Applied Epidemiology in Australia

BRIGITTA OSTERBERGER

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Communicable Disease Epidemiology and
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Field supervisors:
Ms Anna-Jane Glynn-Robinson
Mr Timothy Sloan-Gardner

Academic supervisors:
Professor Martyn Kirk
Dr Benjamin Polkinghorne

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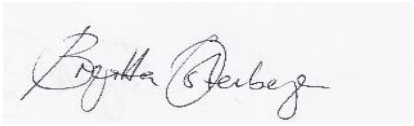
ORIGINALITY STATEMENT

'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 is explicitly acknowledged in the thesis. I also declare that the intellectual content of this thesis is 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'.



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involved for the successful surveillance of a mass gathering but also what effective communication, interpersonal and leadership skills entail. I am truly grateful for this experience and thankful to the Gold Coast PHU staff and Ross Andrews for making it happen.

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ABSTRACT

My field placement for Master of Philosophy in Applied Epidemiology (MAE) program was within the Communicable Disease Epidemiology and Surveillance Section in the Office of Health Protection at the Australian Government Department of Health. I present the four projects I completed for the MAE program:

For my epidemiological study I described the national trend in *Salmonella* spp. infection in Australia from 1 July 2008 through 30 June 2017 by financial year using Joinpoint regression analysis.

I conducted a descriptive review of investigated foodborne and probable foodborne outbreaks where food was prepared in restaurants, take-away (non-franchised), commercial caterers, bakeries, national franchised fast food restaurants, fairs/festivals/mobile services in Australia between 2001 and 2016. This study involved analysis of routinely collected data of foodborne outbreaks from enhanced surveillance undertaken by OzFoodNet. The outcomes of the study provide the evidence the food service industry has been seeking regarding which types of food service businesses, food vehicles and etiological agents are associated with foodborne outbreaks in the Australian food service industry.

I participated in the investigation of two foodborne outbreaks which occurred in the same hotel restaurant within a week of each other in the Australian Capital Territory, Australia. They were caused by two different *Salmonella* Typhimurium multi-locus variable analysis (MLVA) profiles, one of which had not been seen in Australia before or since the outbreak. Whole-genome sequencing was undertaken that showed that the MLVA profiles were also genomically unrelated. Although a common food vehicle was not identified it was clear that the restaurant was the source of infection, possibly caused by cross-contamination in the facility kitchen. The findings of the investigation demonstrate why the public health control of human salmonellosis is particularly

challenging and highlights the importance of ensuring food safety through improved food-handling practices by food service businesses.

I evaluated the National Human Rabies Immunoglobulin Database (NHRID), a centralised surveillance system that monitors human rabies immunoglobulin usage in Australia. My evaluation found that the NHRID does not meet its objectives and requires a complete redevelopment of the data fields and the data collection tool.

This thesis documents my MAE experience, presents four projects to fulfil the core requirements of the program, and the public health impact my work has made.

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ABBREVIATIONS

AAPC	Average Annual Percentage Change
ABLV	Australian bat lyssavirus
ACT	Australian Capital Territory
ACTGAL	ACT Government Analytical Laboratory
ANU	Australian National University
APC	Annual Percentage Change
CDC	Centers for Disease Control and Prevention
CDESS	Communicable Diseases Epidemiology Surveillance Section
CDNA	Communicable Diseases Network Australia
CIDT	culture-independent diagnostic test
ECDC	European Centre for Disease Prevention and Control
EHO	Environmental Health Officer
EU	European Union
HRIg	human rabies immunoglobulin
ICPMR	Institute for Clinical Pathology and Medical Research
MAE	Master of Philosophy in Applied Epidemiology program
MBS	Medical Benefits Schedule
MDU PHL	Microbiological Diagnostic Unit Public Health Laboratory
MLVA	Multiple-Locus Variable number tandem repeat Analysis
NHRID	National Human Rabies Immunoglobulin Database
NNDSS	National Notifiable Diseases Surveillance System
NSW	New South Wales

NT	Northern Territory
OHP	Office of Health Protection
PEP	post-exposure prophylaxis
QLD	Queensland
SA	South Australia
SNP	single nucleotide polymorphism
TAS	Tasmania
UK	United Kingdom
US	United States
VIC	Victoria
WA	Western Australia
WGS	whole genome sequencing
WHO	World Health Organization

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CHAPTER 1 –
INTRODUCTION TO PLACEMENT AND SUMMARY OF PUBLIC HEALTH EXPERIENCE

Description of the field placement

Introduction

I began my field placement for the Master of Philosophy in Applied Epidemiology Program (MAE) on 7 March 2016, in the Australian Government Department of Health, Office of Health Protection (OHP), Health Protection Policy Branch (HPPB), in the Zoonoses, Foodborne and Emerging Infectious Diseases section (ZoFE), located in Canberra, Australia. I was particularly excited about being involved in projects relating specifically to emerging infectious and foodborne diseases.

In this chapter I provide a brief outline of my field placement, describe my experiences in the MAE program, and summarise my projects which were completed to demonstrate a range of competencies in applied epidemiology.

Summary of field placement

The mission of OHP is "to protect the health of the Australian community through effective national leadership and coordination and building of appropriate capacity and capability to detect, prevent and respond to threats to public health and safety".[1] In 2017, the OHP underwent a Division-wide restructure and ZoFE amalgamated with the Vaccine Preventable Diseases Section to become the Communicable Diseases Epidemiology Surveillance Section (CDESS). The CDESS is responsible for the management of the National Notifiable Diseases Surveillance System (NNDSS) and national surveillance, analysis and reporting on all nationally notifiable diseases and other communicable disease. This includes management of Australia's enhanced foodborne disease surveillance system network, OzFoodNet, and liaison with Food Safety Australia New Zealand on current and emerging food safety issues.[2] Additional responsibilities include:

- Providing surveillance advice to inform policy and response activities;
- Liaising with other commonwealth and state and territory government agencies in response to national outbreaks and current and emerging communicable disease issues;

- Managing policy and projects regarding surveillance for Creutzfeldt-Jakob disease;[2]
- Managing, coordinating and monitoring the use of rabies immunoglobulin coordinating policy and program management of antivenoms;[2]
- Meeting international reporting requirements, such as providing disease statistics to the World Health Organization (WHO) under the International Health Regulations (2005)[3]; and
- Supporting quarantine activities conducted by the Australian Government.[3]

Between 2016 and 2018, my involvement in the routine activities in my placement included:

- Editing articles submitted to be published in *Communicable Diseases Intelligence*;
- Working on a summary comparison document between the original and revised Avian Influenza Series of National Guidelines (SoNG) for public health units;
- Monitoring sources such as ProMed and government websites or UN agency websites to write the International Report for the Communicable Diseases Network Australia (CDNA);
- Participating in fortnightly meetings with epidemiologists to monitor communicable diseases data;
- Chairing the section meeting on a rotational basis;
- Attending the CDNA meetings (face-to-face or teleconference);
- Researching literature to respond to a range of questions and providing a list of citations in relation to the definition of 'elderly' in an Australian and foodborne disease context;
- Volunteering as a Watch Officer, in the Health Emergency Management Branch (HEMB) within OHP, acting as the first point of contact for the National Incident Room and World Health Organization's National Focal Point for Australia;
- Attending a Risk Assessment Team meeting in response to Ebola cases overseas and working through the Assessment form to evaluate the risk to Australia; and

- Attending and taking minutes for OzFoodNet routine and multijurisdictional outbreak investigation teleconferences.

Public health experience

I was very fortunate with the diverse public health experiences afforded to me. I worked at both the local and national level, giving me a very broad experience in public health and an understanding of the different components of the surveillance and control of communicable disease.

National response to communicable diseases of public health concern

Throughout my MAE, I had the opportunity to be involved in a variety of ways in the national surveillance and in the national outbreak response to disease such as Zika virus infection in 2016 and multiple multijurisdictional foodborne-related outbreaks.

Zika virus infection surveillance, 2016

I immediately started work on my first project, the enhanced surveillance of Zika virus infection when I commenced my placement, which was an emerging public health concern in 2016. As part of my project, I drafted a comprehensive list of all proposed fields for enhanced surveillance for confirmed and probable cases of Zika virus infection. These data were to be collected via a nationally collated database separate to the NNDSS. I provided a spreadsheet of a draft list of all the possible fields for which data could be collected by States/Territories when interviewing confirmed/probable Zika virus cases. I sourced these fields from the Queensland Department of Health's Zika Virus Case Report Form and a case report form used by the Australian Paediatric Surveillance Unit at the Kids Research Institute to collate data on rare childhood diseases (e.g. Acute Flaccid Paralysis Initial Questionnaire). Within the spreadsheet, fields were listed under Field Groupings with additional information to be collected for the specific field listed in the Comments section. Colour coding was used to identify information to be collected at the different levels (jurisdictions, National). The jurisdictions were to be the primary source of data collection and provide the data for the specific fields of interest to the Australian Government Department of Health. I

wrote an agenda paper asking the CDNA Zika virus working group for input and expertise to refine and identify the key fields most useful for Zika virus surveillance by the jurisdictions and Zika virus infection surveillance data collected by the jurisdictions that could be sent to the Australian Government Department of Health for national surveillance. The list was discussed at a teleconference where I presented the data fields. Unfortunately this project did not come to fruition as the scope of the project was reduced to the point that it wasn't a viable project to fulfil the program requirements.

Besides this project, I was also involved in the following routine activities relating to the national Zika virus infection surveillance:

- Making contributions to the daily Zika Epidemiological Updates;
- Updates on Zika virus rumour surveillance using World Health Organization data and publications;
- Reviewing peer-reviewed literature on a weekly basis to maintain an annotated bibliography of Zika virus infection -related publications (Zika virus infection evidence) and disseminating it to internal and external stakeholders;
- Assisting in public health messaging by updating Zika virus fact sheets, made available on the Australian Government Department of Health's website (see Supporting Information for the URLs);
- Managing the correspondence with jurisdictions and collation of responses to CDNA out of sessions items in relation to issues such as Zika virus in pregnant women and updating the advice on sexual transmission of Zika virus.
- Organising a teleconference for the CDNA Zika virus working group and Zika virus SoNG working group to discuss sexual transmission guidelines for Zika virus. This involved writing the agenda paper, preparing documents to be discussed, and writing and disseminating minutes.

Multijurisdictional foodborne outbreaks

Besides taking minutes during the multijurisdictional foodborne outbreak teleconferences, I assisted in public health messaging. In February 2018 during a multijurisdictional outbreak of Listeria monocytogenes infection caused by the consumption of contaminated rockmelon, I drafted a Listeria fact sheet under

outbreak conditions that was published on the Australian Government Department of Health's website (Supporting Information – Listeria fact sheet).

Jurisdictional communicable disease response and control

Aside from working at the Australian Government Department of Health, I also had the opportunity to work in communicable disease response and control at the local level in the in the Communicable Disease Control Section (CDC) at the Australian Capital Territory Department of Health (ACT Health). The CDC's primary function is the minimisation of harm due to the spread of communicable diseases in the ACT through disease surveillance, infection control and coordination of the ACT Immunisation Program.[4] The work I undertook included conducting follow-up investigations, which included undertaking food histories as part of the routine surveillance of notifiable diseases in the ACT, such as *Salmonella*, Dengue and Gonorrhoea.

It is also here that I completed my outbreak investigation component of the core program requirements of the MAE (Supporting Information – Structured questionnaire). I wrote this investigation as an advanced draft of a paper for publication in Chapter 4 of this thesis. I also presented this investigation at the Communicable Diseases Control Conference in Melbourne in June 2017 (Supporting Information – Short Presentation).

Other public health experience and training

In addition, to my projects and routine placement activities, there were numerous highlights during my MAE experience:

Mass surveillance of the 2018 Commonwealth Games, Gold Coast, Australia

The MAE program gave me the invaluable opportunity of assisting the Gold Coast Public Health Unit (GCPHU) with the mass surveillance of the 2018 Commonwealth Games. In April 2018, the Gold Coast hosted the 21st Commonwealth Games, a big multi-sport event, with competitors from 53 Commonwealth nations.[5] It was the fifth time Australia staged the Commonwealth Games and the first time it was held in a regional Australian city.[5] My experience at the GCPHU was varied and provided numerous learning opportunities:

I was the Support Officer in the Emergency Operating Centre and my responsibilities included:

- Taking minutes for meetings and logging activities and decisions,
- Preparing documents for meetings,
- Working with the Duty Officer to maintain the Incident log,
- Liaising with the Sector Commander, Public Health Medical Officer, Epidemiology team and Environment Health team/ leaders for the collation and dissemination of the Ministerial Daily Dot Points and the Situation Report.

As the Support Officer, I was able to attend a number of meetings and observe how information was used to inform real-time decision-making. In this role, I was required to build relationships with members from different teams and work under pressure whilst being adaptable and flexible. I also had to quickly learn new systems and processes. This was however easily achieved through the support and guidance of the generous GCPHU staff.

I accompanied Environmental Health Officers (EHO) to drop off faecal sample kits and collect food samples. I learnt how complicated it can be to determine the origins of food products. I also learnt how to use Open Office, a data management system used by the Environmental Health team for the collection of data on the samples taken by EHOs and their results, and assisted with regular data entry. I observed the different types of tests that are requested for the testing of water, foodborne pathogens or chemical testing to determine gluten presence; and what the lab results look like. This experience provided an insight to how Environmental Health works in practice. I was also given the opportunity to gain experience in undertaking three day food history and entering the data into EpiInfo.

It was a great experience being able to play an active role in the mass surveillance of the 2018 Commonwealth Games.

Australia's Joint External Evaluation (JEE) mission

I attended Australia's Joint External Evaluation (JEE) mission in late 2017 in Canberra. Australia's capacity to "prevent, detect and rapidly respond to public health threats of a natural, deliberate or accidental nature" was evaluated against the International Health Regulations (IHR) 2005. It was fascinating to listen to discussions of key issues by subject matter experts from across Australia and hear Australia's strengths acknowledged and recommendations and priority actions discussed during the JEE. It was an invaluable learning experience and networking opportunity.

Global Outbreak Alert and Response Network (GOARN) workshop

As part of the MAE program I was able to participate in a two-day Global Outbreak Alert and Response Network (GOARN) workshop held at the Australian National University. This training gave me an insight into the different qualities that make an effective epidemiologist in the field. These include interpersonal and cultural sensitivity skills, self-awareness, showing empathy, putting the needs of the team first, coping with the pressure of the disaster situation you are working in and identifying the signs when you need to remove yourself from the field.

Reflections on my MAE journey

Through my projects and my public health experiences, I gained a comprehensive insight of how different activities and processes at the local, jurisdictional and national level interrelate to assist in the control of communicable disease, in particular *Salmonella* spp. Fig 1 is a visual summary of my projects and experiences.

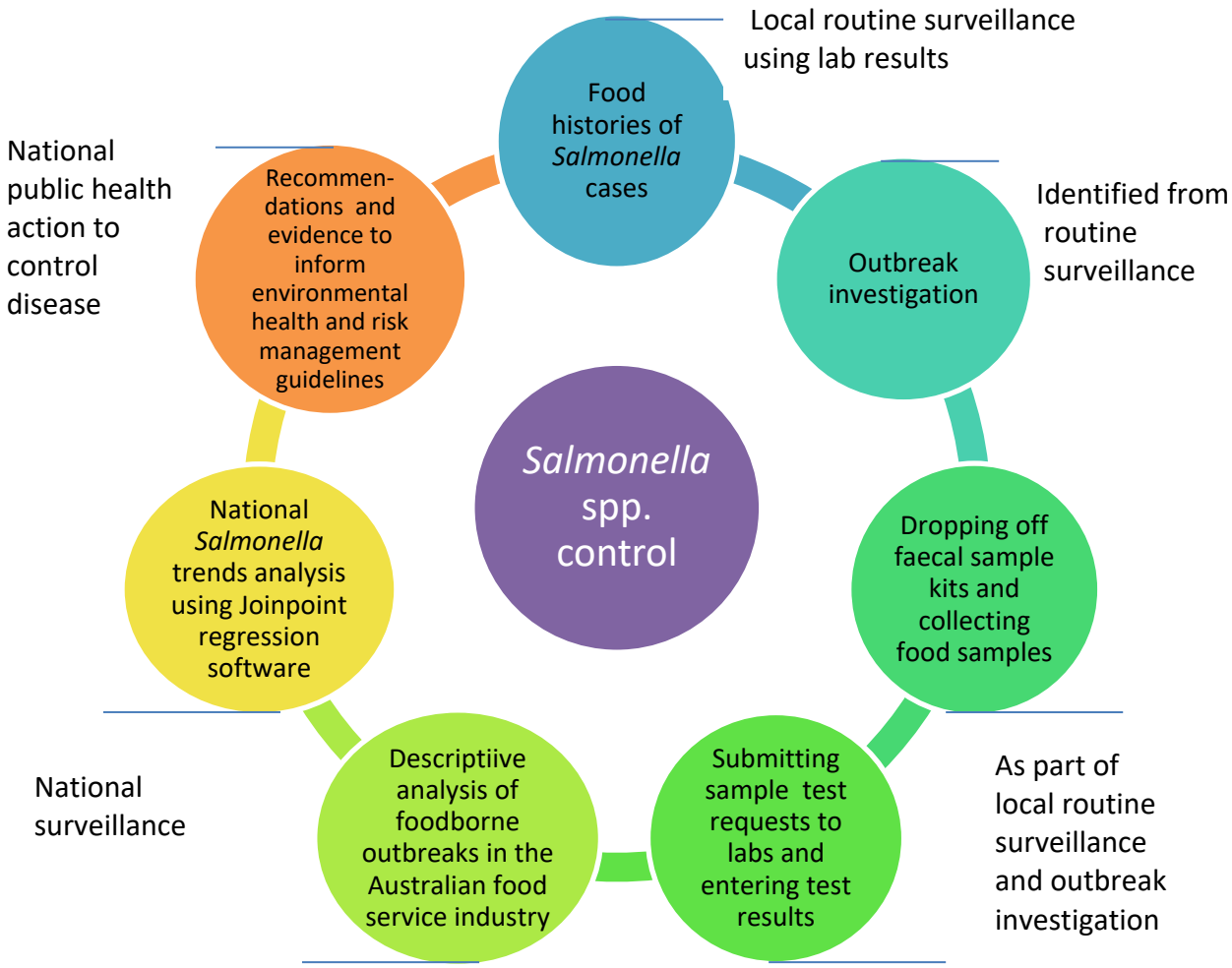

Fig 1. Full circle of my public health experiences relating to *Salmonella* spp control

The major themes I identified during my MAE journey:

1. Collaboration and cooperation

No person, section, branch or department can work in a silo in the control of disease. Throughout my MAE I observed how tasks and actions required the collaboration between teams, for example epidemiologists and environmental health officers; between sections in OHP for example CDESS and Emergency, Preparedness and Response in response to Zika virus infection and Ebola virus outbreaks overseas; and between government departments such as the collaboration between the commonwealth health department and the jurisdictional health departments.

Although each stakeholder has their own priorities, they all have the same goals. The key to working towards a common desired outcome is collaboration and cooperation.

2. Resilience and Perseverance

The working life of an epidemiologist can be a difficult balance between fulfilling your day-to-day work requirements as well as managing competing priorities often under restrictions such as limited resources and time. In addition, the control of disease is a collaborative process which requires the cooperation between stakeholders. This is often a challenging and long process. Resilience to deal with change and persistence in spite of adversity is a skill that will stand me in good stead as I pursue a career as an epidemiologist.

In summary, my MAE journey was a roller coaster of experiences. During my MAE, I had two changes in field supervisors and my placement went through a restructure. I also took leave due to ill health and maternity leave and worked part-time for a period. These added an element of difficulty to my MAE experience. Furthermore, each project presented with its own challenges. However perseverance paid off in so many ways. The MAE provided rigorous training in epidemiology, hands-on experience, networking opportunities (both domestic and internationally) through the MAE network and with subject matter experts. I am grateful for this life changing experience, both in terms of professional and personal growth. I look forward to "leaving my footprint" as an epidemiologist in the future.

Summary of core program requirements

To satisfy the requirements the MAE program, besides the four projects, additional prerequisites include a teaching session; writing a communication for a lay audience; a lesson from the field and a presentation at a national or international conference. The fulfilment of these requirements and in which chapter they can be found are summarised below:

Summary of Core Competencies

MAE Competency	Chapter 1 - Introduction to field placement and summary of experience	Chapter 2 - *Salmonella* trends in Australia	Chapter 3 - Foodborne outbreaks in the Australian food service industry	Chapter 4 - Outbreaks of multiple *Salmonella* Typhimurium MLVA profiles at a hotel restaurant	Chapter 5 - Evaluation of the National Human Rabies Immunoglobulin Database	Chapter 6 - Teaching Experience
Investigate an acute public health problem				✓		
Evaluate a surveillance system					✓	
Analyse a public health dataset			✓			
Design and conduct an epidemiological study		✓				
Literature review		✓	✓	✓	✓	
Communication for a lay audience	✓					
Late draft of a manuscript for publication		✓	✓	✓		
Oral presentation at a scientific conference				✓		
Lessons from the Field						✓

References

1. Department of Health website (accessed 7 March 2016); Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-about.htm
2. Department of Health intranet website (accessed 7 March 2016); Available from:http://www.health.gov.au/internet/main/publishing.nsf/content/ohp-about.htm
3. Department of Health intranet website. Communicable Disease Epidemiology and Surveillance Section 2018 [accessed 23 May 2018]; Available from: http://sharepoint.central.health/divisions/OHP/teams/zofe/SitePages/Home.aspx.
4. ACT Health website [accessed 17 May 2018]; Available from: Communicable Disease Control. http://www.health.act.gov.au/public-information/public-health/communicable-diseases
5. Gold Coast Commonwealth Games 2018 website [accessed 17 May 2018]; Available from: https://www.gc2018.com/

Supporting Information

Zika virus fact sheets

- Zika virus Factsheet – The Basics
  http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-factsheet-basics.htm
- Zika virus – information for clinicians and public health practitioners
  http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-health-practitioners.htm
- Zika virus – information for pregnant women
  http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-fs-pregnant-info.htm
- Information for Travellers about Zika virus testing
  http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-testing.htm
- Interim recommendations for assessment of pregnant women with potential exposure to Zika virus
  http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-pregnant.htm

Listeria fact sheet

This fact sheet on Listeria is located online:

http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-listeria-

Listeria Fact Sheet

Page last updated: 27 February 2018

What is Listeriosis

Listeriosis, is a rare but serious disease caused by the bacteria *Listeria monocytogenes (L. monocytogenes)* that can survive and grow on certain high risk foods. While it is probably common for people to eat foods contaminated with a small amount of the bacteria, only some people are at risk of becoming sick. The people who do get sick may require hospitalisation and it may lead to death.

What are the symptoms?

Listeriosis can cause different symptoms depending on which part of the body has been affected and the usual health of the person. Symptoms can include fever, muscle aches, and sometimes nausea and diarrhoea. Infection with *L. monocytogenes* may also cause septicaemia (blood poisoning) and meningitis (inflammation of the outside of the brain), and death can occur because of these complications.

Pregnant women generally experience mild symptoms themselves; however infections during the pregnancy can lead to miscarriage, stillbirth or infection of the newborn baby.

Symptoms usually start between 3 to 70 days (average 21 days) after eating food contaminated with the bacteria.

How is it spread?

L. monocytogenes is commonly found in the environment (such as soil) and some raw foods. Unlike many other bacteria, *L. monocytogenes* are unusual because they can grow in the refrigerator. Eating foods that contain *L. monocytogenes* does not cause illness in most people however some can become sick. Babies can be born with listeriosis if their mothers eat contaminated food during the pregnancy.

Listeriosis does not spread from person-to-person.

Who is at risk?

Eating foods that contain *L. monocytogenes* does not cause illness in most people. The disease mainly affects the elderly, pregnant women and their unborn and newborn babies, and people with weakened immune systems due to illness or medication (for example, people on cancer treatment or steroids, and people with diabetes, kidney disease, liver disease and HIV infection).

How is it prevented?

Listeriosis can be prevented by avoiding high risk foods and handling food safely.

Avoid high risk foods:

- pre-prepared and pre-packed fruit and vegetable including coleslaw, fresh fruit salad and pre-cut melons
- unwashed fresh fruits (including melons) and vegetables, and drinks made from fresh fruit or vegetables where washing procedures are unknown (excluding canned or pasteurised juices)
- pre-cooked cold chicken
- cold delicatessen meats
- paté
- raw or undercooked meat, chicken or seafood
- soft cheeses such as brie, camembert, ricotta or blue-vein (unless cooked and served hot)
- sprouted seeds and raw mushrooms
- ready-to-eat seafood and smoked seafood (for example, smoked salmon)
- pre-prepared sandwiches, wraps and sushi that contain any of the meats, salads or cheeses mentioned above
- unpasteurised milk or milk products
- soft serve ice creams

Handle and store food safely:

- thoroughly cook raw meat, chicken and seafood
- wash raw vegetables and fruit thoroughly before cutting or eating
- keep raw meat, chicken and seafood separate from all other foods
- use separate knives and cutting boards for different foods - raw meat, unwashed vegetables and ready to eat foods
- wash your hands before, during and after preparing food, going to the toilet, or after handling animals

- wash knives and cutting boards well after preparing uncooked foods
- eat cooked food as soon as possible

The NSW Food Authority provides further information on foods to eat and avoid during pregnancy.

How is it diagnosed?

The diagnosis of listeriosis can be confirmed by blood or other tests requested by a doctor.

How is it treated?

Treatment for listeriosis involves antibiotics and supportive care. When infection occurs during pregnancy, antibiotics can often prevent infection of the unborn baby or newborn.

Listeria in Australia

While listeriosis can be a very severe illness, the number of cases reported in Australia each year is relatively low, with around 80 cases reported each year. Most people infected with listeriosis are not connected to an outbreak, however outbreaks can occur. Outbreaks caused by listeriosis have been associated with delicatessen meats, raw milk, soft cheeses, pre-prepared salads (for example, from salad bars), unwashed raw vegetables, paté, cold diced chicken and pre-cut fruit and fruit salad.

Preventing the spread of listeria in Australia

Listeriosis is mainly acquired by eating contaminated foods. Food safety standards in Australia are designed to minimise the contamination of food with bacteria including *L. monocytogenes.* It is difficult to completely remove the risk as this bacteria is so widespread in the environment. Cases of listeriosis are reported to public health authorities so outbreaks can be identified and managed, and particular causes detected.

Further Information

Talk to your doctor about preventing listeriosis if you are pregnant or if you think you might be at increased risk due to illness or medications.

More information on listeriosis can also be found by contacting your state or territory health department.

Structured questionnaire for the outbreak investigation

SUSPECTED EVENT OUTBREAK

Respondent number:	Illness status: ☐ Sick ☐ well

EVENT DETAILS

CALL INTRODUCTION

Hi, my name is…… and I'm calling from ACT Health. How are you today?

We are currently investigating an increase in the number of gastroenteritis infections in the community and we are trying to find the potential source for this infection. We are interested if you attended [redacted] on Saturday 14 May 2016 .

The information you provide is kept confidential and identifying information will not be disclosed for any other purpose without your consent.

Do you have time today to speak with me? ☐ Y ☐ N (if no, reschedule)

Interviewer Initials:

Date & time Interviewed?

1	☐
2	☐
3	☐
4	☐
5	☐
6	☐

Person interviewed (if not case):

Call back notes:

☐ *Interpreter used*
☐ *lost to follow up*
☐ *refused interview*

SECTION 1: CASE DETAILS

First Name:	Last Name:	Parent's Name (if applicable):
DOB: Age:	Gender: ☐M ☐F	
Address:	Home Phone:	
	Mobile Phone:	
	Email:	

SECTION 2: EVENT DETAILS

Our first point of call is those who attended [redacted] on Saturday 14 May 2016. Did you attend?

☐ Yes

☐ No - please skip to SECTION 4

Who did you go with?

Name & relation	Contact details

What time did you attend? _____ AM / PM

SECTION 3: What did you eat while you were there?

Canapes	*Food eaten by respondent?*	*Extra Details:*
scallops	☐Y ☐N ☐ DK	
Mini quiches	☐Y ☐N ☐ DK	
Spring rolls	☐Y ☐N ☐ DK	
Samosas	☐Y ☐N ☐ DK	
Entree	*Food eaten by respondent ?*	*Extra Details:*
Butter pumpkin and sage soup with parmesan crouton	☐Y ☐N ☐ DK	
Spinach and ricotta raviolo with creamy sage sauce	☐Y ☐N ☐ DK	
Main		
Salmon fillet with cannellini bean puree and caper and dill lemon dressing	☐Y ☐ N ☐ DK	
Eye fillet potato gratin vine tomato and garlic serve with red wine jus	☐Y ☐N ☐ DK	
Desert		
Chocolate tart and chantilly and strawberry	☐ Y ☐ N ☐ DK	
Sticky date pudding and butter scotch sauce	☐ Y ☐ N ☐ DK	
_____ cake	☐ Y ☐ N ☐ DK	
Drinks		
Alcoholic drinks (beer/wine/cider)	☐Y ☐N ☐ DK	Type:
Soft drinks	☐Y ☐N ☐ DK	Type:
Water	☐Y ☐N ☐ DK	
Other	☐Y ☐N ☐ DK	If yes specify.

Did you eat bread with butter?
Did you eat any other food item(s) _____ not included on the list? ☐Y ☐N ☐ DK

If yes, specify:_____

SECTION 4: OTHER COMMERCIAL VENUES	
Did you eat out at any other commercial venues in Canberra that weekend?	☐Y ☐N ☐ DK
If yes:	Where: _____ Date: _____ Time:_____ What did you eat?
If yes:	Where: _____

Short presentation, Communicable Diseases Control Conference, Melbourne, 28 June 2017

A two cohort, two strain and one food premises *Salmonella* outbreak study

Brigitta Osterberger[1 3], Samuel McEwen[2 3], Laura Ford[2 3]

1. Office of Health Protection, Department of Health, Woden, Australian Capital Territory.
2. Health Protection Service, Population Health, ACT Health, Australian Capital Territory.
3. National Centre for Epidemiology & Population Health, Research School of Population Health, ANU College of Medicine, Biology & Environment, Australian National University, Australian Capital Territory.

ACT Government

Australian Government
Department of Health

Australian National University

Multiple confirmed salmonellosis cases ill after dining on different days and attending different events at same hotel restaurant in Canberra

Outbreak investigation launched:
23 May 2016

Two retrospective cohort studies → **Event A:** 8 May 2016
Event B: 14 May 2016

- **Probable case:** Diarrhoea (≥24 hours) within five days of attending Event A or Event B at hotel restaurant
- **Confirmed case:** Lab-confirmed *Salmonella* infection
- Active case finding, telephone interviews using a standardized questionnaire and environmental investigation commenced
- **MLVA and WGS** of *Salmonella* isolates

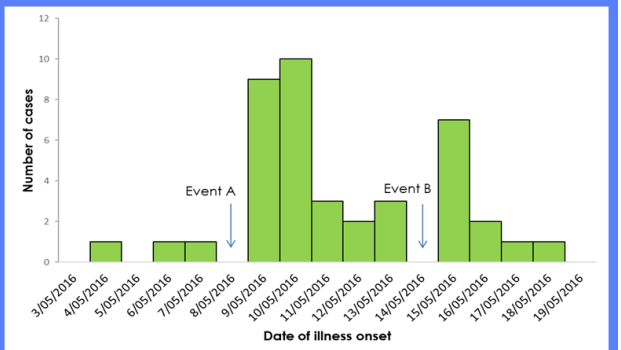

Figure 1: Epidemiological curve of persons ill with gastroenteritis by onset day and event after dining at a hotel restaurant in Canberra, 4 May to 18 May 2016 (n=41)

Findings:

- Multiple gastroenteritis cases caused by **two different *S.* Typhimurium MLVA profiles**
- Uncommon MLVA pattern in Australia: ***S.* Typhimurium (MLVA 03-12-18-14-523)**
- *S.* Typhimurium (MLVA 03-10-14-11-7-496) is a common phage-type
- Two MLVA profiles approx. **90 single nucleotide polymorphisms** apart
- Environmental swabs and food specimens ***Salmonella*-negative.**
- **Salmon sandwiches** significantly associated with illness (RR 4.64, 95% CI1.19-18.1) for Event A

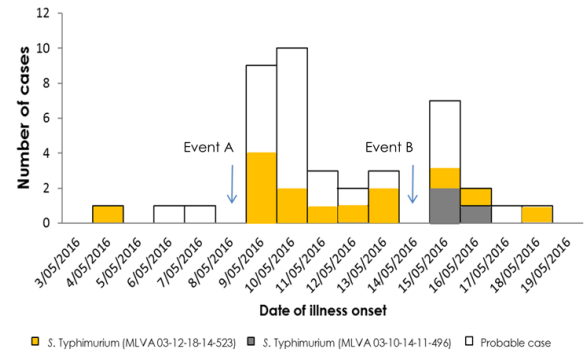

Figure 2: Epidemic curve of attendees ill with gastroenteritis after eating at the hotel restaurant, by MLVA profile, 4 May to 18 May 2016, Canberra, n=41

Conclusions and recommendations: effective food safety measures to control cross-contamination is key

- To our knowledge, this is the **first outbreak** by this uncommon MLVA pattern reported in Australia
- **Cross-contamination** is the most plausible cause of the outbreak
- This outbreak appears typical of food(s) that were available over several days
- MLVA typing identified **2 distinct MLVA patterns** of a common *Salmonella* serotype
- WGS clarified that **the 2 strains are not closely related**
- **Unusual** to see 2 **distinct** MLVA patterns in the one venue
- WGS **complements epidemiological investigations** and improves the **monitoring** of uncommon and persistent *S.* Typhimurium MLVA types

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CHAPTER 2 –
HUMAN *SALMONELLA* TRENDS IN AUSTRALIA, 2008-2017

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Prologue

In Australia, non-typhoidal *Salmonella* spp. infections are one of the most common causes of foodborne gastroenteritis. They are one of the leading causes of hospitalisation and deaths due to foodborne disease in Australia, particularly *Salmonella enterica* serovar Typhimurium (*S*. Typhimurium).[1 2 3]

This study was conducted to analyse national surveillance data for *S.* Typhimurium and non-Typhimurium *Salmonella* serovars from 1 July 2008 through 30 June 2017 by financial year using two different statistical approaches, each with specific advantages. Negative binomial regression analysis was used to assess a change in notification trend over time and the Joinpoint Regression Analysis program was used to determine whether there were any statistically significant changes in trend during the study period. These methods were used to answer three key questions: 1) does analysing *Salmonella* surveillance data by financial year rather than by calendar year give a clearer picture of *Salmonella* incidence, 2) are *Salmonella* notifications increasing or decreasing in Australia, and 3) are any changes in reported incidence of *Salmonella* infection explained by changes in laboratory testing practices. This study has high public health importance with the control of salmonellosis continuing to be a substantial public health and food safety problem in Australia.

My role

I conducted the following tasks as part of this project:

- Developed the research proposal;
- Cleaned and analysed the dataset using Microsoft Excel, Stata and Joinpoint Regression Analysis program;
- Conducted a literature review; and
- Prepared an advanced draft of a paper for publication in a national or international peer-reviewed journal.

Lessons learnt

For this project, I had the opportunity to do something innovative, both in terms of the statistical analysis using financial year as the period. I learnt how to use the National Cancer Institute's Joinpoint Regression Analysis program. This project highlighted that

data can be analysed in many ways, such as by calendar year or financial year, which may provide different results. It is important to analyse data within the context of the disease under investigation. Furthermore, using alternative tools such as Joinpoint regression analysis program to identify statistically significant changes in trend can highlight any changes in trend and if these coincide with potential events that may have influenced the epidemiology of communicable diseases during a study period.

Public health implications of this work

Before this study, *Salmonella* notifications were analysed by calendar year, which did not take into account the peak incidence of *Salmonella* in summer. Therefore, *Salmonella* incidence reporting did not provide a true indication of *Salmonella* incidence in Australia. A simple change from calendar year to financial year shows that it is much more sensible to analyse *Salmonella* data by financial year, which takes into account that the main season of this disease crosses two calendar years. This approach may be useful for other communicable diseases of public health importance, particularly gastrointestinal disease caused by enteric pathogens that also display a peak incidence in the summer season crossing two calendar years.

In this study, I used a novel regression technique developed for cancer surveillance and applied it to *Salmonella* infections in Australia. This statistical methodology describes changing trends over sequential time segments and defines the amount of change (increase or decrease) within each period of time. This type of analysis is useful to determine if and when a statistically significant change in trend has occurred and if changes can be attributed to events such as change in testing practices or regulatory change. This method would be useful for the surveillance of other communicable diseases to determine if an observed decrease coincides with the implementation of public health messaging, targeted public health interventions or regulatory change.

Master of Philosophy (Applied Epidemiology) core activity requirement

- Conduct and interpret an epidemiological study;
- Literature review that demonstrates skills in conducting a targeted literature search and synthesis; and
- Preparation of an advanced draft of a paper for publication in a national or international peer-reviewed journal.

Advanced draft of paper for publication

Human *Salmonella* infections in Australia: a novel approach to *Salmonella* surveillance data analysis, 2008-2017

Brigitta Osterberger[1, 2], Benjamin Polkinghorne[1], Anna-Jane Glynn-Robinson[2] and Martyn Kirk[1]

[1] National Centre for Epidemiology and Population Health, Research School of Population Health, ANU College of Health and Medicine, Australian National University.

[2] Communicable Diseases Epidemiology and Surveillance Section, Office of Health Protection, Australian Government Department of Health.

Corresponding author:

Mrs Brigitta Osterberger

Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
Phone: 02 6232 8985
Email: Brigitta.Osterberger@health.gov.au

Abstract

Introduction: *Salmonella* is one of the leading causes of foodborne gastrointestinal illness in Australia. *Salmonella enterica* serovar Typhimurium (*S*. Typhimurium) is the most commonly reported serovar of *Salmonella* cases and has been displaying an increasing trend nationally.

Methods: We conducted a retrospective epidemiological study using negative binomial regression and Joinpoint regression analysis to analyse national *Salmonella* surveillance data by financial year for 2008/09 to 2016/17, for *S.*Typhimurium and non-Typhimurium *Salmonella* serovars. Incidence rate ratios, adjusted for age and sex to show trends over time, were estimated and statistically significant changes in trend investigated. Estimated resident population data were obtained from the Australian Bureau of Statistics to calculate crude, age and sex-specific and age-standardised rates. Medicare Australia Statistics pathology data was used as the denominator in an alternative analysis to assess the potential impact of changes to laboratory diagnostic practices on *Salmonella* notifications.

Results: A total of 114,751 *Salmonella* infection notifications with serovar, age, and sex information were recorded in Australia between 2008/09 and 2016/17. Overall, *S*. Typhimurium (IRR 1.03, 95% CI 1.02–1.03) and non-Typhimurium *Salmonella* (IRR 1.06, 95% CI 1.06–1.07) infections showed signicant increases in trend. New South Wales (NSW) was the only jurisdiction that showed a decrease in *S*. Typhimurium notification trend (IRR 0.99, 95% CI 0.98-1.01). Analysis of *Salmonella* notifications by financial year showed a clearer pattern compared to analyses by calendar year. Joinpoint regression analysis identified changes in *S*. Typhimurium notification trend by jurisdiction: Victoria (VIC) and Northern Territory in 2010/11 and Queensland (QLD) in 2014/15. Western Australia (WA) was the only jurisdiction to show two changes trend for both *S*. Typhimurium (2010/11 and 2013/14) and non-Typhimurium *Salmonella* (2010/11 and 2014/15).

Conclusion: Our results suggest that the use of culture independent diagnostic tests is having an impact on the public health surveillance of *Salmonella* in NSW, QLD and WA while improved regulation of food safety for eggs and egg products may have contributed to a change in trend in VIC and WA. Our study highlights the use of a novel methodological approach to *Salmonella* surveillance data analysis by identifying

statistically significant changes in trend and the potential impact changes to laboratory diagnostic practices is having on *Salmonella* notifications in Australia. The use of these methods provides an improvement on current traditional surveillance methods.

Keywords: public health surveillance, culture independent diagnostic tests, *Salmonella* Typhimurium, financial year, Australia, Joinpoint regression, faecal culture tests

Introduction

Human non-typhoidal *Salmonella* infections are a global public health problem resulting in considerable burden of disease.[4] In Australia, circa 2010, non-typhoidal *Salmonella* spp. infections were one of the most common causes of foodborne gastroenteritis and one of the leading causes of hospitalisation and deaths due to foodborne disease.[1,4] *S.* Typhimurium is the most frequently notified *Salmonella* serovar in Australia[1 2, 3], accounting for nearly 44% of notifications between 2000 and 2013.[1]

Salmonella infections display a strongly seasonal pattern in Australia[5, 6], with the highest rates of infection in warmer months.[7-9] *Salmonella* replicates faster in higher temperatures, increasing the contamination risk throughout the farm-to-table chain[6] and subsequently leading to increased incidence of salmonellosis.

Since 2016, national surveillance figures derived from the National Notifiable Diseases Surveillance System (NNDSS) suggested that the incidence of *S.* Typhimurium infections was decreasing nationally, despite jurisdictions such as Western Australia (WA) and Australian Capital Territory (ACT) reporting increases in *S.* Typhimurium notifications. The NNDSS is a surveillance system managed by The Australian Government Department of Health (DoH). It is a passive surveillance system that collects data on 52 notifiable communicable diseases or disease groups at the national level. These data are the collation of notifications of communicable diseases from medical practitioners, hospitals and laboratories, received by the six state (New South Wales, Victoria, Queensland, Western Australia, South Australia and Tasmania) and two territory (the Australian Capital Territory and the Northern Territory) health departments in Australia. The NNDSS employs a national case definition for each disease, which overcomes some of the different methods of surveillance in each State

and Territory. States and Territories send to the NNDSS de-identified notification data on: 1) 25 core and mandatory data fields, and where applicable on 2) the species, serogroups/subtypes and phage types of isolated organisms, and 3) on the cases' vaccination status. The DoH collates, analyses and disseminates notification data for the purpose of monitoring national communicable disease incidence trends to inform public health action. [10, 11]

Historically, surveillance summaries for *Salmonella* have been produced for calendar years, i.e. 1 January to 31 December. However, this splits the Australian salmonellosis season in half. By analysing surveillance data by the Australian financial year (fiscal year), which starts on 1 July and ends on the next 30 June, an entire salmonellosis season can be included.

Previous studies reporting on *Salmonella* trends have used traditional statistical methods to show trends over time.[1] Joinpoint regression models characterise the trend behaviour in the data by identifying the significant points where changes occur. Its usefulness lies in its ability to detect sudden changes and describe changing trends over time. These models are widely used in epidemiological studies to calculate disease incidence trends in a population.[12] A study conducted by Wright et al. [13] used Joinpoint regression analysis and identified a significant change in trend in the average rate of *Salmonella* Enteriditis outbreaks in the United States (US). The use of Joinpoint regression analysis to assess whether any statistically significant changes in trends have occurred in the national incidence of *Salmonella* infection in Australia would provide valuable information in the assessment of testing practices, public health interventions and regulatory change.

Multiple factors may influence disease burden and trends and lead to an apparent increase that is due to changes in testing practices rather than a true change in the disease incidence over time. The primary source of *Salmonella* infection notifications in Australia are private pathology laboratories whereby positive test results are reported to jurisdictional surveillance systems. Due to their commercial availability, Australian pathology laboratories have increasingly been moving from microscopy and culture to molecular diagnostics, such as culture independent diagnostic tests (CIDT) using multiplex polymerase chain reaction (PCR) panels, for the diagnosis of enteric

pathogens in faecal specimens.[14] The advantages of CIDTs compared to traditional culture methodology include reduced cost[15], increased sensitivity[15-17]; ease of use[17, 18]; speed and the detection of multiple pathogens in the one test.[15, 17] Multiplex PCR panels have the ability to detect 10 enteric bacterial and parasitic pathogens simultaneously in faecal specimens, including: *Salmonella* spp., *Campylobacter* spp., *Shigella/*entero invasive *Escherichia coli* spp., *Yersinia enterocolitica*, Aeromonas spp., Entamoeba histolytica, *Crytosporidium* spp, Dientamoeba spp., and *Blastocystis homini*. Therefore, its qualities allow for early diagnosis as well as reporting of foodborne diseases. Subsequently, they are attractive to general practitioners[15] and pathology laboratories.[19-22] However, the high sensitivity of CIDTs also has its disadvantages and introduces challenges from a public health perspective. These include increased testing, high sensitivity and low specificity for pathogenic strains.[20] In addition, CIDTs do not provide isolates required to identify serovars or genotypes, such as *S.* Typhimurium, which are essential for monitoring incidence trends, illness cluster detection, and outbreak investigations.[18, 21, 23]

Rates of faecal sampling testing may affect the number of positive tests.[24] May et al.[25] investigated the impact of changed testing procedures on four pathogens in Queensland (QLD), Australia, between 2010 and 2014. Their findings showed that the introduction of CIDT using a multiplex PCR in two QLD private pathology laboratories in late 2013 led to a substantial increase and proportion of faecal specimens testing. Therefore, PCR diagnostic testing had a significant impact on the public health surveillance of enteric pathogens, including *Salmonella,* in QLD. Faecal sampling rates or the application of laboratory denominators to quantifying enteric pathogen incidence rates have been documented by limited studies.[24, 26-28] The use of faecal sampling rates when investigating salmonellosis trends in Australia would be beneficial to determine the impact of laboratory diagnostic practices on national *Salmonella* notifications.

The aim of this study was to 1) analyse national surveillance data for *S.* Typhimurium and non-Typhimurium *Salmonella* serovars from 1 July 2008 through 30 June 2017 by financial year; 2) use Joinpoint regression analysis to determine whether there were

any statistically significant changes in trend during the study period; 3) estimate the national trend in *Salmonella* notifications to determine if there was an increase or decrease in the notification of disease; and 4) assess whether these changes in reports of *Salmonella* infection might be explained by changes in faecal culture rates.

Materials and Methods

Study design

For this descriptive epidemiological study, the *Salmonella* spp. data from the National Notifiable Diseases Surveillance System (NNDSS) was accessed, to describe trends in notification from *S*. Typhimurium and non-Typhimurium *Salmonella* infections for the period 2008/09 to 2016/17.

Data collection

Notifiable disease data

Salmonellosis is a nationally notifiable disease in Australia. Jurisdictional health departments report all laboratory confirmed *Salmonella* infections to NNDSS.[29] To investigate disease trends, de-identified and aggregated notification data on human salmonellosis by jurisdiction for the reporting period were accessed. This study used a NNDSS dataset extracted in July 2017 that was analysed by the date of diagnosis to estimate disease activity within the reporting period. *Salmonella enterica subspecies* I, was grouped with *S.* Typhimurium if they have an H = i in the antigenic formula or a known Typhimurium phage type (commonly known as monophasic *S***.** Typhimurium). All *Salmonella* infection cases where the serovar, age, or sex were missing were excluded as were infections due to invasive serotypes *S*. Typhi, *S***.** Paratyphi A, *S*. Paratyphi B (except for biovar Java), and *S*. Paratyphi C. The number of notifications reported by financial year within the reporting period were analysed in single year age groups from 0 to 4 years old and then grouped in five year age groups until the 85+ age group.

Population denominator data

Estimated resident populations by age and sex for each jurisdiction between 2008 and 2016 served as the population denominators and were obtained from the Australian Bureau of Statistics (ABS).[30] They were used to calculate the notification rates per 100,000 population for the total population, stratified by age, sex, financial year, and

by jurisdiction by financial year. Age- standardised rates per 100,000 population by financial year and by calendar year were calculated using the direct method using the estimated 2001 Australian population as the reference population.[30] Age-standardised rates were also calculated for two age groups (<5 years and ≥5 years) for the Joinpoint regression analysis.

Faecal test denominator data

To examine if testing practices had an influence on *Salmonella* notifications, the number of culture performed were also used as a denominator in an alternative analysis. Statistics reports on Pathology Item 69345 in the Medicare Medical Benefits Schedule (MBS), by financial year for the reporting period 1 July 2008 to 30 June 2017, by jurisdiction, were obtained from the MBS Item Statistics Reports produced and made available online by Medicare Australia Statistics.[31] The Medicare MBS is part of the Medicare Benefits Scheme, Australia's national health insurance scheme, where healthcare services , prescription medicines and treatment as a public patient in a public hospital are provided for free or subsidised by the Australian Government. The Medicare MBS is a list of services (medical, procedural and diagnostic) for which Medicare either pays a subsidy or benefit. Pathology item 69345 is defined as:

> Culture and (if performed) microscopy without concentration techniques of faeces for faecal pathogens, using at least 2 selective or enrichment media and culture in at least 2 different atmospheres including (if performed):
>
> (a) pathogen identification and antibiotic susceptibility testing; and
> (b) the detection of clostridial toxins; and
> (c) a service described in item 69300;
> - 1 examination in any 7 day period.

The figures in the MBS Item Statistics Reports comprise of '...only those services that are performed by a registered provider, for services that qualify for Medicare benefit and for which a claim has been processed by Medicare Australia'.[31]

As per Medicare Australia, State/Territory is based on the patient's address (at the time the claim is made) and the Month is based on the date the service was processed by Medicare Australia, not the service delivery date.[31]

Ethics

The Australian National University Human Research Ethics Committee [protocol 2017/728] approved the conduct of this study.

Statistical analysis

The most recent nine years (2008/09–2016/17) were selected as the timeframe for examining temporal trend changes, as this analysis was an update of a previous study on *Salmonella* trends in Australia.[32] *S.* Typhimurium and non-Typhimurium *Salmonella* serovars were analysed separately. Descriptive analyses were undertaken in Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA). Direct standardisation (as mentioned above) was used with the jurisdiction-, financial year-, age-, and sex-based population as the reference population to calculate age- standardised incidence rates. Negative binomial regression was performed using Stata version 13 (StataCorp LP, College Station, TX, USA), to estimate incidence rate ratios (IRR) and calculate 95% confidence interval adjusted for sex, age groups and jurisdiction to capture any statistically significant difference in *Salmonella* trends.

Three types of notification rates were calculated: crude, specific (age- and sex-specific) and age-standardised (expressed per 100 000 persons). Age-specific notification rates were calculated for all ages and within 5-year age groups. Temporal notification and age-standardised trends in *S.* Typhimurium and non-Typhimurium *Salmonella* infections were assessed using Joinpoint regression analysis (https://surveillance.cancer.gov/Joinpoint/). Permutation tests were used to identify the minimum number of Joinpoints by determining the most appropriate combination of line segments and change points.[33] This approach works well for incidence and mortality data. Kim et al.[34] explain the theory of the Joinpoint model in more detail. The bivariables were sex and jurisdiction. The results are displayed as straight lines connected at Joinpoints on a log-linear scale. Log transformation is the method of choice when working with rates that arise from a Poisson distribution which is skewed.[12] The maximum number of Joinpoints allowed for each analysis was two, as determined by the number of data points. The minimum numbers of observations from a Joinpoint within the study period, and between Joinpoints were 2 and 2 respectively, which were the default settings for grid search in Joinpoint 4.5.0.1. To determine the significance of trends of *Salmonella* annual age-standardised

notification rates are characterised by an annual percentage change (APC) between successive change points. In addition, average annual percent change (AAPC) was calculated to characterise trends in *Salmonella* notification rates over the total study period (2008/09-2017/18). All estimates are presented with 95% confidence intervals (CIs). $P < 0.05$ was considered statistically significant. The trends in crude incidence rates for jurisdictions using Medicare culture data as the denominator was also examined.

In a sensitivity analysis, the same Joinpoint regression analysis was performed by calendar years to compare crude *Salmonella* notification rates by calendar years and financial years.

Results

Between 1 July 2008 and 30 June 2017, Australian jurisdictions reported 122,201 notifications of *Salmonella* infection to the NNDSS (Fig 1). Of these notifications, 94.1% (114,937/122,201) included serovar information and of those, 99.8% (114,751/122,000) included age and sex data. During the study period, a total of 34,950 *Salmonella* isolates were typed in Australia using multiple-locus variable-number of tandem repeats analysis (MLVA). Of these, 96.7% (34,127/34,950) of MLVA typing was performed for *S*. Typhimurium isolates (Supplementary Information Table S1), excluding cases with missing data on serovar, age, or sex. Together, the top five most commonly notified MLVA profiles for *S.* Typhimurium accounted for 16.3% (5,688/34,950) of all MLVA profiles reported nation-wide between 1 July 2008 and 30 June 2017 (Supplementary Information Fig S1).

Between 1 July 2008 and 30 June 2017, approximately 6% (7,238/121,989) of *Salmonella* notifications lacked a serovar entry. The number of *Salmonella* notifications with no serovar was stable between 2008/09 and 2012/13 however increased threefold in 2013/14 (n=829), nearly doubled in 2014/2015 (n=1,373) and peaked in 2015/16 (n=1,922). Supplementary Information Table S2 shows the number and proportion of *Salmonella* notifications without serovar data by state and territory. Queensland (8.6%, 2,841/32,977) had the highest number and proportion of *Salmonella* notifications without serovar data in Australia during the study period.

Incidence trends of *Salmonella* in Australia, 2008/09 to 2016/17

In Australia, the crude notification rate by financial year was lowest in 2008/09 (40.2 per 100,000), after which it increased to 66.8 per 100,000 in 2014/15 and decreased to 61.9 per 100,000 at the end of the study period (Fig 1). Nationally, the most commonly notified *Salmonella* serovar was *S*. Typhimurium, which was responsible for 49.5% (56,761/114,751) of all notified infections over the study period (Fig 1). *S.* Enteriditis was responsible for 6.3% (7,256/114,751) of notifications, followed by *S.* Virchow (n=5,490, 4.8%), *S.* Saintpaul (n=4,754, 4.1%) and *S*. Paratyphi B (n=2,629, 2.3%).

