Island Dreaming: Applied Epidemiology in the Pacific Region

Dr Meru Sheel

Academic Supervisor: Assoc Prof Martyn Kirk

Field Supervisors: Dr Frank Beard, Dr Aditi Dey, Dr Helen Quinn

November 2017

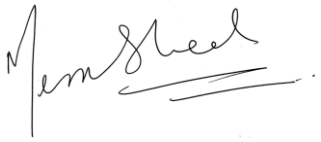
A thesis submitted for the degree of Master of Philosophy in

Applied Epidemiology

The Australian National University

Declaration

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university. To the best of the author's knowledge, it contains no material previously published or written by another person, except where due reference is made in the text.



Meru Sheel

10 November 2017

Acknowledgments

Thank you to everyone who has contributed to my field epidemiology training. I have collaborated and worked with over 30 public health professionals from all around the world, and I am grateful to have learnt something from each one of them.

Sincerest thanks to my academic supervisor, Associate Professor Martyn Kirk, for his leadership, guidance and teachings during the MAE. Martyn, thank you for encouraging me to strive for excellence.

Thank you to my NCIRS field supervisors, Dr Frank Beard, Dr Aditi Dey, Dr Helen Quinn Professor Peter McIntyre, and Associate Professor Kristine Macartney, for your guidance and wisdom. I would like to express my gratitude for your generosity and support that enabled me to undertake two international projects as part of my MAE training. Thank you to Dr Eric Nilles, Dr Colleen Lau, Dr Patricia Graves and Dr Christine Selvey, who directly supervised some components of my MAE.

I am grateful to my mentors Dr Sue Van Leeuwen and Professor Paul Effler, for their mentorship and continuous interest in my professional development. Sue, thanks for guiding me through my leadership journey. Paul, thank you for inspiring me and nurturing my passion for global health!

Thank you to my colleagues at NCIRS, your friendship and support has been invaluable. Working with all of you has been a wonderful and enriching experience. Thank you to my colleagues from the Western Sydney Public Health Unit and Health Protection New South Wales for sharing your knowledge and expertise in public health.

Thank you to the MAE cohort of 2016, for your collegiality and friendship. Particular thanks to Mr Sam McEwen and Ms Alyson Wright for their friendship, endless banter and for shared passion of improving health outcomes for the world's marginalised populations. The MAE would not have been the same without your friendship and camaraderie. I look forward to being inspired by your work in the coming years.

Heartfelt thanks to my family and friends for their constant support and faith in me. Thanks to my brother, Mr Soumya Sheel, for listening to all my crazy stories from the field. I hope you will one day work for "Engineers without Borders", and together we shall change the world! Thank you to my parents for their endless encouragement in all my endeavours.

This research is supported by an Australian Government Research Training Program (RTP) Scholarship.

Abstract

This bound volume describes four significant public health problems in Australia and the Pacific Island Countries of Fiji and American Samoa. The four main epidemiological components are:

1) Australian vaccine preventable disease epidemiological review series: varicella-zoster virus infections, 1998–2015. The review was conducted to assess the impact of the national varicella immunisation program and provide a baseline for monitoring the impact of the national herpes zoster immunisation program. The national varicella immunisation program led to significant reductions in varicella. In Australia, the burden of herpes zoster is substantial, and high quality and timely surveillance will be crucial to assess the impact of the national herpes zoster immunisation program.

2) Investigation into increased lymphogranuloma venereum (LGV) in New South Wales, Australia. LGV is a sexually transmitted infection (STI) caused by L1-L3 serovars of chlamydia, and can lead to irreversible complications. LGV is notifiable condition in New South Wales (NSW). Following a noticeable increase in number of LGV notifications, I conducted a retrospective case series of all cases diagnosed between 1 January 2016 and 31 March 2017. During this period, all reported cases were among men who have sex with men. This chapter examines factors contributing to increase in LGV cases in NSW in 2016. It also describes the challenges associated with investigating STI outbreaks in NSW.

3) An evaluation of an early warning alert and response system (EWARS in a Box) implemented after Cyclone Winston, Fiji 2016. The World Health Organization recommends implementation of early warning systems for timely disease surveillance and early detection of outbreaks during humanitarian emergencies. This chapter describes the EWARS system, and its usefulness at timely monitoring of communicable diseases trends during a national health emergency. Findings include strengths and limitations of the system at conducting surveillance, along with practical recommendations for improving surveillance using EWARS.

