An Infectious Interest: Epidemiology of Communicable Diseases in Australia

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

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Originality statement

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

Signed:

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I am indebted to my MAE cohort for their collective wisdom, boundless enthusiasm and enduring support of each another. I am incredibly proud to be associated with people of such high calibre, academically and personally.

I would like to thank the staff at the National Centre for Epidemiology and Population Health for equipping me with the skills I need to be a budding epidemiologist, and the Australian Government Department of Health for funding my placement. I am also grateful to the staff at ACT Health and the Gold Coast Public Health Unit for providing me with opportunities to extend my skillset and for taking the time to share their knowledge and experiences with me.

I owe all of my sanity in the last two years to my husband, Stuart. His limitless patience and generosity made room in our lives for me to pursue my passion, and his intelligence helped me navigate many of the challenges I came across. Thank you for having confidence in my abilities, and so selflessly supporting them. I am also grateful to my friends and magnificent family, who provided willing ears for me to recount the most intricate and mundane aspects of my projects, and who supported me in more ways than I can describe.

Thesis Abstract

While placed in the Communicable Disease Epidemiology and Surveillance Section in the Office of Health Protection at the Australian Government Department of Health, I focused on five projects.

Using the World Health Organization's (WHO) Pandemic Influenza Severity Assessment (PISA), I established parameters and thresholds to measure the transmissibility, seriousness and impact of circulating influenza in Australia. I found that when these measures were applied to the 2017 influenza season, they aligned with the characterisation of the season by the National Influenza Surveillance Committee based on expert opinion and historical ranges. My implementation of PISA is now being used nationally to make evidence-based, reproducible assessments of the influenza season in real-time. To gain international experience with PISA, I am interning with WHO's Global Influenza Programme following thesis submission.

I conducted an evaluation of the Australian Paediatric Surveillance Unit's surveillance of acute flaccid paralysis using the United States Centers for Disease Control and Prevention's *Guidelines for Evaluating Public Health Surveillance Systems*. I found the surveillance system to have high stability, acceptability, representativeness and predictive value positive. To increase the usefulness of the system, I recommended that timeliness should be enhanced by reducing the complexity of the system, and that facilitation of increased stool sampling to exclude poliovirus infection should be improved.

I used data from the National Enhanced Listeriosis Surveillance System to describe and analyse predisposing risk factors and outcomes amongst nationally notified listeriosis cases in Australia from 2010-17. When compared to the population without each risk factor, I found the risk of listeriosis was 658 times higher in organ transplant recipients, 174 times higher in those with non-haematological cancers, and a range of 1.5-38 times higher in those with other chronic conditions, cases >45 years, pregnant women and those with international backgrounds. The study also highlighted a higher rate of meningitis and death amongst cases without identified susceptibility risk factors compared to cases with any risk factors.

In 2017-18, an unusual *Salmonella* Typhimurium (*S*Tm) multiple-locus variable-number tandem repeats analysis (MLVA) profile (3-25-13-12-523) appeared in the Australian Capital Territory. I undertook a retrospective case-case analysis to generate a hypothesis about the infectious source. As part of this I compared two case-control selection methods; one using MLVA-differentiated *S*Tm case-controls, and the other using case-controls selected from other *Salmonella* serovars. When cases were compared to *S*Tm case-controls, significantly higher egg consumption was detected in cases through multivariate analysis. No significant exposures were found when cases were compared to non-*S*Tm case-controls. This study provided a hypothesis for the source of infections and demonstrated that MLVA may be useful in expanding case-control selection to include those from the same *Salmonella* serovar.

I was also involved in communicable disease surveillance and response for the Gold Coast Commonwealth Games. I established a system of international disease surveillance and reporting, and participated in local monitoring and response through placement at the Gold Coast Public Health Unit.

Each of these projects has informed disease surveillance, prevention and control in Australia and has contributed to the understanding of the diseases' epidemiology.

Chapter 1: Masters of Philosophy in Applied Epidemiology (MAE) experience

Overview of experiences and meeting of course requirements

"I have yet to see any problem, however complicated, which, when you look at it in the right way, did not become still more complicated"

- Poul Anderson

Overview of placement and experiences

For the duration of my Masters of Philosophy (Applied Epidemiology) (MAE), I was placed in the Communicable Disease Epidemiology and Surveillance Section within the Office of Health Protection (OHP) at the Australian Government Department of Health.

Working at the federal level provides you with unique insights into the diversity of communicable disease events across all states and territories and offers opportunities to be involved in national and international policy, surveillance and response activities. It also provided me with the chance to share my work with multiple national committees and see my work being put into practice.

As part of my project work, I had the opportunity to present two of my analyses to national committees including the National Influenza Surveillance Committee and the Polio Expert Panel. My work was also provided to the Communicable Diseases Network Australia (CDNA) and was included in the National Certification Committee for the Eradication of Poliomyelitis's Annual Progress Report to the World Health Organization (WHO). Additionally, I was able to present to departmental staff from Health Emergency Management, the Medical and Scientific Advisory Unit and OHP executive.

Outside of my project work, I had the opportunity to be involved in monitoring multi-jurisdictional outbreaks and addressing national surveillance challenges. Notably, I matched and analysed surveillance and whole genome sequencing data on the meningococcal W outbreak in central Australia to present to the CDNA. In the initial stages of the multi-jurisdictional listeriosis outbreak in February 2018, I conducted a case-case analysis that suggested rockmelon was the most likely source of infections. Later, environmental detections confirmed rockmelons as the source, and the resulting public health action prevented the outbreak (consisting of 22 cases and six deaths) from continuing. I also undertook a stock take of national gonococcal antimicrobial resistance data, analysed survey responses from jurisdictions, met with a variety of stakeholders and presented my findings and recommendations to the National Surveillance Committee.

During my placement, I was involved in many internationally focused activities. As part of a monthly roster, I took part in routine international disease surveillance and

reporting to CDNA. I was also involved in multiple rapid assessment and incident management teams in response to international communicable diseases outbreaks of concern. This included risk assessment and preparations for outbreaks of Lassa fever in Nigeria, Nipah virus in India, poliovirus in Papua New Guinea and Ebolavirus in the Democratic Republic of the Congo. In 2017, the WHO conducted a Joint External Evaluation (JEE) of Australia's International Health Regulations compliance. I was fortunate enough to be invited to review surveillance input and observe deliberations and presentations by the JEE Mission team. I also participated in Watch Officer duty where I was the contact point for the National Focal Point of Australia and the National Incident Room. As part of this, I was responsible for maintaining national and international communications for communicable disease threats, and conducting contact tracing for international disease exposures.

I was fortunate enough to gain experiences outside the department during my MAE as well. I spent time at ACT Health at multiple points in my placement, which gave me hands-on experience in a public health unit and a new perspective on public health at the local level. While there, I learnt about managing acute disease outbreaks; the ways in which environmental health, communicable disease nurses and immunisation teams work collaboratively with epidemiologists; and about local data management and disease notification processes. I also had the opportunity to conduct interviews with notified salmonella cases to try and establish any relevant exposures, one of which lasted two hours (I learnt to bring sustenance to future interviews). Later, I had the opportunity to spend time at the Gold Coast Public Health Unit during the Commonwealth Games. This provided me with another set of perspectives and learnings about the functioning of a public health unit and afforded me unique insights into preparation, monitoring and response during a global event and mass gathering.

My experiences based at the local, state and federal level will be rounded out with international experience at the WHO where I am interning for six weeks with the Global Influenza Programme between thesis submission and my oral examination.

Table 1: Masters of Philosophy in Applied Epidemiology course activity requirements and how they were met

MAE competency	Chapter 2: Establishing parameters and thresholds for influenza severity assessment in Australia	Chapter 3: Evaluation of the Australian Paediatric Surveillance Unit's acute flaccid paralysis surveillance	Chapter 4: Risk factors for invasive listeriosis in Australia	Chapter 5: An unusual DNA macrorestriction pattern amongst *Salmonella* typhimurium cases in the Capital	Chapter 6: Peer-to-peer teaching
Design and conduct an epidemiological study					
Evaluate a surveillance system					
Analysis of a public health dataset					
Investigation of an acute public health problem					
Literature review*					
Conference abstract and presentation					
Peer-reviewed publication					
Report for a non-technical audience					
Lessons from the field					
Teaching first year MAE scholars					

**A literature review was undertaken for every project.*

Chapter 2: Epidemiological study

Establishing parameters and thresholds for Pandemic Influenza Severity Assessment in Australia

"The goal is to transform data into information, and information into insight"

– Carly Fiorina

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Chapter 2 - Prologue

My role

The World Health Organization's Pandemic Influenza Severity Assessment (PISA) guidance was released in 2017 with the goal of Member States implementing the assessment into routine surveillance (Appendix 2A). I was tasked with implementing the PISA in Australia. This involved selecting existing data sources to appropriately measure aspects of influenza severity and developing thresholds for each parameter based on temporal trends using data from 2012-2016. I met with a variety of stakeholders from different surveillance systems to discuss and negotiate use of their systems' data. After establishing these measurements, I tested the parameters and thresholds by applying them to the 2017 influenza season. I assessed the consistency of measurements between data sources and compared the outputs to the assessment of the season by the National Influenza Surveillance Committee (NISC), which is based on expert opinion and historical ranges. I presented this work to NISC in December 2017 at their annual face-to-face meeting and they agreed to trial the PISA real time in 2018 (Appendix 2B). I created a routine report to NISC on circulating influenza severity, which is provided to them and discussed at each of their seasonal monthly meetings. I published my implementation of PISA in the Bulletin of the World Health Organization in August 2018 (provided as my project write up). I was also invited to present my work at the Australian Public Health Conference in September 2018 (Appendix 2C) and the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET) conference in November 2018.

To write for a non-technical audience, I developed a new format for the Australian Influenza Surveillance Report, which is published on the department's website every fortnight during the influenza season (Appendix 2D). There was an identified opportunity for the report to provide more easily accessible messaging about national influenza activity for the media and the public. Where the report traditionally describes each data source, I reformatted the document to group data sources based on the aspect of influenza severity and circulation they were measuring. I incorporated tailored summaries of each severity indicator that made the report more accessible to a lay audience and provided meaning and context to data measurements for non-technical readers.

As a result of my work on PISA, I have been offered an internship with the World Health Organization's Global Influenza Programme which I am undertaking between October and December 2018. A key part of this will be participating in a multi-national meeting about PISA in November.

Lessons learnt

Prior to starting this project, I had no experience with anything beyond descriptive data analysis and had not used any statistical packages before. As an introduction to more complex analysis, this project provided me with a steep learning curve to say the least. I chose to use a particular epidemic modelling package to develop thresholds which involved teaching myself to use R, including everything from starting a script to modelling influenza epidemic timing. I sought advice from the Statistical Consulting Unit at ANU about the package I was using and learnt about the background calculations that were being employed to produce thresholds, and why some functions worked for Australian data and others didn't.

Choosing data sources to measure severity taught me a lot about influenza surveillance, how complicated it is to accurately measure activity and the diversity of surveillance mechanisms we have in Australia. I learnt the benefits and deficits of laboratory-confirmed and syndromic measurements, and the complexity of comparing and integrating these different surveillance systems to illustrate national influenza activity. I became intimately familiar with the National Influenza Surveillance Scheme and learnt how to clean and analyse multiple datasets.

Another key learning in this project was the publication process. Coming from the public service and not academia, I had no insight into how this world worked. Summarising months of work in a succinct cover letter, adhering to journal-specific style, the peer-review process, and editing practices, provided me with a whole new appreciation of the literature I routinely read.

Public health impact

At a national level, the influenza season and whether a given level of activity is expected, has traditionally been assessed using expert opinion and historical ranges. This study has established thresholds that enable evidence-based, reproducible

measurements of influenza activity and severity in Australia. I have also created internationally standardised parameters that measure the transmissibility, impact on society and seriousness of circulating influenza. This quantification of influenza severity enables clear characterisation of the season and provides evidence-based boundaries from which public health action, communications and resourcing can be planned and instigated. It also allows Australia to contribute to a global assessment of influenza severity, which can enable monitoring and swift response to a severe pandemic.

Acknowledgements

My academic supervisor, Aparna Lal, provided me with invaluable guidance and practical help throughout this project. When I first explained to her what I was planning for my epidemiological study, she did not discourage me but did ensure that I was aware of how large and challenging it was going to be for me. I am very grateful that she instituted this kind of 'informed consent', and I am even more appreciative that she supported me in taking on the challenge. I would like to thank her for providing me with instant answers to R questions that countless days of foraging the internet could not, and for sharing her time and advice so liberally with me throughout this project.

I would like to thank Christina Bareja, who was the national influenza epidemiologist at the time, for her patience, insight and encouragement during my implementation of PISA. Her assistance in navigating the complexities of the National Influenza Surveillance Scheme, her facilitation of stakeholder meetings and her considered, perceptive advice made this project possible. Dr Allison Cairns also provided invaluable moral support and assistance in navigating my way through mountains of influenza data.

I am very grateful for the input and advice of Assoc. Prof. Robert Clark from the ANU Statistical Consulting Unit who helped me apply and understand the necessary statistical packages in R. He provided invaluable guidance and explanation on the processes at work for threshold calculation. I was also very fortunate to be in contact and garner helpful advice from Prof. Jose Lozano, who developed the moving epidemic method package. I very much appreciate the time he took to explain aspects of

package calculations and his assistance in understanding the application to Australian data.

Aparna, Christina and Robert assisted in reviewing my chapter and provided helpful feedback and comments.

I would like to acknowledge NISC members, in particular Prof. Allen Cheng, Dr Craig Dalton, Sandra Carlson, Mica Hartley, Prof. Nigel Stocks and Monique Chilver for their input, interest and assistance in understanding their data.

Course activity requirements met

✓ Design and conduct an epidemiological study

✓ Peer-reviewed publication

✓ Literature review

✓ Report for a non-technical audience (Appendix 2D)

✓ Conference abstract and presentation (Appendix 2B – NISC presentation; Appendix 2C – PHAA Public Health Conference abstract)

Ethics statement

This study was approved by the Science and Medical Delegated Ethics Review Committee of the Australian National University (Protocol number 2017/476).

Research

Establishing thresholds and parameters for pandemic influenza severity assessment, Australia

Kaitlyn Vette,[a] Christina Bareja,[b] Robert Clark[c] & Aparna Lal[a]

Objective To implement the World Health Organization's pandemic influenza severity assessment tool in Australia, using multiple sources of data to establish thresholds and measure influenza severity indicators.

Methods We used data from four reliable sources: sentinel general practitioner surveillance, hospital surveillance, a public health hotline and an influenza-like illness survey system. We measured three influenza severity indicators (transmissibility, impact and disease seriousness) defined using pandemic influenza severity assessment guidelines. We used the moving epidemic method and a seriousness indicator-specific method to set thresholds for indicator parameters using 2012–2016 data. We then applied the thresholds to data from the 2017 influenza season.

Findings We were able to measure and produce thresholds for each severity indicator. At least one laboratory-confirmed influenza parameter was used to measure each indicator. When thresholds were applied to the 2017 season, there was good agreement across all data sources in measuring activity for each indicator. The season was characterized as having high transmissibility and extraordinary impact. Seriousness was characterized as moderate overall and in all age groups except those aged ≥ 65 years for whom it was high. This matched the description of the season produced by the Australian national influenza surveillance committee, based on expert opinion and historical ranges.

Conclusion The pandemic influenza severity assessment and moving epidemic method provide a robust and flexible method to enable an evidence-based assessment of seasonal influenza severity across diverse data sources. This is useful for national assessment and will contribute to global monitoring and response to circulating influenza with pandemic potential.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

Influenza is an important global health challenge, with an estimated 10–20% of the 7.6 billion world population infected annually.[1] Due to the changing presentation of epidemics, the beginning, duration and severity of influenza seasons are difficult to predict.[2] Accurately understanding these factors can inform the timing, focus and scale of public health action.[3] In Australia, national influenza surveillance currently uses historical ranges and expert opinion to determine the start of the season, its severity and whether disease activity is within the expected range.[4]

In 2011, the World Health Organization (WHO) reviewed the response to the 2009 influenza pandemic.[5] The report identified a major challenge in measuring global influenza severity due to differences in population health and services, a lack of comparable data and unstandardized measurements. As a result, the WHO developed the pandemic influenza severity assessment, a tool to enhance influenza surveillance and standardize severity reporting by Member States, with the goal of enabling a global, real-time assessment of influenza severity.[3] The tool defines the severity of influenza using three indicators: (i) transmissibility, (ii) seriousness of disease and (iii) impact.[3] The tool suggests data parameters to measure each severity indicator and recommends a variety of methods to determine thresholds for the parameters.

The pandemic influenza severity assessment recommends that transmissibility and impact indicators are measured using weekly rates, and that disease seriousness is measured using a cumulative value. As such, thresholds for the different measurements are calculated using separate methods. We chose the moving epidemic to calculate transmissibility and impact thresholds,[6,7] and a seriousness indicator-specific method to set thresholds for seriousness of disease.[3] The moving epidemic method is a tool for calculation of influenza activity thresholds based the epidemic curves of historical data. The method has been piloted by WHO and the European Centre for Disease Prevention and Control and has been applied in countries including Spain, the United Kingdom of Great Britain and Northern Ireland and the United States of America.[7–10] In Australia, thresholds for influenza surveillance have previously been established in one jurisdiction, but have not been used in national influenza assessments.[11,12]

In this study we applied the pandemic influenza severity assessment to select appropriate surveillance parameters and set thresholds for assessment of seasonal influenza severity in Australia. In doing so, we sought to demonstrate a country-level implementation of the tool and to create an evidence-based, standardized assessment of influenza severity across Australia that would contribute to the WHO's global severity assessment.

Methods

Data sources

We determined a range of data sources capable of measuring the three influenza severity indicators: transmissibility, disease seriousness and impact. For each indicator we chose at least two sources of Australian surveillance data to calculate the relevant parameters, including one source of

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Table 1. **Australian data sources and parameters used to measure influenza severity indicators**

Severity indicator,[a] by data source	Type of surveillance	Parameter
Transmissibility		
Flutracking	Survey-based weekly surveillance of ILI in the community	Number of people reporting ILI per 1000 survey participants
Healthdirect	Callers to public health hotline	Number of callers reporting ILI per 1000 callers to hotline
Australian sentinel practices research network	Sentinel general practitioner surveillance system	(Number of people with ILI per 1000 general practitioner consultations) x (% of systematic ILI swabs confirmed positive for influenza virus)
Impact		
Flutracking	Survey-based weekly surveillance of ILI in the community	Number of people absent from regular duties per 1000 survey participants with ILI
Influenza complications alert Network	Sentinel hospital surveillance system	Number of laboratory-confirmed influenza admissions per 1000 available hospital beds
Seriousness of disease		
Influenza complications alert network	Sentinel hospital surveillance system	Cumulative number of intensive care unit admissions per 100 laboratory-confirmed influenza admissions
Healthdirect	Callers to public health hotline	Cumulative number of callers with ILI advised to seek urgent medical attention per 1000 callers with ILI (split into age groups: < 15, 15–64 and ≥ 65 years)

ILI: influenza-like illness.

[a] Influenza severity indicators are from the World Health Organization pandemic influenza severity assessment tool.[3] Transmissibility measures how many people in a population get sick from influenza on a weekly basis. Seriousness of disease measures how severely sick individual people get when infected with the influenza virus. Impact measures how the influenza epidemic or pandemic affects society, including the health-care system.

laboratory-confirmed influenza data (Table 1). Four data sources were used in total. Flutracking is a survey-based system that conducts weekly surveillance of influenza-like illness (ILI) in the community from approximately 27 000 participants in all Australian jurisdictions.[4] The public health hotline Healthdirect collects surveillance data on ILI from callers in all jurisdictions except the states of Victoria and Queensland, receiving approximately 640 000 calls annually. The Australian sentinel practices research network is a sentinel general practitioner surveillance system that collects data on consultations for ILI and systematically swab-tests these patients for influenza virus at approximately 200 sites across all jurisdictions. The influenza complications alert network is a sentinel hospital surveillance system that collects information on confirmed cases of influenza and intensive care unit admissions from 17 hospitals in all jurisdictions.

We obtained weekly incidence data for the years 2012–2017 from each surveillance system; there were no missing data. Routine case definitions specific to each system were used (Table 1).

Data analysis

We used data from 2012–2016 to determine thresholds for week numbers 18–39 and then applied them to the 2017 season. We assigned week numbers using the International Organization for Standardization 8601 standard.

Moving epidemic method

To determine the thresholds for the transmissibility and impact parameters we used the moving epidemic method, which models historical weekly rates of influenza activity to determine when the epidemic period is likely to occur and to quantify expected activity levels.[6] We calculated pre-and post-epidemic thresholds, as well as thresholds for moderate, high and extraordinary influenza intensity for each parameter. For threshold calculations we used R software, version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria)[13] and the moving epidemic method R package, version 2.9 (Health Sentinel Network of Castilla y León, Valladolid, Spain).[14]

To create thresholds, the moving epidemic method function *memmodel* was used. Within *memmodel*, there are multiple function options to select from, including the confidence interval levels from which to calculate thresholds; how many seasons of data to use; and how to determine the timing of the epidemic period based on temporal trends (referred to as the optimal timing). We chose the slope method to determine the optimal timing of the epidemic period, which calculates the curve of the minimum number of consecutive weeks with the maximum accumulated proportion of the parameter rates and matches this to the mean slope.[14] The moving epidemic method package recommends the fixed criterium method (matching the maximum accumulated proportion of rates to a predetermined parameter value) to determine the epidemic period.[14] However, the slopes of the epidemic curves in our data were not steep enough to use this method with the predefined parameter value set by the package, based on European data. We generated a data-specific parameter value for one data source, and when we used it in the fixed criterium method we found that this produced near-identical results as using the predefined parameter value and the slope method. We therefore used the slope method for subsequent analyses. Within *memmodel*, we calculated the pre- and post-epidemic thresholds using the one-sided 95% point confidence interval (CI) of the arithmetic mean. We set pre-epidemic values for threshold calculation at −1, allowing the appropriate number of points determined by the number of influenza seasons available. We calculated intensity thresholds using the geometric mean and one-sided point CIs. We used upper limits of the 40%, 90% and 99% CIs for moderate-, high- and extraordinary-intensity thresholds.

For other calculations within *memmodel* we determined the median and its two-sided CI using the KC method (an adaptation of K.C. Carrière's CI calculation using quantiles).[14,15]

Seriousness method

As recommended in the pandemic influenza severity assessment, we used a WHO method specific to influenza seriousness to calculate thresholds for this indicator. To determine the thresholds for moderate, high and extraordinary disease seriousness we used the mean, mean plus 1 standard deviation and mean plus 3 standard deviations of end-of-season values. We analysed data for the seriousness parameters in three age groups (< 15, 15–64 and ≥ 65 years). Calculating an epidemic threshold for this parameter is not recommended, as the measurement is cumulative and stabilizes after the peak of the season. We calculated the seriousness parameter thresholds using Office Excel 2010 (Microsoft Corp., Redmond, United States of America).

Results

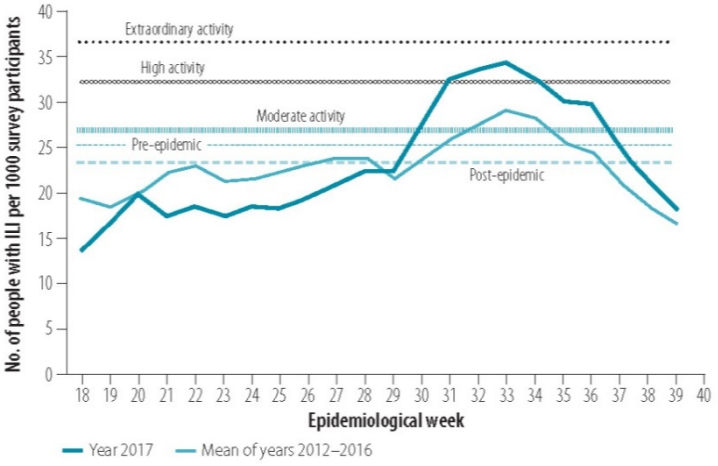
We calculated the weekly mean of the 2012–2016 data and weekly 2017 values for each parameter from week 18–39 or until the post-epidemic threshold was crossed. Detailed interpretations of each data source have been published elsewhere.[4,16]

Transmissibility

Using data from the Flutracking community surveillance system, the thresholds for moderate, high and extraordinary disease transmission were set at 26.8, 32.2 and 36.5 people with ILI per 1000 survey participants, respectively (Fig. 1). The pre- and post-epidemic thresholds were set at 25.4 and 23.4 per 1000, respectively. Transmission in the 2017 season peaked at 34.3 per 1000 in week 33, reaching the definition of high influenza activity.

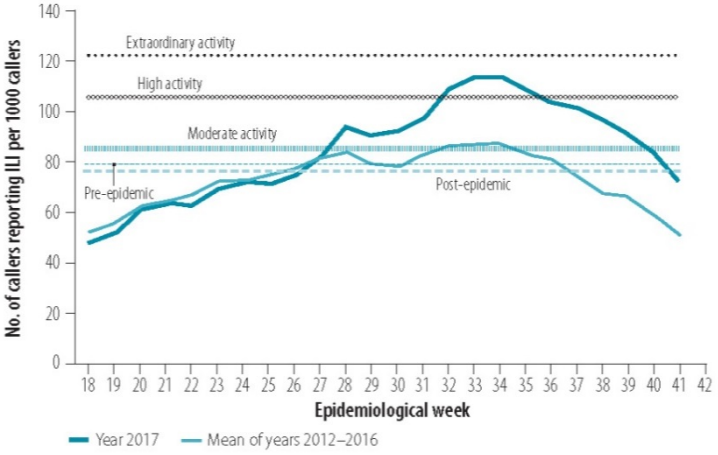
Data from the Healthdirect public health hotline produced thresholds for moderate, high and extraordinary transmission of 85.8, 105.8 and 122.0 people with ILI per 1000 callers to the hotline, respectively (Fig. 2). The pre-epidemic and post-epidemic thresholds were set at 78.8 and 76.6 per 1000, respectively. The 2017 season peaked at 113.5 per 1000 (high activity) in week 34.

Fig. 1. **Influenza transmissibility activity by epidemiological week, Australia, 2017**



ILI: influenza-like illness.
Notes: Thresholds for moderate, high and extraordinary levels of influenza activity were the 40%, 90% and 99% confidence intervals of the geometric mean, respectively. We used data from Flutracking, which conducts weekly surveillance of ILI in the community from approximately 27 000 participants.

Fig. 2. **Influenza transmissibility activity by epidemiological week, Australia, 2017**



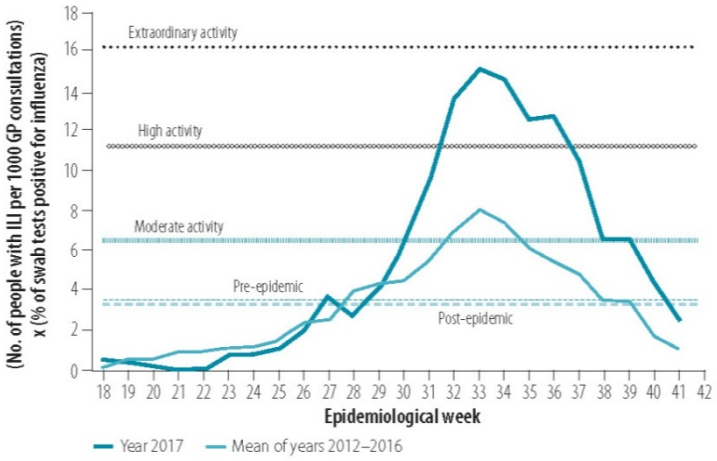
ILI: influenza-like illness.
Notes: Thresholds for moderate, high and extraordinary levels of influenza activity were the 40%, 90% and 99% confidence intervals of the geometric mean, respectively. We used data from Healthdirect public health hotline, which collects surveillance data on ILI, receiving approximately 640 000 calls annually.

Surveillance data from the Australian sentinel practices research network provided a composite measure of transmissibility: (number of people with ILI per 1000 general practitioner consultations) × (number of swabs testing positive for influenza per 100 swabs of people with influenza like illness tested). The thresholds for moderate, high and extraordinary transmission were calculated to be 6.5, 11.2 and 16.2, respectively (Fig. 3). The pre-epidemic and post-epidemic thresholds were set at 3.4 and 3.5, respectively. The peak of the 2017 season was 15.1 (high activity) in week 33.

Impact

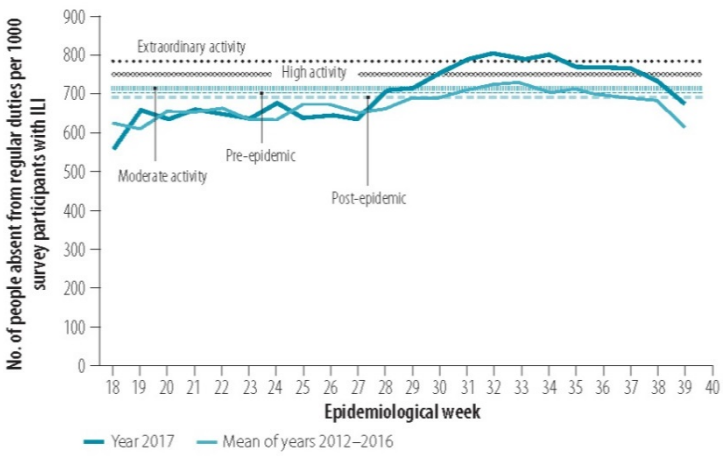
The thresholds for moderate, high and extraordinary disease impact from the

Fig. 3. **Influenza transmissibility activity by epidemiological week, Australia, 2017**



GP: general practitioner; ILI: influenza-like illness.
Notes: Thresholds for moderate, high and extraordinary levels of influenza activity were the 40%, 90% and 99% confidence intervals of the geometric mean, respectively. We used data from ASPREN (Australian sentinel practices research network), which is a sentinel general practitioner surveillance system that collects data on consultations for ILI, including systematic testing for influenza virus in swabs from ILI patients consulting, at approximately 200 sites. The data are a composite measure: (no. of people with ILI per 1000 general practitioner consultations) x (% of systematic ILI swabs confirmed positive for influenza virus).

Fig. 4. **Influenza impact activity by epidemiological week, Australia, 2017**



ILI: influenza-like illness.
Notes: Thresholds for moderate, high and extraordinary levels of influenza activity were the 40%, 90% and 99% confidence intervals of the geometric mean, respectively. We used data from Flutracking, which is a survey-based system that conducts weekly surveillance of ILI in the community from approximately 27 000 participants.

Flutracking system were 713.5, 753.2 and 781.5 people with ILI absent from normal duties per 1000 survey participants with ILI, respectively (Fig. 4). The 2017 season peaked at 796.8 per 1000 in week 32, defined as extraordinary influenza impact.

Data from the influenza complications alert network, a hospital surveillance system, produced thresholds for moderate, high and extraordinary impact of 17.5, 33.6 and 52.5 hospital admissions for influenza per 1000 hospital beds, respectively (Fig. 5). The peak of the 2017 activity was 53.5 per 1000 (extraordinary impact) in week 35.

Seriousness of disease

When the influenza complications alert network data were separated into age groups for the measurement of disease seriousness, the cumulative numerator was less than 10 at the peak of the season for some years; this made the standard error large and impractical to use for measuring seriousness. When analysed without age groupings, the thresholds for moderate, high and extraordinary seriousness were set at 9.2, 10.7 and 13.9 intensive care unit admissions per 100 cumulative hospital admissions for influenza, respectively (Fig. 6). At the end of the 2017 season, intensive care admissions were 9.4 per 100, defined as moderate influenza seriousness.

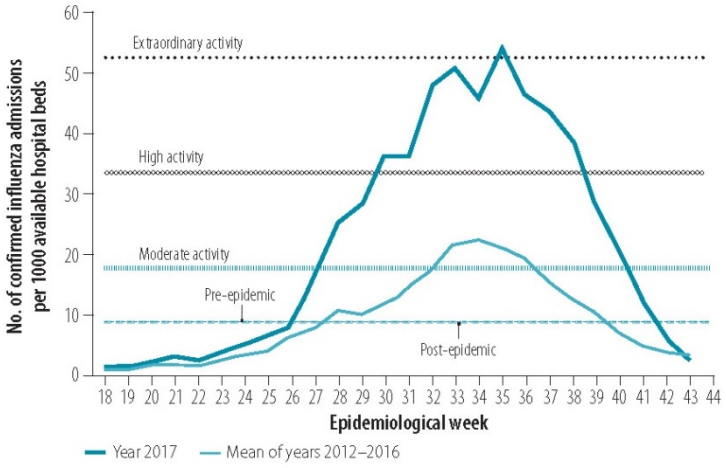
When analysed overall, thresholds for moderate, high and extraordinary seriousness from the Healthdirect system were set at 120.9, 143.0 and 187.0 callers advised to seek urgent medical attention per 1000 cumulative callers with ILI, respectively. The 2017 season ended at 124.2 urgent calls per 1000 (moderate seriousness).

In the youngest age group, Healthdirect thresholds for moderate, high and extraordinary seriousness were set at 121.0, 143.2 and 187.5 urgent callers per 1000 cumulative callers aged < 15 years with ILI, respectively (Fig. 7). At the end of the 2017 season there were 121.3 urgent calls per 1000 callers (moderate seriousness). For the middle age group, thresholds for moderate, high and extraordinary seriousness were set at 120.9, 142.9 and 187.0 per 1000 cumulative callers aged 15–64 years, respectively (Fig. 7). The 2017 season ended with 126.3 urgent calls per 1000 (moderate seriousness). For the oldest age group, thresholds for moderate, high and extraordinary seriousness were set at 120.9, 143.0 and 187.0 urgent calls per 1000 cumulative callers aged ≥ 65 years, respectively (Fig. 7). At the end of the 2017 season there were 151 urgent calls per 1000 (high seriousness).

Discussion

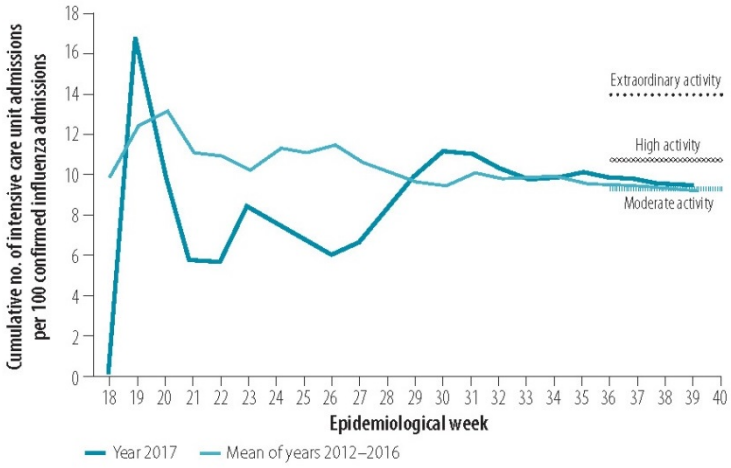
This study has established a standardized assessment of national influenza severity using parameters recommended by the pandemic influenza severity assessment.[3] We were able to

Fig. 5. **Influenza impact activity by epidemiological week, Australia, 2017**



Notes: Thresholds for moderate, high and extraordinary levels of influenza activity were the 40%, 90% and 99% confidence intervals of the geometric mean, respectively. We used data from FluCAN (influenza complications alert network), which is a sentinel hospital surveillance system that collects information on confirmed cases of influenza from 17 hospitals.

Fig. 6. **Influenza disease seriousness activity by epidemiological week, Australia, 2017**



Notes: Thresholds for moderate, high and extraordinary levels of influenza activity were the mean, mean plus 1 standard deviation and mean plus 3 standard deviations of end-of-season values, respectively. Threshold lines start at 36 weeks as seriousness was not assessed until after the peak of the influenza season. We used data from FluCAN (influenza complications alert network), which is a sentinel hospital surveillance system that collects information on confirmed cases of influenza from 17 hospitals.

measure each severity indicator with two independent sources of data, one of which used laboratory-confirmed influenza data to validate ILI measurements. Standardized disease intensity and epidemic thresholds using existing data sources provide a practical, country-specific, yet internationally reportable, method of assessing influenza severity.

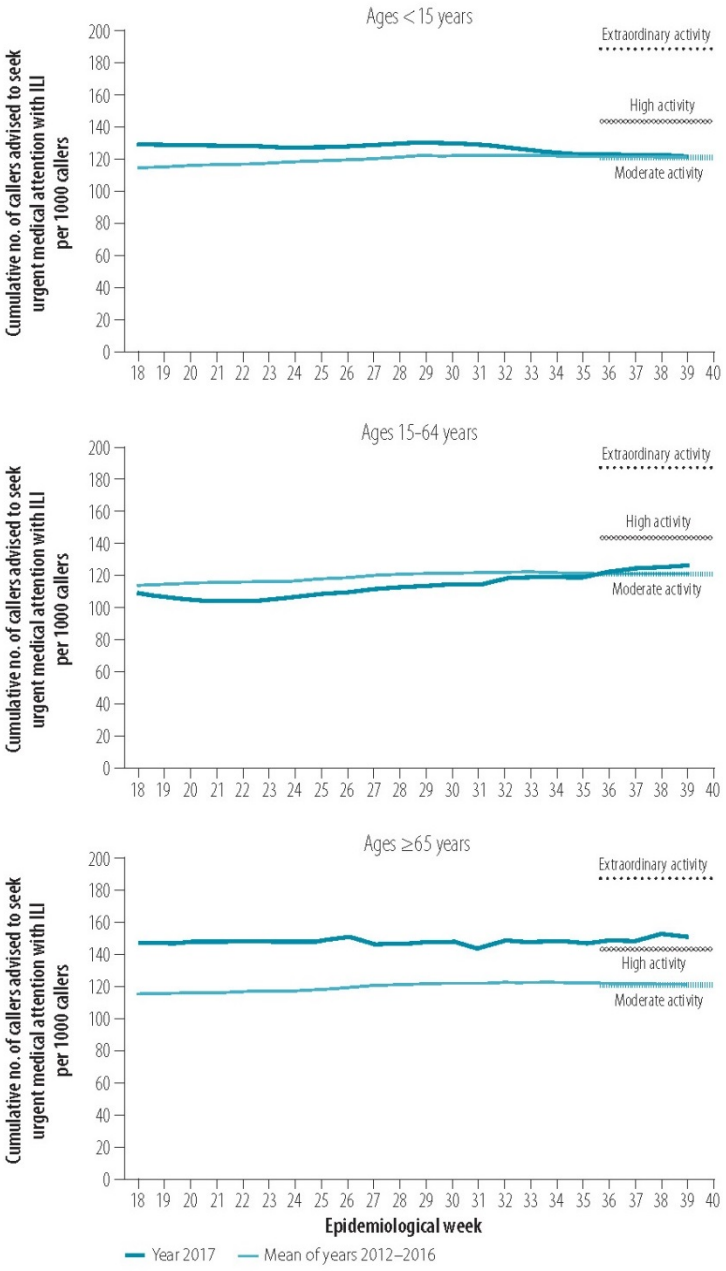
The data sources used in this study have been formally evaluated to have moderate to high timeliness, reliability and data quality (Wright R, Australian National University, unpublished data, 2017; Schicker RF, United States Centers for Disease Control and Prevention, unpublished data, 2016).[17,18] While each source inherently captures data from different geographical areas and demographic groups, they are used as complementary components in routine national surveillance in Australia.[4,16] Fortnightly seasonal analysis has found that the systems detect common trends in influenza activity.[19] Our study also demonstrated conformity across data sources in the measurement of influenza trends; all sources detected the 2017 seasonal peak for each indicator within a 3-week period.

The surveillance systems that collect ILI data (Healthdirect and Flutracking) detect more baseline levels of disease activity than those that capture laboratory-confirmed influenza data (the influenza complications alert network and the Australian sentinel practices research network). This is because ILI surveillance detects more activity by capturing symptomatic influenza cases that might not be confirmed and can inadvertently include other respiratory infections. This is reflected in transmissibility and impact parameter figures where the baseline activity is visibly higher among ILI data sources; and in seriousness parameters where the laboratory-confirmed influenza data are less stable early in the season due to low numbers.

Despite the diversity of surveillance systems used, when we applied thresholds to the 2017 season, we found good agreement between data sources in measuring indicator activity levels. In 2017, each parameter within the transmissibility and impact indicators measured the same activity level at the seasonal peak. For disease seriousness, all parameters measured the same activity level at the end of the season, except the age-separated Healthdirect data, which showed circulating influenza had a greater impact on those aged ≥ 65 years. There were some variations, however, in the start and end dates of the 2017 season according to each parameter. Inconsistencies in detecting the epidemic period could be resolved by defining the seasonal period using the first parameter with laboratory-confirmed influenza data to cross its epidemic threshold. For this study, indicator activity was determined simply by a parameter crossing a threshold. However, future consideration should be given to the value placed on the length of time a parameter exceeds a threshold.

The 2017 Australian influenza season was described by the national influenza surveillance committee as having

Fig. 7. **Influenza seriousness activity by epidemiological week for three age groups, Australia, 2017**



ILI: influenza-like illness.
Notes: Thresholds for moderate, high and extraordinary levels of influenza activity were the mean, mean plus 1 standard deviation and mean plus 3 standard deviations of end-of-season values, respectively. Threshold lines start at 36 weeks as seriousness was not assessed until after the peak of the influenza season. We used data from Healthdirect public health hotline, which collects surveillance data on ILI, receiving approximately 640 000 calls annually.

high influenza activity, very substantial absenteeism and health-system burden and low seriousness in all age groups except the elderly (for whom disease was more serious).[20] This description corresponded with our assessment of activity levels against severity thresholds, which found high transmissibility, extraordinary impact and moderate seriousness in all parameters, except for high seriousness among people ≥ 65 years. While expert opinion is valuable, evidence-based quantification of influenza severity and the epidemic period provides defined, repeatable measurements. Such measurements allow response activities to be planned and instigated, and meaningful comparisons between seasons to be made.

The pandemic influenza severity assessment and moving epidemic method provided useful, flexible methods of selecting and analysing multiple data sources and producing standardized thresholds to assess circulating influenza severity. The recommended threshold for extraordinary disease activity in the pandemic influenza severity assessment method is the upper limit of the one-sided 97.5% CI of the geometric mean.[3,14] When we applied this to Australian data, the extraordinary threshold was close to the 2012–2016 seasonal peaks for some parameters. Consequently, we raised the threshold to the upper limit of the 99% CI, which produced more practical thresholds for assessing activity extremes. The method for detecting the optimal timing of the epidemic period within the *memmodel* function was also flexible in providing alternative options for calculation to suit the data. The epidemic curve for Australian influenza data was less steep than the European data that were used to develop the moving epidemic method. This may explain why we needed to use alternative options within the moving epidemic method functions.[6] The pandemic influenza severity assessment and moving epidemic method are easily tailored to suit the data available in-country, which would enable these methods to be applied in different international surveillance contexts.

The WHO method for measuring disease seriousness was also simple to apply and describes an important facet of influenza severity. As described in the pandemic influenza severity assessment, this indicator is unstable at the beginning of the season and should only be

used to assess activity from the seasonal peak onwards.[3] The seriousness indicator is the most important to examine by age group, as this indicator is relatively stable seasonally, except for differences by age, depending on circulating influenza virus subtypes.[3] The seriousness indicator is very specific and requires the most limited data. As such, it is recommended that a cumulative rate is used to boost the numbers. This approach was effective in enabling analysis of Healthdirect data by age groups, but ineffective in generating sufficient numbers to enable us to measure seriousness using the influenza complications alert network data. In 2017, when Healthdirect data were assessed as a whole, disease activity was measured as reaching a moderate level of seriousness. Assessment by age group in the same season, however, demonstrated that the older population experienced high seriousness. As such, an overall assessment of seriousness without age separation may mask the effect of a season on a particular group. The low numbers of patients in the surveillance of influenza seriousness highlights the importance of having two data sources to validate severity measurements. Broader data capture is needed in Australia to reliably assess severity by age, particularly for seriousness.

Well-established national surveillance made it simple to implement the pandemic influenza severity assessment in Australia. However, the tool requires consistent, reliable and diverse influenza data from long-term surveillance systems. Whether it is feasible to collect such data in low- and middle-income countries has to be considered. Implementation of the tool is an opportunity to build and guide influenza surveillance capacity. Sentinel surveillance of influenza is the most efficient method of collecting high-quality, low-resource, timely data and is a basic recommendation for WHO Member States.[21] Sentinel surveillance of ILI and severe acute respiratory illness in primary and secondary health-care facilities (including a population denominator, intensive care unit admissions and available hospital beds) would provide the necessary information to measure all three severity indicators. While health care may be accessed differently in low-resource settings, these measures should provide an indication of influenza severity relative to a country's recent trends. As such, sentinel influenza surveillance should be prioritized when building capacity in low-and middle-income countries to enable high-value data collection and measurement of indicators.

In addition to the general challenges of influenza surveillance, this study had several limitations. The data sources we used inherently capture different geographic and demographic groups in the population.[4,16] A key consideration is the under-representation of residents from the state of Victoria in transmissibility data sources.

We did not measure transmissibility and impact indicators by age group, nor did we investigate the presence of chronic conditions as a subgroup for analysis. Analysis of the seriousness indicator by age groups demonstrated the importance of separation into age groups; analysis by age for all indicators would be desirable. In applying the pandemic influenza severity assessment, a balance must be struck between a country's need for assessment by age, location and comorbidities and the importance of producing a single, generalized activity level to contribute to global indicator reporting. Although we prioritized creating a national assessment, subgroup analysis should be explored in the future.

Influenza circulates differently in tropical and temperate areas, tending to have multiple epidemic waves and differently timed peaks in tropical regions.[22,23]

Approximately 40% of Australia's landmass lies in a tropical climate, however most of the population reside in temperate areas.[24,25] National influenza data patterns align with predominant population distribution, and represent a temperate pattern with one defined epidemic wave. As a result, we applied the moving epidemic method's temperate climate model. The presence of diverse Australian climatic regions, however, should be considered when actions are being recommended based on pandemic influenza severity assessment assessments. Just as separation into age groups is informative as to the distribution of influenza severity, the division of indicators into climatic regions would be useful in countries with diverse weather systems. Availability of data to describe climatic differences should be explored in Australia and internationally.

Our implementation of the pandemic influenza severity assessment demonstrates how the tool can be applied in practice and its usefulness in the Australian context. The agreement across our diverse data sources and the alignment of expert opinion with our threshold measurements shows the tool's utility in selecting relevant parameters and setting meaningful, consistent thresholds. Routine use and familiarization with the tool will enable measurements to be refined. There is substantial public health benefit in understanding the timing and severity of the influenza season. This can inform responses to seasonal and pandemic influenza, ensuring that funding and prevention and control efforts are directed appropriately. In a season with high transmission levels, symptomatic people can be encouraged to avoid public places. Early detection of a high-impact influenza season could pre-empt extra hospital resourcing. Recognizing a season with high disease seriousness could facilitate targeted prevention activities for those identified as most vulnerable.

On an international scale, having a global view of transmissibility, impact and seriousness patterns can enable early response to influenza pandemics. We hope that this study will encourage other countries to implement the pandemic influenza severity assessment, thereby increasing the strength of international assessment efforts. ■

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Competing interests: None declared.

ملخص

وضع عتبات ومعلمات لتقييم خطورة الإنفلونزا الوبائية، أستراليا

الغرض تنفيذ أداة تقييم شدة الإنفلونزا الوبائية، التابعة لمنظمة الصحة العالمية في أستراليا، باستخدام مصادر متعددة للبيانات بهدف تحديد العتبات وقياس مؤشرات شدة الإنفلونزا.

الطريقة استخدمنا البيانات من أربعة مصادر موثوق بها: مراقبة الممارس العام، ومراقبة المستشفى، والخط الساخن للصحة العامة، ونظام مسح الأمراض المشابهة للإنفلونزا. قمنا بقياس ثلاثة مؤشرات لشدة الإنفلونزا (القابلية للانتشار، والتأثير، وخطورة المرض)، والتي تم تحديدها باستخدام المبادئ التوجيهية لتقييم شدة الإنفلونزا الوبائية. استخدمنا طريقة انتشار الوباء، وطريقة مؤشر الخطورة، لتحديد عتبات معلمات المؤشر باستخدام بيانات 2012 إلى 2016. ثم قمنا بتطبيق العتبات على البيانات من موسم الإنفلونزا لعام 2017.

النتائج كان بمقدورنا قياس وإنتاج عتبات لكل مؤشر شدة. تم استخدام معامل واحد على الأقل للإنفلونزا معزز من جانب المختبر، لقياس كل مؤشر. عندما تم تطبيق العتبات على موسم 2017، كان هناك اتفاق جيد بين جميع مصادر البيانات على قياس النشاط لكل مؤشر. وقد تم وصف هذا الموسم بأنه ذو قابلية عالية للتفشي، وله تأثير غير عادي. وتم وصف الخطورة بأنها معتدلة بشكل عام، وفي جميع الفئات العمرية، باستثناء أولئك الذين تبلغ أعمارهم 65 سنة أو تزيد، حيث كانت الخطورة لديهم مرتفعة. وقد تطابق هذا مع وصف الموسم الذي أصدرته لجنة مراقبة الإنفلونزا الوطنية الأسترالية، بناءً على آراء الخبراء والنطاقات التاريخية.

الاستنتاج يوفر كل من تقييم خطورة الأنفلونزا الوبائية، وطريقة انتشار الوباء، طريقة فعالة ومرنة للتمكين من إجراء تقييم قائم على الأدلة لشدة الإنفلونزا الموسمية عبر مصادر متنوعة للبيانات. ويعد هذا مفيداً للتقييم الوطني، وسوف يسهم في الرصد العالمي، والاستجابة للإنفلونزا المتفشية المحتمل تحولها لوباء.

摘要

确立澳大利亚大流行性流感严重程度评估的阈值和参数

目的 旨在在澳大利亚实施世界卫生组织的大流行性流感严重程度评估工具，使用多种来源的数据以确定阈值并衡量流感严重程度指标。

方法 我们使用来自四个可靠来源的数据：定点全科医生监测、医院监测、公共卫生热线和流感样疾病调查系统。我们衡量了使用大流行性流感严重程度评估指南定义的三种流感严重程度指标（传染性、影响和疾病严重程度）。我们使用 2012 至 2016 年数据，采用流行疫情方法和严重程度指标特定方法来设置指标参数的阈值。然后，将这些阈值应用于 2017 年流感季节的数据。

结果 我们衡量并且生成每个严重程度指标的阈值。至少有一个实验室确认的流感参数被用来衡量各指标。当阈值应用于 2017 年季节时，所有数据来源在各指标的衡量活动中都达成了很好的一致性。该季节的特点是具有高度传染性和特别的影响。除了那些年龄 ⩾ 65 岁的人群以外，各年龄段人群的严重程度均为中等程度。根据专家意见和历史范围，这与澳大利亚国家流感监测委员会提供的季度说明相匹配。

结论 大流行性流感严重程度评估和流行疫情方法提供了一种稳健而灵活的方法，可以对不同数据来源的季节性流感严重程度进行循证评估。这对全国性评估是有用的，并将有助于全球监测和应对可能引起大流行的流行性感冒。

Résumé

Établir des seuils et des paramètres pour évaluer la sévérité de la grippe pandémique en Australie

Objectif Mettre en œuvre l'outil d'évaluation de la sévérité de la grippe pandémique de l'Organisation mondiale de la Santé en Australie, à l'aide de plusieurs sources de données, pour établir des seuils et mesurer des indicateurs de la sévérité de la grippe.

Méthodes Nous avons utilisé des données tirées de quatre sources fiables: surveillance sentinelle des médecins généralistes, surveillance hospitalière, permanence téléphonique en matière de santé publique et système d'enquête sur le syndrome de type grippal. Nous avons mesuré trois indicateurs de la sévérité de la grippe (transmissibilité, impact et sévérité de la maladie) définis à l'aide du guide pour évaluer la sévérité de la grippe pandémique. Nous avons utilisé la Moving Epidemic Method et une méthode propre à chaque indicateur de sévérité afin de définir des seuils pour les paramètres des indicateurs à l'aide de données de 2012-2016. Nous avons ensuite appliqué ces seuils aux données de la saison 2017 de la grippe.

Résultats Nous avons pu mesurer et établir des seuils pour chaque indicateur de la sévérité. Au moins un paramètre de la grippe confirmé en laboratoire a été utilisé pour mesurer chaque indicateur. Lorsque les seuils ont été appliqués à la saison 2017, une forte concordance a été constatée entre toutes les sources de données concernant la mesure de l'activité pour chaque indicateur. La saison a été caractérisée par une transmissibilité élevée et un impact extraordinaire. La sévérité a été définie comme étant modérée dans l'ensemble et dans tous les groupes d'âge, à l'exception du groupe des ≥65 ans pour lequel elle a été définie comme étant élevée. Cela correspondait à la description de la saison faite par le comité national australien de surveillance de la grippe, à partir de l'opinion d'experts et de plages historiques.

Conclusion L'évaluation de la sévérité de la grippe pandémique et la Moving Epidemic Method fournissent une méthode fiable et souple pour permettre une évaluation fondée sur des données scientifiques de la sévérité de la grippe saisonnière à partir de diverses sources de données. Cela est utile pour l'évaluation nationale et contribuera au suivi mondial et à la lutte contre les virus grippaux circulants à potentiel pandémique.

Резюме

Определение пороговых значений и параметров для оценки степени тяжести пандемического гриппа в Австралии

Цель Внедрить в Австралии инструмент Всемирной организации здравоохранения для оценки степени тяжести пандемического гриппа с использованием нескольких источников данных для определения пороговых значений и показателей степени тяжести гриппа.

Методы Авторы использовали данные из четырех надежных источников: дозорного эпиднадзора на уровне врачей общей практики и больниц, горячей линии общественного здравоохранения и системы эпиднадзора за гриппоподобными заболеваниями. Были определены три показателя степени тяжести гриппа (контагиозность, воздействие и серьезность заболевания), определяемые с помощью руководства для оценки степени тяжести пандемического гриппа. Авторы применили метод, основанный на движении эпидемии, а также метод, основанный на показателе серьезности заболевания, чтобы определить пороговые значения для параметров с использованием данных за 2012–2016 гг. Затем полученные пороговые значения были применены к данным по гриппу сезона 2017 года.

Результаты Авторы смогли измерить и создать пороговые значения для каждого показателя степени тяжести. Для измерения каждого показателя использовался по крайней мере один лабораторно подтвержденный параметр гриппа. После применения пороговых значений к сезону 2017 года при измерении активности по каждому показателю наблюдалась хорошая согласованность данных среди всех источников. Сезон был охарактеризован как имеющий высокую контагиозность и чрезвычайно сильное воздействие. Серьезность характеризовалась как умеренная в целом и во всех возрастных группах, за исключением лиц в возрасте ≥ 65 лет, для которых она была высокой. Это соответствовало описанию сезона, подготовленного Австралийским национальным комитетом по эпиднадзору за гриппом, которое основано на экспертном заключении и исторических диапазонах.

Вывод Оценка степени тяжести пандемического гриппа и метод, основанный на движении эпидемии, обеспечивают надежный и гибкий способ, позволяющий провести достоверную оценку степени тяжести сезонного гриппа, используя различные источники данных. Это будет способствовать оценке на национальном уровне, а также глобальному мониторингу и реагированию на распространение гриппа с пандемическим потенциалом.

Resumen

Establecimiento de umbrales y parámetros para evaluar la gravedad de la gripe pandémica, Australia

Objetivo Implementar la herramienta de evaluación de la gravedad de la gripe pandémica de la Organización Mundial de la Salud en Australia, utilizando múltiples fuentes de datos para establecer umbrales y medir los indicadores de gravedad de la gripe.

Métodos Se utilizaron datos de cuatro fuentes fiables: la vigilancia de médicos generales centinelas, la vigilancia hospitalaria, una línea telefónica de salud pública y un sistema de encuestas sobre enfermedades similares a la gripe. Se midieron tres indicadores de gravedad de la gripe (transmisibilidad, impacto y gravedad de la enfermedad) definidos mediante las pautas de la Evaluación de la gravedad de la gripe pandémica. Se siguió el método de epidemia móvil y un método específico de indicador de gravedad para establecer umbrales para los parámetros de los indicadores con los datos de 2012-2016. A continuación, se aplicaron los umbrales a los datos de la temporada de gripe 2017.

Resultados Se midieron y crearon umbrales para cada indicador de gravedad. Se utilizó al menos un parámetro de gripe confirmado por laboratorio para medir cada indicador. Cuando se aplicaron los umbrales a la temporada 2017, todas las fuentes de datos coincidieron en medir la actividad de cada indicador. La temporada se caracterizó por una alta transmisibilidad y un impacto extraordinario. La gravedad fue moderada en general y en todos los grupos de edad, excepto para los de ≥ 65 años, para los que fue alta. Esto coincidió con la descripción de la temporada elaborada por el comité nacional australiano de vigilancia de la gripe, basada en la opinión de los expertos y en los rangos históricos.

Conclusión La Evaluación de la gravedad de la gripe pandémica y el método de epidemia móvil proporcionan un método robusto y flexible para permitir una evaluación basada en la evidencia de la gravedad de la gripe estacional a través de diversas fuentes de datos. Esto es útil para la evaluación nacional y contribuirá a la vigilancia y respuesta mundial a la gripe circulante con potencial pandémico.