Between 1 July 2008 and 30 June 2017, crude notification rates gradually increased for both *S*. Typhimurium and non-Typhimurium *Salmonella* with crude notification rates suggesting breaks in the trend, observed in 2010/11 and 2014/15 (Fig 1).

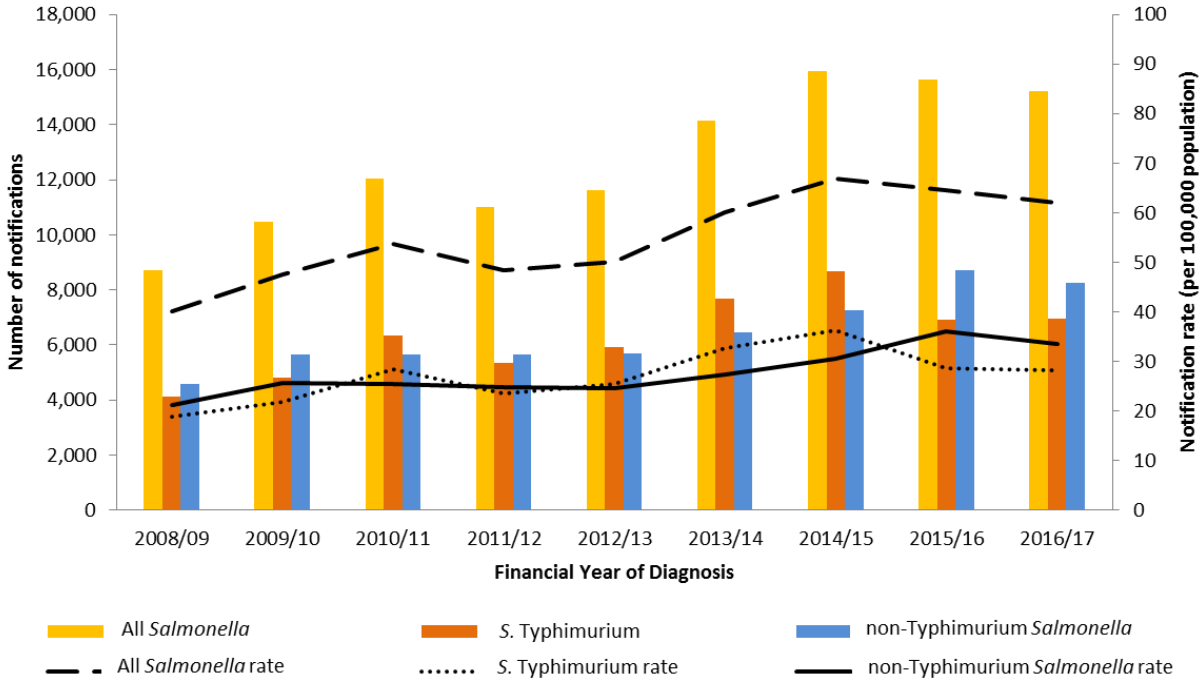


Fig 1. National trend of salmonellosis excluding cases with missing data on serovar, age, or sex, 1 July 2008 to 30 June 2017 (National Notifiable Diseases Surveillance System; n=114,751)

Age distribution trends

Between 1 July 2008 and 30 June 2017, the overall median age at onset of *Salmonella* infection was 25 years (range <1 –108 years), which was similar for S. Typhimurium cases included in this study (median age 25 years (range <1 –108 years)) and non-Typhimurium *Salmonella* cases (median age 26 years (range <1–102 years)). The

highest age-specific rate of *Salmonella* infection was 212 cases per 100,000 population in children aged 0–4 years old. The crude notification rates of non-Typhimurium *Salmonella* in children aged <1 years was substantially higher than for children aged <1 years infected with *S*. Typhimurium (Supplementary Information Fig S2).

Overall, 52.4% (29,727/56,761) of *S*. Typhimurium and 50.3% (29,167/57,990) of non-Typhimurium *Salmonella* notifications were females (Table 1).

Table 1. Characteristics of S. Typhimurium and non-Typhimurium Salmonella notifications by sex, age, MLVA type, serovar and jurisdiction, Australia, 1 July 2008–30 June 2017 (National Notifiable Diseases Surveillance System; excluding cases with missing data on serovar, age, or sex; n=114,751)

Characteristic	*S.* Typhimurium N (%)	Non-Typhimurium *Salmonella* N (%)
Sex		
Female	29,727 (52.4)	29,167 (50.3)
Male	27,034 (47.6)	28,823 (49.7)
Age groups (years)		
0	2,807 (4.9)	7,378 (12.7)
1	3,065 (5.4)	4,879 (8.4)
2	2,542 (4.5)	2,004 (3.5)
3	2,016 (3.6)	1,211 (2.1)
4	1,641 (2.9)	938 (1.6)
5-9	5,068 (8.9)	2,889 (5.0)
10-14	3,157 (5.6)	1,863 (3.2)
15-19	3,357 (5.9)	2,401 (4.1)
20-24	4,604 (8.1)	4,019 (6.9)
25-29	4,596 (8.1)	4,144 (7.1)
30-34	3,794 (6.7)	3,269 (5.6)
35-39	2,915 (5.1)	2,644 (4.6)
40-44	2,671 (4.7)	2,619 (4.5)
45-49	2,414 (4.3)	2,728 (4.7)
50-54	2,258 (4.0)	2,904 (5.0)
55-59	2,024 (3.6)	2,666 (4.6)
60-64	1,861 (3.3)	2,541 (4.4)
65-69	1,703 (3.0)	2,223 (3.8)
70-74	1,360 (2.4)	1,773 (3.1)
75-79	1,121 (2.2)	1,204 (2.1)
80-84	958 (1.7)	967 (1.7)
85+	829 (1.5)	726 (1.3)
State or territory		
New South Wales	17,219 (30.3)	12,378 (21.4)
Victoria	15,431 (27.2)	9,315 (16.1)
Queensland	10,858 (19.1)	19,278 (33.2)
Western Australia	4,785 (8.4)	7,846 (13.5)
Northern Territory	750 (1.3)	3,506 (6.1)
South Australia	5,576 (9.8)	3,649 (6.3)
Tasmania	667 (1.2)	1,390 (2.4)
Australian Capital Territory	1,475 (2.6)	628 (1.1)
MLVA[a]	34,127 (60.1)	823 (1.4)
Total	56,761 (100)	57,990 (100)

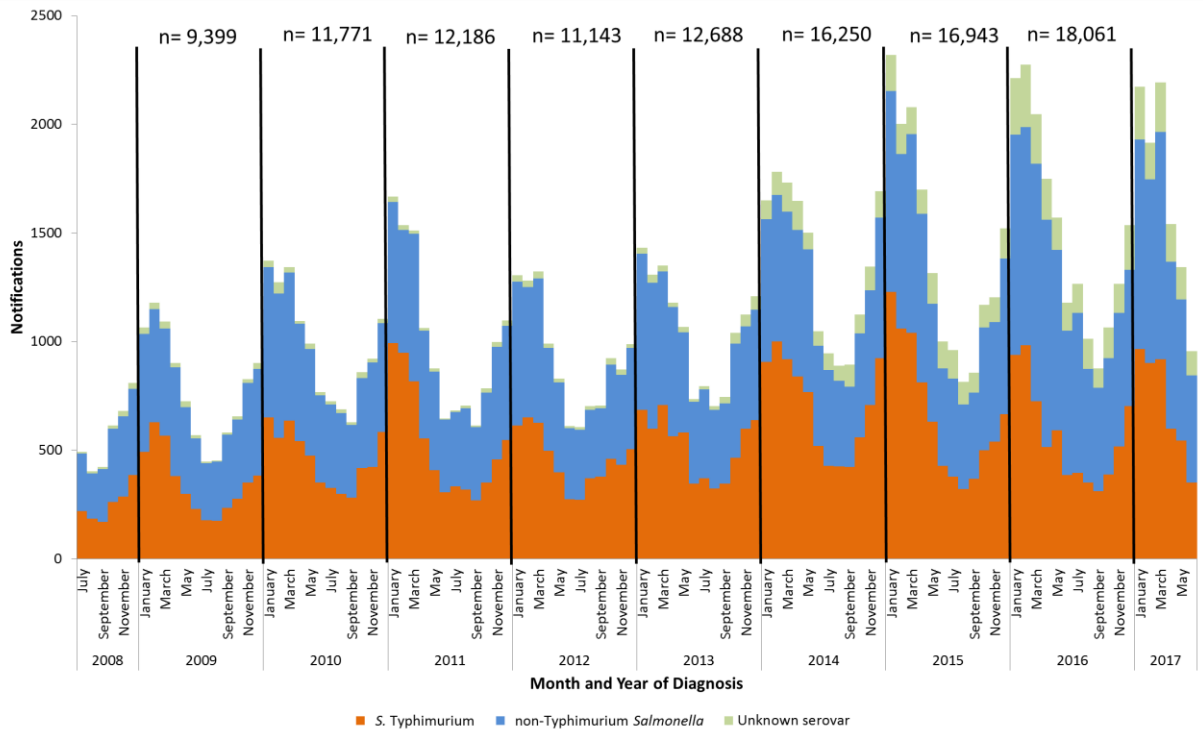
[a] multiple-locus variable-number of tandem repeats analysis

Seasonal distribution

The greatest proportion of *Salmonella* notifications occurred between January and March (36.4%, 44,422/122,000; Fig 2) and the smallest proportion between July and September (16.1%, 19,621/122,000), indicating strong seasonal peaks in summer months, and troughs during winter months. This seasonal pattern was consistent for *S*. Typhimurium and non-Typhimurium *Salmonella* notifications.

Fig 2 shows the distribution of all *Salmonella* notifications (i.e. *S*. Typhimurium, non-Typhimurium *Salmonella* and *Salmonella* notifications with no serovar) by calendar year (Fig 2a) and financial year (Fig 2b). The figures in the graphs represent the number of *Salmonella* notifications. Fig 2a shows that *Salmonella* notifications were largely stable between 2009 and 2012 and subsequently increased steadily each calendar year since 2013. In contrast, Fig 2b illustrates that *Salmonella* notifications have increased since 2011/12 and remained relatively stable since 2014/15.

2a)



2b)

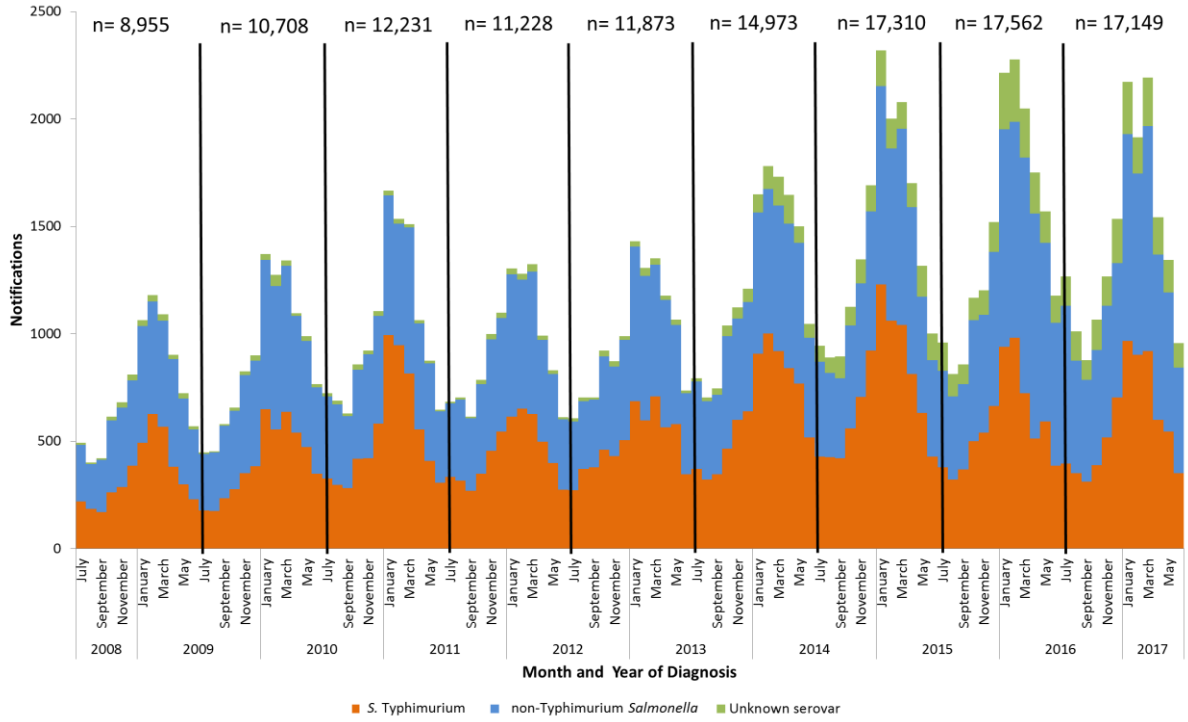


Fig 2. Seasonal distribution of *Salmonella* notifications - *S*. Typhimurium, non-Typhimurium *Salmonella* and *Salmonella* notifications with unknown serovar, Australia, 1 July 2008 to 30 June 2017, National Notifiable Diseases Surveillance System, excluding cases with missing data on age or sex, (n=114,751). Black lines outline notifications by calendar year (2a) and financial year (2b)

Temporal trends of *Salmonella* infection

During the study period, rates of both *S*. Typhimurium (IRR 1.03, 95% CI 1.02–1.03) and non-Typhimurium *Salmonella* (IRR 1.06, 95% CI 1.06–1.07) increased (Table 2).

Between 2008/09 and 2016/17, there was no significant difference between the sexes for non-Typhimurium *Salmonella* infection by jurisdiction, but higher rates of *S*. Typhimurium infection notifications were observed in females (Table 2; IRR 1.13; 95% CI 1.10–1.17). Notification rates of *S*. Typhimurium increased in all jurisdictions, except New South Wales (NSW), which showed a statistically nonsignificant rate decline (IRR 0.99, 95% CI 0.98-1.01). The highest significant increase in *S*. Typhimurium notification rates over the study period were identified in WA (IRR 1.20; 95% CI 1.18–1.22) and QLD (IRR 1.12; 95% CI 1.10–1.13) (Table 2). Notification rates of non-Typhimurium *Salmonella* increased in all jurisdictions, except Northern Territory (NT), which did not show a statistically significant change during the study period (IRR 1.00; 95% CI 0.99–1.02) (Table 2).

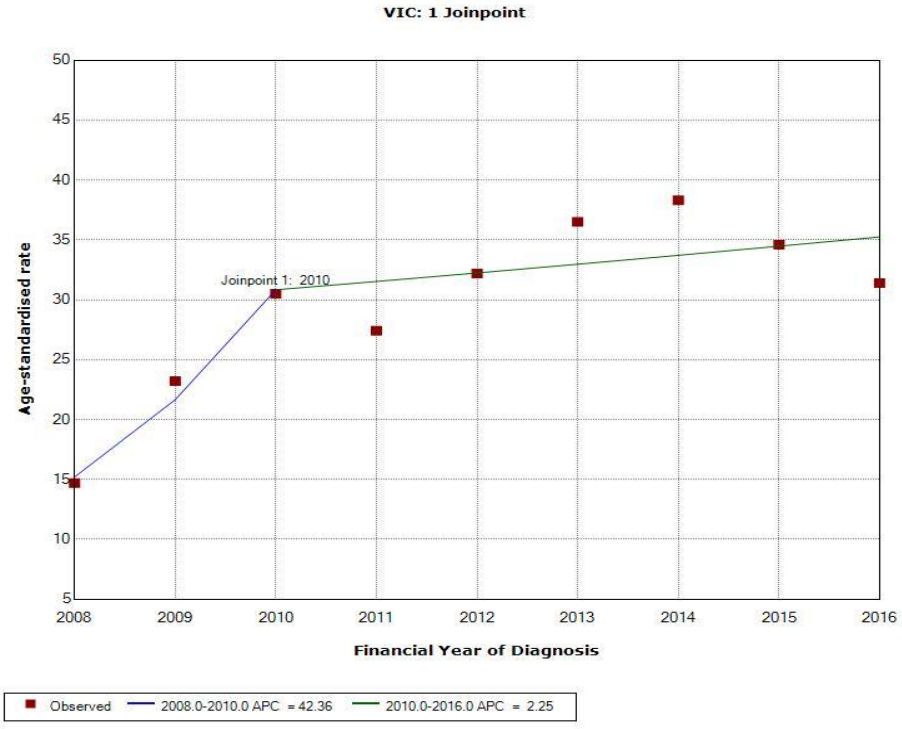
Table 2. Incident rate ratios calculated using negative binomial regression of *S*. Typhimurium and non-Typhimurium *Salmonella* by sex, age, jurisdiction and time, 1 July 2008 to 30 June 2017

Characteristic	***S*. Typhimurium**			**Non-Typhimurium *Salmonella***		
	IRR[a]	95% CI[b]	P-value	IRR[a]	95% CI[b]	P-value
Sex (reference = Male)						
Female	1.13	1.10-1.17	<0.001	1.06	1.03-1.09	<0.001
Age groups (reference =<1)						
1	1.04	0.94-1.14	0.47	0.69	0.63-0.75	<0.001
2	0.82	0.74-0.90	<0.001	0.29	0.26-0.32	<0.001
3	0.64	0.58-0.70	<0.001	0.17	0.16-0.19	<0.001
4	0.53	0.48-0.59	<0.001	0.13	0.12-0.15	<0.001
5-9	0.33	0.30-0.36	<0.001	0.08	0.07-0.09	<0.001
10-14	0.22	0.20-0.24	<0.001	0.06	0.05-0.06	<0.001
15-19	0.22	0.20-0.25	<0.001	0.07	0.07-0.08	<0.001
20-24	0.28	0.25-0.30	<0.001	0.11	0.10-0.12	<0.001
25-29	0.26	0.24-0.29	<0.001	0.11	0.10-0.12	<0.001
30-34	0.23	0.21-0.25	<0.001	0.09	0.08-0.10	<0.001
35-39	0.18	0.16-0.20	<0.001	0.07	0.07-0.08	<0.001
40-44	0.16	0.15-0.18	<0.001	0.07	0.07-0.08	<0.001
45-49	0.16	0.14-0.17	<0.001	0.08	0.07-0.09	<0.001
50-54	0.15	0.14-0.16	<0.001	0.09	0.08-0.09	<0.001
55-59	0.14	0.13-0.16	<0.001	0.09	0.08-0.09	<0.001
60-64	0.15	0.13-0.16	<0.001	0.09	0.08-0.10	<0.001
65-69	0.16	0.14-0.17	<0.001	0.09	0.09-0.10	<0.001
70-74	0.17	0.15-0.19	<0.001	0.10	0.09-0.11	<0.001
75-79	0.18	0.16-0.21	<0.001	0.09	0.08-0.10	<0.001
80-84	0.21	0.19-0.24	<0.001	0.10	0.09-0.11	<0.001
85+	0.18	0.16-0.20	<0.001	0.08	0.07-0.09	<0.001
Trend over time by jurisdiction (2008-2017)						
NSW	0.99	0.98-1.01	0.28	1.08	1.06-1.09	<0.001
VIC	1.08	1.07-1.10	<0.001	1.09	1.07-1.10	<0.001
QLD	1.12	1.10-1.13	<0.001	1.10	1.08-1.11	<0.001
WA	1.20	1.18-1.22	<0.001	1.07	1.06-1.09	<0.001
NT	1.01	0.98-1.05	0.36	1.00	0.99-1.02	0.71
SA	1.10	1.08-1.11	<0.001	1.10	1.08-1.12	<0.001
TAS	1.05	1.02-1.09	<0.001	1.05	1.03-1.08	<0.001
ACT	1.03	1.01-1.06	0.01	1.07	1.04-1.11	<0.001

[a] incidence rate ratio; [b] confidence interval; ACT, Australian Capital Territory; NT, Northern Territory; SA, South Australia; TAS, Tasmania; WA, Western Australia; QLD, Queensland; NSW, New South Wales; VIC, Victoria

Joinpoint regression analysis showed a significant increase in *S*. Typhimurium incidence in males over 5 years, increasing 8.2% per year during the study period (95% CI 2.2–14.6). A change in age-standardised notification trend for *S*. Typhimurium was observed in four jurisdictions: Victoria (VIC; Fig 3a), NT (Fig 3b) and WA in 2010/11 and QLD in 2014/15 (Fig 4a). WA was the only jurisdiction to display two Joinpoints suggesting that there were two changes in the trend line during the study period, with an additional Joinpoint detected at 2013/14 (Fig 4b).

3a



3b

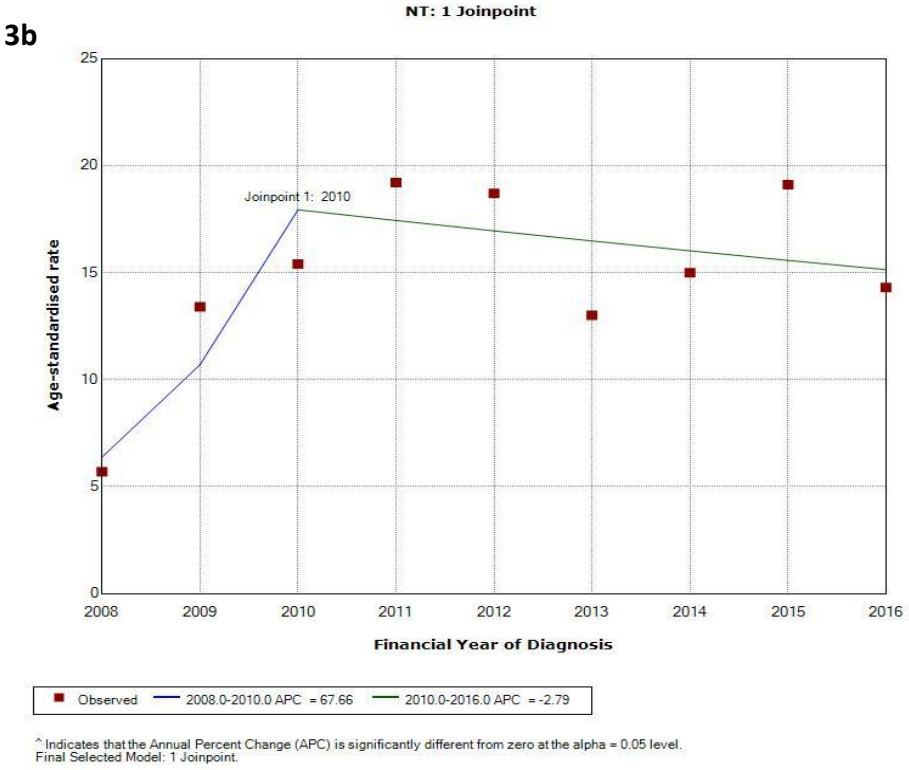
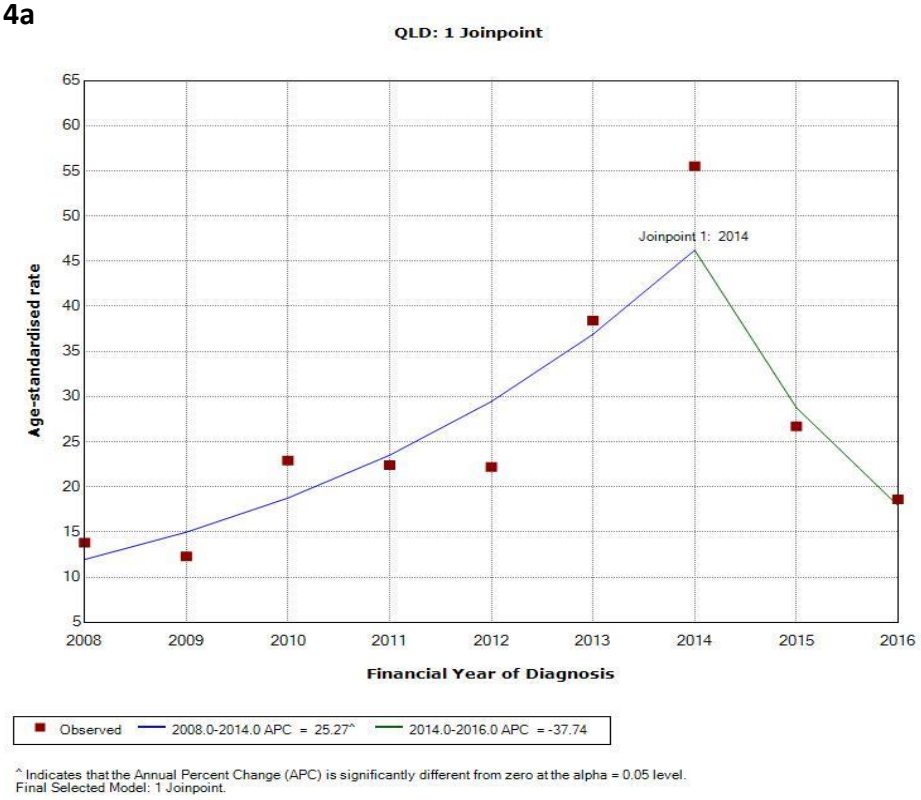


Fig 3. Crude notification rate (dots) and age-standardised *S*. Typhimurium notification rates (per 100,000 population) showing Joinpoint at 2010/11 indicating change in trend over the period 2008/09 to 2016/17, by financial year, for Victoria (3a) and Northern Territory (3b). APC= annual percentage change. Note the years represent financial years, e.g. 2008= 2008/09, 2009=2009/10 etc.

4a



4b

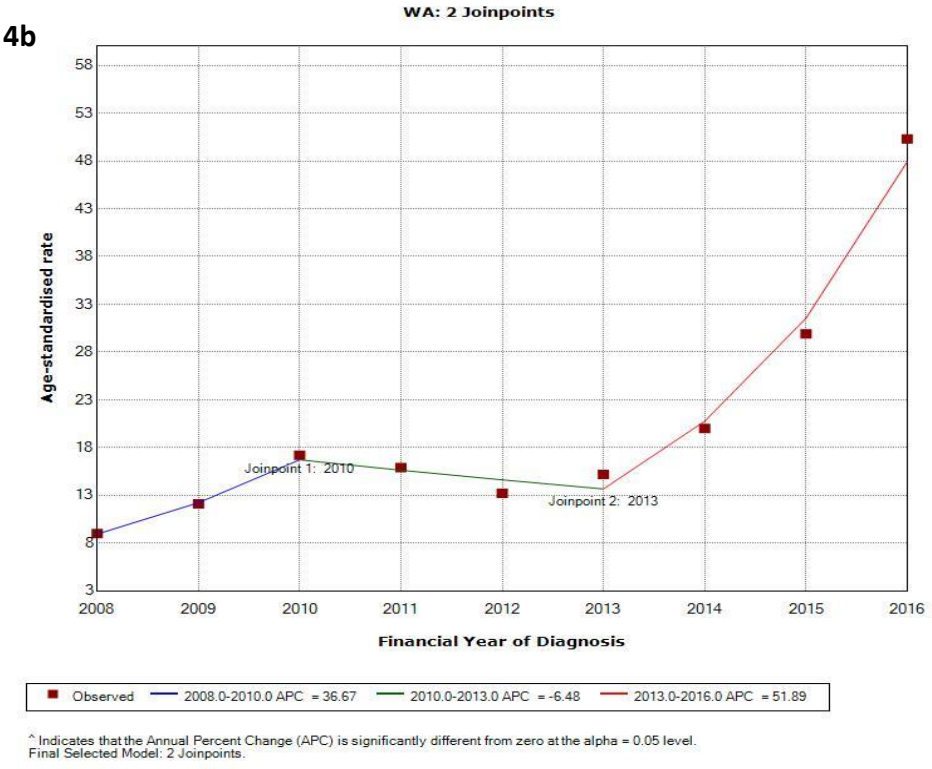


Fig 4. Crude notification rate (dots) and age-standardised *S*. Typhimurium notification rates (per 100,000 population) showing Joinpoint indicating change in trend over the period 2008/09 to 2016/17, by financial year, for Queensland (4a; 2014/15) and Western Australia (4b; 2010/11 and 2013/14). APC= annual percentage change. Note the years represent financial years, e.g. 2008= 2008/09, 2009=2009/10 etc.

For non-Typhimurium *Salmonella*, WA was the only jurisdiction to display a change in notification trend with a Joinpoint detected in 2010/11 and 2014/15 (Fig 5).

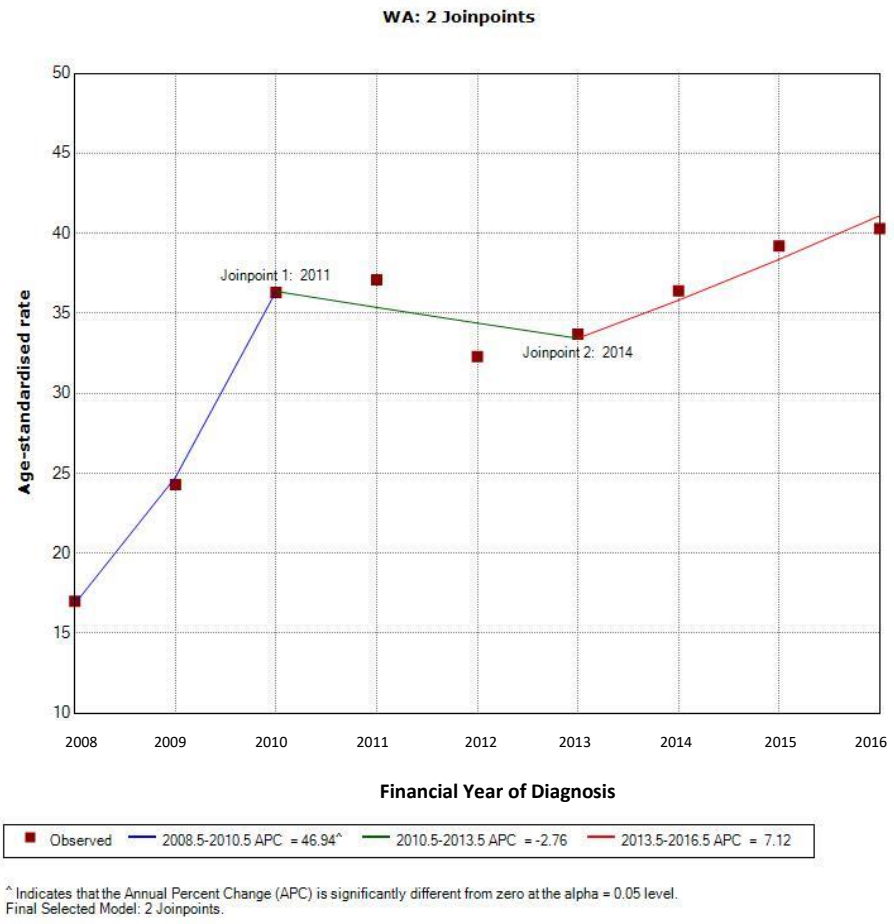


Fig 5. Crude notification rate (dots) and age-standardised non *S*. Typhimurium notification rates (per 100,000 population) showing Joinpoint in 2010/11 and 2014/15 indicating change in trend over the period 2008/09 to 2016/17, by financial year, Western Australia. APC= annual percentage change. Note the years represent financial years, e.g. 2008= 2008/09, 2009=2009/10 etc.

Salmonella notification rates in relation to culture rates

For *S*. Typhimurium, four of the eight jurisdictions, namely VIC, NT, TAS and ACT, displayed similar trends where the age-standardised notification rate showed a different trend to the crude rate trend (using culture as the denominator) (Supplementary Information Table S3). Of these jurisdictions, VIC, TAS and ACT showed a decline in the crude rate trend whilst the age-standardised notification rate increased. In NT, the crude rate trend was constant, decreasing during the study

period, whereas a Joinpoint was observed in the age-standardised rate trend as described above. The results in TAS were reversed, where a Joinpoint was observed in the crude rate trend at 2010/11 and the age-standardised rate trend was constant, increasing during the study period. The annual percentage change was greater when *S*. Typhimurium notification data was plotted by financial year compared to calendar year when comparing crude population rates with crude culture rates (Supplementary Information Fig S4 to Fig S11).

There was no significant change in the national trend for non-Typhimurium *Salmonella* notification rates using culture as the denominator. In four of the eight jurisdictions, namely QLD, WA, NT and TAS, the age-standardised non-Typhimurium *Salmonella* notification rate trend differed from the crude rate trend (using culture as the denominator). Of these jurisdictions, QLD, WA and TAS showed a decline in the crude rate trend whilst the age-standardised rate increased. Between 2008/09 and 2016/17, NT was the only jurisdiction to display a significant change in trend for crude non-Typhimurium *Salmonella* notification rates using culture data as the denominator (Supplementary Information Table S6). NT displayed two periods when there were changes in the trend line during the study period: there was a significant decrease in incidence of non-Typhimurium *Salmonella* with a Joinpoint detected in 2010/2011, followed by a significant increase in 2013/14 (Supplementary Information Table S6).

Discussion

The analysis of temporal patterns of *Salmonella* is essential to assist health authorities in monitoring the effectiveness of pathogen-reduction policies.[35] Laboratory-based surveillance systems are the foundation of today's communicable disease surveillance.[36] Our study demonstrated that while Australia has some of the highest rates of reported salmonellosis in the industrialised world recent increases may be due in part to increases in rates of faecal culture. With the current development of *Australia's Foodborne Illness Reduction Strategy 2018–2021*[+37] to reduce foodborne disease, stakeholders who monitor annual surveillance data will base the apparent success of implemented food safety strategies on the detection of reductions in reported *Salmonella* infections. Statistical methods that identify not only trends over time but also changes in trend, taking into account the whole *Salmonella* season, will

provide invaluable information on the public health effects of policies to control this disease.

Current efforts to control salmonellosis in Australia appear not to have made an impact on the national reduction of *Salmonella* during the study period. Australia continues to have higher notification rates of *Salmonella* infection compared to the US, European Union (EU), and England and Wales. In 2016/17, the crude notification rate for salmonellosis in Australia was 61.9 per 100,000 population. In the US, the laboratory notification rate was 15.2 per 100,000 population in 2013[38], while in the EU 22.2 (range 1.8–97.5) per 100,000 in 2012[39], and 14.8 per 100,000 population in England and Wales in 2015.[40] In particular, *S*. Typhimurium rates have been increasing in Australia causing most foodborne *Salmonella* outbreaks nationally. A variety of sources have been associated with *S*. Typhimurium related foodborne outbreaks, although eggs and poultry are the most common.[2] The number of *S*. Typhimurium outbreaks associated with eggs in Australia increased from 2001 to 2011.[1] In an attempt to reduce egg-associated incidence of disease, the Primary Production and Processing Standards (PPPS) for Eggs and Egg products (Australian New Zealand Food Standards Code) was introduced in Australia in 2011.[41] However, our results indicate that the trend in *Salmonella* infections in Australia is increasing. In comparison, in the EU, since surveillance began in 2007 and the implementation of targeted control measures for poultry, reported cases of *Salmonella* had been showing a constant decline. However, the *Salmonella* trend reportedly plateaued between 2012 and 2016 with *S*. Enteriditis incidence increasing in both humans and laying hens in the EU.[42] In the US, a decrease in *S.* Typhimurium notification rates has been observed, attributable to two main factors focusing on poultry: the combination of the implementation of a live attenuated Typhimurium vaccine and more rigorous performance targets for *Salmonella* contamination of poultry remains.[19]

Although we were unable to observe reductions in national *Salmonella* notifications that may have been due to regulatory measures, we did see reductions at the jurisdictional level that may have been the result of local controls. The *S*. Typhimurium age-standardised rate trend in 2010/11 followed by a markedly less sharp increase thereafter in VIC and NT and a decrease in trend in WA. Besides regulatory changes,

changes in testing methodology can also influence the observed illness.[21] *Salmonella* surveillance relies on the reporting of serovars to determine which serotypes are increasing and for the identification and investigation of outbreaks. Our study supports previous studies[32], which identified that *Salmonella* notifications with no reported serovar are increasing in number and proportion. Monitoring non-serotyped isolates is important to understand how much CIDT is impacting public health surveillance of *Salmonella*.

Our findings suggest that faecal specimens are increasingly not being cultured, either concurrently (parallel) or reflexively (CIDT-positive specimens are cultured for potential referral to pathology laboratories) and therefore the number of faecal specimens without an isolate for further characterisation is increasing. The *S*. Typhimurium trend in QLD suggests that the decrease in *S*. Typhimurium notification rates is related to a decrease in culture practices and thus the serotyping of *Salmonella* isolates. We identified a peak and change in trend in *S*.Typhimurium notifications in 2014/2015 in QLD, which was followed by a declining trend thereafter in both age-standardised *S*. Typhimurium notification rates and crude rate using culture as the denominator. It coincides with the increased number of *Salmonella* notifications in Australia in 2014 by 28% from 2013.[29] This was the largest number of recorded NNDSS notifications since records began in 1991.[29 43] The increase in rate followed the first full year that CIDT using multiplex PCR was widely used in Australian pathology laboratories. This compliments the findings of May et al.[14], which identified that the introduction of CIDT using PCR in late 2013 in QLD led to a significant proportion of positive faecal specimens not yielding an isolate to enable strain characterisation despite an increase in the number of faecal specimens being submitted for testing. In 2014, approximately one fifth of faecal specimens in QLD were PCR positive only for *Salmonella*, either culture negative or no culture performed, thus limiting the further characterisation of *Salmonella* strains by typing.[14]

In our study, NSW was the only jurisdiction to show a decreasing trend in *S*.Typhimurium age-standardised notification rates and in the crude rate using culture as the denominator. Whilst the change was not statistically significant, our result

differs from previous research which found an increasing trend of *S*. Typhimurium between 2000 and 2013.[32] The reduction in *S*. Typhimurium notification trends in NSW in the recent nine financial years may be a combination of a decrease in faecal specimen testing and a downward epidemiological trend in the population, as suggested by the decrease in the crude rate using culture as the denominator.

On the other hand, our use of Joinpoint regression indicate that for some jurisdictions there was a true increase in *S*. Typhimurium and non-Typhimurium *Salmonella* notifications. Results from this study suggest that the change in trend in 2010/11 for VIC align with the reported change in *Salmonella* notifications in 2011 when salmonellosis rates were higher in VIC compared with the 5-year mean in 2011, with a percentage increase of 48%.[2] This suggests that there has been a true increase in *S*. Typhimurium notification in VIC since 2010/11. Furthermore, during the study period the increase in non-Typhimurium *Salmonella* incidence in QLD, WA and TAS was not associated with increased culture practices.

Similar studies have found a reverse trend between notification rates and faecal testing rates. A Swiss study[24] investigated laboratory positivity rates of *Campylobacter* and *Salmonella* infection diagnostic tests from five private laboratories between 2003 and 2012. They found that whilst faecal testing increased during the study period, *Salmonella* notification rates decreased, thus suggesting an apparent reduction of notifications in the population. A study undertaken by Janiec et al.[44] found that reported *Salmonella* incidence declined in Wales despite faecal sampling rates rising steadily.

In contrast, the national co-claiming of Medicare Pathology item numbers suggests that PCR testing has led to an increase in *Salmonella* culture. Pathology practices recommend when ordering faeces microscopy and culture that a request is also made for multiplex PCR panels.[45-51] The analysis of co-claiming of Pathology Item 69345 (faecal culture) and Item 69496 (three or more PCR tests) shows that by calendar year the co-claiming of these services has increased from 3,000 in 2012 to 340,000 in 2016, representing an annual rate of growth of over 200%.[31] This would imply that an increase in *S*.Typhimurium and non-Typhimurium *Salmonella* notifications may be

related to an increase in PCR testing. Item 69345, used in the denominator in our study, does not take into account the testing of public patients in state hospitals and patients in community health centres.[52] This potentially may increase the number of faecal tests undertaken by as much as 10%. Even though these single patient episodes are rarely subject to coning (i.e. when more than three pathology items are requested by a medical practitioner and Medicare benefits are only payable for the three most expensive items), the potential underreporting of faecal tests in the Australian MBS data adds an element of complexity to the monitoring of changes in the pathology test request practice [52] and needs to be taken into account when interpreting the impact of faecal sampling rates on the epidemiological trend of *Salmonella* in Australia.

Limitations

Our study has several limitations. First, notification data represents only confirmed cases of *Salmonella* infection. Based on this study, there were an average of 12,750 notified cases of *Salmonella* in Australia per financial year between 2008/09 and 2016/17. However, cases are significantly underreported in surveillance data due to persons not pursuing medical care for mild episodes of gastroenteritis.[2, 53] It is estimated that for every notified case in Australia, seven exist in the community.[54] Subsequently, the number of notifications reported in this study is an under-representation of the true burden in the population. Second, a variety of factors may affect the number of observed illness, including population growth, spatial or temporal clustering of disease occurrence, and hygiene and food safety knowledge in consumers across the country.[35] Third, distinct characteristics such as “climate, biodiversity, relative geographic isolation and an extensive livestock population in Australia” are associated with enteric pathogen related disease.[32, 55]

Implications and future work

The findings from this study present the recent changes in epidemiology, particularly the impact of period of surveillance and potential impact of non-culture based methods. Our analysis of Salmonella notifications by financial year has shown to emphasise the public health importance of considering including the whole peak season of diseases especially when undertaking analysis of communicable disease

surveillance data. This study illustrates the importance of denominator data on surveillance limitations such as faecal sampling practices.

The rise in the continued uptake of CIDT poses a potential hindrance in the assessment and interpretation of change, particularly for the public health surveillance of serotypes such as *S*. Typhimurium, deemed a public health concern. To capture the *Salmonella* trend more accurately and to improve interpretation of salmonellosis notification trends seen in the NNDSS, future analysis should include the national assessment of the proportion of positive tests of all diagnostic tests performed (laboratory positivity rates).[24] Additional considerations for future analyses include the likelihood of false-positive CIDTs and of CIDTs that possess increased sensitivity compared to routine culture methods.[56]

Historically, public and private laboratories in Australia bore the expense associated with the reflexive culturing and referral of specimens to reference public health laboratories. However, with the increasing shift from culture to CIDTs the cost and higher workloads involved in yielding isolates solely for public health surveillance purposes have been reported as prohibitive for many laboratories.[57] Two unpublished reports which examined the potential implications of CIDT on public health surveillance in Australia suggest that this problem can be overcome by changes to the MBS through the introduction of an item that reimburses pathology laboratories for: 1) reflexive culture and 2) specimen or isolate transfer to public health laboratories for molecular characterisation.[57, 58] This will provide pathology laboratories with an incentive to perform reflexive culture on CIDT-positive *Salmonella* specimens and allow the testing for antimicrobial susceptibility, genotyping, phenotyping, serotyping and whole genome sequencing (WGS) required for public health surveillance.[57]

Amid the rise of CIDT uptake, WGS, due to its characterisation and discriminatory power[59], has concurrently been progressively introduced in public health surveillance. With continued advances in technology, WGS will increasingly become available for routine *Salmonella* typing and characterising pathogens. This will be notably beneficial for non-Typhimurium *Salmonella* serovars that currently lack an established typing system.[60] Until then, the culture of isolates and referral for molecular characterisation will need to be continued.[32]

Moving forward, national surveillance of salmonellosis will need to adapt to the change to CIDTs. Case definitions will have to be expanded to include positive CIDT reports and eventually WGS results, as they currently are defined by culture-confirmed infection.[56]

Conclusion

Our results have potentially important implications for epidemiological surveillance of *Salmonella* infection in Australia, which is essential to achieve timely control of this disease. Our application of a novel methodological approach in the analysis of *Salmonella* notifications highlights that the inclusion of a single summer season in the year for the analysis of enteric disease is an improvement to current surveillance practices. Using Joinpoint regression analysis and faecal sampling rates to investigate changes in national *Salmonella* notifications, our results suggest that the introduction of the use of multiplex PCR panels is having an impact on the public health surveillance of *Salmonella* in Australia. Our findings suggest that its implementation is associated with changes in trend in age-standardised *S.* Typhimurium notification rates in 2013/14 and 2014/15, particularly the increase in *Salmonella* notifications in QLD and WA. Consequently, health authorities should consider using the financial year rather than calendar year for the routine analysis of surveillance data and the use of Joinpoint regression analysis to complement traditional statistical methods. Given the implementation of a national reduction strategy to improve food safety, the use of these methods would be advantageous in the monitoring of *Salmonella* infection epidemiology and burden in Australia. However, the identification of significant changes in incidence of *Salmonella* will require the ability to distinguish between serovars. The absence of serovar data will profoundly restrict the detection and investigation of outbreaks nationally and Australia's response to international events of public health concern.

Acknowledgements

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Supporting Information

Table S1. Number and proportion of MLVA typing undertaken for S. Typhimurium and non-Typhimurium Salmonella, Australia, 1 July 2008-30 June 2017, National Notifiable Diseases Surveillance System (NNDSS), excluding cases with missing data on serovar, age, or sex

Jurisdiction	***S.* Typhimurium** N (%)	**Non-Typhimurium *Salmonella*** N (%)
New South Wales	14,978 (43.9)	782 (95.0)
Victoria	7390 (21.7)	13 (1.6)
Queensland	5,784 (16.9)	12 (1.5)
Western Australia	1,703 (5.0)	15 (1.8)
Northern Territory	3,719 (10.9)	1 (0.1)
South Australia	216 (0.6)	0 (0)
Tasmania	337 (1)	0 (0)
Australia	34,127 (100)	823 (100)

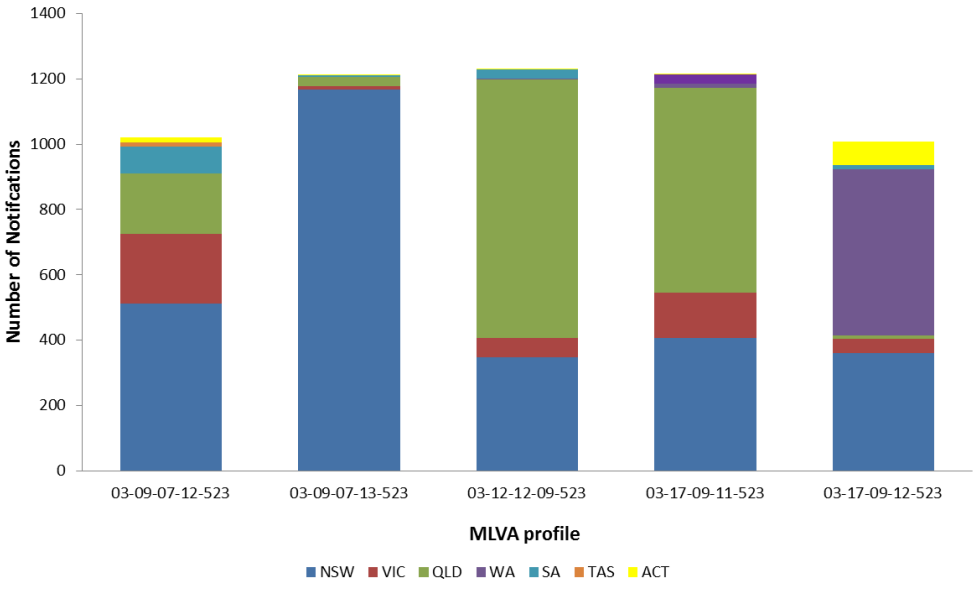


Fig S1. Top 5 MLVA profiles by jurisdiction, Australia, 1 July 2008– 30 June 2017, National Notifiable Diseases Surveillance System (NNDSS), excluding cases with missing data on serovar, age, or sex

Table S2. Number and proportion of Salmonella notifications without serovar data by jurisdiction, Australia, 2008/09-2016/17, excluding cases with missing data on age, or sex

Jurisdiction	Number of notifications without serovar data	Total number of notifications	Proportion of notifications without serovar data (%)
New South Wales	2,638	32,235	8.2
Victoria	894	25,640	3.5
Queensland	2,841	32,977	8.6
Western Australia	345	12,976	4.8
Northern Territory	194	4,450	2.7
South Australia	181	9,406	1.9
Tasmania	55	2,112	2.6
Australian Capital Territory	77	2,180	3.5
Australia	7,225	122,976[a]	5.9

[a] 26 entries are missing a serovar entry and are excluded from analysis

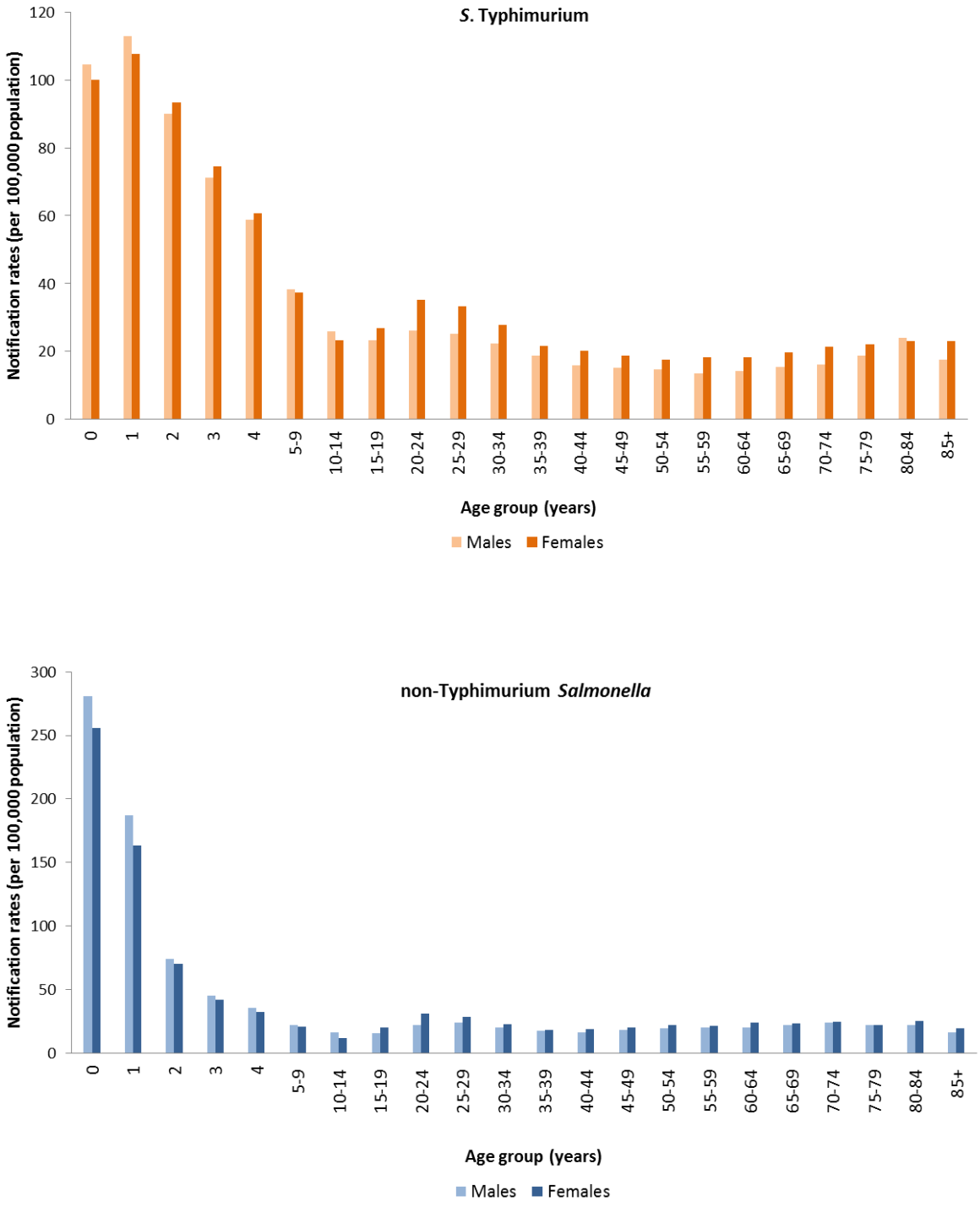


Fig S2. Crude notification rates (per 100,000 persons) of *S*. Typhimurium and non-Typhimurium *Salmonella* notifications in Australia by sex and age, 1 July 2008 to 30 June 2017, National Notifiable Diseases Surveillance System (NNDSS), excluding cases with missing data on serovar, age, or sex. Note the differing y-axis scales