4) Identifying residual transmission of lymphatic filariasis in post-mass drug administration surveillance phase: Comparing school-based versus community-based surveys – American Samoa, 2016. This study compares the effectiveness of two cross-sectional survey designs, a school-based and a community-based survey, for assessing transmission of lymphatic filariasis. Under the Global Programme for Elimination of Lymphatic Filariasis, American Samoa conducted seven rounds of mass drug administration (MDA) from

2000-2006. The World Health Organization recommends systematic post-MDA surveillance for epidemiological assessment of recent lymphatic filariasis transmission. Finger prick blood samples were collected from study participants to measure the prevalence of circulating filarial antigen (CFA). I recruited 1143 grade 1 and 2 school students from 29 elementary schools. For the community survey, 30 out of 70 villages were randomly selected, from which 2507 community members were recruited. The school survey was cheaper and logistically easier to implement. The estimated CFA prevalence by school survey was 0.7%, and was significantly lower than the community survey (6.2%). The community survey was more effective for collecting information required for identifying residual transmission of lymphatic filariasis. Both surveys provided evidence of ongoing lymphatic filariasis transmission in American Samoa.

Table of Contents

List of Abbreviations

ABS	Australian Bureau of Statistics
AIHW	Australian Institute of Health and Welfare
ANU	Australian National University
CDC	Centers for Disease Control and Prevention
CFA	Circulating Filarial Antigen
CI	Confidence interval
CIDM	Centre for Infectious Diseases and Microbiology - Public Health
Ct	*Chlamydia trachomatis*
DEC	Diethylcarbamazine
DMO	Divisional Medical Officer
DPS	Division of Pacific Technical Support
EBS	Event-based Surveillance
EWARN	Early Warning Alert and Response Network
EWARS	Early Warning Alert and Response System (EWARS in a Box)
FCCDC	Fiji Centre for Communicable Disease Control
FPC	Finite population correction
FSSS	Fiji Syndromic Surveillance System
FTS	Filariasis Test Strip
GOARN	Global Outbreak Alert and Response Network
GP	General practitioner
GPELF	Global Programme to Eliminate Lymphatic Filariasis
GPS	Geographic Positioning Systems
HIV	Human immunodeficiency virus
HNE	Hunter New England
HZ	Herpes zoster
IBS	Indicator-based Surveillance
ICD-10-AM	International Statistical Classification of Diseases, 10th Revision, Australian Modification
ICT	Immunochromatographic test
IHR	International Health Regulations
IRR	Incidence rate ratio
LF	Lymphatic filariasis
LGV	Lymphogranuloma venereum
LHD	Local Health Districts
MAE	Masters of Philosophy in Applied Epidemiology
MDA	Mass drug administration
Mf	Microfilaria
MoHMS	Ministry of Health and Medical Services in Fiji
MSM	Men who have sex with men
NCIMS	NSW Notifiable Conditions Information Management System
NCIRS	National Centre for Immunisation Research and Surveillance
NDMO	National Disaster Management Office
NIP	National Immunisation Program
NNDSS	National Notifiable Diseases Surveillance System
NSW	New South Wales

PHN	Post-herpetic neuralgia
PHU	Public Health Unit
PrEP	Pre-exposure prophylaxis
PSSS	Pacific Syndromic Surveillance System
PSU	Primary sampling unit
SDMO	Sub-divisional Medical Officer
SEALS	South Eastern Area Laboratory Services
SES PHU	South-East Sydney Public Health Unit
SO	Surveillance officer
STI	Sexually transmissible infections
STIGMA	Sexually Transmissible Infections in Gay Men Action Group
TAS	Transmission Assessment Survey
TFGH	Taskforce for Global Health
The Act	NSW Public Health Act 2010
VZV	Varicella-zoster virus
WHO	World Health Organization
WHO DPS	WHO Division of Pacific Technical Support

Chapter 1

Introduction

Island Dreaming: Applied Epidemiology in the Pacific Region

As the title suggests, this bound volume describes my work and experiences in the Pacific Region while undertaking the Masters of Philosophy in Applied Epidemiology (MAE) program. I use the word *Island* in the context of my work in Australia and other Pacific Island Countries. The word *Dreaming* is adopted from the Aboriginal Dreamtime, in my aspiration to understand the world's public health issues and tell great stories. The MAE has augmented my long-term passion for global health, encouraged me to conduct science that makes a difference and anticipate the *"So what?"*.