References

1. Cox NJ, Subbarao K. Global epidemiology of influenza: past and present. Annu Rev Med. 2000;51(1):407–21. doi: http://dx.doi.org/10.1146/annurev.med.51.1.407 PMID: 10774473
2. Hale BG, Albrecht RA, García-Sastre A. Innate immune evasion strategies of influenza viruses. Future Microbiol. 2010 Jan;5(1):23–41. doi: http://dx.doi.org/10.2217/fmb.09.108 PMID: 20020828
3. Pandemic Influenza Severity Assessment (PISA): a WHO guide to assess the severity of influenza epidemics and pandemics. Geneva: World Health Organization; 2017. Available from http://apps.who.int/iris/bitstream/handle/10665/259392/WHO-WHE-IHM-GIP-2017.2-eng.pdf?sequence=1 [cited 2018 Jun 17].
4. Sullivan S, Pennington K, Raupach J, Franklin L, Bareja C, de Kluyver R, et al. A summary of influenza surveillance systems in Australia, 2015. Available from: http://www.health.gov.au/flureport#nat-scheme [cited 2017 Sep 2].
5. Strengthening response to pandemics and other public-health emergencies. Report of the Review Committee on the Functioning of the International Health Regulations (2005) and on Pandemic Influenza (H1N1) 2009. Geneva: World Health Organization; 2011.
6. Vega T, Lozano JE, Meerhoff T, Snacken R, Mott J, Ortiz de Lejarazu R, et al. Influenza surveillance in Europe: establishing epidemic thresholds by the moving epidemic method. Influenza Other Respir Viruses. 2013 Jul;7(4):546–58. doi: http://dx.doi.org/10.1111/j.1750-2659.2012.00422.x PMID: 22897919
7. Vega T, Lozano JE, Meerhoff T, Snacken R, Beauté J, Jorgensen P, et al. Influenza surveillance in Europe: comparing intensity levels calculated using the moving epidemic method. Influenza Other Respir Viruses. 2015 Sep;9(5):234–46. doi: http://dx.doi.org/10.1111/irv.12330 PMID: 26031655

8. Green HK, Charlett A, Moran-Gilad J, Fleming D, Durnall H, Thomas DR, et al. Harmonizing influenza primary-care surveillance in the United Kingdom: piloting two methods to assess the timing and intensity of the seasonal epidemic across several general practice-based surveillance schemes. Epidemiol Infect. 2015 Jan;143(1):1–12. doi: http://dx.doi.org/10.1017/S0950268814001757 PMID: 25023603
9. Biggerstaff M, Kniss K, Jernigan DB, Brammer L, Bresee J, Garg S, et al. Systematic assessment of multiple routine and near-real time indicators to classify the severity of influenza seasons and pandemics in the United States, 2003–2004 through 2015–2016. Am J Epidemiol. 2018 May 1;187(5):1040–50. doi: http://dx.doi.org/10.1093/aje/kwx334 PMID: 29053783
10. Bangert M, Gil H, Oliva J, Delgado C, Vega T, DE Mateo S, et al.; Epidemiology Working Group of the Spanish Influenza Sentinel Surveillance System. Pilot study to harmonize the reported influenza intensity levels within the Spanish Influenza Sentinel Surveillance System (SISSS) using the Moving Epidemic Method (MEM). Epidemiol Infect. 2017 03;145(4):715–22. doi: http://dx.doi.org/10.1017/S0950268816002727 PMID: 27916023
11. Watts CG, Andrews RM, Druce JD, Kelly HA. Establishing thresholds for influenza surveillance in Victoria. Aust N Z J Public Health. 2003;27(4):409–12. doi: http://dx.doi.org/10.1111/j.1467-842X.2003.tb00418.x PMID: 14705303
12. Tay EL, Grant K, Kirk M, Mounts A, Kelly H. Exploring a proposed WHO method to determine thresholds for seasonal influenza surveillance. PLoS One. 2013 10 11;8(10):e77244. doi: http://dx.doi.org/10.1371/journal.pone.0077244 PMID: 24146973
13. R: a language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2017.
14. Lozano JE. The moving epidemic method R Package v2.9 [internet]. Castilla y León: Health Sentinel Network of Castilla y León; 2017. Available from: https://github.com/lozalojo/mem [cited 2018 Mar 18].
15. Concept: confidence interval of median. Winnipeg: University of Manitoba; 2000. Available from: http://mchp-appserv.cpe.umanitoba.ca/viewConcept.php?printer=Y&conceptID=1092#a_sas [cited 2018 May 25].
16. Data considerations for the Australian influenza surveillance report, 2017. Canberra: Australian Government Department of Health; 2017. Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm/$File/2017-AISR-data-considerations.pdf [cited 2017 Dec 15].
17. Fitzgerald T-L. The epidemiology of communicable disease in the Hunter New England region, New South Wales. Canberra: Australian National University; 2015.
18. Burroughs A. Applied epidemiology of communicable disease at a national level. Canberra: Australian National University; 2016.
19. Australian influenza surveillance report and activity updates. Australian Government Department of Health; 2017. Available from: http://www.health.gov.au/flureport [cited 2017 Jun 1].
20. 2017 influenza season in Australia. Canberra: Australian Government Department of Health; 2017. Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm/$File/2017-season-summary-22112017.pdf [cited 2017 Dec 5].
21. Global epidemiological surveillance standards for influenza. Geneva: World Health Organization; 2014.
22. Shek LP-C, Lee B-W. Epidemiology and seasonality of respiratory tract virus infections in the tropics. Paediatr Respir Rev. 2003 Jun;4(2):105–11. doi: http://dx.doi.org/10.1016/S1526-0542(03)00024-1 PMID: 12758047
23. Viboud C, Alonso WJ, Simonsen L. Influenza in tropical regions. PLoS Med. 2006 Apr;3(4):e89. doi: http://dx.doi.org/10.1371/journal.pmed.0030089 PMID: 16509764
24. Geography and climate. Year book Australia, 2012. Canberra: Australian Bureau of Statistics; 2012. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/mf/1301.0 [cited 2018 December 15].
25. Regional population growth, Australia, 2016. Canberra: Australian Bureau of Statistics; 2017. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/mf/3218.0 [cited 2017 Dec 15].

Appendix 2A – Pandemic Influenza Severity Assessment Guidance

GLOBAL INFLUENZA PROGRAMME

May 2017

PANDEMIC INFLUENZA SEVERITY ASSESSMENT (PISA)

A WHO guide to assess the severity of influenza in seasonal epidemics & pandemics

World Health Organization

WHO/WHE/IHM/GIP/2017.2

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1 SCOPE OF THE DOCUMENT

1.1 Background and development history

The events of the 2009 H1N1 pandemic revealed that WHO and national organizations did not have a robust and standardized method for making a timely assessment of the severity of pandemic influenza. They also showed that Member States were not fully prepared to rapidly assess the severity of a pandemic, or to implement the necessary risk management and communications plans.

In 2011, the World Health Assembly adopted a report by the Review Committee on the Functioning of the International Health Regulations (2005) and on Pandemic Influenza (H1N1) 2009[(1)]. The committee recommended that WHO should develop and apply measures that can be used to assess the severity of every influenza epidemic, whether seasonal or pandemic. A severity assessment provides the information needed to determine the timing, scale, emphasis, intensity and urgency of pandemic response actions. The report stated that, "by applying, evaluating and refining tools to measure severity every year, WHO and Member States can be better prepared to assess severity in a timely manner in the next pandemic" [(1)].

Severity assessments should be conducted in the early phase of a pandemic and regularly thereafter as the pandemic evolves. Since the World Health Assembly highlighted this need, WHO has made great progress on developing a framework on pandemic influenza severity assessment (PISA)[(2)]. The framework was developed through several meetings, expert consultations, collaborative WHO projects and the establishment of a technical working group (TWG) on pandemic influenza severity assessment. The framework defines influenza severity in terms of three indicators: transmission, seriousness of disease and impact.

In April 2014, WHO convened a meeting of the TWG to review the scope of surveillance data currently collected by Member States. The TWG reviewed surveillance data in the selected Member States to identify strengths and gaps, and areas for improvement, all of which varied dramatically among Member States.

Interim guidance describing a structured way of assessing influenza severity was developed, based on the results of previous meetings, work that WHO did with the Robert Koch Institute (Germany), a pilot study performed by Member States in the southern Hemisphere (Australia, Chile, New Zealand and South Africa) in 2014, and ongoing conference calls and expert consultations. Development of this framework formed the basis of discussion for the second and third meetings of the TWG, held in November 2014 and June 2015, respectively.

From 2014 to 2016, pilot testing of the interim guidance continued in selected Member States: Australia, Bangladesh, Canada, Chile, China, Egypt, France, Germany, India, Iran, Ireland, Japan, Madagascar, New Zealand, Norway, Portugal, Singapore, South Africa, Spain, Thailand, the United Kingdom of Great Britain and Northern Ireland, and the United States of America.

The guidance was further refined based on the findings and experience from the pilot testing. In March 2017, the PISA approach was launched and Member States were encouraged to start implementation. The immediate use of the tool to assess seasonal epidemic severity will highlight the need for strong baseline data; in addition, it will encourage Member States to refine their available data and familiarize themselves with the severity assessment tool, which would also be used during a pandemic.

1.2 Purpose of the guidance document

This guidance has been developed by WHO to be used by Member States and WHO as part of the pandemic influenza risk management guidance (PIRM)[3] to assess the severity of influenza in seasonal epidemics and pandemics, when sustained human-to-human transmission occurs. The assessments will take place continuously during seasonal epidemics or a pandemic, with a conclusive assessment being undertaken once transmission has subsided.

During a pandemic, time and resources are limited. Therefore, countries need to become familiar with the tool as soon as possible (i.e. during seasonal influenza epidemics), and operationalize the methods and outputs in their routine seasonal influenza situation assessments and reports. This will allow countries to assess severity more easily and efficiently during a pandemic.

This guidance does not apply to the alert phase situation[3]; that is, before sustained human-to-human transmission of zoonotic influenza viruses, when the aim is to define the risk of pandemic spread. Other tools are available from WHO for this purpose; for example, the Rapid risk assessment of acute public health events[4] or the tool for influenza pandemic risk assessment (TIPRA)[5].

Information to assess severity early and throughout the course of a pandemic will also be provided through special studies and modelling. However, this guidance focuses mainly on the information collected during routine influenza surveillance.

1.3 Target audience

This document is intended for use primarily by public health professionals at the national level, who perform or plan to perform national influenza severity assessments, and who can contribute to global influenza severity assessments. It is a living document that will be further updated as needed, and will serve as guidance for seasonal and pandemic influenza severity assessments.

2 AIM OF THE INFLUENZA SEVERITY ASSESSMENT

The aim of the influenza severity assessment at the national level is to [3]:

- describe the epidemiological situation and assess the severity of an influenza epidemic or pandemic based on all available information;
- inform national and global risk assessments; and
- inform public health preparedness, response and recovery measures, as well as resource allocation.

The global influenza severity assessment will be used by WHO to monitor and understand the global situation, and to inform and support global decisions and recommendations on public health interventions.

3 Influenza severity assessment concept & definitions

3.1 Indicators

Based on consultations between external experts and WHO staff between 2011 and 2015, influenza (pandemic) severity is defined in terms of three indicators: transmissibility of an influenza virus, seriousness of influenza disease and impact. These terms are defined in detail below and in Table 1.

3.1.1 Transmissibility

The transmissibility indicator reflects the ease of movement of the influenza virus between individuals and communities. Thus, a virus with high transmissibility will spread rapidly from one person to another. Several factors affect transmissibility: the ability of the virus to spread from person to person, the dynamics of the spread and the susceptibility of the exposed population. Transmissibility will be influenced by social and climatic factors. During seasonal influenza epidemics, transmissibility is usually measured by routine surveillance systems using a proxy (e.g. how many people are seeking health care for influenza-like illness). The actual dynamics of the spread (the reproductive number) and the susceptibility of the exposed population would be measured by ad hoc special studies during a pandemic.

3.1.2 Seriousness of disease

The seriousness of disease (also referred to as "severity of infection") indicator describes the extent to which individual people get sick when infected with the influenza virus. It describes the frequency of clinical symptoms, complications of influenza illness and outcomes following influenza infection. The seriousness of disease depends on the virus; for example, an influenza virus with a high level of clinical severity can result in a disproportionate number of people with serious illnesses, some of whom will be hospitalized and some of whom will die. Seriousness of disease also depends on the host; for example, the presence of underlying medical conditions that predispose individuals to develop severe illness, a history of vaccinations that may be protective (e.g. for influenza and pneumococcal disease), the person's age and the availability of health care. An infection is likely to be much more severe for some segments of a population than for others, and descriptions of the groups that are at increased risk will be an important part of this indicator. During seasonal influenza, seriousness of disease is measured with routine, hospital-based surveillance; for example, the case fatality ratio among people hospitalized or admitted to intensive care units (ICU) due to influenza.

3.1.3 Impact

The impact indicator generally describes how the influenza epidemic or pandemic affects society. It represents the impact on the health-care sector; for example, the impact on health-care use (hospitalization and ICU admissions), on the health-care workforce and on society (including excess mortality). The impact will be affected by the implementation of public health measures, public concern and the behaviour of the affected population. If the health-care sector impact is high, there may be stress on health-care resources. The public health impact may also result in societal and economic consequences, such as absenteeism from workplaces and schools, loss of critical infrastructure, and decreases in trade and tourism.

Table 1. Summary of the indicators used to describe influenza severity

INDICATOR	DESCRIBES	INFLUENCED BY	INFORMED BY
Transmissibility	How many people in a population get sick from influenza on a weekly basis	• Ease of movement of virus between individuals (virus shedding, viral replication, and viral binding) • Immunity and vaccination status • Age, contact patterns and health-seeking behaviour • Climatic factors	Routine surveillance parameters
Seriousness of disease	How severely sick individual people get when infected with the influenza virus	• Virus factors • Host factors • Context (e.g. access to health care and availability of ventilators)	Hospital-based surveillance parameters
Impact	How the influenza epidemic or pandemic affects the health-care system (and society)	• Public health interventions • Health-care use • Public concern	• Hospital-based surveillance • Vital statistics (e.g. death records) • School and work absenteeism

3.2 Parameters

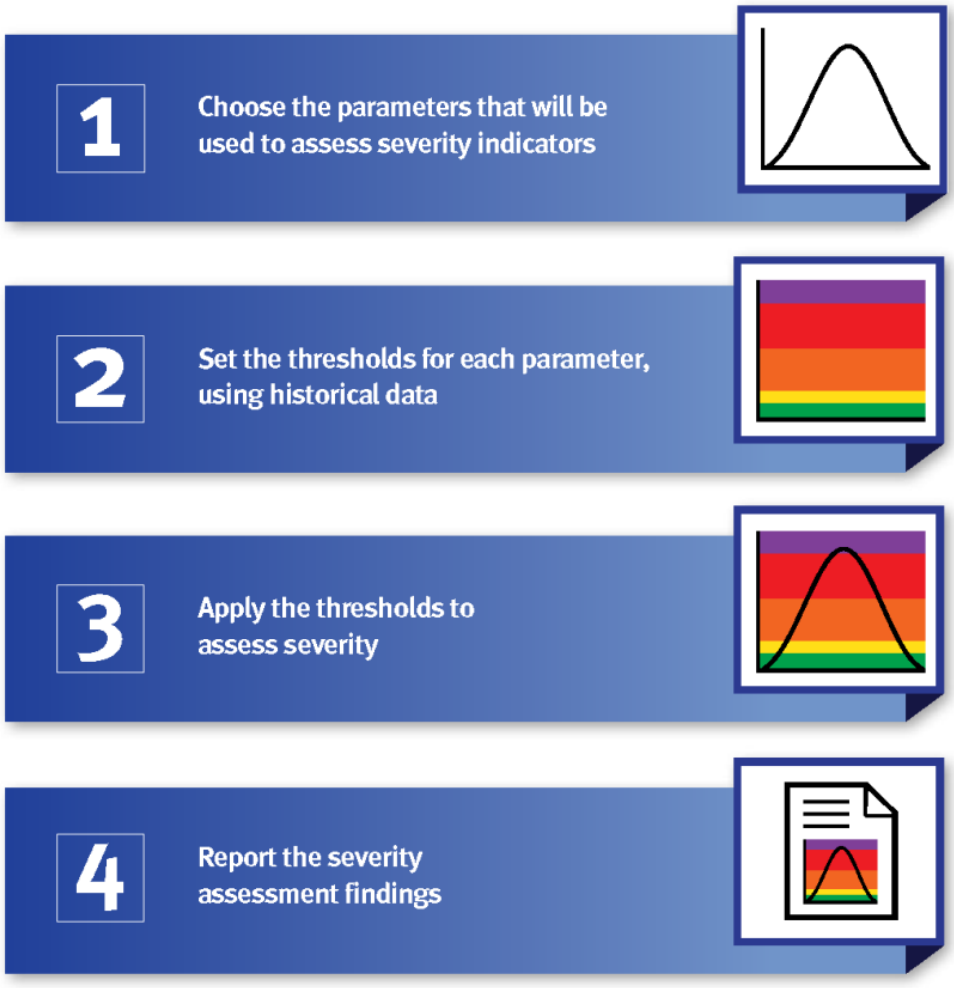
Each indicator described above is derived from various parameters that come from virological and epidemiological surveillance and clinical sources. These parameters are often collected on a routine basis by a country's public health surveillance systems[6]; alternatively, they may be measured in specific investigations (special studies). This guidance document focuses on the information collected through routine surveillance; information from special studies would only be obtained during influenza pandemics or other unusual events.

This guidance is intended to be flexible and should be adapted to the country implementing it. Each country has unique surveillance systems and has to choose the parameters (based on their experience) from their surveillance systems that could feed into the three indicators. For assessment of influenza severity, countries are encouraged to identify those parameters that are collected by established routine surveillance systems.

4 Steps for Assessing Influenza Severity

There are four key steps to assessing influenza severity, as shown in Figure 1.

Figure 1. Steps for assessing influenza severity



Step 1: Choose parameters

Certain criteria should be considered when selecting the parameters that will be used to assess the three severity indicators:

- Parameters must be:
  - indicative of influenza activity; therefore, at least a subset of samples should be laboratory tested for influenza viruses;
  - reliable and come from a surveillance system that is stable over time (or from a system in which changes that occur are well-documented);
  - timely;
- Historical data must be available (on historical seasonal epidemics or pandemics) for the parameters; and
- Where possible, denominators should be available to calculate (representative) proportions or rates.

The parameters considered to be most useful as defined by the WHO TWG are shown in Table 2.

Table 2. Useful parameters for assessing severity

INDICATOR	PARAMETERS (examples) [a]
Transmissibility	• Weekly ILI or MAARI cases as a proportion of total visits, or incidence rates • Composite (product) of weekly ILI or MAARI rates and weekly percentage positivity rates for influenza
Seriousness of disease	• Cumulative death: hospitalization ratio (ideally confirmed influenza cases and cases with outcome or discharge data) • Cumulative ICU: hospitalization ratio (ideally for confirmed influenza) • SARI:ARI or SARI:ILI ratios
Impact	• Weekly number or proportion of SARI cases, with percentage of SARI cases that are influenza positive • Weekly excess P&I or all-cause mortality (ideally stratified by age) • Weekly number of confirmed influenza cases admitted to ICU, or weekly number of confirmed influenza cases admitted to hospital

ARI: acute respiratory infection; **ICU:** intensive care unit; **ILI:** influenza-like illness; **MAARI:** medically attended acute respiratory illness; **P&I:** pneumonia and influenza; **SARI:** severe acute respiratory infection

[a] Other possible parameters that may reflect the impact on the society are school closures, hospital beds occupied, work absenteeism and school absenteeism. These non-health-care-related parameters might not be reported to the disease surveillance units in a country; rather, they might be captured by the ministry of education or social security systems. Such parameters were not tested during the pilot period.

Where possible, and when enough data are available, the parameters should be looked at by age groups. The minimum age groups are: under 15 years, 15–64 years and 65 years or over. If more age groups are used (e.g. >2 years or <5 years), it is important to ensure that they can aggregate to previously proposed age groups. Data might be insufficient at the beginning of the season to stratify by age groups, but it is important to collect age-specific information from the start.

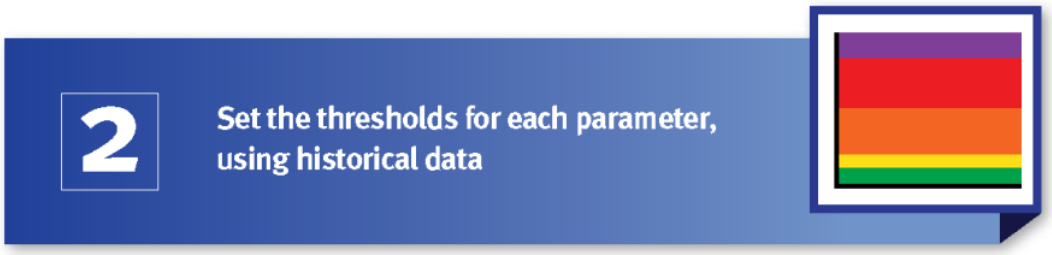
For the seriousness of disease and impact indicators, the parameters should, where possible, take into account the presence or absence of underlying chronic diseases or conditions known to be linked with severe outcomes for influenza (asthma, HIV/AIDS, pregnancy, heart or lung disease, for example). Refer to appendix 3 of the WHO global epidemiological surveillance standards for influenza for further information on pre-existing conditions.[6]

In addition to these proposed parameters, Member States can include other parameters based on their own surveillance system, provided they have confidence in the data.

INFLUENZA SEVERITY ASSESSMENT:

Step 1: Key points

- At the beginning of the assessment, use the criteria included in this guidance to select the parameters you will use.
- Document the following information on the selected parameters:
  - **data source** (e.g. outpatient sentinel or hospital surveillance);
  - **number of years** of data available;
  - **strengths** of this parameter;
  - **limitations** of this parameter; and
  - **proportion of data** that is laboratory confirmed.



Step 2: Set thresholds

Surveillance systems differ widely from one country to another; hence, the absolute values of the parameters cannot be used to make meaningful comparisons between countries. However, within a country, it is possible to see how a parameter compares with previous seasons and, more specifically, how the parameter's value compares with the peak value of previous seasons. Thus, using historical data, each country can describe an epidemic's (or pandemic's) activity compared with previous seasons, using qualitative descriptions such as:

- no activity or below seasonal threshold
- low
- moderate
- high
- extraordinary.

These qualitative assessments can then be compared both within a country over time and between countries.

It is useful to set thresholds or define ranges (using historical data) for the parameters that allow for qualitative categorization by describing the levels of activity. This involves defining the start of the epidemic (or pandemic) and then setting thresholds for each parameter to define the different levels of activity, as outlined below.

Defining the start of an epidemic

To define the beginning of the influenza epidemic (seasonal or pandemic), the following methods can be used:

- calculating the epidemic threshold using the moving epidemic method (MEM) [7, 8]; or
- using the weekly positivity rate (ratio of influenza-confirmed samples to all collected samples) to determine the virological threshold.

Thresholds for transmissibility and impact parameters

To set the thresholds for the transmissibility and impact parameters, the following methods can be used:

- MEM [7, 8];
- WHO method [6]; and
- country-specific statistical or empirical approaches, depending on the intrinsic properties of the systems.

The pilot testing indicated that MEM works well in most countries with the transmissibility and impact parameters, but more work is needed in tropical settings.

Country-specific approaches to threshold setting might have to be derived locally using national historical data, and should be comparable to the thresholds derived by MEM and the WHO method. The thresholds have been set in such a way that about 50–60% of the season peaks should be above the moderate threshold, ±10% above the high threshold and ±2.5% above the extraordinary threshold.

Table 3 provides proposed cut-off points for transmissibility and impact parameters used by WHO and in MEM.

Table 3. Cut-off points by method for threshold setting for transmissibility and impact

RANGES OF ACTIVITY	MEM	WHO
No activity or below seasonal threshold	**Below the seasonal threshold** as set by MEM	**Below the seasonal threshold** as set by the WHO method (annual median value)
Low	**Between the seasonal threshold and the upper limit of the 40% one-sided** CI of the geometric mean	**Between the seasonal threshold and the upper 40%** CI of the mean peak value[a] of the average curve
Moderate	**Between the upper limit of the 40% and 90%** one-sided CIs of the geometric mean	**Between the upper limit of the 40% and 90%** CIs of the mean peak value[a] of the average curve
High	**Between the upper limit of the 90% and 97.5%** one-sided CIs of the geometric mean	**Between the upper limit of the 90% and 97.5%** CIs of the mean peak value[a] of the average curve
Extraordinary	**Above the upper limit of the 97.5%** one-sided CI of the geometric mean	**Above the upper limit of the 97.5%** CI of the mean peak value[a] of the average curve

CI: confidence interval; **MEM:** moving epidemic method; **WHO:** World Health Organization

[a] When the peak values are very different from one season to another, it is best to use the geometric mean of the peak values instead of the arithmetic mean.

Thresholds for seriousness of disease parameters

The pilot testing indicated that the parameters for the seriousness of disease indicator (e.g. the cumulative measurements) fluctuate at the beginning of the epidemic and only become stable when the peak of the influenza activity occurs. From season to season, peak values are fairly stable, with differences by age group depending on circulating influenza subtypes. However, the values might be very different during a pandemic. Therefore, country-specific means and standard deviations should be calculated using end-of-season values of previous seasons and thresholds should be refined using historical data including pandemic data, as shown in Table 4. Age-specific thresholds should be set when data are available.

Table 4. Example of threshold setting for seriousness of disease

RANGES OF ACTIVITY	
No activity or below seasonal threshold	< Mean outside of the epidemic period
Low	< Mean
Moderate	Mean to mean+1SD
High	Mean+1SD to mean+3SD
Extraordinary	> Mean+3SD

ICU: intensive care unit; **SARI:** severe acute respiratory infection; **SD:** standard deviation

INFLUENZA SEVERITY ASSESSMENT:

Step 2: Key points

- **Define** the beginning of the epidemic or pandemic and document the cut-off values.
- **Set thresholds for qualitative levels** of activity for each parameter, and document the threshold values for each parameter.
- **Describe the methods** and the historical data used.

Step 3: Apply the thresholds

The severity assessment at the national level is mainly driven by quantitative data, expertise and experience. A country will come to a qualitative assessment for each indicator by looking at all parameters for a specific indicator; categorizing the values for the current situation in relation to their own historical data (ideally five seasons), or otherwise available comparable data; and taking into account additional available information. When performing the qualitative assessment, additional information needs to be considered; for example, timeliness, reporting biases and relative reliability of information from different systems.

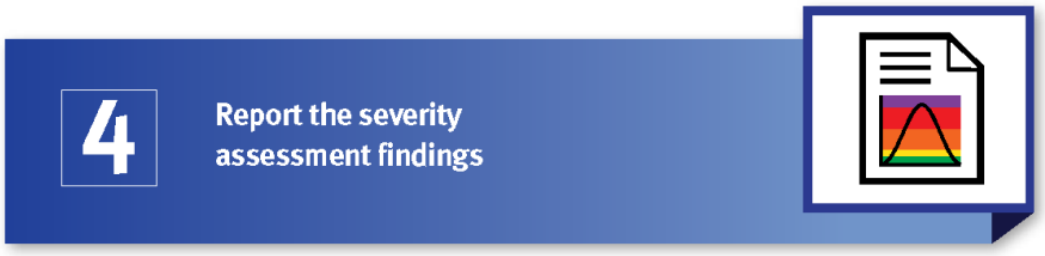
Ideally, on a weekly basis, after the beginning of the epidemic or pandemic, the thresholds should be applied to the contemporary parameter data for transmissibility and impact indicators. As discussed earlier, assessing the seriousness of disease indicator should be done once influenza activity has peaked.

At a minimum, the three indicators should be assessed at the middle of the epidemic and at the conclusion of the epidemic. Where data allow, it is important to also check whether there are differences in specific age groups or risk groups. The assessments, including confidence levels, should be used for national risk assessments and to inform public health decisions.

INFLUENZA SEVERITY ASSESSMENT:

Step 3: Key points

- At a minimum, **assess the contemporary data** for each indicator at the midpoint and end of the epidemic. Transmissibility and impact indicator data can be assessed on a weekly basis.
- **Examine data** for any differences between age groups or risk groups.
- **Use the findings** from the assessments, including confidence levels, to inform national risk assessment.
- **Document the parameters and thresholds used**, the parameters that were most reliable and gave most weight in the overall assessment, how the interpretation was done and how you combined the information of the different parameters to give a judgement on each indicator.



Step 4: Report the findings

The qualitative assessment by countries for each indicator, together with a confidence level and any indicator-specific comments, should be reported to WHO ideally on a weekly basis but at a minimum at the midpoint and end of the epidemic (Figure 2).

Where there are differences in the estimates by age groups or groups with underlying conditions, the final assessment should be based on the aggregated data (all age groups). However, if the estimate for a specific age group or risk group is in a higher category, this should be flagged in the comment field.

Figure 2. Indicators and categories for severity assessment

Transmissibility	☐ No activity or below seasonal threshold	☐ Low	☐ Moderate	☐ High	☐ Extraordinary
	Level of confidence:	☐ Low	☐ Medium	☐ High	
	Comments:				
Seriousness of disease	☐ No activity or below seasonal threshold	☐ Low	☐ Moderate	☐ High	☐ Extraordinary
	Level of confidence:	☐ Low	☐ Medium	☐ High	
	Comments:				
Impact	☐ No activity or below seasonal threshold	☐ Low	☐ Moderate	☐ High	☐ Extraordinary
	Level of confidence:	☐ Low	☐ Medium	☐ High	
	Comments:				

INFLUENZA SEVERITY ASSESSMENT:

Step 4: Key points

- **Report the overall assessment** for each indicator using all available information and the level of confidence in an Excel file that can be uploaded through the PISA SharePoint site (***workspace.who.int/sites/influenza/pisa/default.aspx***).

  Include the following:

  - **weekly qualitative assessments** for transmissibility and impact indicators;
  - **at the peak of the season and at the end of the season**, a qualitative assessment for the seriousness of disease indicator; and
  - **any comment you have in the comment box** (e.g. whether certain age groups are more affected or whether a high proportion of cases did not have underlying chronic conditions that put them at risk for severe disease).

5 Presentation of influenza severity assessments at the global level

The severity assessment results from countries will be visible to participants reporting data (i.e. there will be user-restricted access). Outputs will include heat charts for each indicator by week and by country, with comments fields visible when the user scrolls over the chart. Maps with results for each indicator will be included, showing assessments per country at a certain time point. WHO will further refine the display of the information received by Member States, but some of the potential outputs are shown in Figure 3 and Figure 4.

WHO will monitor the three indicators on a regular basis and will provide mid-season and end-of-season reports describing the severity in terms of transmission, seriousness of disease and impact, for the temperate northern and southern hemisphere influenza seasons. WHO will also provide situation updates whenever an unusual event is happening or during a pandemic. WHO is encouraging countries to become familiar with these indicators, to apply severity assessments during influenza seasons routinely, and to facilitate communication on national and international influenza events.

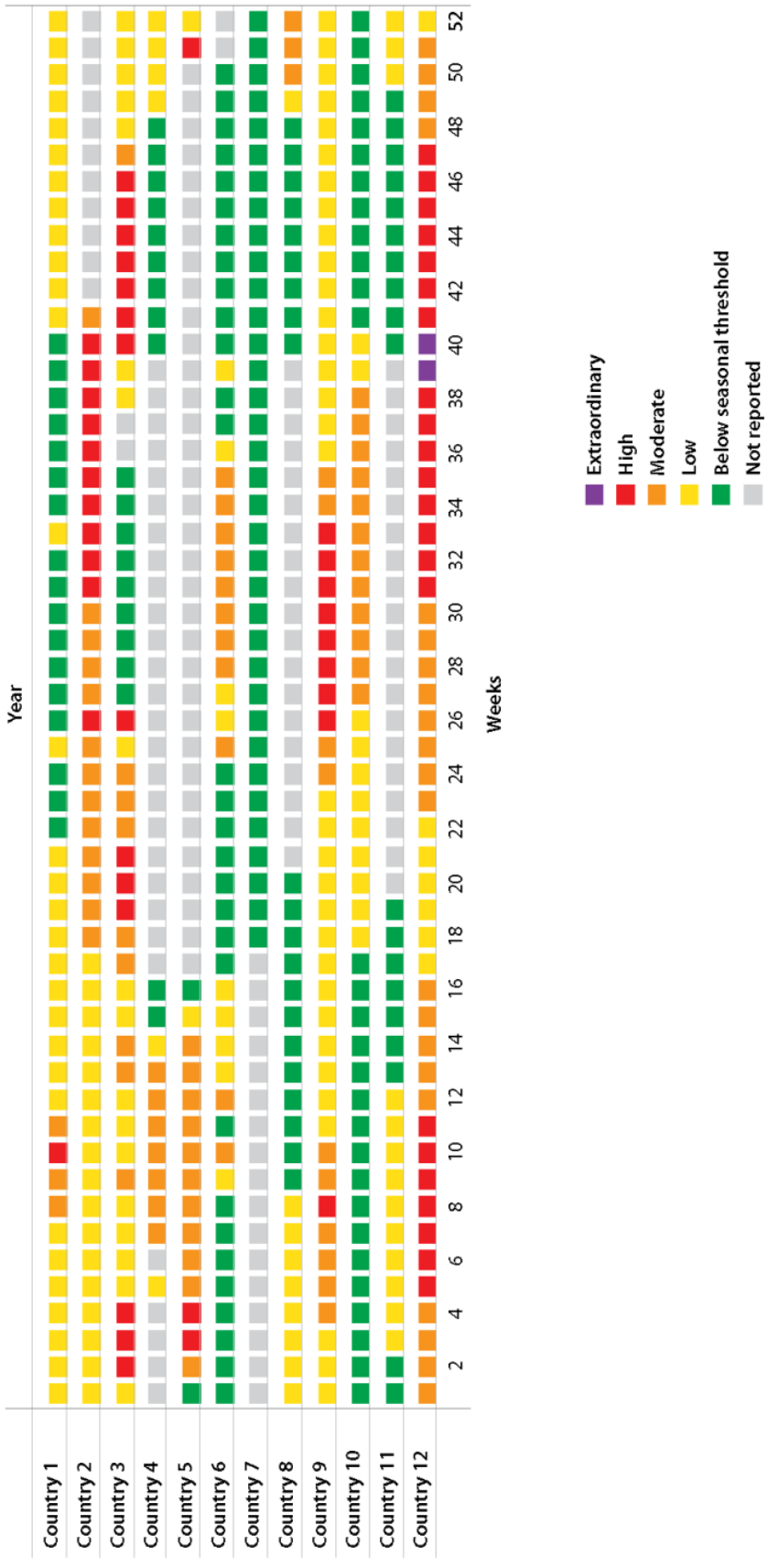


Figure 3: Heat chart for transmissibility indicator

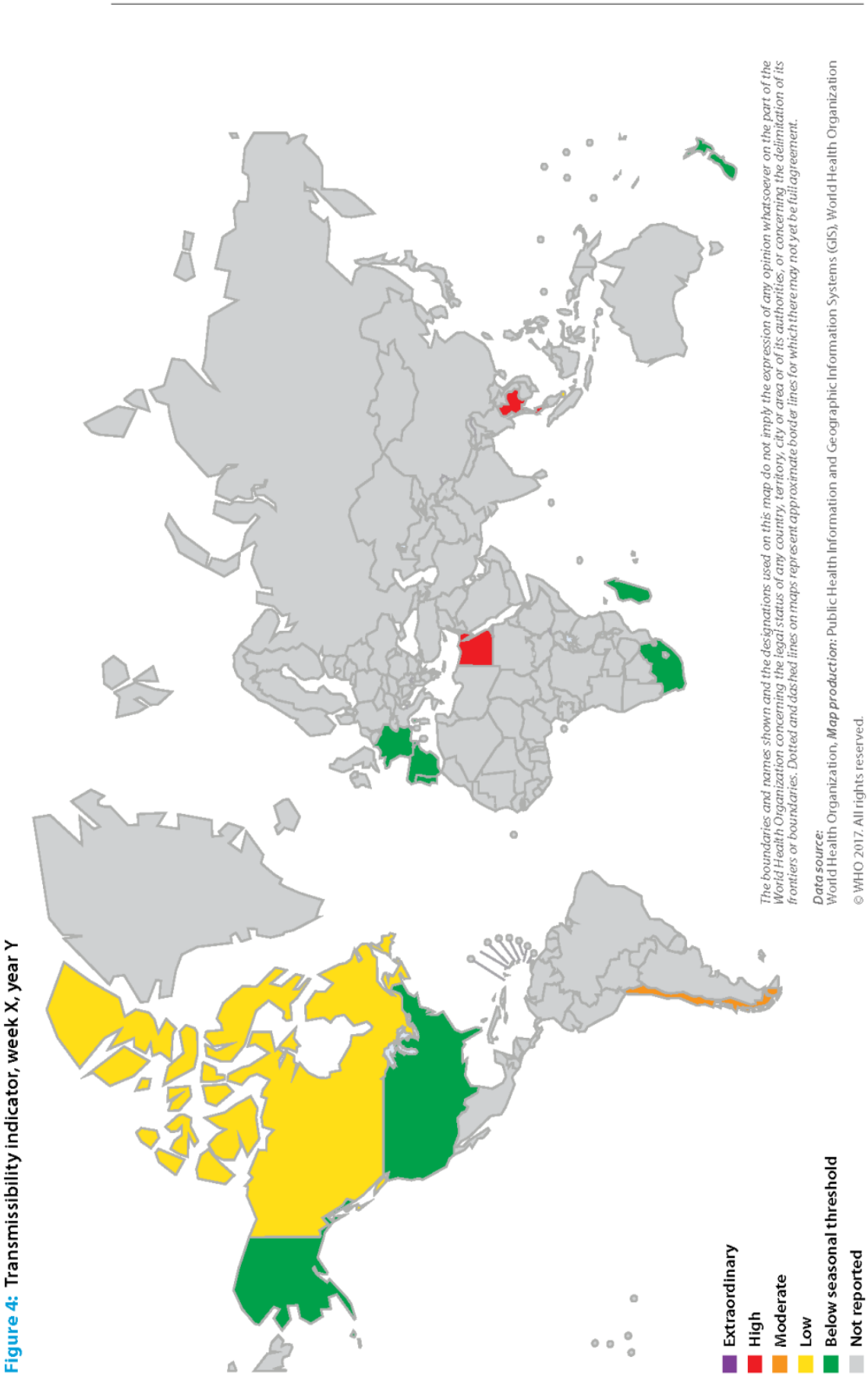


Figure 4: Transmissibility indicator, week X, year Y

6 References

1 **WHO.** *Strengthening response to pandemics and other public-health emergencies: Report of the Review Committee on the Functioning of the International Health Regulations (2005) and on Pandemic Influenza (H1N1) 2009.* Geneva: World Health Organization (WHO); 2011 (*http://www.who.int/ihr/publications/RC_report/en/, accessed May 2017*).

2 **WHO.** *Pandemic influenza severity assessment (PISA).* Geneva: World Health Organization (WHO); 2017 (*http://www.who.int/influenza/surveillance_monitoring/pisa/en/, accessed June 2017*).

3 **WHO.** *Pandemic influenza risk management: A WHO guide to inform & harmonize national & international pandemic preparedness and response.* Geneva: World Health Organization (WHO); 2017 (*http://www.who.int/influenza/preparedness/pandemic/influenza_risk_management_update2017/en/, accessed May 2017*).

4 **WHO.** *Rapid risk assessment of acute public health events. Geneva: World Health Organization (WHO);* 2012 (*http://www.who.int/csr/resources/publications/HSE_GAR_ARO_2012_1/en/, accessed May 2017*).

5 **WHO.** *Tool for influenza pandemic risk assessment (TIPRA).* Geneva: World Health Organization (WHO); 2016 (*http://www.who.int/influenza/areas_of_work/human_animal_interface/tipra/en/, accessed May 2017*).

6 **WHO.** *WHO global epidemiological surveillance standards for influenza.* Geneva: World Health Organization (WHO); 2014 (*http://www.who.int/influenza/resources/documents/influenza_surveillance_manual/en/, accessed May 2017*).

7 **Vega T, Lozano JE, Meerhoff T, Snacken R, Beaute J, Jorgensen P et al.** *Influenza surveillance in Europe: comparing intensity levels calculated using the moving epidemic method.* Influenza Other Respir Viruses. 2015;9(5):234–246 (*https://www.ncbi.nlm.nih.gov/pubmed/26031655, accessed May 2017*).

8 **Vega T, Lozano JE, Meerhoff T, Snacken R, Mott J, Ortiz de Lejarazu R et al.** *Influenza surveillance in Europe: establishing epidemic thresholds by the moving epidemic method.* Influenza Other Respir Viruses. 2013;7(4):546–558 (*https://www.ncbi.nlm.nih.gov/pubmed/22897919, accessed May 2017*).

Appendix 2B – Presentation to the National Influenza Surveillance Committee

Australian Government
Department of Health

Establishing severity indicators and thresholds for Australian influenza surveillance

Kaitlyn Vette
Office of Health Protection, Department of Health
Australian National University

Australian National University

Annual face to face meeting of the National Influenza Surveillance Committee
12 December 2017

Australian Government
Department of Health

Outline

- Pandemic Influenza Severity Assessment (PISA)
- Threshold setting
- 2017 season by parameter
- 2017 season overall
- PISA use going forward

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WHO Pandemic Influenza Severity Assessment[1] (PISA)

Severity Indicators and Recommended Parameters		
Transmission	**Impact**	**Seriousness of disease**
• Weekly ILI or MAARI cases as a proportion of total visits, or incidence rates • Composite (product) of weekly ILI or MAARI rates and weekly percentage positivity rates for influenza	• Weekly number or proportion of SARI cases, with percentage of SARI cases that are influenza positive • Weekly excess P&I or all-cause mortality (ideally stratified by age) • Weekly number of confirmed influenza cases admitted to ICU, or weekly number of confirmed influenza cases admitted to hospital	• Cumulative death: hospitalization ratio (ideally confirmed influenza cases and cases with outcome or discharge data) • Cumulative ICU: hospitalization ratio (ideally for confirmed influenza) • SARI:ARI or SARI:ILI ratios • School closures, hospital beds occupied, work absenteeism and school absenteeism.

1. World Health Organization. Pandemic influenza severity assessment. Geneva: World Health Organization, May 2017.

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PISA - Australian data parameters

Severity Indicators					
Transmission		**Impact**		**Seriousness of disease**	
System	**Parameter**	**System**	**Parameter**	**System**	**Parameter**
Flutracking	Rate of ILI per 1000 survey participants	Flutracking	Rate of absenteeism from regular duties per 1000 survey participants with ILI	Healthdirect	Cumulative rate of callers with ILI advised to seek urgent medical attention per 1000 Healthdirect callers with ILI (by age group:<15, 15-64 and 65+)
Healthdirect	Rate of ILI per 1000 callers	FluCAN	Rate of confirmed influenza admissions per 1000 available hospital beds	FluCAN	Cumulative rate of ICU admissions per 100 confirmed influenza admissions
ASPREN	(Rate of ILI per 1000 consultations) x (% positivity of swab testing)				

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PISA – Recommended parameters used

Severity Indicators and recommended parameters[1]		
Transmission	**Impact**	**Seriousness of disease**
• Weekly ILI or MAARI cases as a proportion of total visits, or incidence rates	• Weekly number or proportion of SARI cases, with percentage of SARI cases that are influenza positive	• Cumulative death: hospitalization ratio (ideally confirmed influenza cases and cases with outcome or discharge data)
• Composite (product) of weekly ILI or MAARI rates and weekly percentage positivity rates for influenza	• Weekly excess P&I or all-cause mortality (ideally stratified by age)	• Cumulative ICU: hospitalization ratio (ideally for confirmed influenza)
	• Weekly number of confirmed influenza cases admitted to ICU, or weekly number of confirmed influenza cases admitted to hospital	• SARI:ARI or SARI:ILI ratios
	• School closures, hospital beds occupied, work absenteeism and school absenteeism.	• Cumulative proportion of those with ILI advised to seek urgent medical attention

1. World Health Organization. Pandemic influenza severity assessment. Geneva: World Health Organization, May 2017.

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Thresholds: Moving Epidemic Method[1] and Seriousness method[2]

Activity levels and thresholds	MEM threshold	Seriousness threshold
Extraordinary activity		
EXTRAORDINARY THRESHOLD	Very high - 99% CI	Mean + 3SD
High activity		
HIGH THRESHOLD	High - 90% CI	Mean + 1SD
Moderate activity		
MODERATE THRESHOLD	Medium - 40% CI	Mean
Low activity		
EPIDEMIC THRESHOLD	Pre/post epidemic	-
No activity		

1. Vega T, Lozano JE, Meerhoff T, Snacken R, Mott J, Ortiz de Lejarazu R, et al. Influenza surveillance in Europe: establishing epidemic thresholds by the moving epidemic method. Influenza and other respiratory viruses. 2013;7(4):546-58.
2. World Health Organization. Pandemic influenza severity assessment. Geneva: World Health Organization, May 2017

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PISA - Australian data parameters

Severity Indicators					
Transmission		**Impact**		**Seriousness of disease**	
System	**Parameter**	**System**	**Parameter**	**System**	**Parameter**
Flutracking	Rate of ILI per 1000 survey participants	Flutracking	Rate of absenteeism from regular duties per 1000 survey participants with ILI	Healthdirect	Cumulative rate of callers with ILI advised to seek urgent medical attention per 1000 Healthdirect callers with ILI (by age group:<15, 15-64 and 65+)
Healthdirect	Rate of ILI per 1000 callers	FluCAN	Rate of confirmed influenza admissions per 1000 available hospital beds	FluCAN	Cumulative rate of ICU admissions per 100 confirmed influenza admissions
ASPREN	(Rate of ILI per 1000 consultations) x (% positivity of swab testing)				

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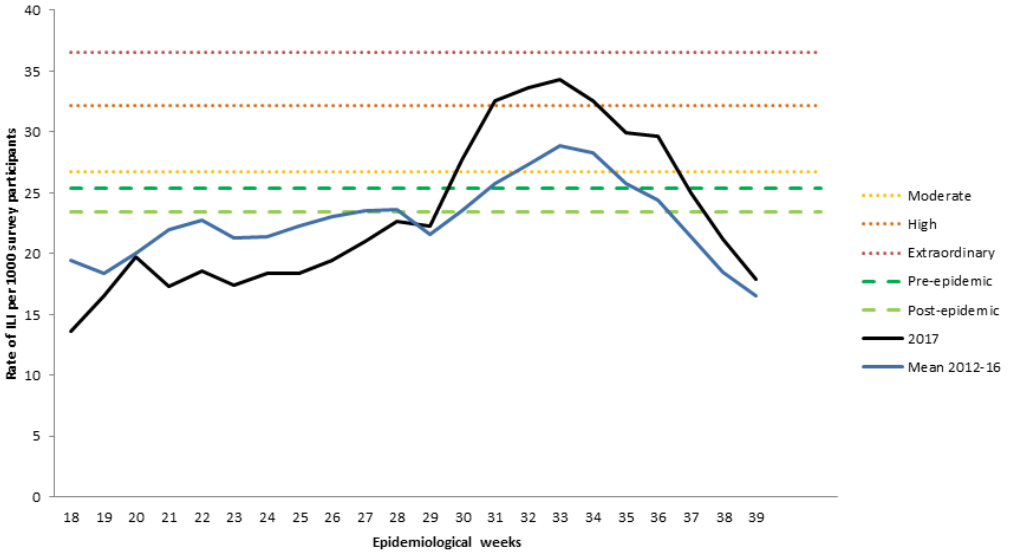
Transmission indicator – parameter 1

Rate of ILI per 1000 **Flutracking** survey participants, by epidemiological week, 2012-2017



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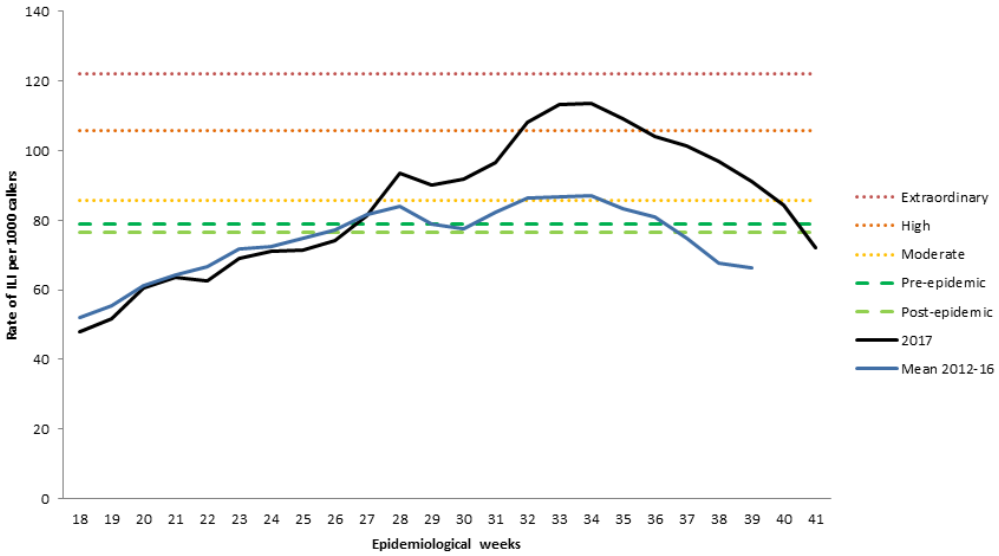
Transmission indicator – parameter 2

Rate of ILI per 1000 **Healthdirect** callers, by epidemiological week, 2012-2017



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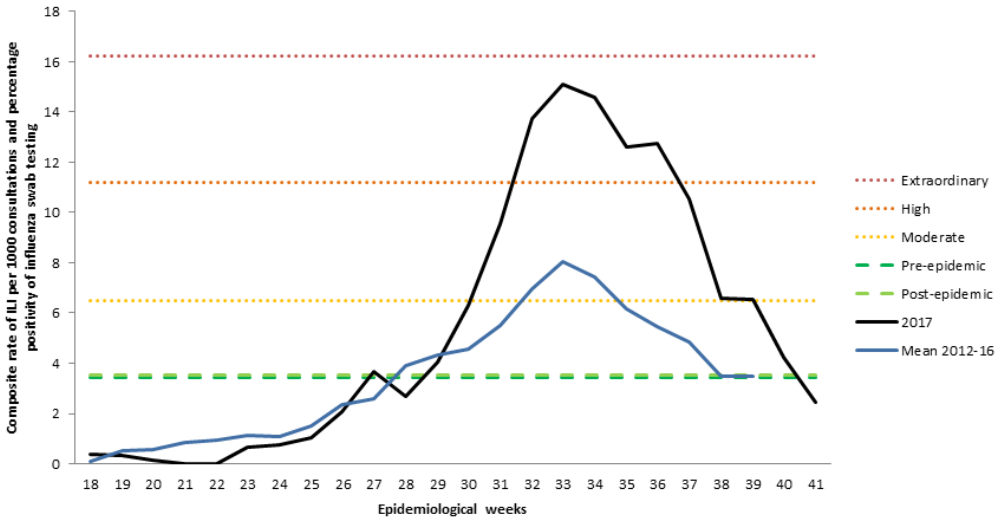
Transmission indicator – parameter 3

Composite rate of ILI per 1000 consultations and percentage positivity of influenza swab testing at **ASPREN** sites, by epidemiological week, 2012-2017



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PISA - Australian data parameters

Severity Indicators					
Transmission		**Impact**		**Seriousness of disease**	
System	**Parameter**	**System**	**Parameter**	**System**	**Parameter**
Flutracking	Rate of ILI per 1000 survey participants	Flutracking	Rate of absenteeism from regular duties per 1000 survey participants with ILI	Healthdirect	Cumulative rate of callers with ILI advised to seek urgent medical attention per 1000 Healthdirect callers with ILI (by age group:<15, 15-64 and 65+)
Healthdirect	Rate of ILI per 1000 callers	FluCAN	Rate of confirmed influenza admissions per 1000 available hospital beds	FluCAN	Cumulative rate of ICU admissions per 100 confirmed influenza admissions
ASPREN	(Rate of ILI per 1000 consultations) x (% positivity of swab testing)				

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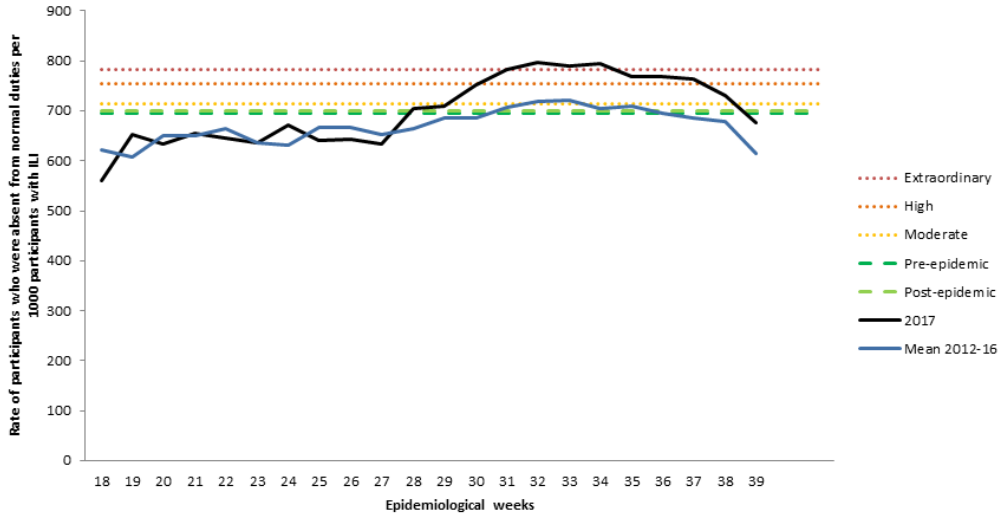
Impact indicator – parameter 1

Rate of survey participants who were absent from normal duties per 1000 **Flutracking** survey participants with ILI, by epidemiological week, 2012-2017



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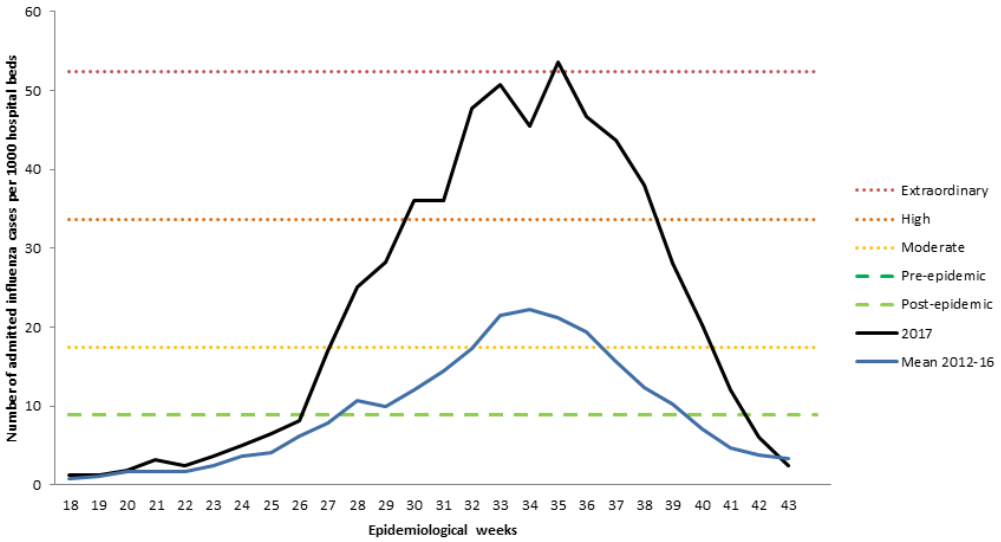
Impact indicator – parameter 2

Rate of confirmed influenza admissions per 1000 available hospital beds in **FluCAN** hospitals, by epidemiological week, 2012-2017



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PISA - Australian data parameters

Severity Indicators					
Transmission		**Impact**		**Seriousness of disease**	
System	**Parameter**	**System**	**Parameter**	**System**	**Parameter**
Flutracking	Rate of ILI per 1000 survey participants	Flutracking	Rate of absenteeism from regular duties per 1000 survey participants with ILI	Healthdirect	Cumulative rate of callers with ILI advised to seek urgent medical attention per 1000 Healthdirect callers with ILI (by age group:<15, 15-64 and 65+)
Healthdirect	Rate of ILI per 1000 callers	FluCAN	Rate of confirmed influenza admissions per 1000 available hospital beds	FluCAN	Cumulative rate of ICU admissions per 100 confirmed influenza admissions
ASPREN	(Rate of ILI per 1000 consultations) x (% positivity of swab testing)				

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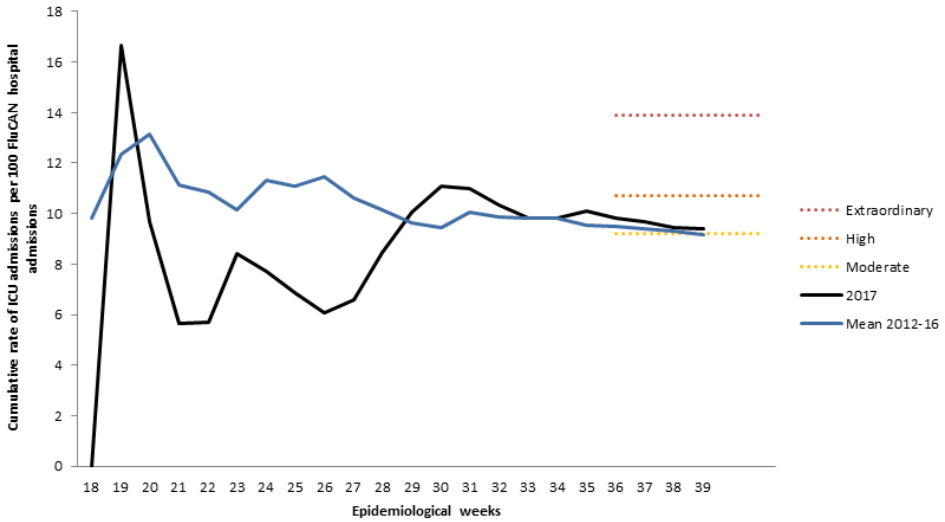
Seriousness indicator – parameter 1

Cumulative rate of ICU admissions per 100 confirmed influenza admissions to **FluCAN** hospitals, by epidemiological week, 2012-2017



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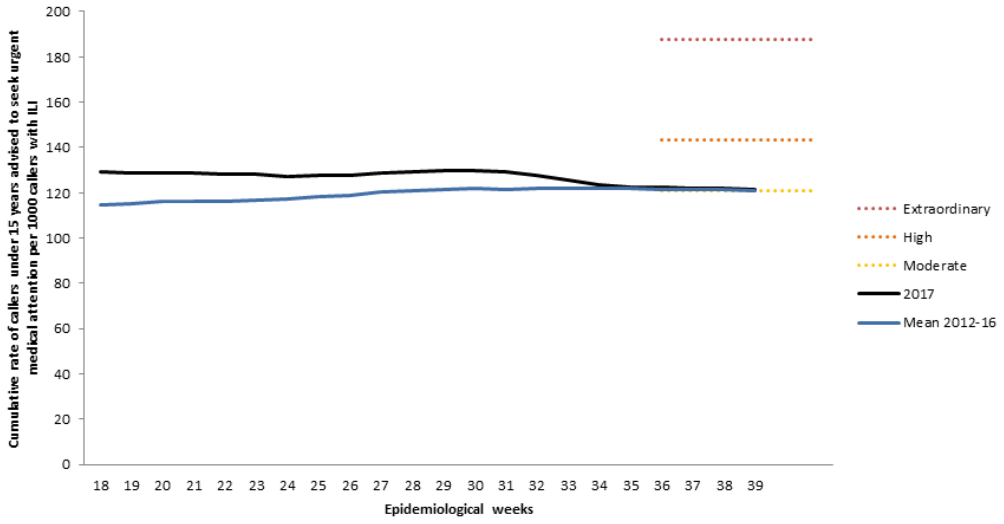
Seriousness indicator – parameter 2a

Cumulative rate of callers under 15 years advised to seek urgent medical attention per 1000 **Healthdirect** callers with ILI, by epidemiological week, 2012-2017



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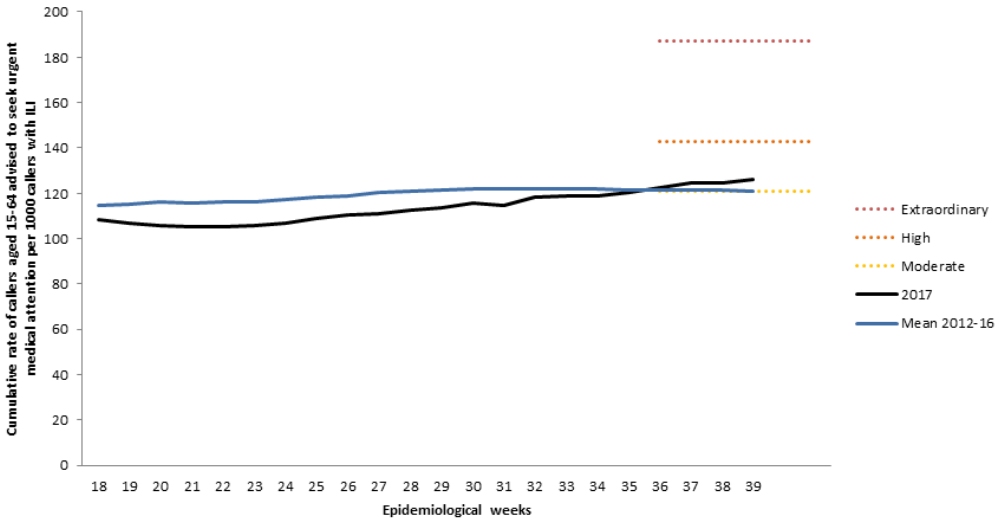
Seriousness indicator – parameter 2b

Cumulative rate of callers aged 15-64 advised to seek urgent medical attention per 1000 **Healthdirect** callers with ILI, by epidemiological week, 2012-2017



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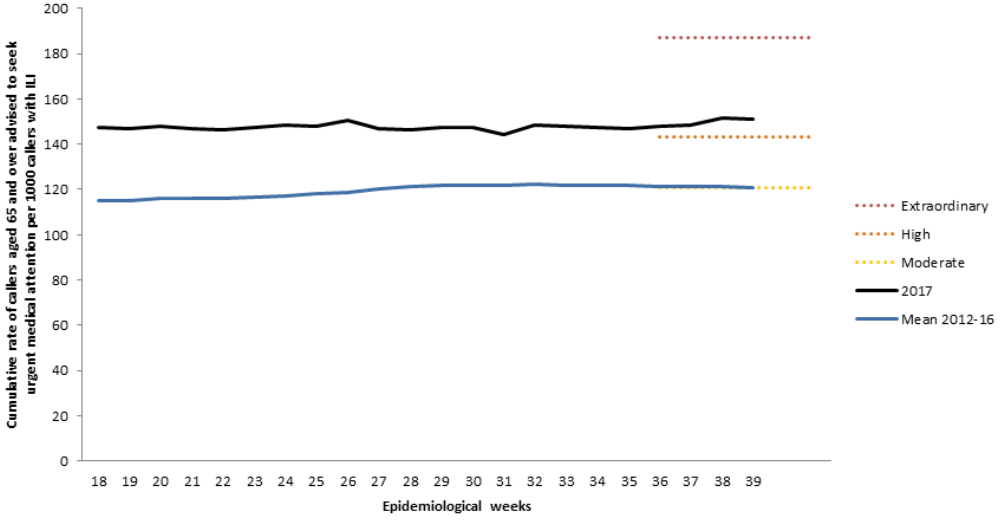
Seriousness indicator – parameter 2c

Cumulative rate of callers aged 65 years and over advised to seek urgent medical attention per 1000 **Healthdirect** callers with ILI, by epidemiological week, 2012-2017



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2017 season

Parameter	Epidemic start week	Epidemic end week	Peak week	Threshold reached
TRANSMISSION				
Flutracking	30	38	33	High
Healthdirect	27	41	34	High
ASPREN	27/29	41	33	High
IMPACT				
Flutracking	28	39	32	Extraordinary
FluCAN	27	42	35	Extraordinary
SERIOUSNESS				
Healthdirect <15	N/A	N/A	N/A	Moderate
Healthdirect 15-64	N/A	N/A	N/A	Moderate
Healthdirect ≥65	N/A	N/A	N/A	High
FluCAN	N/A	N/A	N/A	Moderate

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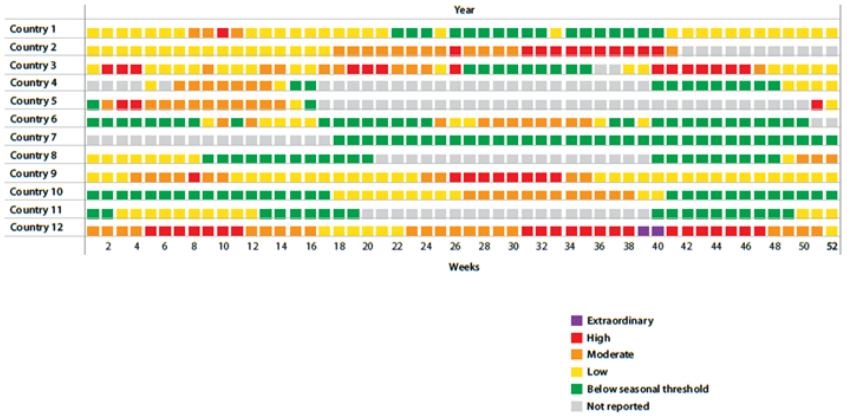
Going forward

- Updating thresholds
- National assessment
- International assessment



Source: World Health Organization. Pandemic influenza severity assessment. Geneva: World Health Organization, May 2017.