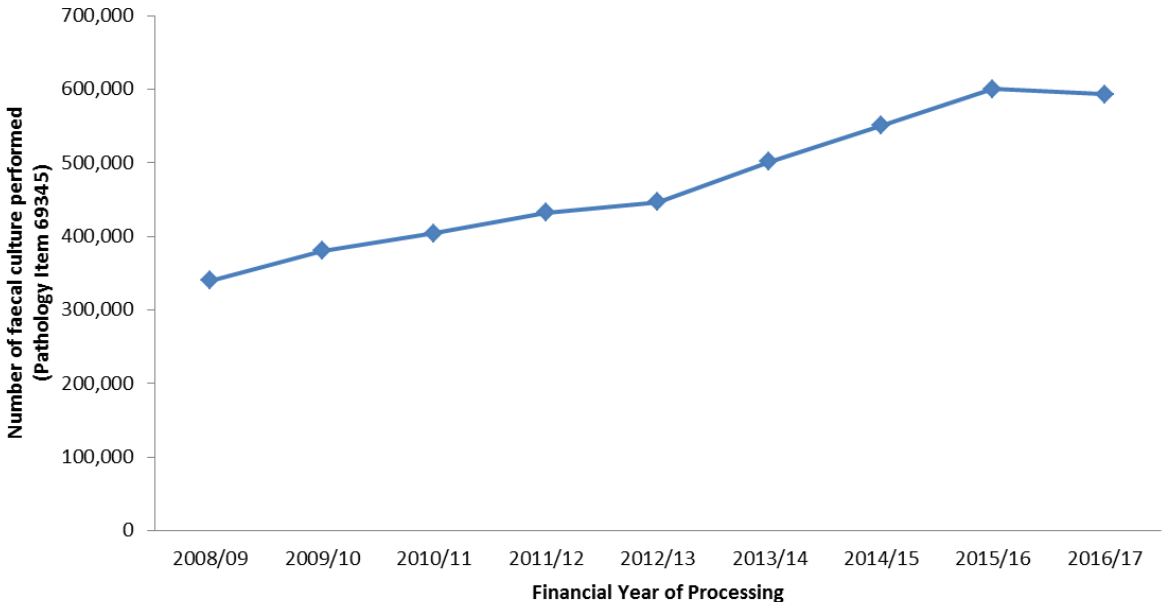
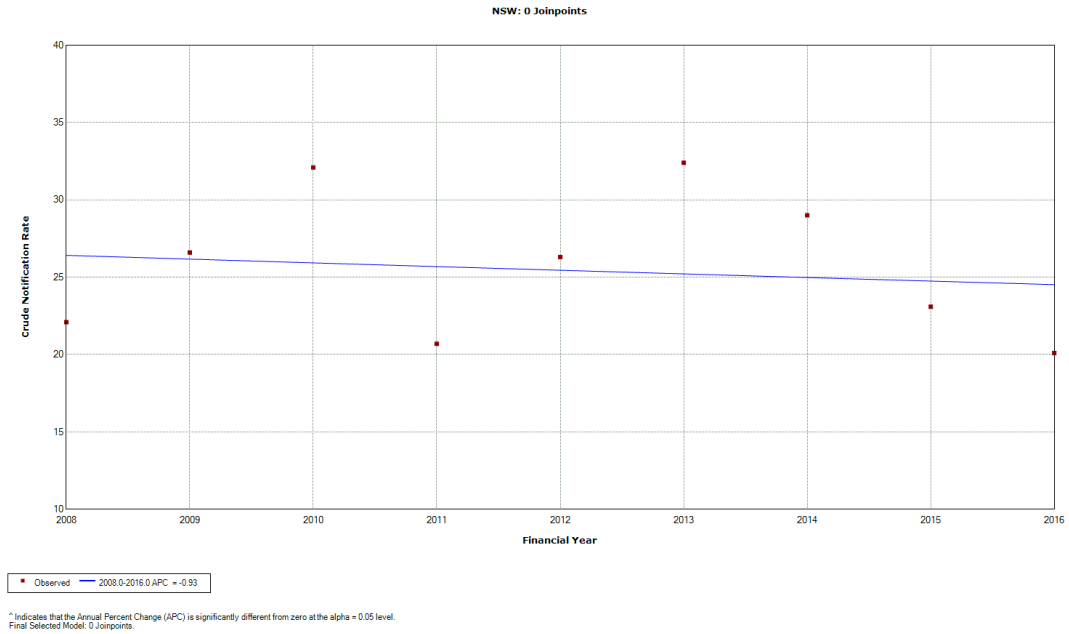


Fig S3. Number of faecal culture (Pathology Item 69345) performed over the period 2008 to 2017, by financial year of processing, (Medicare Australia Statistics; n=4,247,882)

Crude *S*. Typhimurium notification rates by calendar year versus financial year

S. Typhimurium - New South Wales



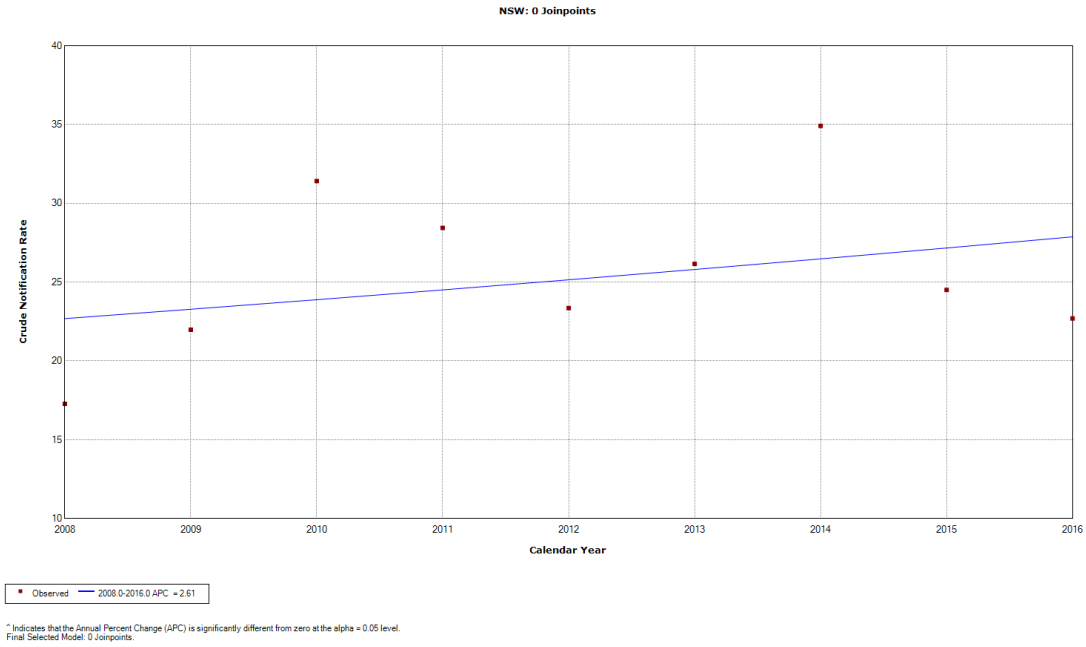


Fig S4. Crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by calendar year (bottom graph) displaying statistically significant change over the period 2008 to 2017, New South Wales (^significantly different from zero at alpha = 0.05). APC= annual percentage change

S. Typhimurium - Victoria

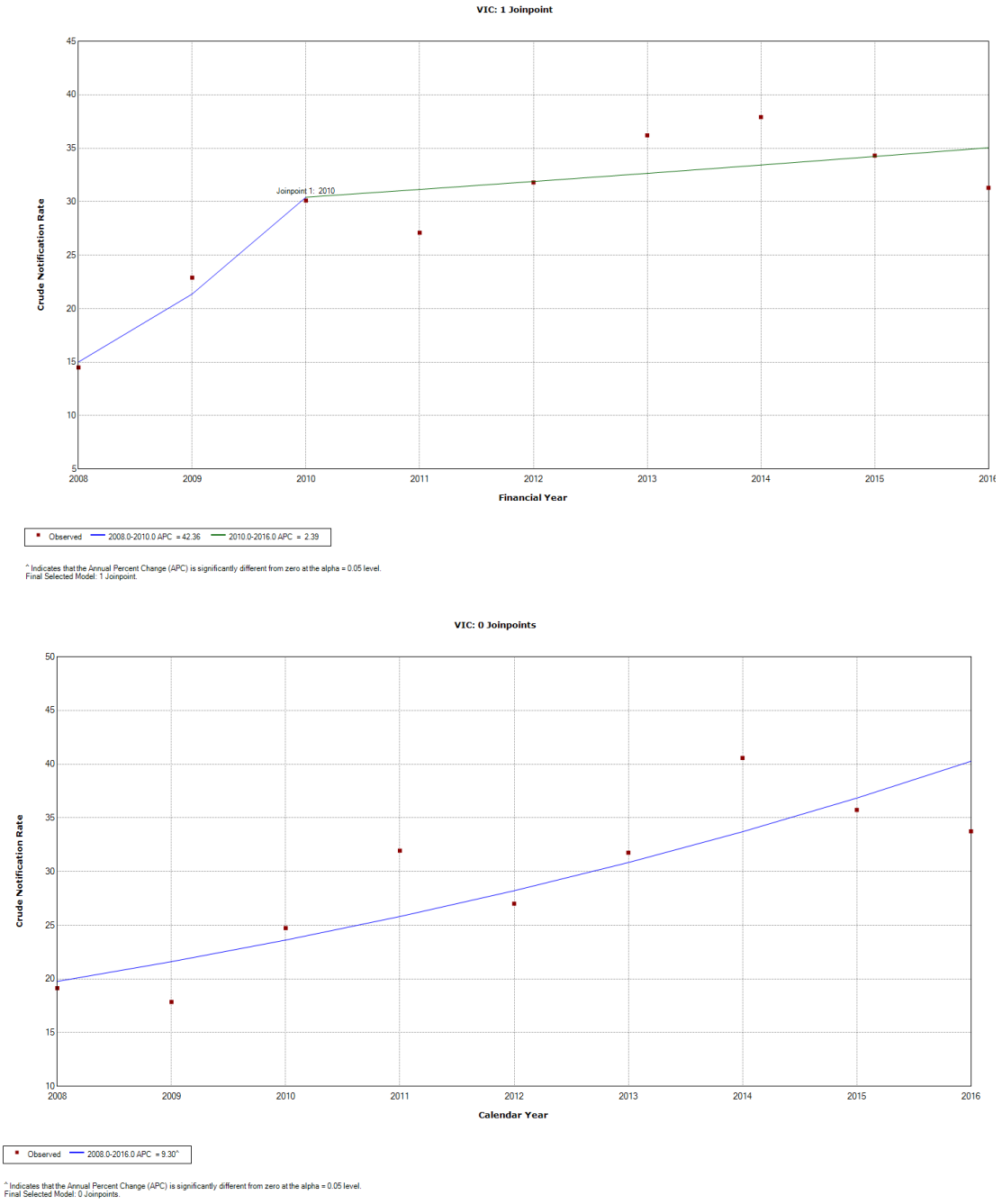
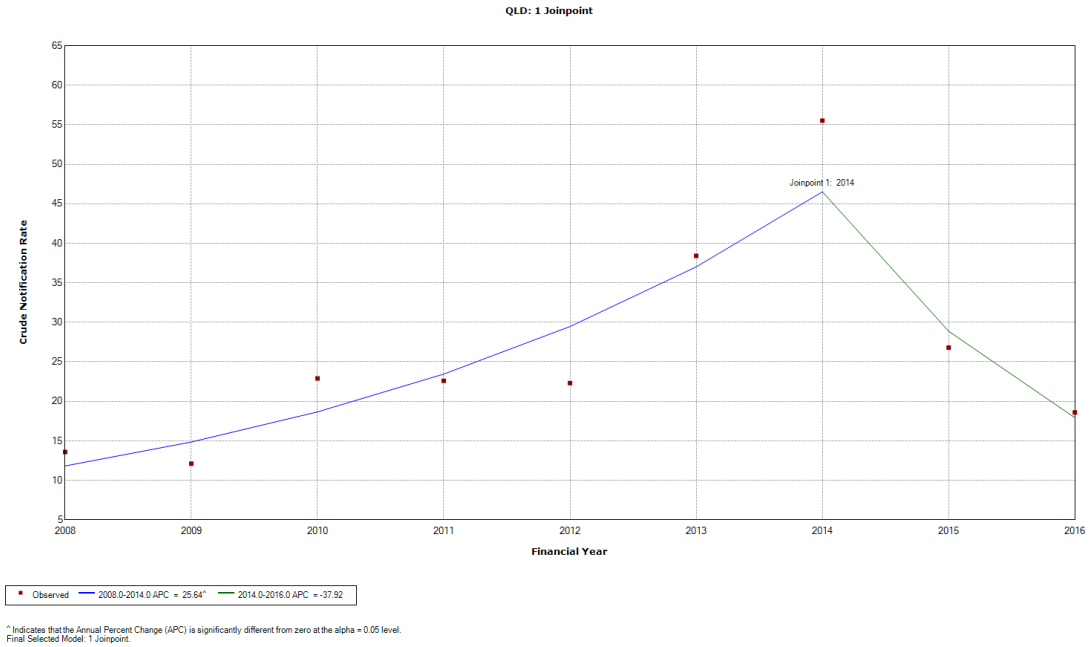


Fig S5. Crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by calendar year (bottom graph) displaying statistically significant change and Joinpoint indicating change in trend over the period 2008 to 2017, Victoria (^significantly different from zero at alpha = 0.05). APC= annual percentage change

S. Typhimurium - Queensland



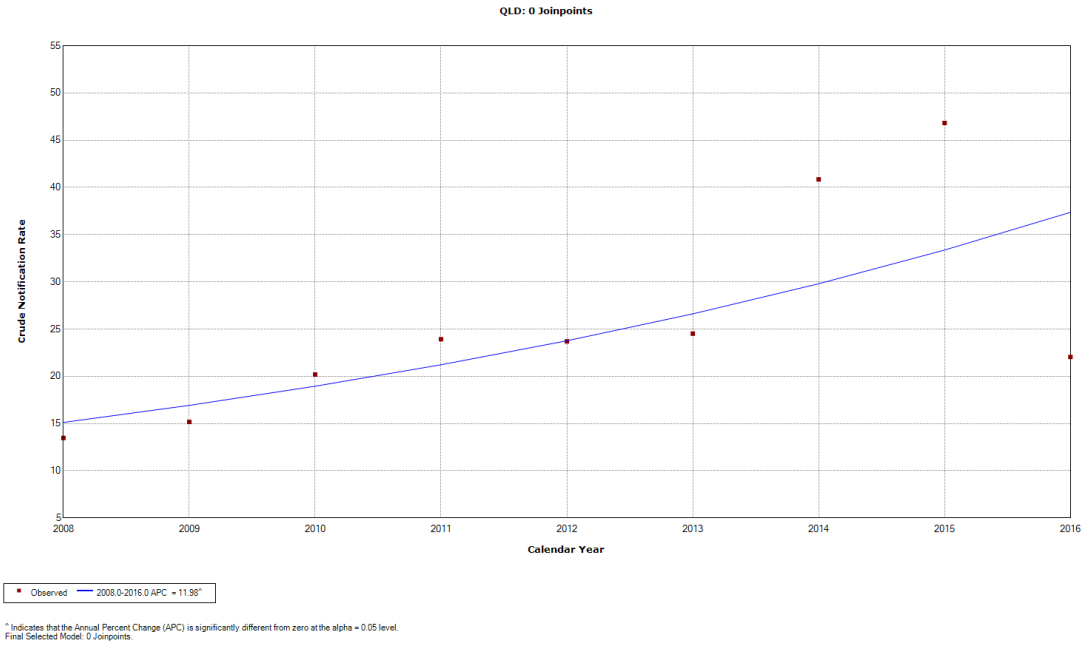


Fig S6. Crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population as the denominator by calendar year (bottom graph) displaying statistically significant change and Joinpoint indicating change in trend over the period 2008 to 2017, Queensland (^significantly different from zero at alpha = 0.05). APC= annual percentage change

S. Typhimurium - Western Australia

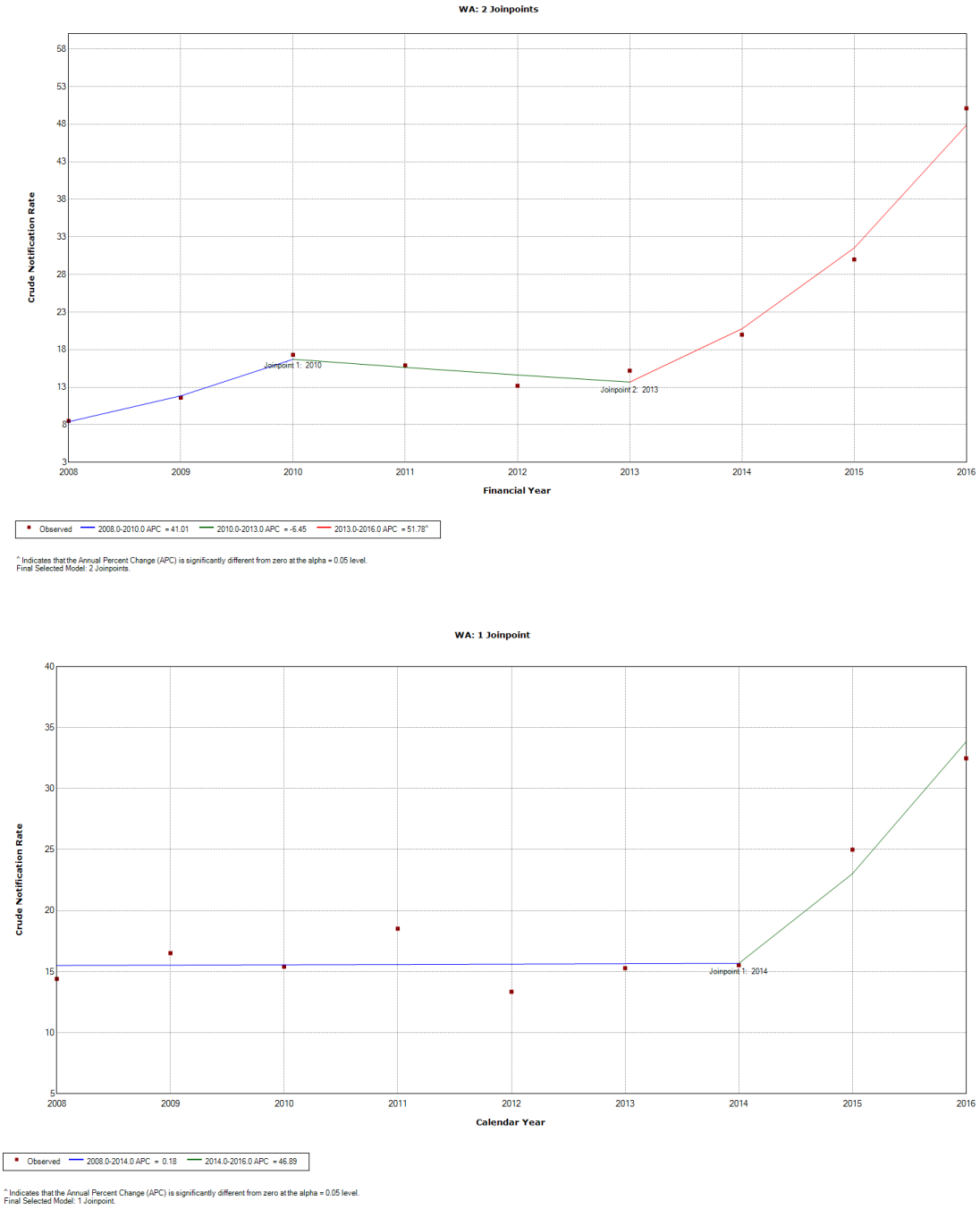
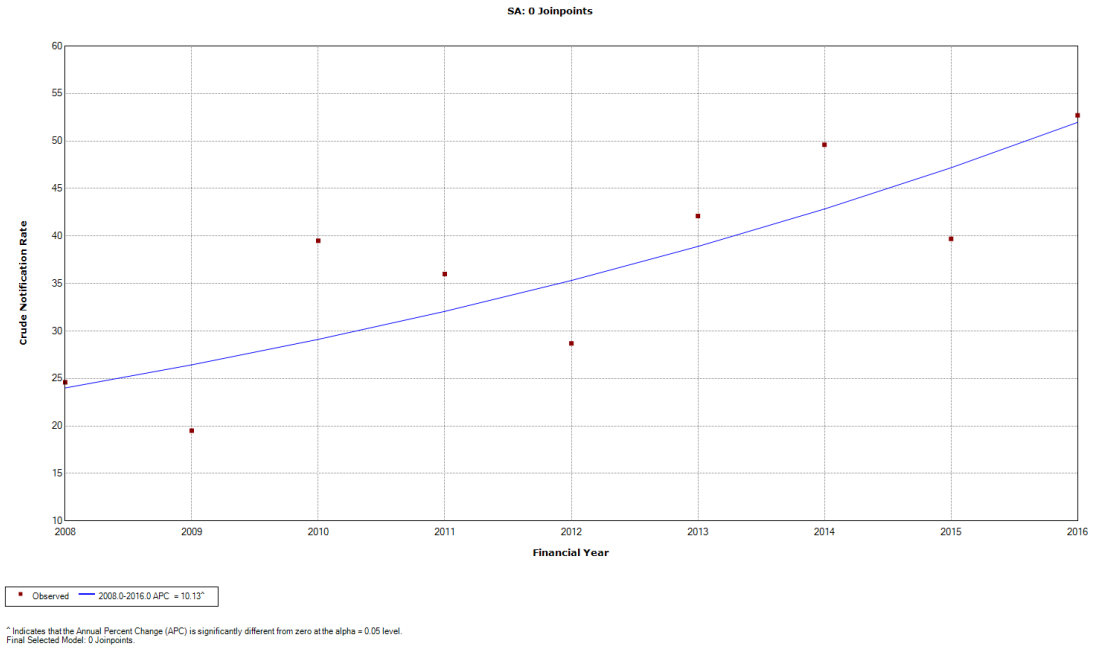


Fig S7. Crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by calendar year (bottom graph) displaying statistically significant change and Joinpoints indicating change in trend over the period 2008 to 2017, Western Australia (^significantly different from zero at alpha = 0.05). APC= annual percentage change

S. Typhimurium - South Australia



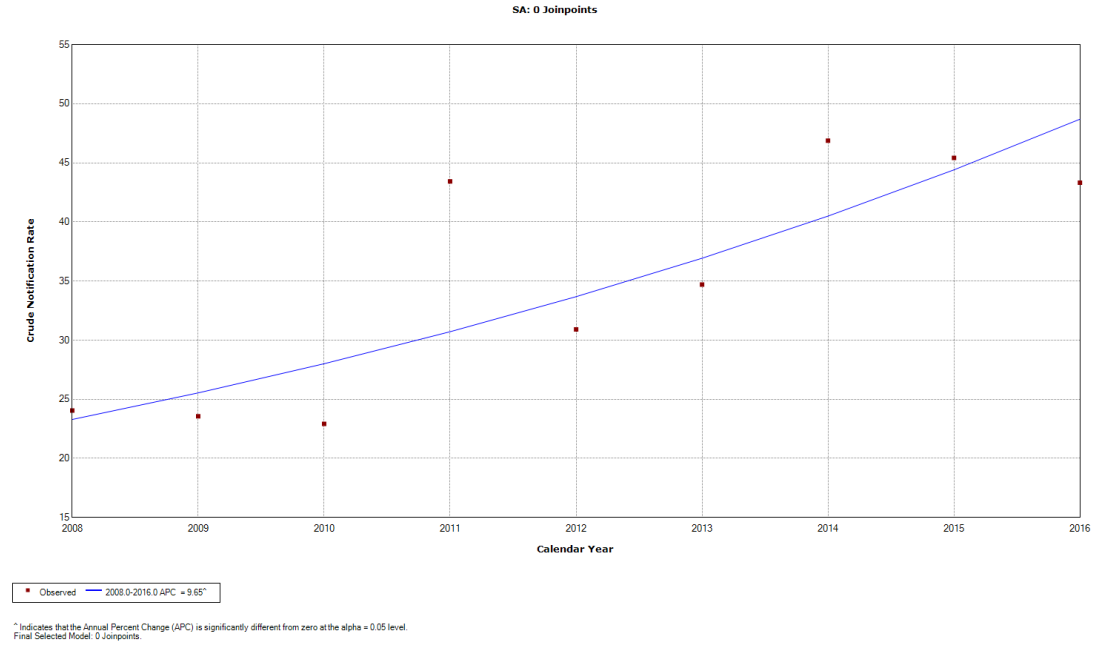
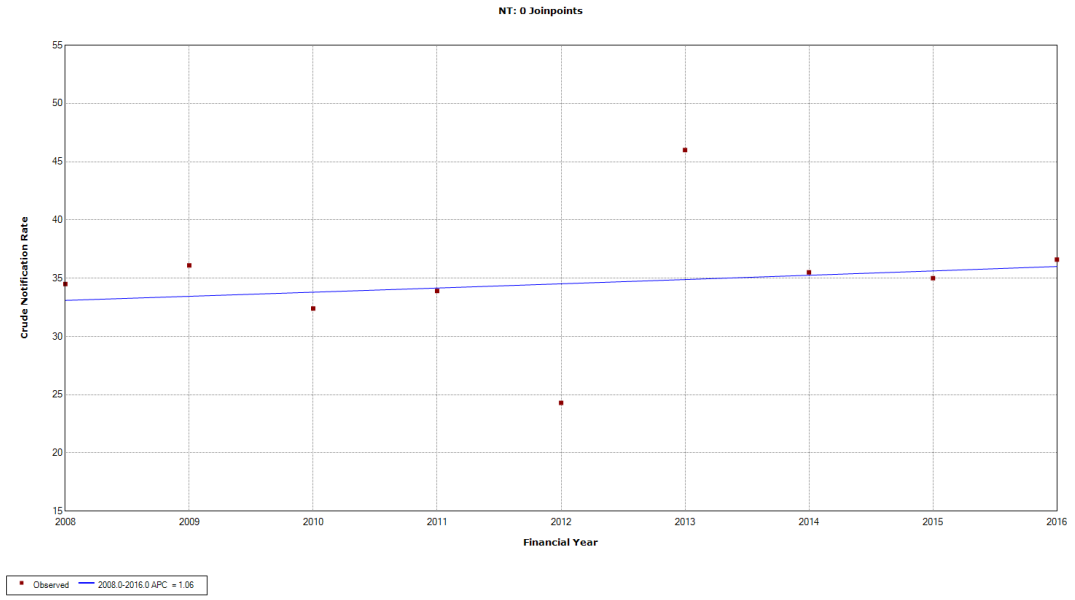


Fig S8. Crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by calendar year (bottom graph) displaying statistically significant change over the period 2008 to 2017, South Australia (^significantly different from zero at alpha = 0.05). APC= annual percentage change

S. Typhimurium - Northern Territory



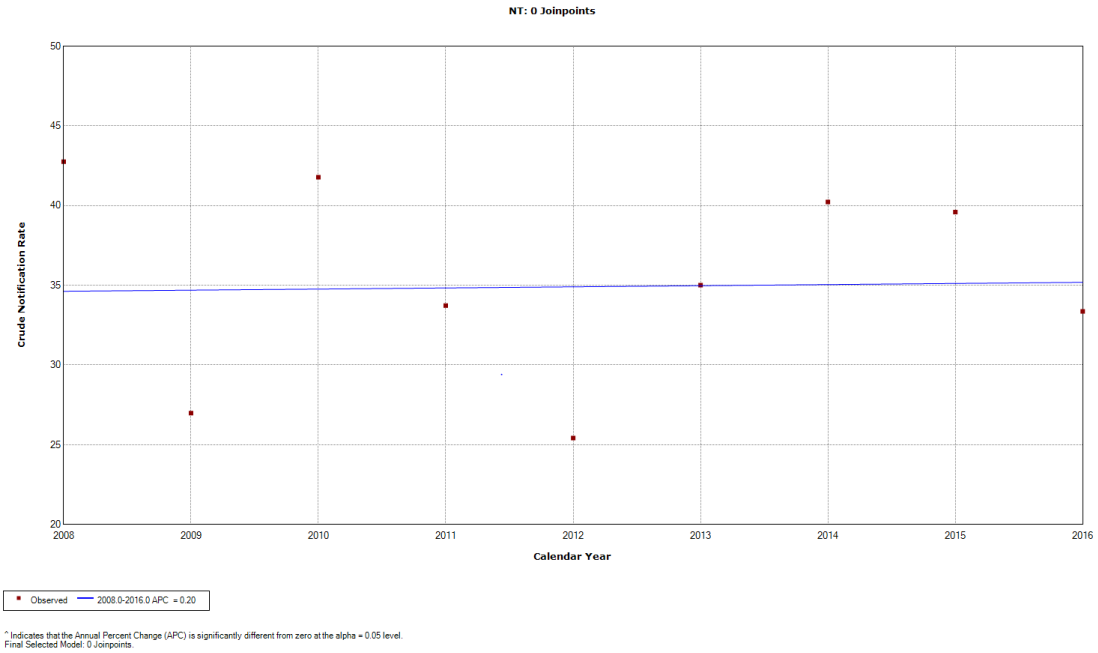
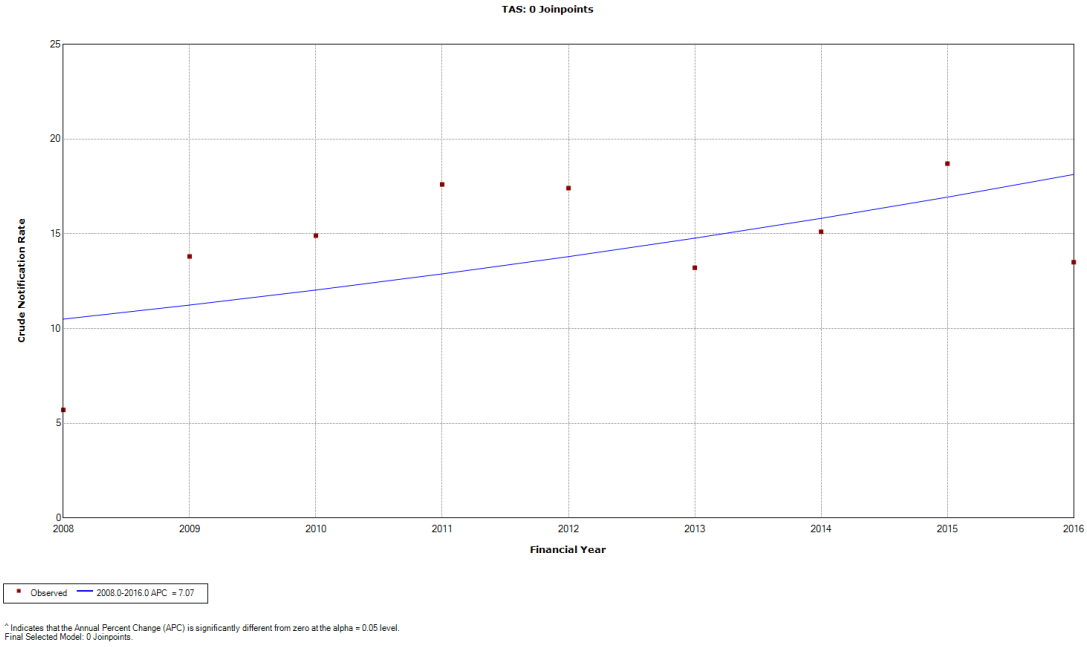


Fig S9. Crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by calendar year (bottom graph) not displaying statistically significant change over the period 2008 to 2017, Northern Territory. APC= annual percentage change

S. Typhimurium - Tasmania



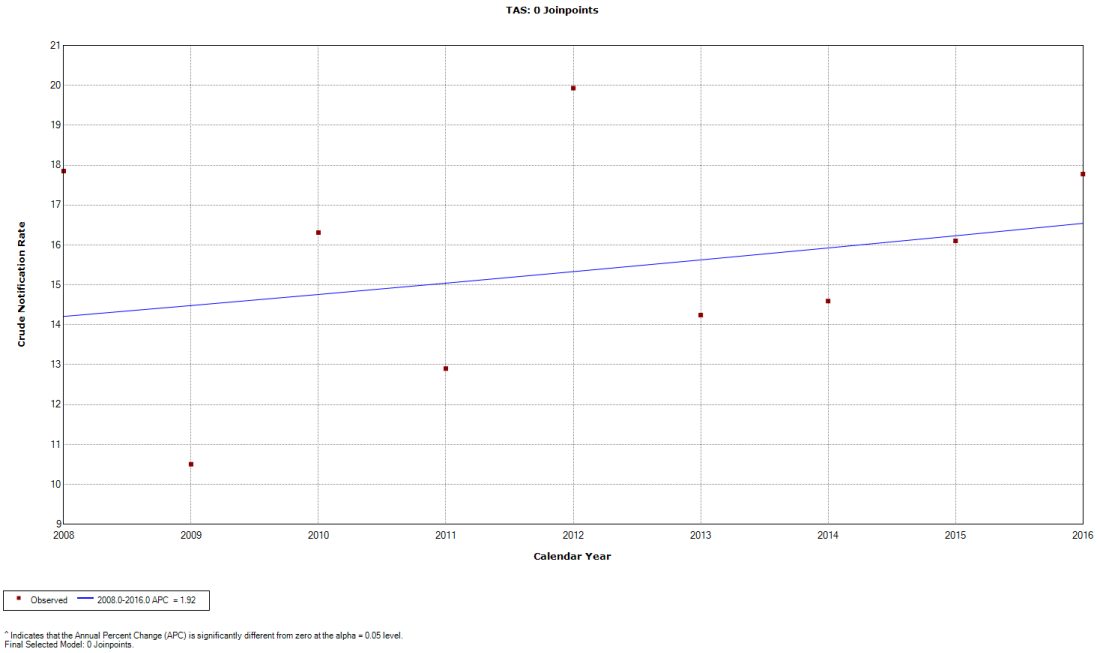
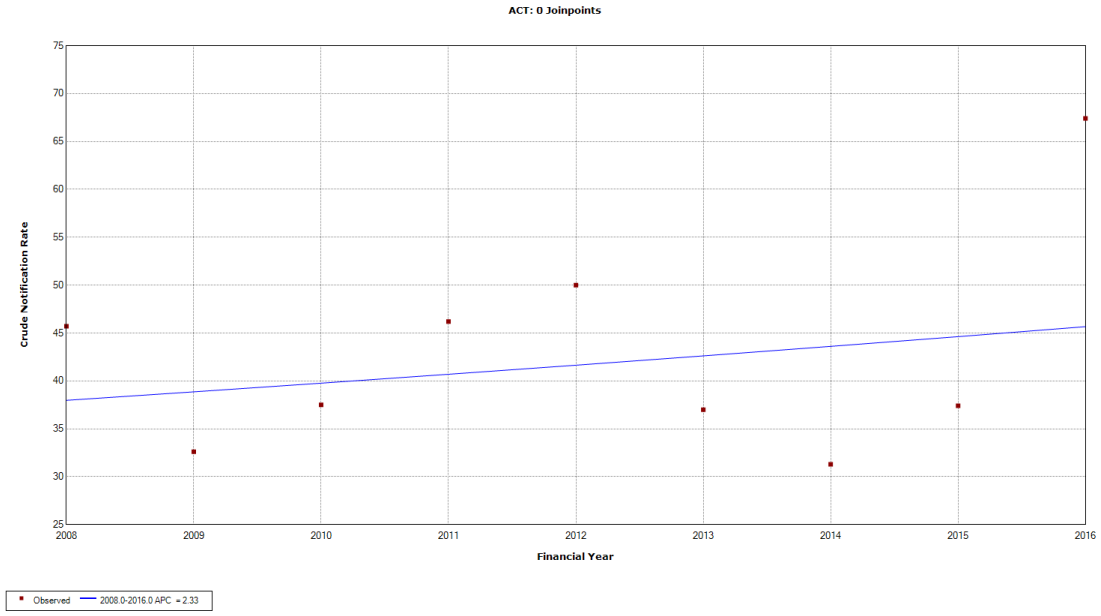


Fig S10. Crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by calendar year (bottom graph) displaying statistically significant change over the period 2008 to 2017,Tasmania (^significantly different from zero at alpha = 0.05). APC= annual percentage change

S. Typhimurium - Australian Capital Territory



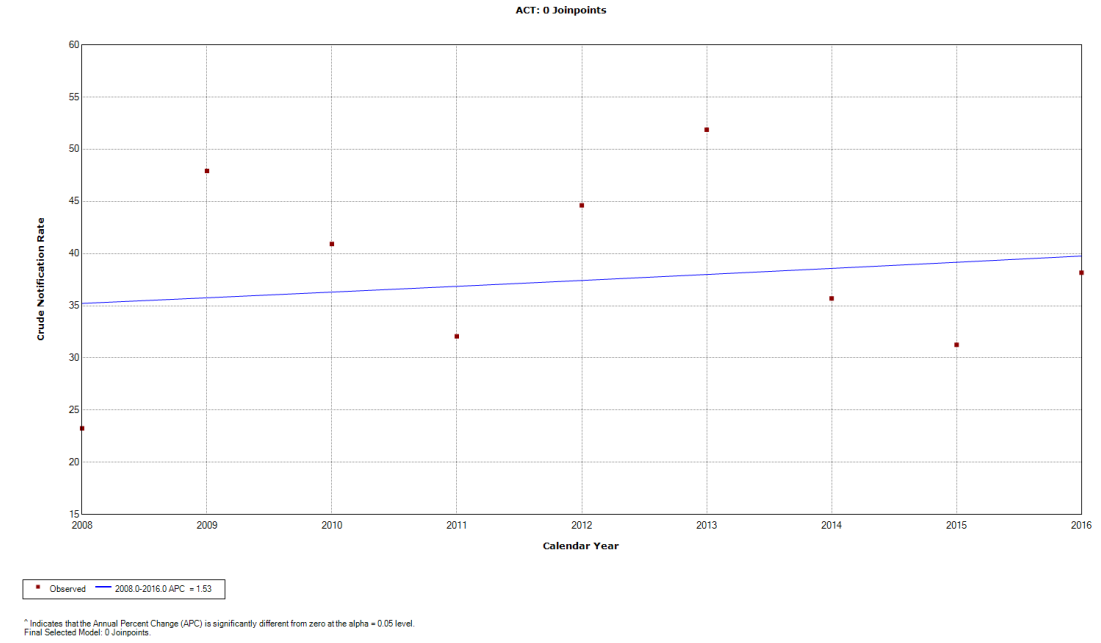


Fig S11. Crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by financial year (top graph) and crude *S*.Typhimurium notification rates (per 100,000 population) using population data as the denominator by calendar year (bottom graph) displaying statistically significant change over the period 2008 to 2017, Australian Capital Territory (^significantly different from zero at alpha = 0.05). APC= annual percentage change

Table S3. Trends in age-standardised incidence rates of *S*. Typhimurium infection and Joinpoint regression analysis by jurisdiction, Australia, 2008/09 to 2016/17

Jurisdiction	Age-standardised rate (per 100,000 population)		2008/09 to 2016/17		Joinpoint analysis		
	2008/09	2016/17	AAPC[2]	95% CI[1]	Time period	APC[3]	95% CI[1]
NSW	22.1	20.3	-0.8	-6.5, 5.2		No Joinpoint	
VIC	14.7	31.4	11.1^	1.1, 22.1	2008/09-2010/11	42.4	-11.7, 129.6
					2010/11-2016/17	2.3	-5.7, 10.9
QLD	13.8	18.6	5.2^	-10.1, 23.1	2008/09-2014/15	25.3	9.5, 43.3
					2014/15-2016/17	-37.7	-71.9, 38.0
WA	9.0	50.3	23.3^	15.6, 31.6	2008/09-2010/11	36.7	-42.5, 24.8
					2010/11-2013/14	-6.5	-60.7, 122.3
					2013/14-2016/17	51.9	-1.5, 134.2
TAS	29.7	36.5	2.4	-2.9, 8.0		No Joinpoint	
SA	25.7	53.9	10.0	3.2, 17.3		No Joinpoint	
NT	5.7	14.3	11.4	-2.8, 27.7	2008/09-2010/11	67.7	-15.8, 233.8
					2010/11-2016/17	-2.8	-13.5, 9.2
ACT	44.2	67	2.8	-4.7, 10.9		No Joinpoint	
Australia	16.9	29.2	7.2^	1.8, 12.8		No Joinpoint	

[1] confidence interval

[2] average annual percentage change

[3] average percentage change; estimated with the best-fitting Joinpoint model

^ significantly different from zero at alpha = 0.05

Number of Joinpoints is decided by the model

ACT, Australian Capital Territory; NT, Northern Territory; SA, South Australia; TAS, Tasmania; WA, Western Australia; QLD, Queensland; NSW, New South Wales; VIC, Victoria

Table S4. Trends in age-standardised incidence rates of non-Typhimurium *Salmonella* infection and Joinpoint regression analysis by jurisdiction, Australia, 2008/09 to 2016/17

Jurisdiction	Age-standardised rate (per 100,000 population)		2008/09 to 2016/17		Joinpoint analysis		
	2008/09	2016/17	AAPC[2]	95% CI[1]	Time period	APC[3]	95% CI[1]
NSW	12.6	24.9	7.2^	3.9, 10.6		No Joinpoint	
VIC	10.1	22.3	8.9^	4.9, 13.1		No Joinpoint	
QLD	31.6	58.7	8.9^	6.3, 11.5		No Joinpoint	
WA	17.0	40.3	11.8^	9.0, 14.7	2008/09-2010/11	46.9^	4.5, 106.6
					2010/11-2013/14	-2.8	-30.8, 36.7
					2013/14-2016/17	7.1	-9.7, 27.0
TAS	22.9	32.9	5.3	1.7, 8.9		No Joinpoint	
SA	16.4	29.3	9.6^	5.0, 14.4		No Joinpoint	
NT	156.9	164.3	0.2^	-5.4, 6.2		No Joinpoint	
ACT	13.3	21.9	7.1^	2.5, 12.0		No Joinpoint	
Australia	18.8	34.6	7.3^	5.0, 9.7		No Joinpoint	

[1] confidence interval

[2] average annual percentage change

[3] average percentage change; estimated with the best-fitting Joinpoint model

^ significantly different from zero at alpha = 0.05

Number of Joinpoints is decided by the model

ACT, Australian Capital Territory; NT, Northern Territory; SA, South Australia; TAS, Tasmania; WA, Western Australia; QLD, Queensland; NSW, New South Wales; VIC, Victoria.

Table S5. Trends in incidence of *S*. Typhimurium and Joinpoint regression analysis using culture data as the denominator, Australia, 2008/09 to 2016/17

Jurisdiction	Age-standardised rate (per 100,000 population)		2008/09 to 2016/17		Joinpoint analysis		
	2008/09	2016/17	AAPC[2]	95% CI[1]	Time period	APC[3]	95% CI[1]
NSW	1,307.1	872.7	-5.2	-10.9—1.0		No Joinpoint	
VIC	983.7	1,372.1	5.2	-0.8—11.6	2008/09-2010/11	39.7^	0.5, 94.3
					2010/11-2016/17	-2.3	-6.6, 2.0
QLD	897.7	617.9	-4.2	-14.8—8.0	2008/09-2014/15	11.9^	1.0, 23.9
					2014/15-2016/17	-39.8	-67.1, 10.1
WA	931.4	2,224.4	11.2^	7.4—15.2	2008/09-2009/10	15.4	-5.6, 41.1
					2009/10-2013/14	-11.2^	-16.7, -5.4
					2013/14-2016/17		38.5, 69.3
TAS	1,387.7	1,287.0	- 2.3	-6.7, 2.3		No Joinpoint	
SA	1,260.5	1,933.6	5.0	-1.7, 12.1		No Joinpoint	
NT	366	575.3	5.9	-3.9, 16.7	2008/09-2010/11	103.9^	8.1, 284.5
					2010/11-2016/17	-7.1	-14.7, 1.1
ACT	2,274.0	2,556.2	-1.9	-9, 5.7		No Joinpoint	
Australia	1,104.2	1,173.1	0.3	-4.2, 5.0		No Joinpoint	

[1] confidence interval

[2] average annual percentage change

[3] average percentage change; estimated with the best-fitting Joinpoint model

^ significantly different from zero at alpha = 0.05

Number of Joinpoints is decided by the model

ACT, Australian Capital Territory; NT, Northern Territory; SA, South Australia; TAS, Tasmania; WA, Western Australia; QLD, Queensland; NSW, New South Wales; VIC, Victoria.

Table S6. Trends in incidence of non-Typhimurium *Salmonella* and Joinpoint regression analysis using culture data as the denominator, Australia, 2008/09 to 2016/17

Jurisdiction	Age-standardised rate (per 100,000 population)		2008/09 to 2016/17		Joinpoint analysis		
	2008/09	2016/17	AAPC[2]	95% CI[1]	Time period	APC[3]	95% CI[1]
NSW	743.3	1,074.5	2.6	-0.5, 5.8		No Joinpoint	
VIC	685.4	978.3	3.1	-0.3, 1.1		No Joinpoint	
QLD	2,042.2	1,961.9	-1.2	-3.5, 1.1		No Joinpoint	
WA	1,829.8	1,795.9	-2.4	-5.3, 0.6		No Joinpoint	
TAS	1,451.5	1,372.6	-1.0	-4.6, 2.8		No Joinpoint	
SA	821.3	1,057.8	4.6^	0.3, 9.0		No Joinpoint	
NT	7,116.2	6,234.8	-0.9	-6.2, 4.7	2008/09-2009/10	15.9	-14.1, 56.5
					2009/10-2013/14	-16.9^	-28.4, -3.4
					2013/14-2016/17	10.9^	0.9, 21.9
ACT	659.7	836.4	2.8	-1.3, 7.1		No Joinpoint	
Australia	1,234.5	1,394.9	0.5	-1.6, 2.5		No Joinpoint	

[1] 95% confidence interval

[2] average annual percentage change

[3] average percentage change; estimated with the best-fitting Joinpoint model

^ significantly different from zero at alpha = 0.05

Number of Joinpoints is decided by the model

ACT, Australian Capital Territory; NT, Northern Territory; SA, South Australia; TAS, Tasmania; WA, Western Australia; QLD, Queensland; NSW, New South Wales; VIC, Victoria.

CHAPTER 3 –
FOODBORNE OUTBREAKS IN THE AUSTRALIAN FOOD SERVICE INDUSTRY, 2001-2016

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Prologue

In Australia, foodborne disease outbreaks are a public health concern due to the human health implications and effects on the food industry. This study was conducted to describe investigated outbreaks associated with the preparation of food in restaurants, take-away (non-franchised), cafés, commercial caterers, bakeries, national franchised fast food restaurants, fairs/festivals/mobile services in Australia between 2001 and 2016. The outcomes of the study will improve the understanding of factors leading to outbreaks of human illness linked to food service businesses in Australia, and provide an evidence base for targeting public health interventions and inform policy and guideline formulation.

My role

I conducted the following tasks as part of this project:

- Developed the data analysis plan;
- Conducted a literature review;
- Cleaned and analysed the dataset using Stata and Microsoft Excel; and
- Prepared an advanced draft of a paper for publication in a national or international peer-reviewed journal.

Lessons learnt

Due to data issues in the OzFoodNet Outbreak Register, associated with the extensive use of free text fields, I had to do a lot of recoding in Microsoft Excel and Stata. Issues that I encountered include an inconsistency in entries due to different spellings of etiological agents, spelling mistakes of food vehicles, extra spaces, and varying classification of food vehicle information (e.g. eggs benedict or hollandaise sauce) and the amount of detail entered per outbreak. The analysis of free text field is not impossible but it is time-consuming and complicated. A standardised data entry approach with limited free text options would significantly improve the data analysis process.

I initially started my analysis using a US Centers for Disease Control and Prevention[1, 2] method of food categorisation, whereby implicated foods are assigned to predefined food categories using recipes. Foods are grouped into three broad categories (aquatic

animals, land animals and plants) and 17 sub-categories based on ingredients of the implicated food to calculate attribution percentages. However I found this method assigned composite foods, such as sandwiches, predominantly to a complex category (multiple ingredients), which I considered unlikely to be useful information in terms of informing public health action. I subsequently used the food categories from the updated but not yet implemented OzFoodNet Outbreak Register data dictionary to categorise the implicated food vehicle for my analysis. These food categories allow the implicated food to be categorised into broad and more specific food categories, rather than ingredients. My experience identified that even with this improved method, certain foods remain difficult to categorise, such as custard buns/éclairs, cream buns/cakes, kebabs, and sandwiches/burger/rolls. However, overall, my experience of using these food categories for my study indicates that once implemented by OzFoodNet they will greatly simplify the analysis of OzFoodNet Outbreak Register data compared to using an ingredient-based analysis method.

Public health implications of this work

The results of this study provide OzFoodNet with information about the risk factors leading to outbreaks of human illness following the consumption of food at food service establishments in Australia between 2001 and 2016. The findings of this study can be used to inform the development of national risk management policies in Australia.

This study highlights the lack of completeness of fields relating to contributing factors. This information is important to making recommendations for reducing cross-contamination and improving hygiene in food service businesses.

Master of Philosophy (Applied Epidemiology) core activity requirement

- Analyse a public health dataset;
- Undertake a literature review that demonstrates skills in conducting a targeted literature search and synthesis; and
- Prepare an advanced draft of a paper for publication in a national or international peer-reviewed journal.

Advanced draft of paper for publication

Foodborne outbreaks in the Australian food service industry, 2001 to 2016: what are the risks?

Brigitta Osterberger[1, 2], Benjamin Polkinghorne[1], Anna-Jane Glynn-Robinson[2] and Martyn Kirk[1]

[1] National Centre for Epidemiology and Population Health, Research School of Population Health, ANU College of Health and Medicine, Australian National University

[2] Communicable Diseases Epidemiology and Surveillance Section, Office of Health Protection, Australian Government Department of Health

Corresponding author:

Mrs Brigitta Osterberger

Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
Phone: 02 6232 8985
Email: Brigitta.Osterberger@health.gov.au

Abstract

Introduction: Outbreaks caused by foodborne disease have a considerable public health impact, with food service businesses frequently implicated in foodborne illness.

Methods: To describe the epidemiology of foodborne outbreaks associated with the Australian food service industry, we analysed foodborne and probable outbreaks reported to the OzFoodNet Outbreak Register from 2001 to 2016.

Results: There were 1,276 food service industry –associated outbreaks reported between 2001 and 2016, affecting 20,450 people, leading to 1,697 hospitalisations and 12 deaths. The percentage of foodborne outbreaks in the food service industry increased from 5.3% (67/1,276) in 2008 to 9.2% (118/1,276) in 2016. The median annual number of outbreaks was 80 (interquartile range 65-92). The most commonly reported food service businesses were restaurants (67.4%, 860/1,276), commercial caterers (12.2%, 156/1,276) and non-franchised take-aways (11.9%, 152/1,276). Approximately 60% (12,198/20,450) of cases ate at restaurants. *Salmonella* infection was the major cause of foodborne outbreaks (37.6%; 480/1,276), outbreak-associated illnesses (46.1%; 9,436/20,450) and deaths (83.3%, 10/12). The consumption of poultry meat, egg sauce/dressing, and Vietnamese rolls (Bánh mì) were the most commonly implicated foods. The most frequently reported contributing factors were related to food worker health and hygiene (20%, 255/1,276) and food handling and preparation practices (18.9%, 241/1,276). Foodborne outbreaks were more frequently reported in the warmer months (40%, 540/1,276). An increase in the number of outbreaks was identified around the “Christmas party season “and commercial caterers accounted for 21.1% (12/57) of foodborne outbreaks around Melbourne Cup Day.

Conclusion: Targeted public health initiatives to improve food safety practices particularly whilst undertaking high-volume food production and consumer education on the risk of the consumption of undercooked poultry meat and raw egg and foods where it may not be apparent that raw egg is an ingredient could further reduce foodborne outbreaks.

Keywords: foodborne disease, restaurants, infectious disease epidemiology, outbreaks, food service business, risk factors, public health

Introduction

Foodborne disease is a public health concern and a common cause of morbidity and mortality globally.[3] The World Health Organization estimated the burden of foodborne diseases in 2010 to be 600 million foodborne illnesses and 420,000 deaths per year worldwide.[3, 4]

The developing world has the highest incidence rates and death rates attributable to foodborne disease.[3, 4] However, foodborne illness affects industries and consumers worldwide regardless of level of country development.[5] Foodborne disease outbreaks cause substantial public health impacts and drain resources[6] as well as lead to major ramifications for the food service industry[7] through lost business revenue, legal action and damaged consumer trust.[8] Although largely preventable through effective food safety[9], foodborne outbreaks continue to occur in the food service industry.

International studies have shown that eating in a food service business is associated with an increased risk for acquiring a foodborne illness.[10] In particular, sit-down dining style restaurants[11-15] are the most common setting for reported restaurant-associated foodborne disease outbreaks.

OzFoodNet – Australia's national surveillance system of foodborne diseases – has conducted surveillance of gastroenteritis and foodborne disease and identified outbreaks of foodborne or probable foodborne illness since 2000.[16] OzFoodNet epidemiologists in all eight states and territories send outbreaks investigated by their jurisdiction to the Australian Government Department of Health where it is stored in a Microsoft Access database, the OzFoodNet Outbreak Register. Investigating the epidemiology of foodborne disease outbreaks associated with the Australian food service industry would be beneficial to determine what the risk factors are for foodborne outbreaks associated with food prepared by a food service business in Australia.

The aim of this study was to describe epidemiological characteristics of investigated foodborne and probable foodborne outbreaks where food was prepared by restaurants, take-away (non-franchised), commercial caterers, bakeries, national

franchised fast food restaurants, fairs/festivals markets/mobile service in Australia between 2001 and 2016.

Materials and Methods

Study design

A retrospective descriptive data analysis using data obtained from the OzFoodNet Outbreak Register was conducted. Information collected for each outbreak includes state or territory of outbreak, the year and month the outbreak occurred, setting where food was prepared, median age of cases, percentage of cases by sex, median duration of outbreaks, number of illnesses, hospitalisations and deaths, food vehicle, the etiological agent, contributing factors, and a free text remarks field. In this study, the mode of transmission (e.g. foodborne or probable foodborne) and the food vehicle as entered into the register by the OzFoodNet epidemiologists was accepted and used for the analysis. Supplementary Information Table S1 summarises the case definitions and the evidence required for the mode of transmission and food vehicle used in this study.