My field placement was at the National Centre for Immunisation Research and Surveillance (NCIRS). NCIRS is co-located with the Kids Research Institute and is situated next door to the Children's Hospital at Westmead. NCIRS conducts epidemiological, clinical and social research into vaccine preventable diseases. NCIRS provides technical support to the Australian Technical Advisory Group on Immunisation (ATAGI) and for the Australian Immunisation Handbook. NCIRS's research is aimed at reducing the incidence of vaccine preventable disease and improving vaccine uptake in Australia. At NCIRS, I had the opportunity to interact and learn from experts in the field of immunisation and epidemiology of vaccine preventable diseases. I participated in regular meetings and seminars. I also presented at the Centre's journal clubs and internal seminar series.

At NCIRS, I completed one major project on the epidemiology of varicella (chicken pox) and herpes zoster (shingles) in Australia. I analysed notification, hospitalisation and mortality data for varicella and herpes zoster for the years 1998 to 2015. In 2005, the National Immunisation Program implemented a vaccine to prevent varicella, for children aged 18 months. In 2016, the National Immunisation Program implemented a vaccine for herpes zoster for adults aged 70-79 years. I assessed the impact of the varicella vaccine and provided a baseline for herpes zoster for monitoring the impact of the herpes zoster vaccine. The findings from this work were summarised for publication in the Communicable Diseases Intelligence and are presented in Chapter 2. An additional piece of work was published in the Medical Journal of Australia on the 6th November 2017 (Appendix 2A). The latter compared hospitalisation rates for herpes zoster in Aboriginal and Torres Strait Islander people with other Australians. I reported that Aboriginal and Torres Strait Islander people were hospitalised at almost double the rate at a younger age of 60 years. Considering only a small proportion of Aboriginal and Torres Strait Islander people live beyond the age of 70 years, the data presented in the short report provided evidence for

vaccinating Aboriginal and Torres Strait Islanders at a younger age. These findings were also presented to ATAGI for review of the funding policy for herpes zoster immunisation program.

NCIRS has a close relationship with the Western Sydney Public Health Unit (PHU), which is co-located in the Westmead Complex (Cumberland Hospital). In January 2017, I worked with the infectious diseases team performing everyday public health activities such as follow up of notifiable diseases including typhoid, hepatitis A, invasive meningococcal disease, influenza and other notifiable diseases. The Western Sydney PHU services a densely populated area, with many migrants and visitors from countries where the incidence of infectious disease is high. Therefore, this was a perfect environment to learn about routine public health activities but also about the contribution of imported diseases on New South Wales' public health system. At the Western Sydney PHU, I investigated the Western Sydney measles outbreak in March-April 2017. During the period 1 January 2017 to 20 April 2017, NSW Health reported 23 confirmed cases of measles, of which 17 were locally acquired. All cases were geographically clustered in Western Sydney but epidemiological links could not be established for all the cases. As part of the outbreak investigation, I performed contact tracing of persons who might have been exposed to measles, participated in team meetings and assisted with running of the measles immunisation clinic at the Hillsong Church in Baulkham Hills, New South Wales.

From April-November 2017, I completed a part time placement with the Communicable Diseases Brach of Health Protection New South Wales. I was placed within the Blood Borne Virus and Sexually Transmitted Infections (STI) team with whom I investigated the 2016 lymphogranuloma venereum (LGV) outbreak in New South Wales. All LGV cases were diagnosed in men who have sex with men, residing mostly in metropolitan Sydney. I conducted a retrospective case series of all LGV cases diagnosed between 1 January 2016 and 31 March 2017. This was a challenging experience as I was unaware of the complexities and cultural sensitives of working in the field of STIs. Further, limitations under the New South Wales *Public Health Act 2010* and societal stigma against STIs often limit the scope of public health response. The outcomes and challenges I faced during this outbreak investigation are summarised in Chapter 3