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Acknowledgements

Dr Aparna Lal (ANU)
Ms Christina Bareja (Department of Health)
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Australian National University

Appendix 2C – Abstract and presentation for the Australian Public Health Conference

'Leadership in public health: Challenges for local and planetary communities' - Accepted for presentation in Cairns, 28 September 2018

Quantifying influenza severity in Australia

Context

Australian influenza surveillance traditionally uses historical ranges and expert opinion to determine the influenza seasonal period and its severity. The World Health Organization has recently published Pandemic Influenza Severity Assessment (PISA) guidance for in-country implementation to standardise and enhance global capacity to monitor severe and pandemic influenza. As globalisation increases the interface between communities of animals and humans, the threat of emerging influenza strains and transmission between populations makes detecting severe influenza increasingly important.

Process

National data from sentinel GP surveillance, hospital surveillance, a public health hotline and an influenza-like illness survey system were used to measure PISA's severity indicators (transmission, impact and seriousness). Thresholds for indicator parameters were set using 2012-2016 data and then applied to 2017 seasonal data.

Analysis

Multiple sources of Australian data measured and produced thresholds for each severity indicator, including confirmed influenza data to validate measurements. When thresholds were applied to the 2017 season, there was good agreement between all data sources in measuring each indicator's activity. The season was characterised as having high transmission and extraordinary impact. Seriousness was characterised as moderate in all groups except those aged ≥65 years where it was high.

Outcomes

Evidence-based, internationally comparable, timely measurement of national influenza severity is now possible in Australia. This measurement can inform the scale, focus and timing of activities in response to seasonal and pandemic influenza and maximise the impact of activities. By leading the way globally through the application of PISA in Australia, we hope to encourage adoption of severity assessment internationally.

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Department of Health

Quantifying influenza severity in Australia

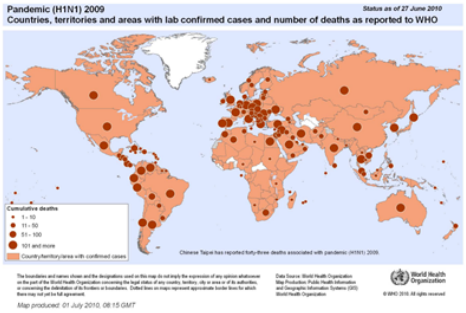
Kaitlyn Vette
Australian National University
Office of Health Protection, Department of Health

28 September 2018

Australian National University

Australian Government
Department of Health

Development of the Pandemic Influenza Severity Assessment



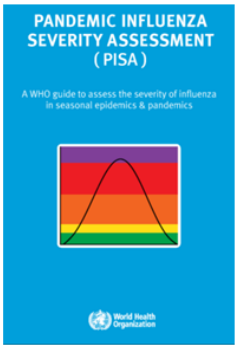


Image sources: World Health Organization. Pandemic influenza severity assessment. Geneva: World Health Organization, 2017.
Getty images, 2009

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Australian data parameters for severity assessment

Flutracking – ILI survey system

FluCAN – hospital-based influenza surveillance

HealthDirect – public health hotline

ASPREN – GP-based ILI and influenza surveillance

Severity Indicators					
Transmission		**Impact on society**		**Seriousness of disease**	
System	**Parameter**	**System**	**Parameter**	**System**	**Parameter**
Flutracking	Rate of ILI per 1000 survey participants	Flutracking	Rate of absenteeism from regular duties per 1000 survey participants with ILI	HealthDirect	Cumulative rate of callers with ILI advised to seek urgent medical attention per 1000 callers with ILI (by age group: <15, 15-64 and 65+)
HealthDirect	Rate of ILI per 1000 callers	FluCAN	Rate of confirmed influenza admissions per 1000 available hospital beds	FluCAN	Cumulative rate of ICU admissions per 100 confirmed influenza admissions
ASPREN	(Rate of ILI per 1000 consultations) x (% positivity of swab testing)				

ILI: Influenza-like illness, ICU: Intensive care unit, GP: general practitioner

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The 2017 season

Peak activity of severity indicators by data source in 2017

Thresholds and activity levels	Transmission	Impact on society	Seriousness
Extraordinary activity		**Flutracking** (ILI absenteeism rate) **FluCAN** (hospital beds taken up by flu cases)	
EXTRAORDINARY THRESHOLD			
High activity	**Flutracking** (incidence rate) **HealthDirect** (incidence rate) **ASPREN** (composite incidence rate and percent influenza positive)		**HealthDirect ≥65 yrs** (rate of ILI directed to hospital)
HIGH THRESHOLD			
Moderate activity			**HealthDirect 15-65 yrs** (rate of ILI directed to hospital) **HealthDirect <15 yrs** (rate of ILI directed to hospital) **FluCAN** (Flu ICU admission rate)
MODERATE THRESHOLD			
Low activity			
EPIDEMIC THRESHOLD			
No activity			

ILI: Influenza-like illness, ICU: Intensive care unit

Vette K, Bareja C, Clark R & Lal A. Establishing thresholds and parameters for pandemic influenza severity assessment, Australia. Bulletin of the World Health Organization. 2018 ;96(8):558.

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Appendix 2D - Writing for a non-technical audience: remodelling of the Australian Influenza Surveillance Report

Australian Government
Department of Health

AUSTRALIAN INFLUENZA SURVEILLANCE REPORT

No. 06, 2018
30 July to 12 August 2018

The Department of Health acknowledges the providers of the many sources of data used in this report and greatly appreciates their contribution.

KEY MESSAGES

- **Activity –** Person to person transmission of influenza and influenza-like illness (ILI) in the community is low and remains within or below the bounds of previous years. Rhinovirus was the most common respiratory virus detected in patients presenting with ILI to sentinel general practices this fortnight.
- **Severity –** Due to low numbers and the instability of data early in the season, there is no indication of the potential severity of the 2018 season at this time.
- **Impact –** Currently, the impact of circulating influenza on society is low.
- **Virology –** This fortnight, the majority of confirmed influenza cases reported nationally were influenza A (87%). Where subtyping information was available, influenza A(H1N1)pdm09 was most common.

ANALYSIS

Introduction

Each year, the influenza virus changes and different strains can circulate in the population. Particular strains and subtypes of influenza can affect different groups of the population more than others. Depending on the susceptibility of the population, the strains that are circulating and the changes to the virus itself, the influenza season can be very different year to year. Our surveillance systems help us to understand influenza activity, severity of the infection in individuals and impact of the illness on society in Australia. We are also able to monitor which influenza strains are circulating, which populations might be more affected, the effectiveness of the vaccine, and any resistance to antiviral drugs that has developed.

1. Activity

Activity measures the capacity of circulating influenza to spread from person to person and may be measured indirectly through systems that monitor symptoms of influenza-like illness and more directly through systems that monitor laboratory confirmed influenza. In temperate climates, influenza most commonly circulates in the winter months and in tropical climates it can have multiple peaks of activity during the year. While Australia has diverse subnational climates, national surveillance represents a temperate pattern with one epidemic wave generally between April and October.

Influenza-like illness (ILI)

Overall, ILI in the community is low and is within historical ranges.

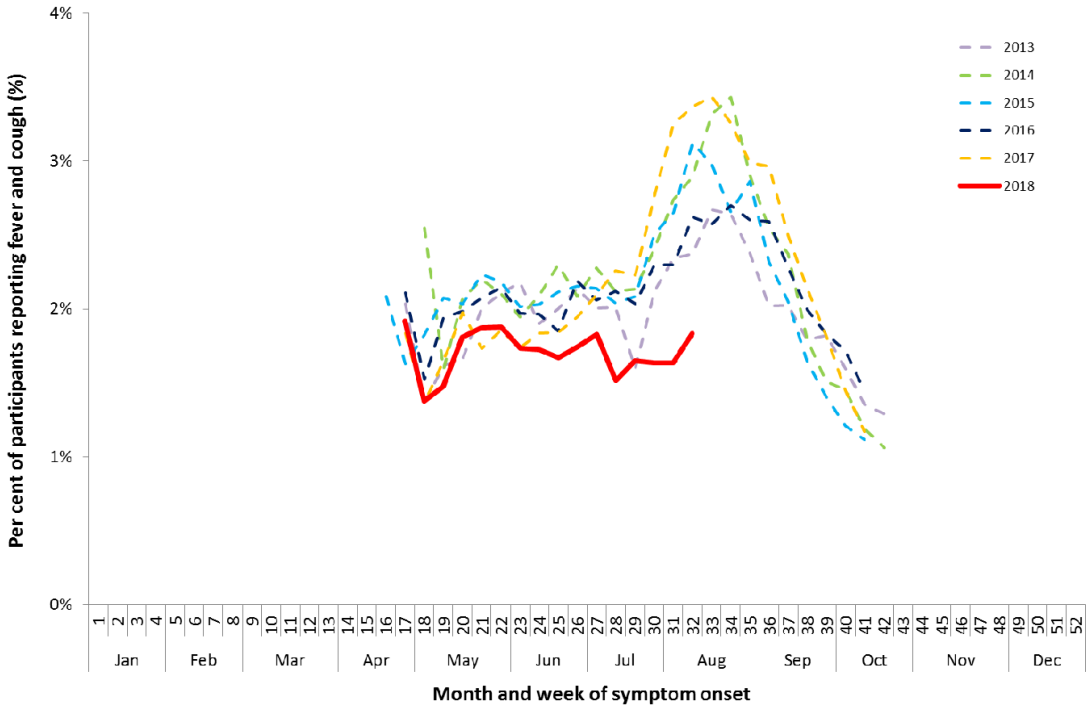
- **Flutracking:** 1.8% of Flutracking participants reported ILI (fever and cough) in the week ending 12 August 2018 (week 32; Figure 1). This is a slight increase from the proportion reported in week 31 (1.6%). Activity remains consistently low. This fortnight is below the range of the levels in August for the last five years.
- **Healthdirect:** 6.8% of calls to the Healthdirect public health hotline were related to ILI in weeks 31 and 32 (Figure 2). When compared to trends in recent years, the level of ILI activity amongst callers is on the low end of the historical range. In the last fortnight, the number of ILI-related calls as a percentage of all calls remained the same as the week prior, with an overall downwards trend since mid-July.
- **Sentinel General Practitioners (ASPREN):** 6.1 per 1,000 consultations in sentinel general practices were attributed to ILI in week 32 (Figure 3). ILI consultations are below the historical range for this time of year and have an overall increasing trend in activity.

Confirmed influenza

Influenza is circulating at very low levels and is not a major cause of ILI this fortnight.

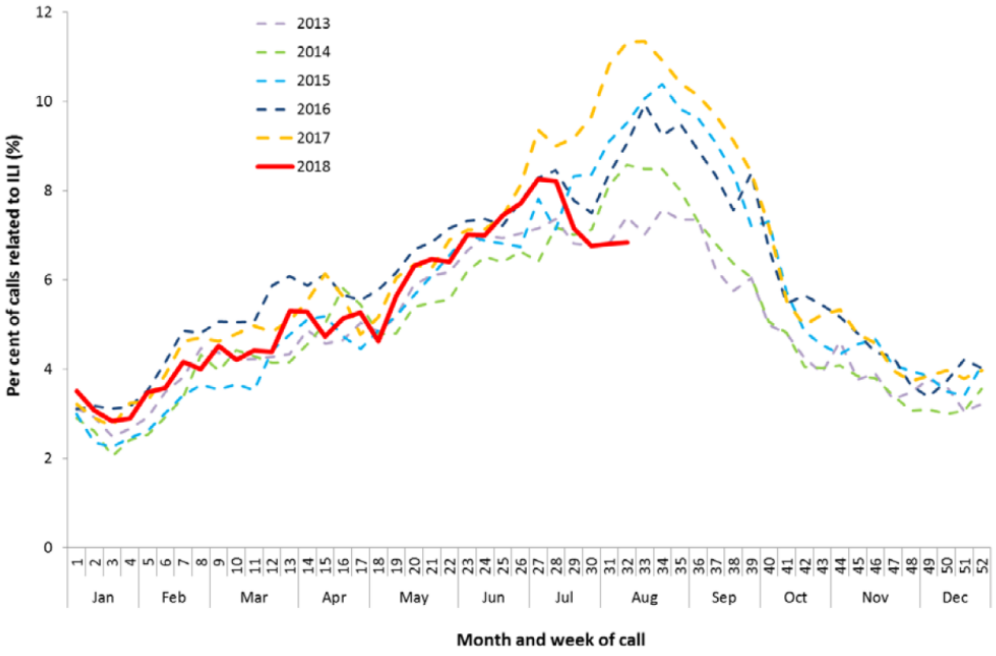
- **Proportion of ILI with confirmed influenza seen by sentinel GPs:** Of the 111 ILI cases presenting to sentinel ASPREN GPs this fortnight who were tested for influenza, 9 (8.1%) had a positive result. This is a decrease from the previous fortnight when 8.4% (13/154) of swabbed ILI patients tested positive for influenza. Rhinovirus was the most common respiratory virus detected in swabbed patients this fortnight (n=19, 17.1%).
- **Proportion of ILI with confirmed influenza in sentinel labs:** Detections of influenza across all sentinel laboratories this reporting fortnight remained low (Figure 4). The pooled unweighted percentage of tests positive for influenza across all sentinel laboratories was 5.3% in week 32, which was an increase from 3.2% reported in week 31. Respiratory syncytial virus (RSV) was the respiratory virus most commonly detected by PathWest and the Institute of Clinical Pathology and Medical Research (ICPMR) in this reporting fortnight. The most commonly detected respiratory viruses detected by the Victorian Infectious Disease Reference Laboratory (VIDRL) was RSV in week 31 and RSV and picornavirus in week 32. The respiratory virus most commonly detected by Tasmania was rhinovirus in both weeks.
- **NNDSS notifications**: This fortnight there were 2,248 notifications of laboratory confirmed influenza to the National Notifiable Diseases Surveillance System (NNDSS), which is an increase in reported cases compared to the previous fortnight (n=1,534). There have been 21,831 notifications year to date. While national notifications of laboratory confirmed influenza were higher than usual in January and February, consistent with high activity experienced in the Northern Hemisphere at that time, notifications returned to normal range by March (Figure 5).
- **FluCAN:** Since seasonal sentinel hospital surveillance began on 3 April 2018, a total of 203 people have been admitted with confirmed influenza (Figure 6). This is fewer hospitalisations than the 5 year average for the same period (n=810).

Figure 1. Proportion of fever and cough among FluTracking participants, Australia, between May and October, 2013 to 2018, by month and week.



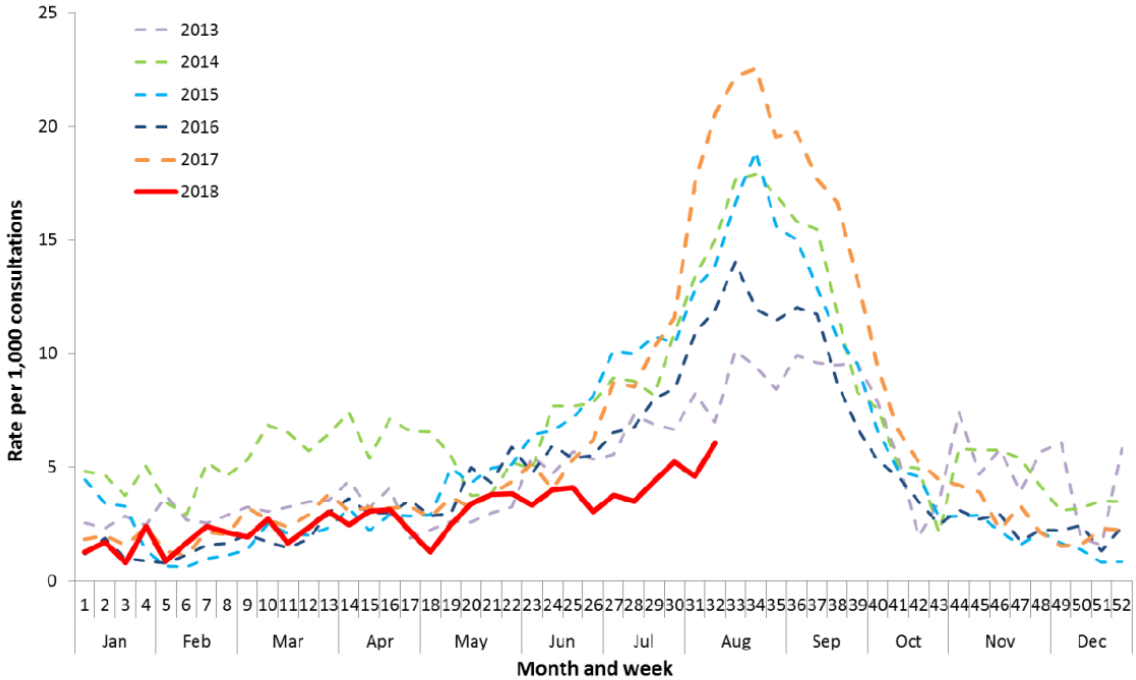
Source: FluTracking

Figure 2. Per cent of calls to Healthdirect related to ILI, Australia, 1 January 2013 to 12 August 2018, by month and week of call.



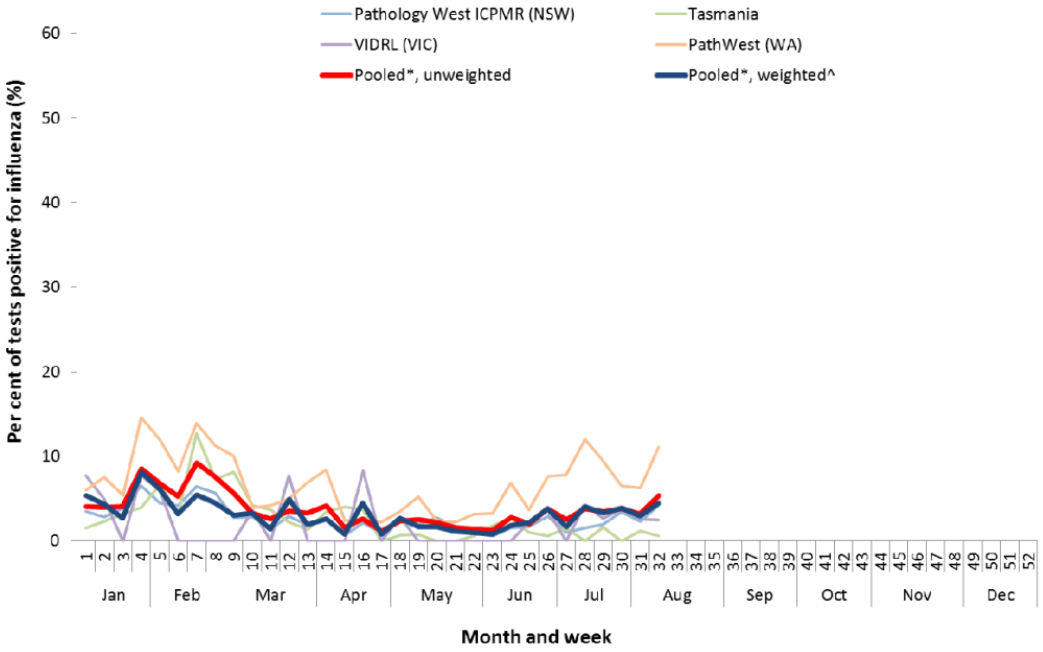
Source: Healthdirect

Figure 3. Unweighted rate of ILI reported from sentinel GP surveillance systems, Australia, 1 January 2013 to 12 August 2018, by month and week.



Source: ASPREN and VicSPIN (weeks 31 and 32 of 2018 do not include VicSPIN data)

Figure 4. Proportion of sentinel laboratory tests positive for influenza, 1 January to 12 August 2018, by contributing laboratory or jurisdiction and month and week.

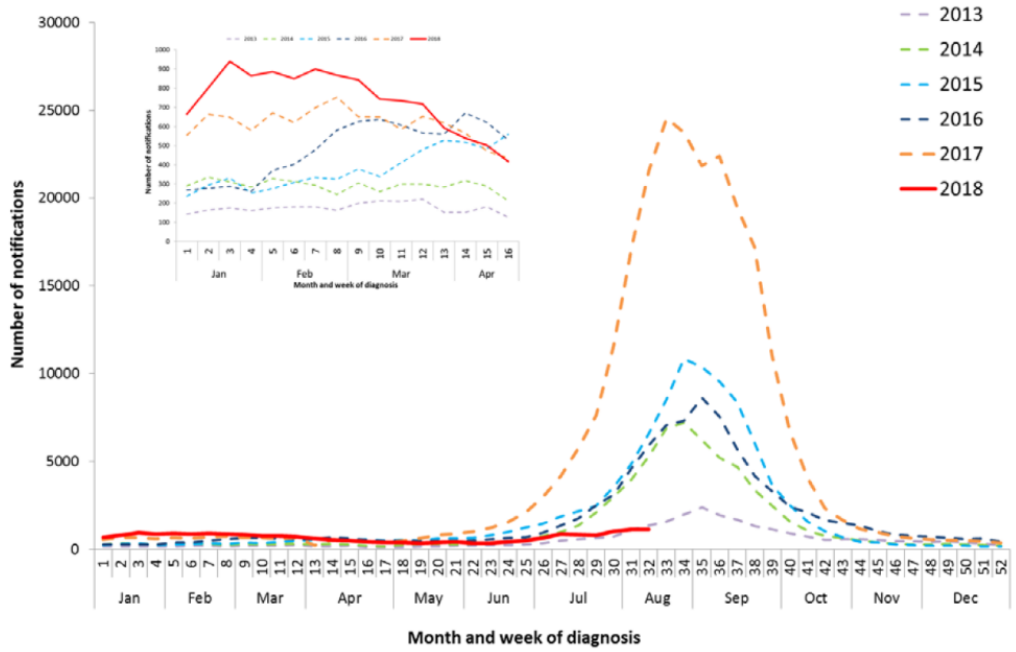


* Pooled percentage positive indicators should be interpreted with caution, noting that collectively pooled contributing laboratories are not representative of testing across Australia and individually contributing laboratories may not be representative of the jurisdiction in which they are located.

^ Weighted according to jurisdictional population in which laboratories are located.

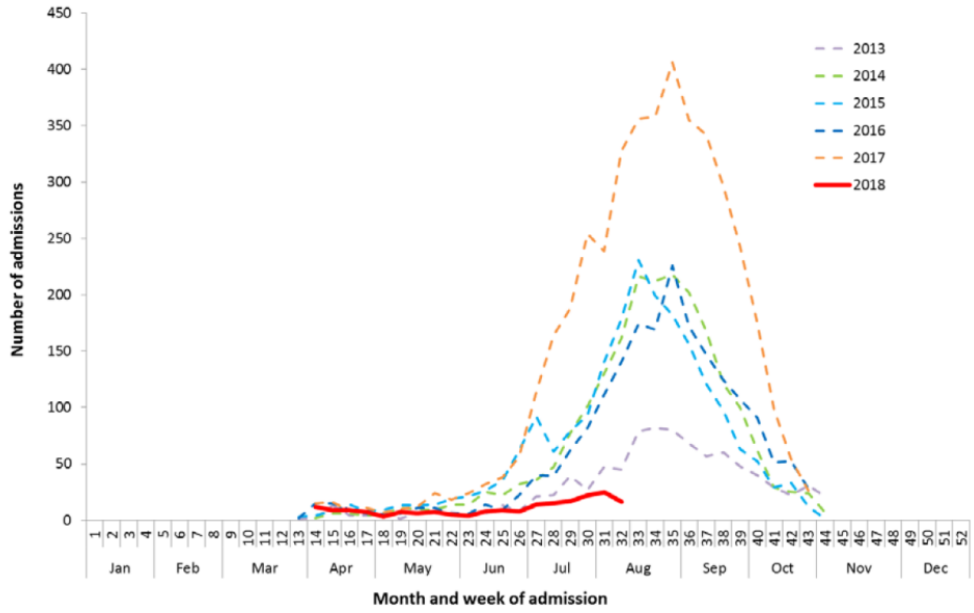
The percentage of tests positive for influenza in the interseasonal period should be interpreted with caution due to small numbers of tests being undertaken in this time, resulting in high variability in the indicators.

Figure 5. Notifications of laboratory confirmed influenza, Australia, 1 January 2013 to 12 August 2018, by month and week of diagnosis.



Source: NNDSS

Figure 6. Number of influenza hospitalisations at sentinel hospitals, between March and October, 2013 to 2018 by month and week.



Source: FluCAN

Geographical distribution of activity

- **Jurisdictional reports**: In the fortnight ending 12 August 2018, the geographic spread of influenza activity was reported by state and territory health departments as being sporadic in the Australian Capital Territory (ACT), both regions of Northern Territory (NT), the Tropical and Central regions of Queensland (QLD), Tasmania (TAS) and the Northwest region of Western Australia (WA). Activity was reported as being localised in the Southern region of QLD, South Australia (SA), Victoria (VIC) and the Rural south region of WA. New South Wales (NSW) reported regional activity levels and the Perth metro region of WA reported widespread levels of activity. There was no change in influenza activity compared to the previous fortnight in ACT, the Central Australia region of NT, SA and all regions of WA. An increase in activity was reported for NSW, the Top End region of NT, all regions of QLD, and Victoria. Tasmania reported a decrease in activity. (Figure 7).
- **NNDSS**: Of the 2,248 notifications of influenza reported to the NNDSS in the last fortnight, 981 were from NSW, 682 from QLD, 240 from WA, 226 from VIC, 79 from SA, 23 from ACT, 11 from TAS and 6 from NT (Figure 8). Of the 21,831 notifications of influenza reported to the NNDSS this year to 12 August 2018, 7,120 from NSW, 6,697 were from QLD, 3,225 from VIC, 2,593 from WA, 1,687 from SA, 217 from ACT, 158 from TAS and 134 from the NT.

For further information regarding influenza activity at the jurisdictional level, please refer to the following State and Territory health surveillance reports:

- ACT: Influenza report (http://health.act.gov.au/node/41)
- NSW: Influenza Surveillance Report (http://www.health.nsw.gov.au/Infectious/Influenza/Pages/reports.aspx)
- QLD: Statewide Weekly Influenza Surveillance Report (https://www.health.qld.gov.au/clinical-practice/guidelines-procedures/diseases-infection/surveillance/reports/flu)
- SA: Weekly Epidemiological Summary (Influenza section) (http://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/about+us/health+statistics/surveillance+of+notifiable+conditions)
- TAS: fluTAS Reports (http://www.dhhs.tas.gov.au/publichealth/communicable_diseases_prevention_unit)

- VIC: Influenza Surveillance Reports (https://www2.health.vic.gov.au/public-health/infectious-diseases/infectious-diseases-surveillance/seasonal-influenza-reports)
- WA: Virus WAtch (http://ww2.health.wa.gov.au/Articles/F_I/Infectious-disease-data/Virus-WAtch)

Figure 7. Map of influenza activity by state and territory, Australia, 30 July to 12 August 2018.

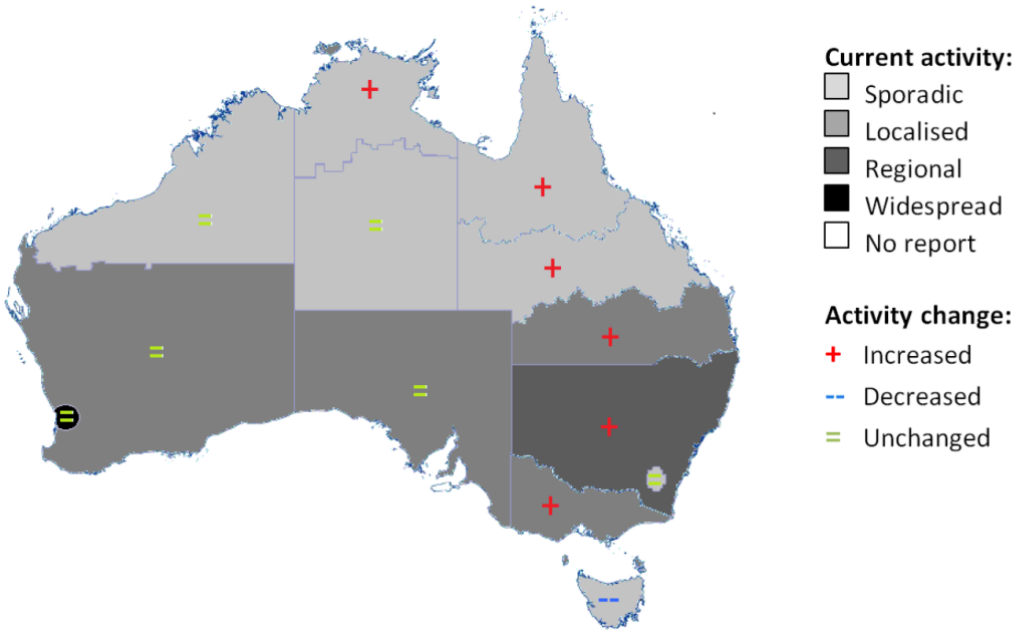
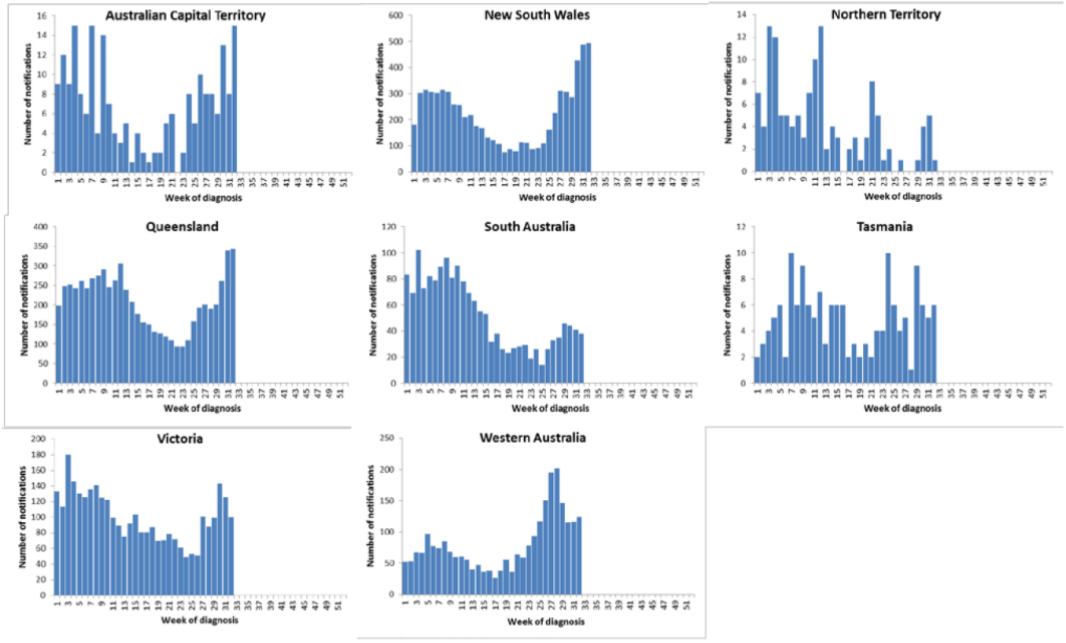


Figure 8. Notifications of laboratory confirmed influenza, 1 January to 12 August 2018, by state or territory and week.



Source: NNDSS

2. Severity

Severity is a measure of adverse outcomes or complications as a result of influenza or influenza-like illness (ILI) such as hospital referrals, admissions, need for intensive care and deaths. Measuring and understanding the severity of circulating influenza is difficult to establish at the beginning of the influenza season. The proportion of confirmed influenza cases with serious outcomes might be skewed initially because there are only a small number of people with influenza at the beginning of the season. This means that the measure of severity will vary substantially fortnight to fortnight until after the peak of the season when there is enough data for measurements to stabilise. An assessment of severity will be provided once the signals become clearer.

Intensive care admissions

- **FluCAN**: This fortnight, five of the 41 people admitted to sentinel hospitals with confirmed influenza were admitted to ICU. Since seasonal sentinel hospital surveillance began on 3 April 2018, 9.4% (n=19) of the 203 people admitted to sentinel hospitals with confirmed influenza were admitted to ICU.

Deaths in confirmed influenza cases

- **NNDSS**: So far in 2018, 35 influenza associated deaths have been notified to the NNDSS. The majority of deaths were due to influenza A (77.1%, n=27). Of the notifications where influenza A subtyping information was available (n=7), A(H3N2) was most common (n=4). The median age of deaths notified was 79 years (range 2 to 100 years). The number of influenza-associated deaths reported to the NNDSS does not represent the true mortality associated with this disease. The number of deaths is reliant on the follow up of cases to determine the outcome of their infection. The follow up of cases is not a requirement of notification, and are only inclusive of laboratory-confirmed cases of influenza. Due to retrospective revision, the variation across jurisdictions in methodology, representativeness and timeliness of death data, and reporting of an outcome of infection not being a requirement of notification, year on year comparisons of deaths in notified cases of influenza may not be reliable.

3. Impact

Impact measures how the influenza epidemic affects society, including stress on health-care resources and societal and economic consequences.

Overall this fortnight, impact on society caused by circulating influenza is low.

Absenteeism

- **Flutracking**: 1.3% of Flutracking survey respondents reported having ILI and taking time off regular duties while unwell in the weeks 31 and 32. This is a low level of impact when compared to trends in recent years, the five year average for week 32 is 2.2%.

Use of hospital beds

- **FluCAN:** Since seasonal sentinel hospital surveillance began on 3 April 2018, 2.9% of hospital beds available in FluCAN hospitals were occupied by patients with confirmed influenza. This is a low level of impact when compared to temporal trends.

4. Virology

Influenza A and B are the two main types of influenza virus. Influenza A can be can be categorised into multiple subtypes and influenza B can be grouped into two lineages.

National notification data

- **NNDSS:** In the reporting fortnight, 87.0% of notifications of laboratory confirmed influenza to the NNDSS were influenza A (76.6% influenza A(unsubtyped), 8.2% influenza A(H1N1)pdm09 and 2.2% influenza A(H3N2)), and 12.6% were influenza B (Figure 9).
- **NNDSS:** For the year to 12 August 2018, 66.9% of notifications of laboratory confirmed influenza to the NNDSS were influenza A (57.0% influenza A(unsubtyped), 6.4% influenza A(H1N1)pdm09 and 3.4% influenza A(H3N2)), 32.6% were influenza B and less than 1.0% were influenza A&B co-infections or untyped. The proportion of all notifications year to date reported as influenza A has ranged across jurisdictions from 54.5% in the NT to 75.4% in WA (Figure 10).

Reference Laboratory data

- **World Health Organization Collaborating Centre for Reference and Research on Influenza (WHOCC):** From 1 January to 13 August 2018, the WHOCC characterised 399 influenza viruses. Of these, 45% were influenza A(H1N1)pdm09, 31% were influenza A(H3N2), 22% were influenza B Yamagata lineage and 1% were influenza B Victoria lineage.

Sentinel laboratory surveillance

- In the reporting fortnight, 96.3% of influenza positive samples detected in sentinel laboratories were influenza A (48.5% were influenza A(unsubtyped), 43.3% influenza A(H1N1)pdm09, and 4.5% were influenza A(H3N2)) and 3.7% were influenza B (Figure 11).

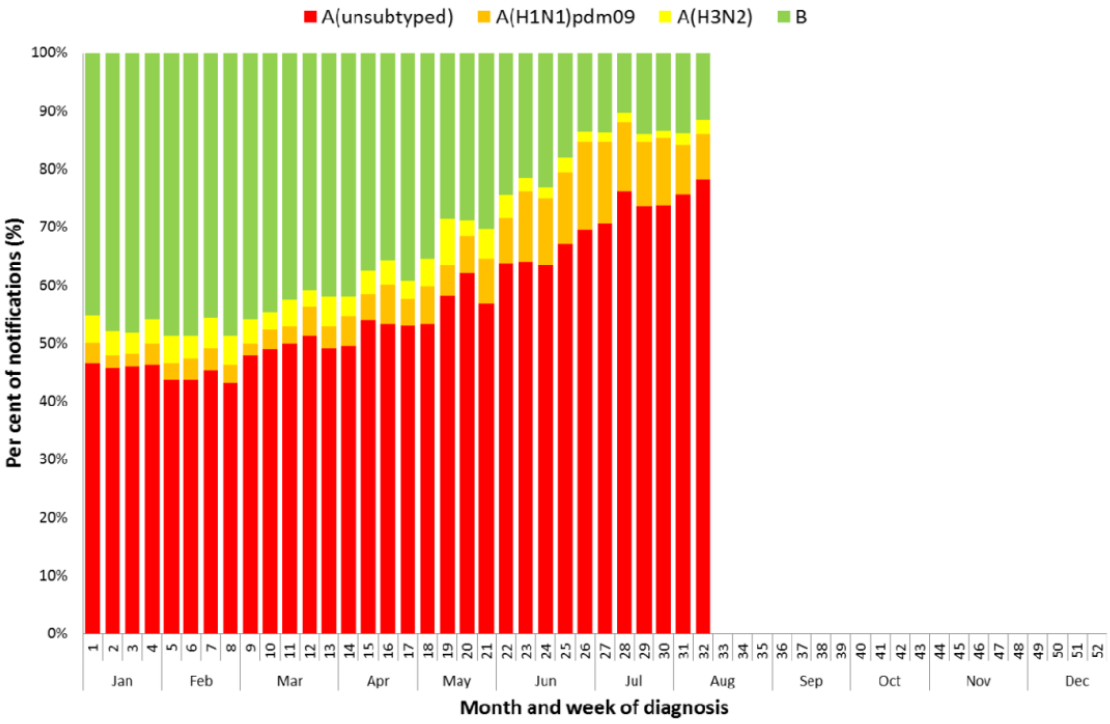
Sentinel GP surveillance

- **ASPREN**: Of the nine influenza positive samples detected this fortnight through swab testing patients presenting with ILI to ASPREN sentinel GPs, seven were influenza A (H1N1), one was Influenza A (H3N2) and one was influenza B (Figure 12).

Sentinel hospital surveillance

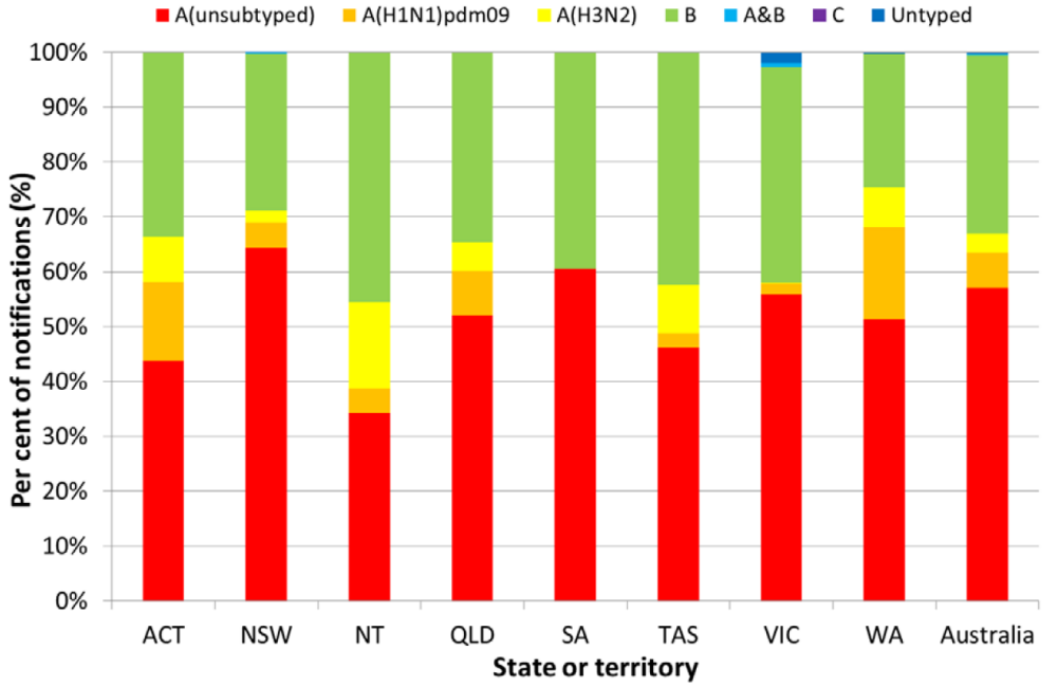
- **FluCAN**: Since seasonal sentinel hospital surveillance began on 3 April 2018, 77.3% of confirmed influenza to sentinel hospitals were influenza A (54.7% A(unsubtyped), 21.7% influenza A(H1N1)pdm09 and 1.0% influenza A (H3N2)) and 22.7% were influenza B. (Figure 13).

Figure 9. Per cent of laboratory confirmed influenza, Australia, 1 January to 12 August 2018, by subtype and week.



Source: NNDSS

Figure 10. Per cent of notifications of laboratory confirmed influenza, Australia, 1 January to 12 August 2018, by subtype and state or territory.



Source: NNDSS

Figure 11. Proportion of sentinel laboratory tests positive for influenza and total number of specimens tested, 1 January to 12 August 2018, by subtype and month and week.

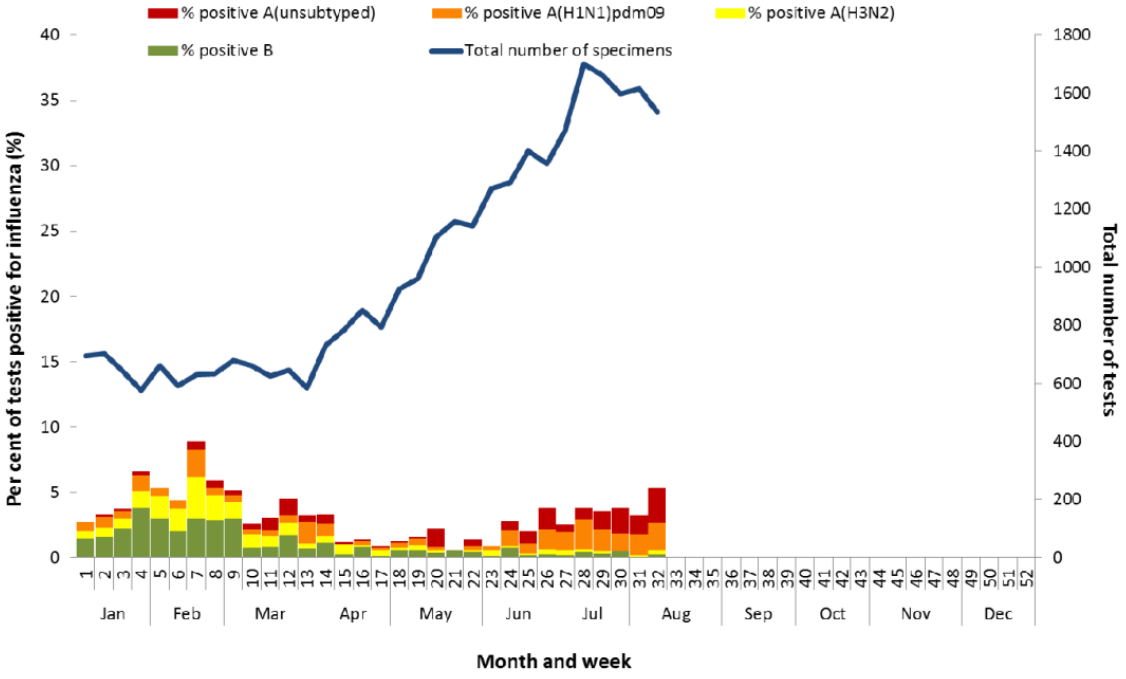
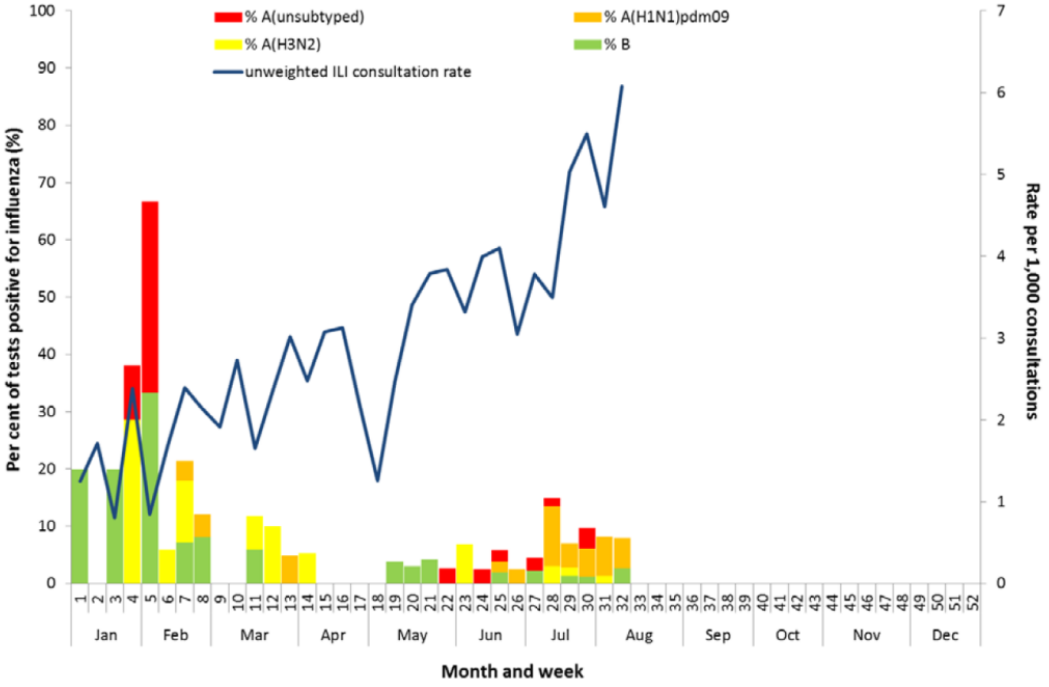
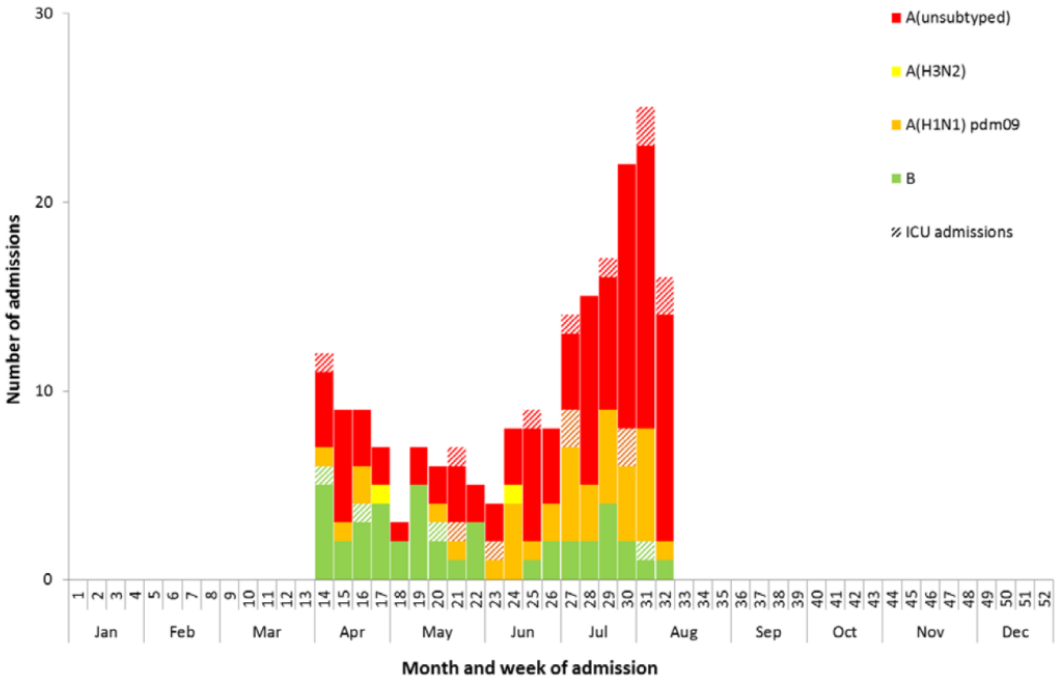


Figure 12. Proportion of respiratory viral tests positive for influenza in ASPREN ILI patients and ASPREN ILI consultation rate, Australia, 1 January to 12 August 2018, by month and week.



Source: ASPREN

Figure 13. Number of influenza hospitalisations at sentinel hospitals by subtype and ICU admission, 3 April to 12 August 2018, by month and week.



Source: FluCAN

5. At-risk Populations

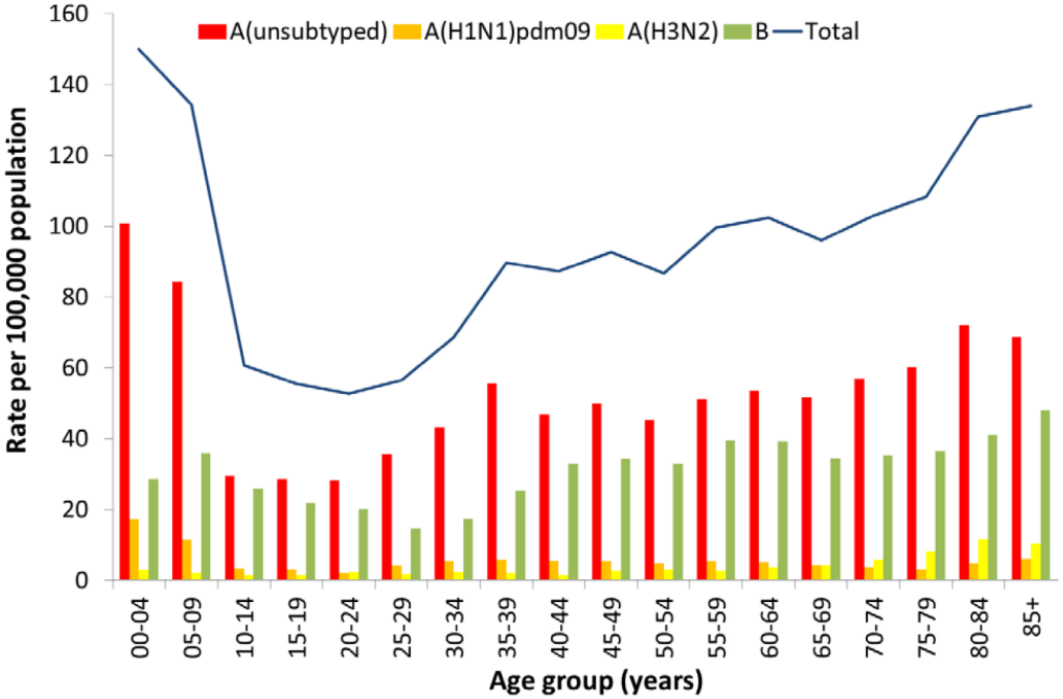
National notification data

- **NNDSS:** So far in 2018, notification rates have been highest in children under 10 years (142.2 notifications per 100,000), with a secondary peak in adults aged 80 years or older (132.5 notifications per 100,000) (Figure 14). Where subtyping information is available, notifications of influenza A(H1N1)pdm09 were highest in children aged less than 4 years (17.3 per 100,000) and notifications of influenza A(H3N2) were highest in adults aged 80-84 years (11.6 per 100,000). The rate of influenza B was highest in those aged over 80 years (44.7 notifications per 100,000).