Outbreak and setting definitions

The analysis was restricted to investigated confirmed foodborne and probable foodborne outbreaks (hereafter referred to as 'foodborne outbreaks') with an onset between 2001 and 2016 inclusive and where food was prepared in a food service business in Australia. As per the OzFoodNet Register data dictionary, a foodborne outbreak was defined as an incident where ≥2 persons experienced illness after consuming a common meal or food and analytical epidemiological and/or microbiological evidence implicated the food or meal as the source of illness. A probable foodborne outbreak was defined as an incident where ≥2 persons experienced illness after consuming a common meal or food and the specific meal or food is probable, but other transmission modes cannot be ruled out.[17] For this analysis, outbreaks associated with the food service industry was defined as the setting where food was prepared and listed as restaurants, take-away (non-franchised), national franchised fast food restaurants, commercial caterer, bakery, and fair/festival/markets/mobile service. The definitions for the settings used in this study are described in Table 1.

Table 1. Definitions used for outbreaks and settings where food was prepared

Term	Definition
Restaurant	Includes cafés and sit-down dining in hotels and food courts.
Take-away (non-franchised)	Consists of milk bars and fast food outlets where the food was eaten off-site from where it was prepared and purchased.
National franchised fast food restaurants	National franchised fast food restaurant such as large hamburger, pizza, or chicken franchises that sell food nation-wide.
Commercial caterer	A setting in which food was produced for a commercially catered special function or group (e.g. wedding or other function, or airlines) where the food was prepared off-site from where it was served.
Bakery	Venue that produces and sells baked bread, pastries and sweet products.
Fair/festival/markets/mobile service	Fair, festival, markets or other temporary or mobile food service.

Source: [17]

Etiological agent classification

All foodborne outbreaks with a single etiological agent, either confirmed or suspected, were included in the etiology analyses. These were categorised according to the US Centers for Disease Control and Prevention (CDC) guidelines[18], except for rotavirus, bacterial and fish toxins. Rotavirus is not an etiology listed in the CDC guidelines, therefore it was categorised like norovirus as per the CDC guidelines. Bacterial toxins were classified into five etiological categories, as per May et al[19]:

- "*Bacillus cereus*" (if listed as the sole etiology);
- "*Clostridium perfringens*" (if listed as the sole etiology);
- "*Staphylococcus aureus*" (if listed as the sole etiology);
- "Preformed toxin" (if etiology was listed as preformed toxin or both *Staphylococcus aureus* and *Bacillus cereus*); and
- "*In vivo* toxin" (if etiologies were listed as both *Clostridium perfringens* and *Bacillus cereus*).

For outbreaks due to fish toxins such as scombroid toxin and ciguatoxin, only epidemiological (or microbiological) evidence was required. The remainder of the etiologies were grouped into either a "Suspected etiology" category if the identified etiological agent didn't meet the CDC guidelines; or an "Unknown" category if not enough information was available to identify a specific etiology.

Food vehicle classification

Implicated foods were categorised using the new food categories from the updated, but not yet implemented, 2016 OzFoodNet Outbreak Register data dictionary.[20] Outbreaks selected for inclusion were identified after third party review to determine the allocation of outbreaks into the food categories and for inclusion in the final study. Food vehicles were grouped into two levels of classification: Level 1 foods include 13 broad first tier food categories and Level 2 breaks the foods into 64 specific second tier food categories. Supplementary Information Table S1 summarises the Level 1 and 2 food categories used in this study. Food vehicles as they were listed in the OzFoodNet Outbreak Register were allocated into these food categories. Food was categorised as a composite food (i.e. consisting of multiple ingredients) when a specific contaminated ingredient could not be identified or the category that best fit their description. A process was established to assign foods that were identified as difficult to assign (e.g. sandwiches). Assignment criteria for these food vehicles are shown in Supplementary Information Table S2.

Contributing factors classification

Contributing factors were grouped into four categories for analysis, adapted from Angelo et al[8]: food worker health and hygiene, food contamination before arrival at the food service business, food handling and preparation practices in the food service business, and other contamination factors. The remainder of the etiologies were grouped into an "Unknown" category.

Data analyses

Univariate frequencies of outbreak characteristics were calculated, including demographic (number of cases, median age, sex,); outcomes (number of persons ill, hospitalisation, deaths); geographical distribution by state and territory; reported etiologies; food service business where food was prepared; and contributing factors. A

total of 9,950 outbreaks were excluded after applying inclusion and exclusion criteria, resulting in 447 foodborne and 829 probable foodborne outbreaks included in the study. A summary of the inclusion and exclusion process is shown in Fig 1.

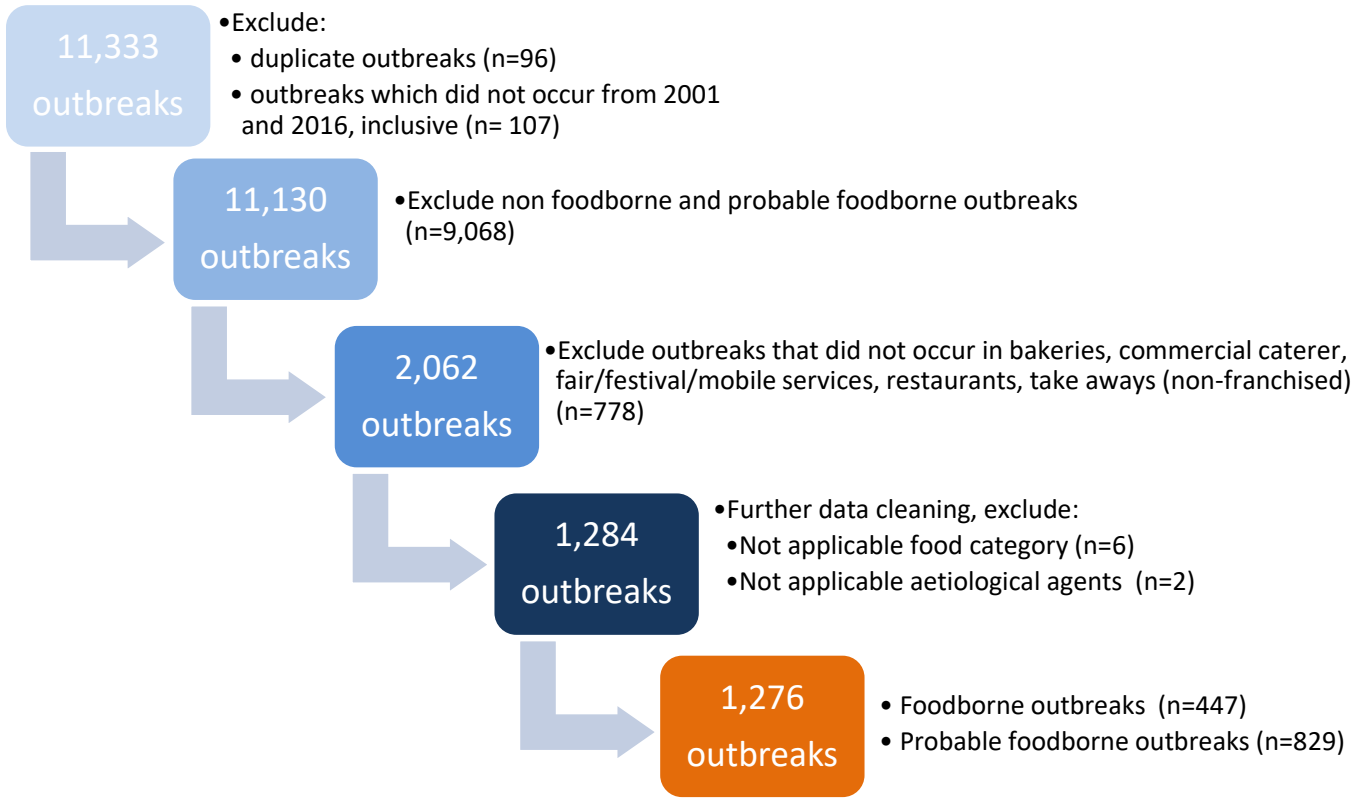

Fig 1. Flowchart of the number of reported outbreaks after inclusion/exclusion criteria are applied, OzFoodNet Outbreak Register, 2001 to 2016

The median values and interquartile (IQR) ranges were calculated for the number of cases, hospitalisations, deaths, and age. The crude rate per 1 million population of reported food service setting-associated foodborne outbreaks for each state and territory per year was calculated using Australian Bureau of Statistics[21] estimated population data as the denominator.

The application of inclusion and exclusion criteria, data cleaning and analysis was performed in Microsoft Excel 2010 (Microsoft, Redmond, WA) and Stata SE version 13 (Stata Corp, 2013; Stata Statistical Software: Release 13; StataCorp LP, College Station, TX, USA).

Ethics

The Australian National University Human Research Ethics Committee [protocol: 2016/272] approved the conduct of this study.

Results

During 2001–2016, a total of 11,226 gastrointestinal disease outbreaks were reported in the OzFoodNet Outbreak Register. Of these, 2,062 were foodborne or probable foodborne outbreaks. During the study period, there were 1,276 reported foodborne outbreaks in the food service industry in Australia. This constitutes 61.9% (1,276/2,062) of all reported foodborne outbreaks during the study period. Of these outbreaks, 35% (447/1,276) were foodborne and 65% (829/1,276) were probable foodborne. As a result of foodborne outbreaks associated with the food service industry, 20,450 persons became ill, 6,927 persons sought treatment from a medical practitioner and 1,697 were hospitalised (Table 2). Twelve deaths were associated with these outbreaks, equating to a case fatality rate of 0.1% (12/20,450). The median number of outbreaks per year was 80 (interquartile range (IQR) 65-92) and the median outbreak size was 8 persons (IQR 4-17).

Table 2. Characteristics of food service industry-associated foodborne disease outbreaks, OzFoodNet Outbreak Register, 2001-2016 (n=1,276)

Characteristics		Food service business setting where food is prepared N (%)						
		Restaurants	Commercial caterer	Take-away (non-franchised)	Bakeries	National franchised fast-food restaurants	Fairs, festivals, markets, mobile service	Total
Demographics	Total number of cases	12,198 (59.6)	3,960 (19.4)	2,133 (10.4)	1,467 (7.2)	279 (1.4)	413 (2)	20,450 (100)
	Median age (IQR)	35 (27-44)	38 (30-47)	28 (24-37)	32.5 (25.5-38)	31 (20.5-38)	30 (24-39.5)	34 (26.5-43)
	Male (median %)[a]	43	50	50	50	53.5	40	44
	Female (median %)[a]	53	50	50	50	46.5	60	50
Outcomes	Presented to a medical practitioner	3,854 (55.6)	657 (9.5)	1,032 (14.9)	883 (12.7)	131 (1.2)	370 (5.3)	6,927 (100)
	Hospitalisations	868 (51.1)	156 (9.2)	255 (15)	336 (19.8)	41 (2.4)	41 (2.4)	1,697 (100)
	Deaths	4 (33.3)	4 (33.3)	2 (16.7)	2 (16.7)	0 (0)	0 (0)	12 (100)
Total number of outbreaks		860 (67.4)	156 (12.2)	152 (11.9)	63 (4.9)	28 (2.2)	17 (1.3)	1,276 (100)

IQR = interquartile range

[a] 178 outbreaks missing entries

In Australia, the annual number of food service industry –associated outbreaks and the number of persons ill has increased steadily over time (Fig 2). Besides a decrease in number of outbreaks observed in 2012, the percentage of foodborne outbreaks increased from 2008 (5.3%, 67/1,276) to 2016 (9.2%, 118/1,276).

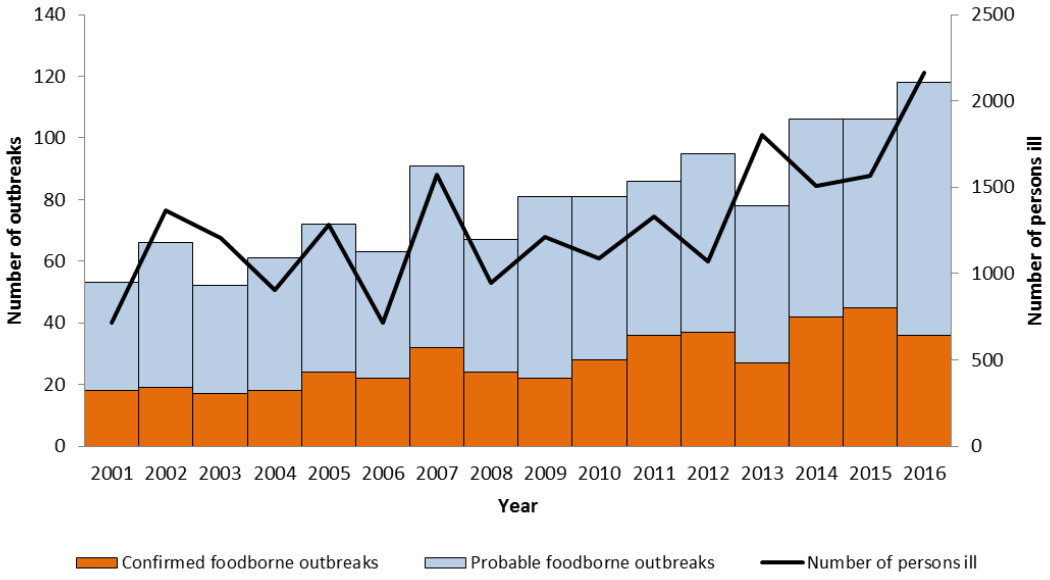

Fig 2. Number of foodborne outbreaks (confirmed and probable foodborne outbreaks) associated with food service industry and number of persons ill, by year, OzFoodNet Outbreak Register, 2001-2016

The total number of food service industry-associated outbreaks by state and territory over the study period ranged from 29 outbreaks (2.3 %) in Tasmania to 559 outbreaks in New South Wales (NSW) (43.8%). The average number of outbreaks per million population by state and territory for the 16-year period was highest in the Northern Territory (11.2 per 1 million population), Australian Capital Territory (ACT) (7.4 per 1 million population) and NSW (5 per 1 million population).

Food vehicles implicated in outbreaks

The most common food vehicle associated with outbreaks in the food service industry was “Meats” (12.4%, 158/1,276; Table 3). Of these, meals consisted primarily of poultry meat (chicken, duck, quail or pigeon) (47.5%, 75/158). In the majority of outbreaks where “Meats” were implicated, foods were prepared in a restaurant (59.5%, 94/158, affecting 1,029 persons). The consumption of “Meats” and “Salads” accounted for one-third (1,322/3,960) of cases who consumed these foods prepared by commercial caterers (Table 3).

Although “Eggs” were the second most commonly reported food category, implicated in 139 (10.9%) outbreaks, they caused the most outbreak-associated illness (12%; 2,453/20,450) and hospitalisations (26.6%, 451/1,697) during the study period. Of these egg-related outbreaks, the majority (94.2%, 131/139) were found to be due to contamination with *Salmonella*. “Eggs” also accounted for the majority of cases (20.1%, 2453/12,198) in restaurants (Table 3).

After “Multiple foods” (84/1,276; where multiple food items had the potential to result in illness), Egg sauce/dressing (6%, 77/1,276) was the most commonly reported level 2 food category, followed by Composite foods (3.9%, 53/1,276), Fish (3.3%, 42/1,276) and Rolls (3.2%, 43/1,276). Of the latter, Vietnamese rolls (i.e. Bánh mì) (81.4%, 35/43) was the main implicated food vehicle. The consumption of Vietnamese rolls was responsible for nearly 30% (539/2,133) of cases who ate food prepared by a non-franchised take-away and nearly 20% (301/1,697) of all hospitalisations during the study period.

Table 3. Number of food service industry-associated foodborne disease outbreaks and number of persons affected by implicated food, etiological agent and food service business setting, OzFoodNet Outbreak Register, 2001-2016

Food vehicle category (Level 1)	**Food service business setting where food is prepared** Number of outbreaks (number of persons affected)[c]						
	Restaurants	Commercial caterers	Take-away (non-franchised)	Bakeries	National franchised fast-food restaurants	Fairs, festivals, markets, mobile service	Total
Meats	94 (1,029)	25 (663)	31 (281)	1 (17)	6 (26)	1 (10)	158 (2,026)
Eggs	115 (2,453)	2 (82)	15 (282)	5 (93)	0 (0)	2 (25)	139 (2,935)
Specialty/Ethnic	23 (163)	6 (87)	26 (611)	16 (641)	8 (57)	0 (0)	79 (1,559)
Seafood	58 (559)	2 (46)	7 (22)	1 (1)	0 (0)	1 (3)	69 (631)
Desserts	18 (336)	6 (129)	4 (72)	22 (505)	1 (48)	1 (6)	52 (1,096)
Salads	28 (495)	12 (659)	2 (51)	0 (0)	0 (0)	0 (0)	42 (1,205)
Grains	14 (192)	6 (152)	6 (233)	5 (69)	0 (0)	2 (10)	33 (656)
Dairy	25 (460)	0 (0)	0 (0)	1 (10)	1 (4)	0 (0)	27 (474)
Produce	7 (92)	2 (62)	0 (0)	0 (0)	1 (36)	2 (7)	12 (197)
Beverages	2 (40)	0 (0)	1 (6)	0 (0)	1 (6)	0 (0)	4 (52)
Miscellaneous[a]	83 (1,543)	34 (846)	19 (198)	6 (74)	6 (29)	2 (282)	150 (2,972)
Unknown[b]	393 (4,836)	61 (1,234)	41 (377)	6 (57)	4 (73)	6 (70)	511 (6,647)
Total	860 (12,198)	156 (3,960)	152 (2,133)	63 (1,467)	28 (279)	17 (413)	1,276 (20,450)

[a] "Miscellaneous" group comprises of herbs/spices (n=2), sauces (n=6), condiments (n=7), composite food (n=50), and multiple foods consumed (n=81).

[b] "Unknown" is defined as not enough information to identify a specific food vehicle.

[c] Total number of persons affected includes suspected and confirmed

Etiological agent

The most common etiological agent to cause outbreaks in the food service industry was *Salmonella*, with 37.6% (480/1,276) of outbreaks affecting 46.1% (9,436 /20,450) of all cases (Fig 4). *Salmonella* infection accounted for 27.9% (156/559) of food service industry-associated outbreaks in NSW to 78.3%, (65/83) in South Australia. Approximately half of foodborne outbreaks in the food service industry in Western Australia (48.9%, 44/90) were attributed to *Salmonella* infection.

Norovirus was the second most frequently reported etiological agent (7.1% of outbreaks comprising of 2,710 cases). Bacterial toxins caused a total of 69 outbreaks (5.4%) and affected 1,332 persons (6.5%).

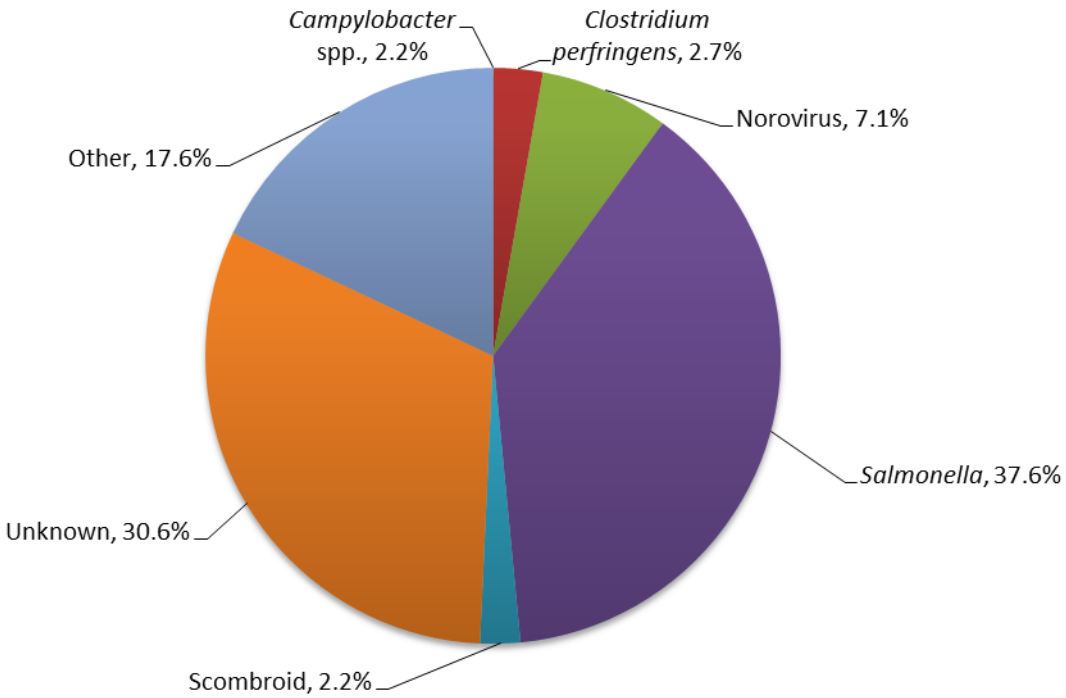

Fig 2. Percentage of foodborne disease outbreaks associated with food service business setting by the most common etiologies, OzFoodNet Outbreak Register, 2001-2016

The majority of deaths (83.3%, 10/12) associated with outbreaks were due to the consumption of foods contaminated with *Salmonella* (case fatality rate of 0.1% [10/9,436]), followed by *Clostridium perfringens* (case fatality rate 0.1% [1/683]) and *Listeria monocytogenes* (case fatality rate 16.7% [1/6]).

The most common etiological agent-food category pairs causing outbreaks with a specified etiological agent and food vehicle were *Salmonella* in "Eggs" (10.5%, 134/1,276), *Salmonella* in "Meat" (3.4%, 43/1,276), and *Salmonella* in "Specialty/ethnic food" (3.2%, 41/1,276).

Food preparation setting

The most frequently reported food service setting where implicated food was prepared was restaurants, which was associated with the greatest number of outbreaks (67.4%, 860/1276), cases (59.6%; 12,198/20,450), and number of persons who sought treatment at a medical practitioner (55.6%, 3,854/6,927). Nearly one-quarter of outbreaks were attributed to food prepared by a commercial caterer (12.2%, 156/1,276, affecting 3,960 persons), or non-franchised take-away (11.9%, 152/1276, affecting 2,133 persons) accounting for approximately one-third of all cases during the study period combined (29.8%, 6,093/20,450).

The majority of outbreaks associated with the consumption of food prepared by non-franchised take-aways (63.8%, 97/152), restaurants (45%, 387/860) and bakeries (31.7%, 20/63) were reported in NSW. Over one-third (50/156) of commercial caterer related foodborne outbreaks were reported in Victoria.

Salmonella infection was responsible for the majority of outbreaks across all food service settings (37.6%; 480/1,276) (Table 4). In particular, bakeries and fairs/festivals/markets/mobile services, where 81% (51/63) and 58.8% (10/17) of outbreaks in these settings were attributed to *Salmonella* infection, respectively.

Table 4. Number of food service industry-associated foodborne disease outbreaks and number of persons affected, by etiological agent and food service business type, OzFoodNet Outbreak Register, 2001-2016

Etiological agent	Food service business setting where food is prepared Number of outbreaks (number of persons affected)[d]						
	Restaurants	Commercial caterers	Take-away (non-franchised)	Bakeries	National franchised fast-food restaurants	Fairs, festivals, markets, mobile service	Total
Bacteria							
Salmonella	315 (5,513)	30 (922)	65 (1,447)	51 (1,293)	9 (151)	10 (110)	480 (9,436)
Campylobacter spp.	19 (217)	5 (165)	4 (12)	0 (0)	0 (0)	0 (0)	28 (394)
Listeria monocytogenes	2 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)
Escherichia coli	1 (8)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	2(11)
Shiga toxin-producing *Escherichia coli*	0 (0)	0 (0)	1(6)	0 (0)	0 (0)	0 (0)	1(6)
Vibrio parahaemolyticus	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
Yersinia enterocolitica	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)
Bacterial total	339 (5,749)	35 (1,087)	71 (1,468)	51 (1,293)	9 (151)	10 (110)	515 (9,858)
Virus							
Norovirus	61 (1,742)	25 (894)	1 (13)	2 (54)	1 (7)	0 (0)	90 (2,710)
Hepatitis A	3 (28)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (28)
Rotavirus	1 (14)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)
Viral total	65 (1,784)	26 (900)	1 (13)	2 (54)	1 (7)	0 (0)	95 (2,758)
Toxin							
Scombroid toxin/Histamine	23 (90)	1 (9)	3 (11)	1 (1)	0 (0)	0 (0)	28 (111)
Clostridium perfringens	19 (202)	12 (386)	3 (89)	0 (0)	1 (6)	0 (0)	35 (683)
Bacillus cereus	4 (56)	3 (83)	3 (26)	0 (0)	1 (6)	0 (0)	11 (171)

Etiological agent	Food service business setting where food is prepared Number of outbreaks (number of persons affected)[d]						
	Restaurants	Commercial caterers	Take-away (non-franchised)	Bakeries	National franchised fast-food restaurants	Fairs, festivals, markets, mobile service	Total
Toxin cont.							
Staphylococcus aureus enterotoxin	5 (32)	4 (104)	1 (5)	0 (0)	2 (14)	1 (272)	13 (427)
Preformed toxin[a]	6 (26)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	7 (28)
In vivo toxin[b]	0 (0)	2 (16)	0 (0)	0 (0)	0 (0)	1 (7)	3 (23)
Wax ester (escolar fish poisoning)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)
Toxin total	59 (411)	22 (598)	11 (133)	1 (1)	4 (26)	2 (279)	99 (1,448)
Suspected etiologies	99 (1,404)	25 (474)	14 (149)	2 (32)	2 (7)	2 (5)	144 (2,071)
Other[c]	22 (393)	8 (124)	3 (22)	0 (0)	1 (18)	0 (0)	34 (557)
Unknown	278 (2,457)	40 (777)	52 (348)	7 (87)	11 (70)	3 (19)	390 (3,758)
Total	860 (12,198)	156 (3,960)	152 (2,133)	63 (1,467)	28 (279)	17 (413)	1,276 (20,450)

[a] Preformed toxin: heat-resistant bacterial toxins are ingested in food. No microbial growth within the person is necessary to cause illness.

[b] *In vivo* toxin: bacterial toxins are formed in the digestive tract after food is consumed.

[c] "Other" includes etiologies such as mixed infection (n=4) and miscellaneous viruses (n=30)

[d] Total number of persons affected includes probable and confirmed

Contributing factors reported for outbreaks

Of the 1,276 food service industry-associated outbreaks, 615 (48.2%) outbreaks contained information on a major contributing factor. Of these, food worker health and hygiene (41.5%, 255/615) and food handling and preparation practices (39.2%, 241/615) were the most commonly reported contributing factor categories. In particular, "ingestion of contaminated raw products" (37.1%, 228/615) and "cross-contamination from raw ingredients" (23.6%, 145/615) were the major reasons for contamination.

Of the outbreaks with a reported reason for microbial growth (30.2%, 385/1,276), the major contributing factor for bacterial growth or toxin production in food that led to the outbreak were "food left at room or warm temperature" (31.7%, 122/385) and "insufficient cooking" (27.3%, 105/385).

Only 25% of outbreaks had a response for microbial survival (337/1,276). The major reason reported for microbial survival in food was "insufficient time/temperature during cooking" (50.4%, 170/337).

Seasons, national holidays and observances

Seasonality

Over 40% (540/1,276) of foodborne outbreaks in the food service setting were reported in November through February (i.e. warmer months). A higher incidence of outbreaks caused by bacterial etiological agents was observed during these months (Fig 5) with *Salmonella* spp. infection the main risk factor causing gastroenteritis in over 40% (227/540) of outbreaks in the warmer months. Nearly 50% (43/90) of norovirus-associated foodborne outbreaks were reported in October through December, with the greatest number of outbreaks reported in November (22.2%, 20/90) (Fig 5). Of these, a food vehicle was specified in 13 outbreaks (14.4%, 13/90) and predominantly associated with the consumption of "Salads" (46.2%, 6/13) prepared by restaurants (66.7%, 4/6) and commercial caterers (33.3%, 2/6).

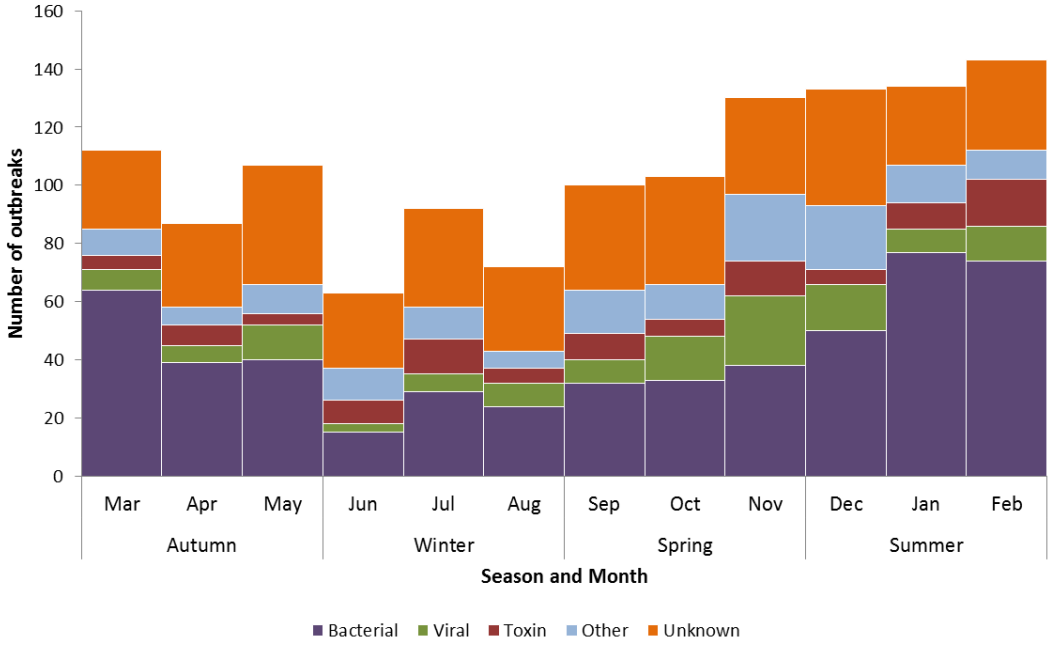

Fig 3. Number of foodborne disease outbreaks associated with food service business setting, by month and season, OzFoodNet Outbreak Register, 2001-2016

National holidays and observances

The highest increases in the number of foodborne outbreaks in the food service industry occurred during the "Christmas party season" (i.e. the weeks leading up to Christmas when work Christmas parties occur, weeks 47 to 50), with a total of 163 outbreaks (12.8% of all foodborne outbreaks) occurring during these four weeks. The majority of outbreaks in the "Christmas party season" were associated with the consumption of a meal prepared in a restaurant setting (69.9%, 114/163).

However, an increase in the number of outbreaks associated with consumption of food prepared by a commercial caterer can also be identified at the beginning of the "Christmas party season" (Fig 6). Over 20% (12/57) of outbreaks occurring around the time of Melbourne Cup Day (weeks 44 and 45), Australia's most popular horse racing event, were attributable to food prepared by commercial caterers.

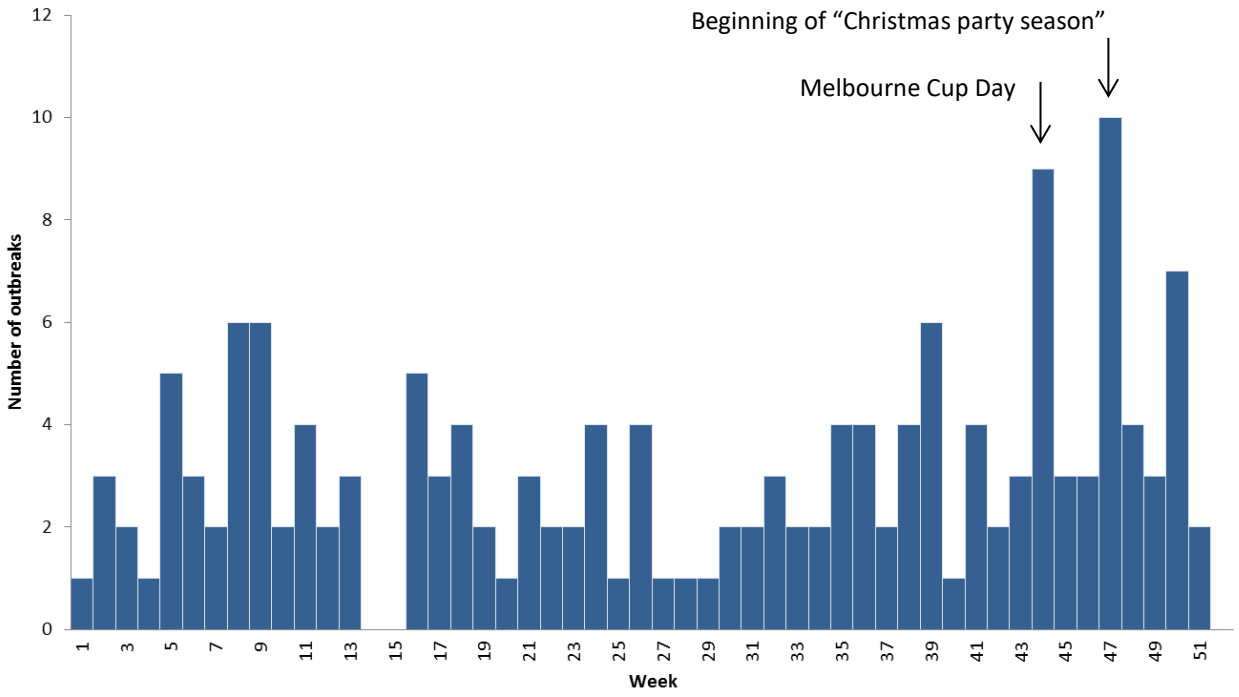

Fig 4. Number of foodborne outbreaks associated with food prepared by commercial caterers, by week, OzFoodNet Outbreak Register, 2001-2016

Discussion

Our study shows that the number of food service industry-associated foodborne outbreaks and the number of persons affected are increasing in Australia. Food service business owners are required by state and territory legislation, governed by the Australia and New Zealand Food Standards Code, to sell safe food. Our results highlight that government food safety guidelines regarding the handling and storage of high risk foods are not being followed consistently. Understanding the risk factors most commonly implicated with foodborne illness in the Australian food service industry is key to informing public health strategies to reduce foodborne outbreaks in Australia and the implications of these on the public and the food service industry.

Current challenges and strategies to reduce foodborne illness

In Australia, restaurants and cafés comprised half of the 85,284 eating out establishments in 2017 and Australians ate out on average two to three times/week, accounting for over 50 million meals/week.[22] We found

restaurants accounted for over two-thirds of foodborne outbreaks in the Australian food service industry between 2001 and 2016. A myriad of possible factors may explain why restaurants are the most commonly reported setting where food is prepared in the food service industry. By their nature, restaurants are predisposed to foodborne outbreaks.[12] The high volume of food that is served and the "cook-to-order" preparation of food may increase the likelihood of preparation errors[10, 13] leading to more illnesses. Food is also generally consumed in a group setting in restaurants facilitating the identification and epidemiological linkage of ill persons.[13] Customers are more likely to consume raw foods in a restaurant compared to fast –food restaurant or take-away[13] and ill persons may be more prone to associate illness with a commercially prepared food compared to other possible sources.[10] Consequently, evidence suggesting that restaurants are an important source of foodborne infection must be interpreted with caution. This finding does, however, corroborate the results of previous surveillance summaries using foodborne outbreak data carried out in Australia.[9, 23]

The implementation of measures to prevent foodborne disease outbreaks should be an incentive for the food service industry to avoid potential economic consequences. A recent US study[8] estimated that the cost of a single foodborne disease outbreak ranged from approximately US$4000 to US$2.6 million, excluding costs associated with lost revenue, lawsuits, legal fees or fines worth up to 101% of annual profits and revenue. International studies have shown that hygiene and food safety rating programs can lead to an improvement in hygiene standards of food service businesses.[24] Businesses which aim for the best hygiene score by following good hygiene and food safety practices reduce foodborne illness outbreaks.[25] They also provide consumers with information regarding the hygiene results of their establishment of choice promoting competition.[26] In Australia, similar food safety management strategies have been implemented including the voluntary "Scores on Doors" in NSW[27], and the mandatory "Eat Safe" food safety star rating scheme implemented by the Brisbane City Council (BCC).[28] Following the implementation of their star rating system in 2010, the BCC found that consumers' awareness of food hygiene

issues had increased as well as their interest in reporting them. A 20% decrease in the number of businesses identified with low compliance with food safety legislation was also observed as resources were able to be targeted to low performing businesses.[29]

Our study supports findings that in many developed countries, the main cause of foodborne disease outbreaks associated with the food service industry is salmonellosis with *Salmonella* outbreaks predominantly due to poultry meat and eggs.[30] Compared to red meat, poultry meat has been identified to have a higher *Salmonella* risk rating.[31] In the US from 1998 to 2008, nearly 60% of *S.* Enteritidis outbreaks were associated with food products containing eggs.[2] In Australia, the crude annual rate of salmonellosis increased from 30.6 per 100,000 in 2000 to 53 per 100,000 in 2013[32] with a significant increase of foodborne salmonellosis outbreaks linked to eggs.[33] Egg producers are required to comply and demonstrate compliance in the implementation of food safety control measures. In addition, a voluntary and independent quality assurance program in the egg industry, Egg Standards Australia, requires adherence to best practice standards of production in areas including egg quality, biosecurity, hen welfare, the environment and food safety.[34] However, implementation of effective management strategies to mitigate *Salmonella* contamination of eggs has proven to be challenging.[35]

We identified that consumption of Vietnamese rolls (Bánh mì), prepared in bakeries and non-franchised take-aways was a key source of foodborne disease outbreaks. Vietnamese rolls contain multiple high-risk ingredients such as barbequed pork or chicken, pork liver pâté and raw egg butter or homemade mayonnaise using raw egg. In this study, Vietnamese rolls were frequently listed as the implicated food vehicle, however, mayonnaise using raw egg or raw egg butter was often identified as the source of the contamination. Vietnamese pork rolls have caused foodborne outbreaks in Australia since the 1990s.[36-42] Pasteurisation is crucial in the reduction of foodborne illness risks.[35] The food service industry should consider using pasteurised eggs as an alternative to raw eggs. Given that nearly 20% of hospitalisations of all foodborne outbreaks in

our study were due to the consumption of Vietnamese rolls this finding strongly highlights that the use of raw egg products such as homemade mayonnaise and raw egg butter should be avoided by food service businesses as it presents an unacceptable risk to the consumer.

The occurrence of outbreaks in the food service settings was highest following two well-established national holidays and observances in Australia. Melbourne Cup Day and the "Christmas party season" are ingrained in Australian workplace culture and result in increased numbers of foodborne outbreaks. Traditionally, work Christmas parties are celebrated in restaurants whilst Melbourne Cup Day is a catered event celebrating an international horse race. Due to the popularity of these events, restaurants and commercial caterers would be undertaking excessive production of foods to cater for the large numbers of patrons, which could potentially lead to lapses in food safety controls.

Catering for large numbers such as special events has been found to represent a potential public health risk.[43] This is particularly evident for food service businesses that do not regularly cater for large numbers[44, 45], as it places additional pressures on food preparation systems particularly food handlers. Factors such as "being busy, having to perform multiple tasks at the same time, managers not being around to remind them, lack of support following training, and fatigue"[46] result in lapses in food safety behaviours and ultimately the contamination of food. In the US, food handling and preparation practices were the most frequently reported reasons for contamination in restaurant-associated foodborne disease outbreaks.[13] The most commonly implicated reasons for contamination leading to outbreaks in England and Wales, depending on cuisine type prepared, were cross-contamination and inadequate thermal treatment.[12] Our findings complement these studies and suggest that foods and ingredients are contaminated upstream from the restaurant, i.e. they arrive already contaminated. Failure to meet food safety procedures within a restaurant such as cooking poultry meat and eggs to required temperature, adequate cleaning of hands, equipment or utensils, or appropriate storage to avoid drippage or spillage are not followed to remove the pathogen once in the restaurant, resulting in potentially preventable foodborne outbreaks.[13]

One of the greatest challenges that the food service industry faces relates to staffing issues, including the transient nature of casual staff.[22] High staff turnover, resulting in understaffing, creates situations where food handlers are responsible for multiple tasks such as cleaning bathrooms and then returning to food preparation.[46] Younger staff tend to have little previous training in food safety[10] and experienced staff may rely on judgement rather than follow food safety practices such as using sensory judgements (sight, smell, or taste checks) instead of a thermometer to assess if foods are adequately cooked.[46] International studies have found that having a certified kitchen manager in the facility was associated with the prevention of foodborne outbreaks. [24] In Australia, Queensland, Victoria, NSW and ACT have regulations that requires a minimum of one trained Food Safety Supervisor to be employed in the food business and formal training occurs through registered accredited training organisations.

Implications and future work

Current measures to reduce foodborne outbreaks in the food service industry need improvement. Our study highlights that new multi-pronged approaches to foodborne disease control is needed. A recently published project report by Nuffield Australia, an organisation that provides scholarships for Australian primary producers to undertake research to improve Australian agriculture, focused on international egg production and food safety regulation and ways Australia could improve the safety of eggs. It recommended that a national mandatory accreditation system to ensure best practice standards in egg production should be implemented and enforced consistently across Australia. This would benefit Australia's egg farmers by maintaining high standards within the industry and allow accredited egg producers to stay commercially competitive.[47] Food service businesses should strive to implement consistent food safety practices and strengthen food safety skills and knowledge through upskilling staff in 1) the safe preparation and storage of high-risk food items, 2) the use of pasteurised eggs or commercially made mayonnaise and dressings as alternatives, 3) the importance of cooking through poultry meat to avoid bacterial survival, and 4) the preparation, refrigeration and handling of raw eggs

and egg products to mitigate bacterial growth and decrease the food safety risks associated with food service businesses carrying out such practices. Furthermore, consumer awareness of high-risk foods especially where the risks are not immediately evident, such as Vietnamese rolls, should be increased.

Since the trend in foodborne outbreaks in the food service industry showed a steady increase during the study period, it is predicted that this trend will continue into the future given the popularity of eating out in Australia. The average Australian household spends approximately $5000 a year on eating out. In 2017 alone, the total revenue of the food and beverage industry in Australia was $45 billion.[22] Furthermore, the variety of food choices available for consumption in Australia has increased in recent decades.[48] Annual market research suggests that Australians are showing greater interest in healthy fast food alternatives or choosing healthier cuisines such as Japanese or seafood.[22] In addition, home delivery of restaurant meals by delivery services has emerged in Australia, however the growth of this new trend and its impact on foodborne disease incidence remains uncertain.[22] Our study emphasises the benefits of systematically collecting information about food categories implicated in foodborne outbreaks associated with the food service industry. Future research should monitor if the change in food choices, and cuisines, is reflected in a change in the epidemiology of etiological agents causing foodborne outbreaks in the Australian food service industry. Our study emphasises the benefits of systematically collecting information about food categories implicated in foodborne outbreaks associated with the food service industry. Future research should monitor if the change in food choices, and cuisines, is reflected in a change in the epidemiology of etiological agents causing foodborne outbreaks in the Australian food service industry. This information could inform *Australia's Foodborne Illness Reduction Strategy 2018-2021*[+] and future strategies developed to achieve a nationally-consistent approach to reducing foodborne illness

Limitations

Our study is subject to some limitations. Firstly, the coverage of the OzFoodNet surveillance system in the early years did not cover the full country until 2002.[49]

This means that we may not have included some outbreaks in the earlier years. Outbreaks reported into the Outbreak Register do not represent all foodborne outbreaks that occurred in Australia as not all outbreaks are identified and investigated. Thus, the numbers are likely to be an underestimate of the real magnitude of foodborne disease outbreaks in Australia. Secondly, the majority of foodborne disease cases are mild and ultimately resolve themselves without treatment. Less than 30% of affected people seek medical treatment.[7, 50] Consequently, surveillance data constitutes only a small portion of what is actually occurring in the community.[7, 50] Thirdly, the sensitivity of surveillance and investigation methods may have varied between state and territories. However, OzFoodNet attempted to standardise investigative procedures and surveillance methods. Fourth, the vehicle or the contaminated ingredient is not always identified during outbreak investigations. An implicated food was not reported in 40% of food service industry–associated outbreaks during the study period. The identification of a common food exposure is necessary to attribute food to an outbreak. However, establishing which food item is responsible is often challenging as ill persons can potentially be exposed to numerous common foods.[13] Finally, contributing factors were reported for only approximately half of the foodborne outbreaks in the OzFoodNet Outbreak Register, which limited our ability to generalise contributing factors for outbreaks in this setting.

Conclusion

Eating out is a national pastime in Australia[22] and around the world. Our study investigated risk factors for foodborne outbreaks associated with eating food prepared by a food service business in Australia and informs food safety interventions. The identification of Vietnamese rolls as a high risk food vehicle and catering to large numbers of patrons as a risky practice may be important to prevent foodborne illness. Food service businesses must be committed to maintaining a high-performing food safety culture. Investment in staff will result in an engaged food service industry workforce that is more likely to display consistent hygiene and food safety practices. Since over 60% of all reported foodborne outbreaks in Australia during 2001-2016 were attributable to the

food service industry, this sector plays an important role in the overall national foodborne disease control efforts.

Recommendations

This study is the first analysis of Outbreak Register data using the new food categories from the updated Outbreak Register data dictionary prior to their official implementation. In 2016, OzFoodNet developed new data field criteria for its register, two of which allow the reporting of food categories for identification of the food commodity associated with the implicated food vehicle. This new method for assigning implicated foods standardises data entry for national consistency. Prior to the redevelopment of the Outbreak Register data dictionary, this information was not collected and had to be surmised from a food vehicle data field. Previous to this study, these food category data fields had not yet been implemented or trialled to determine what the major causes and health impacts of outbreaks are due to food consumption in Australia. This study showed that the use of these new food categories greatly simplifies the analysis of Outbreak Register data and will make the national surveillance of foodborne outbreaks, including the routine response to data requests, a quicker and less involved process. Based on our experience using the food categories, we recommend creating a separate food category for Vietnamese rolls (Bánh mì), sandwiches/rolls/burgers; and cakes/ buns filled with cream or custard. Furthermore, we recommend a field in the Outbreak Register should be created that allows the identification of the special event (national holiday or observance) when food was prepared that led to the foodborne outbreak, such as Valentine's Day, work Christmas party, Mother's Day, Melbourne Cup Day, wedding, or a mass gathering of another kind.

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Disclosure statement

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Supporting Information

Table S1. Definitions used and evidence required for food vehicle and mode of transmission of outbreaks

Term	Definition
Food vehicle	Food exposure (food or meal) most likely responsible for the outbreak. Description of food vehicle is required for all foodborne/probable foodborne outbreaks.
Mode of transmission – Foodborne	An incident where ≥2 persons experience a similar illness after consuming a common food or meal and there is the following evidence: • Epidemiological: statistically significant results for a food vehicle; or • Microbiological: Pathogen detected in the food vehicle is the same as for the cases.
Mode of transmission – Probable foodborne	An incident where ≥2 persons experience a similar illness after consuming a common food or meal and a specific meal or food is suspected, but person-to-person transmission is also a possible source of illness. Evidence: • Compelling: Symptoms are specific to certain pathogens (e.g. *Listeria monocytogenes*, ciguatoxin, scrombotoxin); the aetiology of the outbreak can only result through foodborne transmission; or there is only one food item the case was exposed to.

Source: [17]

Table S2. Summary of the Level 1 and 2 food categories from the updated OzFoodNet Outbreak Register Data Dictionary

Level 1 Food Categories	Level 2 Food Categories
Dairy	Milk/cream, Cheese, Spreads/fillings, Ice-cream/yogurt, Dairy - other
Desserts	Cake, Candy, Chocolate, Mousse, Pie, Pudding, Raw egg-based desserts, Desserts - other
Eggs	Eggs – single food, Eggs – composite food, Egg drink, Egg sauce/dressing, Eggs - other
Produce	Fresh fruit, Processed fruit, Fresh vegetable, Processed vegetable, Produce - other
Grains	Bakery and bakery wares, Cereals, Pasta/noodles, Rice, Grains - other
Meats	Beef, Poultry, Lamb, Veal, Offal, Pork Processed meats, Game meat, Meats - other
Beverages	Vegetable drink, Fruit drink, Dairy drink, Other beverage
Salads	Seafood based salad, Lettuce based salad, Vegetable based salad, Pasta based salad, Fruit based salad, Salad - other
Seafood	Fish, Shellfish, Seafood - other
Specialty/ethnic	Pizza, Sushi, Rolls, Noodle based dishes, Specialty/ethnic - other
Miscellaneous	Condiments, Herbs/spices, Sauces, Nuts, Composite food, Multiple foods, Miscellaneous - other
Unknown	Not enough information to identify a specific food vehicle
Not applicable	No evidence of foodborne transmission

Source: [20]

Table S3. Assignment rules for identified implicated foods that were difficult to classify into food categories and the subsequent categories they were allocated

Custard in baked goods	Cream in baked goods	Sandwiches/burgers
• E.g. custard eclairs/ custard fruit tart/custard buns/custard cannoli/custard cake =raw-egg based desserts (desserts) •Dessert containing raw egg custard = raw-egg based desserts (desserts)	• E.g. cream and custard cake = cake (desserts) •cream filled cakes/cream puffs/profiteroles = Dessert - other (desserts)	•E.g. sandwich, sandwiches, mixed sandwiches, assorted sandwiches, premade sandwiches = composite food (miscellaneous) •raw egg mayonnaise in chicken sandwich = egg sauce/dressing (eggs) •chicken sandwiches = chicken (meats), if extra info suggests chicken •beef burger = beef (meats), if extra info suggests beef •chicken sandwiches = composite food (miscellaneous), if no extra info available •beef burger = composite food (miscellaneous), if no extra info available
Kebab (doner kebab or meat kebab)	**Vietnamese rolls (Bánh mì)**	**Specialty/ethnic or Miscellaneous**
•Beef kebab = beef (meats) •meat kebab = meats •doner kebab = composite food (miscellaneous) •kebab = allocate as per doner kebab if extra info in free text suggests to do so, otherwise classify as meats	• Vietnamese rolls = rolls (specialty/ethnic) • Vietnamese rolls with raw egg butter = rolls (specialty/ethnic)	• chicken curry = chicken (meats) • "meals containing chicken pieces and pizza of any kind" = multiple foods (miscellaneous) •Various Indian dishes - rice, beef madras, butter chicken, lamb rogan josh, vege curry = multiple foods (miscellaneous) •chinese food = multiple foods (miscellaneous) •curries = specialty/ethnic - other (specialty /ethnic)

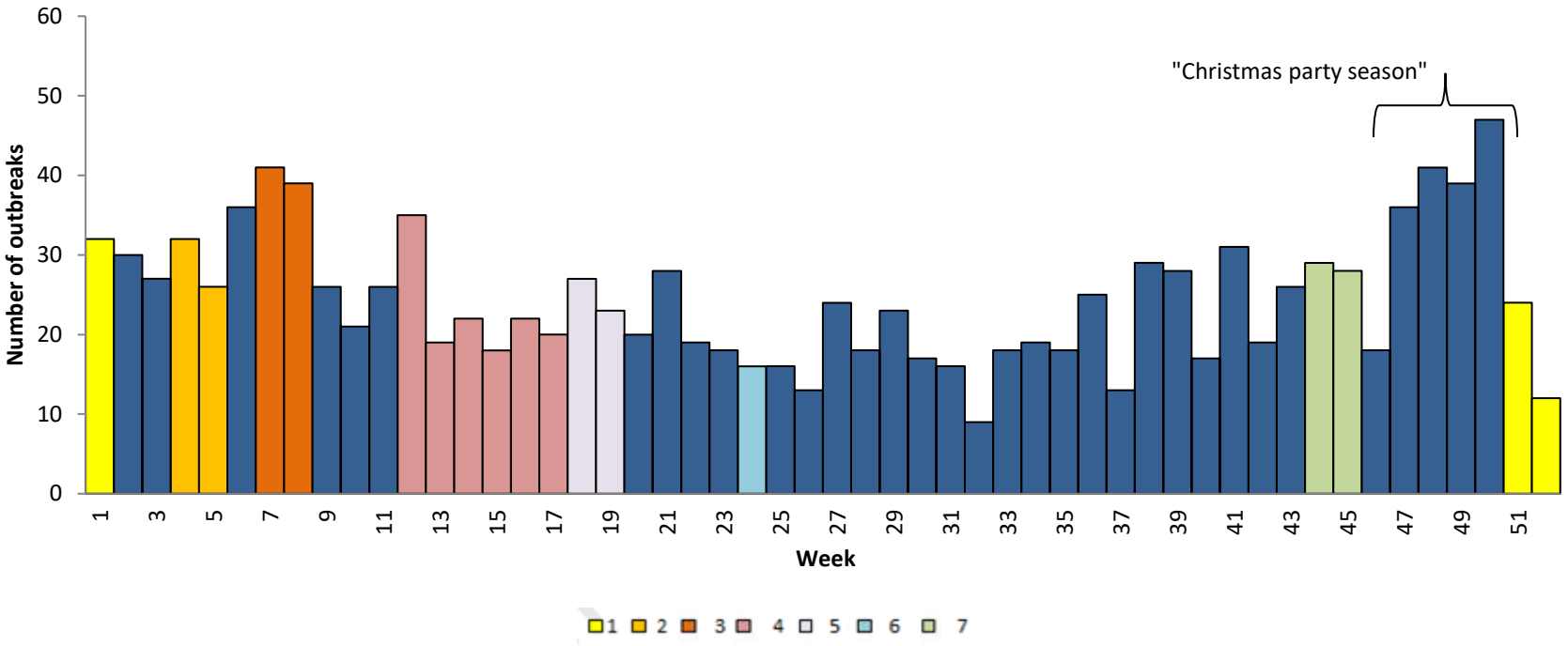

Fig S1. Number of foodborne disease outbreaks associated with food service business setting, by week and national holidays and observances, OzFoodNet Outbreak Register, 2001-2016

Legend: 1= Christmas holiday period (Christmas Eve to New Year's Day); 2= Australia Day (26 January); 3= Valentine's Day (14 February); 4= Easter holiday period (Good Friday to Easter Monday) and Anzac Day (25 April); 5= Mother's Day (13 May); 6= Queen's Birthday (11 June)* except for Western Australia and Queensland; and 7= Melbourne Cup Day (first Tuesday of November). Dark blue represents no public holiday or observance.

