Government Department of Health; 2020. [Accessed on 7 March 2020.] Available from: https://www.health.gov.au/news/australian-health-protection-principal-committee-ahppc-coronavirus-covid-19-statement-on-4-march-2020.
26. Australian Government Department of the Prime Minister and Cabinet. Update on novel coronavirus (COVID-19) in Australia. [Internet.] Canberra: Australian Government Department of the Prime Minister and Cabinet; 2020. [Accessed on 7 March 2020.] Available from: https://www.pm.gov.au/media/update-novel-coronavirus-covid-19-australia-0.
27. Australian Government Department of Health. Australian Health Protection Principal Committee (AHPPC) coronavirus (COVID-19) statement on 8 March 2020. [Internet.] Canberra: Australian Government Department of Health; 2020. [Accessed on 11 March 2020.] Available from: https://www.health.gov.au/news/australian-health-protection-principal-committee-ahppc-coronavirus-covid-19-statement-on-8-march-2020.
28. Australian Government Department of Health. Australian Health Protection Principal Committee (AHPPC) coronavirus (COVID-19) statement on 11 March 2020. [Internet.] Canberra: Australian Government Department of Health; 2020. [Accessed on 13 March 2020.] Available from: https://www.health.gov.au/news/australian-health-protection-principal-committee-ahppc-coronavirus-covid-19-statement-on-11-march-2020.
29. Australian Government Department of Health. Australian Health Protection Principal Committee (AHPPC) coronavirus (COVID-19) statement on 12 March 2020. [Internet.] Canberra: Australian Government Department of Health; 2020. [Accessed on 15 March 2020.] Available from: https://www.health.gov.au/news/australian-health-protection-principal-committee-ahppc-coronavirus-covid-19-statement-on-12-march-2020.
30. Australian Government Department of Health. Australian Health Protection Principal Committee (AHPPC) coronavirus (COVID-19) statement on 13 March 2020. [Internet.] Canberra: Australian Government Department of Health; 2020. [Accessed on 15 March 2020.] Available from: https://www.health.gov.au/news/australian-health-protection-principal-committee-ahppc-coronavirus-covid-19-statement-on-13-march-2020.
31. Australian Government Department of Health. Novel coronavirus 2019 (2019-nCoV) - CDNA national guidelines for public health units. [Internet.] Canberra: Australian Government Department of Health; 2020. [Accessed on 15 March 2020.] Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/7A8654A8CB144F5FCA2584F8001F91E2/$File/interim-COVID-19-SoNG-v2.0.pdf.