Sentinel hospital surveillance

- **FluCAN:** Since seasonal sentinel hospital surveillance began on 3 April 2018, 41.6% of people admitted with confirmed influenza were children aged 15 years and younger, 37.1% were adults aged between 16 and 64 years and 21.3% were adults aged 65 years and older.

Figure 14. Rate of notifications of laboratory confirmed influenza, Australia, 1 January to 12 August 2018, by age group and subtype.



Source: NNDSS

6. Vaccine effectiveness

Australian Influenza Vaccines Composition 2018

The influenza virus strains included in the 2018 seasonal influenza vaccines in Australia are:

- A/Michigan/45/2015, (H1N1)pdm09-like virus;
- A/Singapore/INFIMH-16-0019/2016, (H3N2)-like virus; and
- B/Phuket/3073/2013-like virus, Yamagata lineage.
- B/Brisbane/60/2008-like virus, Victoria lineage.

The best way to determine how well the vaccine protects against circulating viruses during the season is by determining the vaccine effectiveness. These estimates provide an indication of how effective the vaccine was in providing protection against influenza infection, but can only be determined towards the end of the influenza season.

WHOCC

From 1 January to 13 August 2018, 270 isolates were characterised for similarity to the corresponding vaccine components by haemagglutination inhibition (HI) assay (Table 1). Influenza A(H1N1)pdm09 viruses and viruses from both influenza B lineages appeared to be antigenically similar to the corresponding vaccine components. One Influenza A(H1N1)pdm09, two influenza B(Yamagata) and no influenza B(Victoria) isolates were characterised as low reactors. The influenza A(H3N2) isolates that were able to be assessed by HI assay appeared to be reasonably matched, although there are ongoing technical issues that significantly limit the WHOCC's capacity to fully assess the similarity of circulating viruses to the vaccine strain. Three influenza A(H3N2) isolates were characterised as low reactors, and an additional 23 isolates were unable to be characterised in the HI assay due to insufficient haemagglutination titre.

Table 1. Australian influenza viruses typed by HI from the WHOCC, 1 January to 13 August 2018.

Type/Subtype	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	TOTAL
A(H1N1) pdm09	2	37	0	52	5	0	1	17	114
A(H3N2)	3	27	3	39	5	0	0	1	78
B/Victoria lineage	0	1	1	1	0	0	0	0	3
B/Yamagata lineage	3	32	10	22	4	0	0	4	75
Total	8	97	14	114	14	0	1	22	270

SOURCE: WHO CC
Note: Viruses tested by the WHO CC are not necessarily a random sample of all those in the community.
State indicates the residential location for the individual tested, not the submitting laboratory.
There may be up to a month delay on reporting of samples.

7. Antiviral Resistance

The WHOCC reported that from 1 January to 13 August 2018, none of the 176 influenza viruses tested for neuraminidase inhibitor resistance, demonstrated reduced inhibition to the antiviral drugs Zanamivir or Oseltamivir.

8. Data considerations

No one single system, including notification data, provides the full picture on influenza, because influenza is a common disease and its presenting symptoms are non-specific. The epidemiology of influenza is informed by a number of different systems based in the community, laboratories, primary care and hospitals, as well as official deaths and notifiable diseases data. The information in this report is reliant on the surveillance sources available to the Department of Health at the time of production.

Data in this summary is reported by International Organization for Standardization (ISO) 8601 weeks, with the week ending on Sunday. Throughout the summary, where the year to date is presented, this includes data from 1 January to 12 August 2018. NNDSS data were extracted on 17 August 2018. Due to the dynamic nature of the NNDSS and other surveillance systems, data in this report are subject to retrospective revision and may vary from data reported in other national reports and reports by states and territories. Detailed notes on interpreting the data presented in this report are available at the Department of Health's Australian Influenza Surveillance Report website (www.health.gov.au/flureport).

While every care has been taken in preparing this report, the Commonwealth does not accept liability for any injury or loss or damage arising from the use of, or reliance upon, the content of the report. Delays in the reporting of data may cause data to change retrospectively. For further details about information contained in this report please contact the Influenza Surveillance Team (flu@health.gov.au).

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Chapter 3: Evaluation of a surveillance system

Evaluation of the Australian Paediatric Surveillance Unit's surveillance of acute flaccid paralysis

"Without knowledge action is useless, and knowledge without action is futile"

– Abu Bakr

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Chapter 3 - Prologue

My role

The Australian Paediatric Surveillance Unit (APSU) has been conducting acute flaccid paralysis (AFP) surveillance in Australia since 1995. While there have been recent evaluations of national polio surveillance and the APSU as a whole (including their surveillance of 42 other conditions), there was an identified need to conduct a more focused evaluation of APSU's AFP surveillance. I completed a detailed evaluation using the United States Centers for Disease Control and Prevention's *Updated Guidelines for Evaluating Public Health Surveillance Systems* (CDC guidelines). I engaged heavily with the APSU, the National Enterovirus Reference Laboratory (NERL) and the Polio Expert Panel (PEP) to conduct the evaluation. I presented my results to PEP and provided my report to the APSU, NERL, the National Certification Committee for the Eradication of Poliomyelitis, and the Australian Government Department of Health.

Lessons learnt

This project provided me with an understanding of the complexities of polio surveillance and the importance of AFP as a mechanism for sensitive detection and control of the virus. It's quite remarkable the ways in which epidemiologists and public health experts have instigated innovative solutions to challenging surveillance issues. AFP surveillance is a clear example of this, and how important it is to think outside the box and work with what you have available to you.

Having worked in national communicable disease surveillance for a number of years, I had a broad understanding of key surveillance attributes. However, systematically applying the CDC guidelines gave me a much more practical appreciation of the features necessary for surveillance systems to meet their goals, and a new lens through which to consider my previous experiences.

This project also introduced me to the ethical considerations involved in enrolling participants in a study. As all of my other projects made use of existing data, I had not previously had to consider this aspect of study design. It was good experience to develop a participant information sheet and think about the ways in which you can appropriately gain informed consent from study participants.

Public health impact

AFP surveillance is the primary mechanism of sensitive case-based detection of poliovirus infections. As polio eradication comes within reach, the importance of sensitive AFP surveillance becomes increasingly paramount in informing and ensuring the end of virus circulation. The recent outbreak of vaccine-derived polio virus in Papua New Guinea highlights the importance of polio detection closer to home, and means that Australia must ensure that our AFP surveillance is the best it can be.

The findings of my evaluation show APSU's strengths, and highlight some changes that could be made to make surveillance more timely, simple and useful in detecting AFP. I hope that my recommendations will be helpful in strengthening AFP surveillance in Australia.

Acknowledgements

My field supervisor, Amy Bright, was key in navigating me to an evaluation project and was supportive when other iterations of an evaluation fell through. I would like to thank her, and Aparna Lal, for helping me plan and review this evaluation and for their time, perspectives and input.

I would like to thank NERL, PEP and APSU for their contributions to this evaluation and for providing the expert perspectives that gave this project shape. I particularly appreciate the efforts of Assoc. Prof. Bruce Thorley, Linda Hobday, Assoc. Prof. Yvonne Zurynski, Dr David Durrheim and Prof. Elizabeth Elliott, who provided me with the information I needed to conduct the evaluation, and who took the time to share historical context and insights about polio and AFP surveillance in Australia with me.

Anna Glynn-Robinson, the vaccine preventable diseases epidemiologist at the Department of Health, was very generous with her time in helping me to understand polio, its surveillance and the stakeholders involved across Australia. Jennie Hood, the director of the Communicable Diseases Epidemiology and Surveillance Section at the time, was very helpful in providing oversight and guidance throughout this project. I would also like to thank Jennie, as well as Katrina Knope and Patiyan Andersson for helping to review and validate my stakeholder survey.

Course activity requirements met

✓ Evaluate a surveillance system

✓ Literature review

Ethics statement

This study was approved by the Science and Medical Delegated Ethics Review Committee of the Australian National University (Protocol number 2017/623).

Abstract

Background: Surveillance of acute flaccid paralysis (AFP) is key to detecting cases of polio and achieving polio eradication. Polio elimination was achieved in the Western Pacific Region in 2000 and ongoing vigilance in surveillance is essential to ensure progress towards global polio eradication is sustained. This study aims to evaluate a primary mechanism of AFP surveillance in Australia, the Australian Paediatric Surveillance Unit (APSU).

Methods: The United States Centers for Disease Control and Prevention's (CDC) *Updated Guidelines for Evaluating Public Health Surveillance Systems* (CDC guidelines) was used to frame the assessment of APSU's AFP surveillance attributes. A survey of experts was conducted and data parameters were inspected to assess these attributes. Surveillance system managers were consulted to establish the current structure of the system and flow of data.

Results: The APSU was found to have high stability, acceptability, representativeness and predictive value positive. It was found to have moderate flexibility and data quality as well as sensitivity when combined with other systems. Simplicity, timeliness and usefulness were identified as needing improvement.

Conclusion: The APSU is an important component of AFP surveillance in Australia. In order to enhance the usefulness of the system, actions should be taken to increase the timeliness of surveillance by reducing complexity and focusing on facilitation of increased stool sampling to exclude poliovirus infection.

Introduction

Polio is a highly contagious, potentially debilitating illness that has contributed a significant disease burden globally, infecting millions of people prior to the launch of global eradication efforts (1). The disease can lead to the permanent paralysis of areas of the body and death through immobilisation of the breathing muscles (2). Poliovirus is predominantly spread person to person, through the faecal-oral route (3). Once ingested the virus replicates in the gastrointestinal tract and there is a short period of viremia during which the poliovirus may cross the blood-brain barrier and infect the cerebro-spinal fluid. If this occurs, an attack of lower motor neurons is possible, resulting in acute flaccid paralysis. Most infections are subclinical, however one in 150 cases develops paralysis. The case fatality rate is between 2-5% in children and 15-30% in adults, increasing to 25-75% when paralysis is present (4).

The disease came to prominence in the late 19th century, with a series of outbreaks across the world which escalated into major epidemics in the 20th century (3). The introduction of a vaccine for polio in 1955 signalled the first step in the decline of the disease and was followed by subsequent vaccines and control measures. Despite these interventions, in the 1980s it was estimated that there were still over 350,000 cases per year across 125 countries(5).

In the late 1980s, the focus shifted towards rapidly reducing the incidence of polio. The presence of an effective vaccine, diagnostic tools sufficiently able to detect transmissible virus and the lack of a non-human reservoir, meant that polio eradication is achievable (6, 7). In 1988, the World Health Assembly passed a resolution to eradicate the disease, resulting in the formation of the Global Polio Eradication Initiative (GPEI)(1). International efforts have resulted in a 99.99% reduction in the global incidence of polio since 1988 with only 118 wild and circulating vaccine-derived polio cases occurring globally in 2017. The virus is now only endemic in three countries: Pakistan, Afghanistan and Nigeria. Since the Western Pacific Region was declared polio-free in 2000, there has been one case of polio in Australia, imported from Pakistan in 2007 (8).

Surveillance of acute flaccid paralysis (AFP) is the primary method for sensitive case-based detection of poliovirus disease worldwide (5). Surveillance of the condition as a mechanism for detecting polio began with the emergence of polio eradication efforts in the Americas (9). With a decline in polio incidence, came a decrease in clinical suspicion of infection with the virus in people presenting with AFP. As paralysis occurs in less than 1% of polio cases, and AFP can have numerous other causes unrelated to polio, it became more likely for clinicians to attribute paralysis to other conditions (10). In order to ensure that cases of true paralytic polio were being investigated and identified, surveillance of AFP was introduced internationally. This aims to capture all children presenting with AFP within the high-risk age group and enable systematic assessment of these cases to categorise them as having polio or non-polio AFP. The gold standard for this assessment is stool sampling to test for the presence of the virus. Surveillance was initially limited to those under the age of five, as historically >80% of cases occurred in this age group (7). However, the epidemiology of the infection has changed as a result of sanitation and vaccination programs such that those aged less than 15 years are now considered most susceptible and are the target of surveillance activities (D. Durrheim, personal communication, 19 January 2018).

The World Health Organization and GPEI have well-documented international AFP surveillance standards, poliovirus containment requirements and polio-free accreditation processes that are part of a strategy for eradication (5). As part of maintaining polio-free certification, Australia is required to detect at least one non-polio AFP case per 100,000 people aged under 15 years annually to demonstrate that surveillance is adequately sensitive(5). Eighty percent of these cases should have two stool specimens collected more than 24 hours apart within 14 days of onset of paralysis in order to determine whether reported AFP is caused by poliovirus.

Routine AFP surveillance has been conducted in Australia since 1995 through the Australian Paediatric Surveillance Unit (APSU), who conduct monthly surveys of paediatricians around the country (11). Since 2001, the National Enterovirus Reference Laboratory (NERL) at the Victorian Infectious Diseases Reference Laboratory (VIDRL) has coordinated AFP surveillance in Australia in collaboration with APSU (12). Queensland is the only jurisdiction in which AFP is a notifiable condition and this has been in place since 2001. In 2007, the Paediatric Active Enhanced Disease Surveillance

(PAEDS) network began working in conjunction with APSU and NERL to detect AFP nationally through research nurses matching hospital data to case definitions (13).

The Polio Expert Panel (PEP) and the National Certification Committee for the Eradication of Poliomyelitis (NCC) play a key role in AFP surveillance in Australia. Established in 1998, PEP is an expert panel that review all cases identified through AFP surveillance and classify them as 'non-polio AFP', 'AFP more information required', 'polio compatible - zero evidence or polio not excluded' (when there is a lack of information to classify the case otherwise or exclude polio as a cause), or 'poliomyelitis' (wild poliovirus infection, vaccine associated paralytic poliomyelitis or vaccine derived poliovirus)(14). The NCC is an independent, non-statutory committee of the Australian Government Department of Health who review and report to the Regional Certification Committee on the performance of AFP and polio surveillance, polio immunisation and laboratory containment activities in Australia, and advise on maintenance of polio-free certification (15).

This study was undertaken to investigate the function and benefit of the APSU's AFP surveillance in the context of polio policy and response in Australia. It builds on previous investigations into Australian polio surveillance and the APSU. In 2009, the APSU's surveillance of 43 childhood conditions was evaluated through a survey of clinicians, researchers and public health officers (16). An evaluation of national polio surveillance in Australia in 2013 looked at virological and enterovirus surveillance, environmental surveillance, the National Notifiable Disease Surveillance System, as well as AFP surveillance by PAEDS, APSU and mandatory notification in Queensland (13). As previous evaluations have been broad in scope, this evaluation provides important insight through a focused review of the attributes of a key component of AFP surveillance in Australia, the APSU.

Methods

The United States Centers for Disease Control and Prevention's (CDC) *Updated Guidelines for Evaluating Public Health Surveillance Systems* (CDC guidelines) was used to assess the APSU's AFP surveillance system and its attributes(17). Scoping meetings were conducted with managers of APSU and NERL to gather information on the history of APSU's AFP surveillance as well as the current structure and flow of data. Attributes

were assessed through inspection and analysis of the data collected by the surveillance system and via a survey of polio and AFP surveillance and policy experts.

Survey questions were developed and necessary AFP data parameters identified based on the surveillance system attributes outlined in the CDC guidelines as per Table 1 (survey questions available at Appendix 3A). The survey measured the simplicity, flexibility, stability, acceptability, usefulness, data quality and timeliness of the system. The questions used were validated through review by four independent surveillance professionals and epidemiologists at the Australian Government Department of Health who were not part of the survey sample. SurveyMonkey Inc. was used to distribute the survey and collect responses. Twenty one key stakeholders were invited to participate in the survey including members of PEP, NCC, APSU and NERL and the designated national polio policy officer, medical advisor and epidemiologist at the Australian Government Department of Health. Participants were not asked to identify themselves as part of the survey, with only their interaction with the system in broad categories requested.

Relevant data parameters were requested from APSU and NERL to investigate the data quality, timeliness, sensitivity, predictive value positive, usefulness, acceptability and representativeness of the surveillance system (Table 1). The 2016 estimated resident population was used to describe the geographical distribution Australian population under 15 years(18). Where incidence rates were calculated, the estimated resident population from the year described was used.

To focus on the recent performance of the system, data was requested from 2012-2017 and survey participants were asked to consider and refer to their experiences with the system over the same period.

Table 1: List of attributes to be evaluated, by their measurement and data sources

Attribute	Description (17)	Measurement	Survey	Data inspection	APSU/ NERL
Simplicity	The structure of the system and the ease of extracting information for surveillance purposes	• Method of data collection and dissemination • Amount and type of data needed to meet the case definition • Integration with other systems	✓		
Flexibility	How the system can accommodate changes in information needs or operating conditions	• Response to a change in procedure, information collection or funding (e.g. incorporation of another AFP surveillance system)	✓		
Stability	The reliability (ability to collect, manage and distribute data without failure) and availability (ability to perform when needed) of the surveillance system	• Reported functions of, and interactions with the system, including storage of information, the operation of the database and access to data	✓		✓
Acceptability	The willingness of stakeholders to provide and utilise the system's data	• How readily the information is used and what it is used for • Reporting clinician participation rate	✓		✓
Usefulness	The extent to which AFP data from APSU meets its objectives and is used for the purposes it is needed	• Achievement of objectives • The scope of activities the data is used for • Use in policy and response	✓		✓
Data quality	The completeness of the data	• Completeness of essential data fields and examine for completeness • Determine if other data is needed that isn't captured	✓	✓	
Timeliness	The time taken between steps in the surveillance system and ability to enable time-sensitive public health action	• The time it takes from a case's onset to a selection of key points in surveillance • The timeliness of data for public health action	✓	✓	
Sensitivity	The proportion of cases of AFP in the population that are detected by the system	• Rate of detection of non-polio AFP per 100,000 population under 15 years (19)		✓	✓
Predictive Value Positive	The proportion of reported cases that actually have the condition under surveillance	• Of all the AFP reported by APSU, how many are classified as AFP by PEP		✓	
Representativeness	Accurately describes the occurrence of AFP over time by person and place	• Geographical comparison of the distribution of the population under surveillance and the spread of reporting clinicians		✓	✓

AFP: Acute flaccid paralysis, APSU: Australian Paediatric Surveillance Unit, NERL: National Enterovirus Reference Laboratory

Ethics statement

This study was approved by the Science and Medical Delegated Ethics Review Committee of the Australian National University (Protocol number 2017/623).

Results and discussion

System description

Operation and integration

The APSU currently conducts surveillance of 18 rare childhood diseases and conditions, including AFP (19). Surveillance is based around the reporting of whether or not cases have been seen in the month prior by approximately 1,500 paediatricians and child health specialists (neonatologists, surgeons, geneticists and neurologists) who are part of the APSU register. This register of clinicians is maintained primarily through contact with the Royal Australasian College of Physicians, who facilitate the invitation of new medical graduates to enrol in the APSU register.

Each month every clinician in the network is sent a report card by email (96%) or post (4%) asking whether they have seen patients with any of the 18 diseases or conditions being studied, including AFP (Figure 1). The AFP case definition used by APSU is the "acute onset of flaccid paralysis in one or more limbs or acute onset of bulbar paralysis"(20). Clinicians return these report cards to the APSU, indicating whether a case has been seen by the clinician during the previous month (via a simple case count number). Instructions on the report card encourage clinicians to also report cases immediately to NERL. Following receipt of the report card, APSU may then request the case's date of birth and initials to make identification for acquisition of additional clinical information simpler. These initial reports are then passed on to NERL via email in a weekly report or as they come in.

NERL proceed to email clinicians to request clinical details about the case. A clinical questionnaire (Appendix 3B) is filled in by clinicians which provides a range of information to determine the cause of the AFP and assess polio risk factors including vaccination history, clinical features and investigations, outcome and clinical diagnosis (21). At this point, clinicians are also prompted to provide stool samples on the questionnaire. Once this information is returned to NERL, case information is entered into the National AFP Surveillance Database and clinical details are entered into a separate AFP Clinical Information Database. Both databases are relational and are accessed through SQL. There are circumstances where clinicians will send through an APSU clinical questionnaire directly after reporting a case, or without being prompted

by a report card. When a case is reported directly to NERL by phone, the clinician is asked to fill in the APSU questionnaire as well. As part of AFP being notifiable in QLD, clinicians are advised to concurrently report the case to their local health authorities and are advised to use APSU's AFP questionnaire to provide details directly to NERL(22). AFP cases from other sources such as PAEDS or directly from clinicians are also included in these NERL databases. Every two months PEP meets to classify the AFP cases as 'non-polio AFP', 'AFP more information required', 'polio compatible – zero evidence or polio not excluded' (when there is a lack of information to classify the case otherwise or exclude polio as a cause), or 'poliomyelitis' (wild poliovirus infection, vaccine associated paralytic poliomyelitis or vaccine derived poliovirus)(14). Extraordinary PEP meetings can be arranged if high suspicion of polio infection is highlighted by a clinician or initial laboratory results. NERL coordinates PEP meetings, provides the data and collates outcomes to update case information in their databases. While some information on cases is provided back to APSU, they do not store clinical or case information beyond initial notifications. Figure 1 provides a visual representation of the flow of APSU's AFP data and integration with NERL and PAEDS.

The Poliomyelitis Outbreak Response Plan for Australia is a framework that details agreed situations in which pre-determined actions should be taken to appropriately contain the risk of spread of polio in Australia. This plan was last updated in 2014. If an AFP case is classified as poliomyelitis or polio compatible (when there is a lack of information to classify the case otherwise or exclude poliovirus as a cause), activation of the plan and response activities are triggered. The Australian Government Department of Health works closely with PEP and the affected jurisdiction when activating the plan.

PEP classifications of AFP cases are incorporated into the national surveillance case definition for poliovirus infection, which are used to report cases to the National Notifiable Diseases Surveillance System. Under the national surveillance case definition, a probable case aligns with the 'polio compatible' case classification made by PEP(23).

Objectives

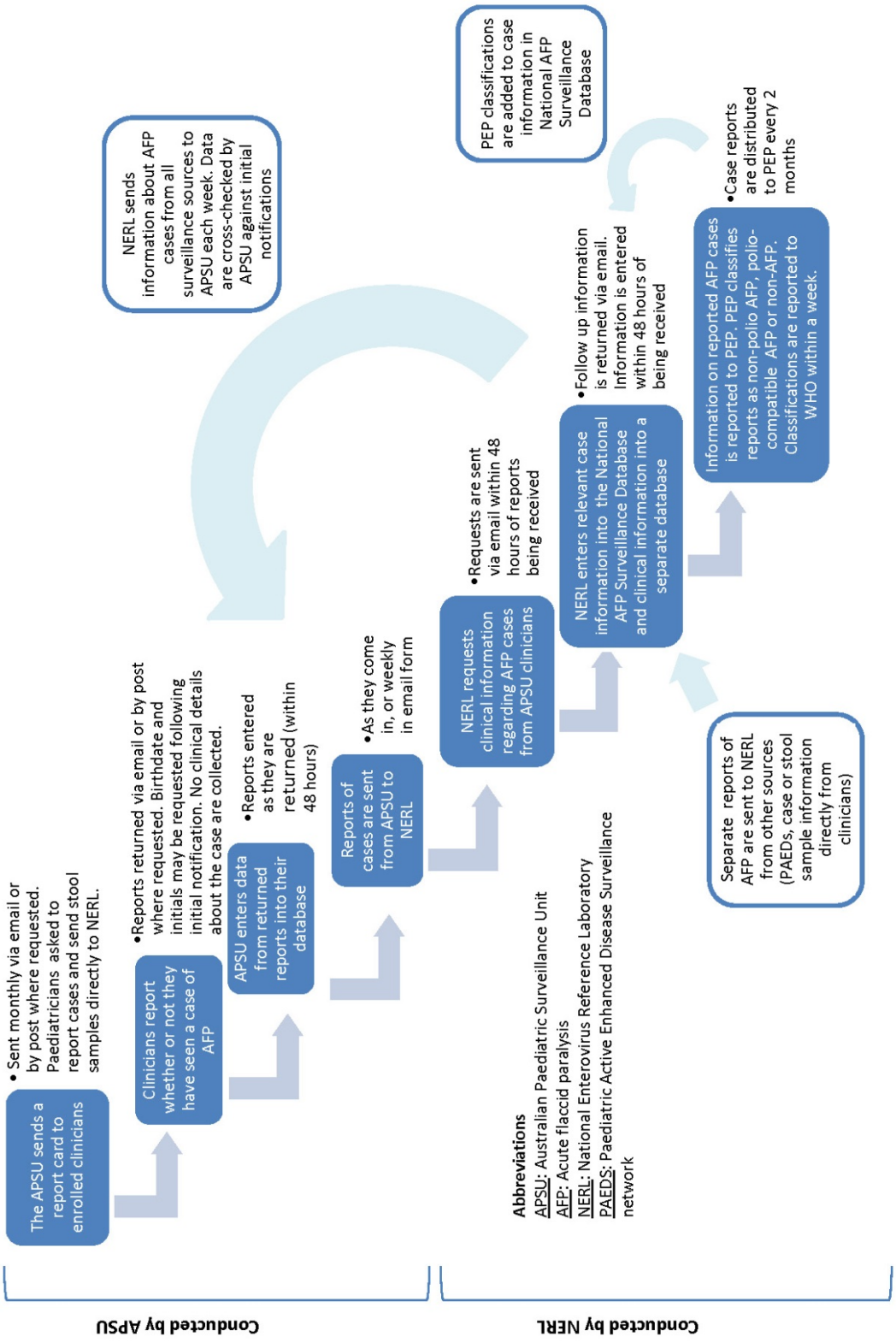
The APSU has three objectives in their surveillance of AFP(20). Firstly, to determine whether AFP is caused by poliovirus infection and if so, whether it is wild or vaccine strain poliovirus. Secondly, to document the reported rate of AFP over time and to assess the adequacy of AFP surveillance according to World Health Organization (WHO) criteria. Lastly, to monitor the aetiology, clinical features and outcome at 60 days of non-polio AFP. APSU conducts AFP surveillance in conjunction with PAEDs and NERL with the overall purpose of ensuring that polio cases are detected and minimising the risk of an outbreak (13). As per the standards set by GPEI, the population under surveillance is all children under the age of 15 years across Australia.

Other components of the system

Data is collected by APSU and NERL under the *National Health Security Act 2007*, specifically Section 8(e)(24). APSU are funded by the Australian Government Department of Health to conduct surveillance of AFP amongst eight other rare diseases and conditions. The Department funds NERL under a separate agreement to coordinate national AFP surveillance and conduct laboratory testing and environmental surveillance for poliovirus. PAEDS is another key AFP surveillance system in Australia. It is comprised of a network of clinicians and researchers in seven tertiary hospitals, where research nurses actively review hospital records for cases(25). PAEDS and APSU AFP data both feed into the National AFP Surveillance Database and are reviewed in conjunction by PEP. There is oftentimes overlap in case detection by both systems as a result of paediatricians enrolled in APSU also working in a PAEDS hospital. PAEDS is funded separately for AFP surveillance and is not the focus of this evaluation.

Entry of data at APSU and NERL is manual and is conducted by specific members of staff. Transfer of data between clinicians, APSU, NERL, the WHO, the Australian Government Department of Health and committees is primarily via email. Alongside other polio related surveillance sources, APSU's AFP data are reported to the WHO weekly and are included in an annual report to the Regional Certification Committee to demonstrate Australia's polio-free status (L. Hobday, personal communication, 7 February 2018).

Figure 1. Flow chart of APSU's AFP surveillance data



System attributes

Of the key stakeholders who were invited to participate in the survey of their experiences with the APSU's AFP surveillance, 71% responded (n=15/21).

Simplicity

A simple system is defined by its structure, the data collection process, integration with other systems, the ease of extracting data and the amount of information necessary to meet the case definition (Table 1).

The structure of APSU's surveillance and integration with other systems was understood by most survey participants (80%), who reported no difference between their understanding of the system and the way it is shown to work in Figure 1. A majority of participants saw the logistics of the system as being simple (20% very simple, 73% reasonably simple and 7% not simple). Suggested improvements were focused around the lack of online systems to report case information.

Integration of APSU systems and data with NERL was seen as reasonably simple by the majority of participants (13% very simple, 73% reasonably simple and 13% not simple). Participants commented that the provision of patient identifiers at the point of first notification would make acquisition of clinical case details much simpler. Integration of PEP's AFP classifications was seen as simple by most respondents (40% very simple, 47% reasonably simple and 7% not simple).

The process of data collection including the initial notification through APSU and follow up by NERL was seen as simple by a slim majority of participants (7% very simple, 53% reasonably simple), but notably 40% reported it not to be simple. Participants commented that the multi-step data collection process and time between notification and follow up means that clinical case details may be incomplete and appropriate testing not undertaken. Difficulty identifying patients, reliance on good note taking and movement of clinicians were identified as contributing to this.

Of the participants that had requested APSU's data (27%), most found it simple (25% very simple, 50% reasonably simple, 25% not simple). Respondents who had extracted APSU's data (40%) found it to be simple (17% very simple, 83% reasonably simple). It

was noted that having all AFP data from multiple surveillance sources in a centralised database at NERL was useful.

APSU's AFP case definition is met using clinical judgement only. The definition is deliberately broad to ensure the sensitivity of syndromic surveillance and means that case ascertainment is simple and not resource intensive. The case definition is based on the WHO's definition and matches that used by PAEDS, allowing simple integration with other data.

Overall, APSU's AFP surveillance was found to be reasonably simple by those that use the system and its data. The process of data collection whereby APSU prompts clinicians for initial case reports and NERL later requests clinical information was found to be the least simple aspect of the system. Decreasing the steps involved in collecting data would simplify surveillance and enhance the capacity of the system and the quality of its data.

Flexibility

A flexible surveillance system can adapt to changes in information needs or operating conditions without impact on surveillance activities or need for additional resources. The integration of the PAEDS surveillance system into AFP surveillance in 2007 was used to assess the flexibility of APSU (Table 1).

Prior to beginning the survey, 93% of participants were aware that PAEDS began conducting surveillance of AFP in collaboration with APSU in 2007. Approximately half of respondents were involved in AFP surveillance during that time (47%). Respondents thought that APSU's AFP surveillance system responded somewhat well to this change (33% very well, 13% reasonably well, 13% not well, and 40% unsure). It was noted that PAEDS is a valuable complement to APSU, enabling the achievement of the necessary AFP detection rate. It was also noted that with the introduction of the new surveillance component, some clinicians in PAEDS hospitals stopped reporting to APSU based on the assumption that their cases would be picked up by PAEDS, which is a less labour intensive surveillance system for the clinician. Participants noted that while PAEDS and APSU work well together, having two systems can complicate the clarity of the number of AFP cases being notified.

Respondents most frequently reported that the APSU would respond well to a future change in procedure, funding or system structure (20% very well, 40% reasonably well, 13% not well, and 27% unsure). It was noted that the system may benefit from a more modern database in order to assist in being flexible in the future.

APSU's system of reporting is inherently flexible in that diseases can be added or removed easily from report cards. In terms of AFP surveillance, there are many components to the collection of surveillance data, and this may increase the complexity of changes in information needs or operating conditions. Overall, APSU was perceived to respond reasonably well to a recent change in surveillance structure. However, reducing the number of steps in the system would make it more flexible.

Stability

Stability of the system is determined by its reliability (ability to collect, manage and distribute data without failure) and availability (ability to perform when needed) (Table 1).

Survey participants thought the APSU's AFP surveillance system and data was reliable in terms of APSU's ability to collect, manage and provide data without failure (40% very reliable, 47% reasonably reliable, 7% not reliable, 7% not sure). Approximately half of participants hadn't experienced difficulty accessing APSU's AFP data or system due to a system outage or other disruption and others were unsure (47% no issues with system or data availability, 7% partial issues, 47% unsure). Respondents commented that the APSU does not always have the most recent information on their cases and that NERL is more reliable and accurate for retrieving APSU's data.

Representatives from both APSU and NERL reported that there has not been an outage in any database holding APSU's data in working memory. APSU have 1.6 full time equivalent (FTE) staff members who manage surveillance of all 18 conditions under investigation by the APSU. As a result, quantifying the resources dedicated to AFP surveillance alone is challenging. NERL have 3.8 FTE staff to perform all polio surveillance activities, of which 0.4 FTE are dedicated to managing AFP surveillance specifically.

APSU collects and stores notifications of AFP, however information about APSU's AFP cases and the clinical details required for public health action are collected by NERL and are stored on databases at NERL's facility. APSU does not have access to these databases except through NERL. While APSU receives weekly emails from NERL with some case information, they cannot produce line list data or clinical details of cases independently.

The Australian Government Department of Health funds APSU through a contract for surveillance of AFP and eight other conditions. While there is often uncertainty with Departmental funding, there is a recognised need and obligation to upkeep AFP surveillance, and funding has been consistently provided to APSU for this purpose since 1995. This suggests a relatively high level of stability for a nationally funded surveillance system. NERL is funded by the Department under a separate agreement to coordinate national AFP surveillance and conduct laboratory testing for poliovirus, the funding for which has been in place since 1997 and is perceived to be stable as well.

The surveillance system was perceived as having a high level of stability, however it is noted that there is a gap in APSU's immediate access to surveillance data as a result of NERL completing APSU's data collection.

Data quality

Data quality is determined by the level of completeness of the data captured and recorded by a surveillance system (Table 1).

Survey participants were asked whether there was any information that is necessary for AFP surveillance that isn't currently captured by APSU. Respondents were most frequently satisfied with the breadth of information collected by APSU (64% no further information needed), however 29% noted that additional information was needed and 7% were unsure. Respondents noted that the multistep data collection process can result in incomplete data and that patient identifiers should be collected at the time of notification to make clinical follow up simpler and enable more complete data collection. Others said that more aetiological and imaging data would be desirable as is collected through PAEDS. It was noted again here that APSU itself does not have the most up to date data and that NERL is more reliable for retrieving high quality data on APSU's AFP cases.

To examine the quality of APSU's data in NERL's National AFP Surveillance Database, the completeness of 16 essential fields was assessed. From 2012-2017, 93% of the total available fields contained complete data for the 203 notifications recorded during this time. Most notably, fields that indicate timeliness had the most missing data including the date the clinical questionnaire was sent and received. Some data entry errors were revealed during inspection of the data. These were primarily in the classification (n=1) and classification date fields (n=11). Assessing the validity of all entries was beyond the scope of this evaluation.

The quality of the data in the separate AFP Clinical Information Database was also investigated through inspection of the completeness of fields necessary for PEP's classification of cases. Due to the many conditions that may cause AFP and the resulting complexity of excluding polio in the absence of adequate stool samples, the necessary information for case classification can vary. For the purposes of this evaluation, lumbar puncture, nerve conduction studies and MRI were chosen as the fields most informative for classification of cases by PEP and were inspected for completeness. At the time of data inspection, 198 out of the 203 notified AFP cases in the database from 2012-2017 had been assessed by PEP. During this time, clinical questionnaires were received for 87% of reported cases that had been assessed by PEP (n=172/198). Of the cases where questionnaires were received, 90% of the total fields were filled (n=1140/1265). This meant that 78% of cases had necessary clinical fields filled.

Through investigation of timeliness, it became apparent that APSU did not have data to reflect how long it takes clinicians to respond to initial report cards. While this data may not be essential for surveillance activities, it is an important administrative measure that indicates system functionality and should be recorded with case information.

APSU's AFP data quality was found to be reasonably good in terms of the completeness of essential data fields, noting that clinical information was less complete than case information. Completion of clinical information could be enhanced through the reduction of time and steps between initial case notification and follow up for completion of the clinical questionnaire. Data quality would also benefit from data

collection being linked directly to a database to reduce manual errors and automatically collect information about system functionality.

Acceptability

Acceptability of the surveillance system is defined as the willingness of stakeholders to provide and utilise the system's data (Table 1).

Survey participants reported using APSU's AFP data for a variety of purposes, including committee work (86%), national and international reporting (57%), describing the epidemiology of AFP (57%), system administration (43%), policy development (14%), informing response activities (14%) and cluster investigation (14%). For the purposes participants used the system and data for, most found it useful (64% very useful, 36% reasonably useful). Most participants used the system or data every two months (14% annually, 36% bimonthly, 14% weekly, 29% daily, 7% aren't currently using the data).

Based on total initial report cards sent and returned, the response rate of clinicians enrolled in APSU surveillance from 2012-2016 was 93% (n=67,637/72,905). Yearly response rates ranged from 90%-96%.

The response rate of clinicians in filling in the clinical questionnaire for all cases notified and classified between 2012-2017 was 87% (172/198).

APSU's AFP surveillance was found to be acceptable. It provides important information for a variety of purposes in polio policy and response. The data was found to be useful to those that need it, and the system is well accepted by reporting clinicians, as reflected in their response rates and ongoing participation. The decline in response from initial questionnaire to clinical follow up should be addressed by reducing the steps necessary for surveillance.

It is important to note that this study did not attempt to interview reporting clinicians. This has been done in previous studies, however the ongoing views and self-reported practices of paediatricians in AFP surveillance would be worth investigating in future evaluations(13).

Timeliness

The timeliness of the system is determined by the time taken between key steps in surveillance and whether this enables time-sensitive public health action (Table 1).

Most survey participants thought that the APSU's AFP data was reasonably timely (20% very timely, 67% reasonably timely and 13% not timely). Participants commented that follow up can take several months, can be dependent on the clinician and is delayed by the multistep process. It was noted that the timeliness varies for data collection depending on how close to the monthly reporting date the case is seen by the clinician, and for data dissemination, how close to the PEP meeting it is reported. It was noted that the length of time it takes to collect a full clinical report and classify an APSU AFP case usually surpasses the window of opportunity to request the necessary stool samples.

When participants were asked whether they had ever experienced a delay in APSU's AFP surveillance data that resulted in delayed public health action, 60% said they hadn't and 40% were unsure.

Respondents were asked about whether APSU detects AFP and disseminates data in a timely way to permit identification of a potential polio case and actioning of appropriate response activities. Just over half of participants thought that detection and data dissemination was timely for this purpose (60%), while 20% thought it was partially timely, 13% said it wasn't timely and 7% didn't know if it was timely enough. It was noted that clinician response time may contribute to a lack of timeliness. Participants reported that while retrospective monthly reporting may not be timely enough to illicit appropriate actions for a polio case, clinical suspicion and rapid reporting directly to NERL is (as instructed on the monthly APSU report cards). Respondents said that online clinical data collection would enhance capacity of the system to detect and act on potential polio cases in a more timely way.

APSU reported that 100% of report cards are sent on the first or last day of the month to all active clinicians who are not on leave. APSU did not have data to reflect how long it took clinicians to respond to initial report cards.

Inspection of APSU's data held by NERL showed the time taken between four key steps in the surveillance system; date of onset of paralysis, date of first notification to NERL, date of clinical questionnaire receipt and the date that classifications were finalised via reporting to WHO (Figure 2).

Figure 2. Time taken between key steps in APSU's AFP surveillance from 2012-2017*

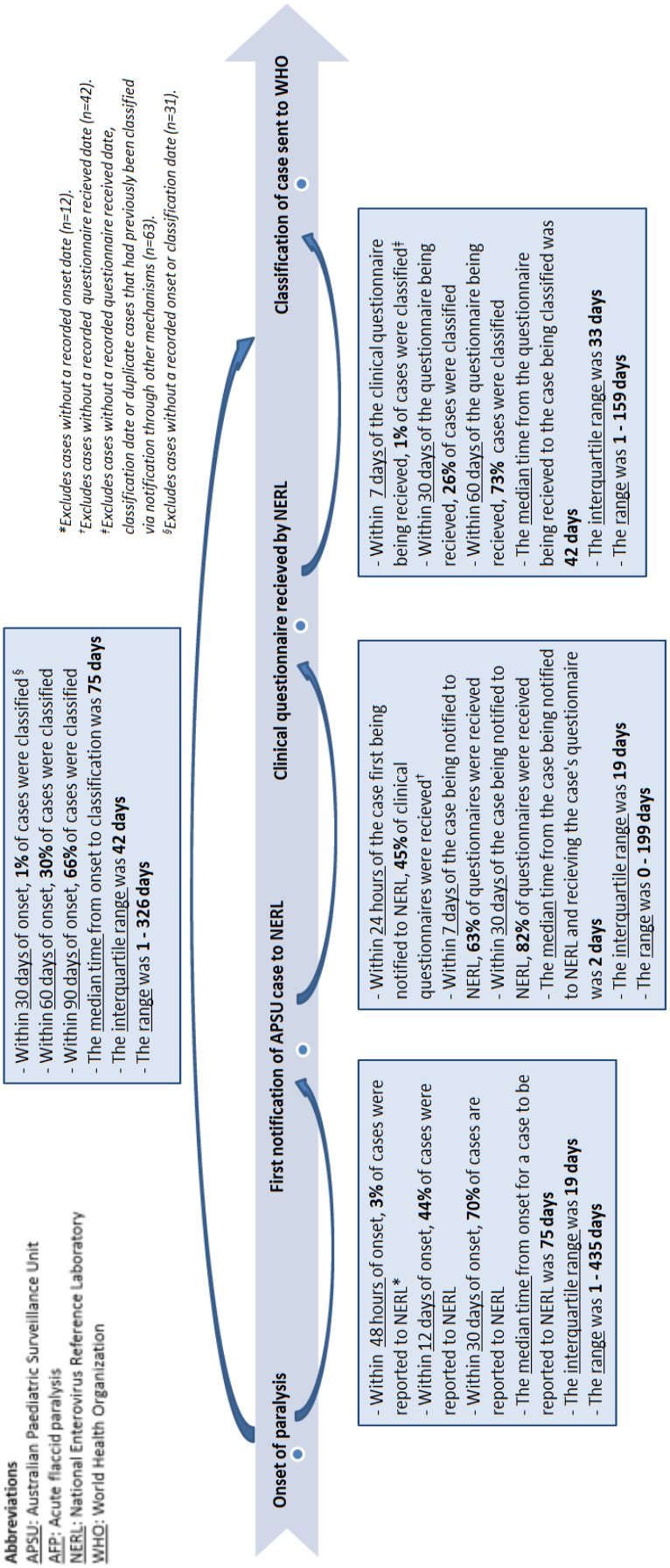


*Figure is restricted to cases identified by APSU. This includes cases reported in duplicate through PAEDS, however APSU notification timeframes are reported.

The WHO standards for surveillance of polio recommends that 80% cases of AFP under 15 years old should be reported immediately and investigated within 48 hours (26). The APSU study protocol instructs clinicians to immediately contact NERL when an AFP case presents. While the data fields used don't account for how long it takes from onset for a patient to present to the reporting clinician, NERL were notified of 3% of cases within 48 hours of onset between 2012-2017. The period of time between onset and reporting is also crucial for prompting the requisite collection of two stool samples more than 24 hours apart within 14 days of onset. The last time point at which NERL can encourage adequate stool sample collection would be 12 days and 44% of cases were reported within this time (Figure 2). The majority of cases being reported within 30 days aligns with the clinician reporting schedule held by APSU.

Clinician provision of the clinical questionnaire to NERL was quite timely, with two thirds of cases (63%) having relevant clinical information available within a week of notification and a within a median timeframe of two days. The receipt of the clinical questionnaire is an important time point, as an initial assessment of the case is conducted by NERL whereby a potential polio case may be flagged.

The step between clinical questionnaire receipt and finalised classification of cases was less timely (median=42 days). A majority of cases (73%) were classified within 60 days from receipt of questionnaire, which aligns with PEP's bimonthly meeting schedule to classify cases.

Overall, APSU's AFP surveillance was perceived as timely by a majority of those who use it, but inspection of the time taken between key surveillance points and consideration of the goals of AFP surveillance shows that the system as a whole is not timely. AFP surveillance is undertaken with the overall aim of detecting polio in the community in order to prevent further cases (26). In this way, it is important for AFP surveillance to enable timely identification of potential polio cases, including the exclusion of polio through stool sampling within 14 days of onset. While the whole process from onset to notification is lengthy, the need for increased timeliness is more important for some steps in surveillance than others. It is noted that retrospective bimonthly classification of cases by PEP may be appropriate as it is the last step in the process; however other steps in surveillance where safeguards are in place, such as the

window for stool sample collection and review of the clinical questionnaire, should be made more timely. Reduction in the time from onset to notification and elimination of the step between notification and clinical follow up would be beneficial to enhance timeliness and meet the goals of AFP surveillance more broadly.

Representativeness

A representative system is defined as accurately describing the occurrence of the condition over time by person and place (Table 1).

To provide an indication of whether APSU's clinician distribution is representative of the distribution of Australia's population <15 years, the proportion of enrolled clinicians and those <15 years in each jurisdiction were compared (Table 2) (18). It was found that the distribution of clinicians across jurisdictions closely matches the distribution of the <15 year old age group, with slight underrepresentation of clinicians in Victoria and Queensland and over representation in New South Wales. This demonstrates that surveillance activity is broadly representative of population spread. It was also noted by survey participants that APSU provides important representation of non-paediatric and private hospital settings as well as suburban and regional areas that are not covered by PAEDS. As discussed in the sensitivity of the system (below), the expected rate of non-polio AFP in the population under surveillance is one case per 100,000 children aged under 15 years annually. This has been achieved by the surveillance system in conjunction with other data sources since 2007, meaning that detection is representative of the expected occurrence of the condition nationally.

A recent study investigated the distribution of AFP detection rates (from all sources) at the statistical local area level four and found that while national AFP detection rates were met, subnational analysis revealed underrepresented areas (27). Similarly, while the broad distribution of the age group under surveillance matches clinicians enrolled in surveillance by jurisdiction, this does not mean distribution within the jurisdiction is representative. Assessing representativeness geographically within jurisdictions and demographically within the under 15-year-old age group was beyond the scope of this study. As AFP is a serious clinical condition, it is plausible that children presenting with AFP in geographically diverse areas would be referred to a tertiary paediatric hospital

captured by AFP surveillance. However, representativeness within jurisdictions should be investigated in the future.

Table 2. Number and proportional distribution of clinicians and Australian population <15 years by jurisdiction

	Clinicians		Population <15 years old	
Jurisdiction	Number	Proportion of total enrolled (%)	Number	Proportion of total population <15 years old (%)
NSW	573	36	1,452,958	32
VIC	369	23	1,140,283	25
QLD	270	17	954,598	21
SA	112	7	304,338	7
WA	172	11	496,568	11
TAS	26	2	93,463	2
NT	20	1	53,607	1
ACT	31	2	76,264	2
Total	1573	100	4,572,079	100

As AFP is a notifiable condition in QLD, APSU reporting may duplicate notification processes, and reporting to APSU may occur differently in this jurisdiction as a result of heightened reporting requirements. Subnational clinician reporting behaviours was not a focus of this evaluation and as such was not specifically investigated, but may warrant further evaluation.

Sensitivity

The sensitivity of the system is determined by the proportion of cases of AFP in the population that are detected by the system (Table 1).

The international surveillance target of detecting one case of non-polio AFP per 100,000 children aged under 15 years was met annually in Australia from 2012-2016 (Table 3). The 2017 rate is not yet finalised as not all cases have been classified. From 2012-2016, APSU detected 20% of eligible cases uniquely (not duplicated by other sources of reporting) and contributed to 47% of case detection when duplicates also detected by PAEDS were included.

Table 3. Rate of detection of AFP per 100,000 children aged <15 years and source of contributing case numbers by year

AFP detections	2012	2013	2014	2015	2016
National non-polio AFP rate (per 100,000)	1.26	1.44	1.32	1.2	1.38
Expected number of non-polio AFP cases (n)	43	43	44	44	45
Cases classified as non-polio AFP from all sources* (n)	54	62	58	53	62
Unique eligible cases notified by APSU (n)	18	12	13	7	9
Unique eligible cases notified by PAEDS (n)	28	26	36	33	30
Eligible cases notified by both APSU and PAEDS (n)	8	24	9	13	23
Proportion of unique eligible cases notified by APSU (%)	39	32	27	18	23
Proportion of total cases (including duplicates) notified by APSU (%)	48	58	38	38	52

AFP: Acute flaccid paralysis, APSU: Australian Paediatric Surveillance Unit, PAEDS: Paediatric Active Enhanced Disease Surveillance
** Includes polio compatible AFP. There were two AFP cases classified by the PEP as "polio compatible" in 2012-2017; one case in 2012 and one in 2016.*

APSU provides approximately half of the notifications to detect AFP at an adequately sensitive rate to match the expected number of cases in the population under surveillance. While not sensitive enough to conduct AFP surveillance alone, national surveillance would not currently meet AFP sensitivity targets without APSU. The goals of the surveillance system should be updated to reflect the fact that APSU forms only part of the system designed to document the rate of AFP over time.

As previously outlined, while national surveillance of AFP is adequately sensitive, this may mask subnational gaps in surveillance (27). Subnational sensitivity should be routinely assessed and efforts should be made to enhance surveillance in areas identified to have lower than expected case detection.

Predictive value positive

A surveillance system with a high predictive value positive (PVP) is one where a high proportion of the cases reported actually have the condition under surveillance (Table 1).

All cases of AFP reported by clinicians to APSU are assessed by PEP to determine whether cases are true AFP. Of all APSU'S AFP cases that have been assessed by PEP between 2012-2017 (n=179), 26 were found not to meet the case definition. The PVP for this time period was found to be 85%.

PVP can be important in determining whether alarm is being unduly raised as a result of a surveillance system detecting false positives. For AFP surveillance, it is more important to ensure detection and investigation of all potential polio cases than to avoid falsely detecting AFP. Despite this, APSU still has a high PVP, giving confidence to the initial case reports and any evidence of clustering.

Usefulness

A useful system is one that meets its stated objectives and contributes to the prevention and control of a disease through timely identification and recognition of changes in incidence (Table 1).

The first objective of APSU's AFP surveillance is determining whether AFP is caused by poliovirus infection and if so, whether it is 'wild' or vaccine strain poliovirus. Most survey participants thought this objective is partially met by APSU (33% met, 60% partially met, and 7% unsure). It was noted that APSU provides a trigger for investigation, but does not explicitly determine whether cases are caused by polio. Participants said that meeting this objective is dependent on stool sampling and the work of NERL.

APSU's data in NERL's National AFP Database was inspected to investigate achievement of the first objective. From 2012-2017, 31% of cases had adequate stool samples collected (two samples collected more than 24 hours apart within 14 days following paralysis onset)(26). Notably, there were two cases within this time period that did not have adequate stool samples collected that were classified as polio compatible (polio not excluded). This means that based on their clinical and diagnostic

information, polio could not be excluded and adequate stool samples were not collected to demonstrate whether polio was the cause of their symptoms.

The second objective is to document the reported rate of AFP over time and assess the adequacy of AFP surveillance according to WHO criteria. Most participants thought this objective is met or partially met (60% met, 30% partially met, and 7% unsure). Respondents noted that adequately documenting the reported rate of AFP is only achieved in conjunction with PAEDS, and that assessing the adequacy of surveillance is conducted by the NCC not APSU. It was also noted that there is an ongoing need for subnational analysis to look for underrepresented geographical areas.

The third objective is to monitor the aetiology, clinical features and outcome at 60 days of non-polio AFP. Most respondents didn't think or didn't know whether this objective is fully met (40% met, 27% partially met, 13% not met, 20% unsure). Despite this being an official objective of the system, in 2001 PEP decided to stop actively requesting 60 day follow up information if the case had made a full recovery. Since 2007, clinicians are only contacted if PEP is unable to classify the case based on the information at hand. Respondents noted that APSU's multi-step reporting process was inhibitory to long term case monitoring.

Survey participants described which actions they believed should be taken in the event of an AFP case being found to be polio compatible. These included further investigation (seeking additional laboratory and clinical information), analysis of clustering, reporting to the WHO's Western Pacific Regional Office, informing the clinician and notifying health authorities. Four out of 15 responses appropriately identified that the Poliomyelitis Outbreak Response Plan should be activated, while others in part identified steps in the plan. Respondents noted that the polio compatible classification includes AFP cases without adequate clinical or laboratory evidence to exclude them as non-polio AFP. As part of the current response plan, polio compatible cases can be 'zero evidence', where there is insufficient clinical, diagnostic and specimen evidence, or 'polio not excluded', where there is insufficient specimen evidence. At present, both of these polio compatible case classifications are grounds to activate the response plan. Respondents most frequently thought the actions they had identified would be taken or partially taken in the event of a polio compatible AFP

case being identified (47% actions would be taken, 27% actions partially taken, 7% actions wouldn't be taken, 20% unsure). Participants most frequently believed the actions they had identified to be adequate or partially adequate in preventing further cases in the event that the polio compatible case was a true case of polio (47% would be adequate, 27% partially adequate, 7% not adequate, and 20% unsure). Respondents noted that by the time PEP review and classify cases that the window of time to request a stool sample to exclude polio has almost always passed.

Overall, participants were asked to describe what APSU's AFP surveillance contributes to the identification and control of polio in Australia. Respondents noted that APSU provides access to surveillance data from non-paediatric and private hospital settings as well as suburban and regional areas that are not covered by PAEDS. This ensures achievement of surveillance targets whilst enabling broader case ascertainment. Other benefits noted include zero reporting providing reassurance of surveillance activity, reminding clinicians to consider the presence of polio, and enhancing awareness of the importance of stool sample collection.

The APSU's surveillance of AFP was found to be useful in contributing to the surveillance of AFP in Australia but was not found to meet its objectives. Overall, less than half of those that use the system believe that it meets its stated objectives (44% met, 40% partially met, 4% not met and 11% unsure). The system was found to be most useful in its contribution to documenting the rate of AFP over time, enabling detection at a rate that meets international surveillance targets when combined with other data sources. Many aspects of the objectives of the system are not achievable by APSU alone and updating the goals of the system would allow the system to more readily meet its objectives and demonstrate its usefulness.

Many other attributes of a system contribute to its usefulness and ability to prevent and control a disease through identification of changes in incidence. By nature of the fact the system is sensitive when combined with other AFP data sources, it is capable of detecting changes in incidence and as such should be able to identify clustering. As the system is not timely, the usefulness in detection of clustering may be limited in terms of prompting response activities to control an outbreak of polio.

Benefits, limitations and recommendations

Identified benefits of the system

The APSU is an important component of Australia's AFP surveillance, providing a stable, acceptable, representative system that collects part of the data essential to detect and respond to a potential case of polio. Collection of AFP cases by APSU in conjunction with PAEDS and other sources of data enables adequately sensitive detection at a rate that meets international surveillance targets. Participants noted that the system has a broad geographical reach and is useful in providing national surveillance coverage in non-urban and private settings that are not accessed by other AFP surveillance methods. APSU's AFP surveillance was found to be highly acceptable to the people who use the system and its data, as well as to enrolled clinicians as reflected in their high reporting rates. The system and its data were also found to be available and reliable when needed. A key benefit of APSU was found to be that the monthly report cards serve as a reminder to clinicians to consider the presence of polio in their patient, an important aspect and founding rationale for AFP surveillance. This monthly reminder serves to educate clinicians about eradication initiatives and the importance of stool sample collection. The reporting of zero cases was also found to be an important reassurance offered by APSU in AFP surveillance.

Recommendations and the limitations addressed

1. **Introduce single-step collection of case and clinical information.**

There are currently seven steps in APSU's surveillance of AFP (Figure 1). The time taken between each of these steps was found to culminate in an extended period between onset of AFP and classification, which hampers the time-sensitive goals of surveillance. Introducing collection of clinical information at the point of the initial report would reduce this to a three-step process. APSU's monthly request for reports of AFP should be updated to include a web link to the clinical questionnaire so that this information can be provided at the same time. It is noted that this is currently being investigated by NERL and APSU and it should be implemented as a matter of priority. This will involve requiring the 4% of clinicians who still report by post to transition into online

reporting. It is important that this questionnaire has a function to save and return to the form to accommodate clinician's competing priorities. Ideally, the questionnaire would be linked to a database or have automated data exportation.

It is anticipated that single-step case and clinical information collection would enhance:

- Simplicity of the system by reducing the components necessary for surveillance.
- Timeliness of surveillance by reducing steps required prior to classification.
- Data quality by reducing the time and steps between case presentation and clinical information being reported. At present, completeness of case information can suffer as a result of difficulty identifying patients for clinical follow up and reliance on clinician consistency and recall of case information long after presentation.
- Flexibility of the system by reducing the number of steps to be impacted by a change in procedure. In addition, flexibility of staff will be increased as a result of less time being spent facilitating the extra steps in data collection. Collecting identifying case details at the point of notification will also reduce the resources spent following up duplicate notifications individually.
- Usefulness by increasing capacity to encourage appropriate testing to rule out polio. By decreasing the time between onset and case information being obtained, it is more likely that stool samples can still be requested within the required timeframe.

2. Encourage active, real time reporting while sending monthly reminders.

The period of time between onset and reporting is critical in prompting the collection of adequate stool samples to detect or exclude poliovirus infection. Requesting case reports monthly means that if incidence is evenly distributed across the month, more than half of cases might be reported too late to prompt collection of adequate stool samples within 14 days. The APSU reporting structure could benefit from a shift in methodology, whereby clinicians are encouraged to report in real time and monthly emails are reminders and function as a zero-report step rather than the primary request for cases. It is noted that the current system accepts reports at any time and encourages clinicians to contact NERL as soon as a case is seen. This should be

enhanced by changing the focus of the monthly report cards to being reminders for real time reporting. This may also assist in increasing reporting and investigation of cases within 48 hours as per WHO AFP surveillance recommendations.