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CHAPTER 4 –
OUTBREAKS OF MULTIPLE *SALMONELLA* TYPHIMURIUM MLVA PROFILES AT A HOTEL RESTAURANT

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Prologue

Salmonellosis is a notifiable condition in the Australian Capital Territory (ACT), Australia. As part of routine surveillance, laboratory-confirmed cases of *Salmonella* infection notified to the Communicable Disease Control Section (CDC) at ACT Health Protection Service are interviewed and investigated.

On 18 May 2016, CDC identified that three persons with laboratory-confirmed salmonellosis had dined at the same hotel restaurant in Canberra during their incubation period. Follow up of *Salmonella* notifications identified five laboratory-confirmed cases of salmonellosis dined at the same hotel restaurant between 3 - 17 May 2016. These cases dined on different days and attended different events held at the same hotel restaurant (à la carte and Event A). The Environmental Health Officer undertook a food premises inspection which didn't identify any food safety issues or ill food handlers. Following these inspections, an additional laboratory-confirmed case of salmonellosis identified through routine surveillance reportedly attended a second event (Event B) at the hotel restaurant. The identification of two cohorts of affected persons prompted the launch of an Acute Response Team (ART) meeting and subsequently an outbreak investigation comprising of two cohort studies: the attendees of the Event A and the attendees of Event B, to confirm an outbreak, identify the source of infection and implement strategies to prevent the spread of illness.

My role

After the ACT Health Protection Service initiated an outbreak investigation, I was requested to assist with the investigations as part of the ART to search for the source of the disease.

I conducted the following tasks as part of the outbreak investigation:

- telephone interviews of Event B attendees;
- contributing to Situation Reports;
- entering case questionnaire data and managed Microsoft Excel database used for recording case information (data entry, cleaning and analysis);
- retrospective analysis of outbreaks using STATA and Microsoft Excel;

- report and manuscript writing; and
- present the findings at the Communicable Diseases Control conference held in Melbourne during June 2017.

Lessons learnt

This was my first experience of an outbreak investigation and it gave me a better appreciation and understanding of the complexities of disease outbreak investigations. There are a number of limitations to successful outbreak investigations. For example, a sufficient number of people may be interviewed as part of the investigation as required for an adequately statistically powered study. However, there may not be enough ill persons in the study which can affect the identification of a statistically significant difference in exposure between the ill and the non-ill group. In addition, left-over food specimens may be unavailable for collection and testing. Nevertheless, even where specimens are available, results may not reveal the causative organism. Furthermore, the epidemiological study may not be supported by environmental health investigations that may not find a causative organism or any major breaches to food safety. Yet, the identification of numerous ill persons who ate at the same venue strongly suggests at least one failure in food safety. Through this experience I learnt that outbreak investigations can be challenging and sometimes require resourcefulness.

Key components of outbreak investigations are perseverance and creativity. In the outbreak investigation for Event B, the event organiser initially refused to release any contact details (name and phone numbers) for the attendees as they were embarrassed their guests would find out that the venue may have made people ill. We made a number of attempts to find the phone numbers of names mentioned from the initial attendees we interviewed because although they knew their name they didn't have their phone number. The first method we used was to look at the event organiser's Facebook page to see who their friends were. However the persons we were looking for weren't on their list of friends. When that didn't work we noticed that the surname of one of the attendees was the same as the surname of a MAE scholar in our cohort who originally was from Canberra. We contacted the MAE scholar and asked if they had a brother with the same first name, which they confirmed. We then

asked if their brother had attended this type of event on this particular day. It turned out that their brother had the same first name, had attended the same type of event on the same day – but in another city. We were just about to give up the investigation because our window of opportunity was closing - the investigation started 10 days after Event B had occurred – when the event organiser contacted us to advise that family members had become ill. They finally agreed to supply contact details for five attendees. We subsequently contacted them and asked for contact details of other attendees. Through active case finding we managed to obtain contact details for 43 (78%) of the 55 Event B attendees.

This investigation showed how dependant investigators are on the public's participation. It revealed that investigations can't progress if the public doesn't want to cooperate and agree to participate in interviews or supply specimens, as they are not obligated to provide information to assist with outbreak investigations. Consequently, outbreak investigators need to be able to establish and maintain relationships through communication to achieve collaboration not only with each other and management but also the public.

I learnt during the analysis of this outbreak the time-efficient Stata syntax to calculate a summary table for cohort studies, "cstable case". This command followed by each exposure (name of variable) undertakes a univariate cohort analysis for each exposure and summarises the results into one table. In addition, I learnt that if you're dealing with expected numbers that are smaller than 5, which some of the exposures in the outbreak had, then I needed to use Fishers exact test. Furthermore, I wanted to sort my table by p-value. Therefore, in this analysis I modified the command to "cstable case *[variable]*, exact pvalue".

Public health implications of this work

The investigation revealed that *S.* Typhimurium was implicated in this outbreak of gastrointestinal illness. Due to its prevalence and serovar diversity, *S*. Typhimurium needs further subtyping for surveillance or outbreak investigations. Two different MLVA profiles were responsible for this outbreak; furthermore, one of the profiles identified through MLVA subtyping was *S.* Typhimurium MLVA 3-12-18-14-523, a strain that has not been seen previously in Australia or since the outbreak. The two MLVA

profiles were also shown to be genetically different using whole-genome sequencing. It's unusual to find multiple MLVA profiles in the one outbreak. The multiple outbreaks in the one location imply lapses in proper food preparation practices. Food service businesses have an obligation to their patrons to recognise the risks of poor food handling and minimising these by following food safety practices meticulously. These outbreaks also highlight the requirement for food service businesses to document food preparation activity. The chef at the hotel restaurant was unable to recall the canapés that had been served for Event B; therefore, the canapés included in the investigation were based on the responses from the attendees. In addition, there were conflicting responses amongst the attendees as to what canapés were served. Therefore it is not clear which ingredients they may have consisted of. Furthermore, no canapé samples were available for testing which could have helped their identification. Lastly, no information regarding the foods prepared or served for events identified following the investigation was available. Thus, food service businesses should log not only how the food they serve is prepared and but also what is served to patrons.

This outbreak investigation highlights the important role of collaboration of the public in the investigation of disease outbreaks. Another two potential outbreaks were identified in the same time period at the hotel restaurant following the initial outbreak investigation (Event C and Event D). Persons notified with confirmed *Salmonella* infection had eaten at two additional functions at the hotel restaurant in the same time period and microbiological results showed they had the same MLVA profile as Event A. However, these could not be further investigated as contact details could not be obtained from these function attendees. Road blocks occurred when persons did not see the value of participating in an interview if they themselves or people they knew weren't affected by gastroenteritis. To accomplish effective public cooperation, education campaigns could be implemented to educate the public on the importance of outbreak investigations in preventing further spread of disease.

Master of Philosophy (Applied Epidemiology) core activity requirement

- Investigate an acute public health problem or threat (includes outbreaks);
- Prepare of an advanced draft of a paper for publication in a national or international peer-reviewed journal; and

- Present at a national or international scientific conference or forum

Advanced draft of paper for publication

Outbreaks of multiple *Salmonella* Typhimurium MLVA types at a hotel restaurant in Canberra, Australia, May 2016

Brigitta Osterberger[1, 2], Laura Ford[2], Samuel McEwen[3], Sam Durant[3], Martyn Kirk[2], Benjamin Polkinghorne[2], Anna Glynn-Robinson[1] and Timothy Sloan-Gardner[3]

[1] Office of Health Protection, Department of Health, Woden, Australian Capital Territory.

[2] National Centre for Epidemiology & Population Health, Research School of Population Health, ANU College of Health and Medicine, Australian National University, Australian Capital Territory .

[3] Health Protection Service, Population Health, ACT Health, Australian Capital Territory.

Corresponding author:

Mrs Brigitta Osterberger

Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
Phone: 02 6232 8985
Email: Brigitta.Osterberger@health.gov.au

Abstract

Introduction: In May 2016, routine public health surveillance of salmonellosis notifications identified two cohorts of affected persons who reported eating at the same hotel restaurant on different days in the Australian Capital Territory (ACT). An investigation was launched to identify and control the source of the infection.

Methods: We conducted two retrospective cohort studies using telephone interviews of attendees of two events (Events A and B) held at the same venue using a standardised questionnaire and an environmental health inspection was conducted at the implicated restaurant. ACT Health forwarded *Salmonella* isolates for serotyping, genotyping via multi-locus variable-number tandem-repeat analysis (MLVA), and whole genome sequencing (WGS). Data were analysed descriptively using Stata to summarise data and calculate relative risks for food exposures.

Results: Two unrelated *S.*Typhimurium MLVA profiles were identified. Eight isolates from ill Event A attendees were typed as *S.* Typhimurium (MLVA 03-12-18-14-523), a very rare MLVA profile in Australia. Three isolates from ill Event B attendees were typed as *S.* Typhimurium (MLVA 03-10-14-11-496). WGS revealed that the isolates of these two MLVA profiles were approximately 90 single nucleotide polymorphisms apart. Smoked salmon and avocado dip sandwiches served at Event A were the only food item significantly associated with illness (relative risk 4.64, 95% confidence interval 1.19-18.1). Environmental investigations did not detect *Salmonella* species on the premises.

Discussion: This outbreak highlights the complex nature of foodborne outbreaks. While WGS is in the process of being implemented across Australia, our study shows that MLVA is still useful in the public health surveillance of *S*. Typhimurium infections. Cross-contamination may have been the cause of infection and emphasises the importance of food safety practices to prevent food contamination. This outbreak identified two distinct genomic profiles of *S*. Typhimurium in the one venue, which is unusual and rarely reported.

Keywords: public health surveillance, restaurant, disease outbreaks, *Salmonella* Typhimurium, Australia, salmonellosis, retrospective cohort study, MLVA, whole-genome sequencing

Introduction

Salmonella enterica serovar Typhimurium (*S*. Typhimurium) is the most frequently notified *Salmonella* serovar in Australia, accounting for nearly 44% of notifications between 2000 and 2013.[1] *S*. Typhimurium is the most common aetiological agent linked to outbreaks caused by consumption of contaminated food[1] with over 90% of foodborne salmonellosis outbreaks attributed to *S*. Typhimurium in Australia in 2011.[2] *S*. Typhimurium trends have increased in Australia particularly in the Australian Capital Territory (ACT) where *S***.** Typhimurium increased at 12% (95% confidence interval 10–14%) each year.[1] However, single large restaurant-based outbreaks can strongly influence the rates in a small jurisdiction, such as the ACT. The prevention and control of *Salmonella* continues to be a considerable public health and food safety concern and challenge in Australia.[1]

In Australia, subtyping methods for *Salmonella* are transitioning from multi-locus variable-number tandem-repeat analysis (MLVA) to whole genome sequencing (WGS).[3] MLVA typing has been used successfully in several *S*. Typhimurium outbreak investigations nationally[4-6] and internationally.[7-9] However, Australia is rapidly moving towards WGS for the surveillance of all foodborne bacteria [10-12], due to its characterisation and discriminatory power.[13] WGS is getting faster, cheaper, and more accurate[13], and is increasingly being employed around the world and nationally.

Salmonellosis is a notifiable condition in the ACT. In May 2016, during routine follow up of *Salmonella* notifications, the Communicable Disease Control Section (CDC) at ACT Health Protection Service identified five microbiologically-confirmed cases of salmonellosis who had all dined at the same hotel restaurant in Canberra in May 2016. The identification of two separate cohorts of affected persons prompted the initiation of an outbreak investigation comprising of two cohort studies to confirm the existence of an outbreak, identify the source of infection and implement strategies to prevent the further spread of illness.

Materials and Methods

Epidemiological investigation

We initiated an outbreak investigation comprising of two retrospective cohort studies, consisting of attendees of Event A and Event B, to identify the possible exposures causing infection in these distinct cohorts.

A structured telephone questionnaire was administered to all persons with a contact phone number, who either attended Event A or Event B. We included standardised questions in the questionnaire to obtain demographic, clinical and potential food exposure information, as used in previous outbreak investigations conducted by the CDC. Food items were identified from the menus for each respective event, which were obtained from the hotel restaurant. For Event B, canapés in the questionnaire were based on the responses from the attendees. Canapés were listed as "Hot and cold canapés" and no record was kept of which had been served on the day. We interviewed persons identified from the hotel restaurants' booking list for Event A and Event B attendee details were obtained from the event organiser and interviewed attendees. All persons were asked if they had dined at any other commercial venues in the ACT, or had any other common exposures.

The case definition for a clinical case of gastroenteritis was a person that ate at the hotel restaurant and developed gastrointestinal symptoms including diarrhoea ≥six hours after eating at the venue, lasting ≥24 hours and within five days of eating at the hotel restaurant.

Event A and Event B attendees reporting gastrointestinal symptoms consistent with the case definition were asked to supply a faecal specimen to aid with the epidemiological investigation.

For the descriptive analysis of each cohort study, continuous variables were summarised using median and range. The association between food exposures and illness was quantified by estimation of the relative risk (RR) and the respective 95% confidence interval (CI) using the Pearson chi-square test. Age and sex were compared using a Student's t-test and the Pearson chi-square test, respectively. Statistical significance was assumed when *p*-values were <0.05 and the 95% CI of the RR did not

include 1. Where expected numbers were small (<5), we used the Fisher's exact test. Data analysis was carried out in Stata® version 13 (StataCorp., USA).

Environmental health investigation

ACT Health Protection Service conducted an environmental health inspection of the hotel restaurant's kitchen facilities on 19 May 2016. Environmental swabs were taken of the work surfaces and seven food samples were collected, which were sent for microbiological analysis. Food handling procedures, premises, staff hygiene practices and record keeping of temperature control and cleaning were reviewed. Follow up inspections of the hotel restaurant were conducted with additional swabbing performed and food specimens collected for microbiological analysis testing. Copies of the complete list of suppliers, booking list for Event A, function list for the period 5-15 May 2016, including contact names and telephone numbers, as well as menus, were obtained.

A copy of the staff roster and details on staff illness and absenteeism were requested. The staff roster was examined to identify food handlers who had worked on the days the events took place and cross-referenced with the details on staff illness and absenteeism.

Microbiological investigation

Local pathology companies, ACT Pathology, Capital Pathology, or Laverty Pathology tested faecal samples were tested for enteric pathogens using standard laboratory methods.[14-16] *Salmonella* -positive specimens or isolates were forwarded to state reference laboratories: the Microbiological Diagnostic Unit - Public Health Laboratory, Victoria (MDU PHL) or the New South Wales Enteric Reference Laboratory, Institute for Clinical Pathology and Medical Research (ICPMR) for serotyping and MLVA if the serotype was Typhimurium.

MDU PHL and ICPMR performed phenotypic serotyping and MLVA on all *S.* Typhimurium isolates as described by Ford et al.[17] Additionally, environmental swabs and food specimens collected from the hotel restaurant were tested for *Salmonella* by the Microbiology Unit at ACT Government Analytical Laboratory (ACTGAL), ACT Health Protection Service, using standard food and environmental laboratory methods. *Salmonella* isolates from this outbreak were included in a pilot project to evaluate the

use of whole-genome sequencing for the public health surveillance of *S.* Typhimurium in the ACT.[17]

Ethics and permissions

Ethics approval was not sought for this investigation as it was conducted under public health legislation.[18]

Results

Epidemiological investigation

A total of 33 cases were identified who attended either Event A or Event B (Fig 1). There were 26 cases attending Event A with 35% (9/26) confirmed and 65% (17/26) clinical. There were seven cases attending Event B with 43% (3/7) confirmed and 57% (4/7) clinical.

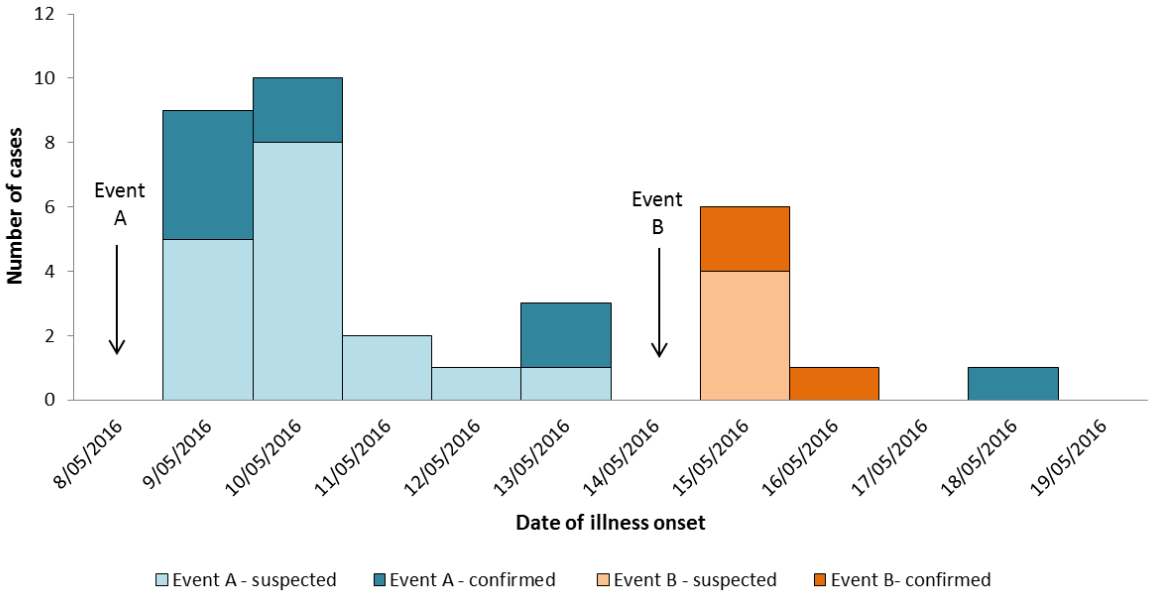

Fig 1. Epidemiological curve of microbiologically-confirmed and clinical outbreak cases by onset day and event after dining at a hotel restaurant in Canberra, May 2016 (n=33)

Event A Cohort

We interviewed 81% (81/100) of people estimated to have attended Event A. The overall attack rate for gastroenteritis among the cohort was 33% (26/81). The median incubation period was 35.5 hours (range: 11.5-228 hours). The longest incubation period was 10 days for a person with underlying co-morbidities, which may have led to delayed onset of symptoms.

Diarrhoea was reported by 100% (26/26) of cases, with abdominal pain in 76.9% (20/26), nausea 69.2% (18/26) and fever 69.2% (18/26). Nearly one-fifth of the cases reported blood in their faeces (5/26).

Additional symptoms mentioned by cases included vomiting with 23.1% (6/26), lethargy 88.5% (23/26), headache 69.2% (18/26), muscle and body aches 15.4% (4/26), dizziness 3.8% (1/26) and light-headedness 3.8%(1/26).

Over 45% (12/26) of cases sought medical attention at a general practitioner or emergency department and two cases required hospitalisation.

Event B Cohort

A total of 55 adult guests and 6 children attended Event B. Children were excluded from the cohort study as they ate from a different menu and none reported experiencing gastroenteritis. Of these, 84% (46/55) of attendees were interviewed. The overall attack rate for gastroenteritis was 15% (7/46).

The median incubation period was 21 hours (range 7-27.5 hours). Diarrhoea was reported by 100% (7/7) of cases, with abdominal pain 71.4% (5/7), nausea 71.4% (5/7) and fever 57.1% (4/7). Two cases reported blood in their faeces. Chills (42.9%, 3/7), fatigue (85.7%, 6/7), vomiting (14.3%, 1/7) and weakness (14.3%, 1/7) were additional symptoms reported. Nearly one-third (2/7) of ill attendees sought medical attention at a general practitioner with none requiring hospitalisation.

Analytical Analysis

Event A and Event B had different menus with few overlapping foods and requiring separate analysis (Table 1). In univariate analysis, a statistically significant association with illness were smoked salmon and avocado dip sandwiches (RR 4.64, 95% CI 1.19-18.1), served at Event A. Although salmon was served at both events, smoked salmon was used for the salmon sandwiches served at Event A and salmon fillet portions were served at Event B.

No statistically significant differences in becoming ill were identified for age or sex for Event A or Event B.

Table 1. Univariable analysis to identify epidemiological associations between food exposures and salmonellosis among attendees of Event A (n=81) on 8 May 2016 and Event B (n= 46) on 14 May 2016 at a hotel restaurant in Canberra

Food exposure	Exposed			Not Exposed			RR[c]	95% CI[d]	*p*-value
	Cases	Total	AR[b]%	Cases	Total	AR[b]%			
Event A									
Smoked salmon and avocado dip sandwich[a]	23	57	40	2	23	9	4.64	[1.19-18.1]	<0.01
Berry macaron	13	55	24	8	19	42	0.56	[0.28-1.14]	0.12
Apple crumble	7	36	19	12	34	35	0.55	[0.25-1.23]	0.14
Cherry friand	6	35	17	11	34	32	0.53	[0.22-1.27]	0.14
Lemon slice	6	33	18	13	40	33	0.56	[0.24-1.31]	0.17
Mini quiche	22	65	34	2	14	14	2.37	[0.63-8.93]	0.21
Scones	24	79	30	1	1	100	0.30	[0.22-0.42]	0.31
Chocolate square	17	47	36	9	32	28	1.29	[0.66-2.51]	0.46
Panna cotta	16	60	27	5	14	36	0.75	[0.33-1.69]	0.52
Ricotta maple cream	24	78	31	1	2	50	0.62	[0.15-2.56]	0.53
Nut tart	11	46	24	8	26	31	0.78	[0.36-1.68]	0.53
Berry compote	23	76	30	2	4	50	0.61	[0.21-1.71]	0.59
Apricot friand	8	33	24	9	35	26	0.94	[0.41-2.15]	0.89
Cucumber sandwich	20	64	31	4	14	29	1.09	[0.44-2.70]	1.00
Event B									
Canapés									
Scallops	5	20	25	2	25	8	3.13	[0.68-14.1]	0.21
Mini quiche	6	31	19	1	13	8	2.52	[0.34-18.9]	0.65
Samosa	2	9	22	5	31	13	1.38	[0.32-5.95]	0.64
Spring rolls	3	16	19	4	26	12	1.63	[0.37-7.1]	0.66
Entree									
Pumpkin soup	6	23	26	1	21	5	5.48	[0.72-41.8]	0.10
Spinach and ricotta Raviolo	2	24	8	5	20	25	0.33	[0.07-1.54]	0.22
Main course									
Salmon fillet	6	27	22	1	19	5	4.22	[0.55-32.3]	0.21
Eye fillet	3	25	12	4	21	19	0.63	[0.16-2.50]	0.69
Dessert									
Cake	6	26	23	1	20	5	4.62	[0.60-35.3]	0.12
Chocolate tart	2	21	10	5	24	21	0.46	[0.10-2.11]	0.42
Sticky date pudding	4	27	15	3	19	16	0.94	[0.24-3.72]	1.00

[a] Statistically significant
[b] Attack rate
[c] Relative Risk
[d] Confidence Interval

Environmental health investigation

ACT Health only noted minor non-compliances such as minor cleanliness issues in the kitchen facilities. Swabs were taken from door handles knobs, preparation bench and boards, fixtures and utensils. Food safety procedures, and staff hygiene facilities and practices appeared to comply with food safety requirements. ACT Health issued an Improvement Notice based on minor violations, which was followed-up during a subsequent inspection.

Microbiological investigation

In total, 39% (13/33) of all cases who dined at the hotel restaurant at Event A or Event B submitted a stool sample. All specimens, except one, tested positive for *Salmonella* species. All *Salmonella* isolates were subsequently serotyped as *S.* Typhimurium. All (8/8) confirmed cases from cohort A were typed as *S*.Typhimurium (MLVA profile 03-12-18-14-523). Furthermore, routine surveillance identified six additional salmonellosis cases that reported eating at the restaurant between 3 and 12 May 2018 who were not part of either cohort A or B and all of these specimens were also typed as MLVA 03-12-18-14-523 (Fig 2). In contrast, all three confirmed cases from Event B were typed as *S.* Typhimurium (MLVA 03-10-14-11-496).

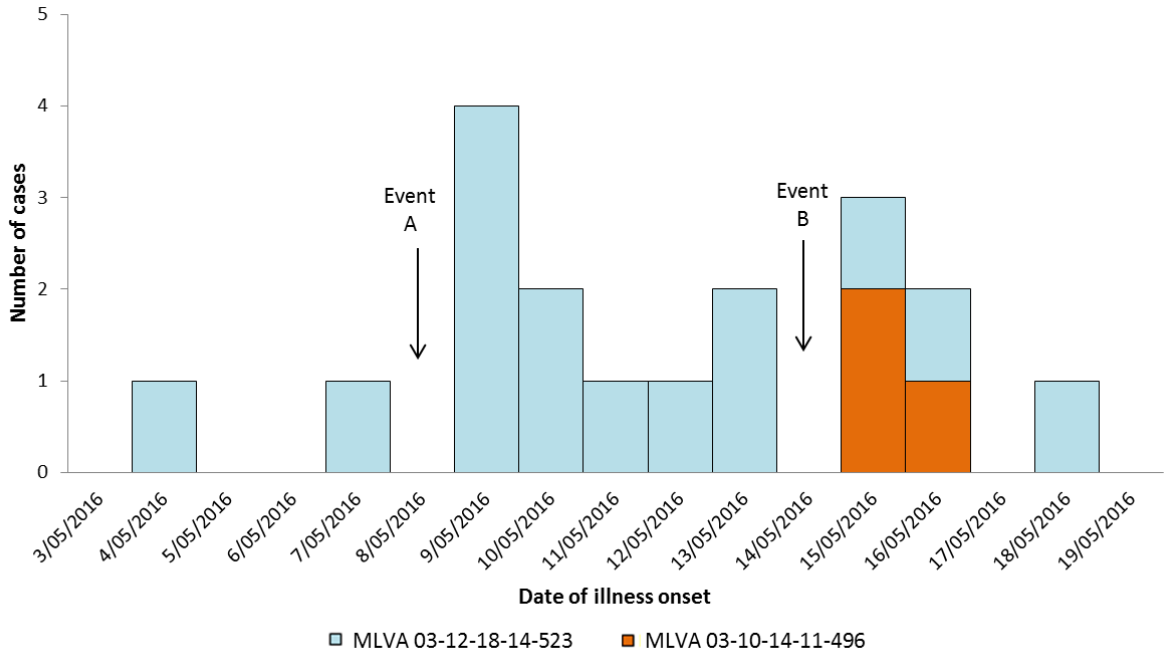

Fig 2. Epidemiological curve of MLVA profiles of *Salmonella* Typhimurium infection, by onset day, after dining at a hotel restaurant in Canberra, May 2016 (n=18)

The sequencing results for isolates related to this outbreak investigation were only received after the epidemiological investigation had concluded. WGS showed that isolates with the two MLVA profiles were approximately 90 single nucleotide polymorphisms (SNPs) apart.[17]

All environmental swabs and food specimens collected from the hotel restaurant tested negative for *Salmonella*.

Discussion

We investigated two well-defined point source cohorts within an intermittent source outbreak occurring at the same hotel restaurant, where illness was caused by two distinct MLVA profiles of *S*. Typhimurium. WGS confirmed that these strains were distinctly different, which is unusual for foodborne outbreaks in the same premises in a similar time period. The hotel restaurant was the common source of infection of the outbreaks; however we could not identify obvious common food exposures between the cohorts or between the two cohorts and the additional cases. Infections ceased spontaneously. According to the head chef at the hotel restaurant the functions were served different food items at each event, except for mini quiches, which showed an elevated, but not statistically significant risk of illness. The cohort study of Event A participants identified a statistically significant association with smoked salmon and avocado dip sandwiches, which is a potential food vehicle for this particular point source outbreak. Given the different MLVA profile associated with each cohort study, it is possible that the cause of infection was cross-contamination in the facility kitchen by two sources of infection or one source infected with two strains. However, this was not supported by the environmental investigation. Our investigation could not identify the food source that introduced *S*. Typhimurium onto the premises and the contamination events leading to human illness may never be identified. Nonetheless, there are many uncertainties surrounding the food served. Although there was no direct indication of eggs in this investigation, we don't know what sauces were served with the canapés, which may have contained raw egg as an ingredient. Consequently, a biological plausibility is that the outbreaks occurred due to cross-contamination with contaminated raw egg as the source.

S. Typhimurium infections have been linked to a range of food vehicles including meat such as chicken, pork, beef; milk products, nuts, and fresh produce.[1 2, 19] Outbreaks associated with *S.* Typhimurium infection are increasingly being attributed with a diverse range of sources and via a variety of pathways[19] and the identification of a novel *S.* Typhimurium MLVA profile could be an indication of a new source of infection. Nevertheless, eggs are a major source of *S.*Typhimurium outbreaks in restaurants or other commercial food settings in Australia, with raw egg use the main reason for contamination.[20] Egg handling procedures together with kitchen cleanliness reduce the risk of infection, however evidence suggests that *Salmonella* spp. can survive and persist on eggshells, with only 10^2 colony forming units of pathogenic strains of *Salmonella* capable of causing disease in vulnerable persons.[21] Consequently, eggs are potential causes of cross-contamination in the food service kitchen environment.

There are several limitations associated with our study. Although Event B results showed a number of foods associated with an increased risk, the small number of outbreak cases may have prohibited finding any strong food association for this outbreak. A further limitation includes potential recall bias, as persons who experienced gastrointestinal illness may be more likely to reflect on the foods they consumed than those unaffected by illness. In addition, there may have been recall bias around canapé items at Event B. The menu only stated 'Hot and cold canapés' for this event and it is unclear what was actually served. As the head chef was not able to provide details about the canapés, we were unable to verify what was served with these items such as dipping sauces, and how they were prepared. Consequently, how they were cooked (or potentially undercooked) could not be verified. Furthermore, in relation to canapés served, it is also difficult to recall which dipping sauces were served to accompany the canapés. It is thus important that accurate records of food prepared and served for each event is a standard that should be implemented by food service businesses not only for their own purposes but also to assist in the case of an outbreak, as testing leftover food specimens is not always possible to ascertain food served.

Food handlers who worked at the hotel restaurant were not interviewed to confirm reports that they had not experienced gastroenteritis symptoms. Therefore it is

possible that food handlers were a source of infection[22] but is highly unlikely given the two separate MLVA strains and human-to-food-to-human outbreaks are very rare with *Salmonella.* [23]

All environmental swabs and food specimens collected from the hotel restaurant tested negative for *Salmonella*. However, food items with short shelf lives would not have been available for testing at the time of the outbreak investigation. In addition, the food sampled may not have contained the pathogen or high enough doses resulting in a potential false-negative test.[24]

Finally, after the completion of the outbreak investigation two additional potential cohorts of persons with microbiologically-confirmed *Salmonella* infection who dined at the same restaurant were identified but could not be further investigated. The faecal test results for these cases identified the causative agent as the uncommon MLVA profile; *S.* Typhimurium (MLVA 03-12-18-14-523). Not being able to interview additional attendees of these events limited the study by not obtaining information regarding potential common food consumed.

Despite these limitations, our study identified that MLVA typing still presents itself as a powerful tool in the surveillance of *S*. Typhimurium. MLVA has been implemented progressively in Australia since 2008, and since 2016 for routine reporting in the ACT. The National Notifiable Disease Surveillance System contains MLVA data from 2008 onwards and, to date, our study was the first and only time *S.* Typhimurium (MLVA profile 03-12-18-14-523) was reported for an outbreak. Only one additional case of this novel MLVA profile was identified in South Australia (SA), Australia, in May 2016, around the same period our outbreaks occurred in the ACT. However, the source was unknown. As phage typing is still practiced in SA, the isolate was phage-typed as *S*. Typhimurium phage-type 9. This rare strain also appears to be new in the ACT, but ACT Health has only been routinely reporting MLVA typing information to NNDSS since 2016 (unpublished data, MDU PHL). The other strain, *S.* Typhimurium (MLVA profile 03-10-14-11-496), is also a phage-type 9. In Australia, phage type 9 strains have been commonly associated with chicken meat[25] and eggs.[2] Since 2016, three percent (9/352) of *S*. Typhimurium notifications in the ACT have been associated with *S.*

Typhimurium (MLVA 03-10-14-11-496), including the outbreak-associated cases we report.[26]

Our investigation shows MLVA to be sufficient for the identification of point source outbreaks. WGS confirmed that the two distinct MLVA profiles were approximately 90 single nucleotide polymorphisms (SNPs) apart[17] thus unrelated genomically. Octavia et al.[10] retrospectively examined *S.* Typhimurium isolates from epidemiologically confirmed outbreaks using WGS. Their results showed, with the exception of one outbreak, that the majority of the isolates (human and environmental) established to be epidemiologically implicated in the outbreaks varied by one or two SNPs or were genomically identical.[10]

The presence of multiple MLVA profiles, including a novel type, over several days in the one physical location demonstrates why the public health control of human salmonellosis is particularly challenging. Published studies reporting multiple MLVA profiles of *Salmonella* infection like in our study are not easily found. Although no major non-compliances in food safety practices were observed, the number and spread of cases associated with this outbreak investigation indicates this hotel restaurant was the common source of infections over several days. This strongly suggests multiple failures of food safety. Furthermore, the variety of foods prepared for each event makes cross-contamination of food via contaminated equipment or surfaces likely.

Thus, our study reinforces the importance that appropriate food handling and storage processes are followed by food service businesses to minimise risks of foodborne illness in patrons. Factors such as inadequate hygiene practices and design of equipment, and deficiencies in the control of ingredients have been linked to *Salmonella* cross-contamination and recontamination events.[27] Businesses that greatly handle the food that they produce have been found to be more likely to contaminate food with pathogenic bacteria.[28] Hence, food service businesses should ensure safe handling of foods, like eggs and egg products, and provide appropriate ongoing training of staff on food safety.[21] Ensuring food safety through improved food-handling practices by food service businesses is a key component to the control of

Salmonella in Australia. A commitment to identifying effective control measures also needs to be emphasised at the national level.

Australia's Foodborne Illness Reduction Strategy 2018-2021[+29] is an important step towards a nationally-consistent approach to reducing foodborne illness associated with *Campylobacter* and *Salmonella.* With high rates of *S*. Typhimurium notifications a national concern, it will otherwise inevitably remain a substantial public health burden and food safety challenge in Australia in the future.

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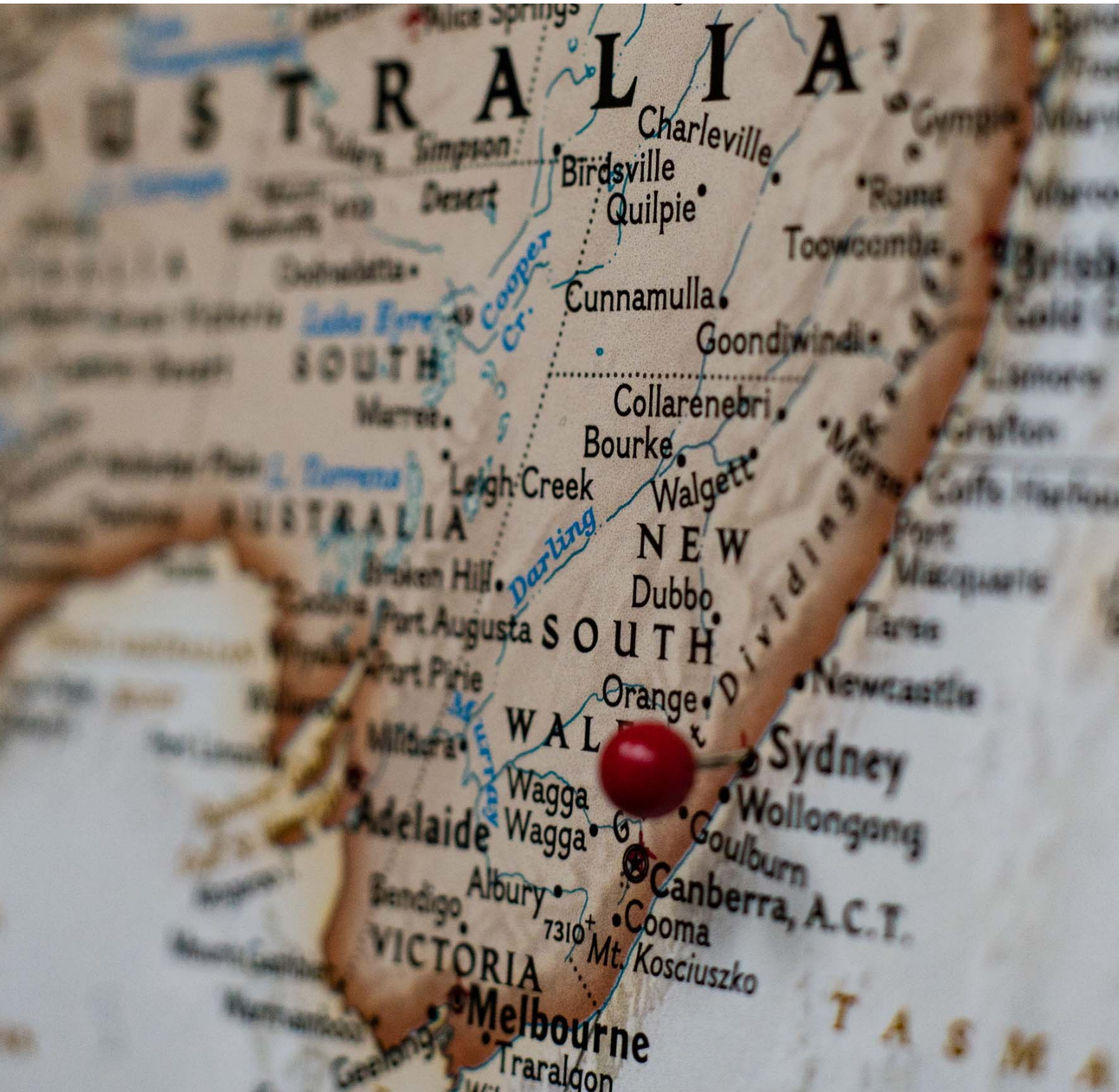
CHAPTER 5 –
EVALUATION OF THE NATIONAL HUMAN RABIES IMMUNOGLOBULIN DATABASE



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Prologue

This project was conducted to systematically and objectively evaluate the attributes of the National Human Rabies Immunoglobulin Database (NHRID) as a national surveillance system to monitor the usage of Human Rabies Immunoglobulin (HRIg), determine if the purpose and objectives are being met and if the surveillance system should continue as it stands. The analysis of its data has been undertaken by previous Master of Philosophy in Applied Epidemiology (MAE) Scholars; however, to date no comprehensive evaluation of the NHRID had been done since its inception on 1 January 2010.

This chapter outlines the evaluation methods, findings and recommendations.

My role

I was responsible for this evaluation, which included completing the following tasks:

- Literature review;
- Questionnaire design;
- Stakeholder consultation;
- Data analysis;
- Describe and evaluate the NHRID; and
- Development of:
    - Executive summary report and recommendations
    - Suggestions for the revision of the data fields for NHRID data collection
    - Design of a data collection tool that the Office of Health Protection, Australian Government Department of Health, can disseminate to jurisdictions to obtain HRIg usage associated exposure and risk factor information for biannual reporting or ad hoc, if required; and
    - An annual short report template for publishing findings in a public report.

Lessons learnt

After doing this evaluation, I have a clearer understanding for the premise of data collection. The collection of data into a national surveillance system should always have a purpose and clear public health actions. The collection of data without its

analysis is pointless. This project highlighted to me the importance of evaluation as a tool to ensure that a public health surveillance system is meeting a current need. Regular evaluation of surveillance systems ensure data collected is used to effectively inform public health action or to inform the future of the system such as amendments or cease of its use.

The findings of this project stressed that for the implementation of effective public health actions, it is important that staff are supported through the provision of tools that allow them to do their work effectively and use their time efficiently. The data in the NHRID was never used to inform how human rabies immunoglobulin is used in Australia mainly because of the difficulties getting data from the jurisdictions into the NHRID. The data management systems in Queensland and New South Wales did not integrate with the NHRID and Victoria had a backlog of paper forms that could not be entered into the NHRID in a timely manner to inform regular and frequent reporting. From the outset the NHRID could not provide a complete national picture of human rabies immunoglobulin use. Wherever possible, processes and tools including surveillance systems need to be planned and implemented with input from stakeholders who will be using them, both at the Commonwealth and in the jurisdictions.

Public health implications of this work

Based on the findings of my evaluation of the NHRID, I recommended reducing the number of data fields and the type of data that should be captured. I assessed the existing NHRID data fields and compared data fields used in the jurisdictions and centralised surveillance systems monitoring HRIg usage around the world, based on available published literature. Moving forward, I recommended a new selection of aggregate data fields to be used in the interim whilst a long term data collection system is developed and implemented.

I recommend that the NHRID should be moved off its current platform and that a different data collection tool should be implemented in the long term – one that captures HRIG usage data, both in the current era where HRIg is not in short supply and during critical supply shortages. This will allow the Australian Government

Department of Health to be well-prepared for the public health response associated with another HRIg supply shortage.

I recommended the use of an interim data collection template to allow HRIg usage and exposure and risk factor data to be captured in a format that is easy for jurisdictions to use whilst ensuring that the data still has public health value for the Office of Health Protection (OHP), Australian Government Department of Health. As part of this recommendation, I developed a proposed interim data collection template for OHP.

I recommended that the HRIg usage and exposure and risk factor data should be analysed, reported and disseminated to jurisdictions, the research community and the public. Consequently, I proposed the structure and content for an annual short report template as a reporting and dissemination tool to circulate findings to internal and external stakeholders via a public report. I suggested the option of creating a short report of 1) the usage of HRIg and the demographic, exposure and risk factors of potential exposures occurring domestically and overseas, or 2) a rabies and Australian bat lyssavirus (ABLV) post-exposure prophylaxis short report that captures both HRIg and rabies vaccine usage in Australia.

I presented my recommendations to the Communicable Diseases Network Australia (CDNA) members at the CDNA Face to Face Meeting on 28 June 2018, in their role as the decision makers on the future of the NHRID. All, except for two, of my recommendations were accepted and endorsed by CDNA on 17 July 2018 (Table 5F and 5G). I also provided the stakeholders who participated in my evaluation with a copy of the executive summary, recommendations and the outcomes from the CDNA meeting.

Acknowledgements

I would like to express my gratitude to all the persons, at the jurisdictional level and at the Australian Government Department of Health, who are either responsible for data entry into NHRID or use the data from the NHRID, for their time and involvement in this evaluation. Particularly, I'd like to thank the following persons for their assistance: Professor Martyn Kirk and Dr Ben Polkinghorne at the National Centre for Epidemiology and Public Health, ANU; Anna Glynn-Robinson, Phil Wright, Katrina

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Master of Philosophy (Applied Epidemiology) core activity requirement

- Evaluate a surveillance system
- Literature review that demonstrates skills in conducting a targeted literature search and synthesis

Abstract

Background

The National Human Rabies Immunoglobulin Database (NHRID) captures data, as reported by States and Territories in Australia, on persons who received human rabies immunoglobulin (HRIg) as part of their post-exposure prophylaxis treatment following a potential exposure to rabies virus overseas or Australian bat lyssavirus in Australia. The aim of this evaluation was to determine if the NHRID was meeting its objectives of collecting and reporting on national data on people who receive HRIg in Australia due to potential exposure to rabies virus overseas and Australian bat lyssavirus (ABLV) in Australia; identifying possible risk factors for these potential exposures; reporting on the approximate national HRIg usage*;* and informing the redistribution of HRIg in Australia.

Methods

The attributes of the NHRID were assessed against these objectives using the Centers for Disease Control and Prevention's *Updated Guidelines for Evaluating Public Health Surveillance Systems* and the European Centre for Disease Prevention and Control's *Data quality monitoring and surveillance system evaluation – A handbook of methods and application* frameworks.

Results

The evaluation found that the national collection and reporting of potential exposures to rabies virus overseas and ABLV in Australia and possible risk factors for these potential exposures in persons who receive HRIg in Australia is not only useful but essential to inform targeted risk-minimisation advice. These data have been used to inform policy on HRIg usage and led to a campaign to raise awareness of potential exposures to rabies virus whilst overseas. The NHRID was however found to require the improvement of stability, acceptability, representativeness, flexibility, data quality, simplicity, timeliness and usefulness. Stakeholder consultation found that difficulties transferring data from jurisdictions into the NHRID due to the legacy platform it sits on, and the loss of historical knowledge of the NHRID as a result of staff turnover, were barriers to the acceptance of the system. Three jurisdictions do not enter data directly into the NHRID and nearly one third (2,490/8,409) of entries in the NHRID do not state

how much HRIg was administered. Consequently, the data captured by the NHRID is not representative of the actual national HRIg usage.

Conclusion

To obtain data that is of high quality and useful to inform public health action, a redevelopment of the data fields and the data collection mechanism is required.

1. Introduction

1.1 Project rationale

In 2016, a review of the National Human Rabies Immunoglobulin Database (NHRID) to improve its usefulness and provide justification for the current collection of information was supported by the Communicable Disease Network Australia (CDNA). Previous MAE Scholars conducted data analyses using data from the NHRID in 2011 and 2014, respectively. Although the redevelopment of the NHRID was initiated it was changed to an evaluation as no comprehensive evaluation of the NHRID had been undertaken since its inception on 1 January 2010.

1.2 Aims and objectives

In this evaluation, I systematically and objectively evaluate the attributes of NHRID, to determine if the purpose and objectives were being met and if the database should continue as it currently stands. The objectives of this evaluation were to:

1. Assess the performance and effectiveness of the existing NHRID surveillance system, against the objectives determined by the Australian Government Department of Health in 2016;

2. Assess the extent to which NHRID influences decision making relating to the redistribution of HRIg;

3. Determine what system modifications or improvements would be worth making; and

4. Make recommendations to CDNA.

1.3 Methods

The Australian Government Department of Health will be referred to from here onwards as 'the Department' and the Australian States and Territories as 'jurisdictions'. The data that is collected in the NHRID such as Human Rabies Immunoglobulin (HRIg) usage, demographics, exposure and risk factors, health status, and past use of rabies vaccine will be referred to as 'NHRID data'.

Stakeholders

The primary users of the NHRID were the main stakeholders of this evaluation (Table 1). This group consists of decision makers from jurisdictions and the Department who will ultimately use the information generated from this evaluation to inform whether the NHRID is meeting its purpose and objectives and subsequently the future of the surveillance system. The secondary audience consists of groups who may find the outcomes of the evaluation useful but ultimately do not decide on the future of the surveillance system.

A list of primary users, those involved in the database operations and those served or affected by the surveillance system are summarised in Table 1.

Table 1. Primary and secondary target audience for the evaluation of the National Human Rabies Immunoglobulin Database

Primary users of the evaluation	
Communicable Diseases Network Australia (CDNA) members	
Office of Health Protection, Australian Government Department of Health	
Secondary audience	
Those involved in database operations	Jurisdictional health department/ public health unit epidemiologists
	Jurisdictional health department/ public health unit data entry personnel
Those served or affected by the database directly or indirectly	Australian Technical Advisory Group on Immunisation (ATAGI) working groups
	National Surveillance Committee (NSC)
	Australian National University

Eighteen consultations were held with stakeholders, who participate in the system (data entry) or use data generated by the system. Stakeholders included Office of Health Protection (OHP) staff (n=4), and jurisdictional staff identified by a list of

contacts from a previous review of the NHRID in 2016 and through referral (n=14). All stakeholders were emailed an invitation to participate in the consultation process through an un-structured telephone interview. The number of stakeholders consulted and their role and location is summarized in Table 2.

Table 2. Stakeholder consultation for the evaluation of the National Human Rabies Immunoglobulin Database

State/Territory	Number of stakeholders consulted	Role of stakeholders
Queensland	2	Epidemiologist Data manager
New South Wales	2	Epidemiologist Public Health Nurse
Victoria	1	Epidemiologist
Western Australia	2	Public Health Nurse Manager Public Health Nurse
South Australia	2	Epidemiologist Public Health Nurse
Australian Capital Territory	2	Epidemiologist Immunisation Officer
Tasmania	2	Epidemiologist Public Health Nurse
Northern Territory	1	Public Health Nurse
Commonwealth	4	2 x Epidemiologist Medical Officer Assistant Director
TOTAL	**18**	

Framework

The framework for the evaluation of the NHRID was based on the Centers for Disease Control and Prevention's Guidelines for Evaluating Public Health Surveillance Systems[1,2] and the European Centre for Disease Prevention and Control's *Data quality monitoring and surveillance system evaluation – A handbook of methods and applications*.[3]

Assessment of attributes and usefulness of the NHRID

This is the first time the NHRID has been comprehensively evaluated to identify if the system has been meeting its objectives since its establishment in 2010. Therefore, according to the ECDC[33], for an initial evaluation the appropriate attributes to be

evaluated include simplicity, flexibility, and usefulness. This evaluation also included acceptability, representativeness and stability.

The evaluation included quantitative data analyses, and qualitative analyses of information gathered from key stakeholders of the system.

The evaluation attributes are shown in more detail in Table 3.

Table 3. Evaluation attributes and key questions

Evaluation attributes	Key questions/Indicator
Undertake a review of the literature for public health importance	1. Total number of cases, incidence and prevalence of rabies 2. Indicators of severity, such as the mortality rate and the case-fatality ratio, disability-adjusted life years (DALYs) 3. Preventability 4. Costs associated with rabies and ABVL infections
Acceptability	1. Willingness of persons to use the database 2. Timeliness (speed between steps) indicator 3. Completeness indicator - percentage of missing information by required field. The number of completed data fields out of the total number of data fields' (unknown and missing items should be included in the denominator)[1] 4. Validity indicator - Proportion of coding errors within a dataset[1.] 5. Data quality indicator - evaluated by assessing the completeness and validity
Stability	1. Reliability (i.e. the ability to collect, manage, and provide data properly without failure)[1] 2. Availability (the ability to be operational when needed) of the surveillance system[1] 3. Adequacy (refers to the ability of the surveillance system to address its objectives)[1]
Usefulness	1. Participants were asked whether they use NHRID, what they used it for, what they think the objectives of database should be and their opinions about the strengths and weaknesses of NHRID. 2. Review the outcomes from data collected from NHRID (policy, practice, research)
Simplicity	Rating of the simplicity of the surveillance system by implementers and users of the system1: 1. Data necessary to complete the form 2. Other additional data collected on persons 3. Departments/organisations involved in receiving reports from a surveillance unit 4. Steps in the system 5. What information is required and would they want to receive on a regular basis 6. Amount of follow-up that is necessary to update data on the person 7. Method of managing the data, including time spent on transferring, entering, editing, storing, and backing up data 8. Time spent on system maintenance, if applicable
Flexibility	Rating of the ability of the surveillance system to adapt to changing needs, as perceived by the users and evaluators: 1. Capacity of the system to cope with inclusions/exclusions, changes in data fields, etc.) 2. Can it be easily integrated with other systems?
Representativeness	Rating of the surveillance system's ability to accurately describe a health-related event occurrence by time, place and person

[1] Based on European Centre for Disease Prevention and Control. Data quality monitoring and surveillance system evaluation – A handbook of methods and applications. Stockholm: ECDC; 2014.

As recommended in the CDC guidelines, the successful evaluation also includes the following steps[1, 2], which were incorporated into this evaluation:

a. Refer to the legal authority for the collection of the data.
b. Describe where the system sits within the organisation, including the context in which the system evaluation will be undertaken.
c. Describe if and how integration with other systems occurs, if applicable.
d. Create a flowchart diagram of the system.

The sensitivity and positive predictive value of NHRID are not applicable attributes for this evaluation. Sensitivity is associated with specificity, positive predictive value and negative predictive value. These four attributes are generally used in relation to case definition evaluations and the ability of a system to detect an event. [3]

Data analysis

Responses from the stakeholder interviews were analysed for common themes. Operating costs of the NHRID were estimated by calculating the time data entry personnel, who in most jurisdictions were public health nurses, stated they spent entering data into the NHRID by multiplying that time by the average hourly rate ($49.60/hour). In addition, the cost associated with extraction and analysis of NHRID data was estimated by calculating the time the Department data manager and epidemiologist spent extracting and analysing NHRID data by multiplying that time by the average hourly rate ($55.2/hour).

The usefulness of the system was examined by reviewing the objectives of the surveillance system; interviewing stakeholders from OHP in the Department and staff who were responsible for data entry into the NHRID in the jurisdictions; and reviewing the output of the system, including public health actions. Public health actions for the period 1 January 2010 to 1 February 2018 were identified through reviewing archival Departmental documents such as emails, papers, minutes, media communications, data requests and letters, and past MAE theses; and through interviews with the OHP staff. The simplicity, flexibility, stability and acceptability of the system were examined through unstructured interviews with OHP and jurisdictional staff, and by describing the flow of information through the system. Timeliness of reporting was evaluated by determining the period between the notification to the jurisdictional staff of a case

who had received HRIg treatment, and when their details were entered. To assess the completeness of the case records in the NHRID, the last date of data entry by jurisdiction was reviewed in Microsoft Excel 2010. Completeness of data fields in the NHRID was determined by the frequency of data fields that were blank or had unknown responses using Stata 13 (Stata Corp, College Station, TX, USA). Data completeness was defined as: Percentage of data completeness = (total notifications – missing or unknown) / total notifications x 100. The representativeness was assessed by the completeness of the NHRID.

Ethics

Ethics approval was sought for this study and granted by the Australian National University Human Research Ethics Committee [protocol: 2017/909].

2. Evaluation of the National Human Rabies Immunoglobulin Database

2.1 The public health importance of rabies virus and Australian bat lyssavirus

Human rabies is a neurological disease transmitted via saliva from rabid mammals to humans, via bite or scratch wounds or licking of mucous membranes.[4] This disease is caused by highly neurotropic viruses in the order *Mononegavirales,* in the family *Rhabdoviridae* and genus *Lyssavirus*.[5, 6] Rabies virus (genotype 1) and Australian bat lyssavirus (ABLV; genotype 7), a rabies-like virus unique to Australia[7], are members of the *Lyssavirus* genus which cause rabies disease.[5]

All mammals are vulnerable to infection with rabies virus. However, the single most important reservoir of the rabies virus are dogs (order *Carnivora*) followed by bats (order *Chiroptera*).[8, 9,10] Up to 99% of human rabies cases in rabies-endemic regions are attributable to rabies virus transmission via bites from domestic dogs.[11, 12] Australia is free of terrestrial rabies [11, 13] and ABLV infection is extremely rare.[7] The reservoir for ABLV are Australian pteropid fruit bat (or 'flying fox') species[14, 15, 16,17]and

insectivorous bats.[7,14,15]ABLV prevalence is less than 1% in the wild bat population[14] however increases to 5% to 10% in ill, wounded, or orphaned bats.[18 19 20]
Despite having the highest case fatality rate of any infectious disease (99.9%)[5, 8], human rabies remains a neglected disease. [11, 7, 8, 21, 22] It is a major global public health burden and affects mainly disadvantaged and vulnerable populations residing in remote rural areas [23] where vaccination of domestic dogs does not occur.[24] Rabies is a vaccine-preventable disease yet effective vaccines are not readily available, accessible or affordable to those who need them most.[10, 11] The prevention of clinical rabies, even after confirmed exposure to a lyssavirus, is almost 100% effective through the provision of post-exposure prophylaxis (PEP).[9,25,26,27] Once clinical symptoms present, however, there is no proven curative treatment. Thus rabies almost invariably results in painful death.[9]

Globally, nearly 60,000 people die of rabies every year[10,11, 28, 29], with an associated annual loss of over 3.7 million disability-adjusted life years (DALYs).[11, 28] Premature death of rabies victims (YLL) accounts for over 99% of DALYs lost (3.68 million).[10] However, due to its similarity with other encephalitic diseases, rabies is often misdiagnosed.[4, 30, 31,26]

Treatment for a rabies exposure can place a disastrous financial burden on those with limited financial resources: the average cost of rabies PEP is $40 (USD) in Africa, and $49 (USD) in Asia[12], whilst the typical daily income in these regions is approximately 1–2 USD per person.[12, 24] For these reasons, over 75% of victims die at home with no medical attention.[32,33,34] Thus no official record of their deaths exist[10] resulting in the underreporting of rabies in many rabies-endemic countries[12] and ultimately the lack of robust surveillance data.

The overall global economic costs associated with rabies were estimated as $8.6 billion (USD) (95% CIs: 2.9–21.5 billion).[10] These costs were predominantly linked to three causes: 1) loss of productivity from premature deaths ($2.27 billion [USD]), 2) PEP treatment costs ($1.70 billion [USD]), and 3) lost income as a result of seeking PEP treatment ($1.31 billion [USD]).[10] However, as mentioned above, the true burden of this disease is likely to be underestimated due to chronic underreporting.[12]

A direct link between human behaviour and potential exposure to rabies virus and ABLV exists resulting in the need for public awareness-raising to improve public health. Australian travellers, particularly female travellers, are interacting with animals such as monkeys and dogs whilst on holiday overseas and being exposed (e.g. being bitten or scratched). [35, 36] However, review of NHRID data suggests that persons are suffering animal-related injuries due to a variety of animals such as "cat, squirrel, horse, Asian cat bear, rat, tiger, pizote (badger), lion, orang-utan, hutia (banana rat), cheetah, mongoose, coati (racoon), civet, cow, leopard, lemur, otter, tree rat and mouse". [36] In Australia, humans are moving further into bat habitats leading to bat camps in metropolitan areas and increasing human-bat interaction[37], especially with sick or injured bats which have the highest risk of ABLV. Based on previous studies, males account for over half of persons requiring HRIg after potential exposure to ABLV in Australia. [35, 36] Changing human behaviour however is not straight forward and interventions require time to achieve results. Thus longer-term strategies should be considered to achieve long-term changes in behaviour to reduce potential exposure and thus the need for treatment with HRIg to prevent the onset of rabies disease.

Preventability of human rabies

Currently, rabies prevention involves the implementation of two strategies: dog vaccination to interrupt virus transmission to humans, and human vaccination.

The prevention of rabies via human vaccination is highly effective in preventing clinical rabies[9, 25, 27, 38] and prevents an estimated 327,000 annual deaths.[39] Human vaccination comprises of the use of purified cell-culture and embryonated egg-based vaccines (CCEEVs) either before (pre-exposure prophylaxis [PrEP]) and/or after (PEP) suspected or proven exposure to a lyssavirus. [11]

Pre-exposure prophylaxis (PrEP)

Persons who are prone to occupational and/or travel-related exposure to rabies virus in specific settings or over a prolonged period, such as veterinarians, laboratory workers, certain travellers, and children living or visiting rabies endemic areas, are

recommended to receive PrEP (i.e. be vaccinated against rabies).[40, 41] PrEP consists of a series of rabies vaccines, followed by booster vaccinations in case of exposure (Fig.1).

Post-exposure prophylaxis (PEP)

The indicated PEP procedure is determined by the category of exposure.[11] Table 4 shows the lyssavirus exposure type categories, which describe the rabies virus exposure risk based on the type of contact with the animal potentially infected with rabies virus.

Table 4. Lyssavirus exposure categories and recommended post-exposure prophylaxis (PEP), WHO (2018)

Exposure type category	Description	Post-exposure prophylaxis measures
Category I	Touching or feeding animals, licks on intact skin	None
Category II	Nibbling of uncovered skin, minor scratches or abrasions without bleeding	Immediate vaccination and local treatment of the wound
Category III	Single or multiple transdermal bites or scratches, licks on broken skin; contamination of mucous membrane with saliva from licks, contacts with bats.	Immediate vaccination and administration of rabies immunoglobulin; local treatment of the wound

PEP is required for all category II and III exposures which have been assessed as a potential risk of developing rabies. This risk is increased if the following attributes are also present [12]:

- "the biting mammal is a known rabies reservoir or vector species;
- the exposure occurs in a geographical area where rabies is still present;
- the animal looks sick or displays abnormal behaviour;
- a wound or mucous membrane was contaminated by the animal's saliva;
- the bite was unprovoked;
- the animal has not been vaccinated".

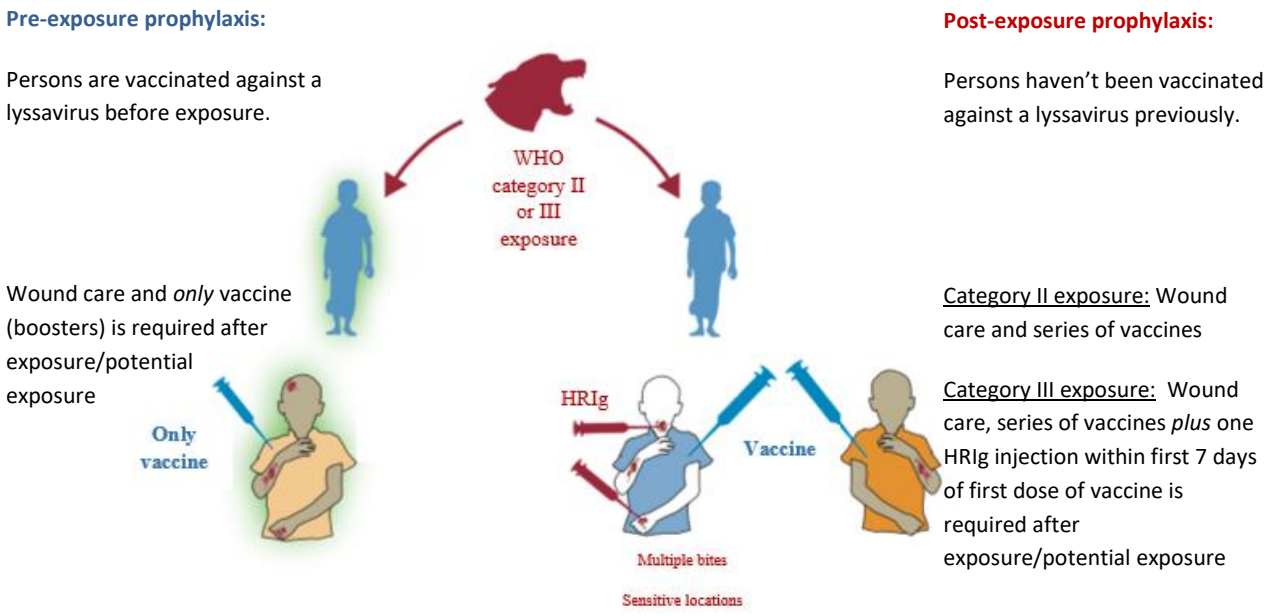

Fig 1. The two main WHO immunisation strategies to prevent human rabies (pre-exposure prophylaxis and post-exposure prophylaxis) and the therapy required after possible exposure (Adapted from: Rabies vaccines and immunoglobulins: WHO position; World Health Organisation, 2018).

Legend: HRIG = human rabies immunoglobulin

As recommended by the World Health Organization (WHO), PEP is promptly administered following a potential exposure and includes three components:

1) Immediate, rigorous wound care;
2) Active immunisation using rabies vaccines; and
3) Passive immunisation using HRIg.

The first component reduces the viral inoculum at the wound site.[11, 42] Both active and passive immunisation prevent the virus from reaching the central nervous system (CNS). Active immunisation is initiated following the administration of a series of intradermal or intramuscular rabies vaccines over 7−28 days. Antibodies lower the risk of lyssavirus entering peripheral nerves after a bite from an infected animal.[43, 44] As outlined in the Rabies vaccines: April 2018 WHO position paper, HRIg is recommended for category III exposure.[45] It is administered once and must be administered within the first seven days since the first dose of vaccine to avoid HRIg from potentially interfering with the immune response to the vaccine.[9, 46 ,45, 12] There are three post-exposure prophylaxis regimens, Institut Pasteur du Cambodge (IPC), Essen and Zagreb.

The IPC regimen lasts seven days with rabies vaccine administered intradermally on 2 sites on days 0 (immediate), 3 and 7. In the Essen regimen the PEP course is administered intramuscularly over 14-28 days with rabies vaccine administered on days 0, 3, 7, and between day 14 to 28. In the Zagreb regimen, rabies vaccine is administered in two different sites intramuscularly on day 0, followed by a single dose of rabies vaccine on day 7 and 21, respectively.[45] Figure 2 provides a summary of these regimens.

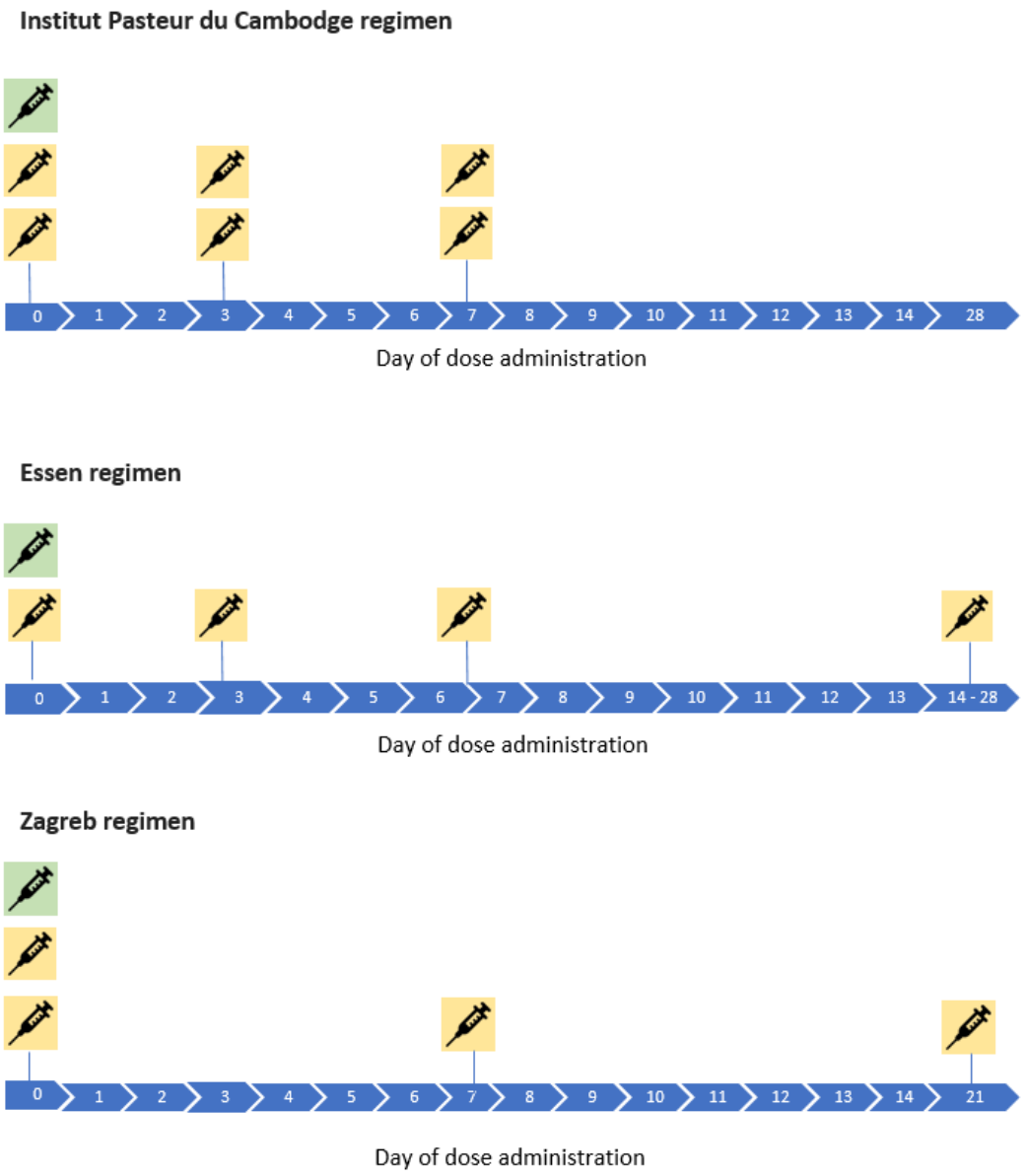

Fig 2. Post-exposure prophylaxis for persons with category III exposure who did not receive pre-exposure prophylaxis, by regimen. (Adapted from: *Rabies vaccines and immunoglobulins: WHO position April 2018*)

Legend: Yellow syringe = Rabies vaccine. Green syringe = Human rabies immunoglobulin

The administration of HRIg into and around the wound early in the vaccination regimen neutralises the lyssavirus at the wound site and provides additional protection before the immune system can respond to the vaccine. This extra protection is especially important for patients with severe and/or multiple wounds.[11]

In the absence of PEP, the average probability of developing rabies following a bite by an infected animal increases the closer the bite is located to the CNS: lower limb (12%), the trunk (9%), upper extremity (22%), the head (55%).[11, 47,46]

PEP administration in Australia

The *Australian Immunisation Handbook 10th edition* [48] and the CDNA National Guidelines (SoNG) for Public Health Units: *Rabies virus and other Lyssavirus (including Australian bat lyssavirus) exposures and infections* [49] (Rabies and ABLV SoNG), are guided by the WHO's position paper on rabies vaccines.[25] At the time of the evaluation, the Rabies and ABLV SoNG was being updated.

The *Australian Immunisation Handbook 10th edition* are guidelines approved by the Chief Executive Officer (CEO) of the National Health and Medical Research Council (NHMRC) for clinical practice and provides guidance in use of HRIg. The Rabies and ABLV SoNG provides nationally consistent guidance to public health staff and is publicly available on the Department's website. [50] In Australia, the following post-exposure prophylaxis (PEP) for unvaccinated immunocompetent persons is recommended:

- Four doses of rabies vaccine with the first dose given as soon as possible (day 0), with successive doses given on days 3, 7 and 14; and
- HRIg is administered at the same time as the first dose (day 0) of the rabies vaccine at 20 International Units (IU/ml) per kilogram of body weight, where indicated.

Similar to the WHO categories, the recommended PEP depends on the type of contact with the suspected rabid animal. Algorithms that have been modified from the Australian Immunisation Handbook for potential exposure to classical rabies virus from a terrestrial animal overseas and potential exposure to lyssavirus from bats in Australia or overseas are summarised in Table 5. The table depicts when HRIg should be administered (orange).

Table 5. Post-exposure prophylaxis administration for potential exposure to classical rabies virus and lyssavirus

Exposure	Category I	Category II	Category III
Classical rabies virus from terrestrial animal overseas	No prophylaxis	Non-immune/ immunocompetent = Vaccine only	Non-immunised/ immunocompetent = Vaccine and HRIg
		Previously immunised = Vaccine only	Previously immunised = Vaccine only
Lyssavirus from bats in Australia or overseas	No prophylaxis	Previously immunised = Vaccine only	
		Non-immunised/immunocompetent = Vaccine and HRIg	

(Adapted from: The *Australian Immunisation Handbook 10th edition)*

2.2 PEP surveillance systems

Based on limited published literature, Canada, France, Poland, England and Wales are the only countries that have a national surveillance system that collects data on HRIg usage. Their systems collect data on the two components of PEP: HRIg and rabies vaccine usage.

Canada uses an online disease surveillance system, the integrated Public Health Information System (iPHIS), for the collection of data on the exposure incident when PEP is recommended.[51] Each record includes demographic information, notification and exposure date , animal type, exposure type, the rabies status of the animal, and a free- text field for additional information.[52] In Europe, France and Poland have centralised surveillance systems to monitor national PEP usage.[53] In France, delivery of PEP is only allowed through an official network of Antirabies Medical Centers (ARMC) located across continental France. A standard case-report form collects data on geographic location, consultation date, exposure type, animal type, exposure date and clinical decision about PEP. Summary reports describing the individuals visiting ARMC and those receiving PEP are released on an annual basis.[54] In the United Kingdom (UK), the public health agencies of each part of the UK have responsibility for provision of PEP following an appropriate risk assessment using a request form for rabies post

exposure treatment. The arrangements for monitoring usage therefore vary between Public Health England, Public Health Wales, Health Protection Scotland and the Public Health Agency of Northern Ireland. [55] Public Health England centrally compiles stock reports and annual reports on PEP.[56] The Wales Specialist Virology Centre delivers a national service for rabies prophylaxis for Public Health Wales. [57]

Australia on the other hand has a national surveillance system that monitors HRIg usage and the associated potential exposures and risk factors, but not rabies vaccine usage.

The following section outlines the HRIg surveillance system in Australia, which was implemented to capture data on persons who received HRIg as part of their post-exposure prophylaxis treatment following a potential exposure to rabies virus overseas or ABLV in Australia.

2.3 HRIg surveillance in Australia

In this section, I present the findings regarding the operation of the surveillance system, including the legal basis, the monitoring of stock levels, the history of the system, the surveillance case definition and purpose, data sources, flow of data, and the human resources required to operate the system. This provides the context in which to discuss the attributes of the NHRID, in section 3.

Legal basis

Rabies virus and other lyssavirus (including ABLV) exposures and infections are considered an important public health priority in Australia. The surveillance of these diseases covers the whole Australian population. The *National Health Security Act 2007* (NHS Act) provides the legal framework for sharing information between the Department and the jurisdictions. Rabies virus and ABLV are diseases included on or under:

- Jurisdictional government legislation[58-65];
- The National Notifiable Diseases List (NNDL), which is a legislative instrument under the NHS Act;

- National Notifiable Diseases Surveillance System that collects information on diseases on the NNDL; and
- National List of Notifiable Diseases of Terrestrial Animals, notifiable to the World Organization for Animal Health (OIE).

There is no legal basis for the collection of HRIg usage data. However, in the Rabies and ABLV SoNG it does state that the collection and reporting of de-identified data on potential human exposures to rabies virus or other lyssaviruses, including ABLV, and the usage of HRIG in Australia is to be undertaken. In addition, it mentions entering the rabies virus or other lyssaviruses (including ABLV) exposure data into NetEpi (i.e. NHRID) and/or jurisdictional database, as appropriate. According to the Rabies and ABLV SoNG, data should be collected to better inform prevention strategies, including travel advice.

The Rabies and ABLV SoNG also includes guidelines regarding the management of potential human exposure to rabies virus or other lyssaviruses, including ABLV. The definition of a potential human exposure is outlined in Box 1.

Box 1: Definition of potential human exposure to rabies or other lyssaviruses

Potential human exposure is defined as:
"Any bite or scratch from, or mucous membrane or broken skin contact with the saliva or neural tissues of, a bat in Australia or elsewhere in the world, or a wild or domestic terrestrial mammal in a rabies-enzootic country. The latter includes Bali, Indonesia from August 2008 onwards.

Any bite or scratch from, or mucous membrane or broken skin contact with the saliva or neural tissues of a wild or domestic terrestrial mammal in Australia, where there is laboratory confirmation of infection with any lyssavirus, should also be managed as a potential exposure."

Source: The SoNG: Rabies virus and other Lyssavirus (including Australian bat lyssavirus) exposures and infections, 2014

History of HRIg surveillance in Australia

A number of reasons have led to an additional demand on HRIg supplies in Australia. Firstly, the detection of rabies amongst dogs in Bali, Indonesia, in late 2008 with subsequent human cases and secondly, the detection of rabies in Bali and the ensuing increase in the number of returning unvaccinated travellers potentially exposed to rabies virus that require PEP. Consequently, the Department implemented a data collection tool to monitor and reduce unnecessary usage of HRIg – the National Human Rabies Immunoglobulin Database (NHRID). The *Shortage of Rabies Immunoglobulin and Post Exposure Treatment for Rabies and Australian Bat Lyssavirus Protocol* (2009), commonly known as the HRIg rationing Protocol, provides guidance in the event that rationing of HRIg is required to improve supply (when HRIg supplies are low and shipments of new supplies are not foreseen) and reduce unnecessary use of HRIg in Australia. The HRIg rationing Protocol, endorsed by the Australian Health Protection Committee (AHPC), mentions the development of a national database (i.e. NHRID) to monitor "*post exposure management including exposure details (type of injury, animal and geographic location) and testing of bats implicated in human exposures in Australia"* to ensure Australia has an accurate assessment of the amount of HRIg likely to be used in each season. At the time of the evaluation, the HRIg rationing Protocol was not in force.

The original aims for the implementation of the NHRID included:

1. Monitoring of HRIg usage for post exposure management including exposure details (type of injury, animal and geographic location) and testing of bats implicated in human exposures in Australia.
2. Provide an accurate assessment of the amount of HRIg used in each season and to determine critical minimum HRIg levels upon which HRIg stock would require redistribution.

The NHRID was reviewed for redevelopment in 2016 to determine if it was effectively monitoring and describing HRIg usage, as well as the extent to which NHRID influences decision making relating to the redistribution of HRIg. As part of the redevelopment, the objectives of the NHRID were redefined. Box 2 describes the objectives of the NHRID as proposed by the Department in 2016.

Box 2: Objectives of the National Human Rabies Immunoglobulin Database

1. *Collect and report national data on people who receive HRIg in Australia due to potential exposure to rabies virus overseas and ABLV in Australia.*
2. *Identify possible risk factors for these potential exposures.*
3. *Report on the approximate national HRIg usage in Australia.*

Source: Redevelopment plan for the National Human Rabies Immunoglobulin Database, 2016

The NHRID monitors HRIG usage in Australia as part of post-exposure prophylaxis treatment in unvaccinated individuals who have been potentially exposed to a notifiable disease(s), namely rabies virus or other lyssaviruses such as ABLV. Box 3 outlines the case definition.

Box 3: National Human Rabies Immunoglobulin Database case definition

A case is defined as:

A person who requires HRIg and received HRIg in Australia on or after 1 January 2010.

Source: Case protocol for Rabies Immunoglobulin National Database, 2009

Since the implementation of the NHRID, additional factors have led to a further demand on HRIg supplies in Australia:

1. Increased reporting of potential exposures to ABLV in Australia following the death of a Queensland child in February 2013;
2. The death of two infected horses in Queensland from ABLV in May 2013. These horses were the first known cases of ABLV identified in an animal other than a bat [66-68,]; and
3. A television program in June 2013, which focussed on a death associated with ABLV.

Two large increases in persons receiving HRIg for potential exposures were observed in response to the above events. The first increase was after the death in Queensland in

2013 and the second increase coincided with the deaths of the infected horses and the airing of the television program. [36]

The main indications for rabies PEP in Australia are presented in Box 4.

Box 4: Main indications for rabies PEP in Australia

There are two main indications for rabies PEP in Australia:

- *"travellers who have had animal bites/scratches in a geographic location where rabies is known to be endemic in animal populations; and*
- *people in Australia, where Australian bat lyssavirus (ABLV) is endemic, who have had bites/scratches from bats"*.

Source: Case protocol for Rabies Immunoglobulin National Database

Monitoring HRIg stock levels

Monitoring HRIg usage to avoid critical stock levels ensures all persons potentially exposed to rabies virus overseas or ABLV in Australia have access to HRIg for post exposure treatment, preventing onset of clinical symptoms and inevitable death. HRIg remains in short supply globally [69,53] as it is manufactured from human blood plasma of suitable human donors which results in a high cost of production. [70, 71, 72] Worldwide, a maximum of five million doses of HRIg are produced and sold every year.[53]

Sanofi Pasteur is the primary supplier of the only registered HRIg product in Australia, *Imogam Rabies Pasteurized* – Sanofi Pasteur Pty Ltd human rabies immunoglobulin (IMOGAM®). The Department maintains an inventory of IMOGAM® stock held by Sanofi Pasteur and monitors supply issues. Each vial of IMOGAM® contains the active ingredient, human rabies immunoglobulin. The final formulation is a liquid and the potency is assessed in IU/ml. There are at least 300 IU of human rabies immunoglobulin in each 2mL vial. The Department liaises regularly with Sanofi Pasteur to determine how much IMOGAM® stock they have available. In recent years, Australia has on occasion experienced critically low levels of IMOGAM®. Following a shortage of IMOGAM® in February 2011, the Department successfully negotiated with Sanofi Pasteur to increase Australia's allocation for future years to provide a buffer against increased demand. However, should Sanofi Pasteur only have four weeks of stock left, the Department has access to alternate supplies of HRIg. A backup wholesaler, Link Healthcare, sources *KamRAB Rabies Immune Globulin* (KamRAB™), an unregistered HRIg product from

Israel, through a Special Access Scheme (Category A) managed by the Therapeutic Goods Administration. To date, 12 orders of KamRAB™ had been placed since the first delivery in 2013. At the time of the evaluation, there was no critical level of HRIg in Australia.

In Australia, the total HRIg usage of IMOGAM® between 2010 and 2017 was 45,667 vials which equates to roughly $13.7 million spent on HRIg treatment (~ $2 million/year). This is approximately 9,134 treatable cases at 5 vials (10mL) per case.

The Department advises jurisdictions when national surveillance indicates critical levels of HRIg are anticipated. It facilitates redistribution of stocks and implementation of rationing procedures. In the event a jurisdiction has low levels of HRIg stock the Department redistributes the available stock in Australia between jurisdictions. Box 5 outlines the algorithm to determine when the critical minimum level has been reached.

Box 5: Identification of critical supply levels of HRIg

Minimum HRIg required – A mls x (B+C) weeks

A = anticipated use of HRIg: mls per week
B= weeks until next shipment into Australia
C= allowance (4 weeks) for any supply chain delay

Source: Shortage of Rabies Immunoglobulin and Post Exposure Treatment for Rabies and Australian Bat Lyssavirus Protocol, 2009

Description of the NHRID

The NHRID sits within OHP at the Department. It is a national, passive surveillance system where information is collated through an online surveillance database system hosted on NetEpi. In 2010, NetEpi was the only system administered by the Department that had web-enabled data sharing capabilities that could support timely and simultaneous collection of data by multiple jurisdictions centrally.

NetEpi was developed by the Centre for Epidemiology and Research, at the New South Wales (NSW) Department of Health, following the global Severe Acute Respiratory Syndrome threat in 2003. [73] Its primary purpose was the collection of structured information about cases and contacts of disease through the internet. [74] Currently, NetEpi hosts the NHRID and OzFoodNet's National Enhanced Listeriosis Surveillance

System (NELSS). It is also available for jurisdictional use for foodborne disease or other disease outbreaks. However, NetEpi is now a legacy system that is no longer supported or maintained by the Department. The server was last updated in 2008 and formal IT support of NetEpi within the Department ceased in 2011.

The NHRID is an indicator surveillance system that captures HRIg usage-related information of every human exposure requiring rabies post-exposure prophylaxis in Australia. Although the backend of the NHRID has database properties, it is a flat file (i.e. only has one table) and is not a relational database management system (RDBMS), the standard for databases. NetEpi does not have the ability to house data in multiple tables with linkages between them thus the case details of a person can be entered multiple times. NetEpi also does not have an in-built mechanism to prevent duplicates. Consequently, the case details of an individual can exist within the NHRID multiple times if they received HRIg in multiple jurisdictions over a number of years.

Information collected

The population under surveillance are persons who received HRIg in Australia after having an animal-related injury and potentially exposed to rabies virus or ABLV from 1 January 2010. The purpose of the NHRID is outlined in Box 6.

Box 6: Purpose of the NHRID

"*This national database of cases of possible rabies/lyssavirus exposure will record post-exposure prophylaxis involving the use of RIG and document possible animal exposures. Information sought will include details on exposure (type of injury, animal and geographic location), post-exposure prophylaxis and testing of bats implicated in human exposures in Australia*".

Source: National Human Rabies Immunoglobulin Database, 2010

The system uses a questionnaire that collects 45 data fields (see Supplementary Information Table S1). Each record contains information pertaining to the person who received HRIg as part of their post exposure management and includes demographic information, dates of interest (i.e. exposure date, wound assessment date and treatment date), the type of exposure (e.g., bite, scratch exposure, country of

exposure), the type of wound and location, the type of animal, the type of risk factor (e.g. occupational risk, travelling), the past use of rabies vaccine, the rabies status of the animal, the immunocompromised status of individual, the treatment details of individual, as well as a free-text “notes” field for reporting other relevant information such as clinical or other facts.

Data sources

In Australia, each jurisdiction has their own notification form for collecting data on persons requiring HRIg as part of their post exposure management. Generally, these forms are in hardcopy or fillable PDF format. Supplementary Information Table S2 provides a summary of HRIg usage-related information captured in jurisdictional rabies forms against NHRID data fields currently collected.

The notification form is either completed by the public health unit/jurisdictional health Department if they were contacted directly or completed by the health practitioner. Subsequently the form is emailed/faxed to a public health unit/jurisdictional health Department. At present, all except three jurisdictions (Victoria [VIC], NSW and Queensland [QLD]), enter data directly from forms into NHRID. QLD, VIC and NSW do not upload data directly into NHRID because their systems do not integrate with NetEpi. Their NHRID data is provided to the Department upon request only, after which it is uploaded into the NHRID by the Department. The remaining jurisdictions, except for South Australia (SA) and Western Australia (WA), undertake double manual data entry of the information from the form: the information is entered manually into their local database (Microsoft Excel spreadsheets) and then also into the NHRID. The only jurisdiction that uses the NHRID on NetEpi as its primary HRIg usage database is SA and WA uploads a CSV file into the NHRID.

The following flowchart diagram (Fig 3) summarises the data flow for the NHRID:

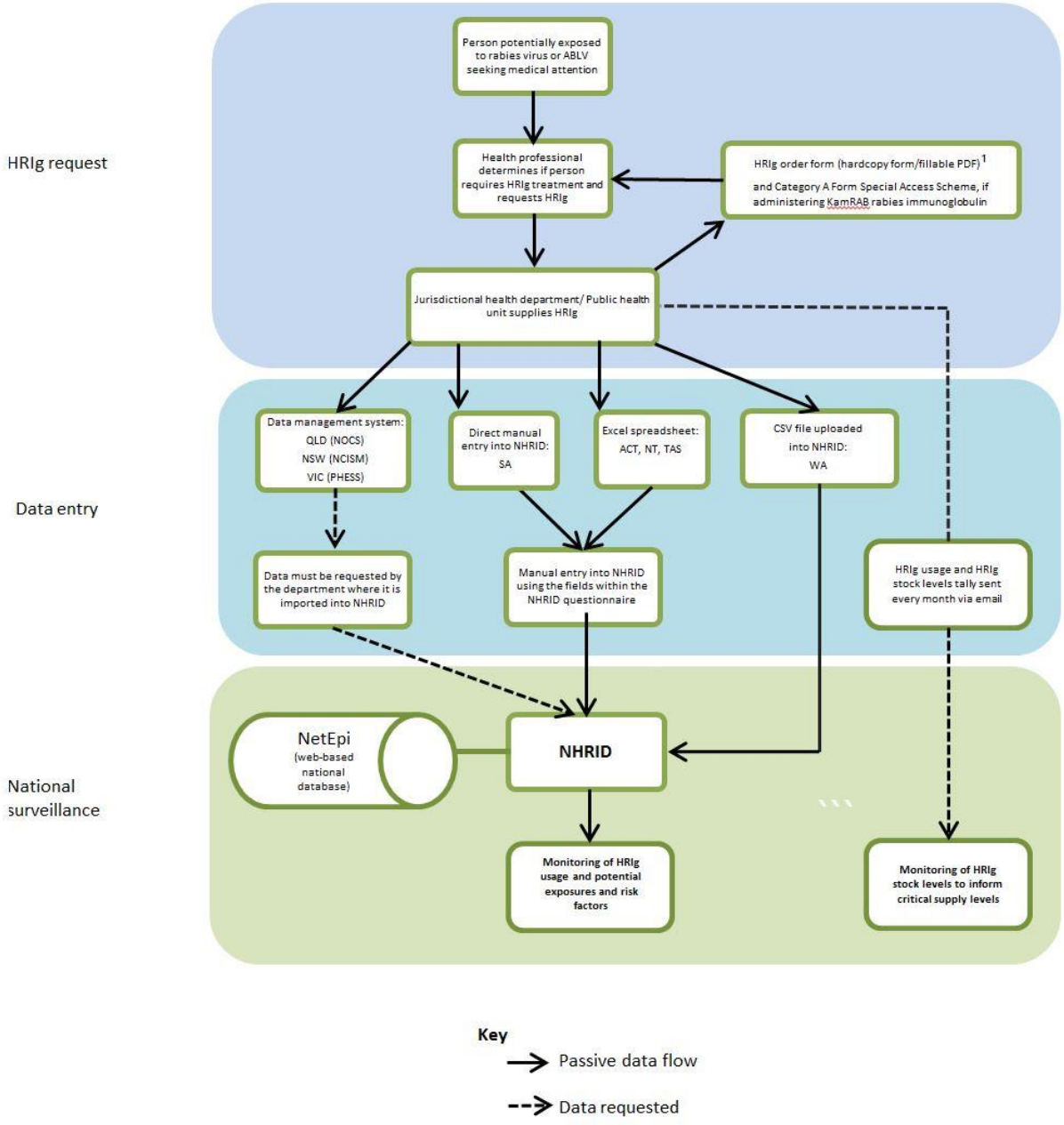

Fig 3. Data flow for National Human Rabies Immunoglobulin Database

Legend: ABLV, Australian bat lyssavirus; HRIg, Human Rabies Immunoglobulin; ACT, Australian Capital Territory; NT, Northern Territory; SA, South Australia; TAS, Tasmania; WA, Western Australia; QLD, Queensland; NSW, New South Wales; VIC, Victoria; NHRID, National Human Rabies Immunoglobulin Database; NOCS, Notifiable Conditions System; NCISM, NSW Notifiable Conditions Information Management System; PHESS, Public Health Event Surveillance System; CSV, comma separated values file.

Transfer and management of information

There are three data entry and two data export methods for the NHRID. Data entry can be accomplished using the following methods:

1. Upload into NHRID using an import rule file through NetEpi:
2. Adding a case manually (i.e. one case at a time) to the NHRID using a graphical user interface; and
3. Upload into NHRID by the Department.

Export of data from NHRID is accomplished either by exporting data manually or exporting data in a report.

HRIg usage data transfer not involving the NHRID

In addition to the upload into the NHRID, all jurisdictions, except VIC, send the Department an email every month (Fig 3) with the following information:

a. Stock holdings tally
b. Usage tally

} HRIg (IMOGAM® and KamRAB™)

VIC only emails a tally of HRIg stock holdings. This method allows the Department to receive the information it requires in a straightforward and timely fashion. Jurisdictions supply counts of how many 2ml vials and total ml is available of HRIg in their respective jurisdiction. This information is stored in an Excel spreadsheet monitored by a team in OHP responsible for monitoring HRIg stock levels for the Department (Fig 3). Although the Department receives regular HRIg usage tallies via this mechanism it is not routinely collated or monitored. Therefore, it is not used to inform national HRIg stock levels nor is it used to monitor national HRIg usage.

Data management of the NHRID data is currently not undertaken. The NHRID was last accessed by the Department in 2016.

Analysis, reporting and dissemination

NHRID data has not been cleaned, analysed, reported nor disseminated by the Department since 2014. This work involved extensive effort to update and clean the data. Analysis of NHRID data at the national level has been undertaken twice since its inception to determine HRIg usage in Australia (Fig 4). However, since its implementation, national routine surveillance of HRIg usage using data from the

NHRID have not been undertaken for the purpose of monitoring HRIg usage in Australia.

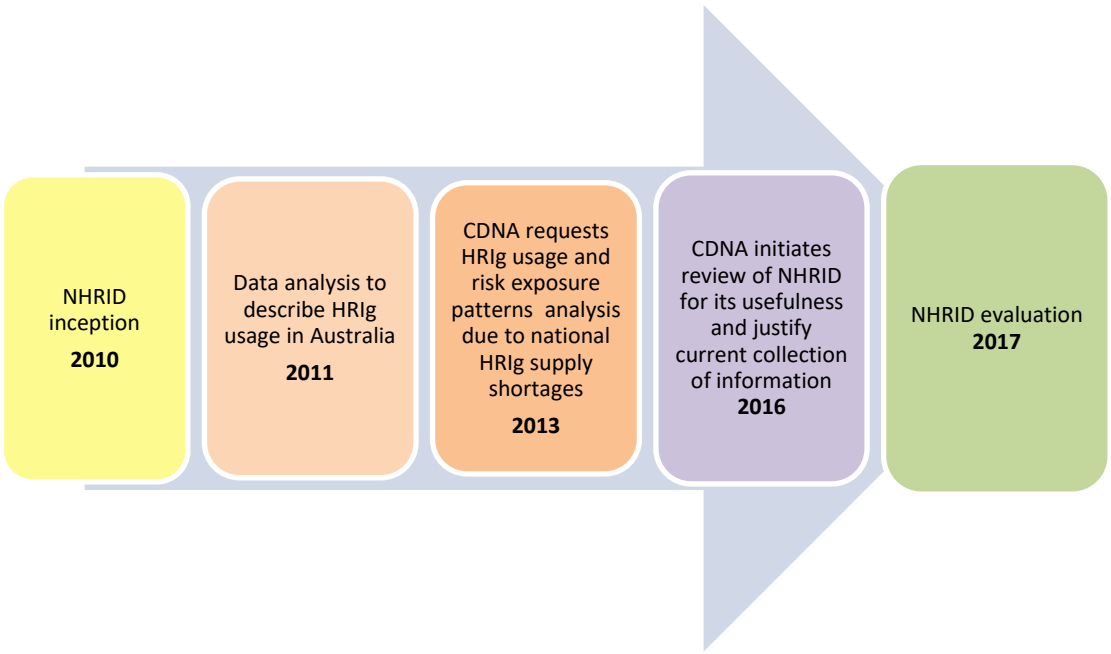

Fig 4. Timeline of data analysis undertaken of NHRID data

Resources and costing of NHRID

At the Department, one staff member is currently responsible for monitoring HRIg stock levels, the redistribution of HRIg stocks to the jurisdictions and access to alternate supplies of HRIg. The last time the Department had to implement this backup supplier was in April and June of 2016. Consultation revealed that the data from the NHRID however did not inform this process.

There is one epidemiologist at the Department who is responsible for the analysis of the NHRID data. However, analyses of these data are not a routine task and are undertaken on an as-needed basis.

Quality control or maintenance of the NHRID data is not routinely undertaken at the Department. The jurisdictions also do not allocate resources for quality control of data in the NHRID.

The number of cases that need to be entered into the NHRID depends on the season (school holidays) when more people are potentially exposed to rabies virus whilst overseas requiring HRIg treatment when they return.

In addition, the resources and cost are difficult to estimate for the jurisdictions who supply NHRID data to the Department for upload, as it varies by jurisdiction. An upload by the Department can take three days to several weeks, depending on complexity and size of the data being provided.

3. Evaluation of the attributes of the NHRID

The following section outlines the results of the evaluation based on the system attributes. I also make recommendations which may apply to more than one attribute.

The evaluation found that the collection and reporting on national data on people who receive HRIg in Australia through the NHRID serves a public health function by informing rationale use of HRIg through targeted risk-minimisation advice. These data have been used to inform policy on HRIg usage and led to a campaign to raise awareness of potential exposures to rabies virus whilst overseas. However, since its inception in 2010, the data contained in NHRID have not provided a complete national picture of HRIg usage or the potential exposures to rabies overseas and ABLV in Australia and the possible risk factors. In addition, data from the NHRID is currently inadequate to inform the redistribution of HRIg in Australia. The NHRID contains identifiable data (from one jurisdiction) and sits on an out-dated and insecure platform. Transfer of data into the NHRID is not simple or efficient. NHRID is neither a user-friendly nor intuitive system affecting its acceptability by the Department and the jurisdictions that use it. Furthermore, too many data fields are collected in the NHRID (n=45) with over 25% (n=12) of these as free text fields. Thus, data entry is too cumbersome and the level of information collected is too detailed for the purpose of monitoring HRIg usage. I therefore recommended to CDNA to undertake the following actions to simplify the system to improve timeliness and usefulness:

1. Define the objectives of the NHRID;
2. Phase out data collection on NetEpi;
3. Agree to a national consistent case definition;
4. In the interim, change the collection from case-based to aggregate data;
5. Collect data using data fields that only collect the necessary information to meet the objectives; and

6. In the long term, provide an alternate tool for data collection to the jurisdictions.

In addition to the above actions, I gave the following general recommendations.

Recommendations

- CDNA to continue to collect HRIg usage and related data to inform policy on HRIg usage and awareness campaigns to reduce potential exposures to rabies virus whilst overseas and ABLV in Australia.
- CDNA to agree to the interim objectives of the NHRID.

The following parts explain the key recommendations in detail.

Simplicity

The evaluation concludes that the current NHRID lacks simplicity.

The CDC Guidelines suggest that surveillance systems should be as simple as possible (in their structure and ease of operation) while still meeting their objectives. [1, 2] The overall design of NHRID has not changed since 2010, besides adding the number of vials used for individuals who weigh more than 140 kilos in 2016. It is not automated end-to-end and measures that monitor data quality do not exist. The structure of NHRID is simple however its operation is complex: the cumbersome user interface of NetEpi, difficulty uploading/exporting data from the NHRID and ambiguity of questions has contributed to the lack of analysis, interpretation, reporting and dissemination of NHRID data by the Department.

A key element of a successful surveillance system is to clearly define what data should be collected. Currently, different case definitions are documented. The case definition in the *Case protocol for Rabies Immunoglobulin National Database* (2009) is not comprehensive enough and is described by the jurisdictions as ambiguous. It does not clearly state that only persons who need HRIg treatment due to a Category III or a Category II or Category III are to be entered into the NHRID. The case definition in the NHRID is different and is defined as: "*a case is a person who requires rabies immunoglobulin in Australia after being bitten or scratched or had an exposure of*

concern from an animal potentially infected with rabies or Australian bat lyssavirus from 1 January 2010". A comprehensive case definition should be agreed upon and used in all relevant documents.

Recommendation

- CDNA to make the case definition clearer and more specific.

Proposed new case definition to be considered by CDNA:
"a case is a person who from 1 January 2010 onwards received human rabies immunoglobulin in Australia as part of post-exposure prophylaxis following a Category III exposure from an animal in a rabies-endemic area or a Category II or Category III exposure from a bat potentially infected with rabies virus overseas or Australian bat lyssavirus in Australia."

The NHRID and supporting documents lack clarity. Firstly, review of the manual revealed that it lacks clarity in terms of the different system functions and capabilities and the instructions aren't specific to the NHRID. Secondly, most jurisdictions stated that whilst the current data fields are appropriate they did need clarification. For example, for the question "Had the exposed person previously received rabies vaccination?" it is not clear if this refers to rabies vaccine in the past or as part of the post exposure rabies prophylaxis for the current incident. For the field "Date when the wound was assessed", jurisdictions had reporting date, notification date, date of presentation instead in their forms. Only Victoria had the same wording. Furthermore, the wording for the question "Was the animal that caused the wound tested for rabies?" should include ABLV, as stated in the description of the question, to avoid ambiguity.

Although a data dictionary had been developed at the time of the evaluation, none of the jurisdictions mentioned receiving it or using it. In addition, issues identified in previous studies including 1) ongoing training for database users on the aims of the database to ensure all persons administered HRIg are entered, and 2) improving the instructions and the wording of questions in the NHRID questionnaire, were still pending.

A variety of forms and systems are used for the collection of HRIg usage information in Australia. Seven of the eight (88%) jurisdictions collect HRIg usage and related data, which are generally compatible with the information captured in the NHRID questionnaire. This difference places a burden on jurisdictions to gather additional data through time-consuming follow-up with the HRIg administering health practitioner. One jurisdiction stated that the forms are sometimes completed by persons other than the health practitioner administering HRIg such as receptionists. Review of the NHRID data reveals that in 1.5% (127/8409) of entries, the person receiving HRIg themselves or a relative or friend on behalf of a case completed the form. However, this is considered to be an underestimation.

Once all the required information has been collated, the time required to complete the NHRID questionnaire on the NHRID is 15 minutes per person receiving HRIg. For smaller jurisdictions this may take 1-2 hours per month due to the smaller number of case records required to be entered. However, for larger jurisdictions such as QLD, NSW and VIC, this process of data entry would be implausible. Therefore, only necessary data fields should be collected for the purpose of national surveillance of people who receive HRIg in Australia due to potential exposure to rabies virus overseas and ABLV in Australia and associated risk factors.

The majority of jurisdictions (7/8) use their own disease management systems as their primary mechanism to house NHRID data to inform 1) the monthly reporting to the Department; 2) inform jurisdictional expenditure due to HRIg usage, and 3) identify exposure factors for public health messaging. Therefore, there is an issue of double entry of records into the jurisdictional database in addition to the NHRID.

NetEpi does not integrate with other systems, consequently QLD, NSW and VIC cannot upload their data directly into the NHRID from their systems. Furthermore, besides WA, the remaining three jurisdictions aren't aware of the ability of a direct upload of the spreadsheets. Subsequently, case information is uploaded manually into NHRID, thus placing a burden on the jurisdictions.

Consultation with data entry staff in the jurisdictions and those who use the information from NHRID revealed that neither training nor a manual or standard operating

procedure (SOP) on how to enter or export data from NHRID was provided to them. The exception is SA that received a manual in 2012 and WA when they received the CSV template in 2013. Review of archival documents reveals that CDNA members weren't aware that data could be uploaded directly into NHRID. Therefore, one of the recommendations from a previous review included that the Department develop a manual outlining the import rules, and a SOP to show the steps jurisdictions would need to follow to assist with data transmission. Review of Departmental documents revealed that these documents already exist.

Recommendation

- CDNA to start tracking events/changes to the system and data fields and the reasons for these changes to allow for historical documentation at the Department.

As discussed, NHRID is difficult to use because historical knowledge has been lost due to staff turnover at both the Department and in the jurisdictions. There also seems to be a general lack of training for NetEpi for the staff that collects the data. There is no training for new staff and there seems to be no awareness that a manual and SOP for the NHRID exists. Combined, this may lead to missing data since the staff does not know how to fill in the questionnaire correctly and thus leave it blank or enter it into free text fields. It also increases the chance for different interpretations of questions and what is supposed to be filled in for each data field. This can cause reliability problems in the form of inconsistent reporting. Currently, time and effort are required for staff to explore how to use or make changes to the NHRID. These resources do not exist and are better served getting a better system.

The Department plays a crucial role in improving the recording of NHRID data nationally. It could encourage jurisdictions' commitment to reporting NHRID data by providing a tool that enables the easy and timely transfer of information, both aggregate and case data. Case data may be required in the event of a critical shortage of HRIg. The Department is currently putting together a business case to move towards a common, national surveillance system (interoperable system) to ensure data quality,

national consistency and timeliness for reporting purposes and for the detection, monitoring and control of outbreaks and reducing communicable disease. Although the NHRID consists of data on HRIg usage of individuals potentially exposed to rabies virus or ABLV, and their exposure and risk factor details rather than of persons with confirmed rabies virus or ABLV infection, this should be seriously considered as a long term solution to house NHRID data as enhanced surveillance data. In the interim, alternatives with similar qualities are required until the national interoperable surveillance system is implemented.

Recommendations

Interim recommendation

- Jurisdictions to use the draft of proposed interim data collection template for the reporting of aggregate data fields annually to the Department for interim reporting purposes (Supplementary Information – Executive Summary).

Long term recommendation

- The Department to phase out the use of the NHRID on NetEpi and provide a secure, user-friendly data collection system capable of collecting case data. This will improve data quality, national consistency and timeliness of HRIg usage and potential exposure and risk factor data.

- CDNA to agree to the collection and sending of de-identifiable case data to the Department once a long term data collection system is implemented.

Flexibility

Based on its structure, the evaluation finds the current NHRID is not a flexible system.

According to the CDC guidelines, "a flexible public health system can adapt to changing information needs, or operating conditions with little additional time, personnel, or allocated funds."[1, 2] The NHRID is hosted on NetEpi which is a system where changes in data fields or the inclusion of new data fields are not easy to do without the appropriate programming skills. To implement changes it would thus require existing staff to spend time learning the system or funds to hire programmers to make the required changes would need to be sourced.

Consultation with staff and review of the data revealed that it is difficult to document and identify tourists, mobile/transient persons, or persons that may move between jurisdictions. This makes it difficult to follow the PEP treatment of these persons for a number of reasons. Jurisdictions can only see details of cases in their respective jurisdiction and HRIg can be administered up to 7 days. It is therefore difficult to ascertain what these persons have been administered and when, based on the NHRID. However, jurisdictions stated that they generally communicate informally if someone who has started PEP will continue treatment in another jurisdiction. Consequently, in 2016, the "Country of residence/birth" data field was suggested, to identify overseas persons receiving treatment, and a "State of residence" data field, to document persons receiving treatment in a jurisdiction other than where they reside.

Recommendations

- CDNA to create a data field that collects data on the circumstances (risk behaviour) that led to the potential exposure to rabies overseas or ABLV in Australia.
- CDNA to create a data field that identifies HRIg recipients with an overseas residential address (tourists). This will inform the demographic characteristics of HRIg recipients in Australia.

At present, jurisdictions do not receive any feedback from the Department on a regular basis. Currently, the Department does not have a dissemination procedure in place. The collection of data on exposures and risk factors adds to the epidemiological knowledge of the potential exposures and risk factors occurring due to potential exposure to rabies virus overseas and ABLV in Australia. Previous studies used NHRID data to determine HRIg usage and risk factor patterns in Australia, which have led to public health actions to minimise risk behaviours of travellers with the aim to reduce the HRIg usage. Therefore, the data that NHRID captures is potentially useful and could be applied to target public health messaging campaigns to reduce risk behaviours leading to potential exposure to rabies virus and ABLV. There is the opportunity to make savings in Australia's use of HRIg if travellers avoided exposures whilst in rabies's listed countries and persons in Australia avoided handling bats.

Recommendations

- The Department to collate and analyse the data annually and report to CDNA.
- CDNA to review the annually analysis of HRIg use and identify any issues and develop strategies to implement public health actions, if required.
- CDNA publish a HRIg surveillance short report or a Rabies and Australian bat lyssavirus post-exposure prophylaxis surveillance short report on an annual basis in a public report to relay findings to the jurisdictions, research community and the public.

Stability

The evaluation finds that based on the lack of dedicated resources in the Department to maintain and support the NHRID; the current NHRID is not a stable system.

Stability reflects the public health surveillance system's ability to collect, manage, and provide data properly without failure (reliability) and its ability to be operational when it is needed (availability).[1, 2] The NHRID can collect, manage and provide data properly without failure however because it is not an intuitive system it requires training or a manual to use it efficiently and effectively. None of the OHP staff and the five jurisdictions that enter data directly into the NHRID mentioned any technical difficulties involved with the NHRID usage and it was operational when needed. Due to the simplicity of the setup of the NHRID it is not exposed to issues such as unscheduled outages or down times for the system's computer. It is however potentially vulnerable to virus attacks since its servers are no longer able to be upgraded. The NHRID is covered by usual Information Technology security practices at the Department meaning servers and backups are kept in a secure location. The NHRID is managed by the data managers for the National Notifiable Diseases Surveillance System in OHP, but this is limited to database access and monitoring of database use. However, the server hasn't been updated since 2008 and formal IT support for NHRID ceased in 2011. The server cannot be upgraded and the skill set (knowledge in programming language) to maintain NetEpi does not exist at the Department anymore. Thus the Department should phase out the use of the NHRID on NetEpi.