3. **Move APSU's AFP data collection and primary storage to a web-based platform with questionnaire functionality**

Utilisation of a secure web-based platform for data collection and storage would increase the simplicity of the system and enhance the quality and accessibility of APSU's AFP data. At present, cases are tracked across two organisations and data is entered manually across multiple systems. Case information is held by NERL, meaning APSU does not have immediate access to the data they are funded to collect. Data entry and accessibility could be improved by providing clinicians with a questionnaire that functions as a data entry form for an online database. In line with previous recommendations, this questionnaire should be accessible for real time reporting online and a reminder link should be embedded in the monthly reminder email. This solution is intended specifically for APSU's data and it is noted that integration with national data from all sources at NERL is important. Data from the web-based platform should be easily exportable for integration with other AFP data at NERL. In the long term, a web based platform for integration of AFP data from all sources would be ideal.

It is anticipated that the introduction of web-based collection and storage of APSU's AFP data would enhance:

- Data quality by removing the possibility of manual entry errors and increasing completeness of administrative fields such as questionnaire received date through automatic generation.
- Usefulness and stability by increasing the availability of data to APSU.
- Flexibility by enabling easy addition and removal of fields on the questionnaire.
- Timeliness by reducing the time taken to enter data.

4. **Review APSU's role in collection of AFP case information and clinical data**

As NERL collects the actionable surveillance data for APSU's reported AFP cases, it should be clarified how roles and responsibilities are distributed between the two organisations and whether the division of work is appropriate.

5. Update objectives of APSU's AFP surveillance

Overall, a large proportion of people who use the system and its data believe that the objectives of the system are not being met. The objectives of the system are based on the AFP surveillance indicators set by GPEI and encapsulate a range of aspects of the condition's surveillance (28). As noted by survey participants, many facets of these objectives are not achievable by APSU alone and rely on the contribution of PAEDS and the actions of NERL, PEP and the NCC. Determining whether poliovirus infection is the cause of AFP is primarily the job of NERL and PEP, while APSU provides the trigger and information to facilitate these investigations. Assessing the adequacy of AFP surveillance according to WHO criteria is the responsibility of the NCC and monitoring the outcome at 60 days of non-polio AFP is no longer attempted in Australia. While it is not realistic for APSU to achieve the stated objectives alone, the system has a key role in facilitating their achievement through the collection and provision of timely and sensitive surveillance data. It is recommended that the APSU's objectives in the surveillance of AFP should be streamlined and made more specific to their role, enabling the realistic fulfilment of their aims. It is proposed that the APSU should aim to:

- Contribute to the documentation of the reported rate of AFP over time in those under 15 years in Australia with the aim of sensitively detecting and enabling response to polio compatible cases.
- Collect necessary case and clinical information to enable classification of reported AFP cases by PEP.
- Enable and encourage clinicians to report case information in a timely way to facilitate further clinical investigations and prompting of appropriate stool sample collection.
- Ensure appropriate subnational geographical coverage of surveillance activities.

6. Increase awareness of appropriate pre-determined procedures in response to identification of polio compatible AFP cases

A key purpose of AFP surveillance is to treat all AFP cases as a potential polio infection until poliovirus is excluded as the cause of AFP. Classification of a polio compatible AFP case (both 'zero evidence' and 'polio not excluded') is a trigger for activation of the current Poliomyelitis Outbreak and Response Plan. Polio compatibility is defined in the

response plan as being an AFP case that cannot be classified as non-polio. The inability to determine an alternative causative agent for AFP or exclude polio as a cause means that precautionary response activities should be initiated. Only four of the 15 survey participants in this study appropriately identified that classification of an AFP case as polio compatible should activate the response plan. Survey participants noted that polio compatible cases do not necessarily amount to suspected polio, as there can simply be a lack of evidence to classify the case otherwise. While there may not be evidence to classify a case as non-polio AFP, if there is no evidence to exclude polio as a cause, it is stated in the current plan that response activities should be taken. It is noted that the response plan is currently undergoing review, whereby the types of evidence available for polio compatible cases will indicate the need for the response plan's activation. Increasing awareness of the response plan and it's agreed actions amongst key stakeholders is important to enable an orderly, pre-determined response and to ensure that potential polio cases are acted upon and not overlooked.

Conclusion

The APSU is an important component of AFP surveillance in Australia. The surveillance system was found to be acceptable, stable, representative and have a high PVP. It proved to be moderately flexible, have relatively high data quality and be sensitive when combined with other data sources. The system was perceived to be relatively simple overall but the multistep process of data collection impacts negatively on many other aspects and attributes of the system including timeliness, usefulness, acceptability, flexibility, usefulness and data quality. APSU proved to be useful in contributing to recording the rate of AFP in <15 year olds in Australia over time but was found not to meet its objectives as a system. APSU's data collection was found to be untimely in facilitating the overall purpose of AFP surveillance in detecting and responding to a case of polio. In order to address identified limitations of the system, efforts should be made to consolidate the number of steps involved in surveillance, encourage and facilitate real time case reporting and update methods of data collection and storage. Only 31% of APSU's AFP cases had appropriate stool samples taken in order to detect or exclude poliovirus between 2012-2017. Two cases during this time were identified as polio compatible based on their clinical and diagnostic information, and adequate stool samples were not adequately collected to determine

whether these were true poliovirus infections. This demonstrates that substantial effort is needed to increase the proportion of APSU's reported AFP cases with adequate stool samples collected. Increasing the timeliness of reporting, and enhancing NERL's capacity to contact and prompt clinicians about stool samples within 14 days, will contribute to the quality of APSU's AFP surveillance and Australia's capability to detect and respond to polio more broadly.

References

1. World Health Organization. Poliomyelitis 2017 [Available from: http://www.who.int/mediacentre/factsheets/fs114/en/.
2. Ochmann S, Roser M. Polio: Published online at OurWorldInData.org; 2017 [Available from: https://ourworldindata.org/polio.
3. Nathanson N, Kew OM. From emergence to eradication: the epidemiology of poliomyelitis deconstructed. American journal of epidemiology. 2010;172(11):1213-29.
4. Centers for Disease Control and Prevention. Poliomyelitis. In: Hamborsky J, Kroger A, Wolfe S, editors. Epidemiology and prevention of vaccine-preventable diseases: US Department of Health & Human Services, Centers for Disease Control and Prevention; 2015.
5. Global Polio Eradication Initiative. Polio eradication and endgame strategic plan (2013–2018). Geneva, Switzerland: World Health Organization; 2013.
6. Dowdle WR. The principles of disease elimination and eradication. Bulletin of the World Health Organization. 1998;76(Suppl 2):22.
7. Hull HF, Ward NA, Hull BP, Milstien JB, de Quadros C. Paralytic poliomyelitis: seasoned strategies, disappearing disease. The Lancet. 1994;343(8909):1331-7.
8. Stewardson AJ, Roberts JA, Beckett CL, Prime HT, Loh P-S, Thorley BR, et al. Imported case of poliomyelitis, Melbourne, Australia, 2007. Emerging Infectious Diseases. 2009;15(1):63.
9. Tangermann RH, Lamoureux C, Tallis G, Goel A. The critical role of acute flaccid paralysis surveillance in the Global Polio Eradication Initiative. International Health. 2017;9(3):156-63.
10. Horstmann D, Paul, JR. . The incubation period in human poliomyelitis and its implications. Journal of the American Medical Association. 1947;135(1):11-4.
11. Zurynski Y, Srikanthan S, Elliott E, (eds). Australian Paediatric Surveillance Unit: 20 Years of Research into Rare Diseases. Sydney: Australian Paediatric Surveillance Unit; 2013.
12. Victorian Infectious Diseases Reference Laboratory. Acute Flaccid Paralysis Surveillance 2018 [Available from: http://www.vidrl.org.au/laboratories/poliovirus-reference/afp-surveillance/.
13. Paterson B, Durrheim D. Review of Australia's polio surveillance. Communicable Diseases Intelligence. 2013;37(2):E149-55.
14. Communicable Disease Network Australia. Polio Expert Panel: Terms of Reference and Operating Guidelines. 2016.
15. National Certification Committee for the Eradication of Poliomyelitis. Committee Terms of Reference. 2016.
16. He S, Zurynski YA, Elliott EJ. Evaluation of a national resource to identify and study rare diseases: The Australian Paediatric Surveillance Unit. Journal of paediatrics and child health. 2009;45(9):498-504.
17. German RR, Lee L, Horan J, Milstein R, Pertowski C, Waller M, et al. Updated guidelines for evaluating public health surveillance systems. MMWR Recomm Rep. 2001;50(1-35).
18. Australian Bureau of Statistics. Population by Age and Sex, Regions of Australia, 2016 2017 [Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3235.02016?OpenDocument.

19. Australian Paediatric Surveillance Unit. Current Studies 2018 [Available from: http://www.apsu.org.au/studies/current/.
20. Australian Paediatric Surveillance Unit. Study Protocol: Acute Flaccid Paralysis 2014 [Available from: http://www.apsu.org.au/assets/current-studies/AFP-Study-Protocol-June-2014.pdf.
21. Australian Paediatric Surveillance Unit and Victorian Infectious Diseases Reference Laboratory. Acute Flaccid Paralysis Initial Questionnaire 2016 [Available from: http://apsu.org.au/assets/current-studies/AFP-Initial-questionnaire-Oct-2016.pdf.
22. Queensland Government. Acute Flaccid Paralysis 2014 [Available from: https://www.health.qld.gov.au/cdcg/index/afp.
23. Australian Government Department of Health. Poliovirus Infection Case Definition 2015 [14 April 2019]. Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-nndss-casedefs-cd_polio.htm.
24. Cth. National Health Security Agreement (2007). 2017;Compilation no. 15.
25. Paediatric Active Enhanced Disease Surveillance. About PAEDS 2019 [Available from: http://www.paeds.edu.au/about-us/.
26. World Health Organization. WHO-recommended surveillance standard of poliomyelitis 2018 [Available from: http://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/poliomyelitis_standards/en/.
27. Butler M, Paterson BJ, Martin N, Hobday L, Thorley B, Durrheim DN. 'Silent'and 'noisy'areas: acute flaccid paralysis surveillance at subnational level, Australia, 2001–2015. International Health. 2017;9(3):190-4.
28. Global Polio Eradication Initiative. Polio surveillance indicators [Available from: http://polioeradication.org/polio-today/polio-now/surveillance-indicators/.

Appendix 3A - Survey questions

Australian Paediatric Surveillance Unit's surveillance of Acute Flaccid Paralysis - Stakeholder Survey

1.

Thank you for taking the time to fill in this survey. All questions relate to the Australian Paediatric Surveillance Unit's (APSU) surveillance of acute flaccid paralysis (AFP). This evaluation is focusing on any AFP data that is collected by APSU and subsequent surveillance actions conducted by the National Enterovirus Reference Laboratory (NERL) and the Polio Expert Panel (PEP) using APSU's AFP case reports. APSU surveillance and data will be defined as such for the purposes of this survey. The Paediatric Active Enhanced Disease Surveillance network (PAEDS) is not included in this evaluation. Please focus your answers around your recent experience with APSU surveillance (within the last 5 years). As outlined in the participant information sheet, confidentiality of responses will be maintained throughout this process and reporting will not include any identifying factors.

1. What is the primary purpose of your interaction with APSU's surveillance of AFP?

- ◯ System administration
- ◯ Policy work
- ◯ Committee work

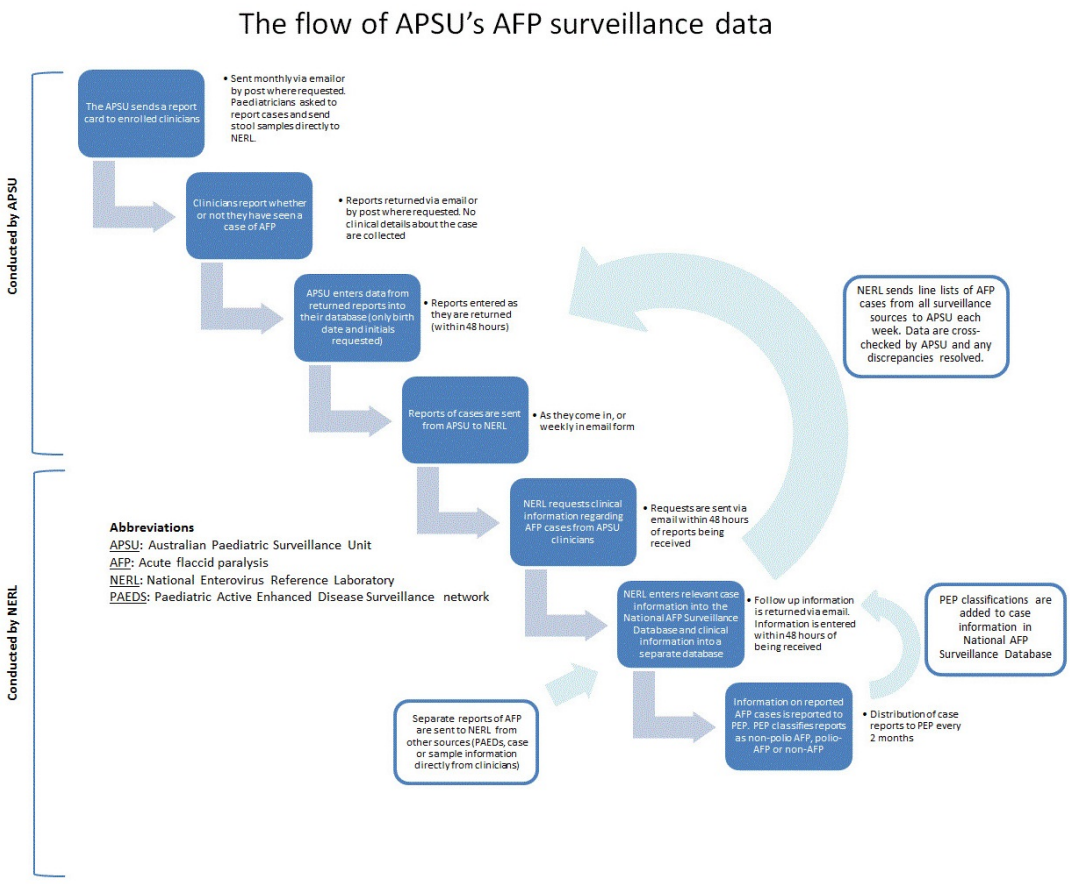
Other (please specify)

Australian Paediatric Surveillance Unit's surveillance of Acute Flaccid Paralysis - Stakeholder Survey

2. Simplicity

These questions relate to the simplicity of the system. In particular, these questions relate to the structure of the system and integration with other systems. Please refer to *Attachment A - Flow of APSU's AFP surveillance data* in order to answer the questions.

Attachment A - Flow of APSU's AFP surveillance data



2. Please look at *Attachment A - Flow of APSU's AFP surveillance data* Prior to this survey, did you have an understanding of how APSU's surveillance of AFP worked?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

3. Are there any differences between the way you understood APSU's surveillance of AFP to work and the way it is shown to in *Attachment A - Flow of APSU's AFP surveillance data*?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

If there were differences, please expand:

4. With reference to *Attachment A - Flow of APSU's AFP surveillance data*, how simple do you think the logistics of APSU's AFP surveillance is?

- ◯ Very simple
- ◯ Reasonably simple
- ◯ Not simple
- ◯ Don't know

If not simple, please expand:

5. With reference to *Attachment A - Flow of APSU's AFP surveillance data*, how simple do you think the integration of APSU and NERL systems are for AFP surveillance?

- ◯ Very simple
- ◯ Reasonably simple
- ◯ Not simple
- ◯ Don't know

If not simple, please expand:

6. With reference to *Attachment A - Flow of APSU's AFP surveillance data*, how simple do you think the integration of AFP classifications by PEP is to APSU surveillance?

- ◯ Very simple
- ◯ Reasonably simple
- ◯ Not simple
- ◯ Don't know
- ◯ If not simple, please expand:

3. Simplicity

These questions relate to the simplicity of the system. In particular, these questions relate to the collection of data.

7. How simple do you think the process of collection of information about AFP cases is (both the initial collection of cases by APSU and follow up by NERL)?

- ◯ Very simple
- ◯ Reasonably simple
- ◯ Not simple
- ◯ Don't know

If not simple, please expand:

These questions relate to the simplicity of the system. In particular, these questions relate to the the dissemination of data.

8. If you have previously requested APSU's AFP data (or APSU data through NERL), how simple have you found this process?

- ◯ Very simple
- ◯ Reasonably simple
- ◯ Not simple
- ◯ I haven't requested APSU's data before

If not simple, please expand:

9. If you have previously extracted APSU's AFP data (or APSU data through NERL), how simple have you found this process?

- ◯ Very simple
- ◯ Reasonably simple
- ◯ Not simple
- ◯ I haven't extracted APSU's data before

If not simple, please expand:

5. Flexibility

These questions relate to the flexibility of the system. In particular, these questions relate to the the ability of the system to accommodate recent changes in procedure and system structure.

10. Prior to beginning this survey, were you aware that in 2007 PAEDS began conducting AFP surveillance in collaboration with APSU?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

11. Were you involved in AFP surveillance during this change?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

12. How do you think APSU's AFP surveillance (including NERL) responded to this change?

- ◯ Very well
- ◯ Reasonably well
- ◯ Not well
- ◯ Don't know

If not well, please expand:

13. Based on your experience with APSU, how well do you think the system would respond to a future change in procedure, funding or system structure?

- ◯ Very well
- ◯ Reasonably well
- ◯ Not well
- ◯ Don't know

If not well, please expand

6. Stability

These questions relate to the stability of the system. In particular these questions relate to the system's ability to collect, manage and distribute data without failure and when needed.

14. How reliable is the APSU's AFP surveillance system or data when you need it (i.e. able to collect, manage and provide data without failure)?

- ◯ Very reliable
- ◯ Reasonably reliable
- ◯ Not reliable
- ◯ Don't know

If not reliable, please expand:

15. Has the APSU's AFP surveillance system or data ever been unavailable when you needed it (e.g. due to a system outage)?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

If yes, please expand

7. Acceptability

These questions relate to the acceptability of the system. In particular they relate to the willingness of stakeholders to utilise the system's data.

16. For what purposes do you use APSU's AFP surveillance system or data? Please select all that apply.

- ☐ Administering the system
- ☐ Committee work
- ☐ Developing policy
- ☐ Describing the epidemiology of AFP
- ☐ Informing response activities
- ☐ National reporting
- ☐ Cluster investigation
- ☐ International reporting

Other (please specify)

17. How useful do you find the APSU's AFP surveillance for this purpose?

- ◯ Very useful
- ◯ Reasonably useful
- ◯ Not useful
- ◯ Don't know

If not useful, please expand:

18. How often do you use the system or data? Please select one option

- ◯ Daily
- ◯ Weekly
- ◯ Monthly
- ◯ Every 2 months
- ◯ Every 6 months
- ◯ Annually

Other (please specify)

8. Data quality

These questions relate to the system's data quality. In particular, these questions relate to the completeness of the data collected.

19. Is there any information that you think is necessary for AFP surveillance that isn't currently captured by APSU?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

If yes, please expand:

9. Usefulness

These questions relate to the usefulness of the system. In particular this relates to whether their objectives are met as a surveillance system.

The APSU has 3 objectives in their surveillance of AFP:

1. To determine whether AFP is caused by poliovirus infection and if so, whether it is 'wild' or vaccine strain poliovirus.

2. To document the reported rate of AFP over time and to assess the adequacy of AFP surveillance according to WHO criteria.

3. To monitor the aetiology, clinical features and outcome at 60 days of non-polio AFP.

20. Do you think Objective 1 is met by the surveillance system (i.e. determining whether AFP is caused by poliovirus infection and if so, whether it is 'wild' or vaccine strain poliovirus)?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

If not, please provide details of why the objective is not met and what could be done differently to assist in achieving it:

21. Do you think Objective 2 is met by the surveillance system (i.e. documenting the reported rate of AFP over time and assessing the adequacy of AFP surveillance according to WHO criteria)?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

If not, please provide details of why the objective is not met and what could be done differently to assist in achieving it:

22. Do you think Objective 3 is met by the surveillance system (i.e. monitoring the aetiology, clinical features and outcome at 60 days of non-polio AFP)?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

If not, please provide details of why the objective is not met and what could be done differently to assist in achieving it:

10. Usefulness

These questions relate to the usefulness of the system.

23. In the event of PEP classifying a case of AFP as polio compatible, what actions do you believe should be taken?

24. Do you think these actions are (or would be) taken when this occurs?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know
- ◯ If no, please expand:

25. Do you think these actions are adequate in preventing further cases in the event that the AFP case has poliomyelitis?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

Other (please specify)

11. Timeliness

These questions relate to the timeliness of the system. In particular these questions relate to the availability of information to enable the meeting of surveillance objectives.

26. For the purposes that it is collected (the system's objectives), how timely do you think APSU's AFP data is?

- ◯ Very timely
- ◯ Reasonably timely
- ◯ Not timely
- ◯ Don't know

If not timely, please expand:

27. Have you ever experienced a delay in APSU's AFP surveillance data that resulted in delayed public health action?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

If yes, please expand:

28. Do you think that APSU detects AFP and disseminates data in a timely way to permit identification of a potential polio case and actioning of appropriate response activities?

- ◯ Yes
- ◯ No
- ◯ Partially
- ◯ Don't know

If not, please expand:

29. All things considered, what do you think APSU's AFP surveillance contributes to the identification and control of polio in Australia?

13. You're finished!

Thank you for providing details of your experience with APSU's surveillance of AFP. As outlined in the participant information sheet, confidentiality of responses will be maintained throughout this process and reporting will not include any identifying factors. A copy of the final evaluation report will be sent to all stakeholders invited to participate.

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Appendix 3B - Acute flaccid paralysis case clinical questionnaire

ACUTE FLACCID PARALYSIS INITIAL QUESTIONNAIRE (Revised October 2016)
Australian Paediatric Surveillance Unit – Victorian Infectious Diseases Reference Laboratory
Please keep a record of the child's unit number in your APSU folder.
Enquires Dr Bruce Thorley at VIDRL ph: (03) 9342 9607 to discuss this questionnaire or Prof Elizabeth Elliott on (02) 9845 3005 for clinical queries.
Please return questionnaire in the addressed reply-paid envelope to: AFP Surveillance, Victorian Infectious Diseases Reference Laboratory, The Doherty Institute, 792 Elizabeth Street, Melbourne, Victoria 3000 fax: (03) 9342 9665 email: enterovirus@mh.org.au

FOR INFORMATION REGARDING REFERRAL OF SPECIMENS TO VIDRL PLEASE SEE http://www.vidrl.org.au/surveillance/afp-surveillance/

If this patient is primarily cared for by another physician who you believe will report the case, please complete the reporting clinician and patient details only and return to VIDRL. If no other report is received for this child we will contact you for information requested in the remainder of the questionnaire.
The primary clinician caring for this child is: ***Name:*** ***Hospital:***

REPORTING CLINICIAN'S DETAILS

1. APSU Dr Code ☐☐☐☐ 2.Month/Year of Report ...../.....
3. Dr Name_____ 4. Dr Address_____
5. Dr Telephone: (0)_____ Fax: (0)_____ Email_____

PATIENT DETAILS

6. First 2 letters of Surname ☐☐ 7. First 2 letters of Given Name ☐☐ 8.Hospital Of Admission _____
9. Date of Birth: ☐☐/☐☐/☐☐ 10. Sex ☐M ☐F
11. Postcode ☐☐☐☐ 12. Of Aboriginal/Torres Strait Islander descent? ☐Yes ☐No ☐Unsure

PATIENT VACCINATION HISTORY

13. Has the patient ever been immunised with a vaccine including polio? ☐Yes ACIR/written record; ☐Yes self-report; ☐No ☐Unknown
14. Number of doses? _____ If known, date of last dose? Date /...../...../..... ☐Unknown
15. Has the patient been in contact with someone who received oral polio vaccine within the 6 weeks prior to onset of symptoms? ☐Yes ☐No ☐Unsure
16. Has the child travelled overseas in the last 3 months? ☐Yes ☐No ☐Unsure. IF YES, specify where _____
17. Has the patient had contact with anyone who has travelled overseas OR visited from overseas in the last 3 months? ☐Yes ☐No ☐Unsure.
IF YES, specify country of travel or origin and relationship to patient_____
18. In the 6 weeks prior to presentation did the child;
a) receive influenza vaccine? ☐Yes ☐No ☐Unsure IF YES, type of vaccine:_____Date given...../...../.....
b) receive any other vaccine? ☐Yes ☐No ☐Unsure IF YES, which vaccine(s) 1:_____Date given...../...../.....
2:_____Date given...../...../.....

CLINICAL FEATURES & INVESTIGATIONS

19. Date of onset of paralysis (dd/mm/yy) ☐☐/☐☐/☐☐
20. Site of paralysis _____
21. In the 6 weeks prior to presentation did the child
a) have an influenza-like illness? ☐Yes ☐No ☐Unsure IF YES, please describe symptoms:_____
b) was the child tested for influenza? ☐Yes ☐No ☐Unsure IF YES, result:_____ IF POSITIVE Date of positive specimen...../...../.....
22. In the 6 weeks prior to presentation did the child have any other infective illness ☐Yes ☐No ☐Unsure IF YES,
a) please describe symptoms:_____
b) did the child have laboratory testing? ☐Yes ☐No ☐Unsure IF YES, result:_____IF POSITIVE Date of positive specimen...../...../.....
23. Was the patient hospitalised? ☐Yes ☐No ☐Unsure
24. Was the patient immunosuppressed? ☐Yes ☐No ☐Unsure IF YES, specify_____
25. Was a sensory level detected on examination? ☐Yes ☐No ☐Unsure IF YES, specify_____
26. Was there cranial nerve involvement? ☐Yes ☐No ☐Unsure IF YES, specify_____
27. Was there bladder and/or bowel involvement? (eg. Urinary retention/incontinence) ☐Yes ☐No ☐Unsure IF YES, specify_____
28. Was a lumbar puncture done? ☐Yes ☐No ☐Unsure
29. IF YES, CSF: protein _____g/L glucose _____mmol/L Number of PMN_____ Lymphocyte_____ RBC_____ other_____
30. Were nerve conduction studies and/or EMG performed? ☐Yes ☐No ☐Unsure IF YES, specify results _____
31. Was an MRI done? ☐Yes ☐No ☐Unsure IF YES, brain ☐ or spinal ☐
If YES, specify findings_____
32. How many faecal specimens were sent for viral culture? ☐None ☐One ☐Two ☐Unsure

OUTCOME

33. Did the patient survive the illness? ☐Yes ☐No ☐Unsure IF NO, please give number of days between onset of paralysis and death ☐☐ days
34. Does the patient have any residual paralysis? ☐Yes ☐No ☐Unsure IF NO, duration of paralysis? ☐☐ days
35. If YES, specify level sensory_____ motor _____
36. Is there residual sphincter dysfunction? ☐Yes ☐No ☐Unsure

DIAGNOSIS
Please turn to PAGE 2 to complete the questionnaire.

Thank you for contributing to AFP surveillance and the WHO polio eradication program
PLEASE USE PAGE 2 OF THIS QUESTIONNAIRE IF YOU HAVE ANY FURTHER INFORMATION THAT MAY HELP US

ACUTE FLACCID PARALYSIS INITIAL QUESTIONNAIRE (Revised October 2016)
Australian Paediatric Surveillance Unit – Victorian Infectious Diseases Reference Laboratory
Please keep a record of the child's unit number in your APSU folder.
Enquires Dr Bruce Thorley at VIDRL ph: (03) 9342 9607 to discuss this questionnaire or Prof Elizabeth Elliott on (02) 9845 3005 for clinical queries.
Please return questionnaire in the addressed reply-paid envelope to: AFP Surveillance, Victorian Infectious Diseases Reference Laboratory, The Doherty Institute, 792 Elizabeth Street, Melbourne, Victoria 3000 fax: (03) 9342 9665 email: enterovirus@mh.org.au

PATIENT DETAILS

First 2 letters of Surname ☐☐ First 2 letters of Given Name ☐☐

Date of Birth: ☐☐ / ☐☐ / ☐☐

Sex M ☐ F ☐

DIAGNOSIS

37. In light of currently available evidence, what is the patient's diagnosis?

Peripheral neuropathy	Acute myelopathy	Systemic disease
❑ Guillain-Barré syndrome (acute post- infectious polyneuropathy)	❑ Transverse myelitis	❑ Acute porphyria
❑ Acute axonal neuropathy	❑ Acute disseminated encephalomyelitis (ADEM)	❑ Critical illness neuropathy/ myopathy
❑ Neuropathies of infectious diseases	❑ Spinal cord ischaemia	❑ Conversion disorder
❑ Acute toxic neuropathies(heavy metals)	❑ Spinal cord injury or compression eg.Tumour, trauma	Disorders of neuromuscular transmission
❑ Focal mononeuropathy	❑ Peri-operative complication	❑ Botulism
Anterior horn cell disease	Muscle disorders	❑ Insecticide *e.g: organophosphate poisoning*
❑ Acute poliomyelitis	❑ Polymyositis, dermatomyositis	❑ Tick bite paralysis
❑ Vaccine-associated poliomyelitis	❑ Periodic paralyses	❑ Myasthenia gravis
❑ Other neurotropic viruses	❑ Mitochondrial diseases (infantile type)	❑ Snake bite
	❑ Viral myositis	Other
	❑ Drug-induced paralysis (specify)_____	(specify)_____

Thank you for contributing to AFP surveillance and the WHO polio eradication program
PLEASE USE PAGE 2 OF THIS QUESTIONNAIRE IF YOU HAVE ANY FURTHER INFORMATION THAT MAY HELP US

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Chapter 4: Analysis of a public health dataset

Risk factors for invasive listeriosis in Australia

"If the statistics are boring, you've got the wrong numbers"

- Edward Tufte

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Chapter 4 - Prologue

My role

Since 2010, the National Enhanced Listeriosis Surveillance System (NELSS) has collected information about notified listeriosis case risk factors, including broad exposure and susceptibility data. While food-based exposures are routinely described and analysed, national data on pre-disposing risk factors such as underlying conditions and medication usage have not previously been analysed. I was tasked with conducting an analysis of these risk factors. To do this, I extracted and cleaned (and cleaned and cleaned) NELSS data, looked thoroughly at cases by multiple risk factors, and calculated risk ratios for underlying conditions, age group, pregnancy, speaking a language other than English at home and being born outside Australia. I drafted the report that forms this chapter and shared it with the Communicable Diseases Network Australia. I plan to share this with OzFoodNet and would like to eventually disseminate my key findings more broadly through publication.

Lessons learned

NELSS taught me many things, the first of which was how to clean a very complex dataset. Luckily, there was an existing do-file that is used for routine outbreak investigation, which gave me some helpful clues for cleaning demographic and clinical information. I quickly learnt that the reason the susceptibility data hadn't been analysed before is likely because there are many duplicate fields, different formats for data entry, and the case questionnaire had changed over time and was used differently depending on the jurisdiction. This provided me with a great opportunity to learn how to go through a dataset with a fine-tooth comb, identify what was important and make it fit for analysis.

Through this analysis I learnt to think about risk calculations from a new perspective. Prior to this, my 'exposure' to calculating associations with illness was based around traditional case-control or cohort studies where food or environmental exposures were the culprit. Reviewing the literature led me to understand that the data I had could be used to calculate risk ratios.

This project required a lot of thinking and I learnt a great deal from reading the literature and speaking to the coordinating OzFoodNet epidemiologist and departmental medical advisors. I had to look at the data from all angles to try and understand the complex interactions between multiple risk factors and stretched myself to come up with explanations for susceptibility, increased risk and severe outcomes. I also gained a new appreciation for the fascinating space between chronic and communicable disease.

Public health impact

Invasive listeriosis is an infection with severe outcomes that can be avoided to a large extent if the appropriate information is provided to highly susceptible populations. This investigation has shed light on the groups that are most at risk of listeriosis in Australia. As such, it has provided the information required to undertake targeted public health action and reduce unnecessary cases amongst high-risk groups. I hope that through dissemination of this work, actions may be taken to educate those at risk about relevant exposures and increase awareness amongst clinicians of those most at risk.

Acknowledgements

I would like to thank Dr Ben Polkinghorne, who was the OzFoodNet epidemiologist when I began this analysis. He conceptualised the project and provided me with insights into listeriosis epidemiology in Australia and the context of surveillance activities. I am also very appreciative of the input provided by the current OzFoodNet coordinating epidemiologist, Rose Wright. She patiently answered all of my late-night questions, helped navigate study design and generously indulged my need to think out loud. I am very grateful for the advice provided to me by Dr Gary Lum and Dr Anna Colwell, who offered invaluable insights into the clinical presentation and management of listeriosis. They afforded me the context I needed to conceptualise explanations for what the data showed. I would also like to thank Aparna Lal for helping me to solidify my methodology and for being so helpfully decisive at difficult points in my project. Ben and Aparna helped to review my chapter and provided helpful guidance and comments throughout.

I would like to acknowledge the work of Kate Astridge and Tim Sloan-Gardner, who created the department's Stata do-file that is used to clean NELSS data for hypothesis generation during cluster investigations. This provided me with somewhat of a road map to begin tackling the data set.

I would also like to thank Dr Alice Richardson who assisted in checking my methodology and ensuring I could answer the question on every epidemiologist's mind; 'compared to what?'.

Course activity requirements met

✓ Analysis of a public health dataset

✓ Literature review

Ethics statement

This study was approved by the Science and Medical Delegated Ethics Review Committee of the Australian National University (Protocol number 2018/199).

Abstract

Background: Invasive listeriosis is an important cause of foodborne illness that can incite severe disease in people with a range of risk factors, particularly those who are pregnant or immunosuppressed. In Australia, the risk of listeriosis amongst older adults and those with various underlying conditions has not been assessed. The National Enhanced Listeriosis Surveillance System (NELSS) contains comprehensive exposure and risk factor data on all nationally reported cases since 2010. This study describes and analyses the first eight years of these data.

Methods: Nationally reported listeriosis cases from 2010-2017 were extracted from NELSS and described by risk factors and outcomes. Rates of listeriosis in risk factor populations were calculated using population estimates from national agencies or publications. Crude risk ratios were calculated by comparing listeriosis in populations with risk factors to those without risk factors.

Results: From 2010-2017, 566 Australian-acquired listeriosis cases were recorded in NELSS (0.3 cases per 100,000 population annually). Overall, 79% of cases were born overseas or were from a non-English speaking background, 64% were on a medication, 63% were ≥65 years, 11% were pregnancy-related and 90% of non-pregnancy related cases had an underlying condition. When compared to the population without each risk factor, the risk of developing invasive listeriosis was 658 times higher in organ transplant recipients, 174 times higher in those living with non-haematological cancers, and a range of 4-38 times higher in those with haematological cancers, kidney disease, heart disease, diabetes, rheumatological conditions, chronic lung disease, those ≥45 years and pregnant women. Cases born overseas or who spoke a language other than English at home were 1.5-2 times more at risk of listeriosis. The case-fatality rate (CFR) was 15% in non-pregnancy related cases and 16% in neonates. High risk of listeriosis was not reflective of severe outcomes. There was a higher rate of presentation with meningitis and death amongst cases with no identified susceptibility risk factors compared to cases with any risk factors. Cases with chronic lung disease (CLD), non-haematological cancer and heart disease also had a high case fatality rate.

Conclusion: This study highlights that people with particular underlying conditions are at significantly higher risk of listeriosis than the Australian population without these

conditions. The risk of listeriosis should be communicated through targeted activities to groups identified as high risk in this study. In particular, transplant recipients and people with non-haematological cancers should be prioritised as groups to target in raising awareness of listeriosis and its exposure sources. Reduction of poor outcomes in those with chronic lung disease and non-haematological cancers, and clinician consideration of listeria-meningitis and rapid testing of young, otherwise healthy cases should also be a priority.

Introduction

Listeria monocytogenes is an important cause of severe foodborne gastrointestinal illness, causing approximately 0.3 cases per 100,000 people in Australia each year (1). While less common than other foodborne illnesses, infection more often results in serious invasive outcomes including more frequent mortality in the form of a higher case-fatality rate (CFR) than other pathogens (2). *L. monocytogenes* is a very resilient organism capable of surviving and multiplying in high salt, low moisture, anaerobic, acidic, and notably low temperature environments that enable its endurance in food (3).

Listeriosis in otherwise healthy people is typically non-invasive and often asymptomatic or can present as a mild illness including fever and gastroenteritis (4). Invasive listeriosis, where the bacteria penetrate normally sterile sites, occurs more commonly in people with increased susceptibility such as those with impaired immunity. Cases with invasive listeriosis present with more severe conditions such as septicaemia and meningitis and infection results in an almost 100% hospitalisation rate and a CFR of approximately 25.90%(5, 6). In pregnant women where the infection crosses the placenta; miscarriage, stillbirth, preterm delivery or neonatal infection may result, and the CFR amongst neonates is estimated to be 14.90%(5).

A number of risk factors have been associated internationally and in Australia with an increased risk of listeriosis due to heightened susceptibility or exposure. Immunosuppression (particularly cell-mediated), being an older adult, and living with a range of chronic conditions including diabetes, cancer, kidney disease, liver disease, organ transplantation, chronic lung disease and heart disease have been shown to increase the risk of susceptibility listeriosis (7-15). Being recently hospitalised, being of a non-English speaking background (NESB) and being born outside Australia have also been shown to increase exposure to listeriosis as a result of lower awareness of high risk foods (16-18). A variety of medications may also increase susceptibility via immunosuppression or altering of gastric pH (16, 19, 20).

In Australia, listeriosis is a nationally notifiable condition. Surveillance only endeavours to capture invasive cases where the bacteria are detected in normally sterile sites (21). Routine data is collected by state and territory health departments and transmitted to the National Notifiable Diseases Surveillance System (NNDSS). Since its establishment in 2010, the National Enhanced Listeriosis Surveillance System (NELSS) has been collecting enhanced surveillance data on all reported cases of listeriosis in Australia. NELSS includes information about each case's risk factors and exposures including demographic information, pregnancy details, underlying conditions, medications and a comprehensive food history. NELSS has been previously evaluated to be adequately timely and representative and have high sensitivity and data quality (22).

Population-level data has not yet been used to describe and calculate the risks associated with a range of susceptibility and exposure factors amongst listeriosis cases in Australia. Being of a NESB, being born overseas, using a range of medications, and hospital exposure have previously been shown to be risks for listeriosis in Australia through a case-control study (16).

This study aims to investigate the distribution of demographic variables, underlying conditions, medication usage, international background, hospital exposure, clinical presentation and outcomes amongst reported listeriosis cases in Australia. We aim to estimate the risks associated with underlying conditions, pregnancy, age and being born overseas or of NESB to identify populations most at risk of infection, and inform prevention activities to reduce unnecessary and severe cases of listeriosis.

Methods

Data and definitions

Data were exported from NELSS as at 1 February 2018. A case was defined as a confirmed case of listeriosis as per the Communicable Diseases Network Australia case definition with reported onset from 2010-2017 (21). Cases were laboratory confirmed through isolation of *L. monocytogenes* from a normally sterile site in any person or foetus ≥20 weeks gestation. Alternatively (as of 1 January 2017), they were confirmed where there was clinical evidence of infection in one person in a maternal-foetal pair and the other person was confirmed by laboratory evidence. Subtyping was

undertaken by jurisdictional reference laboratories and was recorded in NELSS. All cases were interviewed as they were reported to local health authorities using a standardised OzFoodNet listeriosis questionnaire (Appendix 4A). Cases were excluded if they reported having international travel during the incubation period.

The onset date of illness was defined as the date of symptom onset and where that date was not available, the date of hospital admission, specimen collection, notification, pregnancy outcome, or the date of interview or data collection were used as proxy onset dates in such order. The reporting state was used as the place of residence. Reported underlying conditions and medication usage were obtained from both the cases and their medical practitioner. Hospital exposure during incubation period, clinical presentation, hospitalisation following infection and outcome were collected through specific case questionnaire fields. Whether or not cases were associated with a known outbreak (through epidemiological and/or laboratory link) was recorded in NELSS.

We attempted to find an estimate of the Australian population with each risk factor of interest (those recorded in case interviews). Those with available estimates are recorded in Table 1 alongside the source of the estimates. The derived fields for cases' underlying conditions, pregnancy, language, birth country, age and sex are also reported in Table 1. Jurisdictional incidence rate calculations used the 2016 national estimated resident population and the mean number of annual cases (23). Risk factor specific calculations used the mean annual estimated residential estimate population from 2010-2017.

Table 1. Sources of case and population risk factor data

Risk factor	Case data derivation from interview	Data sources for population with risk factor
Renal disease	Combined questionnaire fields 'renal or kidney disease involving dialysis' and 'other renal disease'	National Health Survey, 2014-15 prevalence (24)
Haematological cancers	Questionnaire free text field where type of cancer was specified. Counted as haematological where leukaemia (acute myeloid and acute and chronic lymphoblastic), lymphoma (Hodgkin and non-Hodgkin), myelodysplastic syndromes and multiple myeloma were specified	Australian Institute of Health and Welfare (AIHW), 2017 prevalence; and Leukaemia foundation, 2014 prevalence (25, 26)
Non-haematological cancers	Questionnaire field 'cancer'. Cases with specified haematological cancers in accompanying free text field were removed	Australian Institute of Health and Welfare (AIHW), 2017 prevalence and Leukaemia foundation, 2014 prevalence (25, 26)
Liver disease	Specific questionnaire field	Gastroenterological Society of Australia and the Australian Liver Association, 2013 prevalence (27)
Diabetes	Combined questionnaire fields 'diabetes insulin resistant' and 'diabetes non-insulin resistant'	Diabetes Australia, 2015 prevalence (28)
Heart disease	Specific questionnaire field	National Health Survey, 2014-15 prevalence (24)
Chronic lung disease (excluding asthma)	Specific questionnaire field	National Health Survey, 2014-15 chronic obstructive pulmonary disease prevalence (24)
Organ transplant recipient	Specific questionnaire field	Australian Organ and Tissue Donation and Transplantation Authority, 2015 incidence (29)
Rheumatological conditions	Specific questionnaire field	Publication, 2010 autoimmune rheumatic disease prevalence (30)
Pregnancy	Combined questionnaire fields 'perinatal case', 'mother case' 'outcome pregnancy' and 'foetal or neonatal outcome'	Australian Institute of Health and Welfare, 2015 births (31)
Born overseas	Questionnaire field 'country of birth'	Australian census, 2016 (32)
Non-English speaking background	Questionnaire field 'language other than English spoken at home'	Australian census, 2016 (32)
Age	Specific questionnaire field	National estimated resident population, 2016 (23)

Description and analysis

Data was cleaned and risk ratios were calculated using Stata version 13.1 (StataCorp, College Station, United States of America). Descriptive statistics, figures and tables were produced using Microsoft Excel 2010.

The number of listeriosis cases reported in NELSS and the NNDSS were compared. NNDSS case numbers were selected based on onset date, and when onset was unknown, notification date (which can have a lag of a number of weeks from onset).

Demographic, clinical and laboratory characteristics, outbreak-associated cases and the frequency of risk factors including underlying conditions, medications used, pregnancy, hospital admission during the incubation period, birth country and NESB amongst cases were described. Cases without any recognised risk factors were also described. The proportion of cases that were hospitalised or died, their clinical presentation and their risk factors were described.

Age-group specific, jurisdictional and risk factor specific mean annual listeriosis incidence rates were calculated. The rate of listeriosis amongst those with specific risk factors was calculated using the mean annual number of listeriosis cases who reported having the risk factor and the estimated Australian population with that risk factor. To calculate the population without the risk factor, the population with the risk factor was subtracted from the mean Australian residential estimate population from 2010-2017.

Crude risk ratios (RR) were calculated for risk factors where an estimate of the population with the risk factor in Australia was available (as per Table 1). Methodology was based on that described by Goulet et al (9). The mean annual rate of listeriosis in each risk factor population was divided by the mean annual rate of listeriosis in the population without the specified risk factor to calculate RRs. All results were considered significant at the 5% level.

Data completeness was not a focus of this analysis, however the completeness of each of the fields used in the results was described.

Ethics statement

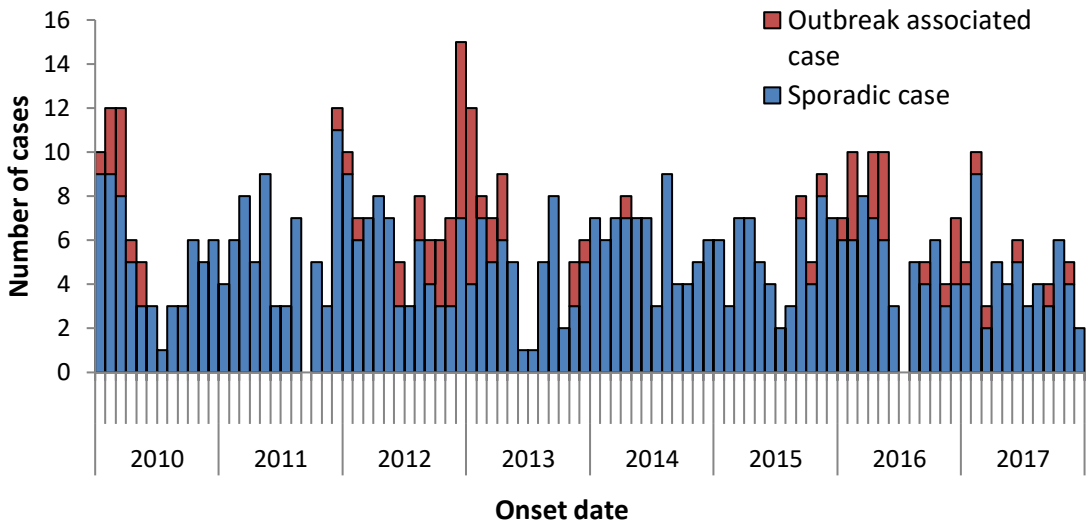
This study was approved by the Science and Medical Delegated Ethics Review Committee of the Australian National University (Protocol number 2018/199).

Results

NELSS recorded 601 listeriosis cases from 2010-2017. Of these, 35 were excluded due to international travel and 566 cases were included in analysis. Overall, the mean annual rate of listeriosis in the population from 2010-2017 was 0.28 cases per 100,000 population. This ranged from 0.29 cases per 100,000 in 2017 to 0.41 cases per 100,000 in 2012. Of the cases with a known serotype from 2010-2017 (94.52%, 535/566), *L. monocytogenes* isolates were most frequently serotype 4b, 4d, 4e (40.75%, n=218), followed by 1/2a, 3a (27.48%, n=147), and 1/2b, 3b, 7 (23.55%, n=126).

Of the cases in NELSS, 13.96% of cases were associated with outbreaks (n=79/566). Outbreaks, like sporadic cases, had a seasonal pattern, with clustering in the summer months (Figure 1). When the number of cases reported to NELSS (n=601) were compared to those reported to NNDSS, there was one additional case in NNDSS (n=602) (33). We were unable to compare the cases to account for the discrepancy.

Figure 1. Listeriosis cases by known outbreak association, 2010-2017



Case demographics

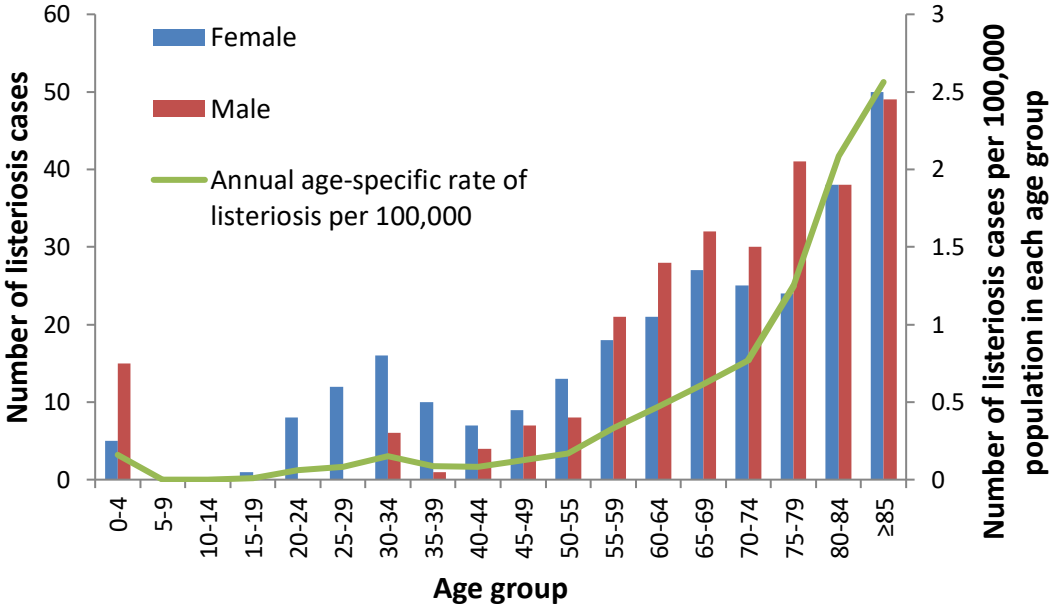
Cases were almost equally male (49.65%, n=281) and female (50.35%, n=285). Where age was reported (99.64%, n=564), cases ranged in age from 0 – 98 years old. The

median age was 70 years and the interquartile range was 26 years. A majority (62.76%, n=354) of cases were aged ≥65 years.

The age-group specific mean annual rate of listeriosis was eight times higher in those aged ≥65 years (1.20 per 100,000 population), than in those <65 years (0.15 per 100,000 population). Amongst five year age-groups, the annual incidence rate increased for each group aged ≥45 years. The five year age-group with the most cases and highest mean annual incidence was the 80-84 year old group (13.48%, n=76/564, 2.56 cases per 100,000 population), followed by the 75-79 year old group (11.52%, n=65/564, 2.09 cases per 100,000 population) (Figure 2).

Where location was recorded (n=563), cases were most frequently reported in New South Wales and Victoria (NSW: 35.70%, n=201, VIC: 31.08%, n=175). The mean annual incidence rate of cases in the population by jurisdiction was highest in Tasmania (0.39 per 1000,000 population), followed by the Northern Territory (0.36 per 100,000 population) and Victoria (0.35 per 100,000 population) and ranged from 0.21-0.32 per 100,000 population in the remaining states and territories (34).

Figure 2. Mean annual listeriosis cases by age, sex and age-specific rate per 100,000 population, 2010-2017



Pregnancy-related cases

One tenth of reported cases were pregnancy-related (10.60%, n=60/566). Of these 60 cases, 42 were mothers and 18 were reported foetal (≥20 weeks gestation) or neonatal cases. The outcomes of 38 pregnancies were known; 16 resulted in live neonates, three resulted in neonatal deaths, 12 resulted in foetal deaths, three resulted in deaths where the stage of pregnancy was not specified, and four women were still pregnant at diagnosis (Table 2). The CFR for foetuses and neonates where their mothers had listeriosis and the outcome was known was 52.94% (n=18/34). All mothers survived.

Table 2. Outcomes amongst pregnancy-related listeriosis cases, 2010-2017

Type of pregnancy-related case	Cases that lived (n)	Cases that died (n)	Cases with unknown outcome (n)	Total cases (n)	CFR where outcome is known (%)
Mothers	42	0	0	42	0.00%
Foetus (≥20 weeks gestation)	0	12	0	12	100.00%
Neonate (within first month of life)	16	3	3	22	15.79%
Gestational age unspecified	0	3	1	4	100.00%
Still pregnant	4	0	0	4	0.00%

CFR: Case-fatality rate

Cases born overseas and from non-English speaking backgrounds

Amongst all cases where language at home or birth country was known (n=466), 79.35% were born overseas or were from a NESB (n=365). The proportion of those born overseas or from a NESB was higher in pregnant mothers (94.44%, n=34/36) than non-pregnancy related cases (77.94%, n=318/408).

Language at home was known in 40.28% of all cases (n=228/566), of which 28.07% spoke a language other than English at home (n=64). Commonly spoken languages amongst cases included Chinese (7.46%, n=17/228), Italian (4.82%, n=11) and Vietnamese (3.95%, n=9).

Country of birth was known for 76.86% of cases (n=435/566), of which 45.06% were born overseas in 55 different countries (n=196). Internationally-born cases were most frequently born in the United Kingdom (6.67%, n=29/435), China (4.83%, n=21), Italy (3.91%, n=17) and Vietnam (2.76%, n=12). In the general population, 21% of

Australians speak a language other than English at home and 33% are born overseas (32).

A majority of pregnancy-related adult cases where a country of birth was specified (n=33), were born in a country other than Australia (66.67%, n=22). These were most commonly China (9.09%, n=3/33), India (6.06%, n=2), Sudan (6.06%, n=2) and the United Kingdom (6.06%, n=2). Of the pregnancy-related cases where language at home was specified (n=11), 45.45% spoke a language that was not English (n=5).

Underlying conditions amongst cases

Amongst non-pregnancy related cases, 90.51% had at least one underlying condition (n=458/506) and 67.98% had two or more (n=344). When pregnancy related cases were included, 84.98% of cases had at least one underlying condition (n=481/566) and 61.31% had two or more (n=347).

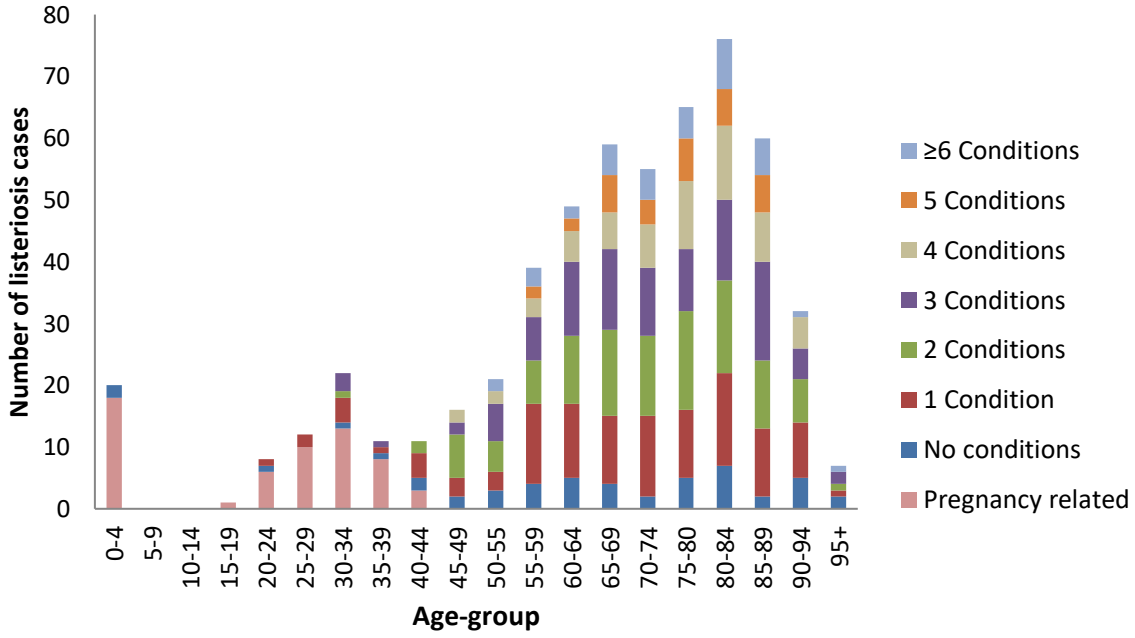
Where specific conditions were collected, cases (including pregnancy related) were reported to most commonly have cancer (n=195, 34.45%), heart disease (n=187, 33.04%) and diabetes (n=131, 23.14%) (Table 3). Where conditions that were not specifically collected were described (83.04%, n=184/224), illnesses were diverse but were most commonly autoimmune, gastric or circulatory diseases such as lupus, arthritis, Crohn's disease, ulcerative colitis, irritable bowel syndrome and hypertension.

The proportion of cases with several underlying conditions increased with age, with the presence of four or more conditions occurring only in cases ≥45 years (Figure 3). The proportion of all cases with no underlying conditions was also almost four times higher in those under 65 years (28.57%, n=60/210) than in cases over 65 years (7.63%, n=27/354).

Table 3. Underlying conditions amongst reported listeriosis cases, 2010-2017

Underlying condition	Number of cases with condition (n)	Proportion of all cases (n=566) with condition (%)
Other illness	224	39.58%
Cancer (all)	195	34.45%
Cancer (non-haematological)	*145*	*25.62%*
Cancer (haematological)	*50*	*8.83%*
Heart disease	187	33.04%
Diabetes	131	23.14%
Kidney disease	109	19.26%
Rheumatological condition	93	16.43%
Liver disease	70	12.37%
Chronic lung disease (excluding asthma)	58	10.25%
Organ transplant	19	3.36%
Number of underlying conditions		
Any condition	479	84.62%
No condition	87	15.37%
1 condition	132	23.32%
2 conditions	112	19.79%
3 conditions	102	18.02%
4 conditions	61	10.78%
5 conditions	34	6.01%
≥6 conditions	38	6.71%

Figure 3. Number of listeriosis cases in each age-group by number of underlying conditions and pregnancy relatedness, 2010-2017



Medication use amongst cases

Of all cases, 64.13% reported taking one or more medications (n=363/566). Where specific medications were collected, cases were reported to most commonly be taking corticosteroids (n=180, 31.80%), antibiotics (n=143, 25.27%) and gastric acid medication (n=142, 25.09%) (Table 4).

Table 4. Medication use amongst reported listeriosis cases, 2010-2017

Medications	Number of cases on medication (n)	Proportion of all cases (n=566) on medication (%)
Corticosteroids	180	31.80%
Antibiotics	143	25.27%
Gastric acid medication	142	25.09%
Antacids	132	23.32%
Chemotherapy	79	13.96%
Other immune affecting drugs	70	12.37%
Antidiarrheal medicine	23	4.06%
Radiation therapy	20	3.53%
Cyclosporines	15	2.65%
Number of medications*		
No medications	203	35.87%
1 medication	136	24.03%
2 medications	109	19.26%
3 medications	62	10.95%
4 medications	29	5.12%
5 medications	16	2.83%
≥6 medications	11	1.88%

**Reflects the number of each category of medications listed in medications*

Hospital exposure during incubation period

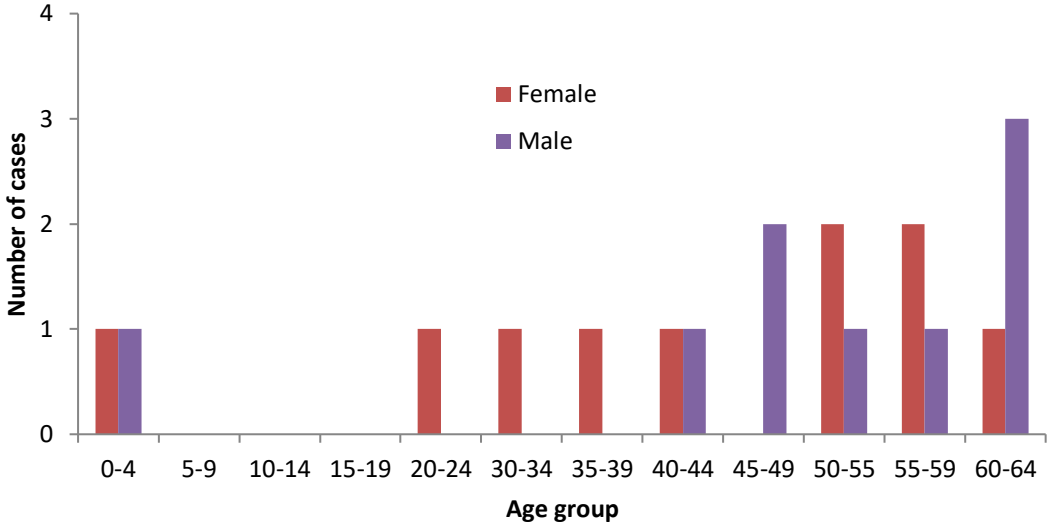
Of all cases where hospitalisation in the three months prior to onset was known (88.52%, n=501), 34.93% were admitted (n=175). Of these, 94.35% had a specified underlying condition or were pregnancy-related (n=167).

Cases without recognised susceptibility risk factors

There were 19 non-pregnancy related cases with no reported underlying conditions, who did not report taking any medications and who were under 65 years of age. These cases were almost equally male (47.37%; 9/19) and female (52.63%; 10/19) (Figure 4). Their distribution across jurisdictions was similar to that of overall cases.

Cases without susceptibility risk factors were most commonly aged 40-65 (73.68%; 14/19) (Figure 4).

Figure 4. Number of listeriosis cases without recognised susceptibility factors by sex, 2010-2017



Risk ratios for risk factors

When compared to the population without each condition, the risk of listeriosis was 658 times higher in organ transplant recipients, 174 times higher in those with non-haematological cancer, 38 times higher in those with haematological cancer and 27 times higher in those with kidney disease (Table 5). All other specified conditions were significantly associated with an increased risk of listeriosis when compared to populations without the conditions, except liver disease, which was found not to be associated with infection (RR=0.4). When non-alcoholic fatty liver disease (NAFLD) was excluded from the Australian population with liver disease (5,538,677 people estimated to have NAFLD; 640,610 estimated to have other types of liver disease), the condition became significantly associated with risk of listeriosis (RR 5.03, P<0.0001, 95% CI 3.86-6.47).

Pregnant mothers were found to be six times more likely to have listeriosis than the non-pregnant population. Those aged ≥65 years were nine times more likely to have listeriosis, and those aged ≥45 were seven times more likely to have the infection than their younger counterparts. Being born overseas or being from a NESB increased the risk of listeriosis by one and a half to two times when compared to those born in Australia and who speak English at home.

Table 5. Risk associated with known risk factors amongst reported listeriosis cases, 2010-2017

Condition	People with risk factor in the Australian population (n)	Cases with risk factor (n)	Cases where risk factor is singular (n, %)	Annual mean cases with risk factor (n)	Cases per 100,000 population with risk factor (n)	Risk ratio (95% CI)*	*P* value
Organ transplant	1239	19	0 (0.00%)	2.38	191.69	658.23 (392.06 - 1042.21)	<0.0001
No organ transplant	*23479124*	*547*		*68.38*	*0.29*		
Cancer (non-haematological)	46340	145	36 (24.83%)	18	39	174.17 (143.52 - 211.27)	<0.0001
No non-haematological cancer	*23434023*	*421*	-	*52.63*	*0.22*		
Cancer (haematological)	60000	50	1 (0.02%)	6.25	10.42	37.82 (27.71 - 50.63)	<0.0001
No haematological cancer	*23420363*	*516*		*64.50*	*0.28*		
Kidney disease	203400	109	0 (0.00%)	13.63	6.70	27.30 (21.95 - 33.71)	<0.0001
No kidney disease	*23276963*	*457*	-	*57.13*	*0.25*		
Heart disease	1200000	187	14 (7.49%)	23.38	1.95	9.16 (7.66 - 10.95)	<0.0001
No heart disease	*22280363*	*379*	-	*47.38*	*0.21*		
Rheumatological condition	545825	93	1 (0.01%)	11.63	2.13	8.26 (6.54 - 10.34)	<0.0001
No rheumatological condition	*22934538*	*473*	-	*59.13*	*0.26*		
Diabetes	1200000	131	11 (8.40%)	16.38	1.36	5.59 (4.56 - 6.83)	<0.0001
No diabetes	*22280363*	*435*	-	*54.38*	*0.24*		
Chronic lung disease (excluding asthma)	600300	58	1 (1.72%)	7.25	1.21	4.35 (3.26 - 5.72)	<0.0001
No chronic lung disease	*22880063*	*508*	-	*63.50*	*0.28*		
Liver disease	6179287	70	5 (7.14%)	8.75	0.14	0.40 (0.30 - 0.51)	<0.0001
No liver disease	*17301076*	*496*	-	*62.00*	*0.36*		
Any specified condition	10036391	479	132 (27.44%)	59.88	0.60	7.38 (5.86 - 9.37)	<0.0001
No specified conditions	*13443972*	*87*	-	*10.88*	*0.08*		
Pregnancy							
Pregnancy	304268	42	24 (57.14%)	5.25	1.73	6.11 (4.35 - 8.37)	<0.0001
No pregnancy	*23176095*	*524*		*65.50*	*0.28*		
Age group							
≥65 years	3673511	354	-	44.25	1.20	9.42 (7.92 - 11.22)	<0.0001
<65 years	*20537298*	*210*	-	*26.25*	*0.13*		
≥45 years	9614311	*479*	-	59.875	0.62	6.80 (7.92 - 11.22)	<0.0001
<45 years	*11597686*	85	-	*10.625*	*0.09*		
International background							
Born overseas	6163667	196	-	24.5	0.40	2.08 (1.71 - 2.52)	<0.0001
Born in Australia	*15614835*	*239*	-	*29.875*	*0.19*		
NESB	4930876	64	-	8	0.16	1.47 (1.08 - 1.97)	<0.0001
English spoken at home	*18549486*	*164*	-	*20.5*	*0.11*		

** Risk ratio: rate of listeriosis in the population with a risk factor / rate of listeriosis in the population without the risk factor.*
CI: Confidence Interval, NESB: Non-English speaking background

Clinical presentation, hospitalisation and outcome

Of the cases where clinical presentation was specified, 69.70% had septicaemia (n=368/528), 12.63% had meningitis (n=61/483) and 72.82% had one or both presentations (n=344/479). The proportion of cases with septicaemia was higher in those with one or more underlying conditions than those with no underlying conditions and no susceptibility risk factors (non-pregnancy cases with no underlying conditions or medication usage and under 65 years) (Table 6). The proportion of cases with meningitis was higher in those with fewer or no underlying conditions, and highest in those with no recognised susceptibility risk factors. No pregnancy-related cases reported experiencing either of these presentations. Cases <65 years old more often presented with meningitis (17.65%, n=33/187) than those ≥65 years (9.46%, n=29/296), and less frequently presented with septicaemia (50.51%, n=100/198) than those over ≥65 years (81.21%, n=268/330 (Figure 5).

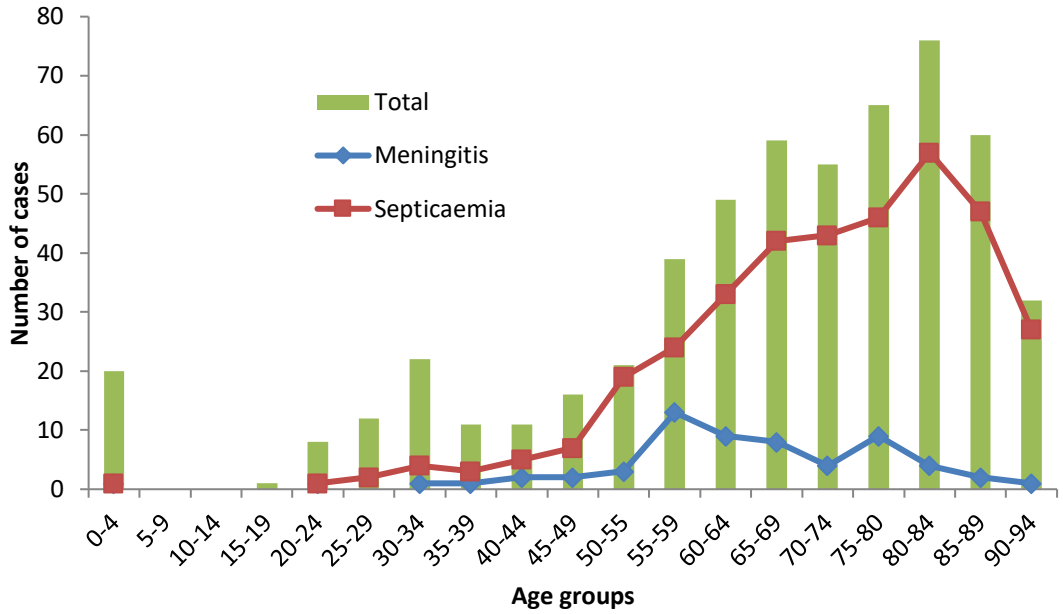
Table 6. Clinical presentation amongst listeriosis cases by number of underlying conditions and cases with no susceptibility risk factors

Number of conditions	Cases with each number of conditions with known septicaemia status (n)	Proportion of cases with each number of conditions with septicaemia (%, n)*	Cases with each number of conditions with known meningitis status (n)	Proportion of cases with each number of conditions with meningitis (%, n)*
No conditions	78	28.21% (22)	78	17.95% (14)
1 condition	120	69.17% (83)	110	16.36% (18)
2 conditions	106	75.47% (80)	93	11.83% (11)
3 conditions	96	78.13% (75)	86	12.79% (11)
4 conditions	59	88.14% (52)	53	3.77% (2)
5 conditions	31	83.87% (26)	29	6.90% (2)
≥6 conditions	38	78.95% (30)	34	8.82% (3)
No susceptibility risk factors**	18	50.00% (9)	18	55.56% (10)
Total	528	69.70% (368)	483	12.63% (61)

**Cases with unknown clinical presentation excluded (n=38 unknown septicaemia, n=83 unknown meningitis)*

*** Non-pregnancy cases with no underlying conditions or medication usage and under 65 years*

Figure 5. Number of listeriosis cases by reported clinical presentation and age group, 2010-2017



Amongst adult cases (excluding foetal and neonatal cases) where clinical presentation was known, there was a higher CFR amongst those with septicaemia (16.58%, n=61/368) than those without it (5.63%, n=9/160) (Table 7). The CFR was also higher in those with meningitis (14.75%, 9/61), compared to those without it (11.85%, 50/422). Septicaemia was present in a vast majority of the cases that died (87.14%, 61/70); meningitis was present in 15.25% of cases that died (9/59).

Table 7. Deaths amongst adult listeriosis cases with septicaemia and meningitis, 2010-2017

Clinical presentation	Proportion of cases that died that had the clinical presentation (%, n)	Proportion of cases that lived that had the clinical presentation (%, n)	CFR amongst cases with the clinical presentation (%, n)	CFR amongst cases without the clinical presentation (%, n)
Septicaemia	87.14% (61/70)	67.03% (307/458)	16.58% (61/368)	5.63% (9/160)
Meningitis	15.25% (9/59)	12.26% (52/424)	14.75% (9/61)	11.85% (50/422)

NB: Only cases with known clinical presentation were included in tabulation and calculation. Foetal and neonatal cases excluded.
CFR: Case-fatality rate

Amongst non-pregnancy related cases where hospitalisation status was known (95.65%, n=484/506), almost all cases were hospitalised during illness for listeriosis or other causes (99.38%, n=481/484). There was a range of 97.06% to 100.00% of cases

hospitalised during listeriosis infection for any cause within specified underlying conditions, number of conditions and age-groups (Table 8).

Of non-pregnancy related cases where hospitalisation reason was known (92.49%, n=468), 69.23% were hospitalised for listeriosis specifically (n=324). Listeriosis cases with rheumatological conditions (80.22%), non-haematological cancers (72.87%) and heart disease (70.17%) had the highest proportion of cases admitted to hospital specifically for listeriosis.

The all-cause CFR amongst all non-pregnancy related cases was 15.02% (n=76/506). The all-cause CFR following illness with listeriosis was highest in those with chronic lung disease (20.69%), non-haematological cancers (18.62%) and heart disease (16.58%).

Half of all non-pregnancy related deaths were attributed specifically to listeriosis (n=38/76). The CFR among cases where listeriosis was specified as the cause of death was 7.51% (n=38/506). The listeriosis-specific CFR was highest in those with diabetes (9.52%), heart disease (8.02%) and non-haematological cancers (7.59%).

Those aged ≥65 years had a higher all-cause CFR (15.82%) and listeriosis-specific CFR (8.76%) than younger cases, but had a lower rate of hospitalisation for listeriosis (67.79%) than those <65 years (72.54%).

Cases without recognised susceptibility risk factors had the highest all cause CFR (21.05%) and second highest proportion of listeriosis-specific hospitalisations (76.47%) compared to cases with any risk factor. Of the cases with no susceptibility risk factors that died, 75% (n=3/4) were under 50. Those with no underlying conditions had a higher proportion of hospitalisations for listeriosis, all-cause mortality and listeriosis-specific mortality than those with one or more conditions (75.61%, 18.76% and 12.50% respectively). There was no clear pattern between the proportion of those who were hospitalised and died and the number of underlying conditions.

Table 8. Deaths and hospitalisations among non-pregnancy related listeriosis cases by condition and age-group, 2010-2017

Underlying condition	Number of cases with condition (n)	Cases hospitalised for all causes during illness (%, n)*	Cases hospitalised for listeriosis during illness (%, n)**	All-cause CFR (%, n)	Listeriosis-specific CFR (%, n)
Chronic lung disease (excluding asthma)	58	100.00% (57/57)	69.64% (39/56)	20.69% (12)	3.45% (2)
Cancer (non-haematological)	145	97.89% (139/142)	72.87% (94/129)	18.62% (27)	7.59% (11)
Heart disease	187	99.44% (179/180)	70.17% (127/181)	16.58% (31)	8.02% (15)
Kidney disease	108	99.05% (104/105)	68.63% (70/102)	15.74% (17)	7.41% (8)
Liver disease	70	100.00% (68/68)	61.19% (41/67)	15.71% (11)	5.71% (4)
Diabetes	126	100.00% (122/122)	66.94% (83/124)	13.49% (17)	9.52% (12)
Rheumatological condition	93	100.00% (91/91)	80.22% (73/91)	11.83% (11)	5.38% (5)
Cancer (haematological)	50	100.00% (45/45)	59.57% (28/47)	8.00% (4)	2.00% (1)
Organ transplant	19	100.00% (18/18)	58.82% (10/17)	0.00% (0)	0.00% (0)
Other illness	206	99.50% (200/201)	67.38% (126/187)	13.59% (28)	6.80% (14)
Number of conditions					
Any condition	458	99.32% (437/440)	68.62% (293/427)	14.63% (67)	6.99% (32)
No condition	48	100.00% (44/44)	75.61% (31/41)	18.75% (9)	12.50% (6)
1 condition	114	100.00% (111/111)	68.63% (70/102)	14.91% (17)	7.02% (8)
2 conditions	110	97.06% (99/102)	69.61% (71/102)	11.82% (13)	3.64% (4)
3 conditions	101	98.98% (97/98)	66.32% (63/95)	16.83% (17)	10.89% (11)
4 conditions	61	100.00% (58/58)	72.41% (42/58)	18.03% (11)	9.84% (6)
5 conditions	34	100.00% (34/34)	60.61% (20/33)	11.76% (4)	2.94% (1)
≥6 conditions	38	100.00% (38/38)	72.97% (27/37)	13.16% (5)	5.26% (2)
Age					
<65 years	152	99.31% (143/144)	72.54% (103/142)	13.16% (20)	4.61% (7)
≥65 years	354	99.41% (338/340)	67.79% (221/326)	15.82% (56)	8.76% (31)

Underlying condition	Number of cases with condition (n)	Cases hospitalised for all causes during illness (%, n)*	Cases hospitalised for listeriosis during illness (%, n)**	All-cause CFR (%, n)	Listeriosis-specific CFR (%, n)
No susceptibility risk factors***	19	100% (18/18)	76.47% (13/17)	21.05% (4)	5.26% (1)
All cases	506	99.38% (481/484)	69.23% (324/468)	15.02% (76)	7.51% (38)

** Only cases with known hospitalisation status included*
*** Only cases with known hospitalisation reason included*
**** Non-pregnancy cases with no underlying conditions or medication usage and under 65 years*
CFR: Case-fatality rate

Discussion

This first analysis of enhanced population-level listeriosis risk factor data in Australia establishes the degree to which populations with a variety of predisposing factors are at risk of listeriosis and severe outcomes nationally. This provides evidence to support international trends, agrees with previous Australian case-control studies, and highlights specific Australian risk groups that need increased attention for listeriosis prevention and management. Notably, we found that organ transplant recipients and those living with cancer and kidney disease had the highest risk of listeriosis amongst cases with a range of risk factors. Cases without any recognised susceptibility risk factors (non-pregnancy related cases who are under 65 years with no underlying conditions or medication usage) and those with chronic lung disease, non-haematological cancer and heart disease had the highest CFR when compared to cases with other risk factors. This study also provides a detailed description of the characteristics of population-level reported listeriosis cases from 2010-17. This includes insights into the number of underlying conditions and the variety of medications used by cases which have not previously been well documented at the population level internationally. Overall, we found that 79.35% of cases were born overseas or were from a NESB, 64.13% were on a medication, 62.76% were ≥65 years, 10.60% were pregnancy-related and 90.51% of non-pregnancy related cases had an underlying condition.

When compared to the population without each risk factor, all of the susceptibility and exposure factors investigated in this study were found to significantly increase the risk

of reported listeriosis, except liver disease. Through univariate analysis, organ transplant recipients, those with cancer and those with kidney disease were identified as at highest risk of contracting listeriosis. Cases with other underlying conditions, pregnant women, cases ≥65 years, those born overseas and from a NESB were also found to be at increased risk of contracting or being exposed to the infection. The groups identified as at increased risk emulate those identified in international literature, except for liver disease (7-15).

Liver disease has been shown by other studies to be a significant comorbid risk factor for listeriosis infection (8-10, 12-14). The discrepancy between our results and international trends may be explained by the inclusion of NAFLD in our estimated Australian population with liver disease. NAFLD encapsulates a broad spectrum of abnormalities, of which a majority are mild and many cases remain undiagnosed (35). The Australian Liver Association's estimate of the Australian population with liver disease that was used for risk ratio calculation was largely comprised of NAFLD (90% of liver disease estimate) (35). The NAFLD component of this estimate was based on extrapolations from screening studies rather than population knowledge of their diagnosis (36). The national listeriosis interview questionnaire asks broadly about whether cases have liver disease. It is likely that NAFLD amongst listeriosis cases is underreported because it can commonly be undiagnosed. Additionally, if cases are aware of having NAFLD, they may not think to report it as a comorbidity if it is a mild abnormality. However, because NAFLD was not specifically excluded from the liver disease classification in the questionnaire, we included those with NAFLD in the estimated population with liver disease for comparable rate calculation. As NAFLD may not be captured in our case data, it may be more accurate to compare it to the population with non-NAFLD liver disease. When NAFLD is excluded from the Australian risk factor population, liver disease became significantly associated with listeriosis infection.

While international studies have identified the same groups as at risk of listeriosis, Australia is unique in having organ transplant recipients as the group most at risk of the disease. This may be due to the fact that this study is relatively unusual in having long term population-level data, or it could be explained by a comparative deficiency in prevention activities aimed at transplant recipients in Australia. Another way to

explain our unique results is a difference in methodology. Some studies have assigned each case one underlying illness determined to be most important, which could lead to different risk measurements than our method of including all cases with each risk factor in each calculation (8, 9). Many studies have used multivariable analysis (9, 14, 37). As we have demonstrated, organ transplant recipients invariably have additional comorbid conditions that have led to the need for transplant, or may have been an adverse outcome of immunosuppression (38). As organ transplant is not an independent risk, adjusted risk calculations in a multivariate model are likely to reduce or remove transplantation as a risk. It is also important to note that it was unclear whether listeriosis cases in this study had received an organ transplant in the year of their illness. Data on the prevalence of organ transplant among the population was not able to be sourced, so population incidence was used in calculation of risk. As a result, the at-risk population of transplant recipients may be underestimated and the risk of listeriosis overestimated. While acknowledging this limitation, and that transplantation is not an independent risk as the effect of other comorbidities on risk calculations have not been accounted for, we believe our results highlight an important population that is in need of targeted prevention activities.

A small but important group of listeriosis cases in the study period did not have any recognised susceptibility risk factors. These cases were not pregnancy related, did not report any underlying conditions or medication usage and were under the widely-accepted age for increased risk, 65 years. A large proportion (73.68%) of these cases were aged 45 years and over. The lack of other predisposing risk factors in these cases may indicate that age-related susceptibility begins earlier than currently communicated in Australia (39). This is supported by the significant risk of listeriosis demonstrated in those aged ≥45 years through risk ratio calculation (noting this is not stratified by, or adjusted for, other risk factors). It may also indicate the presence of other unknown risk factors not specifically collected in the data, and more in-depth case review and follow up is necessary to investigate this. Increased susceptibility from 45 years has been demonstrated in a previous study in the United States, and this should be considered in risk communications while this group is further investigated (40).

When compared to international trends reported in a recent meta-analysis, death rates amongst Australian listeriosis cases are lower in non-pregnancy related cases and very slightly higher in neonatal cases (5). In our results, we included the all-cause CFR following infection as well as the CFR for cases where listeriosis was reported as the cause of death. As most cases have multiple underlying conditions, listeriosis may play a role in mortality but may not be attributed as the primary cause of death. When compared to international trends, it is likely that the listeriosis-specific CFR is an underestimate and the all-cause CFR is more representative (5, 9, 11, 12, 41). The less conservative all-cause CFR amongst non-pregnancy related cases in Australia was 15.02%, which is markedly lower than the estimated non-pregnancy related CFR internationally of 25.90% (5). Internationally the CFR amongst neonates is estimated to be 14.90%, and we found the CFR in Australian neonates over eight years to be 15.79% (5). It is important to interpret this number with caution, as there have only been an average of three neonatal cases per year in Australia from 2010-2017. These results indicate that management of listeriosis in the adult population is above average and that infections amongst neonates are very few. However, as a result of the neonatal CFR being slightly higher than that experienced internationally, there is room for increased attention on the management of neonatal listeriosis in Australia.

Our results show that the groups most susceptible to listeriosis infection do not necessarily represent those with the most severe outcomes. Amongst non-pregnancy related cases; those with chronic lung disease, non-haematological cancers and heart disease had the highest all-cause CFR and diabetes replaced chronic lung disease for highest listeriosis-specific CFR. Notably, despite being at high risk of infection, those with organ transplant and haematological cancers had the lowest all-cause and listeriosis-specific CFRs of any underlying conditions and 100% of cases with a transplant lived. A possible explanation for this is that individuals with these conditions are more closely monitored for infection and would be treated earlier with more targeted therapies than those with other conditions (41, 42). Transplant recipients may also be taking antibiotic prophylaxis which could lessen the severity of infection (15). Less severe outcomes as a result of infection amongst populations most at risk of listeriosis have also been found overseas (37).

Cases with no recognised susceptibility risk factors had the highest rate of all cause death and the highest listeriosis-specific hospitalisation rate when compared to cases with any risk factors. We found that cases with no susceptibility risk factors, as well as those with no underlying conditions and younger cases more often presented with meningitis than those in other groups. *L. monocytogenes* is inherently resistant to cephalosporins, which in Australia are recommended for treatment of meningitis before the causative organism is identified (43). Upon presentation with meningitis, immunocompromised people, those over 50 years, alcoholics, and pregnant women are recommended to have benzylpenicillin added to their treatment to target *L. monocytogenes*. As cases with no underlying conditions or recognised risk factors are not often included in these groups but more often present with listeria-meningitis, treatment with an antibiotic that *L. monocytogenes* is susceptible to may be delayed until after the infection is identified. Previous studies have shown that inadequate and delayed antibiotic treatment for listeriosis, including use of cephalosporin monotherapy, is associated with increased risk of mortality (44, 45). We found that amongst cases with no recognised risk factors who died, most were under 50 years, which would have excluded them from recommended benzylpenicillin administration on presentation. It is also plausible that those with no underlying conditions do not present to medical attention until later than those who are otherwise unwell, which may further delay critical care and treatment. Our results suggest that those at most risk of listeriosis may be treated more effectively than cases who are otherwise healthy, resulting in more severe outcomes in cases without recognised risk factors. However, the group of cases without risk factors is small and analysis of presentation and treatment of these cases is based on low numbers.

Overall, the CFR amongst non-pregnancy related cases is still low in comparison to international trends (5). With antimicrobial stewardship in mind, it is not practical to treat all otherwise healthy people presenting with meningitis for listeriosis prior to causative organism identification. Increased community awareness of the signs of meningitis, clinician consideration of listeria-meningitis and rapid testing may be beneficial in increasing early and appropriate listeriosis treatment amongst younger and healthier cases. While those with haematological cancers and transplantation have relatively good outcomes following listeriosis, those with non-haematological cancers,

chronic lung disease, heart disease and diabetes should be an additional focus of early detection and treatment efforts upon presentation to healthcare services.

In addition to individual underlying conditions; age, the number of underlying conditions, and the use of medications are also likely to be important factors in listeriosis susceptibility (14). In Australia, three quarters of cases have at least one underlying condition and two thirds have two or more. The proportion of cases with multiple comorbidities increases with age, particularly from 45 years onwards, where the age-specific rate of infection also increases. A majority of cases are ≥65 years and the age-specific incidence rate is eight times higher in this age-group than in those under 65 years. Over two thirds of cases reported taking one or more medications known to increase susceptibility to listeriosis. In this study we focused on the risk of listeriosis in populations with underlying conditions, however susceptibility in these cases is inevitably affected by age-related immunosenescence, the presence of other conditions, and medication usage (9, 14, 37). Measurements of risk posed by individual conditions are also possible proxies for age, the medications used to manage the illnesses, or other common comorbid conditions (14). Future work to determine an estimate of the general population taking each medication, and with each number of underlying conditions, would be valuable to enable calculation of listeriosis risk in these groups. This would also provide valuable information to enable multivariable analysis that could account for the complex interactions of multiple factors.

Being of a NESB or being born overseas have previously been shown to be associated with increased exposure to listeriosis (16, 18). We found that over three quarters of cases in our study were born outside Australia or spoke a language other than English at home. We found that those with these factors are at significantly higher risk of listeriosis than those born in Australia and who only speak English at home. While the numbers were small and NESB was not well completed, almost 100% of pregnant cases were born overseas or were of a NESB, which was higher than the proportion in non-pregnancy related cases. A previous Australian study found a strong association between pregnant mothers' knowledge of high risk foods and their consumption of these goods (17). The study also found that mothers from a NESB were less likely to have awareness of high risk foods and were more likely to consume them during pregnancy. Our findings support this and highlight the importance of culturally

inclusive prevention strategies in pregnancy and in the broader community of people at risk. Since 2010, one jurisdiction in Australia has publicly provided translated advice on listeriosis in a variety of languages (46). Our findings reiterate the need for resources such as these, and for the promotion of their use in primary health services.

Internationally and domestically, hospitalisation has been demonstrated to be a risk factor for exposure to listeriosis (16, 47). We found that over one third of cases in Australia were hospitalised during the incubation period for their listeriosis infection. This is not unexpected due to the number of underlying conditions experienced by listeriosis cases, however there is evidence from other studies of the infection being acquired in hospital in approximately 25% of cases (47). While we did not examine the risk of nosocomial infection, nor other possible food exposures, it is plausible that the hospital exposures reported amongst cases in this study were the source of a proportion of the infections. Further analysis is needed to estimate the risk posed by nosocomial listeriosis at a population level in Australia. However, the demonstrated susceptibility to listeriosis amongst people with high contact with health services means that safe food preparation in hospital settings should always be a priority.

The NELSS data used in this study have previously been evaluated and found to have adequate representativeness and high data quality (22). Adding to this, we found a close match in the number of listeriosis notifications in NNDSS and those in the enhanced dataset. Listeriosis surveillance only endeavours to capture invasive cases where the bacteria are isolated from normally sterile sites. Because these are severe infections, they are likely to be captured through compulsory healthcare notification processes, however it is broadly accepted that notifications can only represent a proportion of total incidence (48). Non-invasive cases, which are likely asymptomatic or cause mild illness in otherwise healthy people, are not captured by surveillance in Australia. Data completeness was not formally evaluated as part of this study, however there were some data fields that were less complete than others. Completeness was described for each of the fields used in the results.

This study has several limitations. Case information was obtained through self-report and as such is subject to recall and reporting bias. Because many of the cases with listeriosis are very unwell or may have died, family members or medical practitioners

may answer interview questions on their behalf which would increase possible biases. The accuracy of the calculated RRs is dependent on the precision of the estimated number of people in the population with each risk factor. If the determined population with the risk is an overestimate, the RR is rendered an underestimate, and vice versa. Calculations of risk in populations that aren't captured through population-level registers such as heart and liver disease are likely to be less accurate. We did not account for the presence of multiple conditions in RR calculations, so the susceptible population is likely to be an overestimate because it does not exclude the population with other conditions of interest. As a result, the RRs may be underestimated. Risk amongst organ transplant recipients was calculated using annual incidence of organ transplant as the population denominator. Transplant risk factor information collected from listeriosis cases does not specify a timeframe for when a transplant was received. Depending on how this is interpreted during interview, it is possible that case information could reflect prevalence. As a result of utilising incidence data for the population denominator, risk may be overestimated.

Confounding and effect modification were not accounted for in this study, and are highly likely to be present amongst the complex interactions of multiple risk factors. While established in previous studies, the association between birth country, NESB and knowledge of listeriosis risk factors has not been explored in this study and may impact the validity of the results. Data was extracted for all years on 1 February 2018. Due to routine lag in reporting and/or interview there may be cases with onset at the end of 2017 that were not captured in this analysis. Reported underlying conditions were cross-validated with reports by the case's medical practitioner, however there may be underreporting of conditions. It is anticipated that underreporting would be more prevalent in cases with no reported underlying conditions, as they have less interaction with the healthcare system and may be unaware of having some conditions. Underlying condition categories were broad and no standard case definitions were used for interview, so reporting may be inconsistent. Hospitalisation and death due to listeriosis were not based on administrative records and may have also been particularly subjective fields resulting in reporting bias. Analysis of cases without any identified susceptibility risk factors are based on small numbers which may impact the validity of results. Future work to make the OzFoodNet case questionnaire more

specific, to include definitions of underlying conditions and to specify when an organ transplantation was received would improve data quality and be beneficial for future analyses.

Two viable strategies for prevention of listeriosis are to reduce its presence in food and increase awareness of potential sources of infection in susceptible populations (42). Australia has been recognised as having world-class food safety standards (49). It has also been shown that directed public health messaging can reduce high risk exposures and listeriosis infections amongst those targeted (17). While there are a variety of sources of information about listeriosis available to the Australian public, our results indicate that there are clear at-risk populations that need more focused prevention activities. Well defined high risk groups should be prioritised for prevention activities, as they have potential to be best targeted. This could include groups with conditions that involve regular contact with the healthcare system such as those with transplantation, cancer, type 1 diabetes and chronic kidney disease. Awareness should be raised amongst treating specialists about the degree of risk posed to their patients by listeriosis. Just as risk-based food advice is routinely provided to pregnant women by medical practitioners, provision of this advice should be incorporated into standard care for those with high risk underlying conditions (50). More broadly, raising awareness of the risk of listeriosis to immunocompromised people through public health messaging would be beneficial and advice should be provided in multiple languages.

In addition to reducing incidence, it is important to reduce severe outcomes resulting from listeriosis where possible. Enhancing community awareness of the signs of meningitis and increasing clinician consideration of listeria-meningitis, in particular amongst otherwise healthy young people, may be valuable. Increasing the use of rapid diagnostic testing, such as PCR in addition to microscopy and culture of cerebrospinal fluid specimens, may also increase the provision of rapid, targeted treatment for cases without underlying conditions.

This study has provided important insights into the groups most at risk of listeriosis and severe outcomes in Australia. It has provided the information necessary to appropriately focus public health activities to prevent unnecessary infections and

reduce their severity. Further research is needed to understand the effect of multiple risk factors on susceptibility; however, this study has identified communities in which there are significantly high rates of infection and potential for a reduction in incidence. With an ageing population, increasing prevalence of chronic conditions and growing use of immunomodulating drugs, it is of particular importance that groups most vulnerable to listeriosis are identified and equipped with the knowledge to prevent unnecessary infections.

References

1. National Notifiable Diseases Surveillance System Report. Notification Rate of Listeriosis, received from State and Territory health authorities in the period of 1991 to 2017 and year-to-date notifications for 2018 2017 [Available from: http://www9.health.gov.au/cda/source/rpt_4.cfm.
2. Mead PS, Slutsker L, Dietz V, McCaig LF, Bresee JS, Shapiro C, et al. Food-related illness and death in the United States. Emerging infectious diseases. 1999;5(5):607.
3. Food Standards Australia New Zealand. Listeria monocytogenes 2013 [Available from: https://www.foodstandards.gov.au/publications/Documents/Listeria monocytogenes.pdf.
4. Schuchat A, Swaminathan B, Broome CV. Epidemiology of human listeriosis. Clinical microbiology reviews. 1991;4(2):169-83.
5. De Noordhout CM, Devleesschauwer B, Angulo FJ, Verbeke G, Haagsma J, Kirk M, et al. The global burden of listeriosis: a systematic review and meta-analysis. The Lancet Infectious Diseases. 2014;14(11):1073-82.
6. Maertens De Noordhout C, Devleesschauwer B, Maertens De Noordhout A, Blocher J, Haagsma JA, Havelaar AH, et al. Comorbidities and factors associated with central nervous system infections and death in non-perinatal listeriosis: a clinical case series. BMC Infectious Diseases. 2016;16:256.
7. United States Food Safety and Inspection Service & Center for Food Safety and Applied Nutrition. Interpretive summary: Quantitative assessment of the relative risk to public health from foodborne Listeria monocytogenes among selected categories of ready-to-eat foods. United States Department of Health and Human Services & Department of Agriculture; 2003.
8. Mook P, O'Brien SJ, Gillespie IA. Concurrent conditions and human listeriosis, England, 1999–2009. Emerging Infectious Diseases. 2011;17(1):38.
9. Goulet V, Hebert M, Hedberg C, Laurent E, Vaillant V, De Valk H, et al. Incidence of listeriosis and related mortality among groups at risk of acquiring listeriosis. Clinical infectious diseases. 2012;54(5):652-60.
10. Goulet V, Marchetti P. Listeriosis in 225 non-pregnant patients in 1992: clinical aspects and outcome in relation to predisposing conditions. Scandinavian journal of infectious diseases. 1996;28(4):367-74.
11. Jensen A, Frederiksen W, Gerner-Smidt P. Risk factors for listeriosis in Denmark, 1989–1990. Scandinavian journal of infectious diseases. 1994;26(2):171-8.
12. World Health Organization & Food and Agriculture Organization of the United Nations. Risk assessment of Listeria monocytogenes in ready-to-eat foods: technical report. Rome: Food and Agriculture Organization of the United Nations; 2004.
13. Falk L, Fader K, Cui D, Totton S, Fazil A, Lammerding A, et al. Comparing listeriosis risks in at-risk populations using a user-friendly quantitative microbial risk assessment tool and epidemiological data. Epidemiology & Infection. 2016;144(13):2743-58.
14. Friesema I, Kuiling S, Van Der Ende A, Heck M, Spanjaard L, Van Pelt W. Risk factors for sporadic listeriosis in the Netherlands, 2008 to 2013. Eurosurveillance. 2015;20(31):21199.
15. Fernandez-Sabe N, Cervera C, Lopez-Medrano F, Llano M, Saez E, Len O, et al. Risk factors, clinical features, and outcomes of listeriosis in solid-organ transplant recipients: a matched case-control study. Clinical infectious diseases. 2009;49(8):1153-9.

16. Dalton C, Merritt TD, Unicomb L, Kirk M, Stafford R, Lalor K, et al. A national case-control study of risk factors for listeriosis in Australia. Epidemiology & Infection. 2011;139(3):437-45.
17. Bondarianzadeh D, Yeatman H, Condon-Paoloni D. Listeria education in pregnancy: lost opportunity for health professionals. Australian and New Zealand journal of public health. 2007;31(5):468-74.
18. Silk BJ, Date KA, Jackson KA, Pouillot R, Holt KG, Graves LM, et al. Invasive listeriosis in the Foodborne Diseases Active Surveillance Network (FoodNet), 2004–2009: further targeted prevention needed for higher-risk groups. Clinical infectious diseases. 2012;54(suppl_5):S396-S404.
19. Bavishi C, Dupont H. Systematic review: the use of proton pump inhibitors and increased susceptibility to enteric infection. Alimentary pharmacology & therapeutics. 2011;34(11-12):1269-81.
20. Ramsakal A, Nadaminti H, Field T, Vincent AL, Greene JN, Dass V, et al. Listeria infections in cancer patients. Infections in medicine. 2004;21(7):345-9.
21. Communicable Disease Network Australia. Listeriosis case definition 2017 [Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-nndss-casedefs-cd_listera.htm.
22. Astridge K. Bound volume chapter: Evaluation of the National Enhanced Listeriosis Surveillance System. Canberra: Australian National University; 2012.
23. Australian Bureau of Statistics. ABS.Stat: Estimate resident population, by age, sex and jurisdiction, 2016 2017 [Available from: http://stat.data.abs.gov.au/.
24. Australian Bureau of Statistics. National Health Survey: First Results 2014-15. Canberra, Australia: Commonwealth of Australia; 2015.
25. Leukaemia Foundation. Facts and figures about blood cancer 2016 [Available from: https://www.leukaemia.org.au/disease-information/blood-cancer-resources/facts-and-statistics-about-blood-cancer/.
26. Australian Institute of Health and Welfare. Cancer in Australia 2017. Canberra: AIHW; 2017.
27. The Gastroenterological Society of Australia and Australian Liver Association. The economic cost and health burden of liver diseases in Australia. 2013.
28. Diabetes Australia. Diabetes in Australia 2015 [Available from: https://www.diabetesaustralia.com.au/diabetes-in-australia.
29. Australian Organ and Tissue Donation and Transplantation Authority. Australian Organ and Tissue Donation and Transplantation Authority Annual Report 2015-16. Canberra, Australia: Commonwealth of Australia; 2016.
30. Shapira Y, Agmon-Levin N, Shoenfeld Y. Geoepidemiology of autoimmune rheumatic diseases. Nature Reviews Rheumatology. 2010;6(8):468.
31. Australian Institute of Health and Welfare. Australia's mothers and babies 2015. Canberra, Australia; 2017.
32. Australian Bureau of Statistics. 2016 Census data summary: Cultural diversity in Australia 2017 [Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by Subject/2071.0~2016~Main Features~Cultural Diversity Data Summary~30.
33. National Notifiable Diseases Surveillance System. Unpublished data. 2018.
34. Australian Bureau of Statistics. Australian Demographic Statistics, September quarter 2017 2018 [Available from: http://www.abs.gov.au/ausstats/abs@.nsf/mf/3101.0.

35. Dyson JK, Anstee QM, McPherson S. Non-alcoholic fatty liver disease: a practical approach to diagnosis and staging. Frontline gastroenterology. 2013:flgastro-2013-100403.
36. Gan L, Chitturi S, Farrell GC. Mechanisms and implications of age-related changes in the liver: nonalcoholic Fatty liver disease in the elderly. Current gerontology and geriatrics research. 2011;2011:831536.
37. Gerner-Smidt P, Ethelberg S, Schiellerup P, Christensen J, Engberg J, Fussing V, et al. Invasive listeriosis in Denmark 1994–2003: a review of 299 cases with special emphasis on risk factors for mortality. Clinical Microbiology and Infection. 2005;11(8):618-24.
38. Penfornis A, Kury-Paulin S. Immunosuppressive drug-induced diabetes. Diabetes & metabolism. 2006;32(5):539-46.
39. Food Standards Australia New Zealand. Listeria and food - advice for people at risk 2019 [Available from: http://www.foodstandards.gov.au/publications/Pages/listeriabrochuretext.aspx.
40. Pouillot R, Hoelzer K, Jackson KA, Henao OL, Silk BJ. Relative risk of listeriosis in Foodborne Diseases Active Surveillance Network (FoodNet) sites according to age, pregnancy, and ethnicity. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2012;54 Suppl 5:S405-10.
41. De Noordhout CM, Devleesschauwer B, De Noordhout AM, Blocher J, Haagsma JA, Havelaar AH, et al. Comorbidities and factors associated with central nervous system infections and death in non-perinatal listeriosis: a clinical case series. BMC infectious diseases. 2016;16(1):256.
42. Swaminathan B, Gerner-Smidt P. The epidemiology of human listeriosis. Microbes and Infection. 2007;9(10):1236-43.
43. Therapeutic Guidelines Limited. Central nervous system infections Melbourne, Australia: Therapeutic Guidelines Limited; 2014 [updated March 2018. Available from: https://tgldcdp.tg.org.au/viewTopic?etgAccess=true&guidelinePage=Antibiotic&topicfile=central-nervous-system-infections&guidelineName=Antibiotic&sectionId=toc_d1e47 - toc_d1e47.
44. Thønnings S, Knudsen JD, Schønheyder HC, Søgaard M, Arpi M, Gradel K, et al. Antibiotic treatment and mortality in patients with Listeria monocytogenes meningitis or bacteraemia. Clinical Microbiology and Infection. 2016;22(8):725-30.
45. Liatsos GD, Thanellas S, Pirounaki M, Ketikoglou I, Moulakakis A. Listeria monocytogenes peritonitis: presentation, clinical features, treatment, and outcome. Scandinavian journal of gastroenterology. 2012;47(10):1129-40.
46. Victorian Department of Health and Human Services. Health translations: Listeria - the facts 2015 [updated August 2015. Available from: http://www.healthtranslations.vic.gov.au/bhcv2/bhcht.nsf/PresentDetail?Open&s=Listeria_-_the_facts.
47. Silk BJ, McCoy MH, Iwamoto M, Griffin PM. Foodborne listeriosis acquired in hospitals. Clinical Infectious Diseases. 2014;59(4):532-40.
48. NNDSS Annual Report Writing Group. Australia's notifiable disease status, 2014: Annual report of the National Notifiable Diseases Surveillance System 2016 [Available from: http://www.health.gov.au/internet/main/publishing.nsf/content/cda-cdi4001e.htm.
49. The World Health Organization. Joint external evaluation of the IHR core capacities of Australia: Mission report. Geneva, Switzerland: The World Health Organization; 2018.

50. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Maternity care in Australia. Melbourne, Australia: The Royal Australian and New Zealand College of Obstetricians and Gynaecologists; 2017.

Appendix 4A - Sample OzFoodNet listeriosis questionnaire

ozfoodnet

Listeria Case Questionnaire
(Oct16)

Case Initials:	
State ID:	
National ID:	
☐ sporadic case ☐ outbreak case	
Outbreak ref:	

PRIVACY STATEMENT

The information you provide in this questionnaire is for the purpose of trying to prevent further cases of illness. We do this by trying to find out what is likely to have caused your illness and also by providing you with information to reduce the spread of illness to others. The data collected is kept confidential and identifying information will not be disclosed for any other purpose without your consent. You can access your information by contacting the Department of Human Services. A fact sheet is available ("Privacy Legislation & Notification of Infectious Diseases – Information for Patients") if you would like further information Information read ☐

Note: The following preliminary information can be recorded prior to interview if known

CASE DETAILS

First Name:		Last Name:	Parent's Name (if applicable):
DOB: __ / ___ / ___	Age:	Gender: ☐M ☐F	
Address:			
Home Phone:		Mobile Phone:	
Email:			
Born in Australia ☐Y ☐N			
If no, specify where:		Language spoken at home:	
Are [you/the case] of Aboriginal or Torres Strait Islander origin? (check all that apply) ☐No ☐Yes, Aboriginal ☐ Yes, Torres Strait Islander ☐ Not stated			

Interviewer Initials:

Date/time Interviewed	
1	☐
2	☐
3	☐
4	☐
5	☐
6	☐

Person interviewed (if not case):

Call back notes:

Interpreter used ☐
Case lost to follow up ☐

Case admitted to hospital? ☐Y ☐N		Hospital Name:
Date Admitted ____/____/____	Date Discharged: ____/____/____	Hospital UR #:
Notification Date: ____/____/____	Reason for admission ☐ Listeriosis ☐ Other Specify other:	
Treating Doctor:	Phone:	Hospital / Medical Practice:

OCCUPATION (Include part-time/casual/volunteer work) and/or INSTITUTION CONTACT

What is [your/the case's] occupation? Specify
Name of work place:
Address of workplace:
Contact details for work place:

Does the case's occupation involve:
Handling food/drink? ☐Y ☐N
Close contact with sick people? (e.g. health care worker) ☐Y ☐N
Close contact with the children/elderly? (e.g. child care worker?) ☐Y ☐N

If yes, please provided relevant public health advise for exclusion period to the case

Do [you/the case] attend childcare / preschool / school /prison/ aged care facility? ☐Y ☐N
If yes, provide details
Name :
Address :
Contact details :
Please provided relevant public health advise for exclusion period to the case

MEDICAL & DIAGNOSTIC INFORMATION

Typing	Result	Conducted by (lab name):
Serotype (PCR):		
Binary-type:		
MLVA		
Has the isolate been forwarded for further typing? ☐Y ☐N		
MLST		
Other typing:		

☐ **NON-PERINATAL CASE (If Perinatal go to next table)**		
Specimen type: ☐CSF ☐Blood ☐Other specify:	Collection date: ____/____/____	Collection day:
Nature of illness (case):☐ Meningitis ☐ Septicaemia ☐ Other specify:		
Outcome: ☐Survived ☐Died ☐Unknown	Date of death: ____/____/____	Death due to listeriosis? ☐ Y ☐ N

☐ **PERINATAL CASE**			
Mother		Foetus / Neonate	
Culture Site	Specimen collection date	Culture Site	Specimen collection date
☐ Blood	____/____/____	☐ Blood	____/____/____
☐ CSF	____/____/____	☐ CSF	____/____/____
☐ Stool	____/____/____	☐ Gastric aspirate	____/____/____
☐ Placenta	____/____/____	☐ Meconium	____/____/____
☐ Other specify:	____/____/____	☐ Other specify:	____/____/____
Outcome of pregnancy:			
☐ Still pregnant ☐ Foetal death (miscarriage / stillbirth) ☐ Induced abortion ☐ Delivery (live birth) ☐ Other specify:			
Weeks' Gestation		Outcome Date: ____/____/____	
Type(s) of illness in Mother (tick all that apply)		Type(s) of illness in Foetus / Neonate (tick all that apply)	
☐ Bacteraemia / sepsis		☐ Bacteraemia / sepsis	
☐ Meningitis		☐ Meningitis	
☐ Febrile gastroenteritis		☐ Pneumonia	
☐ Amnionitis		☐ Granulomatosis infantisepticum	
☐ Non-specific "flu-like" illness		☐ None	
☐ Unknown		☐ Unknown	
☐ Other specify:		☐ Other specify:	
☐ None			
Mother's outcome		Foetus / Neonate outcome	
☐ Survived		☐ Survived	
☐ Died		☐ Died	
Date: ____/____/____		Date: ____/____/____	
☐ Due to Listeria		☐ Due to Listeria	
☐ Due to other cause (specify)		☐ Due to other cause (specify)	

NOTE: For perinatal cases ask the remaining questions of the mother

CLINICAL
In the 4 week period prior to diagnosis of Listeria, did [you/case] experience any of the following symptoms?

Fever:	☐Y ☐N ☐DK	Chills:	☐Y ☐N ☐DK	Headache:	☐Y ☐N ☐DK
Stiff Neck	☐Y ☐N ☐DK	Confusion:	☐Y ☐N ☐DK	Diarrhoea:	☐Y ☐N ☐DK
Vomiting:	☐Y ☐N ☐DK	Muscle & Body Aches:	☐Y ☐N ☐DK		
Other:	☐Y ☐N ☐DK	***if yes please specify:***			

What was the first symptom [you/case] experienced?

First symptom: First symptom onset date: ____/____/____ Onset time: : ☐am ☐pm

Do you have any of the following illnesses or conditions?

Illness / condition	Case (response)	Doctor (response)
Diabetes- insulin dependent	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Diabetes- non-insulin dependent	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Heart disease	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Renal / kidney disease requiring dialysis	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Other renal disease	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Rheumatological condition	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Blood disorder	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Organ transplant	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Liver disease	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Chronic lung disease (excluding asthma)	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Cancer **Specify:**	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Other illness or condition **Specify:**	☐Y ☐N ☐DK	☐Y ☐N ☐DK

In the 4 weeks prior to illness, were you taking any of the following treatments?

Treatments	Case (response)	Doctor (response)
Corticosteroids (e.g. prednisone)	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Cyclosporine	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Other drugs that affect the immune system	☒Y ☐N ☐DK	☐Y ☐N ☐DK
Chemotherapy	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Radiation therapy	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Antidiarrhoeal medication (e.g. Lomotil, Imodium)	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Antacids (e.g. Mylanta, Mucaine)	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Medications that reduce stomach acid (e.g. Zantac, Tagamet, Somac, Losec)	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Antibiotics **Specify:**	☐Y ☐N ☐DK	☐Y ☐N ☐DK
Other **Specify:**	☐Y ☐N ☐DK	☐Y ☐N ☐DK

DAY VISITS (FOR TREATMENT/CARE)

Did you have any hospital day visits in the 12 weeks prior to illness? ☐Y ☐N

Reason for visit (e.g. dialysis, outpatient Appt)	Date of hospital visit	Hospital	Hospital food consumed	Detail of food consumed

	____/____/____		☐Y ☐N	
	____/____/____		☐Y ☐N	
	____/____/____		☐Y ☐N	

HOSPITAL ADMISSION

Were you admitted to hospital in the 12 weeks prior to illness? ☐Y ☐N

Admission	Discharge	Hospital	Reason for admission	Ward / section
____/____/____	____/____/____			
____/____/____	____/____/____			
____/____/____	____/____/____			

Foods consumed during hospital admission:

High risk hospital foods consumed? ☐Y ☐N ☐Maybe ☐Don't know/Not answered

ENVIRONMENTAL RISK FACTORS

In the 12 weeks prior to illness, did you travel overseas, to another state or territory or anywhere within the state? ☐Y ☐N

International? ☐Y ☐N ☐DK
Domestic? ☐Y ☐N ☐DK
Local? ☐Y ☐N ☐DK

If yes, provide travel details:

Specify location(s):

Name of resort, hotel, etc.:

Departure Date : ____/____/____
Mode of travel:
☐air ☐car ☐train ☐ bus ☐ other, specify:

Name of airline / tour company :

Travel/Flight numbers (if applicable):

Foods consumed on plane or bus etc.

Return Date : ____/____/____
Mode of travel:
☐air ☐car ☐train ☐ bus ☐ other, specify:

Name of airline / tour company :

Travel/Flight numbers (if applicable):

Foods consumed on plane or bus etc.

POTENTIAL FOOD SOURCES

In the 4 weeks prior to illness (____/____/____ to ____/____/____) did you consume any of the following?

Fruits	**Eaten in 4weeks prior to illness**	**Type / brand / description**	**Where purchased or eaten**
Fruit salad (self-serve salad bar)	☐Y ☐N ☐DK		
Fruit salad (delicatessen)	☐Y ☐N ☐DK		

Fruit salad (other source)	☐Y ☐N ☐DK		
Rockmelon / cantaloupe	☐Y ☐N ☐DK		
Watermelon	☐Y ☐N ☐DK		
Honeydew melon	☐Y ☐N ☐DK		
Strawberries	☐Y ☐N ☐DK		
Other berries	☐Y ☐N ☐DK		
Other fruit	☐Y ☐N ☐DK	**Specify:**	
Fresh fruit juice	☐Y ☐N ☐DK	**Specify:**	
Vegetables / salads	**Eaten in 4weeks prior to illness**	**Type / brand / description**	**Where purchased or eaten**
Whole lettuce	☐Y ☐N ☐DK	☐bagged ☐un-bagged **Specify:**	
Bagged processed lettuce (e.g. leaves/shredded)	☐Y ☐N ☐DK	**Specify:**	
Bagged salad other (e.g. rocket/spinach)	☐Y ☐N ☐DK	**Specify:**	
Bagged coleslaw mix	☐Y ☐N ☐DK		
Uncooked mushroom	☐Y ☐N ☐DK		
Alfalfa / pea sprouts	☐Y ☐N ☐DK		
Bean sprouts	☐Y ☐N ☐DK		
Fresh herbs eaten raw	☐Y ☐N ☐DK		
Organic produce	☐Y ☐N ☐DK	**Specify:**	
Home grown produce	☐Y ☐N ☐DK	**Specify:**	
Raw vegetable juice (state type)	☐Y ☐N ☐DK	**Specify:**	
Other raw vegetables	☐Y ☐N ☐DK	**Specify:**	
Dairy	**Eaten in 4weeks prior to illness**	**Type / brand / description**	**Where purchased or eaten**
Brie cheese	☐Y ☐N ☐DK		
Camembert cheese	☐Y ☐N ☐DK		
Blue-veined cheese	☐Y ☐N ☐DK		
Fetta cheese	☐Y ☐N ☐DK		
Ricotta cheese	☐Y ☐N ☐DK		
Mozarella cheese	☐Y ☐N ☐DK		
Cottage cheese	☐Y ☐N ☐DK		
Other soft cheese	☐Y ☐N ☐DK	**Specify:**	
Shredded/grated hard cheese	☐Y ☐N ☐DK		
Raw / unpasteurised cheese	☐Y ☐N ☐DK		
Sour cream	☐Y ☐N ☐DK		
Ice-cream	☐Y ☐N ☐DK		
Gelato	☐Y ☐N ☐DK		
Yogurt	☐Y ☐N ☐DK		
Raw / unpasteurised milk (cow / goat)	☐Y ☐N ☐DK		
Flavoured milk	☐Y ☐N ☐DK		
Other dairy products:	☐Y ☐N ☐DK	**Specify:**	
POTENTIAL FOOD SOURCES Cont.			
Deli	**Eaten in 4weeks prior to illness**	**Type / brand / description**	**Where purchased or eaten**
Dips	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli **Specify:**	
Barbequed chicken	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Cold cooked chicken	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Luncheon / sandwich meat	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	

Ham	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Salami	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Chicken / turkey slices	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Other uncooked meat products	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Pate	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Liverwurst	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Frankfurts / cheerios	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Silverside	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Pre-prepared potato salad (deli)	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Pre-prepared coleslaw (deli)	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Pre-prepared pasta salad (deli)	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli	
Other pre-prepared salads:	☐Y ☐N ☐DK	☐Pre-packaged ☐ Deli **Specify:**	
Cold/uncooked seafood	**Eaten in 4weeks prior to illness**	**Type / brand / description**	**Where purchased or eaten**
Mussels	☐Y ☐N ☐DK		
Crab	☐Y ☐N ☐DK		
Prawns (purchased cooked)	☐Y ☐N ☐DK		
Prawns (purchased raw)	☐Y ☐N ☐DK		
Oysters	☐Y ☐N ☐DK		
Smoked salmon	☐Y ☐N ☐DK		
Other smoked fish / seafood	☐Y ☐N ☐DK		
Sushi / sashimi	☐Y ☐N ☐DK		
Other seafood:	☐Y ☐N ☐DK	**Specify:**	
Sandwiches / burgers / rolls / wraps containing:	**Eaten in 4weeks prior to illness**	**Type / brand / description**	**Where purchased or eaten**
Ham	☐Y ☐N ☐DK	☐Pre-packaged ☐Custom made	
Beef	☐Y ☐N ☐DK	☐Pre-packaged ☐Custom made	
Bacon, lettuce, tomato (BLT)	☐Y ☐N ☐DK	☐Pre-packaged ☐Custom made	
Chicken	☐Y ☐N ☐DK	☐Pre-packaged ☐Custom made	
Turkey	☐Y ☐N ☐DK	☐Pre-packaged ☐Custom made	
Other meat	☐Y ☐N ☐DK	☐Pre-packaged ☐Custom made **Specify:**	
Salad	☐Y ☐N ☐DK	☐Pre-packaged ☐Custom made	
Cheese:	☐Y ☐N ☐DK	☐Pre-packaged ☐Custom made **Specify:**	
Other filling:	☐Y ☐N ☐DK	☐Pre-packaged ☐Custom made **Specify:**	

ACTIONS	
Before this illness with Listeria, did a healthcare worker tell you to avoid certain foods to prevent listeriosis? ☐Y ☐N	
Information on Listeria requested? ☐Y ☐N	Date sent: ____/____/____
Premises/facility inspection required? ☐Y ☐N	**If yes:** Premises to be inspected by:
Will food samples be taken for analysis? ☐Y ☐N	**If yes:** Samples will be collected by (name of organisation or local council)

FOOD EATEN OR PREPARED OUTSIDE THE HOME			
In the 4 weeks prior to illness, did you attend any of the following?			
Restaurants (specify)	**Eaten in 4weeks prior to illness**	Date	Detail of food consumed
1.	☐Y ☐N ☐DK	____/____/____	
2.	☐Y ☐N ☐DK	____/____/____	
3.	☐Y ☐N ☐DK	____/____/____	
Takeaway (specify)	**Eaten in 4weeks prior to illness**	Date	Detail of food consumed
1.	☐Y ☐N ☐DK	____/____/____	
2.	☐Y ☐N ☐DK	____/____/____	
3.	☐Y ☐N ☐DK	____/____/____	
Any left-over high risk foods available for testing? ☐Y ☐N **Specify:**			

Chapter 5: Investigation of an acute public health issue

An unusual DNA macrorestriction pattern amongst *Salmonella* Typhimurium cases in the Capital: a retrospective case-case analysis and comparison of case-control selection methods

"Compared to what?"