The current system does not lack sufficient human resources to record NHRID data. However, staff turnover leading to the loss of knowledge of how to use the system, and consequently the time required to familiarise themselves with a new system, are all factors that can create a backlog of case records, affecting timeliness of the NHRID data. Workforce instability is a major challenge in health-care in general. However, to improve the efficiency of data entry and completeness of NHRID data, improvements should comprise of a tool that allows the straightforward and direct upload of case records. Furthermore, a process of documented handover should be implemented in the Department. In addition, the jurisdictions should be supplied with a manual and SOP to allow for the continuity of the historical knowledge of the system and related modifications.

The NHRID is the main mechanism to collect NHRID data in one jurisdiction, therefore information collected in the NHRID contains personal data such as full name, address, date of birth and sex. User privileges, which are reviewed annually, are assigned, monitored and controlled by the administrators at the Department to limit access to active users only.

Recommendation

- CDNA to collect de-identifiable data going forward and appropriately manage the disposal of existing identifiable data

Acceptability

The acceptability of the NHRID is low because the Department does not use it and jurisdictions do not like using it.

Acceptability reflects the willingness of persons and organisations that operate the system to use the surveillance system. Overall, everyone (except one participant who did not respond to this question) agreed that there was a place for a national surveillance system to monitor HRIg usage to ensure HRIg, a limited resource, is being used appropriately. Five of the eight jurisdictions entered data into the NHRID on a regular basis and did so in the understanding that the data was being used for these purposes. However, since its inception the Department has not used the NHRID or its

data for routine surveillance of national HRIg usage because the data that is captured is not nationally representative.

There was consensus at the Department that the NHRID was not an adequate system as the data being collected was not relevant and was difficult to export. Depending on the data fields and order of the data fields, the process of uploading the data from QLD and NSW can take three days whereas uploading VIC's data can take several weeks.

Data quality is not monitored by the Department or by the jurisdictions. At the Department, cleaning and validation is not occurring as it is currently a low priority. Therefore, a continual process of improving national consistency of HRIg usage surveillance either through quarterly or annual review of data is currently lacking. In addition, as the NHRID data is not analysed, no reports are disseminated internally, to other federal Departments or fed back to the jurisdictions or other interested stakeholders. Therefore, there are no incentives to continue to capture NHRID data.

The NHRID is a cumbersome system to use, both for data entry and to export the data for analysis. Despite the show of support by CDNA members and jurisdictional staff for a national surveillance system for the collection and monitoring of HRIg usage, the lack of its use by the Department makes the NHRID neither adequate nor relevant in its current state.

Timeliness

The evaluation finds that the NHRID is not timely.

According the CDC, timeliness refers to "the speed between steps in a public health surveillance system".[1, 2] Overall, in the smaller jurisdictions (NT, TAS, WA, SA) that enter data directly into NHRID, the data is entered between 24 hours to one month after being notified of its administration, depending on the work load of the person responsible for data entry. Based on the date of last data entry ACT has not entered data into the NHRID since 2015. For the remaining jurisdictions (QLD, VIC and NSW), NHRID data is provided to the Department upon request, after which it is uploaded into the NHRID by the Department. Since the inception in 2010, the Department has requested data from these jurisdictions twice. Therefore, there is considerable variation in the timeliness of reporting by jurisdiction, due to operational and

geographic issues associated with several different data systems in use across jurisdictions as well as staff turnover.

The NHRID was implemented to house HRIg usage data thus it should clearly specify in the Rabies and ABLV SoNG the required timeframe of data entry. However it is not stipulated in this document. Furthermore, the Department's duties and responsibilities relating to the frequency of data analysis, reporting or dissemination of NHRID data are also not specified.

The NHRID is not a timely system because NHRID data is not published to provide feedback to stakeholders and also not used for planning purposes or to inform public health action.

Should a shortage of HRIg supply reoccur in Australia, necessitating the monitoring of HRIg usage and wastage, up-to-date NHRID data will not be readily available. The data contained in the NHRID will have limited utility.

Data quality

The evaluation finds that since the inception of the NHRID the data have not provided a complete national picture of 1) HRIg usage or 2) the potential exposures to rabies overseas and ABLV in Australia and the possible risk factors for these potential exposures. Data from the NHRID are currently inadequate to inform the redistribution of HRIg in Australia.

Data quality reflects the completeness and validity of the data recorded in the public health surveillance system.[1, 2] Examination of the NHRID revealed that records for four of the five jurisdictions that enter data directly into NHRID were up-to-date based on the date of the last data entry (Supplementary Information Table S3). ACT's records suggest underreporting in the NHRID of individuals who have received HRIg treatment in the ACT. Given that QLD, NSW and VIC do not enter data directly into the NHRID, their last date of data entry would reflect the last time NHRID data was requested from the Department, which is not routinely undertaken. As a result, the completeness of the information in the NHRID is very low. Based on the last date of entry (Supplementary Information Table S3), the data available in the NHRID is incomplete and would not reflect the true number of individuals in Australia who have received HRIg treatment due to potential exposure to rabies virus or ABLV.

At the time of the evaluation, there were a total of 8,409 case records in the NHRID. The completeness for each individual data field can be found in Supplementary Information Table S4. The completeness of demographic data fields was overall over 90% (7,715/8,409), ranging from 96.2% (8,089/8,409) for "State" (jurisdiction where HRIG was administered) to 99.3% (8,353/8,409) for "Sex" of HRIg recipient. The completeness of data fields relating to the objectives of the NHRID was high and included country of exposure (95.9%, 8,060/8,409), wound location (90.3%, 7,594/8,409), animal exposure (86.2%, 7.249/8.409) and wound type (82.6%, 6,944/8,409). The completeness of the circumstance of exposure data fields varied widely and ranged from 33.6% (2,821/8,409) for "Case an expatriate or traveller who had spent prolonged periods (i.e. more than a month) in rabies-endemic areas" to 89.7% (7,563/8,409) for the circumstance data field relating to "working with mammals in rabies-endemic areas" . Nearly one third (2,490/8,409) of entries did not state how much HRIg was administered.

The design of the NHRID questionnaire does not aid in data quality. Key issues identified were the number of free text fields, ambiguous questions and the different types of response options available in the NHRID questionnaire. Besides the Notes section of the questionnaire, over 25% (12/45) of data fields are free text fields. Review of these fields identified that entries were made when it either wasn't required (repetition of information) or information unrelated to the question were entered. The analysis of free text fields requires extensive and time-consuming data cleaning.
It is difficult to ascertain the extent of errors of the data within the NHRID because the completeness of the records is so low and cross-checking with original recorded data from the jurisdictional forms was not feasible.

When the NHRID was initially implemented, HRIg wastage was monitored. CDNA members were reminded every month of the importance of the completeness of the NHRID data when they are supplied with the HRIg supply update. CDNA members were reminded to complete an entry in the NHRID for every administration of HRIg, to improve the completeness of data. They were also requested to update previous year's data, if not yet complete. At the time of the evaluation, however, this process

was not being applied because HRIg supply levels were sufficient and didn't require monitoring of product wastage.

The number of indicators was one of the key issues to address if data quality is to be improved. The data fields could be prioritised to a smaller set of key data fields including reducing the number of free text fields. Fewer indicators would also make a system relying on paper forms more manageable. The 2016 review involved work to reduce the number of data fields, including the removal of identifiable fields such as surname and given name, but it is uncertain whether the reduction was substantial enough as these recommendations had not been implemented at the time of this evaluation. Reducing the list of data fields to a manageable size would require the acceptance from the different jurisdictions and the Department. Feedback obtained from the 2016 review shows that there is willingness from jurisdictions to do so. Therefore, reducing the number of data fields and changing from case data to aggregate data may improve the general lack of quality control on NHRID data and help with the implementation of routine analysis, reporting and dissemination of data.

Recommendation

- CDNA to agree on the aggregate data fields to collect data on HRIg usage and potential exposure and possible risk factors (Supplementary Information – Executive Summary).

Representativeness

Based on consultations with jurisdictions, the details of every person who receives HRIg treatment as part of their PEP is collected in the respective jurisdictions. Review of the data in the NHRID shows that the data for QLD, NSW and VIC was last requested in 2016 and 2014, respectively, and data was last entered by the ACT in 2015. Due to missing data for four jurisdictions, the information in the system is incomplete. According to CDC Guidelines "a public health surveillance system that is representative accurately describes the occurrence of a health-related event over time and its distribution in the population by place and person … to generalise findings from surveillance data to the population at large, the data from a public health surveillance system should accurately reflect the characteristics of the health-related event under

surveillance".[2] The data in the NHRID is consequently not representative as it is not possible to use NHRID data to ascertain the actual usage of HRIg in Australia by person, place or time, accurately and in a timely manner. This is due to the system's inability to integrate with other data management systems and the time-consuming process of the manual data entry to transfer data to the Department.

Figure 5 shows a comparison between HRIg usage data received by the Department every month via email to monitor stock levels (blue) and HRIg usage data from the NHRID (red). As the graph indicates, the information in the NHRID does not reflect actual national HRIg usage. This is mainly due to missing entries for QLD, NSW, VIC and ACT.

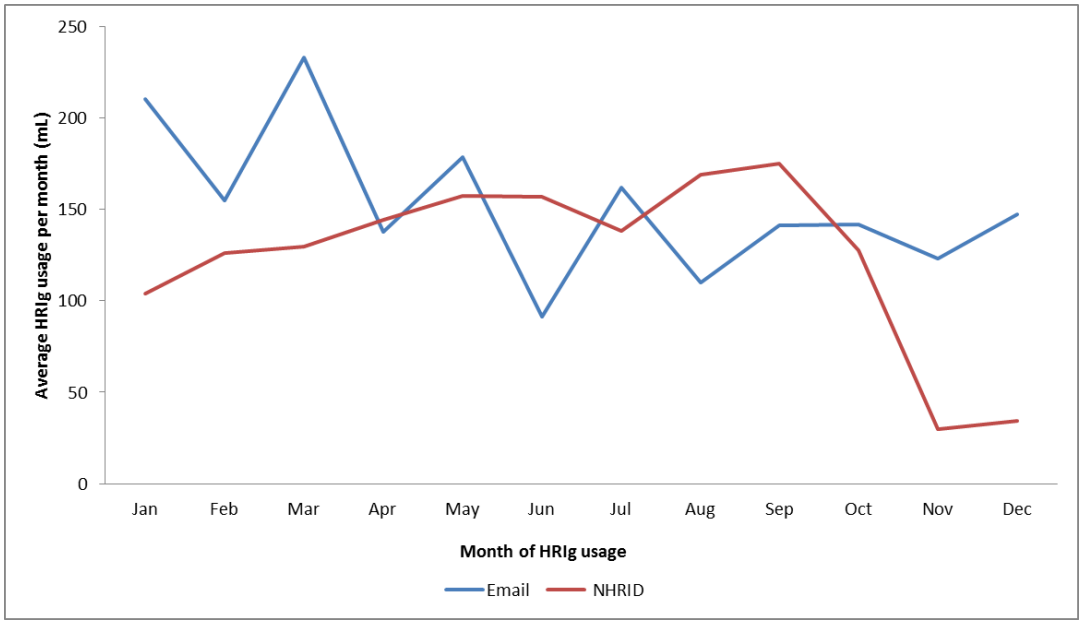

Fig 5. Average monthly HRIg usage (ml) in Australia, National Human Rabies Immunoglobulin Database, 1 January 2010 to October 2017 (n=8,409)* HRIg usage data for QLD, NSW, and VIC not included in NHRID and ACT data only to 2015

Usefulness of NHRID to inform policy and planning

The usefulness of a surveillance system infers that its results are used for public health action.[1, 2] I found during this evaluation that the collection of HRIg usage, potential exposure to rabies virus overseas and ABLV and associated risk factors was useful. However, currently the data are incomplete and of poor quality. Furthermore, the NHRID system itself was also not useful.

An important aspect to this evaluation was the differing viewpoint about the purpose of the NHRID system amongst stakeholders. According to the jurisdictions, the NHRID data were collected to monitor HRIg levels, inform policy and/or the redistribution of HRIg across jurisdictions in times of critical stock levels. Some jurisdictions questioned why the Department was collecting these data. Based on consultations at the Department the objective of the system and the data it collected was for monitoring HRIg wastage, which in the current situation is not relevant and therefore is not being routinely analysed by the Department. The usefulness of the NHRID was deemed high in the jurisdictions but low by the Department.

Most jurisdictions (7/8) thought that having a national surveillance system like NHRID was useful for the monitoring of HRIg usage at the national level to inform policy and/or the SoNG for rabies virus and ABLV. Five of the eight jurisdictions enter data into the NHRID on a regular basis for this sole purpose. SA was the only jurisdiction to record its NHRID data mainly on the NHRID but did not know how to run a report. When asked if data from the NHRID were used to assess risk factors of individuals in their respective jurisdictions who were potentially exposed to rabies virus overseas or ABLV in Australia, responses ranged from infrequently to not at all.

Based on stakeholder consultation at the Department, since its inception in 2010, the NHRID has never been used for the routine reporting on national HRIg usage in Australia. A key factor was the inability of entering Victorian paper forms into the NHRID in a timely manner to inform reporting on a regular basis to CDNA. Currently, the NHRID is considered no longer relevant for the following reasons:

1. A shortage of HRIg stock levels does not currently exist because a backup supplier is available, and therefore;
    a. the information that the NHRID collects is not required; and
    b. analysis of NHRID data to monitor HRIg wastage is not a priority
2. The NHRID system is cumbersome and not user friendly.

Thus, the Department does not currently use the NHRID or its data. However, since 2013, the surveillance and national response to other zoonotic diseases has taken

precedence such as Middle East respiratory syndrome coronavirus, Ebola virus, and Zika virus infection. Therefore, NHRID data analysis has been a low priority.

Neither the Department nor the jurisdictions allocate resources specifically for the quality control or maintenance of data in the NHRID. This is reflected in the low cost associated with running the NHRID over the last seven years as outlined in Table 5. However, the costs in Table 5 do not factor in the time associated with follow up on cases for clarification of information in the rabies prophylaxis forms or due to incomplete forms.

The total estimated ongoing costs for the operation of the NHRID between 2010 and 2017 were $69,117.60. These costs are itemised in Table 6.

Table 6. Estimated ongoing costs of NHRID, Australia, 2010- 2017

Activity	Ongoing cost
Department	
Upload of NHRID data from QLD,NSW and VIC	Year 2011 and Year 2014: EL1 ($55.2/hour) x 150 (37.5hrs x 4 weeks) $8,280 X 2 years = $16,560
	Year 2014 to 2017 =$0
Export of NHRID data	Year 2011 and Year 2014: EL1 ($55.2/hour) x 3hrs $165.6 x 2 years = $331.2
	Year 2014 to 2017 =$0
NHRID support, management and monitoring	Year 2010 to 2011: $55.2/hour x 52 hours =$2,870.4
	Year 2011 to 2017 =$0
Analysis, reporting, dissemination	Year 2011: $961.5 x 4 weeks = $3,846 Year 2014: $961.5 x 4 weeks = $3,846
Total	$27,453.60
Jurisdictions that enter NHRID data	
Data entry[1]	10-15 mins per case 2 hours/month at $49.6/hour $99.2 x 12 months $1,190.4 x 5 jurisdictions $5,952 x 7 years = $41,664
NHRID support, management and monitoring	$0
Analysis, reporting, dissemination	$0
Total	$41,664
TOTAL	**$69,117.60**

[1] Does not include time spent on follow-up

Based on HRIg usage data received by the Department every month via email to monitor stock levels, the usage of HRIg has a seasonal trend with usage increasing during school holiday periods where overseas travel is more frequent. As mentioned previously, HRIg usage in Australia also increased markedly in response to events and media coverage.

Previous analyses highlighted that injuries caused by monkeys in Bali were the main reason for people requiring HRIg treatment in Australia. [35, 36] Prevention strategies informed through these analyses included:

- Policy change in VIC with the Victorian Government committing to the free provision of pre-exposure rabies vaccine to volunteer Victorian wildlife carers.
- Inclusion of data analysis results in an Australian Technical Advisory Group on Immunisation report for CDNA on recommendations of HRIg usage.
- The Department produced an information webpage for the public (http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-rabies-consumer-info.htm)
- The development of Rabies Information Cards as part of a rabies awareness campaign in December 2013. These were developed to complement the Department's information website, information available on the Department of Foreign Affairs and Trade's Smarttraveller website and electronic signage at targeted Australian international airports. In addition, messages were displayed on the Department's twitter feed (@Healthgovau). The campaign was initiated following an increase in the number of travellers returning from Bali, Indonesia, with potential exposure to rabies virus and Australia experiencing critical levels of registered HRIg stock. These cards were distributed at targeted airports or made available through Australian Customs and Border Protection Service (Customs) to educate travellers to Bali, Indonesia, and Thailand on avoiding potential exposure to rabies virus while overseas due to animal injuries. This was undertaken in an effort to reduce potential exposures and national HRIg usage.

The website still provides information to the public on rabies virus and ABLV. The use of the Rabies Information Cards at Australian borders was implemented for one week. Therefore, the information cards are currently not distributed to travellers. However, this campaign could be reintroduced as Customs has kept the travel information cards in storage. Alternatively, dissemination of travel cards at airline check-in points could be implemented as a longer term strategy. This strategy was considered but not pursued by the Department in 2013.

No other uses of the NHRID data by the Department have occurred and at present, there are no other anticipated uses.

A limited number of requests (n=2) from external organisations for NHRID data have been received by jurisdictions and the Department. Requests for data include:

- The total number of people treated with rabies immunoglobulin in 2010, to inform a disease awareness program focusing on Australian travellers to rabies endemic regions; and
- KamRAB™ usage in Australia.

No requests have been received by the Department from jurisdictions asking for national HRIg usage or related information.

From a national perspective, NHRID data has been used to guide public health action. The NHRID has never been used for routine reporting on the approximate national HRIg usage in Australia; however two data analyses conducted by MAE Scholars have led to public health action. [35, 36] Finally, based on the evaluation of the attributes of the NHRID, it is not a simple, flexible, stable, or timely system. It contains incomplete data and acceptability is low by the Department and the jurisdictions.

The goal of collecting data is to be able to analyse it and make decisions about actions to be taken. All jurisdictions stated that they would be interested in receiving annual or biannual reports on national HRIg usage based on types of exposure and risk factors. This information could inform and target public health messaging. In 2010, of the 639,290 arrivals from Indonesia, 537,399 (84%) of these boarded their return flight to Australia from the island of Bali. Around 50% of these arrivals in 2010 were into Perth (265,312; 49%). A study undertaken by Gautret et al.[75] found that over half of animal-related exposures leading to rabies PEP among international travellers between 1997 and 2012 occurred in Thailand, Indonesia, Nepal, China, and India. India is the world's second most populous country and is estimated to account for over 35% of the global rabies burden.[10] In addition, over the next 10 years it is predicted that international travel to India will grow at an average annual rate of approximately 8%.[76] Therefore, monitoring any shifts in travel practices to countries with endemic rabies would be beneficial.

Recommendation

- CDNA to schedule an evaluation of the data collection system chosen and related processes in 5-years' time (or if the objectives change) to ensure that these meet a current need and the data collected is of high-quality.

Limitations, future work and significance

This evaluation is the first comprehensive evaluation of the NHRID. Previous studies analysed data from the NHRID but did not undertake a systematic and objective evaluation of the NHRID attributes to determine if its purpose and objectives were being met.

Limitations were encountered during this evaluation such as a lack of Departmental documentation and access to historical knowledge due to staff turnover at the Department and in the jurisdictions. Therefore, this information would have helped with the interpretation of past events and documents.

Despite the above limitations, the quantitative analyses found NHRID data displayed low completeness in half of the jurisdictions due to the different transfer mechanisms to the NHRID. Three of the largest jurisdictions in Australia only provide NHRID data if requested by the Department, thus the NHRID is not timely. Both issues affect the quality of the data in the NHRID and together contribute to the Departments' low acceptability of the system. Qualitative methods used identified that the NHRID is simple and stable in its structure but in terms of operation it lacked simplicity, flexibility and stability. These factors are a major cause of concern due to the limited dedicated resources by the Department to maintain and support the NHRID. In summary, the system should be appropriately designed to record NHRID data efficiently and effectively, and statistical outputs should be timely, accurately reflect the actual data, fed back to jurisdictions and be used to inform public health action. These features do not pertain to the NHRID.

Participation in the evaluation by jurisdictional and the Department staff was excellent. All, except one participant, answered all questions in relation to the NHRID by sharing their knowledge and experience during the consultation process. Their

cooperation indicates the public health importance of rabies disease and that collection HRIg usage and potential exposure and associated risk factors is useful.

The WHO Expert Consultation on Rabies report[11] states that "governments and responsible agencies should enact regulations to ensure that all people with suspected, probable or confirmed exposure to rabies have timely access to adequate PEP….". Australia is proactively monitoring HRIg stock levels to ensure enough stock is available at all times. In addition, despite all the limitations that the NHRID displays, the concept of having a national surveillance system that monitors HRIg usage and potential exposures and possible risk factors efficiently and effectively is useful. These data could be useful to monitor rabies in the region and ABLV in Australia. They can also help the Department fulfil its responsibility for national surveillance, reporting, and providing national advice and coordination to issues of national concern.

Conclusion

The monitoring of HRIg stock levels at the national level is essential. It ensures Australia has sufficient HRIg, a scarce resource worldwide, for individuals potentially exposed to rabies virus or ABLV, who without it will otherwise develop fatal disease once clinical symptoms occur. However, monitoring HRIg usage and risk behaviours leading to potential exposures to rabies virus overseas and ABLV in Australia also serves a useful public health function as it can feed into prevention efforts.

The Australian national surveillance system on HRIg usage – NHRID – captures information on individuals potentially exposed to rabies or lyssavirus, including ABLV, together with exposure and risk factor details. These data have been used to inform policy on HRIg usage and led to a campaign to raise awareness of potential exposures to rabies virus whilst overseas. Currently, however, the NHRID data does not inform national HRIg usage or the redistribution of HRIg.

In summary, the NHRID is hosted on an outdated and insecure IT platform that is not supported or maintained by the Department because the skill set no longer exists. These factors raise major issues about confidentiality, privacy and usability. Assessment of the performance and effectiveness of the NHRID in monitoring and describing HRIg usage reveals that the NHRID as it stands is not adequate.

Based on these findings, I conclude that the collection of NHRID data requires redevelopment of how data are collected and what is collected. Therefore, the use of the NHRID on NetEpi should be phased out. The system could be improved through the use of more up-to-date, secure and advanced systems. Technology can alleviate some problems, however, several limitations remain; lack of training due to staff turnover, burdensome amount of data collected and the absence of the provision of feedback. The Department could strengthen the summarising of data and its dissemination within government and to non-government users. This could create a stronger link between the data and its use to inform public health action. These problems should be resolved to increase data quality.

Summary of recommendations for moving forward

As this evaluation has shown, changes and improvements to the NHRID are required. In this section, key action points are presented that could be helpful in achieving improved data quality and link these data more strongly to public health action. All recommendations, except for two, were accepted and endorsed by CDNA on 17 July 2018 (Table 5F and 5G).

Priority recommendations

The Department is currently working towards the implementation of the Interoperable Communicable Disease Surveillance and Outbreak Management System (ICDSOMS). However, the operation of this system may not occur for many years. As a result, I provided to CDNA both priority recommendations to be implemented immediately and secondary recommendations that can be implemented in the longer term or once ICDSOMS is operational.

Furthermore, Australia currently only collects data on national HRIg usage. I recommend that CDNA consider the national surveillance of PEP: HRIg and rabies vaccine usage (Recommendation 14 in Table 7). This will provide a complete picture of rabies PEP treatment in Australia.

Table 7. Identified priorities or issues requiring immediate action

Identified issue	Proposed resolution[a]	Outcome
NHRID does not meet its objectives	**Recommendation 1**: CDNA to continue to collect HRIg usage and related data to inform policy on HRIg usage and awareness campaigns to reduce potential exposures to rabies virus whilst overseas and ABLV in Australia. **Recommendation 2**: CDNA to agree to the interim objectives of the NHRID.	**CDNA agreed** **CDNA agreed**
Refining the case definition	**Recommendation 3:** CDNA to make the case definition clearer and more specific. **Proposed new case definition to be considered by CDNA:** *"a case is a person who from 1 January 2010 onwards received human rabies immunoglobulin in Australia as part of post-exposure prophylaxis following a Category III exposure from an animal in a rabies-endemic area or a Category II or Category III exposure from a bat potentially infected with rabies virus overseas or Australian bat lyssavirus in Australia."*	**CDNA did not agree**
Identifiable data in the NHRID	**Recommendation 4**: CDNA to collect de-identifiable data going forward and appropriately manage the disposal of existing identifiable data.	**CDNA agreed**
Collection of case data	**Recommendation 5:** The Department to cease collecting case data and start collecting aggregate data	**CDNA agreed**
Data fields do not reflect the objectives of the system	**Recommendation 6:** CDNA to agree on the aggregate data fields to collect data on HRIg usage and potential exposure and possible risk factors. **Recommendation 7:** CDNA to collect wound type data according to the Australian Immunisation Handbook 10th Edition and the Rabies and other ABLV SoNG exposure categories, which are guided by the World Health Organization's position paper on rabies vaccines. This will achieve a nationally consistent approach of collecting this information	**CDNA agreed** **CDNA agreed** However, when changeover occurs, there will need to be data collected before and data collected after the point of changeover.
Difficulty identifying overseas and transient/mobile persons	**Recommendation 8:** CDNA to create a data field that collects data on the circumstances (risk behaviour) that led to the	**CDNA agreed**

	potential exposure to rabies overseas or ABLV in Australia.	**CDNA agreed**
Too many data fields	**Recommendation 9:** CDNA to create a data field that identifies HRIg recipients with an overseas residential address (tourists). This will inform the demographic characteristics of HRIg recipients in Australia. **Recommendation 10:** CDNA to create a data field that collects data on the HRIg product administered. This will inform the surveillance of the HRIg usage in Australia. **Draft of proposed interim aggregate data fields to be considered by CDNA are outlined in Appendix 1 and include draft data fields proposed in Recommendations 7-10**.	**CDNA agreed**
Outdated and insecure system currently not supported or maintained	**Recommendation 11:** Jurisdictions to use the draft of proposed interim data collection template for the reporting of aggregate data fields annually to the Department for interim reporting purposes. **Proposed interim data collection template for reporting purposes for consideration by CDNA is in Appendix 2.**	**CDNA agreed**
Infrequent review of HRIg usage data and related documents	**Recommendation 12:** The Department to collate and analyse the data annually and report to CDNA. **Recommendation 13:** CDNA to review the annually analysis of HRIg use and identify any issues and develop strategies to implement public health actions, if required.	**CDNA agreed** **CDNA agreed**
Dissemination of findings by the Department	**Recommendation 14:** CDNA publish a HRIg surveillance short report or a Rabies and Australian bat lyssavirus post-exposure prophylaxis surveillance short report on an annual basis in a public report to relay findings to the jurisdictions, research community and the public.	**CDNA agreed**

[a] Proposed resolutions may cover multiple identified issues

Secondary recommendations

Once the ICDSOMS is operational, I recommend that CDNA revisit how HRIg usage data is collected (Table 8). Depending on the functionality of the ICDSOMS, CDNA should decide whether they want to continue with the collection of aggregate data or case data, moving forward.

Table 8. Identified long term priorities for improved national HRIg usage surveillance

Identified issue	Proposed resolution[a]	Outcomes
Outdated and insecure system currently not supported or maintained	**Recommendation 1:** The Department to phase out the use of the NHRID on NetEpi and provide a secure, user-friendly data collection system capable of collecting case data. This will improve data quality, national consistency and timeliness of HRIg usage and potential exposure and risk factor data.	**CDNA agreed**
Data fields do not reflect the objectives of the system	**Recommendation 2:** CDNA to agree to the collection and sending of de-identifiable case data to the Department once a long term data collection system is implemented.	**CDNA did not agree. CDNA considered it too premature as it relates to the ICDSOMS**
Difficulty identifying overseas and transient/mobile persons	**Recommendation 3:** CDNA to develop and agree on national data specifications and ensure only those that meet the national objectives are collected, which include data fields as per Recommendations 7 to 10 in Table 1.	**CDNA agreed with minor amendment to the wording. Change 'collected' to 'sent'**
Too many data fields		
Recording systems reviews, updates and changes	**Recommendation 4:** CDNA to start tracking events/changes to the system and data fields and the reasons for these changes to allow for historical documentation at the Department.	**CDNA agreed**
Future surveillance needs	**Recommendation 5:** CDNA to schedule an evaluation of the data collection system chosen and related processes in 5-years' time (or if the objectives change) to ensure that these meet a current need and the data collected is of high-quality.	**CDNA agreed. CDNA requested that the evaluation be conducted at 12 months following implementation.**

[a] Proposed resolutions may cover multiple identified issues

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Supplementary Information

Data field descriptions

Table S1. Data fields reported in the NHRID questionnaire (n=45)

Data field name	Description
local_case_id	Unique ID used by reporting Stated/territory
case_id	Unique ID automatically generated by NetEpi
indigenous_status	Indigenous status of person receiving HRIg
surname	Surname of person receiving HRIg
given_names	Given names of person receiving HRIg
DOB	Date of birth of person receiving HRIg dd/mm/yyyy
sex	Sex of person receiving HRIg
locality	Locality/Suburb of residence of person receiving HRIg
State	Notifying State
postcode	Residential postcode of person receiving HRIg
notifier_name	Name of person completing NHRID questionnaire
notifier_contact	Contact details of person completing NHRID questionnaire
Exp_date	Date of potential exposure
Wd_1[1]	Wound Type
Wd_Other	Description of “Other” wound type
Wd_2[2]	Location of the wound on the body
Wd_Desc	Wound description in detail, if required
Wd_3	Depth and severity of wounds
Ani_1[3]	The animal that caused the wound
Ani_other	Description of “Other” animal
Animal_b	Behaviour of the animal prior to the injury/exposure, did the animal appear to be unwell or behave in an 'odd fashion'.
Ani_beh_desc	Description of animal behaviour and circumstances
Ani_Test	Was the animal that caused the wound tested for rabies?
Ani_test_1	Results of animal testing for rabies/Australian bat lyssavirus
Ani_test_desc	Description of the laboratory results
Exp_ctry[4]	Country where the patient was exposed to the animal
Indon_Island[5]	If Indonesia, the island where the animal exposure occurred

Ind_Isl_Spec	Description of other country/island
Assess1	Case liable to have received bites or scratches from bats in their everyday activities (this includes bat handlers, veterinarians, wildlife officers and others who come into direct contact with bats).
Assess2	Case an expatriate or traveller who had spent prolonged periods (i.e. more than a month) in rabies-endemic areas.
Assess3	Case working with mammals in rabies-endemic areas
Assess4	Case from a research laboratory - person who work with live lyssaviruses
Prevaccine	Exposed person previously received rabies vaccination
Pstvac1	If yes, number of previous doses
vac_date_Hx	Estimate the date of when the last dose of rabies vaccine was given
Imm_C	HRIg recipient be considered to be immunocompromised as a result of an unrelated illness, condition, or prescribed drug use
Imm_C_Spec	Description on immunocompromising condition
Ass_date	Date when the wound was assessed
Performed_fup	Wound assessor
RIG_date	Date HRIg was administered
Wgt	Weight of person receiving HRIg in kilograms
RIG_Amt	The number of vials of HRIg used
Rab_vac1	Date of first dose of rabies vaccine given as part of PEP
Notes	Description of clinical issues of note
Name_PH	Name and contact details of person completing this survey

[1] Only one option can be selected

[2] Multiple options can be selected

[3] “Fruit bat/Flying fox” (i.e. Australian bats) and “Other types of bat” (i.e. overseas bat category)

[4] 243 countries listed

[5] Options include “Bali”, “Other Indonesian Island”, and “Not applicable”

Summary table of HRIg-related Information captured in jurisdictional rabies form versus NHRID data fields

Table S2. Comparison of HRIg-related information captured in jurisdictional rabies form versus NHRID questionnaire data fields

NHRID fields	ACT	NSW[a]	NT	SA[b]	Tas[c]	Qld	Vic	WA
Unique ID used by reporting Stated/territory	N/A		N/A	N/A	N/A	Yes	N/A	N/A
Unique ID automatically generated by NetEpi	N/A		N/A	N/A	N/A	N/A	N/A	N/A
Indigenous status of person receiving HRIg	Yes		No	Yes	Yes	Yes	Free text	Yes
Surname of person receiving HRIg	Yes		Yes	Yes	Yes	Yes	Yes	Yes
Given names of person receiving HRIg	Yes		Yes	Yes	Yes	Yes	Yes	Yes
Date of birth of person receiving HRIg dd/mm/yyyy	Yes		Yes	Yes	Yes	Yes	Yes	Yes
Sex of person receiving HRIg	Yes		No	Yes	Yes	Yes	Yes	Yes
Locality/Suburb of residence of person receiving HRIg	Address		Address	Yes	Yes	Yes	Yes	Yes
Notifying State	-		Yes	-	-	-	-	-
Residential postcode of person receiving HRIg	Address		Yes	Yes	Yes	Yes	Yes	Yes
Name of person completing NHRID questionnaire	Yes		Yes	Yes	Yes	Yes	Yes	Attending doctor
Contact details of person completing NHRID questionnaire	Yes		Phone number	Yes	Yes	Yes	Yes	Yes
Date of possible exposure	Yes		Yes	Yes	Yes	Yes	Yes	Yes
Wound Type	Bite Scratch Puncture		Bite Scratch Exposure of mucous	Yes	Yes	Bite Scratch Other Unknown	Bite Scratch Lick Other	Bite Scratch Saliva Other

	Lick (to broken skin) Other		membrane to saliva Exposure of open wound/abrasion to saliva Laboratory exposure Other					
Description of “Other” wound type	Yes		Yes	Yes	Yes	Yes	Yes	Yes
Location of the wounds on the body	Free text		Free text	Yes	Yes	Free text	Free text	Free text
Wound description in detail, if required			Yes	No	Free text	Bleed	No	Broken Bleed
Depth and severity of wounds	Free text		Bite or Scratch only	Yes	Yes	No	Free text	Yes and Length
The animal that caused the wound	Free text		Fruitbat / insectivorous bat adult bat / baby bat monkey / dog / unknown other	Yes	Dog Cat Monkey Bat Other	Dog Monkey Other Unknown	Free text	Fruit bat Other bat Dog Monkey Other
Description of “Other” animal			Yes	Yes	Yes	Yes	No	Yes
Behaviour of the animal prior to the injury/exposure, did the animal appear to be unwell or behave in an 'odd fashion'.	Yes		Yes	Yes	Yes	Yes	Yes	Yes
Description of animal behaviour and circumstances	Yes		Yes	Yes	Yes	Yes	No	No
Was the animal that caused the wound tested for rabies?	Yes		Lyssavirus	Yes	Yes	No	No	Yes
Results of animal testing for rabies/Australian bat lyssavirus	Yes		Yes	Yes	Yes	No	No	Yes
Description of the laboratory results	Yes		Yes	Yes	Yes	No	No	No

Country where the patient was exposed to the animal	Free text		Place of exposure (country/region or Stated) Postcode of region where exposure occurred (Australia only) Free text	Free text	Free text	Free text	Free text	Free text
If Indonesia, specify the island where the animal exposure occurred	No			No	No	No	No	Yes
Description of other country/island	No			No	No	No	No	No
Was the case liable to have received bites or scratches from bats in their everyday activities (this includes bat handlers, veterinarians, wildlife officers and others who come into direct contact with bats).	Yes		Free text	Yes	Yes	Circumstances (free text)	No	Included under work and volunteering
Was the case an expatriate or traveller who had spent prolonged periods (i.e. more than a month) in rabies-endemic areas.	Yes			Yes	Yes		No	Yes
Was the case working with mammals in rabies-endemic areas	Yes			Yes	Yes		No	Yes
Was the case from a research laboratory - person who work with live lyssaviruses	Yes			Yes	Yes		No	Included under work and volunteering
Has the exposed person previously received rabies vaccination	Yes Pre and Post exposure		Yes Pre and Post exposure	Yes	Yes	Yes Pre and post exposure	Yes Pre and post exposure	Yes Pre and post exposure
If yes, number of previous doses	Yes		Yes	Yes	Yes	Yes	Yes	Free text
Estimate of the date of when the last dose of rabies vaccine was given	Yes		Yes	Yes	Yes	Yes	Yes	Free text

Could HRIg recipient be considered to be immunocompromised as a result of an unrelated illness, condition, or prescribed drug use.	Yes		No	Yes	Yes	Yes	Yes	Yes
Description of immunocompromising condition	No		No	Yes	Yes	Yes	Yes	No
Date when the wound was assessed	Notification date		Report date	Yes	Yes	Notification date	Yes	Date of presentation
Assessment of wound by	Form completed by		No	Yes	Yes	Treating Doctor (free text)	Yes Only 3 options	Attending doctor (free text)
Date HRIg was used	Yes		Yes	Yes	Yes	Date ordered	Yes[ɣ]	No
Weight of person receiving HRIg in kilograms	Yes		Yes	Yes	Yes	Yes	Yes	Yes
The amount of HRIg used. Describe the number of vials of HRIg used	HRIg dosage (free text)		ml	mls	mls	mls	Yes	Yes
Date of first dose of rabies vaccine was given	Yes		Yes	Yes	Yes	Date ordered	No	No
Description of clinical issues of note	N/A		Yes	N/A	N/A	N/A	N/A	N/A
Name and contact details of person completing this survey	N/A		N/A	N/A	Yes	N/A	N/A	N/A

ACT: Not available online (internal only). Hardcopy form. Does not follow the same order as the NHRID questionnaire.

[a]NSW: Public Health Units enter potential exposure and risk factor data into a free text field in NCSMS. HRIg is ordered using the NSW Vaccine Ordering System.

[b]SA: Uses the NHRID as the main database to capture HRIg usage. Rabies or lyssavirus Post-exposure treatment (PET) form, Available online, Fillable Word document. Does not follow the same order as the NHRID questionnaire.

[c]TAS: Uses the *Rabies virus and other lyssaviruses (including ABLV) post-exposure prophylaxis* form in the Rabies and ABLV SoNG.

QLD: Rabies (Potential Exposure) Case Report Form, Available online, Fillable PDF. Does not follow the same order as the NHRID questionnaire. Includes HRIg history

VIC: Post-exposure rabies – lyssavirus treatment form, Available online, Hard copy form. Fillable PDF, Does not follow the same order as NHRID questionnaire. Asks about Post exposure vaccine and which country they got it. [ɣ]Asks about previous HRIg administration and date it was administered.

WA: Rabies virus and other lyssaviruses exposure assessment form. Available online. Fillable PDF which can be emailed directly, emailed or faxed to the Communicable Disease Control Directorate. Does not follow the same order as the NHRID questionnaire. Includes Exposure category (WHO options I, II, or III). Free text to describe incidence.

NT: Lyssavirus Post-Exposure Prophylaxis Report. Available online, Fillable PDF. Does not follow the same order as the NHRID questionnaire.

Data completeness and quality

Table S3. Completeness of NHRID based on date of last data entry by jurisdiction, January 2010 to November 2017, as at 22 November 2017

Jurisdiction	Completeness (date of last data entry)
Northern Territory	Up-to-date
Western Australia	Up-to-date
Tasmania	Up-to-date
South Australia	Up-to-date
New South Wales	2016
Queensland	2016
Australian Capital Territory	2015
Victoria	2014

Table S4. Proportion of data fields complete in the NHRID, January 2010 to November 2017, as at 22 November 2017 (n=8,490)

Data field	Missing (N)	Completeness (%) (N/8490)
Unique ID used by reporting Stated/territory	0	100% (8,409/8,409)
Unique ID automatically generated by NetEpi	2	99.8% (8,407/8,409)
Indigenous status of person receiving HRIg	2,793	66.8% (5,616/8,409)
Surname of person receiving HRIg [2]	7,995	4.9.% (414/8,409)
Given names of person receiving HRIg [2]	7,996	4.9% (413/8,409)
Date of birth of person receiving HRIg	48	99.4% (8,361/8,409)
Sex of person receiving HRIg	56	99.3% (8,353/8,409)
Locality/Suburb of residence of person receiving HRIg	436	94.8% (7,973/8,409)
Notifying State	320	96.2% (8,089/8,409)
Residential postcode of person receiving HRIg	510	93.9% (7,899/8,409)
Name of person completing NHRID questionnaire	4,886	41.9% (3,523/8,409)
Contact details of person completing NHRID questionnaire	5,572	33.7% (2,837/8,409)
Date of potential exposure	1,230	85.4% (7,179/8,409)

Wound Type [3]	1,465	82.6% (6,944/8,409)
Description of "Other" wound type	Entry required if "Other" entered in previous question: There were 369 entered as "Other" in previous question however there are 1216 entries for this data field.	
Location of the wound on the body [4]	815	90.3% (7,594/8,409)
Wound description in detail, if required[5]	4,031	52.1% (4,378/8,409)
Depth and severity of wounds	2,268	73% (6,141/8,409)
The animal that caused the wound	1,160	86.2% (7,249/8,409)
Description of "Other" animal[5]	Entry required if "Other" entered in previous question: There were 529 entered as "Other" in previous question however there are 760 entries for this data field.	
Behaviour of the animal prior to the injury/exposure, did the animal appear to be unwell or behave in an 'odd fashion'	3,038	63.9% (5,371/8,409)
Description of animal behaviour and circumstances [5]	6,857	18.5% (1,152/8,409)
Was the animal that caused the wound tested for rabies?	4,523	46.2% (3,886/8,409)
Results of animal testing for rabies/Australian bat lyssavirus	5,976	28.9% (2,433/8,409)
Description of the laboratory results[5]	7,987	0.05% (422/8,409)
Country where the patient was exposed to the animal[6]	349	95.9% (8,060/8,409)
If Indonesia, specify the island where the animal exposure occurred	4,418	47.5% (3,991/8,409)
Description of other country/island [5]	7,267	13.6% (1,142/8,409)
Case liable to have received bites or scratches from bats in their everyday activities (this includes bat handlers, veterinarians, wildlife officers and others who come into direct contact with bats)	4,148	50.7% (4,261/8,409)
Case an expatriate or traveller who had spent prolonged periods (i.e. more than a month) in rabies-endemic areas	5,588	33.6% (2,821/8,409)
Case working with mammals in rabies-endemic areas	846	89.9% (7,563/8,409)
Case from a research laboratory - person who work with live lyssaviruses	5,541	34.1% (2,868/8,409)
Exposed person previously received rabies vaccination	2,173	70.6% (5,936/8,409)
If yes, number of previous doses [7]	447	28.9% (182/629)

Estimate the date of when the last dose of rabies vaccine was given	6,935	17.5% (1,474/8,409)
HRIg recipient be considered to be immunocompromised as a result of an unrelated illness, condition, or prescribed drug use.	3,912	53.5% (4,497/8,409)
Description on immunocompromising condition [5]	Entry required if "Yes" entered in previous question: There were 105 entered as "Yes" in previous question however there are 321 entries for this data field.	
Date when the wound was assessed	5,060	39.8% (3,349/8,409)
Wound assessor	4,679	44.4% (3,730/8,409)
Date HRIg was administered	3,422	59.3% (4,987/8,409)
Weight of person receiving HRIg in kilograms[5]	2,438	71.0% (5,971/8,409)
The number of vials of HRIg used	2,490	70.4% (5,919/8,409)
Date of first dose of rabies vaccine given as part of PEP	1,636	80.5% (6,773/8,409)
Description of clinical issues of note [5 and 8]	5,817	30.8% (2,592/8,409)
Name and contact details of person completing the survey [5]	5,003	40.5% (3,406/8,409)

[1] Interpretation of the completeness should be done with caution. Records for QLD, VIC, ACT and NSW are not up-to-date, therefore the reported completeness cannot be interpreted as national representativeness.

[2] Identifiable data fields should not be in the NHRID. Therefore this data field should be 0% complete

[3] Only one option can be selected.

[4] Multiple options can be selected

[5] Free text

[6] 243 countries listed

[7] Entry in this field is only required if "Yes" is entered into previous question

[8] If required

Executive Summary presented to Communicable Diseases Network Australia and provided to stakeholders who participated in the evaluation

Executive summary - Evaluation of the National Human Rabies Immunoglobulin Database

Introduction

Since 2010, Australian State and Territory health departments have supplied data on people receiving human rabies immunoglobulin (HRIg) to a centralised surveillance system—the National Human Rabies Immunoglobulin Database (NHRID), held at the Australian Government Department of Health ('the Department'). In addition to the NHRID, the Department also maintains a separate inventory of HRIg stock around the country and monitors supply issues of HRIg domestically and internationally.

We evaluated the NHRID by examining its system structure and data flows, and through consultations with stakeholders between November 2017 and May 2018. The purpose of the evaluation was to:

1. examine the performance and effectiveness of the NHRID against the objectives proposed by the Department in 2016 following a review by CDNA;
2. Assess the extent to which NHRID influences decision making relating to the redistribution of HRIg stocks;
3. Determine what modifications or improvements could be made to the NHRID; and
4. Provide recommendations to the Communicable Diseases Network Australia (CDNA).

Methods

The interim objectives of the NHRID developed in 2016 were:

1. Collect and report national data on people who receive HRIg in Australia due to potential exposure to rabies virus overseas and Australian bat lyssavirus (ABLV) in Australia;
2. Identify possible risk factors for these potential exposures; and
3. Report on the approximate national HRIg usage in Australia.

Employing a mixed method approach, we evaluated the NHRID against these objectives using the Centers for Disease Control and Prevention's *Updated Guidelines for Evaluating Public Health Surveillance Systems* and the European Centre for Disease Prevention and Control's *Data quality monitoring and surveillance system evaluation – A handbook of methods and application* frameworks.

Findings

The evaluation found that the collection and reporting on national data on people who receive HRIg in Australia through the NHRID is not only useful but essential to inform rationale use of HRIg through targeted risk-minimization advice. These data have been used to inform policy on HRIg usage and led to a campaign to raise awareness of potential exposures to rabies virus whilst overseas.

However, whilst data in the NHRID has been utilized, the evaluation has found that as it currently stands, the NHRID does not adequately fulfill all its 2016 objectives.

Objectives 1 and 2:

Data collated on the NHRID are currently inadequate to identify possible risk factors and report on approximate national usage or inform the redistribution of HRIg in Australia for the following reasons:

1. As there is no specific standard operating procedure for the NHRID, the interface is cumbersome and not user friendly.
2. Staff turnover at the Department and in the jurisdictions over the years has led to the loss of historical knowledge of the NHRID, leading to barriers to acceptance of the system.
3. There is difficulty transferring data from the jurisdictional databases into the NHRID. Currently, only one jurisdiction (South Australia) uses the NHRID as its primary database to collate HRIg usage data, whilst 50% (4/8) of jurisdictions enter their HRIG usage data into their own database and then re-enter it directly into the NHRID. Queensland (QLD), New South Wales (NSW) and Victoria (VIC) cannot upload data into the NHRID as their systems are incompatible with NetEpi. Data from these three states are only provided upon

request. Data on the NHRID for QLD and NSW is only complete up until 2016 and for VIC until 2014.

4. Due the issues with data transfer, data in the NHRID are not nationally representative or timely and therefore do not provide a clear national picture of HRIg use in Australia.
5. The NHRID collects information in 45 fields, of which 25% (n=12) are free text fields. To meet its objectives the NHRID only needs to collect 14 of the 45 current fields.
6. Differences between the jurisdictional and national rabies prophylaxis forms places a burden on jurisdictions to gather additional data through time-consuming follow-up with the HRIg administering health practitioner. Seven of the eight (88%) jurisdictions collect HRIg usage and related data which generally reflect information captured in the NHRID questionnaire.
7. One jurisdiction provides identifiable case data which are not required for the national surveillance and is in contradiction with the Australia Privacy Principles.
8. At present, the production and dissemination of reports is not undertaken by the Department.
9. NetEpi—the platform that hosts the NHRID is out-dated. The NHRID is covered by usual Information Technology security practices meaning servers and backups are kept in a secure location. However, the server hasn't recently been updated and formal IT support for NetEpi in the Department is no longer available. Databases currently on NetEpi are managed by the Data Managers for the National Notifiable Diseases Surveillance System, but this is limited to managing user privileges and controlling access to active users only.

Recommendations to Communicable Disease Network Australia

This report provides a summary of key recommendations that arose from the evaluation of the NHRID. They are divided into priority recommendations, which require immediate implementation or would substantially improve data quality, and secondary recommendations that should be considered for long term planning to provide a stronger link between the data collected and public health action.

Priority recommendations:

Table 1: Identified priorities or issues requiring immediate action

Identified issue	Proposed resolution
NHRID does not meet its objectives	**Recommendation 1**: CDNA to continue to collect HRIg usage and related data to inform policy on HRIg usage and awareness campaigns to reduce potential exposures to rabies virus whilst overseas and ABLV in Australia. **Recommendation 2**: CDNA to agree to the interim objectives of the NHRID.
Refining the case definition	**Recommendation 11:** CDNA to make the case definition clearer and more specific. **Proposed new case definition to be considered by CDNA:** *"a case is a person who from 1 January 2010 onwards received human rabies immunoglobulin in Australia as part of post-exposure prophylaxis following a Category III exposure from an animal in a rabies-endemic area or a Category II or Category III exposure from a bat potentially infected with rabies virus overseas or Australian bat lyssavirus in Australia."*
Identifiable data in the NHRID	**Recommendation 3**: CDNA to collect de-identifiable data going forward and appropriately manage the disposal of existing identifiable data.
Collection of case data	**Recommendation 4:** The Department to cease collecting case data and start collecting aggregate data **Recommendation 5:** CDNA to agree on the aggregate data fields to collect data on HRIg usage and potential exposure and possible risk factors. **Recommendation 6:** CDNA to collect wound type data according to the Australian Immunisation Handbook 10th Edition and Rabies and other ABLV SoNG exposure categories, which are guided by the World Health Organization's position paper on rabies vaccines. This will achieve a nationally consistent approach of collecting this information
Data fields do not reflect the objectives of the system	
Difficulty identifying overseas and transient/mobile persons	
Too many data fields	

	Recommendation 7: CDNA to create a data field that collects data on the circumstances (risk behaviour) that led to the potential exposure to rabies overseas or ABLV in Australia. **Recommendation 8:** CDNA to create a data field that identifies HRIg recipients with an overseas residential address (tourists). This will inform the demographic characteristics of HRIg recipients in Australia. **Recommendation 9:** CDNA to create a data field that collects data on the HRIg product administered. This will inform the surveillance of the HRIg usage in Australia. **Draft of proposed interim aggregate data fields to be considered by CDNA are outlined in Appendix 1 and include draft data fields proposed in Recommendations 5-8**.
Outdated and insecure system currently not supported or maintained	**Recommendation 10:** Jurisdictions to use the draft of proposed interim data collection template for the reporting of aggregate data fields annually to the Department for interim reporting purposes. **Proposed interim data collection template for reporting purposes for consideration by CDNA is in Appendix 2.**
Infrequent review of HRIg usage data and related documents Dissemination of findings by the Department	**Recommendation 12:** The Department to collate and analyse the data annually and report to CDNA. **Recommendation 13:** CDNA to review the annually analysis of HRIg use and identify any issues and develop strategies to implement public health actions, if required. **Recommendation 14:** CDNA publish a HRIg surveillance short report or a Rabies and Australian bat lyssavirus post-exposure prophylaxis surveillance short report on an annual basis in a public report to relay findings to the jurisdictions, research community and the public.

Secondary recommendations:

Table 2: Identified long term priorities for improved national HRIg usage surveillance

Identified issue	Proposed resolution
Outdated and insecure system currently not supported or maintained	**Recommendation 1:** The Department to phase out the use of the NHRID on NetEpi and provide a secure, user-friendly data collection system capable of collecting case data. This will improve data quality, national consistency and timeliness of HRIg usage and potential exposure and risk factor data.
Data fields do not reflect the objectives of the system	**Recommendation 2:** Jurisdictions to agree to the collection and sending of de-identifiable case data to the Department, once a long term data collection system is implemented. **Recommendation 3:** CDNA to develop and agree on national data specifications and ensure only those that meet the national objectives are collected, which include data fields as per Recommendations 6 to 9 in Table 1.
Difficulty identifying overseas and transient/mobile persons	
Too many data fields	
Recording systems reviews, updates and changes	**Recommendation 4:** CDNA to start tracking events/changes to the system and data fields and the reasons for these changes to allow for historical documentation at the Department.
Future surveillance needs	**Recommendation 5:** CDNA to schedule an evaluation of the data collection system chosen and related processes in 5-years' time (or if the objectives change) to ensure that these meet a current need and the data collected is of high-quality.