- Prof. Ross Andrews (and all good epidemiologists)

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Chapter 5 - Prologue

My role

A previously unseen *Salmonella* Typhimurium (STm) Multiple Locus Variable-Number Tandem Repeat Analysis (MLVA) type appeared in the Australian Capital Territory (ACT) in 2017, with a total of 17 confirmed and two probable cases over the proceeding 16-month period. I undertook a retrospective case-case analysis to generate a hypothesis about the source of these infections. I conducted a targeted literature review to assess whether MLVA had been used as a method of case-control selection in salmonellosis and other infectious disease case-case analyses (Appendix 5A). As a result of there being a lack of publications demonstrating MLVA-differentiated case-control selection within *Salmonella* serovars, I took the opportunity to compare two case-control selection methods. I compared cases to case-controls within the same *Salmonella* serovar differentiated through MLVA, and to case-controls from different *Salmonella* serovars. In consultation with ACT Health, I designed the study, entered data from stored paper-based interviews, conducted analyses and drafted a report.

Lessons learned

This project taught me a great deal about case-case study design. When the literature did not provide clear guidance on case-control selection, I decided to incorporate a comparison of selection methods into my analysis. From this I learnt a lot about the technicalities of setting up and interpreting comparisons to case-control groups.

This was also my first practical experience with multivariate analysis. Putting theory into practice really enhanced my understanding of the concepts of data analysis and outbreak investigation.

Public health impact

This investigation provided a hypothesis for the potential infectious source of the unusual STm MLVA profile and will provide a foundation for future investigations. Additionally, my findings through comparison of case-control selection methods should help inform future case-case analyses.

Acknowledgements

I would like to thank Tim Sloan-Gardner from ACT Health for providing me with the opportunity to conduct this investigation and for his guidance and insight into study design, surveillance and salmonellosis. I appreciate the assistance of Ben Polkinghorne in deciphering the available advice on case-case selection methods and his time and assistance in setting up this study. I would like to thank Dr Russell Stafford for his advice on case-case study design and am very grateful for Aparna Lal's and Assoc. Prof. Kathryn Glass's valuable input into the methods and interpretation of my analysis.

Ben, Tim, Katie and Aparna assisted in reviewing my chapter and provided helpful feedback throughout.

Course activity requirements met

✓ Investigation of an acute public health problem

✓ Literature review

Ethics statement

This study was covered by the blanket waiver of consent for outbreak investigations for MAE scholars through the Science and Medical Delegated Ethics Review Committee of the Australian National University (Protocol number 2017/909).

Abstract

Background: Cases of an unusual *Salmonella* Typhimurium (*S*Tm) multiple-locus variable-number tandem repeats analysis (MLVA) profile (03-25-13-12-523) were first notified in the Australian Capital Territory (ACT) in 2017-18. Case-case analyses are routinely used in outbreak investigations, however use of MLVA to select unrelated case-controls within a common *Salmonella* serovar has not been demonstrated in the literature. This study aimed to investigate exposures associated with cases of *S*Tm MLVA 03-25-13-12-523 in the ACT. Additionally, this study compared the use of two different case-control groups; *S*Tm case-controls shown to be unrelated to cases through MLVA typing, and non-Typhimurium *Salmonella* (non-*S*Tm) case-controls.

Methods: A retrospective case-case analysis was used to compare exposures among cases to two case-control groups; notified *S*Tm and non-*S*Tm case-controls. Exposure-based interviews were conducted as part of routine public health follow up of notified cases. Crude and adjusted odds ratios were calculated using univariate and multivariate logistic regression.

Results: In multivariate analysis, cases had significantly higher odds of egg consumption when compared to *S*Tm case-controls. When compared to non-*S*Tm case-controls, no significant exposures were found.

Conclusion: A significant difference in egg exposure, which is known to be a common source of *S*Tm infection in the ACT and Australia in general, was detected when cases were compared to MLVA-differentiated *S*Tm case-controls. As such, MLVA as a method of differentiation may be useful in expanding case-control selection to include those from the same *Salmonella* serovar without eliminating the capacity to detect differences in common infectious exposures. Use of these case-controls could increase the available power of salmonellosis case-case analyses.

Introduction

Non-Typhoidal *Salmonella* is an important cause of foodborne gastrointestinal illness, causing an annual mean of 67.40 cases per 100,000 people in Australia between 2013-2017(1). The serovar *Salmonella* Typhimurium (*S*Tm) is the most frequently notified cause of *Salmonella* infection in Australia, accounting for 48.00% (27.00 cases per 100,000 population) of all *Salmonella* notifications in Australia in 2011(2). This trend is more pronounced in the Australian Capital Territory (ACT), where 72.26% of the 85.10 notified cases of non-typhoidal *Salmonella* per 100,000 population were attributed to *S*Tm in 2017 (ACT Health, unpublished data, 2018).

In 2017, a previously unseen multiple-locus variable-number tandem repeats analysis (MLVA) pattern (03-25-13-12-523) appeared amongst *S*Tm notifications in the ACT and cases have persisted into 2018. There have only ever been 24 notified cases of *S*Tm determined to have this MLVA pattern in Australia, 17 of which have occurred in the ACT since 2017 (Australian Government Department of Health, unpublished data, 2018).

Cases have occurred seasonally in the ACT, with most occurring in February of 2017 and 2018. In addition to the 17 cases confirmed to have this MLVA, there have been two probable cases that were notified with *Salmonella* that had an epidemiological link, by place and time, to confirmed cases. In total, there have been nine sporadic cases, and ten cases clustered at two ACT restaurants since the unusual subtype emerged in the territory. Eight cases ate at one restaurant within a two month period in 2017 (seven cases with *S*Tm MLVA 03-25-13-12-523, one confirmed *S*Tm with an epidemiological link) and two cases ate at another restaurant on the same day in 2018 (one case with *S*Tm MLVA 03-25-13-12-523, and one confirmed *Salmonella* with an epidemiological link). The same egg supplier was used by both restaurants, which initially raised suspicion about a potential common source. Environmental samples at both premises did not detect any *Salmonella.* ACT Health identified the need for a more in depth epidemiological investigation. As the MLVA profile is very specific and relatively unusual, it is likely that cases share a common exposure and there is potential for impactful public health action to prevent further cases.

Selection of an appropriate control group is an important aspect of study validity and the ability to conclude statistically meaningful results. Case-case studies, where cases of interest are compared to other, unrelated cases (case-controls), are a practical alternative to traditional case control studies in routine analysis of public health surveillance data (3). While cases have long been used as controls in cancer studies, the last decade has seen the rise of case-case analyses in communicable disease epidemiology. There are now a variety of publications describing the methodology and application of case-case studies. The demonstrated benefits of these analyses include affordability, rapidity and the removal of many selection and recall biases invariably present in traditional case control studies (3-6). It is widely recommended that case-controls are selected from cases of the same disease with a different subtype, or from cases of other diseases with similar symptoms and notification processes.

With the increasing ability to differentiate groupings within established pathogen subtypes using genetic analyses, there is an opportunity to expand the selection of unrelated cases as case-controls. Progreba-Brown *et. al*. suggest that cases with the same pathogen subtype, shown to be unrelated to cases of interest through pulsed-field gel electrophoresis (PFGE), could be used as case-controls (4). Selection of case-controls through more granular typing than serovars, has not been widely used in salmonellosis investigations in the literature. This may be due to a perceived possibility of case-controls within the same serovar being over-matched on exposure and thus reducing the likelihood of observing an association. However, DNA macrorestriction analysis, such as PFGE, has been used as an alternative to serotyping as a method of case-control selection in published listeriosis, campylobacteriosis and Shiga toxin-producing *Escherichia coli* investigations and has been useful in identifying the source of infections (7-9). One previous study has used phage typing to select case-controls within the same *Salmonella* serovar, however they had difficulty identifying significant exposures amongst cases (10). MLVA provides greater discrimination within *Salmonella* serovars than phage typing and is commonly used to further type Salmonella isolates in Australia (11). To the author's knowledge, MLVA has not yet been used as a method to select case-controls within the same *Salmonella* serovar for case-case investigations in the literature.

This study aims to investigate exposures associated with cases of *S*Tm MLVA 03-25-13-12-523 that have occurred in the ACT in 2017 and 2018. We also aim to compare the use of two different case-control groups; one group selected from notified *S*Tm cases shown to be unrelated through MLVA typing, and the other group selected from notified cases of non-Typhimurium *Salmonella* infections (non-*S*Tm). As part of this we aim to explore whether the common exposure profile amongst cases and case-controls of the same serovar influences the ability to detect associations with the infection.

Methods

Study design

A retrospective case-case analysis was used to investigate the outbreak, whereby two separate analyses were done comparing cases to *S*Tm case-controls and non-*S*Tm case-controls. Case-controls were frequency matched to cases based on quarters within each year. The initial study design attempted to include two case-controls per case; however due to low numbers this was not possible for either case-control group so a one-to-one ratio was used.

Case definitions

Confirmed cases were defined as an ACT-notified case of laboratory confirmed *S*Tm MLVA 03-25-13-12-523 (confirmed case). Probable cases were defined as an ACT-notified case of laboratory confirmed *Salmonella* infection with an epidemiological link (classified as outbreak-associated through common exposure in time and place) to a confirmed case of *S*Tm MLVA 03-25-13-12-523. Cases were excluded if they had overseas travel within seven days prior to onset.

*S*Tm case-controls were defined as an ACT-notified case of laboratory confirmed *S*Tm with an MLVA profile unrelated to 03-25-13-12-523 (differences in the digits at either locus one or locus five, or differences in the digits in more than one of the second, third or fourth loci) (12). Non-*S*Tm case-controls were defined as an ACT-notified case of laboratory confirmed *Salmonella* infection, with a serovar other than Typhimurium. Within both groups, case-controls were excluded if they had not completed an interview; overseas travel within the seven days prior to onset; a known association with an outbreak; no serotyping available; an *S*Tm infection without MLVA typing

(approximately 13% untyped); spent more than one day out of the three days prior to onset outside of the ACT; or had a lack of adequate food history (less than two days).

As per the national surveillance case definition, salmonellosis cases and case-controls for this study were laboratory confirmed through isolation of *Salmonella* in culture or detection of *Salmonella* nucleic acid (with reflex culture and characterisation where necessary) (13). The isolates were referred to the Microbiological Diagnostic Unit (MDU) in Victoria or the New South Wales Enteric Reference Laboratory for further characterisation by serotyping and MLVA where necessary.

Data collection and selection of cases and case-controls

Cases and case-controls were interviewed within 48 hours of their notification as part of routine follow up of all salmonellosis cases in the ACT. Interviews were conducted using the standard OzFoodNet salmonellosis case follow up questionnaire and were stored on paper forms. Interviews collected demographic information, clinical details, potential person-to-person exposures, environmental exposures and travel history in the seven days prior to illness, as well as an open-ended food history for the three days prior to onset.

For this analysis, confirmed cases of *S*Tm MLVA 03-25-13-12-523 were identified through the Notifiable Disease Management System (NDMS) and probable cases through outbreak summary reports which demonstrated the epidemiological link. Interview data was manually entered into Microsoft Excel 2010. A pool of potential case-controls was identified through the NDMS based on matched yearly quarter and *Salmonella* serovar. Potential case-controls were delineated into *S*Tm and non-*S*Tm pools. They were assigned a random number and selected in ascending order for review of interview data against the inclusion and exclusion criteria. *S*Tm case-controls were also assessed upon selection for MLVA relatedness. Where case-controls were eligible for inclusion, their exposure data was manually entered into Microsoft Excel 2010. All data from the NDMS was extracted on 7 May 2018.

Data analysis

Cases were analysed separately against *S*Tm and non-*S*Tm case-controls. Demographic variables were described and compared in cases and case-controls. The distribution of

age in cases and each case-control group were assessed and compared using a Wilcoxon rank sum test. A chi-square or Fisher's exact test (where cell count was less than 5) was used to examine significant differences in sex between cases and each case-control group.

Correlation between exposure variables was assessed and were considered correlated where the correlation coefficient was >0.5. Univariate logistic regression was used to determine crude odds ratios. Age, sex, and any exposures where $p<0.25$ in univariate analysis were included in a multivariate model for further assessment. A forward stepwise approach was used, and as a sensitivity analysis, a backward stepwise approach and manual selection based on biological plausibility were also tried. Adjusted odds ratios (aOR) were calculated and results were considered significant at the 5% level. A likelihood ratio test (LR test) was used to compare the null model (including age and sex) to the final model. All analyses were conducted using Stata version 13.1 (Stata Corp., USA).

Ethics statement

This study was covered by the blanket waiver of consent for outbreak investigations for Master of Philosophy (Applied Epidemiology) scholars through the Science and Medical Delegated Ethics Review Committee of the Australian National University (Protocol number 2017/909).

Results

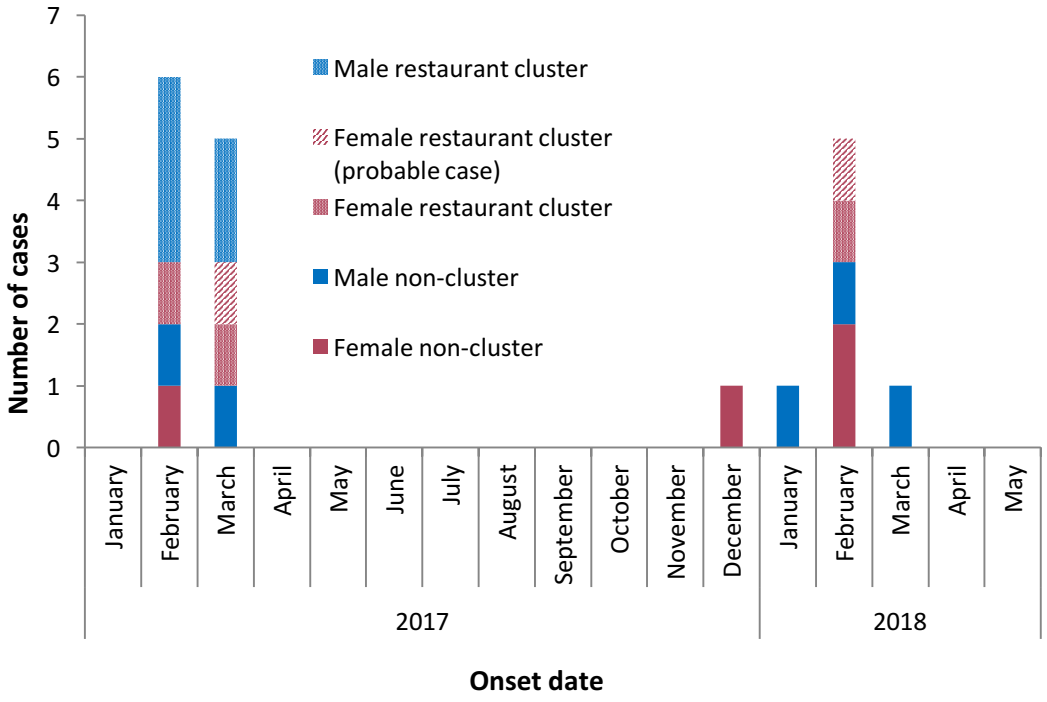
Cases

There were 17 confirmed and two probable cases of *S*Tm MLVA 03-25-13-12-523 reported in the ACT between 1 January 2017 and 7 May 2018. Case sex was almost equally split, with just one more male than female cases (52.63% male, n=10). Cases were most frequently in the 15-34 year old (42.11%, n=8) and 35-54 year old (42.11%, n=8) age groups, with a median age of 34 years and range of 0-66 years. No cases had overseas travel in the seven days prior to onset.

Eleven cases occurred in quarter one of 2017 (57.98%), one in quarter four of 2017 (5.26%), and seven in quarter one of 2018 (36.84%) (Figure 1). Cases were most

frequently in February of both years (n=11). There were nine sporadic cases and ten cases involved in two clusters where there were common restaurant-based exposures (eight cases in 2017 at and two cases in 2018). Five of the cluster of eight cases that ate at one restaurant reported eating sandwiches (with various fillings) and the remaining three did not report common food exposures. The cluster of two cases at another restaurant reported eating the same dish. Environmental health inspections at both restaurants did not identify any issues, and food samples and swabs did not detect any *Salmonella.*

Figure 1. Cases of *Salmonella* Typhimurium MLVA 03-25-13-12-523 in the Australian Capital Territory by onset date, sex and clustering



Analysis of cases and non-*S*Tm case-controls

Non-*S*Tm case-controls were predominantly female (63.16%, n=12) and there was no significant difference in sex between cases and non-*S*Tm case-controls (p=0.33).

Non-*S*Tm case-controls were most frequently in the 15-34 year old (26.32%, n=5) and 35-54 year old (26.32%, n=5) age groups, with a range of 1-58 years and median age of 29 years. When comparing cases to non-*S*Tm case-controls, age was not significantly different (p=0.33). Additionally, cases didn't have higher odds of being in a particular age group when compared to non-*S*Tm case-controls using 0-4 as a reference category in univariate and multivariate analysis.

Assessment of correlation between variables showed correlation between meat and poultry exposures (correlation coefficient=0.62). As such, meat was excluded from analysis. Univariate analysis did not show any significant exposures amongst cases when compared to non-*S*Tm case-controls (Table 1).

Age, sex, animal exposure, consumption of fresh and other vegetables, canned goods and other foods were eligible for inclusion in the multivariate model (p<0.25 in all variables except age and sex). The final multivariate model included all exposures and the LR test indicated that this model was not significantly better than the null model (p=0.07). No exposures were found to be significant (Table **2**).

Analysis of cases and *S*Tm case-controls

*S*Tm case-controls were predominantly female (84.21%, n=16) and sex was significantly different between cases and *S*Tm case-controls (p=0.04). Cases had higher odds of being male than *S*Tm case-controls in both univariate and multivariate analyses (aOR 14.77, p=0.02, CI 1.70-128.10).

*S*Tm case-controls were most frequently in the 15-34 year old age group (36.84%, n=7), with a range of 0-80 years and median of 27 years. When comparing cases and *S*Tm case-controls, age was not significantly different (p=0.21). However, through univariate analysis, cases had significantly higher odds of being aged 35-54 than *S*Tm case-controls, using 0-4 as the reference category (OR 10, p=0.05, CI 1.05-95.46). This was found to be insignificant in multivariate analysis.

No correlation was found between any variables for cases and *S*Tm case-controls. Through univariate analysis, contact with an ill person was found to be the only significant exposure, and cases were found to have lower odds of exposure than case-controls (OR 0.13, p=0.02, CI 0.02-0.73) (Table 1).

Age, sex, contact with illness, shopping at supermarket C, consumption of spreads or sauces, poultry, eggs, fruit, dairy and meat were eligible for inclusion in the multivariate model (p<0.25 in all variables). The final multivariate model included age, sex and egg consumption. When adjusted for demographic variables in the model, cases were found to have significantly higher odds of consuming eggs (aOR 9.86, p=0.04, CI 1.14-85.13) and being male (aOR 14.77, p=0.02, CI 1.70-128.10) than *S*Tm

case-controls (Table 2). The LR test demonstrated that the final model was significantly better than the null model (p=0.02).

Egg brands were collected, however analysis was not undertaken as only 47.37% of case-controls (n=18/38) and 26.31% of cases (n=5/19) reported the egg brand they purchased.

Table 1. Univariate analysis of exposures for *S*Tm MLVA 03-25-13-12-523 infection using *S*Tm and non-*S*Tm case-controls

	Cases (n=19)		Non-STm case-controls (n=19)				STm case-controls (n=19)			
Exposure variable	Number	%	Number	%	OR (95%CI)	P value	Number	%	OR (95%CI)	P value
Environmental exposures										
Interstate travel*	6	31.58%	4	21.05%	1.73 (0.40-7.50)	0.46	6	31.58%	1.00 (0.25-3.93)	1.00
Contact with ill person	2	10.53%	3	15.79%	0.63 (0.09-4.26)	0.63	9	47.37%	0.13 (0.02-0.73)	0.02
Animal exposure	14	73.68%	17	89.47%	0.33 (0.06-1.96)	0.22	13	68.42%	1.29 (0.32-5.28)	0.72
Other environmental exposure	13	68.42%	16	84.21%	0.41 (0.08-1.95)	0.26	14	73.68%	0.77 (0.19-3.16)	0.72
Food exposures										
Shopped at supermarket A	9	47.37%	10	52.63%	0.81 (0.23-2.89)	0.75	12	63.16%	0.53 (0.14-1.92)	0.33
Shopped at supermarket B	11	57.89%	14	73.68%	0.49 (0.13-1.93)	0.31	13	68.42%	0.63 (0.17-2.40)	0.50
Shopped at supermarket C	3	15.79%	2	10.53%	1.59 (0.23-10.82)	0.63	8	42.11%	0.26 (0.06-1.19)	0.08
Shopped at supermarket D	2	10.53%	2	10.53%	1.00 (0.13-7.94)	1.00	4	21.05%	0.44 (0.07-2.76)	0.38
Shopped at supermarket E	1	5.26%	1	5.26%	1.00 (0.06-17.25)	1.00	0	0.00%	1.00(-)	-
Shopped at a butcher	2	10.53%	2	10.53%	1.00 (0.13-7.94)	1.00	1	5.26%	2.12 (0.18-25.55)	0.56
Shopped at markets	5	26.32%	4	21.05%	1.34 (0.30-6.02)	0.70	3	15.79%	1.90 (0.38-9.44)	0.43
Shopped at a farm	0	0.00%	2	10.53%	1.00(-)	-	0	0.00%	1.00(-)	-
Ate home grown produce	3	15.79%	4	21.05%	0.70 (0.14-3.68)	0.68	3	15.79%	1.00 (0.17-5.72)	1.00
All vegetables	19	100.00%	14	73.68%	1.00 (-)	-	18	94.74%	1.00(-)	-
Fresh vegetables	14	73.68%	10	52.63%	2.52 (0.65-9.83)	0.18	11	57.89%	2.04 (0.52-8.00)	0.31
Other vegetables	17	89.47%	13	68.42%	3.92 (0.68-22.70)	0.13	16	84.21%	1.60 (0.23-10.82)	0.63
Seafood	9	47.37%	6	31.58%	1.95 (0.52-7.30)	0.32	9	47.37%	1.00 (0.28-3.57)	1.00
Sandwhich	10	52.63%	7	36.84%	1.90 (0.52-6.96)	0.33	9	47.37%	1.23 (0.35-4.41)	0.75
Spread or sauce	7	36.84%	4	21.05%	2.19 (0.52-9.27)	0.29	11	57.89%	0.42 (0.12-1.56)	0.20
Poultry	14	73.68%	13	68.42%	1.29 (0.32-5.28)	0.72	19	100.00%	2.52 (0.65-9.83)	0.18
Egg alone	10	52.63%	10	52.63%	1.00 (0.28-3.57)	1.00	6	31.58%	2.40 (0.64-9.03)	0.19
Egg and egg based products	11	57.89%	10	52.63%	1.24 (0.34-4.45)	0.74	11	57.89%	1.00 (0.28-3.63)	1.00
Fruit	9	47.37%	9	47.37%	1.01 (0.28-3.57)	1.00	13	68.42%	0.42 (0.11-1.56)	0.19
Canned goods	4	21.05%	8	42.11%	0.37 (0.09-1.53)	0.17	4	21.05%	1.00 (0.21-4.76)	1.00
Desserts	6	31.58%	8	42.11%	0.63 (0.17-2.40)	0.50	6	31.58%	1.00 (0.25-3.93)	1.00
Dairy	14	73.68%	16	84.21%	0.53 (0.11-2.60)	0.43	18	94.74%	0.16 (0.02-1.49)	0.11
Rice products	6	31.58%	9	47.37%	0.51 (0.14-1.92)	0.32	7	36.84%	0.79 (0.21-3.03)	0.73
Meat	12	63.16%	15	78.95%	-	-	16	84.21%	0.32 (0.07-1.51)	0.15
Grain based products	18	94.74%	19	100.00%	1.00(-)	-	17	89.47%	2.12 (0.18-25.55)	0.56
Eating out	19	100.00%	15	78.95%	1.00(-)	-	17	89.47%	1.00(-)	-
Other foods	9	47.37%	5	26.32%	2.52 (0.65-9.83)	0.18	6	31.58%	1.95 (0.52-7.31)	0.32
Frequent café exposures										
Café A	8	42.11%	0	0	1.00(-)	-	0	0	1.00(-)	-
Café B	2	10.53%	0	0	1.00(-)	-	0	0	1.00(-)	-
Demographics										
Age group - 0-4 years	2	10.53%	4	21.05%	1.00(-)	-	5	26.32%	1.00(-)	-
Age group - 5-14 years	0	0.00%	2	10.53%	1.00(-)	-	2	10.53%	1.00(-)	-
Age group - 15-34 years	8	42.11%	5	26.32%	3.20 (0.42-24.42)	0.26	7	36.84%	2.86 (0.42-19.65)	0.29
Age group - 35-54 years	8	42.11%	5	26.32%	3.20 (0.42-24.42)	0.26	2	10.53%	10.00 (1.05-95.46)	0.05
Age group - 55-74 years	1	5.26%	2	10.53%	1.00 (0.05-18.91)	1.00	2	10.53%	1.25 (0.07-22.88)	0.88
Age group - 75+ years	0	0.00%	1	5.26%	-	-	1	5.26%	1.00(-)	-
Male	10	52.63%	7	36.84%	1.90 (0.52-6.96)	0.33	3	15.79%	5.92 (1.29-27.28)	0.20
Female	9	47.37%	12	63.16%	-	-	16	84.21%	-	-

*Case-controls had a maximum of one out of the three days prior to onset outside the ACT

Note: 0-4 years used as reference group for age groups; male used as reference group for females.

OR: odds ratio, CI: confidence interval, STm: *Salmonella* Typhimurium.

Table 2. Multivariate analysis of exposures for *S*Tm MLVA 03-25-13-12-523 infection using *S*Tm and non-*S*Tm case-controls

	Cases (n=19)		Non-STm case-controls (n=19)				STm case-controls (n=19)			
Exposure variable	**Number**	**%**	**Number**	**%**	**aOR (95%CI)**	**P value**	**Number**	**%**	**aOR (95%CI)**	**P value**
Environmental exposures										
Contact with ill person	2	10.53%	3	15.79%	-	-	9	47.37%	-	-
Animal exposure	14	73.68%	17	89.47%	0.22 (0.01-3.53)	0.28	13	68.42%	-	-
Food exposures										
Fresh vegetables	14	73.68%	10	52.63%	2.50 (0.38-32.32)	0.27	11	57.89%	-	-
Other vegetables	17	89.47%	13	68.42%	10.20 (0.61-170.35)	0.11	16	84.21%	-	-
Egg alone	10	52.63%	10	52.63%	-	-	6	31.58%	9.86 (1.14-85.13)	0.04
Canned goods	4	21.05%	8	42.11%	0.11 (0.01-1.02)	0.05	4	21.05%	-	-
Other foods	9	47.37%	5	26.32	0.80 (0.08-7.72)	0.84	6	31.58%	-	-
Demographics										
Age group - 0-4 years	2	10.53%	4	21.05%	-	-	5	26.32%	-	-
Age group - 5-14 years	0	0.00%	2	10.53%	1.00 (-)	-	2	10.53%	1.00(-)	-
Age group - 15-34 years	8	42.11%	5	26.32%	4.34 (0.33-57.62)	0.27	7	36.84%	3.53 (0.41-30.56)	0.25
Age group - 35-54 years	8	42.11%	5	26.32%	4.40 (0.31-61.45)	0.27	2	10.53%	11.94 (0.89-160.99)	0.06
Age group - 55-74 years	1	5.26%	2	10.53%	0.10 (0.00-8.54)	0.31	2	10.53%	3.19 (0.90-113.04)	0.52
Age group - 75+ years	0	0.00%	1	5.26%	1.00 (-)	-	1	5.26%	1.00(-)	-
Male	10	52.63%	7	36.84%	9.79 (0.81-118.49)	0.07	3	15.79%	14.77 (1.70-128.10)	0.02
Female	9	47.37%	12	63.16%	-	-	16	84.21%	-	-

Note: 0-4 years used as reference group for age groups; male used as reference group for females.
aOR: adjusted odds ratio, CI: confidence interval, STm: *Salmonella* Typhimurium.

Discussion

This investigation found that cases of *S*Tm MLVA 03-25-13-12-523 had significantly higher odds of egg consumption when compared to *S*Tm case-controls but not when compared to non-*S*Tm case-controls. A majority of egg-associated outbreaks in Australia are caused by *S*Tm (90%), and a majority of *S*Tm outbreaks are attributed to eggs (52% in 2011) (2, 14). Non-*S*Tm *Salmonella* infections are acquired from more diverse sources including other food vehicles and environmental exposures in Australia. As such, it is notable that comparison of cases to *S*Tm case-controls enabled detection of eggs as a significant exposure amongst cases, as these case-controls were likely to have a high rate of egg exposure as a source of infection. Similarly, it is interesting that non-*S*Tm case-controls did not detect a difference in egg exposure between cases and case-controls, as this group was less likely to have infection-related egg exposures. Our findings demonstrate that it is possible to detect significantly higher odds of exposure amongst cases to a risk factor that is commonly shared with

comparison case-controls from the same *Salmonella* serovar differentiated through MLVA.

Suspicion of eggs as the source of the unusual *S*Tm MLVA pattern was initially raised by ACT Health as a result of the same egg brand being used in both restaurants where clusters of cases occurred. However, further investigation into the risk associated with this egg brand was difficult as only half of case-controls and a quarter of cases reported the egg brands they had purchased prior to onset. Additionally, the presence of a large number of epidemiologically linked outbreak cases and the potential for cross-contamination in restaurant-based exposures may have led to a misrepresentation of exposures. Not all cases that were clustered at restaurants shared food exposures, which means that there are likely to be different routes of transmission that have not been accounted for in this analysis. ORs for the restaurants themselves could not be calculated because no case-controls reported eating at these venues and use of exact logistic regression to assess zero-cells was deemed unnecessary for an investigation of this size. For cases that reported eating similar dishes at the restaurants, it was difficult to identify exact ingredients in meals that may have been a cause of illness. For example, five out of eight cases that ate at one restaurant reported eating sandwiches with various fillings. These sandwich fillings, and notably whether spreads were used, was not well reported. *Salmonella* was not detected in environmental samples at either of the two restaurants. Eggs may be a potential source of infection for this unusual *S*Tm MLVA pattern, but the possibility of cross contamination misrepresenting reported exposures, and the inconsistency in detection of significant case exposures between the two case-control groups reduces confidence in these results.

Use of case-case analysis in this study was efficient, low resource and is likely to have reduced the bias that can be present in traditional case-control investigations. In epidemiological studies, it is important for cases and controls to be comparable to avoid bias and increase the validity of results. It is well-established that cases that are notified to public health authorities are representative of a population with specific health seeking behaviors and susceptibilities (15). This is particularly true of gastrointestinal illnesses such as salmonellosis. Notification requires the case to present to health services, their practitioner to deem a stool sample necessary, the

case to follow through with testing, and a positive laboratory result to eventuate. It is estimated that only 14% of salmonellosis cases in the community are captured through surveillance in Australia (15). As a result of the culmination of demographic, behavioral and biological factors that lead to notification of salmonellosis, notified cases differ systematically from those that are not notified (6). As such, use of unrelated cases as controls reduces selection bias, as cases and controls are identified in the same way. Information about cases is also collected in a uniform manner, and the differential recall bias that can occur when cases are compared to controls that are healthy or have other illnesses is removed in case-case comparisons. As such, recall and selection bias have been substantially reduced as a result of using a case-case analysis in this study.

The identification of different significant associations with exposures amongst cases when compared to different case-control groups highlights the need for a larger sample size, or an additional case-control pool in case-case investigations with small study populations. As there was a temporal pattern of exposure amongst cases, it was considered important to match the case-control population to cases on yearly quarter to allow for the same opportunity for exposure. Use of *Salmonella* notifications as case-controls was a practical method of investigation; however, the sample size was restricted by the number of notifications received within the defined time periods, and the eligibility of case-controls based on inclusion and exclusion criteria. With the concurrent aim of comparing the use of different case-control groups, there were only enough case-controls in each group to select a one-to-one ratio of cases to case-controls. Studies with a small sample size can have low power and results cannot be confidently extrapolated to the population (16). The small sample size in our study means that it is difficult to differentiate between real risk and random variation within our results (17). It is possible that due to the size of our study, the detection of significant odds of case exposure to eggs is type I error, and the lack of detection of significant exposures when compared to the other case-control group is type II error.

An example of the difficulty posed by a small sample size is our finding that cases had significantly higher odds of being male than *S*Tm case-controls. Random selection of case-controls resulted in a high proportion of females in the *S*Tm case-control group, however, *S*Tm and *Salmonella* in general does not normally occur more frequently in

males or females, and is usually notified in relatively equal proportions (14, 18). As such, the high odds of being male amongst cases in this study is more likely a description of random variation amongst the selected case-controls than real risk amongst cases. A larger sample size would increase the chance of the selected case-controls being representative of the comparison population. While the case-case analysis used in this study was helpful for hypothesis generation, a larger sample size would provide more confidence that detection of a significant exposure is not describing random variation. Comparison of cases to two case-control groups provided some validation of the results in this study by highlighting inconsistencies. Our findings indicate that amongst case-case analyses, it may be necessary to have at least a two-to-one ratio of case-controls to cases, or to validate results by comparison to an additional case-control group.

With the increasing granularity in differentiation of subtypes of pathogens, there is a growing opportunity to use MLVA and other DNA macrorestriction analyses to select unrelated cases as case-controls. As case-case studies can rely on small numbers in practice, these typing methods may help to increase the number of available case-controls. *S*Tm is the most commonly notified *Salmonella* infection in Australia. The resulting paradox is that while it causes the majority of outbreaks to investigate, the largest pool of case-controls to use in investigations are excluded if only other serovars are used in case-case analysis. A previous study found it difficult to detect significant exposures amongst cases when comparing to case-controls of the same *Salmonella* serovar that were differentiated through phage typing. MLVA provides greater discrimination of *Salmonella* within serovars than phage typing, which may have allowed this study to more specifically differentiate between relatedness and thus relevant exposures (11).

Based on this study alone it is difficult to say with confidence that a common exposure profile within a *Salmonella* serovar will not influence the ability to detect significant differences in exposure between MLVA-differentiated cases and case-controls. It is important to note that 47% of *S*Tm case-controls in this study had contact with someone who was unwell, compared to 16% of non-*S*Tm case-controls and 11% of cases. Due to random variation, the *S*Tm case-control sample may have had a higher proportion of infections as a result of contact with illness than would normally be seen

amongst *S*Tm cases. This may have increased the ability to detect a significant difference in egg consumption between the two groups, and emphasizes the need for further investigation into the ability to consistently detect differences in exposure when comparing groups within the same *Salmonella* serovar. However, it is plausible that when an unusual MLVA pattern is identified in a number of cases, there is likely to be a specific common source of infection that should be able to be differentiated from other case-controls with adequately detailed exposure information. Further work should be done to trial the use of MLVA to differentiate cases from case-controls in *Salmonella* investigations. Use of these case-controls could bolster the available number of comparison cases and increase the power and ability to reliably detect exposures associated with illness in *Salmonella* case-case analyses.

Case-case analysis is currently used in routine analysis of listeriosis data in Australia at the national level. When a cluster of cases with the same binary and serotype or whole genome sequencing pattern is identified, cases of notified listeriosis with other binary types are used as comparators for rapid hypothesis generation for the source of a potential outbreak. Our results indicate that MLVA-differentiation may be useful in conducting similar hypothesis generation to identify potential infectious exposures amongst identified salmonellosis clusters. As MLVA is the primary mechanism of STm subtyping in Australia, this would be a practical and efficient use of differentiated cases. Given that MLVA typing can take a week or more to be undertaken, this method of case-control differentiation may be useful in the context of long term outbreaks of unknown origin rather than immediate cluster investigations.

In addition to those already discussed, this study has several limitations. As with data on all notified conditions where information on exposures is necessary, there is a time lag between exposure to the infection and the case being interviewed, which can lead to recall bias. This is less prominent in the ACT than other jurisdictions, as all cases are interviewed within 48 hours of notification and not only once a cluster has been detected by MLVA or other typing. Food and restaurant exposures were collected through open ended survey questions and cases were categorised as not exposed if they did not specify consumption of foods or venue attendance. For analyses, food exposure data was recorded in fine detail and then grouped into broader categories. It is possible for these processes to have resulted in misclassification bias. The use of a

large number of specific variables also increased the likelihood of exposures being detected as significant due to chance. Study subjects were excluded if they did not complete an interview, or had less than two days of food history. However, data was still incomplete in some areas. Egg brands had an especially low level of reporting. The study population in this investigation represents a particular group of the population who are tested and notified with an illness. This may limit the external validity of the study. As a result of being a case-case analysis, the biases present in this study should be non-differential.

This study has indicated that eggs may be a potential source of *S*Tm MLVA 03-25-13-12-523 in the ACT. In addition to hypothesis generation, this study has demonstrated that MLVA-differentiated cases and case-controls could be used to identify differences in exposures that are known to be common within a *Salmonella* serovar. As a result of this study, the following is recommended:

1. Further investigation is needed to confidently determine the source of case exposure to *S*Tm MLVA 03-25-13-12-523 in the ACT. A larger study with at least a two-to-one ratio of case-controls to cases would be beneficial. Using the existing data, case-controls could be reselected randomly from a pool of unrelated *Salmonella* cases. *S*Tm cases shown to be unrelated through MLVA typing could be included in this pool to bolster numbers. If cases persist, a prospective study could also be undertaken.
2. The investigation could be expanded to include *S*Tm cases with the unusual MLVA pattern that are reported outside the ACT in analysis, in particular if cases have visited the ACT or its surrounds.
3. Addition of a trawling questionnaire with specific questions about exposures to particular food groups would be beneficial when interviewing cases of salmonellosis in the ACT. While it is acknowledged that the ACT already has a substantial workload as a result of interviewing every case of notified salmonellosis, this type of questionnaire allows for more precise categorisation of exposures and may increase the accuracy of analysis.
4. MLVA differentiation of cases and case-controls should be trialled more broadly to further assess the ability to detect differences in common exposures. The potential of using such cases to bolster numbers in case-case analyses should

also be explored.

References

1. Australian Government Department of Health. National Notifiable Diseases Surveillance System Summary Data 2018 [Available from: http://www9.health.gov.au/cda/source/cda-index.cfm.
2. Moffatt CR, Musto J, Pingault N, Miller M, Stafford R, Gregory J, et al. Salmonella Typhimurium and outbreaks of egg-associated disease in Australia, 2001 to 2011. Foodborne pathogens and disease. 2016;13(7):379-85.
3. Wilson N, Baker M, Edwards R, Simmons G. Case-case analysis of enteric diseases with routine surveillance data: Potential use and example results. Epidemiologic Perspectives & Innovations. 2008;5(1):6.
4. Pogreba-Brown K, Ernst K, Harris R. Case-case methods for studying enteric diseases: A review and approach for standardization. OA Epidemiology. 2014;2(1):7.
5. McCarthy N, Giesecke J. Case-case comparisons to study causation of common infectious diseases. International Journal of Epidemiology. 1999;28(4):764-8.
6. Krumkamp R, Reintjes R, Dirksen-Fischer M. Case–case study of a Salmonella outbreak: An epidemiologic method to analyse surveillance data. International journal of hygiene and environmental health. 2008;211(1-2):163-7.
7. Gaulin C, Levac E, Ramsay D, Dion R, Ismaïl J, Gingras S, et al. Escherichia coli O157: H7 outbreak linked to raw milk cheese in Quebec, Canada: use of exact probability calculation and case-case study approaches to foodborne outbreak investigation. Journal of food protection. 2012;75(5):812-8.
8. De Valk H, Vaillant V, Jacquet C, Rocourt J, Le Querrec F, Stainer F, et al. Two consecutive nationwide outbreaks of listeriosis in France, October 1999–February 2000. American Journal of Epidemiology. 2001;154(10):944-50.
9. Schleihauf E, Mutschall S, Billard B, Taboada E, Haldane D. Comparative genomic fingerprinting of Campylobacter: application in routine public health surveillance and epidemiological investigations. Epidemiology & Infection. 2017;145(2):299-309.
10. Varga C, Middleton D, Walton R, Savage R, Tighe M-K, Allen V, et al. Evaluating risk factors for endemic human Salmonella Enteritidis infections with different phage types in Ontario, Canada using multinomial logistic regression and a case-case study approach. BMC public health. 2012;12(1):866.
11. Boxrud D, Pederson-Gulrud K, Wotton J, Medus C, Lyszkowicz E, Besser J, et al. Comparison of multiple-locus variable-number tandem repeat analysis, pulsed-field gel electrophoresis, and phage typing for subtype analysis of Salmonella enterica serotype Enteritidis. Journal of clinical microbiology. 2007;45(2):536-43.
12. Gilbert GL. Using MLVA to type strains of Salmonella Typhimurium in New South Wales. New South Wales Public Health Bulletin. 2008;19(2):29-31.
13. Communicable Disease Network Australia. Salmonellosis case definition 2016 [Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-nndss-casedefs-cd_salmon.htm.
14. OzFoodNet Working Group. Monitoring the incidence and causes of diseases potentially transmitted by food in Australia: Annual report of the OzFoodNet Network, 2011. Communicable Disease Intelligence. 2015;39(2).
15. Hall G, Yohannes K, Raupach J, Becker N, Kirk M. Estimating community incidence of Salmonella, Campylobacter, and Shiga toxin–producing Escherichia coli infections, Australia. Emerging Infectious Diseases. 2008;14(10):1601.

16. Jones S, Carley S, Harrison M. An introduction to power and sample size estimation. Emergency Medicine Journal. 2003;20(5):453-8.
17. Hackshaw A. Small studies: strengths and limitations. Eur Respiratory Soc; 2008.
18. National Notifiable Diseases Surveillance System. Unpublished Salmonellosis notification data. 2018.

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Chapter 6: Teaching

Peer-to-peer teaching

"In learning you will teach, and in teaching you will learn"

Phil Collins

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Chapter 6 - Prologue

My role

There are two teaching requirements as part of the Masters of Applied Epidemiology (MAE) program – lessons from the field (LFF) for my MAE cohort, and teaching the first-year MAE cohort during course block.

For my LFF I decided to provide my peers with an introduction to the statistical software, R. I knew that my cohort had learnt Stata as part of the data analysis course and I surveyed my LFF group to check if they had experience with R. I had taught myself to use R for my epidemiological study, and I knew how difficult it can be to learn without a structured lesson. As R is a free software that might be more accessible in field-based situations, I thought some basic skill development might be of use to my peers. As I had learnt R in the context of my project on influenza threshold development, I decided to use this as a case study. Following its use as my LFF, the lesson was integrated into the ANU's data analysis course in 2018.

To teach the first-year MAE cohort, I worked with peers from my cohort Julia Maguire, Kelley Meder and Brigitta Osterberger, to provide a lesson on ethical considerations in study participation. A key learning for me as part of my surveillance evaluation project was the process of gaining informed consent from survey participants. The ethical considerations and technicalities involved in developing a participant information sheet was not specifically covered in the MAE curriculum, but is important to understand prior to study commencement. We delivered a lecture on this topic and engaged the class in an interactive exercise. As a whole, our cohort then developed some fun exercises for the first year group, including a donning and doffing of personal protective equipment race, epidemiological pictionary and charades.

In addition to the teaching requirements, my fellow MAE Patiyan Andersson and I delivered a lecture at the National Centre for Epidemiology and Population Health on our establishment of international disease surveillance for the Commonwealth Games (Chapter 7, Appendix 7C).

Lessons learnt

Prior to conducting these sessions, I had limited experience with teaching. It was great working with and teaching fellow MAEs; I learnt a lot from what my peers found challenging, the anecdotes shared and the discussions that resulted during each session. Through peer evaluation of both teaching sessions, I learnt that both lessons were appropriately delivered and that having an interactive component, a comprehensive introduction and critical thinking questions is important (Appendices 6A and 6B). I also learnt a huge amount from the LFFs provided by the other MAEs in my group including cultural and study design challenges in the Pacific Islands, weighted analyses, burden of disease modelling and qualitative data analysis.

Acknowledgements

I would like to thank my teaching collaborators Julia Maguire, Kelley Meder and Brigitta Osterberger for being such an excellent team. I would also like to acknowledge Sophie Phelan, Kelley Meder, Aurysia Hii and Patiyan Andersson for being such a great LFF group. I am also grateful for the guidance and oversight provided by Aparna Lal and Dr Tambri Housen during my teaching experiences.

Course activity requirements met

✓ Lessons from the field

✓ Teaching first year MAE scholars

Lessons from the field

Exercise with answers

Introduction to R using influenza data

The corresponding zoom teleconference has been arranged for 30th May at 11 am AEST.

Instructions: This lesson contains two sections. The first is a brief introduction to the logic and basic functions of R. The second section is a scenario in which you develop a script and analyse data. Download R and R studio. Once downloaded, open R studio.

Learning objectives: By the end of this lesson, you should be able to:

- Understand the basic logic of R
- Assign values to variables, vectors and data frames
- Set a working directory and import data
- Drop and create new variables
- Bind variables to datasets
- Plot variables
- Install and use a package
- Become familiar with influenza data measurements

Section 1: Brief introduction to R

There are four screens in R studio. To begin with, focus on the console where you will be entering your commands. Later we will get to importing data (which will appear in your environment screen), writing a script (in your script and data screen), plotting data and installing packages (in the last remaining screen). There are 3 main data types in R that we will go though in this lesson: variables, vectors and data frames.

Assigning values to variables

A key basic function of R is assigning values to variables. This allows you to store a value or function description under a name. To assign the value 10 to the variable 'x', type the following command into your console and press enter:

```
x<-10
```

Check the value of your variable by typing the name of your variable and pressing enter. You should also be able to see this variable and its corresponding value in your 'environment' window. Now assign the value 5 to the variable 'y'. You are able to do a range of basic arithmetic between these variables. To add variables x and y you would type the command:

```
x+y
```

Now try multiplying and dividing the variables by one another. Provide your code below:

```
x*y

y/x
```

Generating new variables utilises the same process as assigning values to variables. For example, if you are making a new variable and you would like to import data from an existing variable you would use the following code:

```
newvariable<-existingvariable
```

Try assigning the value of y multiplied by 2 to the new variable z. Provide your code below:

```
x<-y*2
```

Creating a vector

A vector is another form of data you can create in R. A vector has more depth than a single variable, in that it can store multiple values much like a row of data. For example, you can make the vector 'a' by assigning it 3 variables through the combine (c) function. Try the following code:

```
a<-c(1, 2, 3)
```

Inspect your vector results by typing `'a'`

Create a new vector 'b' by assigning it the values 1*1, 2*2 and 3*3. Provide your code below:

```
b<-c(1*1, 2*2, 3*3)
```

Data frames

While vectors can become larger and hold more observations and variables, they cannot hold multiple types of data such as characters and numeric variables in one data set. This is where a data frame comes in. We will import and use a data frame later in this exercise.

Starting a script

What you may know as a do file in Stata is called a script in R. In the top left hand corner of your browser click the page with a green plus sign to start a new script and record your commands. Start your script by titling it with your name and the date. In R we use # instead of * to allow for free text comments and titles. It might be useful for you to start including the commands and comments from this exercise in a script for you to keep. To run commands from your script, highlight them and press the 'run button' at the top of your script, or highlight and press Alt+Enter.

Before you go any further, it is important to remember that R is case sensitive. If you can't get a command to work, check capitalisation before flipping a desk!

Section 2: The 'super spreader' influenza situation

It is the first month of the 2017 flu season and the media have already started producing headlines about this season being a 'super spreader'. Your director asks you to come up with a way to measure flu activity and determine whether the level of person-to-person transmission in the 2017 season is expected or unusual. You know of three data sources you could use, each have data by week for the previous 5 years:

- *Data source one*: has the number of people admitted to sentinel hospitals with confirmed influenza and the number of these that are admitted to ICU.
- *Data source two:* has the number of people who report influenza-like illness (ILI) in a regular survey and the number of these that need to take time off work while sick.
- *Data source three:* has the total number of people who call a public health hotline and the number of these who report ILI.

As you are trying to measure the spread of flu through the community, which data source would you use? Why might you not use the others to measure transmission?

I would use data source three. As measuring transmission is essentially an incidence rate, the denominator must be the general community (not people with influenza or ILI). The only data source where the denominator is the community is data source 3.

The denominator for the hospitalisation and survey data are people who have influenza or ILI, so these will not allow you to produce a meaningful indication of the rate of influenza in the community. The hospitalisation data would help you understand seriousness of circulating influenza and the absenteeism data would help you understand the impact on society.

Clearing your workspace

To begin your analysis you need to clear your workspace. Holding down Control+L clears your console and the broom at the top of your 'environment' window clears your data.

Setting working directory

To start off, you would like to know where you can retrieve data from easily and determine a place for your work to be saved. Do this by checking where your current working directory is:

```
getwd()
```

If this location doesn't suit you, change the directory to where you would like it to be using the following code and replacing the location in inverted commas:

```
setwd("\\\\homedrive.anu.edu.au/u5328214/My Documents")
```

Importing data

You decide to use the public health hotline data with the number of total callers and the number of people with ILI. Just as you can assign a value to a variable, you can import a dataset and assign it a name if it is saved in your working directory. If you were importing the dataset called 'my_data.csv', and wanted to call the dataset 'my data', you would use the following code:

```
my_data<-read.csv("my_data.csv")
```

Save the dataset provided into your working directory. Import the data into R and name it 'LFFdata'. Provide your code below:

```
LFFdata<-read.csv("LFFdata.csv")
```

Check the classification of this data using the following code:

```
class(LFFdata)
```

This command allows you to check whether your data is numeric, character-based or logical (True/False). As a data frame can contain multiple classes of data, it is a class of its own. Hopefully you have just confirmed that you now know how to import a data frame.

To inspect your data, you can use the following commands:

```
View(LFFdata)
print(LFFdata)
```

Another useful way to inspect your data is to summarise it. This will provide you with the minimum, 1st quartile, median, mean, 3rd quartile and maximum numbers in each variable. To summarise your data, use the command:

```
summary(LFFdata)
```

Creating new variables using existing variables in a data frame

You decide to start your analysis by looking at the rate of ILI in the community by epidemiological week and year from 2012-2016. To do this, you think it would be best to create new variables to calculate the rates by year. You already know how to create a new variable (hint: `newvariable<-existingvariable`). However, once you have a data frame in R, you need to instruct the program to a variable of interest within the data frame using '$'. For example, if you are using a data frame labelled 'my_data' and you want to refer to the variable 'my_variable', you would use:

```
my_data$my_variable
```

Try looking at the ILI2014 variable in your LFFdata data frame using a command like this. Provide your code below:

```
LFFdata$ILI2014
```

Using this logic, you can derive a rate variable by referring to the variables you would like to use for calculation within the data frame. To create a new variable for the rate of ILI per 1000 public health hotline callers each week in 2012, you would use the following formula:

```
rate2012<-(LFFdata$ILI2012/LFFdata$calls2012)*1000
```

Try creating variables for the rates of ILI for 2013, 2014, 2015 and 2016. Name these variables in the same format as 'rate2012'. Provide your code below:

```
rate2013<-(LFFdata$ILI2013/LFFdata$calls2013)*1000
rate2014<-(LFFdata$ILI2014/LFFdata$calls2014)*1000
rate2015<-(LFFdata$ILI2015/LFFdata$calls2015)*1000
rate2016<-(LFFdata$ILI2016/LFFdata$calls2016)*1000
```

Binding new variables to a data frame

If you view your LFFdata now you will notice that these new variables are not in the data frame. To add these to your data frame you need to bind the variables to the data frame. To bind your new variable 'rate2012' to your 'LFFdata' data frame, you would use the following code:

```
LFFdata$rate2012<-rate2012
```

The logic behind this is that you are assigning the value of your newly created variable (rate2012) to a new column (rate2012) within the data frame (LFFdata).

Now try binding your rate2013, rate2014, rate2015 and rate2016 variables to the LFFdata data frame. Provide your code below:

```
LFFdata$rate2013<-rate2013

LFFdata$rate2014<-rate2014

LFFdata$rate2015<-rate2015

LFFdata$rate2016<-rate2016
```

View your 'LFFdata' to check your new variables are now in the data frame.

Now summarise your LFFdata and look at your new variables. Which year had the highest mean rate of ILI?

2016 with a rate of 87.22 per 1000 population

Plotting variables:

You think that maybe visualising the data might be helpful in investigating ILI trends over the years. The simplest way to do this is to plot each year's rates individually over time. To plot 2012 ILI rates as a line graph with circular data points in the colour red you would use the following code:

```
plot (rate2012, type="o", col="red")
```

Plot the rates in 2013, 2014, 2015 and 2016 in orange, green, blue and purple respectively. Provide your code below:

```
plot (rate2012, type="o", col="red")
plot (rate2013, type="o", col="orange")
plot (rate2014, type="o", col="green")
plot (rate2015, type="o", col="blue")
plot (rate2016, type="o", col="purple")
```

As you enter these commands, graphs should appear in your 'plot' window. You can scroll through them using the arrows in the top left hand corner of the plot window. You can see the different timings of the seasonal peaks, but comparing them and knowing what is expected and what is unusual activity is difficult.

Using a package

A colleague tells you that there are lots of packages you can download into R that can do all kinds of fancy tricks with automated commands. They tell you about a package called the 'moving epidemic method' (MEM) that might be of use in setting thresholds for flu activity. Thresholds might be of use in measuring the 2017 flu season as it happens and determining whether transmission is low, medium, high or very high.

Dropping variables

Your colleague helpfully tells you that the only information that you need for MEM is your rate data by year and week. This means that variables containing epidemiological week, number of calls and number of ILI presentations are not going to be useful to you anymore.

To drop a variable within a data frame, you assign it a 'NULL' value. For example, if you were going to drop the variable 'my_variable' from the data frame 'my_data', you would use the following command:

```
my_data$my_variable<-NULL
```

Individually drop the variables epiweek, calls2012, calls2013, calls2014, calls2015, calls2016, ILI2012, ILI2013, ILI2014, ILI2015 and ILI2016 from your dataset. Provide your code below:

```
LFFdata$epiweek<-NULL
LFFdata$calls2012<-NULL
LFFdata$calls2013<-NULL
LFFdata$calls2014<-NULL
LFFdata$calls2015<-NULL
LFFdata$calls2016<-NULL
LFFdata$ILI2012<-NULL
LFFdata$ILI2013<-NULL
LFFdata$ILI2014<-NULL
LFFdata$ILI2015<-NULL
LFFdata$ILI2016<-NULL
```

To check that your only remaining variables are your yearly rates, inspect the top few rows of your data using the following code:

```
head(LFFdata)
```

Installing and using a package

Install the MEM package with the following code:

```
install.packages("mem")
```

The first thing you do when you use any package is load the package's library. This should automatically be stored in your working directory by nature of you using R to download and install it. Use the following code:

```
library(mem)
```

In the screen where your plots had appeared previously, you should see a packages tab. Look for 'MEM' in this list and click on it. Within this you can see all the possible functions and commands in the package. The colleague that told you about the package very helpfully tells you that you need to use the 'memmodel' function to create thresholds based on your 5 years of data. You could read the function instructions and figure out which commands to put within your code, but your colleague helps you put it together. Use the following code to create your thresholds:

```
LFFdatamem<-memmodel(LFFdata, i.seasons = 5, i.type.threshold = 5,i.level.threshold
= 0.95, i.tails.threshold = 1, i.type.intensity = 6,i.level.intensity = c(0.4,
0.9, 0.975),  i.tails.intensity = 1,i.type.curve = 2, i.level.curve = 0.95,
i.type.other = 3,  i.level.other = 0.95, i.method = 3, i.param = 2.8, i.n.max = -
1,i.type.boot = "norm", i.iter.boot = 10000)
```

You have now created thresholds. All the information about these thresholds is stored in 'LFFdatamem'. To access this information, try 'print' and 'summary' of 'LFFdatamem. What are your medium, high and very high threshold levels?

Intensity thresholds:

	Threshold
Medium (40%)	93.05
High (90%)	120.74
Very high (97.5%)	135.48

To visualise these thresholds and the 5 years of data, you can plot your results. The package has made this much simpler and you do not need to instruct R with all the details on how to plot. Use the following command:

```
plot(LFFdatamem)
```

To demonstrate to your director how these thresholds might represent transmission levels in previous flu seasons, you decide to compare how the previous 5 years would have been measured with these thresholds. Crossing a threshold results in the activity being scaled at that level. For example, if your medium threshold is 100 and your peak activity in a year is 103 people with ILI per 1000 callers, that year would have reached a medium level of transmission activity.

Summarise your 'LFFdata' again. Using the maximum weekly rate from each year, what level of activity (low, medium, high or very high) would each year have reached at its peak?

2012: High (121.29)
2013: Medium (109.07)
2014: Medium (98.4)
2015: Low (86.86)
2016: Very high (138.86)

You present your thresholds to your director, who agrees with the representation of the previous 5 years against these thresholds. They think the thresholds will be helpful in monitoring and managing the 2017 season. Congratulations, your work here is done!