Appendix 1: Draft of proposed suggestions for the interim data fields for HRIg usage and related data collection for consideration by the Communicable Disease Network Australia

Table 1: Draft of proposed suggestions for the HRIg usage and related data elements[a] (n= 18)

Data field	Description
Descriptive data	
Number of notifications by month and year	Count of persons notified with potential exposure to rabies virus or Australian bat lyssavirus, stratified by month and year
HRIg usage by age group (years)	Count of persons who received HRIg by predefined age groups (years): 0-9 10-19 20-29 30-39 40-49 50-59 60-69 65-69 70-79 80+ Not stated/Unknown
HRIg usage by sex	Count of persons who received HRIg by sex 1: M 2: F 3: Indeterminate 9: Not stated/Inadequately described NULL/Blank: No information
HRIg usage by jurisdiction	Count of persons who received HRIg by jurisdiction 1: NSW 2: Vic 3: QLD 4: SA 5: WA 6: TAS 7: NT 8: ACT
HRIg usage by Australian residents who are transient/mobile	0: Yes 1: No 9: Not stated/Unknown NULL/Blank: No information
HRIg usage by country of usual residence	Count of overseas persons by country of usual residence who received HRIg treatment in Australia
HRIg usage by Indigenous status[b]	Whether a person identifies as being of Aboriginal or Torres Strait Islander origin, as represented by a code.

	Count of persons who received HRIg by Indigenous status of person receiving HRIg 1: Aboriginal but not Torres Strait Islander origin 2: Torres Strait Islander but not Aboriginal origin 3: Both Aboriginal and Torres Strait Islander origin 4: Neither Aboriginal nor Torres Strait Islander origin 9: Not stated/inadequately described
HRIg usage	
HRIg usage by HRIg administration date	Count of persons who received HRIg by month and year Month: MM Year: YYYY
HRIg usage by HRIg product	Count of persons who received HRIg by product 0: IMOGAM® 1: KamRAB™ 9: Not stated/Unknown NULL/Blank: No information
HRIg usage by HRIg dosage	Count by mLs and vials of HRIg used (predefined) 0< 2mLs (1 vial of 2mLs) 2<4 mLs (2 vials of 2mLs) 4<6 mLs (3 vials of 2mLs) 6<8 mLs (4 vials of 2mLs) 8>10 mLs (5 vials of 2mLs) 10<12 mLs (6 vials of 2mLs) 12<14 mLs (7 vials of 2mLs) 14<16 mLs (8 vials of 2mLs) 16<18 mLs (9 vials of 2mLs) 18<20 mLs (10 vials of 2mLs) 20<22 mLs (11 vials of 2mLs) 22<24 mLs (12 vials of 2mLs)
HRIg usage by exposure category[c]	Count by WHO lyssavirus exposure category following animal-related injury 1: Category I 2: Category II 3: Category III 5: Other 9: Not stated/Unknown NULL/Blank: No information
HRIg usage by location of wound	Count by Location of the wounds on the body 1: Head 2: Neck 3: Torso 4: Upper arm 5: Lower arm (includes hand) 6: Fingers 7: Upper leg 8: Lower leg (includes foot and toes) 9: Other 10: Not stated/Unknown

	NULL/Blank: No information
Important for public health action	
HRIg usage by animal causing injury	Count by Animal causing injury 1: Fruit bat/ Flying fox (Australia) 2: Overseas bat 3: Dog or canine family 4: Cat 5: Other domestic animal 6: Monkey 7: Wildlife: General (excluding monkeys) 8: Other 9: Not stated/Unknown NULL/Blank: No information
HRIg usage by occupation	Count by occupations 1: Bat handlers 2: Veterinarians 3: Wildlife officers 4: Persons working with mammals in rabies-endemic areas 5: Persons who work with live lyssaviruses (a research laboratory). 6: Volunteers who come into direct contact with bats 7: Other animal-related occupations 8: Non-occupational exposure 9: Not stated/Unknown NULL/Blank: No information
HRIg usage by travel history	Count by Expatriate or Australian traveller who had spent time in rabies-endemic areas. 0: Traveller 1: Expatriate 9: Not stated/Unknown NULL/Blank: No information
HRIg usage by risk behaviour	Incident that provoked the exposure 1: Feeding an animal 2: Playing with an animal 3: Trying to capture an animal 4: Trying to assist an injured animal 5: Disturbing an animal 6: Accidental contact with an animal 9: Not stated/Unknown NULL/Blank: No information
HRIg usage by country of exposure	Count by country of exposure Include Not stated/Unknown, NULL/Blank: No information
HRIg usage by in-country location where potential exposure occurred (i.e. Island name)	Count by location with country of exposure, in case of an island (e.g. Bali in Indonesia) Include “Not applicable”

[a] Aggregate data

[b] Source: http://meteor.aihw.gov.au/content/index.phtml/itemId/291036

[c] Adapted from: WHO Expert Consultation on Rabies, third report. Geneva: World Health Organization; 2018 (WHO Technical Report Series, No. 1012). Licence: CC BY-NC-SA 3.0 IGO.

Table 2: Draft of proposed data fields relating to rabies vaccination (optional inclusion) (n=5)

Data field	Description
Rabies vaccination due to potential rabies exposure	Count of exposed persons that received rabies vaccination as part of the post exposure rabies prophylaxis for a current incident
Rabies vaccination due to potential ABLV exposure	Count of exposed persons that received rabies vaccination as part of the post exposure ABLV prophylaxis for a current incident
Name of rabies vaccine product used as part of current PEP	Count of persons who received rabies vaccine rabies vaccine product used as part of the post exposure rabies/ABLV prophylaxis for the current incident. 0: Mérieux Inactivated Rabies Vaccine 1: Rabipur Inactivated Rabies Virus Vaccine 9: Not stated/Unknown NULL/Blank: No information
Exposed person previously received rabies vaccination	Count of exposed persons who received rabies vaccination in the past (as part of the post-exposure prophylaxis for a previous incident)
Year that rabies vaccine was administered	Year the person notified with potential exposure to rabies or Australian bat lyssavirus received previous rabies vaccination YYYY: year

[a] Aggregate data

Appendix 2: Proposed interim data collection template for reporting purposes for consideration by Communicable Disease Network Australia

To be collected in Microsoft Excel

1. Total HRIg usage

State/Territory:

Year	Human rabies immunoglobulin usage			
	# of persons who received HRIg		# of persons who received HRIg product	
	Month	Year	IMOGAM	KamRAB
2010				
2011				
2012				
2013				
2014				
2015				
2016				
2017				
2018				
Total				

2. HRIg usage by sex

State/Territory:

Year	Human rabies immunoglobulin usage		
	# of persons who received HRIg by **Sex**		
	Female	Male	Not stated/ Unknown
2010			
2011			
2012			
2013			
2014			
2015			
2016			
2017			
2018			

3. HRIg usage by age group

State/Territory:

Year	Human rabies immunoglobulin usage									
	# of persons who received HRIg by **age group (years)**									
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80+	Not stated/Unknown
2010										
2011										
2012										
2013										
2014										
2015										
2016										
2017										
2018										

4. HRIg usage by WHO lyssavirus exposure category

State/Territory:

Year	Human rabies immunoglobulin usage				
	# of persons who received HRIg by **WHO lyssavirus exposure category**				
	Category I	Category II	Category III	Other	Not stated/ Unknown
2010					
2011					
2012					
2013					
2014					
2015					
2016					
2017					
2018					

5. HRIg usage by travel history

State/Territory:

Year	Human rabies immunoglobulin usage		
	# of persons who received HRIg by **travel history**		
	Traveller	Expatriate	Not stated/ Unknown
2010			
2011			
2012			
2013			
2014			
2015			
2016			
2017			
2018			

6. HRIg usage by transient/mobile persons (Australian resident)

State/Territory:

Year	Human rabies immunoglobulin usage		
	# of persons who received HRIg by **Transient/mobile (Australian resident)**		
	Female	Male	Not stated/ Unknown
2010			
2011			
2012			
2013			
2014			
2015			
2016			
2017			
2018			

7. HRIg usage by Indigenous status

State/Territory:

Year	Human rabies immunoglobulin usage				
	# of persons who received HRIg by **Indigenous status**				
	Aboriginal but not Torres Strait Islander origin	Torres Strait Islander but not Aboriginal origin	Both Aboriginal and Torres Strait Islander origin	Aboriginal nor Torres Strait Islande	Not stated/ inadequately described
2010					
2011					
2012					
2013					
2014					
2015					
2016					
2017					
2018					

8. HRIg usage by overseas recipients

State/Territory:

Year	Human rabies immunoglobulin usage									
	# of persons who received HRIg by **overseas recipients**									
	[country]	[country]	[country]	[country]	[country]	[country]	[country]	[country]	[country]	[country]
2010										
2011										
2012										
2013										
2014										
2015										
2016										
2017										
2018										

9. HRIg usage by HRIg dosage

State/Territory:

Year	Human rabies immunoglobulin usage												
	# of persons who received HRIg by **HRIg dosage**												
	0< 2mLs (1 vial of 2mLs)	**2<4 mLs** (2 vials of 2mLs)	**4<6 mLs** (3 vials of 2mLs)	**6<8 mLs** (4 vials of 2mLs)	**8>10 mLs** (5 vials of 2mLs)	**10<12 mLs** (6 vials of 2mLs)	**12<14 mLs** (7 vials of 2mLs)	**14<16 mLs** (8 vials of 2mLs)	**16<18 mLs** (9 vials of 2mLs)	**18<20 mLs** (10 vials of 2mLs)	**20<22 mLs** (11 vials of 2mLs)	**22<24 mLs** (12 vials of 2mLs)	Not stated/ Unknown
2010													
2011													
2012													
2013													
2014													
2015													
2016													
2017													
2018													

10. HRIg usage by Animal causing injury

State/Territory:

Year	Human rabies immunoglobulin usage							
	# of persons who received HRIg by **Animal causing the injury**							
	Fruit bat/ Flying fox	Overseas bat	Dog or canine family	Cat	Other domestic animal	Monkey	Wildlife: General	Other	Not stated/Unknown
2010									
2011									
2012									
2013									
2014									
2015									
2016									
2017									
2018									

11. HRIg usage by Exposure occupation

State/Territory:

Year	Human rabies immunoglobulin usage							
	# of persons who received HRIg by **Exposure occupation**							
	Bat handlers	Veterinarians	Wildlife officers	Persons working with mammals in rabies-endemic areas	Persons who work with live lyssaviruses (a research laboratory).	Volunteers who come into direct contact with bats	Other	Not stated/Unknown
2010								
2011								
2012								
2013								
2014								
2015								
2016								
2017								
2018								

12. HRIg usage by Incident that provoked the exposure

State/Territory:

Year	Human rabies immunoglobulin usage						
	Incident that provoked the exposure						
	Feeding an animal	Playing with an animal	Trying to capture an animal	Trying to assist an injured animal	Disturbing an animal	Accidental contact with an animal	Not stated/Unknown
2010							
2011							
2012							
2013							
2014							
2015							
2016							
2017							
2018							

13. HRIg usage by Country of exposure

State/Territory:

Year	Human rabies immunoglobulin usage									
	# of persons who received HRIg by **country of exposure**									
	[country]	[country]	[country]	[country]	[country]	[country]	[country]	[country]	[country]	[country]
2010										
2011										
2012										
2013										
2014										
2015										
2016										
2017										
2018										

14. HRIg usage by In-country of exposure

State/Territory:

Year	Human rabies immunoglobulin usage				
	# of persons who received HRIg by **In country exposure (example Bali, Indonesia)**				
	[enter name of place here]	[enter name of place here]	[enter name of place here]	[enter name of place here]	[enter name of place here]
2010					
2011					
2012					
2013					
2014					
2015					
2016					
2017					
2018					

HRIg usage short report template for the Office of Health Protection, Australian Government Department of Health

Short report

HUMAN RABIES IMMUNOGLOBULIN USAGE, AUSTRALIA, 2018

The purpose of this short report is to characterise the distribution of human rabies immunoglobulin (HRIg) by Australian Government Department of Health during 2018.

Human Rabies Immunoglobulin usage in Australia

Rabies virus and other lyssavirus, including Australian bat lyssavirus (ABLV), exposures and infections are considered an urgent public health priority in Australia. Human rabies immunoglobulin (HRIg) is an immediate post-exposure prophylaxis (PEP) providing passive immunity following overseas or domestic acquired animal-related injuries important to prevent rabies or ABLV, respectively. It is one component of lifesaving treatment to prevent clinical symptoms in unimmunised people who may have been exposed to a lyssavirus.

The only registered HRIg product in Australia is *Imogam Rabies Pasteurized* – Sanofi Pasteur Pty Ltd human rabies immunoglobulin (IMOGAM®), however, through a Special Access Scheme managed by the Therapeutic Goods Administration, KamRAB Rabies Immune Globulin (KamRAB™) is also administered. For previously unvaccinated persons, rabies PEP involves HRIg given intramuscularly on a per weight basis as soon as possible after exposure, ideally with the first dose of rabies vaccine, and four subsequent doses of rabies vaccine over the following 4 weeks.

Indications for HRIg usage in Australia

Since 1 January 2010, data on all HRIg usage for potential exposures, such as potential ABLV in Australia and potential rabies virus exposure from overseas acquired animal-related injuries in previously unimmunised persons have been collected by the Australian Government Department of Health.

There are two main indications for HRIg usage in Australia:

"travellers who have had animal bites/scratches in a geographic location where rabies is known to be endemic in animal populations; and

people in Australia, where Australian bat lyssavirus (ABLV) is endemic, who have had bites/scratches from bats".

Methods

We reviewed aggregate data on HRIg usage in 2018 as reported by Australian Stated and territory health departments (n=8) and summarised by demographics, exposures and risk factors using Stata 13 (Stata Corp, College Station, TX, USA).

Results

During 2018, Australia supplied HRIg for X persons (mean: X per year, range: X–X) at a notification rate of X per 100,000 population for women and X per 100,000 population for men. Of these X persons, X (X%) were Australian residents and X (X%) identified as Indigenous. A total of X 2-ml vials of HRIg were administered to the X persons at an estimated cost of $X. In 2018, X% (n=X) of persons administered with HRIg in Australia received IMOGAM®, the only l and X& (n=X) were administered KamRAM rabies immunoglobulin. Between 2010 and 2018 the trend of HRIg usage decreased/increased (Figure 1). [Include seasonality]

Of the X persons who received HRIg due to an animal exposure in Australia, X (X%) were male and the age group with the highest incidence was X-X years. Of the X persons who received HRIg due to animal-related injuries overseas, X (X%) were male and the age group with the highest incidence was X-X years. X (X%) were identified as persons with an overseas address and X (X%) were transient or mobile persons who received their HRIg in one Stated or territory and but completed their PEP in another jurisdiction.

[*insert figure here*]

Figure 1: Human rabies immunoglobulin (HRIg) usage by month and year, Australia, 2010 to 2018 [*bar graph indicating school holiday periods*]

Geographical distribution [*display as a map*]

Of the X persons supplied with HRIg in Australia, X (X%) received HRIg in [jurisdiction] and [jurisdiction] (X, X%) (Table 1).

Table 1: Frequency (N) and rates per 100,000[a] of persons who received HRIg for potential exposures to the rabies virus or ABLV by year and jurisdiction, 1 January to 31 December 2018 (n=X)

Stated or territory	Notifications		Total (N, Rate per 100,000)
	N	Rate per 100, 000	
ACT			
NSW			
NT			
Qld			
SA			
Tas			
Vic			
WA			
Australia			

[a] Rates calculated using the ABS mid-year estimated resident populations

Exposures

Category of exposure

In 2018, the most common type of exposure for persons who received HRIg were (exposure type] (Table 2) followed by [exposure type].

Table 2: Human rabies immunoglobulin (HRIg) usage by category of exposure, Australia, 2018

Category of exposure[a]	**2018 (n,%)**
Category I	
Category II	
Category II	
Other	
Not Stated/Unknown	

[a] Modified from the WHO, Australian Immunisation Handbook 10th Edition and Rabies and other lyssavirus SoNG

Animal

Persons exposed to [animal] or [animal] represented X% of all persons who received HRIg due to potential exposure to rabies or ABLV. [animal] exposure was responsible for X% of HRIg usage. Of the X bat exposures in 2018, X occurred in Australia, mainly in [jurisdiction] (X,X%), and X (X%) abroad. Of the animals involved in the X overseas

exposures, X (X%) were [animal], X (X%) were [animal], X (X%) were [animal], and X (X%) were [animal].

Table 3: Human rabies immunoglobulin (HRIg) usage by animal exposure, Australia, 2018

Animal exposure	2018 (n,%)
Fruit bat/Flying fox	
Oversea bat	
Dog or canine family	
Cat	
Other domestic animal	
Monkey	
Wildlife: General	
Other	
Not Stated/Unknown	

Location of wound

In 2018, the most frequently reported wound location was [X].

Table 4: Human rabies immunoglobulin (HRIg) usage by wound location, Australia, 2018

Location of wound	2018 (n,%)

Circumstances of potential exposure

Of the X persons who received HRIg in Australia in 2018, the most common occupation resulting in potential exposure, was [X], followed by [X] at X% and X%, respectively.

Country of potential exposure

Among the X persons potentially exposed to rabies overseas, X% were exposed in Asia, predominately following travel to [country] and [country] (Table 5).

Table 5: Human rabies immunoglobulin (HRIg) usage by country of potential exposure, Australia, 2018

Country of exposure	2018 (n,%)
Top 10	
Not Stated/Unknown	

Risk factors

Of the X persons who received HRIg, X (X%) were exposed to an animal outside of Australia while traveling as a tourist. [risk behaviour] was the main reason for HRIg usage in Australia (Table 3).

Table 3: Human rabies immunoglobulin (HRIg) usage by risk behaviour, Australia, 2018

Risk factor	2018 (n,%)
Risk behavior	
Feeding an animal	
Playing with an animal	
Trying to capture an animal	
Trying to assist an injured animal	
Accidental contact with an animal	
Disturbing an animal	
Other	
Not Stated/Unknown	

Summary

Recommendations [*public health messaging mentioned here*]

Potential rabies virus exposure whilst overseas or ABLV in Australia are serious public health emergencies.

HRIg is a scarce resource worldwide and may not be available in certain countries. Persons traveling overseas should consider consulting a medical practitioner to determine if pre-exposure immunisation against rabies is indicated.

Acknowledgements

Author details

References

Interview questions

Objective	**The Australian Government Department of Health is evaluating the National Human Rabies Immunoglobulin Database (NHRID). This component of the evaluation will assess the value of the data derived from the NHRID and the effectiveness and efficiency of NHRID as a national surveillance system to monitor the usage of Human Rabies Immunoglobulin (HRIg).**
Attributes assessed using semi-structured telephone interviews/ face-to-face interview	➢ Qualitative system attributes (simplicity, flexibility and acceptability) will be assessed through interviews with NHRID users. ➢ Usefulness of and accessibility to NHRID data will also be assessed [some already assessed by Timothy Sloan-Gardner, see below] ➢ Opening and closing questions
Participants	➢ Jurisdictional health Department/Public health unit staff responsible for data entry into NHRID ➢ Department staff with NHRID knowledge

Questions for JURISDICTIONS Semi-structured telephone interviews	
Attributes	**Questions**
Acceptability	➢ In your opinion, are the NHRID and the data still relevant in the collection of HRIg usage and monitoring of stock levels? ➢ What barriers exist to using the database for the collection of HRIg usage and monitoring of stock levels? ➢ How often do you look at the information from NHRID? ➢ What other uses of NHRID data do you think could be made?
Stability	➢ Can you give me any specific examples of technical difficulties you have experienced whilst using the NHRID? What kinds of issues have arisen while you have used NHRID?
Usefulness	➢ From your perspective, what should be the objectives of a national surveillance system to monitor the usage of HRIg? ➢ In your opinion, do you think NHRID meets these objectives? ➢ In your opinion, what are the strengths of the NHRID and data?

	➢ In your opinion, what are the limitations of the NHRID and data? ➢ How has NHRID data been used to inform policy, practice or research in your jurisdiction?
Simplicity (of its structure and ease of operation	➢ How do you access data from NHRID? ➢ In your jurisdiction, where do you receive most of your HRIg information from? ➢ Can you describe to me the steps/process by which data is entered into the NHRID? ➢ Do you receive feedback from the Department on HRIg stock levels? ➢ What kind of feedback on HRIg stock levels do you receive from the Department? ➢ How would you describe the feedback you get from the Department on HRIg stock levels? ➢ How could the feedback you receive from the Department on HRIg stock levels be improved? What information would you want to receive on a regular basis? ➢ How much time per week do you spend preparing/entering/transferring data into NHRID? (in hours) ➢ When do you make updates/corrections to your data based on NetEpi transmission reports from the Department? ➢ What is the time lag between the administration of HRIg and entering the data into NHRID?
Flexibility	➢ In your opinion, can the NHRID adapt to changing information needs and operating requirements (i.e. changes in data fields etc.)? ➢ What is your opinion of what makes the NHRID work well or not well in monitoring the usage of Rabies Immunoglobulin (HRIg) (in regards to the design of the NHRID)?

Questions for AUSTRALIAN ZOONOSES EPIDEMIOLOGIST Face to face interviews with semi-structured questions	
Attribute	Question
Acceptability	➢ In your opinion, are the NHRID and the data useful in the collection of HRIg usage and monitoring of stock levels?? ➢ How relevant is the NHRID and the data in the collection of HRIg usage and monitoring of stock levels? ➢ Are there barriers to using the database for the collection of HRIg usage and monitoring of stock levels? Have you experienced any problems whilst using the NHRID? If so, what kinds of issues have arisen while you have used NHRID? What happened? ➢ How often do you look at the information from NHRID? ➢ What other uses of NHRID data do you think could be made?
Stability	➢ Have you experienced any technical difficulties whilst using the NHRID? If yes, what are they?
Usefulness	➢ From your perspective, what should be the objectives of a national surveillance system to monitor the usage of HRIg? ➢ Do you think NHRID meets these objectives? ➢ In your opinion, what are the strengths of the NHRID? ➢ In your opinion, what are the limitations of the NHRID? ➢ How has NHRID data been used to inform policy, practice or research at the Department? What decisions have been made based on data from the NHRID? ➢ How are the data analysed? How often? ➢ How often are reports disseminated? To whom? How are the reports distributed?
Simplicity (of its structure and ease of operation	➢ How do you access data from NHRID? ➢ At the Department, where do you receive most of your HRIg information from? ➢ Can you describe to me the steps/process by which data is retrieved from the NHRID? ➢ When do you make updates/corrections to your data based on NetEpi transmission reports from jurisdictions?
Flexibility	➢ In your opinion, can the NHRID adapt to changing information needs and operating requirements (i.e. changes in data fields etc.)?

	➢ In regards to the design of the NHRID, what do you think makes the NHRID work well or not well in monitoring the usage of HRIg?

Timothy Sloan-Gardner's redevelopment survey questions	
Question	Attribute
Does the HRIg data collected in your jurisdiction get entered into any local databases? If Yes, what types of databases are they (i.e. your notifiable disease database, an excel spreadsheet, etc.).	Usefulness Simplicity
Do you enter your HRIg data into NetEpi? If Yes, is it manually or by upload?	Simplicity
What is the purpose of collecting HRIg data in your jurisdiction?	Usefulness Acceptability
Are there any changes you would like to see to the NetEpi database?	Usefulness Simplicity Flexibility

Opening questions:

- How long have you been in your role?
- What are your main tasks in relation to NHRID? (Usefulness)

Closing question:

- Do you have any other comments or thoughts about the NHRID you would like to add?

CHAPTER 6 –
TEACHING EXPERIENCE

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Teaching experience

This chapter outlines the Teaching experience component of the MAE. Scholars are required to complete two exercises: 1) provide a Lessons from the Field (LFF) to your cohort, and 2) participate in a teaching exercise to the first year MAE scholars.

Lessons from the Field

The LFF is an opportunity for MAEs to share with their cohort key learnings from their projects or activities that they participated in at their placements. Given that each MAE placement is different, these learnings provide an opportunity to share knowledge of a new topic and thus broaden the MAE's knowledge in applied epidemiology.

Surveillance is undertaken at all levels: local, jurisdiction, national and international. Being an MAE placed in the Office of Health Protection at the Australian Government Department of Health; I participated in the routine national surveillance of communicable diseases for the detection and monitoring of diseases/events of public health concern, both within Australia and internationally. This process comprises of the review of communicable disease data, derived from event-based surveillance (EBS) and indicator-based surveillance (IBS), with subject matter expert epidemiologists on a fortnightly basis. These two types of public health surveillance use different types of data which complement one another. Communicable disease surveillance information deemed relevant or of interest is subsequently provided to the Communicable Diseases Network Australia (CDNA) members for their noting and evaluation to decide if public health action is required.

I developed my LFF on the two routine activities undertaken as part of the national surveillance of communicable diseases to show the process that is followed – rumour surveillance which includes writing a short report, and interpreting communicable disease notifications reported to the National Notifiable Diseases Surveillance System (NNDSS). After learning about EBS and IBS during course block, I thought it would be a valuable exercise for my fellow MAEs to show how EBS and IBS is undertaken in practise at the national level. Based on the feedback I received from my MAE colleagues, they found my LFF interesting and insightful. I conducted my LFF on 16

August 2017 and the lesson with answers is presented in Supplementary Information – Lessons from the Field.

Teaching the first-year MAE scholars

I completed my teaching of the first-year MAE scholars with the 2017 MAE cohort at the course block in March 2018. In a team of four, we developed, planned and implemented a lesson to teach the first-year scholars about what ethical considerations they should keep in mind whilst creating informed consent forms. The team wanted to share information with first-year scholars that they could use once they "hit the ground running" at their placements, especially on a topic that isn't covered during the first course block.

Informed consent is an important component of ethical research. The need for ethical research practices was the result of vulnerable groups being exploited, abused or inadequately protected due to highly unethical/ incorrectly regulated research practices. Infamous cases include the Nazi's experiments on concentration camp prisoners in WWII, the sale of the unlicensed drug Thalidomide to pregnant women in the late 50s/early 60s and the 40 year Tuskegee Syphilis Study on African American men. There is a lot to consider when creating an informed consent form but the key elements that should be included are information, comprehension and voluntary participation:

- The use of simple and clear language and avoidance of jargon and technical terms to explain the purpose of the study,
- Being transparent with any potential costs or risks as well as any benefits to the participant,
- Explaining the participant's role and how long they are being asked to participate in the study,
- Stating the person's ability to ask questions and their right to withdraw at any time without consequence, and
- Outlining how the data collected will be stored and held secure.

This information needs to be included to help a person decide if they want to agree to participate in your study. Furthermore, adolescents (12 to 17 years) give their assent together with their parent's consent and for those under 12; consent is required from

the parents. The use of coercion or undue influence is not allowed. We presented a PowerPoint presentation outlining the above key points and then, in groups, asked the first-year MAE scholars to critique a short informed consent form we developed (Supplementary Information – Teaching materials for the first-year MAEs).

In addition to the individual team lessons, the second-year MAEs ran two exercises for the first-year MAE scholars to participate in, based on the successful 2016 MAE cohort's "Epi-Cranium". The first-year MAEs participated in teams in the following activities: 1) putting on a personal protections suit under time pressure and using glitter spray to determine if the instructions were followed correctly; and 2) epidemiology and communicable disease knowledge gained during course block was tested using charades (to act out the answer), drawing (to produce a picture of the answer) and play doh (to sculpt the answer). These activities required the involvement of all members of the second-year MAE cohort for its successful implementation. Needless to say it was not only a fun but also an effective learning tool. I did however sometimes wonder who was having more fun, the first or second-year MAEs.

Supplementary Information

Lessons from the Field exercise

National Communicable Diseases Surveillance

Learning objectives

By the end of this LFF students should be able to:

1. Conduct rumour surveillance to identify international events/diseases that may pose a threat to Australia and identify resources for rumour surveillance
2. Write a short report to be included in the CDNA surveillance report
3. Review the communicable disease notifications reported to the National Notifiable Diseases Surveillance System (NNDSS) and understand factors that need to be taken into consideration when interpreting data.

Background

In Australia, communicable disease surveillance at the national level comprises of:

- "detecting outbreaks and identifying national trends;
- providing guidance for policy development and resource allocation at the national level;
- monitoring the need for and impact of national disease control programs;
- coordinating a response to national or multi-jurisdictional outbreaks;
- describing the epidemiology of rare diseases that occur infrequently at state and territory levels;
- meeting various international reporting requirements, such as providing disease statistics to the World Health Organization; and
- supporting quarantine activities, which are the responsibility of the Australian government."[1]

As part of this process, communicable disease data are reviewed by epidemiologists at the Australian Government Department of Health on a fortnightly basis and findings

are presented to the Communicable Diseases Network Australia (CDNA) members who evaluate communicable disease surveillance information and decide on public health actions at their jurisdictional level, if applicable.

This LFF is about undertaking two components of routine national surveillance of communicable diseases at the Australian Government Department of Health. It consists of: 1) conducting rumour surveillance of international events/diseases that may pose a threat to Australia, and 2) reviewing the communicable disease notifications reported to the National Notifiable Diseases Surveillance System (NNDSS).

Instructions

Your main tasks in this LFF are to scan multiple resources of information for rumour surveillance, understand the limitations of these resources, interpret the communicable disease notifications reported to the NNDSS, and decide the relevant information to present to decision makers (CDNA) as part of a fortnightly summary on diseases of current interest, including an International Report, and notifications of Australia's nationally notifiable diseases.

Introduction to the LFF – Exercise 1

Communicable Diseases Network Australia

CDNA provides national public health co-ordination and leadership, and supports best practice for the prevention and control of communicable diseases. It includes members from each jurisdiction in Australia, the Australian Government Department of Health, Ministry of Health New Zealand, and other health stakeholders such as OzFoodNet, Food Standards Australia and New Zealand (FSANZ), Australian Society for Microbiology (ASM), the Kirby Institute for Infection & Immunity in Society, and the National Centre for Immunisation Research and Surveillance (NCIRS). CDNA members meet fortnightly to share and evaluate the latest information and developments in communicable diseases surveillance with a view to providing a high quality surveillance of communicable and notifiable diseases.

Question: Given the role of CDNA, what kind of information do you think CDNA would find useful?

Relevant information about national/international communicable disease developments and trends which have specific relevance to public health and emergency response in Australia.

For more information:

- Australian Government Department of Health Communicable Diseases Network Australia http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-cdna-cdna.htm

Scenario 1 – International Report

You are the new Master of Philosophy in Applied Epidemiology (MAE) Scholar undertaking your placement in the Zoonosis, Foodborne and Emerging Infectious Diseases Section within the Office of Health Protection, Australian Government Department of Health. The MAEs who are hosted at the Australian Government Department of Health are responsible for writing the International Report that is completed fortnightly as part of the CDNA surveillance report. You have been rostered to complete the International Report this fortnight. The process that you will follow is summarised as:

Scan: find and read information sources (official and unofficial) on the Internet and electronic-mail-based groups.

Assess: determine the relevance of the information you have found, i.e. focus your search.

Verify: cross-reference and obtain background information to determine accuracy and quality.

Report: compile and report on the events and their context.

Disseminate: disseminate the information to inform decision makers of issues of public health importance, i.e. CDNA, for them to decide on any actions.

Exercise 1.1 - Resources

Scan the resources emailed to you last week (also included below) and answer the following questions:

QUESTIONS:

1. What kind of surveillance are you undertaking?
   Rumour surveillance. "Event-based surveillance is the rapid identification of information about events that are a potential risk to public health. Unlike traditional surveillance systems, there is no systematic collection of routine data and disease/syndrome definitions are not used. The sources of information include rumors and disease reports transmitted through formal and informal channels".[2]
2. What is the purpose of monitoring events?
   Events are monitored to determine the potential impact on public health and whether a response is required, i.e. public health action. Monitoring a range of unofficial information sources and scanning official websites to detect threats of potential public health importance and assessing the accuracy of the information and the risk that the potential threat may pose to the public. This informs whether a public health response is required to minimise illness, and deaths and public health concern.
3. Which sources would you consider official or unofficial sources of information?
   Official: UN agency websites such as WHO, PAHO; ECDC, CDC, UK HPA etc.
   Unofficial: news media, electronic surveillance systems such as ProMED.
4. What do you need to keep in mind when perusing sites such as Reuters/ProMed etc.?

   Sources such as Reuters or ProMed-mail are websites which act as a repository of information. The information on these websites has not been verified, 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.

5. Are there other reliable sources you would also refer to as part of this exercise?
   Government health department websites
   WHO EIS and situational reports (note: requires login details) - http://apps.who.int/ihr/eventinformation/

Resources for task:

- 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
- ECDC - http://www.ecdc.europa.eu/en/press/news/Pages/News.aspx
- Eurosurveillance – http://www.eurosurv.org/
- 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
- PACNET: To be added to PACNET send an email to join-pacnet@lyris.spc.int.
- Reuters alert net - http://www.trust.org/?show=alertnethumanitarian
- FLUTRACKERS - http://www.flutrackers.com/forum/
- HealthMap - http://healthmap.org/en/
- Reliefweb: http://reliefweb.int/

Exercise 1.2 – Information to include in your report

You have perused the resources from Exercise 1. You are now required to write a short International Report. This report will provide a fortnightly summary on diseases of current interest to Australia and will be disseminated to CDNA as well as the public.

To guide you, please read the International Reporting Guideline (in Appendix 1 or attached to email). You can also use the International Report attached to the email as a reference (Appendix 2).

Before completing Exercise 1.2, answer the following questions:

QUESTIONS:

6. Risks to public health have increased due to globalisation, and international travel and trade. Give examples of these types of risks and how they may be transmitted. People (SARS, influenza, Ebola, polio), goods, food, animals (e.g. zoonotic disease) and vectors (e.g. Dengue, Yellow Fever).
7. What criteria should be assessed when considering the inclusion of an event in your report?
    - The scale of the event (both within and outside the Region), for example number of people affected, proportion of population affected, size of geographical area affected, a substantial increase from the norm.
    - The urgency of responding, for example degree of transmissibility of pathogen (does Australia and/or the Region have the vector), speed of international spread (to Australia), and case fatality ratio.
    - The emergence of a new infectious disease (e.g. Zika virus infection).
    - An event that may influence trade or travel.

Please write your International Report (no more than 2 pages) for the fortnight: 31 July 2017 to 14 August 2017. You have 5 hours to complete this task.

Once you have written your short report, please answer the following questions:

QUESTIONS:

1. What core information did you include in your report?
   Time, place and person; threat and potential impact.
2. Which diseases would you consider to be high priority for Australia?
   Diseases where the vector is also present in Australia, for example Dengue (*Aedes aegypti*), Yellow Fever (*Aedes aegypti*), Japanese encephalitis (*Culex* species), Chikungunya (*Aedes aegypti),* malaria (*Anopheles* species); Emerging infectious diseases (avian influenza, SARS, Zika virus infection); Seasonal diseases that cause high morbidity or mortality every year such as Influenza; Sexually transmitted infections such as Gonorrhoea, Syphilis; Diseases considered a public health emergency of international concern such as Poliomyelitis; quarantinable disease like Ebola; or highly infectious diseases like measles.
3. What kind of difficulties did you come across whilst completing this task?

   Broad range of information sources/Time management: Perusing all the websites within the given timeframe. Thus need to be selective. This comes with experience. Best practice is to scan sites everyday so that can identify a change or occurrence quicker as you're already familiar with what is happening. Verifying the information – cross-checking information with official sources. This process can be time-consuming and/or difficult as some government health department websites aren't easy to find or after translating their websites it does not yield useful information. Knowledge of diseases and vectors (is it a threat to Australia or Australian tourists?)

7. Write a sentence or two justifying your choice of each event you have included in your report

   Response should include source of information (whether an official site, if not, were they able to cross-reference with an official site), likelihood of spread and speed of spread in Australia or the Region (e.g. threat or potential impact to Australia or the Region), number of cases and deaths, if applicable.

Before the final step of the process (Disseminate), the events you chose were individually reviewed by epidemiologists at the Australian Government Department of Health and it was decided whether these findings should be presented to CDNA.

You have completed Exercise 1 of this LFF.

Scenario 2 - Review of national communicable disease notifications

You have now also been asked to review the communicable disease notifications reported to the National Notifiable Diseases Surveillance System (NNDSS) for this fortnight (table can be accessed from the link below or attachment).

Introduction to the LFF - Exercise 2

The National Notifiable Diseases Surveillance System (NNDSS)

The NNDSS coordinates the national surveillance of over 50 communicable diseases/ disease groups. Notifications are made to the States or Territory health authority under the provisions of the public health legislation in their jurisdiction. States and Territories provide de-identified data on each notified case to the Australian Government through the NNDSS.

For more information:

- National notifiable diseases: Australia's notifiable diseases status: Annual report of the National Notifiable Diseases Surveillance System: http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-pubs-annlrpt-nndssar.htm

Exercise 2 – Review and interpretation of national communicable disease notification data

You now need to review and interpret the national communicable disease notification data for this fortnight to see if any diseases have seen a change and are worth including in the CDNA surveillance report. Have a look at the table in the previous fortnight's CDNA report (attached or link below).

Fortnight 15 28 07 2017 Communicable D

Resources for Exercise 2:

National Notifiable Diseases Surveillance System – current CDNA fortnightly report http://www.health.gov.au/internet/main/publishing.nsf/Content/cdnareport.htm

Once you have completed Exercise 2, please answer the following questions:

QUESTIONS:

1. The reporting of notifiable diseases is based on what kind of surveillance?
   Indicator-based surveillance. "Indicator based surveillance is the systematic collection and analysis of timely, reliable and appropriate data on priority diseases, syndromes and conditions" for public health action."[3] IBS is considered traditional surveillance. It includes datasets obtained from notifiable disease surveillance, syndromic surveillance, sentinel surveillance, hospital diagnosis and death registers, laboratory-based surveillance, and antimicrobial resistance surveillance.[3]
2. What causes a disease to be 'flagged' (highlighted)?
   The rolling mean is a technique used with time series data to smooth the data to reduce the effect of random variation or short term irregularities (fluctuations), to identify longer term trends. The rolling mean is where the mean average of the data from successive years, often three or five, is plotted instead of, or in addition to, the data points.
   Normally, approximately 95% of the data lie within two standard deviations of the mean. When the actual number in the cell exceeds the mean (either quarterly 5-year rolling mean or yearly 5-year rolling mean) by two standard deviations, it "flags". This suggests a statistical anomaly and something worth investigating/having a closer look at.
3. What could be an explanation for the increase in notifications for "flagged" diseases?
   Important: This is relative to the disease and what would be expected for the disease. For example, some jurisdictions report diseases differently (e.g. STEC in SA) or only recently started reporting it (Campylobacteriosis became a notifiable disease in NSW in 2017). There currently may be an outbreak of a certain disease in a jurisdiction or regions causing it to "flag" for example, infectious syphilis notifications attributable to an on-going outbreak occurring in young Aboriginal and Torres Strait Islander people residing in northern and central Australia and continued increases among men who have sex with men (MSM) in urban areas of Victoria and New South Wales. Or there may be a seasonal increase for the particular disease, such as Influenza, signifying the beginning of the season. However, caution should be exercised when interpreting the 5-year rolling means. Changes in surveillance practice, diagnostic techniques and reporting may contribute to increases or decreases in the total notifications received over a five year period.
4. Why do you think the review of notification data is important?
   Data needs to be interpreted within context. After taking all of context information into consideration, "flagged" diseases are sometimes "unflagged" (removed).
   If they remain "flagged", an explanation is included in the CDNA surveillance report stating whether it's an ongoing issue or a new issue of public health importance.

In summary, event-based and indicator-based surveillance are essential components of a national surveillance system that monitors events to determine the potential impact on public health and whether a response is required.

You have now completed the two exercises for the national surveillance of communicable disease for this fortnight – Well done!

Appendix 1:

International Reporting Guideline

Inclusion criteria

Important considerations:

1. Does the event pose a threat to the health of Australians (human only) either in Australia or overseas?
    - The event may be a communicable disease, infectious agent (e.g. prion), or a foodborne contamination.
    - The threat may be real or perceived (e.g. by the public, politicians or the media).

These may include:

1. Communicable disease outbreaks within our region;
2. Communicable disease outbreaks of significance outside our region;
3. Higher than normal incidence of a communicable disease of significance to Australia;
4. An emerging infectious disease; and
5. 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;
3. Issues provided in previous fortnightly reports - unless significant new information is available.

Appendix 2:

International Communicable Disease Surveillance Report

Reporting period: 17 July – 31 July 2017

Cholera – Republic of Yemen[1]

On 24 July 2017, the Ministry of Public Health and Population (MoPHP) of the Republic of Yemen updated the World Health Organization (WHO) on the current cholera outbreak which was first reported in October 2016. Due to the country's ongoing conflict, the Republic of Yemen is in a state of emergency with the health system unable to contain this unprecedented health and environmental disaster. It is attributed to prevalence of risk factors including disruption of public health and Water, Sanitation and Hygiene services amidst increasingly collapsing basic services, displacement, and inadequate sanitation conditions. Less than 45% of health facilities are fully functional and vulnerable populations and affected communities have reduced access to safe water and sanitation. As of 2 July 2017, the outbreak has resulted in a total of 262,650 suspected cases and 1,587 deaths (case fatality rate (CFR): 0.6%) in 21 of the country's 23 governorates. Children under the age of 5 years account for 18% of cases, and those aged over 60 years represent 32% of fatalities (CFR: 2.9%).

Accidental release of wild poliovirus type 2 (WVP2) update, The Netherlands[2]

On the 13 July 2017, the government of the Netherlands updated the WHO on the factory worker who was infected with WVP2 following its accidental release in a vaccine production facility on 3 April 2017. The infected individual stopped excreting the virus on 1 May 2017, 28 days after having been infected. The virus was last detected in the sewage system downstream of the residence of the infected individual on 3 May 2017. No further spread of the virus has been detected.

Measles outbreak update, European Union[3]

Measles outbreaks continue to occur in European Union/European Economic Area countries. Since last reported to CDNA on 3 July 2017, Romania has reported an additional 1,013 measles cases (as of 21 July 2017). Since the beginning of 2017, a total of 38 measles-related deaths have occurred in: Romania (n=32), Italy (n=3), Germany (n=1), Portugal (n=1), and France (n=1)[3].

Seasonal influenza – Asia[4] [5]

Since April 2017, an unexpected increase in seasonal influenza cases has been reported in Asia, with a significant impact in Hong Kong, Macau and Taiwan. Hong Kong and Macau are experiencing an increasing number of severe influenza cases, while Taiwan

is reporting that the influenza activity has peaked and is decreasing gradually. The main circulating influenza virus type is A (H3N2). Between 5 May 2017 and 26 July 2017, enhanced surveillance for severe seasonal influenza cases (i.e. influenza-associated admissions to intensive care unit or deaths) among patients aged 18 or above, has recorded 379 cases including 255 deaths in Hong Kong. In children, 26 cases of severe influenza-associated complications and four deaths have been detected so far in 2017.

Mumps - New Zealand[6]

There is currently a large outbreak of mumps reported in Auckland, New Zealand. Between 1 April 2017 and 30 June 2017, there were 103 mumps notifications in the Auckland region compared to the same period in 2016 where there were no cases reported. As of 5 July 2017, a total of 148 cases have been notified. The majority of these cases were aged 10 to 29 years and around 80% of the current cases were not fully vaccinated (73% did not receive two mumps containing vaccines).

Mumps – Republic of Marshall Islands[7]

A mumps outbreak is ongoing in the Republic of Marshall Islands. As of 10 June, there were 1,033 cases; 82% of the cases are on Majuro, the capital, and cases are spreading to the outer islands. Outbreak vaccination with the Measles Mumps Rubella vaccine began on 17 April 2017, with mass immunisation for all islands affected with mumps.

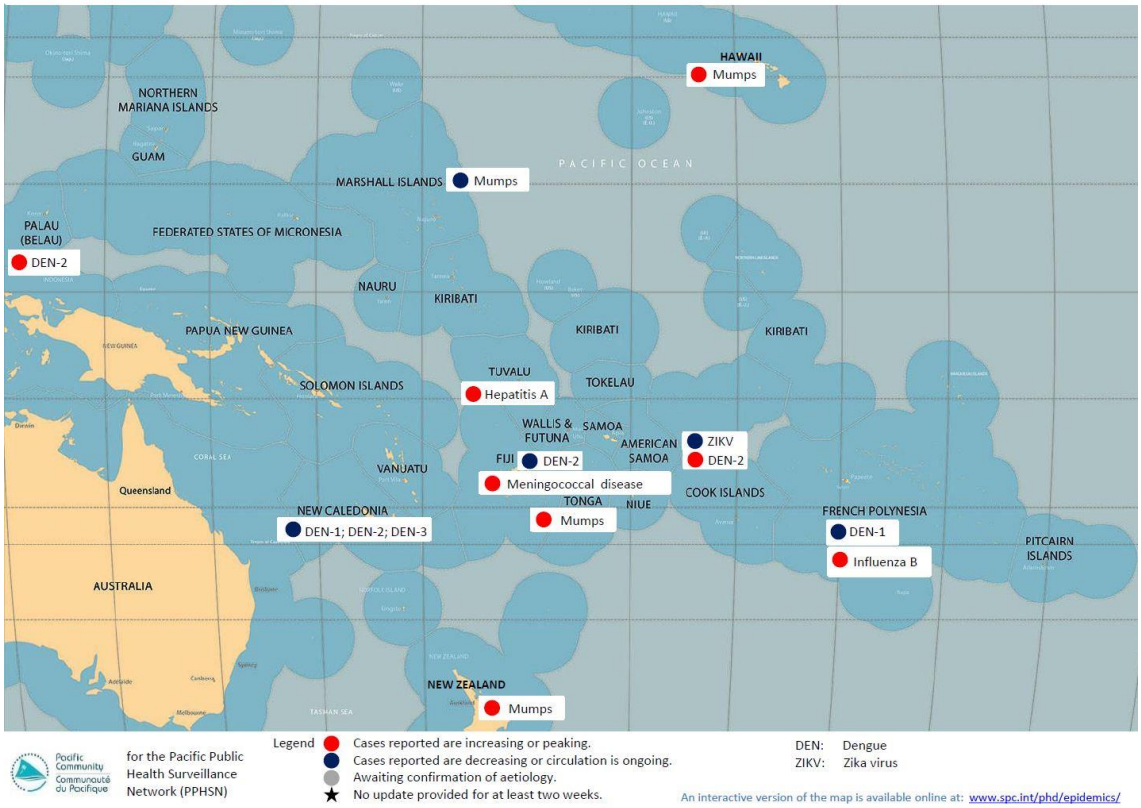
Mumps – Hawaii[8]

The Hawaii State Department of Health continues to investigate an increasing number of cases of mumps infection state-wide. The disease has been confirmed in children and adults, both vaccinated and unvaccinated. As of 27 July 2017, there have been 185 confirmed cases of mumps since the beginning of 2017. Approximately 45% of cases have been in adults aged 18 years and older. To date, none of the infected individuals have required hospitalization for mumps.

Disease alerts in the Pacific[9]

The Pacific Public Health Surveillance Network disease map for the Pacific is shown below. An interactive version is available from http://www.spc.int/phd/epidemics/. Note increasing outbreaks in red.[9]

Epidemic and emerging disease alerts in the Pacific region as of 01 August 2017



This report is designed to provide relevant information on communicable disease outbreaks or incidents occurring overseas with potential relevance or interest to public health in Australia or the region. Updates regarding communicable disease events reported previously will be provided only where there are notable changes.

[1] World Health Organization EIS Update "Cholera - Yemen", 24 July 2017. Available http://apps.who.int/ihr/eventinformation/event/2017-e000187 {accessed 31 July 2017]

[2] World Health Organization. EIS Update "Update on the accidental release of wild poliovirus type 2 in a vaccine production facility in The Netherlands and subsequent infection of an exposed factory worker", 17 July 2017. Available at http://apps.who.int/ihr/eventinformation/event/2017-e000097 [accessed 30 July 2017]

[3] European Centre for Disease Prevention and Control – Epidemiological Update "Epidemiological update: Measles – monitoring European outbreaks, 28 July 2017" Available at https://ecdc.europa.eu/en/news-events/epidemiological-update-measles-monitoring-european-outbreaks-28-july-2017 [Accessed 30 July 2017]

[4] European Centre for Disease Prevention and Control – Publication "Communicable disease threats report, 23 July-29 July, week 30" Available at https://ecdc.europa.eu/sites/portal/files/documents/Communicable-disease-threats-report-29-jul-2017.pdf [accessed 30 July 2017]

[5]Centre for Health Protection, Department of Health, The Government of the Hong Kong Special Administrative Region – Flu Express "Flu Express, Local Situation of Influenza Activity (as of Jul 26, 2017" http://www.chp.gov.hk/files/pdf/fluexpress_web_week29_27_7_2017_eng.pdf [accessed 1 August 2017]

[6] Auckland Regional Public Health Service – Latest News "Disease surveillance for Apr-Jun 2017" Available at http://www.arphs.govt.nz/news/articletype/archiveview/year/2017 {accessed 31 July 2017]

[7]World Health Organization – Western Pacific Region "Pacific syndromic surveillance report, Week 23, ending 11 June 2017. Available at http://www.wpro.who.int/southpacific/programmes/communicable_diseases/disease_surveillance_response/PSS-11-June-2017/en/ [accessed 1 August 2017]

[8]Hawaii State Department of Health– News "Department of Health investigating mumps cases" Available at http://health.hawaii.gov/docd/department-of-health-investigating-mumps-cases/ [accessed 1 August 2017]

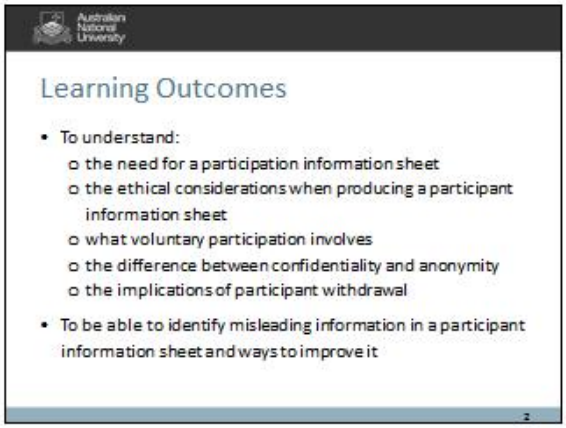
[9] PACNET "Updated map of epidemics in the Pacific as of 1 August 2017"

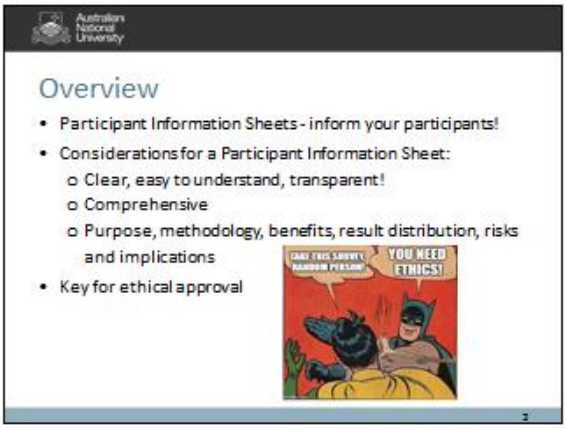
References

1. Australian Government Department of Health. Surveillance systems reported in *Communicable Diseases Intelligence,* 2016. Accessed August 2017. Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-surv_sys.htm
2. WHO Western Pacific Region. A Guide to Establishing Event-Based Surveillance. Manila: World Health Organization, 2008.
3. WHO. Asia Pacific Strategy for Emerging Diseases: 2010. Geneva, Switzerland: World Health Organization, 2011.

Teaching materials for the first-year MAEs

PowerPoint presentation for the first-year MAEs – Ethical considerations in study participation: What you need to know





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

Voluntary Participation & Withdrawal

- Remuneration
- Withdrawal without consequence
- Collecting anonymous information has implications for withdrawal
- Informed consent

Data Storage & Security

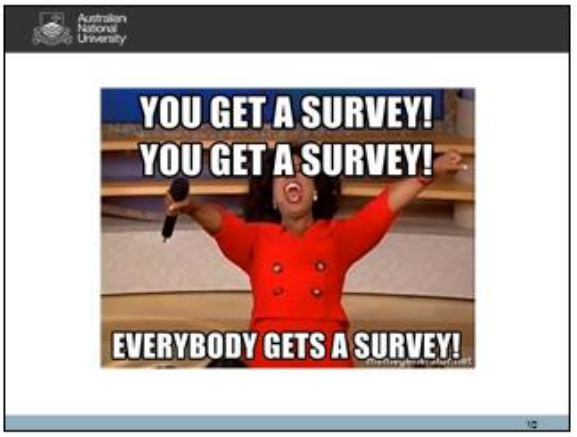
- Where and how
- How long
- Handling of data following the required storage period

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.


Australian National University
Wrap Up
There is more involved with information sheets..
OH YOU THINK YOU KNOW WHAT'S IN A PARTICIPANT INFORMATION SHEET?
TELL ME HOW ETHICS GOES...
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


Australian National University
YOU GET A SURVEY!
YOU GET A SURVEY!
EVERYBODY GETS A SURVEY!

Teaching activity for first-year MAEs: Critique the participant information sheet

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 controlled 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. I intend to interview 10 children with visible facial freckles under the age of 10 years.

Participants: 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 raised money via a golden ticket competition sponsored by Willy Wonka's Chocolate Division.

Participant Involvement:

Voluntary Participation & Withdrawal: *(what is important to explain?)*

_____

_____

_____

_____

_____

_____

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What does participation in the research entail?

You are invited to take part in an interview with the chief investigator, Augustus Gloop, about your chocolate eating habits in 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?)*

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Location and Duration:

Interviews are expected to last approximately 10 minutes, and will be conducted at a place of your choosing – for example, your primary school, at the local supermarket 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, participants will be offered a Willy Wonka chocolate bar.

Risks: *(which 3 points would you mention?)*

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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?)*

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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