Additional reading:

- I would highly recommend the datacamp training for R (https://www.datacamp.com/courses/free-introduction-to-r)
- For additional information on the moving epidemic method and flu surveillance:
    - Vega, T., Lozano, J.E., Meerhoff, T., Snacken, R., Mott, J., Ortiz de Lejarazu, R. and Nunes, B., 2013. Influenza surveillance in Europe: establishing epidemic thresholds by the moving epidemic method. *Influenza and other respiratory viruses*, *7*(4), pp.546-558.
    - Vega, T., Lozano, J.E., Meerhoff, T., Snacken, R., Beauté, J., Jorgensen, P., Ortiz de Lejarazu, R., Domegan, L., Mossong, J., Nielsen, J. and Born, R., 2015. Influenza surveillance in Europe: comparing intensity levels calculated using the moving epidemic method. *Influenza and other respiratory viruses*, *9*(5), pp.234-246.
    - http://www.who.int/influenza/surveillance_monitoring/pisa/en/

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Teaching first year MAEs

Presentation

Ethical Considerations in Study Participation: What YOU need to KNOW!

Brigitta Osterberger
Julia Maguire
Kaitlyn Vette
Kelley Meder

Learning Outcomes

- To understand:
  - the need for a participation information sheet
  - the ethical considerations when producing a participant information sheet
  - what voluntary participation involves
  - the difference between confidentiality and anonymity
  - the implications of participant withdrawal
- To be able to identify misleading information in a participant information sheet and ways to improve it

2

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Overview

- Participant Information Sheets - inform your participants!
- Considerations for a Participant Information Sheet:
  - Clear, easy to understand, transparent!
  - Comprehensive
  - Purpose, methodology, benefits, result distribution, risks and implications
- Key for ethical approval

3

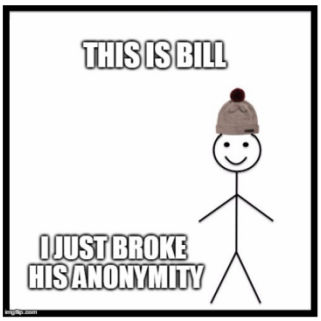
Australian National University

Confidentiality & Anonymity

4

Australian National University

Confidentiality & Anonymity



- Not the same thing
- Anonymous – cannot be identified
- Confidential – identifiable, but kept private
- Confidentiality can only be protected as far as the law allows
- It's ok not to protect confidentiality, as long as you are clear about it

5

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Voluntary Participation & Withdrawal

- Remuneration
- Withdrawal without consequence
- Collecting anonymous information has implications for withdrawal
- Informed consent

6

Australian National University

Data Storage & Security

- Where and how
- How long
- Handling of data following the required storage period

7

Australian National University

Exercise

Augustus Gloop, MAE Scholar at the Willy Wonka Institute of Chocolate Science

The influence of child freckles on the consumption of Theobroma cacao: A randomised controlled trial.

8

Australian National University

Wrap Up

There is more involved with information sheets..

ANU PIS and consent form template online
https://services.anu.edu.au/research-support/ethics-integrity/information-sheets-consent-forms

ANU Code of Research Conduct
https://policies.anu.edu.au/ppl/document/ANUP_007403

Australian National Data Service Guide - 'Indentifiable, re-indentifiable, non-identifiable' data
https://www.ands.org.au/__data/assets/pdf_file/0003/737211/De-identification-edit-2018.pdf

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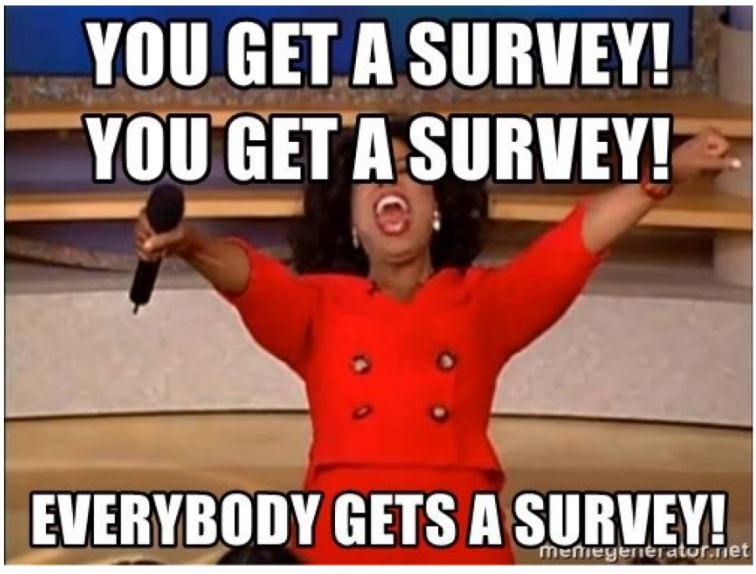


10

Practical exercise: Developing a Participant Information Sheet

Researcher:

My name is Augustus Gloop and I am a Master of Philosophy (Applied Epidemiology) Scholar at the Willy Wonka Institute of Chocolate Science.

Project Title: The influence of child freckles on the consumption of Theobroma cacao: A randomised control trial.

General Outline of the Project:

Description and Methodology: I am conducting research on how freckles in children impacts chocolate consumption. This research seeks to understand how physical features influence chocolate consumption in children.

Participants: I intend to interview 10 children with visible facial freckles under the age of 10 years. Children will be recruited from the confectionary aisle of a grocery store in the Sydney CBD.

Use of Data and Feedback: I will use the data collected for advertising purposes and to produce peer-reviewed published articles. Individual participants will not receive any feedback regarding their involvement or of the study findings.

Project Funding: I have the genius idea of raising money via a golden ticket competition sponsored by Willy Wonka's Chocolate Division.

Participant Involvement:

Voluntary Participation & Withdrawal: *(what is important to explain?)*

_____

_____

_____

_____

What does participation in the research entail? You are invited to take part in an interview with me about your experiences of eating chocolate in your day-to-day life. With your consent, I will record the interview so that I can accurately transcribe it, and the recordings will be destroyed after transcription. During the interview, I may ask some personal questions about how freckles on your face have impacted your chocolate consumption, including your relationship with other food.

Confidentiality: (how would you phrase this?)

_____

_____

_____

_____

Location and Duration: Interviews are expected to last about 10 minutes, and will be conducted at a place of your choosing – for example, your primary school or in a place we can talk in private. I may contact you for another 10 minute interview if I would like to follow up on anything from the first interview.

Remuneration: In recognition of your time, I will offer you a Willy Wonka chocolate bar.

Risks: (which 3 points would you mention?)

_____

_____

_____

_____

Benefits: It is unlikely that you will personally benefit from participation in this research other than happiness after eating the complementary chocolate bar. However, the work will support the chocolate industry.

Data Storage: (what are the 3 headings that you would include?)

_____

_____

_____

_____

Privacy Notice:

In collecting your personal information within this research, the ANU must comply with the Privacy Act 1988. The ANU Privacy Policy is available at https://policies.anu.edu.au/ppl/document/ANUP_010007 and it contains information about how a person can:

· Access or seek correction to their personal information;

· Complain about a breach of an Australian Privacy Principle by ANU, and how ANU will handle the complaint.

Queries and Concerns:

Contact Details for More Information: Call 1800 CHOCOLATE for more information

Ethics Committee Clearance:

The ethical aspects of this research have been approved by the ANU Human Research Ethics Committee (Protocol 20xx/xxx). If you have any concerns or complaints about how this research has been conducted, please contact:

Ethics Manager

The ANU Human Research Ethics Committee

The Australian National University

Telephone: +61 2 6125 3427

Email: Human.Ethics.Officer@anu.edu.au

Modified from Australian National University - Information Sheets and Consent Forms

https://services.anu.edu.au/research-support/ethics-integrity/information-sheets-consent-forms

Practical exercise: Answers

1. GENERAL OUTLINE OF THE PROJECT: What issues might be present in the draft information sheet?

• Project title does not reflect the study, e.g. how is it a randomised control trial?

• Description and methodology - lack of information about study design and analysis.

• Participants - no exclusion criteria, no justification of small sample size.

• Use of data and feedback - should always try to give participants feedback.

2. VOLUNTARY PARTICIPATION AND WITHDRAWAL:

• You may, without negative consequences, decline to take part or withdraw from the research without providing an explanation at any time until the work is prepared for publication (if the participant's data is re-identifiable), or until data are submitted to the researcher (if no personal identifying details are collected, and participation is completely anonymous).

3. CONFIDENTIALITY

• Your confidentiality will be protected as far as the law allows.

4. RISKS FOR PARTICIPANTS

• Describe any **risks, discomforts**, **hazards or side effects** that might arise because of the subject of the research or the research method. For this study in particular, you don't know what we you are participating in, or how your information will be used. Things to think about include:

· A lack of feedback to participants

· Children may feel intimidated and obliged to participate

· No explicit adult consent

· The research is supporting the chocolate industry

· Research will be used for advertisement

· The interview will be recorded

Other considerations – unlikely to be in the information sheet

· Study design is not robust – not an RCT, small sample size

· No established link between freckles and chocolate consumption – no scientific basis for the study

5. DATA STORAGE

• Where, how long (5 years), what will happen at the end of the storage period (destroyed, archived, used further)

Three keen budding MAEs putting their donning and doffing skills to the test

Later that day - second year MAEs celebrating impending marriages with their PPE

Appendix 6A - Evaluation of lessons from the field

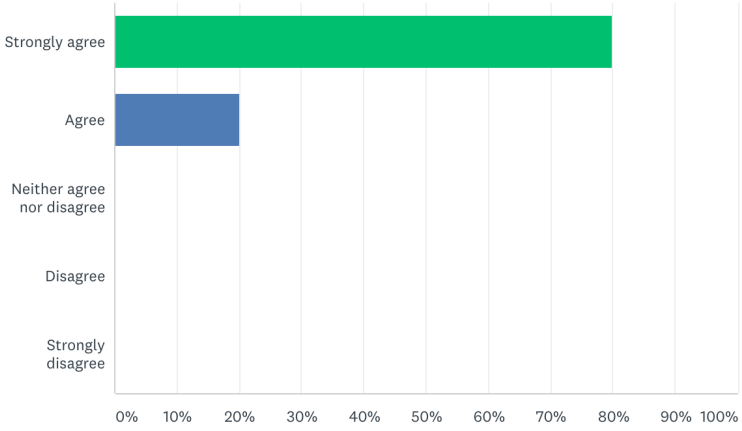
There were five respondents who filled out this survey.

Q1

Customize Export

The objectives of the LFF were to: understand the basic logic of R; assign values to variables, vectors and data frame; set a working directory and import data; drop and create new variables; bind variables to datasets; plot variables; install and use a package; become more familiar with influenza data measurements. Did the LFF meet these objectives?

Answered: 5 Skipped: 0

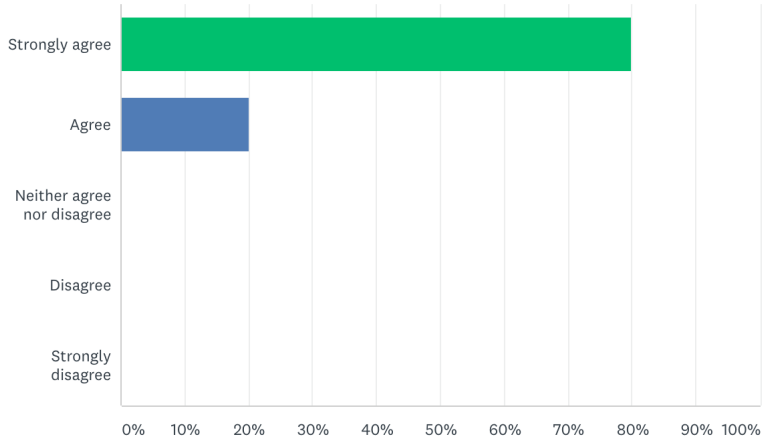


Q2

Customize Export

Tasks outlined were easy to understand

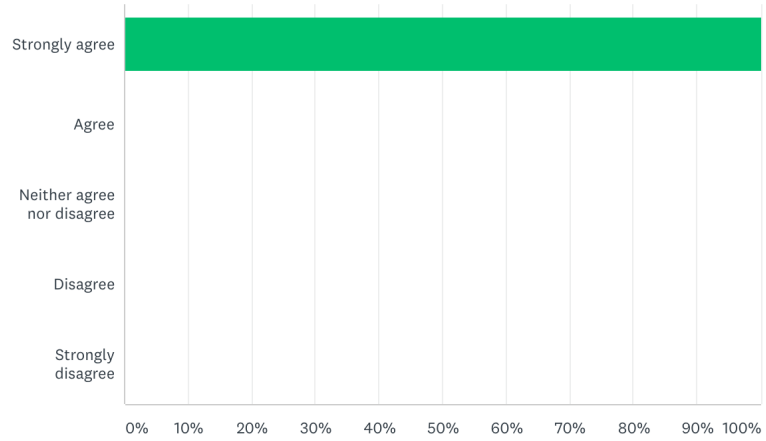
Answered: 5 Skipped: 0



Q3 Customize Export

The time to complete the LFF was reasonable

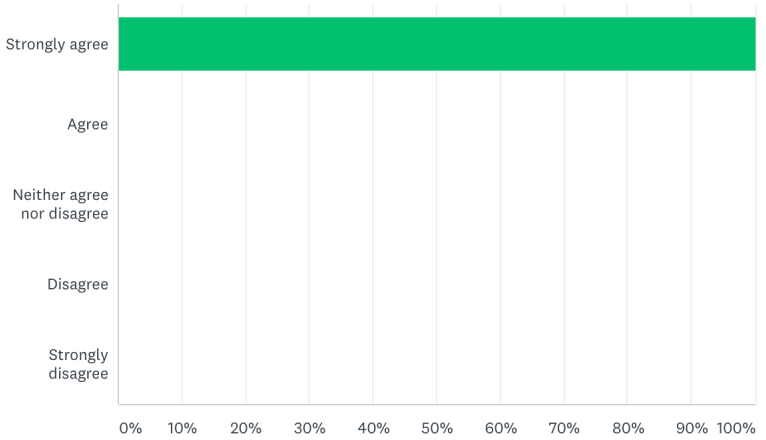
Answered: 5 Skipped: 0



Q4 Customize Export

I have a better understanding of how to use R now

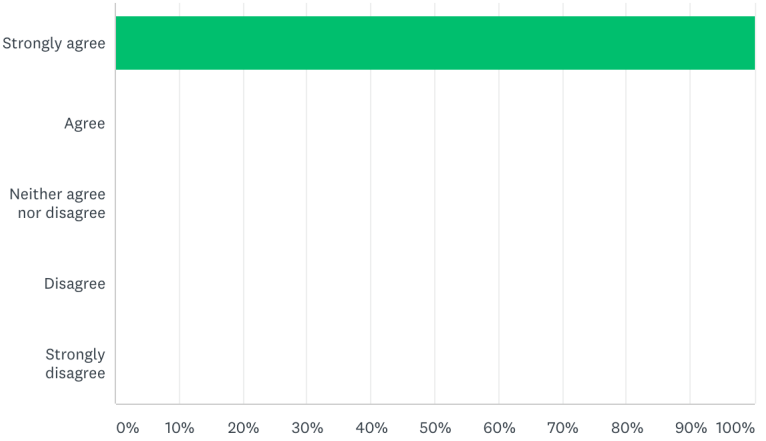
Answered: 5 Skipped: 0



Q5 Customize Export

Kaitlyn provided answers that were easy to understand

Answered: 5 Skipped: 0

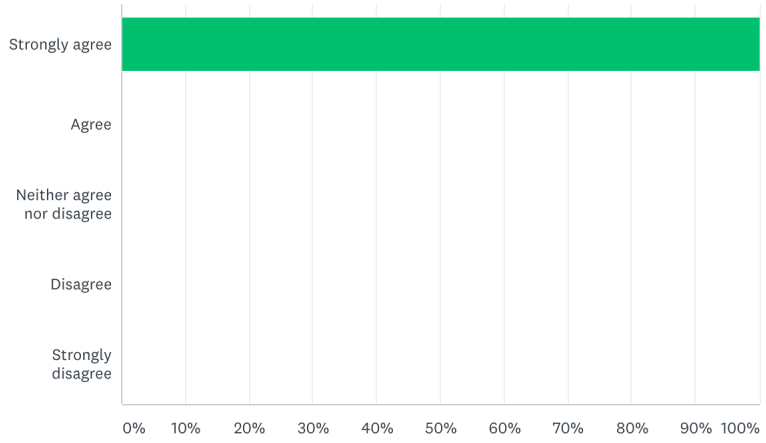


Q6

Customize Export

Kaitlyn was knowledgeable about the LFF content

Answered: 5 Skipped: 0



Q7

Export

Please provide at least one thing you learnt as a result of doing this LFF

Answered: 5 Skipped: 0

RESPONSES (5) TEXT ANALYSIS TAGS (0)

Add Tags Filter by Tag Search responses

Showing **5** responses

How flexible R is but also how much you need to know to be able to use it

6/25/2018 10:35 AM View respondent's answers

Basic R commands

6/14/2018 9:01 AM View respondent's answers

I had not used R to generate plots before. And I had of course not used the MEM before either, and suspect this could become handy in the future.

6/13/2018 7:50 PM View respondent's answers

How to conduct basic data analysis in R and some of the differences between R and stata.

6/5/2018 3:25 PM View respondent's answers

Generally just how to even get started using R! Sometimes that's the most daunting thing - where to start.

6/5/2018 9:47 AM View respondent's answers

Q8

Export

Please provide at least one thing that could have been improved in the LFF

Answered: 5 Skipped: 0

RESPONSES (5) TEXT ANALYSIS TAGS (0)

Add Tags Filter by Tag Search responses

Showing **5** responses

N/A

6/25/2018 10:35 AM View respondent's answers

I thought it was really well done, not sure if I would have changed anything.

6/14/2018 9:01 AM View respondent's answers

Could we learn some more R? It is very difficult to find room for improvement. The LFF was very well structured and easy to follow, providing a good introduction to the stats package/programming language. The lesson did not include any harder questions to think about, but that is very difficult to incorporate when introducing a programming language, specially when the students have little to no base knowledge and the lesson has to start from the most basic level.

6/13/2018 7:50 PM View respondent's answers

Perhaps more open ended questions/discussion questions like the question on which data source you would use, and why.

6/5/2018 3:25 PM View respondent's answers

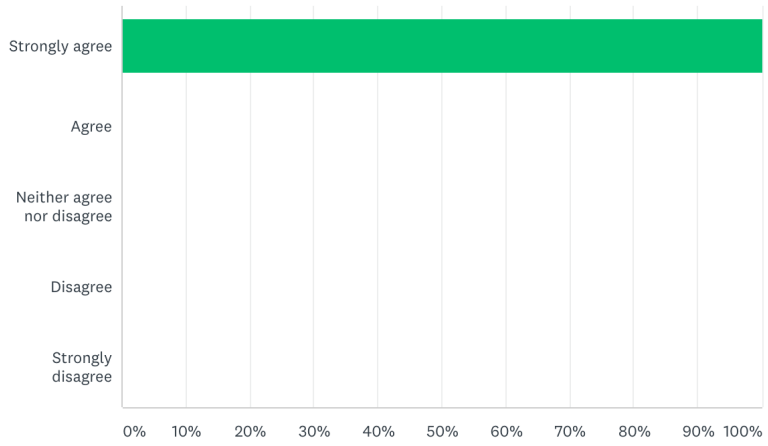
I think in the initial introduction of using R, a bit more explanation of the different windows may have been helpful, but i figured it out in the end. Also realise that its difficult to balance how much information to give in a set of instructions.

Q9

Customize Export

Overall I enjoyed the LFF

Answered: 5 Skipped: 0



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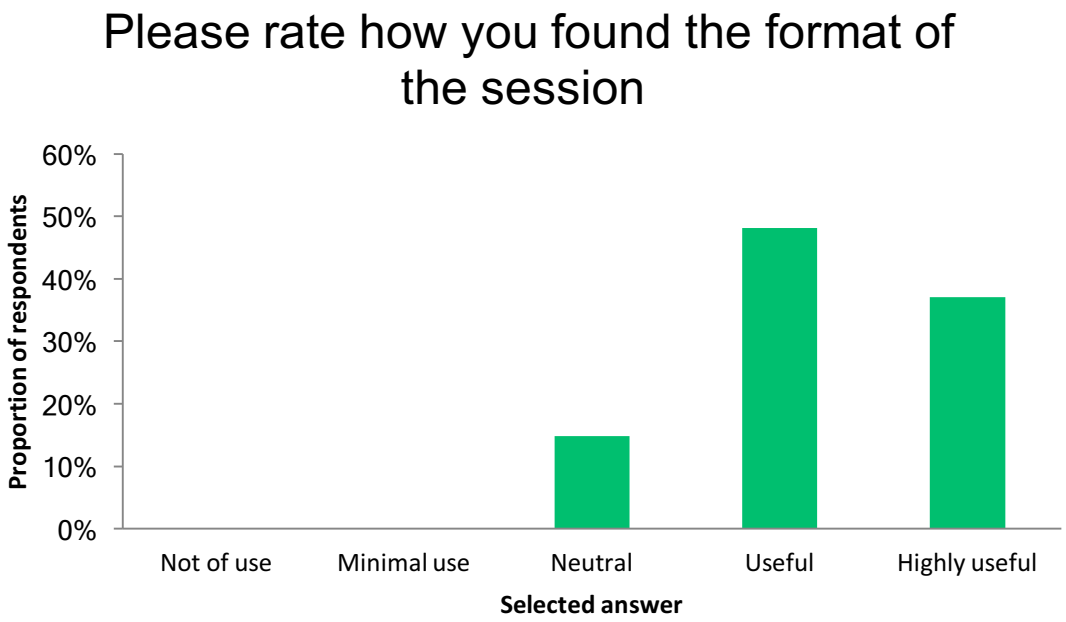
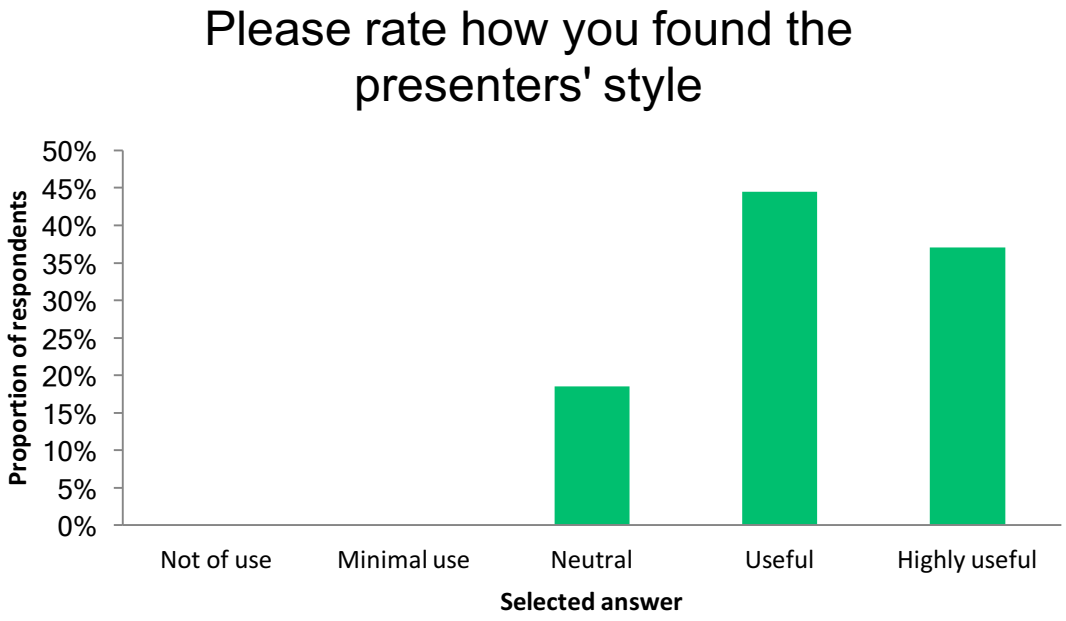
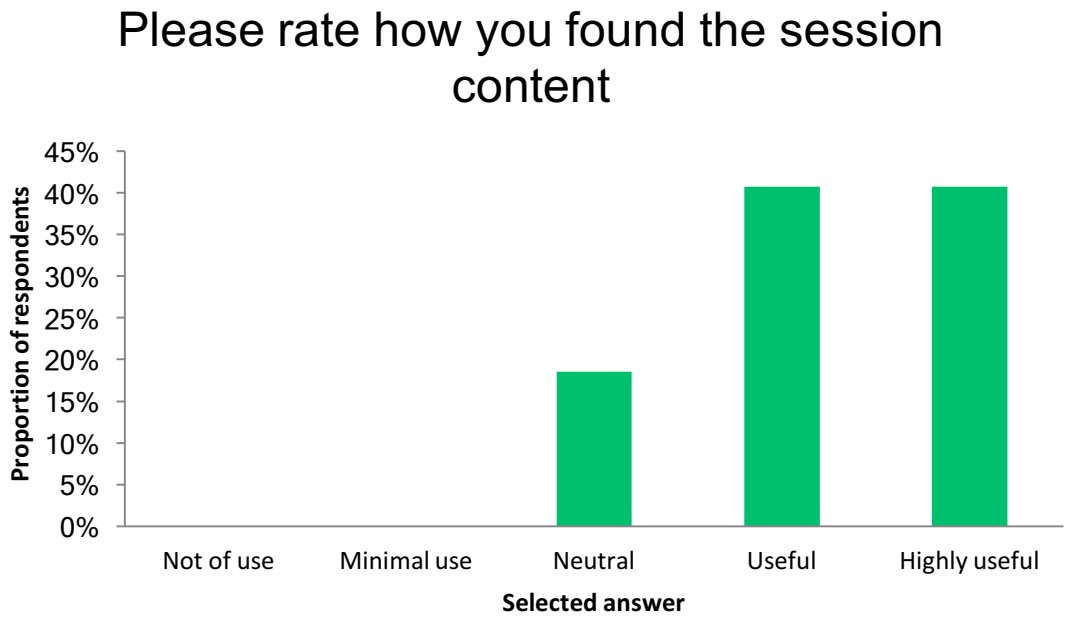
Appendix 6B – Evaluation of first year MAE teaching

There were 27 participants who responded to this survey.






Please rate how you found the session content
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
Proportion of respondents
Not of use
Minimal use
Neutral
Useful
Highly useful
Selected answer

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Chapter 7: The Commonwealth Games

The Commonwealth Games: International and local surveillance

"Be alert, not alarmed"

- Dr Emily Fearnley

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Introduction

From the 4th-15th of April 2018, the Gold Coast hosted the 21st Commonwealth Games (the Games). With 70 participating teams representing one third of the world's population and a large number of spectators anticipated, it was important to be prepared to detect and respond to communicable disease events at the mass gathering. I was involved in two aspects of the Games; conducting international communicable disease surveillance at the Australian Government Department of Health, and taking part in a short-term placement at the Gold Coast Public Health Unit (GCPHU) during the Games.

International communicable disease surveillance

My role

In mid-2017 the GCPHU contacted the Australian Government Department of Health to request international communicable disease surveillance in the lead up to and during the Games period. My fellow MAE Patiyan Andersson and I were tasked with establishing a system of surveillance and reporting for Queensland (QLD) Health. As the mass gathering was drawing a large influx of international visitors, it was necessary for local and national health authorities to be aware of communicable disease events overseas that may be imported into Australia.

Patiyan and I worked together to determine the scope of the surveillance, inclusion and exclusion criteria (Appendix 7A), record keeping processes, distribution of the report, and a reporting structure and schedule (Appendix 7B). We built on existing surveillance processes where possible to keep the system streamlined. Both of our placement areas within the Office of Health Protection needed to be involved in surveillance activities as they were responsible for national epidemiology and surveillance, and health emergency preparedness and response. We consulted with and sought agreement from the GCPHU and our respective departmental areas on our proposed processes and established a standard operating procedure for agreement by all.

Patiyan and I conducted surveillance and compiled a report monthly in January and February, weekly from the end of February to mid-March and daily from then until

four days after the closing of the event in mid-April. Epidemiologists in my team assisted when we were at course block, and first year MAEs Celeste Marsh and Hendrik Camphor became part of the reporting roster when they joined the Office of Health Protection in March.

The surveillance report was disseminated to state public health units, QLD Health epidemiologists, pathologists and general practitioners throughout QLD, the medical functional area of the Commonwealth Games organisers, the Communicable Diseases Network Australia (CDNA), staff in the Office of Health Protection and the Sports Branch of the Australian Government Department of Health.

Following the completion of our surveillance activities, Patiyan and I provided input to a summary report of public health activities during the Games that will be published in the coming months. I also presented on our activities to the first year MAEs during their tour of the National Incident Room, and Patiyan and I delivered a lecture during MAE course block at the National Centre for Epidemiology and Population Health (Appendix 7C).

Lessons learnt

This additional project taught me a lot about the details of setting up a surveillance process and the importance of collaboration and forethought. With so many stakeholders involved, it was essential for processes to be planned and agreed ahead of time.

It was an interesting and challenging experience establishing the scope of our surveillance. Having routinely compiled international disease surveillance for CDNA as part of my placement, I was well experienced in investigating and reporting international events of concern. However, this report needed to be much more sensitive in the breadth of our searches and inclusion criteria. I learnt that while it is important to start with clear inclusion and exclusion criteria, the definition of these only fully crystallise once you start undertaking surveillance. As such, it is essential to keep the overall goal of your activities front-of-mind, and it's important to start conducting surveillance in advance of reporting in order to fully determine why some events and not others should be reported.

I also learnt a lot about Commonwealth countries, and that a trusty map and list of nations to include was essential!

Public health impact

Across the four-month period, 25 reports were compiled and distributed, and 27 international disease events were identified and monitored. Notable events included:

- The largest reported outbreak of Lassa fever in Nigeria, which was ongoing throughout the Games period.
- Dengue activity in the Pacific, known to cause seasonal outbreaks and lead to exported cases.
- A significant outbreak of meningococcal disease in Fiji.
- An ongoing outbreak of mumps in the Pacific, including a large cluster in Auckland, New Zealand.

The surveillance reports provided ongoing situational awareness for decision making and risk assessment by local and national government, primary health care and pathology services.

Acknowledgements

I would like to thank Patiyan Andersson for being such a supportive collaborator throughout this process, for sharing the successes and challenges, and for making this project fun. I also very much appreciate the assistance provided by Hendrik Camphor and Celeste Marsh in daily reporting. I would like to acknowledge and thank the Communicable Disease Epidemiology and Surveillance Section, Emergency Preparedness and Response Section and their branch heads Sarah Norris and Rhonda Owen for their assistance, advice and cooperation during surveillance and reporting. I would also like to thank Dr Satyamurthy Anuradha and Deena Seesaengnom from the GCPHU and those at QLD Health who provided input to the development of our surveillance and reporting processes.

Local communicable disease surveillance

Overview of experiences and role

I was fortunate enough to be placed in the GCPHU from the 9th-18th of April 2018, which included six days in the Games period and three days following its conclusion before the heightened response was stood down. The GCPHU is made up of environmental health (EH), epidemiology (epi), communicable disease nurse (CD nurse) and immunisation teams. There are also two public health physicians in the unit, Dr Satyamurthy Anuradha and Dr Paul Van Buynder. Three MAE scholars were placed in the epi team and one was placed in the temporary emergency operations centre (EOC). I was placed in the epi team, and was fortunate enough to gain some experience assisting CD nurses and going on a site visit with the EH team.

Daily rhythm

Each day someone from the epi team was scheduled to work 6:30am–2:30pm and 8am–4:30pm. A key part of ensuring lateral and vertical information sharing, upholding surveillance activities, and coordinating incident management and response, was maintaining the daily rhythm. The same processes, reports and meetings occurred each day throughout the games period and information was routinely shared between a variety of stakeholders.

Surveillance systems

A risk-based approach was taken to determine what the likely threats to health were, the potential impacts of these threats and how they should be monitored and managed. Gastroenteritis and influenza were the focus of surveillance activities and gastroenteritis was made the priority for monitoring and response efforts. Norovirus was identified as a key threat that was known to be an issue in previous mass gatherings, particular amongst event staff. To conduct surveillance of these priority illnesses, routine notifiable disease surveillance was enhanced using a combination of syndromic, laboratory and event based surveillance. Sentinel health services and partner agencies all supplied essential information to the GCPHU for surveillance. The GCPHU spent years planning, preparing and building these systems and partnerships.

My role

As part of the epi team, I was responsible for reviewing surveillance data each day as part of a rotating roster of responsibility for data sources. Four job cards were shared amongst the team, including two syndromic surveillance tasks, one event-based surveillance task, and one routine notifiable disease surveillance task. MAEs were responsible for managing each of these tasks independently when rostered to them and each involved collection, collation, assessment (including risk detection) and reporting of data.

A large part of our role was conducting, recording and analysing three-day food histories from people with gastroenteritis to try and establish any common exposures. At daily meetings, we were responsible for reporting any signals or risks we had identified so that the EH team could investigate these incidents with site visits.

Lessons learnt

Being part of a small epidemiological unit monitoring and responding to infectious diseases during the Games provided me with rare hands on experience in the specialised area of mass gathering surveillance. It was very interesting to get a sense of the level of the planning, stakeholder engagement and infrastructure implementation that needed to occur in order to establish adequate communicable disease surveillance for the Games. The GCPHU began preparing for the Games in 2015 and there was an enormous amount of consultation, literature review and brainstorming involved in establishing the well-oiled surveillance machine that we stepped into. I learnt that a key part of this planning, was to consider what the ongoing legacy of the surveillance systems and relationships established will be.

I learnt that in planning public health activities, the important questions to ask are ‘what risks are we concerned about?’, ‘how do we know if something unusual is happening?’ and ‘what do we then do about it?’. I also learnt the importance of pre-approved processes being flexible and adaptable to change as needs evolve.

As the response progressed, I learnt the art of the three-day food history interview. As part of this, I gained an understanding that these interviews provide an opportunity to educate the public, and I learnt the importance of consistent public health messaging when interviewing groups of people. One practical and important thing I learnt is to

ask if someone has a fridge before requesting a stool sample from them. I also gained hands on experience managing and consolidating data across multiple systems and using new platforms including Microsoft Access and EpiInfo.

By collecting data and reporting events at meetings with the EH team, CD nurses and public health physicians, I gained a real sense of the immediate importance of data for public health action. Every day the data we had collected was used as actionable disease intelligence and the EH team and CD nurses would conduct inspections and further investigations based on the epidemiological information. The process of event investigation also highlighted the importance of establishing and maintaining networks for communication with a variety of stakeholders.

I was fortunate enough to attend a meeting with an international delegation who were planning for a mass gathering in their home country. This provided me with further context and understanding of how other countries might approach public health planning for large events, and the degree of preparation involved.

It was a very rewarding to experience how a public health unit functions and the ways in which CD nurses, public health physicians, EH officers and epidemiologists work together. Not only did this provide me with context for activities while I was there, but it also provided me insight into the similarities and differences between public health at national and local levels.

Public health impact

As a result of timely, sensitive and well-planned surveillance and response, there were no Games-related outbreaks. Routine disease activity in the Gold Coast community was also managed effectively and did not enter circulation at the mass gathering. There were a number of surveillance systems developed for the Games that will continue on and be the legacy of the work of the GCPHU.

Acknowledgements

I would like to thank the GCPHU, in particular Dr Satyamurthy Anuradha, Sharon Jurd, Deena Seesaengnom and Ian Hunter for this opportunity and for fully immersing us as part of the team. All members of the GCPHU including the epi team, EH officers, CD nurses and public health physicians were exceptionally generous with their time,

sharing of their knowledge and experience, and inclusion of the MAEs in important, real-time activities. I would also like to acknowledge the MAE staff at ANU for organising and facilitating this experience, and thank my fellow MAEs Cushla Coffey, Kelley Meder and Brigitta Osterberger who accompanied me on this placement and made it all the more educational and fun.

I am very grateful to have had the opportunity to gain invaluable experience in this setting. It was an excellent opportunity to put theoretical learnings into practice, and to learn from people who put an enormous effort into preparing and managing a successful mass gathering.

Action in the Emergency Operations Centre

Some of the fantastic GCPHU staff

Two MAE students with an extra helping of nerdy and excitable

Appendix 7A – Standard operating procedure for international communicable disease surveillance for the 2018 Commonwealth Games

Last updated 6 April 2018 by Patiyan Andersson and Kaitlyn Vette

International Reporting Guidelines

Objective of the report

To provide relevant information about international communicable disease outbreaks and trends which have specific relevance to public health and emergency response relevant to the Gold Coast 2018 Commonwealth Games (GC2018) to the Queensland Public Health Authorities and the game organisers.

The GC2018 will run over the time period of 4-15 April 2018. There will be 70 teams competing from the 52 members of the Commonwealth of Nations. An increase in travel associated with the GC2018 is expected, both with respect to competing athletes and their families, as well as spectators of the games. This mean there is a heightened risk of communicable disease transmission over the period surrounding the GC2018. The Commonwealth Department of Health will be providing enhanced rumour surveillance reports to the Queensland Department of Health, with a particular attention to public health events in Commonwealth countries. The enhanced reporting will be operational only for a limited time covering the GC2018 games, with a reporting schedule as set out later in this SOP. During this time period, the enhanced information will be used for the fortnightly CDNA report, and replacing the regular international report section. At the end of the GC2018 enhanced reporting period (last report due 2 May), the international section for the fortnightly CDNA report will return to its regular format.

Inclusion criteria

Important considerations:

1. Does the event have potential to be imported to Australia by international travellers?
    - For example: a communicable disease or infectious agent – human only.
2. Is the affected population likely to be travelling to the games?
    - For example: if transmission is primarily in a disadvantaged population, are they likely to be travelling to the games.
3. Does it have potential to continue transmission if imported?
    - For example: a disease without a competent vector or a food/water-borne disease is unlikely to continue spreading.

These may include:

1. Communicable disease outbreaks or a higher than normal incidence within Commonwealth countries;
2. Communicable disease outbreaks of significance internationally;
3. Higher than normal incidence of a communicable disease of significance to Australia;
4. Only new issues or significant updates (e.g. increase in case numbers or deaths) are to be included in the report.

Exclusion Criteria

Events should be excluded if they meet one or more of the following criteria:

1. Routine reports of communicable diseases such as global reports;
2. Potential threats or situations based on research outcomes alone; or

Last updated 6 April 2018 by Patiyan Andersson and Kaitlyn Vette

3. Issues provided in previous reports - unless significant new information is available.

If unsure, please check with the relevant epidemiologist.

Sources of information

- WHO EIS and situational reports - http://apps.who.int/ihr/eventinformation/
- WHO Disease Outbreak News - http://www.who.int/csr/don/en/
- WHO SEARO surveillance and outbreak - http://www.searo.who.int/entity/emerging_diseases/en/index.html
- WHO WPRO surveillance and outbreak- http://www.wpro.who.int/outbreaks_emergencies/en/index.html
- WHO AFRO surveillance and outbreak – http://www.afro.who.int/health-topics/disease-outbreaks/outbreaks-and-other-emergencies-updates
- ECDC - http://www.ecdc.europa.eu/en/press/news/Pages/News.aspx
- CDC - http://www.cdc.gov/
- CIDRAP - http://www.cidrap.umn.edu/
- UK HPA - http://www.hpa.org.uk/
- ProMED mail - http://www.promedmail.org/
- ProMED Mekong basin: http://www.promedmail.org/mbds
- GPHIN (see "Email lists" section below for instructions on how to access this)
- PacNET: http://www.spc.int/phd/epidemics/

Sources for additional information about known event or threat:

- Reuters alert net - http://www.trust.org/?show=alertnethumanitarian
- FLUTRACKERS - http://www.flutrackers.com/forum/
- HealthMap - http://healthmap.org/en/
- Reliefweb: http://reliefweb.int/

Email lists

- PACNET
  - To be added to PACNET send an email to join-pacnet@lyris.spc.int. They will email you back asking why you want to join.
- CIDRAP Newsletter – Go to http://www.cidrap.umn.edu/newsletter and add your email details
- GPHIN alerts can be read in the Health ops inbox (access to Health ops inbox provided to Watch Officers (WO) – please contact WOs if you require information about GPHIN alerts)

Interpretation of information

When using sources such as Reuters or ProMed ensure you check where the information has originated from and reference the original source as well as ProMed itself. These websites act as repository of information, so it is important to check the sources these websites reference to ensure the information is accurate and plausible. Some media articles are recycled. You should always check the date from the original source and cross-reference with a known credible source such as a government website or UN agency website where possible. For the purposes of Commonwealth Games surveillance, including information without an official source is acceptable if it is of interest.

Last updated 6 April 2018 by Patiyan Andersson and Kaitlyn Vette

Report structure

The Surveillance Issues Log will be used as the depository for the surveillance information collected. The columns and expected content is described below. Once updated, the filters are used to generate a view specific to the Commonwealth Games report and exported to an Excel format.

Heading	Description and format
Issue/Incident Title	"Disease – Country"
Date of update	The day that you made this entry
Date first reported or first aware	The first date of reporting if reported previously (check the log for previous entries).
Disease	Full name of the disease
Countries/regions/areas affected	Can be "country", "continent+countries", "country+specific areas"
Source of information/data	State the source and provide a link
Case numbers	Number of suspected and confirmed cases only. Details should be provided elsewhere.
Affected population	In broad terms (e.g. general population, young people, Indigenous people, urban/rural, occupation-specific)
Background description	Summarise important background information. Any important contextual information for internal record keeping and decision making should be in here.
Summary description	Summarise the most important information. Should be as concise as possible and contain only relevant information pertaining to time, place, and person.
Serious health impact	Does the health event result in a serious health impact, can be significant event if only having local affects. Some sources (such as EIS) will have a risk assessment that can be used. Otherwise look at the assessment from previous instances of similar health events in the surveillance issues log, or ask an epidemiologist in the relevant area.
Unusual or unexpected	Is this health event unusual or unexpected, or is it endemic to the country or has a seasonal recurrence. Some sources (such as EIS) will have an assessment that can be used. Otherwise look at the assessment from previous instances of similar health events in the surveillance issues log, or ask an epidemiologist in the relevant area.
International disease spread	Is the health event likely to result in transmission to neighbouring countries (for instance when borders are porous, conflict zones, affecting displaced populations), or even further international spread (through air travel). Some sources (such as EIS) will have an assessment that can be used. Otherwise look at the assessment from previous instances of similar health events in the surveillance issues log, or ask an epidemiologist in the relevant area.
Likelihood of impacts for Australia	Is the health event is likely to have an effect on Australia (for instance through importation and local transmission, Australian residents travelling overseas). Revisit the key considerations at the beginning of this document.
Include in reports	Tick if the information should be included in the Commonwealth Games report or CDNA report. If it is a Commonwealth country and the other considerations of inclusion are met, it should be included. Even if it is a major health event in a non-Commonwealth country, it could be of relevance for the Commonwealth report as there may still be significant numbers of visitors from this country and risk of onward transmission. All commonwealth games surveillance should be included in the CDNA report, however there may be additional events that are necessary for the CDNA report that are not necessary for the Commonwealth games report (eg non-Commonwealth

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Heading	Description and format
	countries with outbreaks that are unlikely to be imported, but more likely for Australians to visit that country).
Current actions, related reports, documents	Mainly used by the CDESS.
Additional actions that might be required	Mainly used by the CDESS.
Smartraveller updated	Mainly used by the HPPB Surveillance sections. Check Smartraveller website to see if there is advice about the disease and note that.
Current/superseded/closed	Indicate the state of the entry. Please check if there are previous entries about the same disease, ensure to 'supercede these' and make yours current. Ensure to update and close entries (especially your own) when they are no longer active.
Logged by initials	Put in your initials

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Appendix 7B - Example of international communicable disease surveillance report for the 2018 Commonwealth Games

Commonwealth Games international disease surveillance report

Reporting period: 17 April 2018

Issue/Incident Title	Date of update	Date first reported or first aware	Disease	Affected source populations	Case numbers	Summary description	Countries/regions/areas affected	Source of information/data
Lassa fever - Nigeria	18/04/2018	26/01/2018	Lassa fever	Two thirds of the cases are male and the people predominantly affected are between 30 and 50 years.	413 confirmed, 9 probable, 5 awaiting laboratory results	The Lassa fever outbreak in Nigeria continues however new cases reported over the past week (9-15 April) and the epidemic curve indicate that the peak number of cases nationally has passed. However, the Lassa fever period can be expected to continue for another 1-2 months, into June 2018. This is the largest outbreak of Lassa fever ever reported in Nigeria. In the reporting week 15 (9-15 April 2018), 5 new confirmed cases were recorded from 4 States.Between 1 January -15 April 2018, a total of 1849 suspected cases have been reported from 21 states. Of these, 413 were confirmed positive, 9 are probable, 1422 are negative (not a case) and 5 are awaiting laboratory results (pending). Since the start of the 2018 outbreak, there have been 105 deaths in confirmed cases. Case fatality rate in confirmed cases is 25.4 %.	Nigeria	Nigeria Centre for Disease Control week 13: 1 April 2018 http://www.ncdc.gov.ng/diseases/sitreps
Hepatitis A virus - New Zealand	18/04/2018	18/04/2018	Hepatitis A	Children associated with one kindergarten	6	Following diagnosis of 3 children from 2 families associated with a kindergarten in Oamaru last week (reported 7 April), 3 more cases have been confirmed through blood testing of the centre's children and staff. Vaccinations for those at the kindergarten were completed on 13 April 2018. Although the origin of the virus had not been identified, it was thought to be from outside the country.	New Zealand	http://www.promedmail.org/ Archive Number: 20180417.5751276 Otago Daily Times: https://www.odt.co.nz/regions/north-otago/3-more-hepatitis-cases
Measles - Europe	17/04/2018	2/07/2017	Measles	Unvaccinated general population	14,813 cases including 13 deaths	**New information:** There is an ongoing measles outbreak in Europe with 14,813 cases reported across 30 countries between 1 March 2017 and 28 February 2018. Outbreaks of measles are ongoing in France, Greece, Ireland, Italy, Portugal and Romania. As of 14 April 2018, Romania has had the most cases with 1,709 cases so far this year, followed by Greece (1,463), France (1,346), and Italy (411). Most concerning are the case counts in France and Italy, which have almost tripled and more than doubled, respectively, in the last month. Of these cases, where age was known, 35% were in children under five and 47% were in those 15 years or older. Where vaccination status was known, 86% were unvaccinated. Outside of the European Union, Ukraine has continued to experience the largest outbreak, with almost 10,000 cases reported year to date in 2018, including seven deaths. Ongoing outbreaks are also being reported in Albania, Belarus, Georgia, Serbia, and Turkey. Over 500 cases are reported from Russia, which will host country of FIFA 2018 during the 2018 European summer.	European countries	https://ecdc.europa.eu/sites/portal/files/documents/Communicable-disease-threats-report-14-apr-2018.pdf PHE https://www.gov.uk/government/publications/notifiable-diseases-weekly-reports-for-2018
Typhoid fever - Pakistan	16/04/2018	24/01/2018	Typhoid fever - multi drug resistance	Children aged 2-10 years	>850 cases in 14 districts, including at least 4 deaths	**New information:** The first known epidemic of extensively drug-resistant (XDR) typhoid is spreading through Pakistan, infecting at least 850 people in 14 districts since November 2016, according to the National Institute of Health Islamabad. The typhoid strain, resistant to 5 types of antimicrobial agents including ceftriaxone, the antibiotic previously used to treat MDR strains of typhoid, is expected to disseminate globally, replacing weaker strains where they are endemic. Experts have identified only one remaining oral effective antibiotic - azithromycin. Only 4 isolated cases of extensively drug-resistant (XDR) typhoid had previously been reported worldwide. **Background:** Antibiotic resistance is a major problem in Salmonella enterica serovar Typhi, the causative agent of typhoid. Multidrug-resistant (MDR) isolates are prevalent in parts of Asia and Africa and are often associated with the dominant H58 haplotype.	Pakistan	PromedArchive Number: 20180415.5747027 https://www.nytimes.com/2018/04/13/health/drug-resistant-typhoid-epidemic.html ProMED. https://www.thenews.com.pk/print/272217-hyderabad-facing-world-s-first-outbreak-of-drug-resistant-typhoid-aku http://www.coalitionagainsttyphoid.org/the-perfect-storm-in-pakistan-unsafe-drinking-water-and-drug-resistant-typhoid/

Issue/Incident Title	Date of update	Date first reported or first aware	Disease	Affected source populations	Case numbers	Summary description	Countries/regions/areas affected	Source of information/data
Scarlet fever - UK	16/04/2018	5/02/2018	Group A Streptococcus - Scarlet fever	89% of cases are children under 10 years - The age distribution of cases is similar to previous years.	17 103 cases reported in 2018 (to week 14 - ending 8 April)	There has been an unusually high level of scarlet fever circulating in the UK. In the 14 weeks ending 8 April 2018, 17,103 suspected cases of scarlet fever were reported to Public Health England (PHE) across England and Wales. The number of reports to date (8 April) in 2018 is more than double the 2017 figure and much higher than over the same period in the previous 8 years. There were 7,050 cases reported in 2017, compared to 8,360 in 2016, and 1,016 in 2011.	England, Wales	Promed-Archive Number: 20180408.5732644 Public Health England NOIDs Weekly Report - Week 11 ending 18 March 2018 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/692810/NOIDS-weekly-report-week11-2018.pdf Public Health England Health Protection Report - Volume 12 Number 13, 13 April 2018: https://www.gov.uk/government/publications/health-protection-report-volume-12-2018/hpr-volume-12-issue-13-
Measles - New Zealand	13/04/2018	10/04/2018	Measles	Unvaccinated general population	5 confirmed, up from 3 confirmed, 1 probable previously	As of April 11, an additional 2 new confirmed cases have been reported in Nelson and Christchurch, in addition to three previous cases in Queenstown, Wanaka, and Christchurch, bringing the total to 5 confirmed cases in the South Island, with age range 13 months to 46 years old. Investigations are continuing and close contacts are being identified for follow up.	New Zealand	PromedArchive Number: 20180409.5734358 Canterbury Health Wardhttp://www.scoop.co.nz/stories/GE1804/S00008/three-cases-of-measles-confirmed-in-south-island.htm
Dengue - Malaysia (Sabah state)	12/04/2018	12/04/2018	Dengue virus	General population	958 cases of dengue, including 10 deaths, this year up to March 31	According to the Sabah Department of Health, all districts in the state of Sabah have registered an increase in the number of dengue cases in the first quarter of 2018. Sabah has recorded 958 cases of dengue, including 10 deaths up to Sat 31 Mar, 2018. Malaysia as a whole has a similar dengue incidence trend for 2018 (until March 29) compared to previous years according to the WHO WPRO Dengue Situation Update.	Sabah state, Malaysia	ProMED-MBDS: Mekong BasinArchive Number: 20180407.5730876 WHO WPRO:http://www.wpro.who.int/emerging_diseases/dengue_biweekly_report_20180329.pdf?ua=1
Dengue - Pacific	11/04/2018	1/12/2016	Dengue	General population	Approximately 2,000 suspected cases	**New information:** **New Caledonia:** As of 6 April 2018, 528 confirmed cases since 1 January 2018; with co-circulation of dengue serotypes 1 and 2, of which 79.5% is serotype 2. One imported confirmed case of serotype 4 in the capital Noumea. **Background:** As at 25 March 2018, there are ongoing dengue serotype-2 outbreaks in Fiji, New Caledonia, Samoa and Vanuatu. The weekly number of cases (dengue serotype-2) reported is decreasing in Tonga. **Tonga:** As at 19 March 2018, there was an increasing number of dengue cases of dengue serotype-2. **Vanuatu:** As at 22 March, the outbreak of dengue serotype-2 was ongoing. As at 20 March there were 329 suspected cases reported. 52 of these were confirmed with rapid diagnostic test. Age range is 1-85 years old, 42% are children below 14 years of age and 55% are male. **Fiji:** As at 23 March, there is an ongoing outbreak of dengue serotype-2. There were 426 cases reported in January 2018 alone. **American Samoa:** As at 18 March, cases of dengue serotype-2 had peaked and are decreasing in number. **Wallis and Futuna:** As at 20 March, the outbreak of dengue serotype-1 has reportedly slowed. As at 22 January, 31 cases had been reported, 9 of which were confirmed, of which 8 are dengue serotype-1. There have been 5 hospitalised cases and no associated deaths. **Samoa:** As at 8 March, the number of new cases of dengue serotype-1 per week was decreasing but the outbreak is ongoing. There were still almost 50 new clinical cases per week in January 2018. There have been 3,001 clinical cases since August 2017. French Polynesia: As at 7 March, cases of dengue serotype-1 were decreasing but ongoing.	Pacific Islands	PacNet Epidemiological bulletin for New Caledonia PacNET Dengue Vanuatu Sit.Rep.#3, 20 March 2018 PacNET Syndromic Surveillance Report week 10 11 March 2018

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Appendix 7C – Lecture on international communicable disease surveillance report for the 2018 Commonwealth Games

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COMMONWEALTH GAMES INTERNATIONAL SURVEILLANCE REPORT

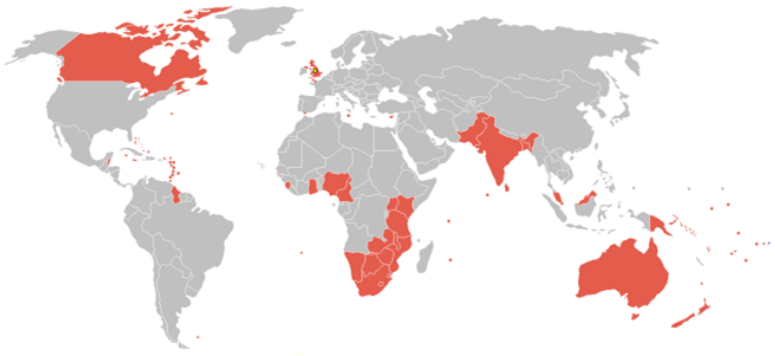
Kaitlyn Vette
Patiyan Andersson

March 2018
National Center for Epidemiology and Population Health

Australian Government
Department of Health

Purpose of the report

- Commonwealth Games on the Gold Coast from 4 - 15 April 2018
- 52 countries, 70 competing teams
- Commonwealth's role
- International communicable disease outbreaks and trends



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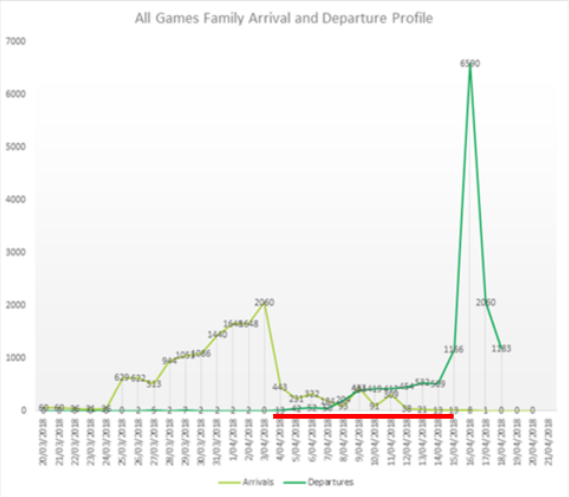
Surveillance period

- **Monthly:** January and February
- **Weekly:** End of Feb to mid March
- **Daily:** Mid March to mid April
- **Weekly:** Until beginning of May



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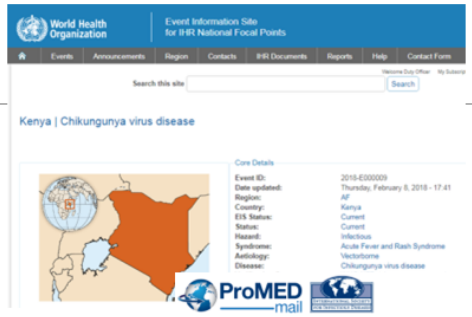
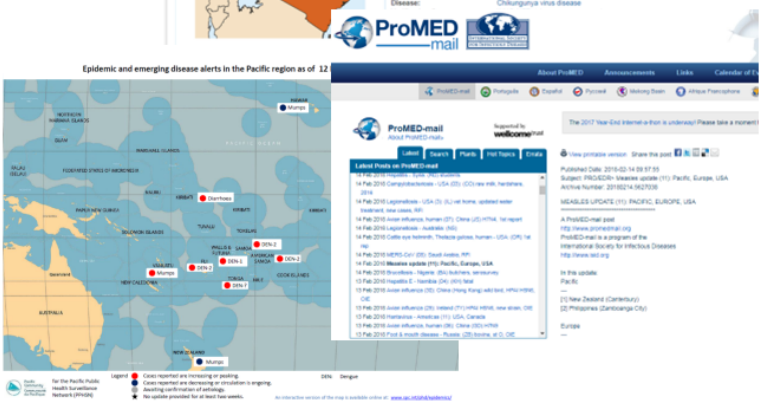
Surveillance sources

- WHO EIS
- WHO disease outbreak news
- WHO SEARO
- WHO WPRO
- ECDC
- CDC
- CIDRAP
- UK HPA
- ProMED
- GPHIN
- PacNET





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What to include

Scope

- Major events
- Commonwealth countries

Inclusion criteria

- Outbreaks and higher than normal incidence
- Likelihood of affected population travelling
- Likelihood of ongoing transmission

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Report structure

- Incident Title
- Date of update
- Date first reported or first aware
- Disease
- Affected source populations
- Case numbers
- Commonwealth country affected?
- Countries/regions/areas affected
- Source of information/data
- Description

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Report dissemination

- Internal staff
- Key epidemiologists in QLD Health
- Public health units in QLD
- Health section of Commonwealth Games organisers
- National Incident Room
- Commonwealth Department of Health sport area

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Key lessons

- Great opportunity
- Coordination
- Coverage
- A lot more commonwealth countries than we knew about
- Beneficial to work as a team

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