In April-May 2016, I was deployed with the Global Outbreak Alert and Response Network (GOARN) to the World Health Organization's Division of the Pacific Technical Support (WHO DPS), Fiji. I worked as an Early Warning and Alert Response Surveillance (EWARS) epidemiologist within the Emergency Surveillance and Response team of WHO DPS. My primary responsibility was to provide technical support to the Fiji Centre for Communicable Diseases Control (FCCDC) for communicable diseases surveillance after Cyclone Winston. In

addition to undertaking surveillance activities, I evaluated the EWARS system. The surveillance system and the findings of the evaluation are summarised in Chapter 4. During that period, FCCDC reported five deaths in pregnant women at the Colonial War Memorial hospital, the main tertiary hospital in Suva, Fiji. All of the patients were diagnosed with influenza A (H1N1) pdm09 related severe acute respiratory infection. Subsequently, FCCDC initiated an outbreak response and was assisted by the WHO DPS. As part of the response team, I analysed surveillance data from the Fiji Syndromic Surveillance System, virological influenza surveillance (laboratory testing of suspected ILI cases) and intensive care unit register at the Colonial War Memorial hospital. I compiled the data into a brief epidemiological review, which was presented during a high level meeting (via teleconference) convened by the WHO DPS and MoHMS, and was attended by WHO Western Pacific Regional Office, WHO Headquarters Geneva, Centers for Diseases Control and Prevention and Victorian Infectious Diseases Reference Laboratory, to assess the severity of the outbreak. During the outbreak, I coordinated and collated the situational reports at WHO DPS. In response to the outbreak, the Western Pacific Regional Office of the WHO organised an immediate donation of 300 courses of Tamiflu. Targeted immunisation with seasonal influenza vaccine of high-risk individuals including pregnant women, health care workers and the elderly was facilitated by the WHO DPS. I used my experience in immunology and vaccine preventable diseases to provide advice and information on the use of seasonal influenza vaccines. A few weeks later, the FCCDC with assistance from WHO DPS also investigated an increase in paediatric severe acute respiratory infections across Fiji. Findings from this outbreak investigation were compiled for publication in the Western Pacific Surveillance and Response Journal by Ms Julie Collins, fellow MAE from the Hunter New England Population Health Unit. I participated in several other activities such as surveillance meetings at the Fiji Ministry of Health and Medical Services and WHO DPS; assisted with the workshop of 'Training on Humanitarian Response Supply Chain Management' and assisted with training of local surveillance officers.

In September 2016, I travelled to American Samoa where I spent two months collecting data for my epidemiological project. Under the Global Programme for Elimination of Lymphatic Filariasis, American Samoa conducted seven rounds of mass drug administration (MDA) from 2000-2006. The WHO recommends systematic post-MDA surveillance using Transmission Assessment Surveys for epidemiological assessment of recent lymphatic filariasis transmission. My study was designed to compare the effectiveness of two survey designs for post-MDA surveillance: school-based Transmission Assessment Survey targeting children aged 6-7 years, and a community-based survey targeting individuals aged ≥8 years. My field experience and primary study findings are summarised in Chapter 5. During my placement in American Samoa,

I trained local field and laboratory teams, and managed the survey logistics. I was invited to present on the advancements in rheumatic heart disease at the national symposium, and judge the American Samoa's national high school science symposium. In 2017, I have continued to support the high school science symposium remotely from Australia.

During the MAE, I also received scholarships to participate in the Croucher Summer Course 2016 on "Vaccinology for Public health and Clinical Practice in the 21st Century" held in Hong Kong in July 2016; and to attend the GOARN Outbreak Response Training held in Cairns in November 2017. Both were rewarding professional experiences and contributed to my MAE training.

To conclude, the MAE has been a wonderful journey and reminds me of the quote by Ralph Waldo Emerson, "Life is a journey, not a destination". Below are my key take home messages from the MAE:

1. Be culturally sensitive and compassionate, but don't be afraid to push the boundaries.

2. Be resilient – don't let people, politics or other circumstantial challenges prevent you from undertaking the work you have been assigned.

3. Be a 'good' epidemiologist – collect good quality data, record as much information as possible and trust your intuition. Avoid the quick and dirty approach, and apply the academic rigour wherever possible.

4. Be a leader – provide leadership wherever possible. Just because you are not the elected leader does not mean you cannot use your leadership skills.

Summary of MAE program requirements

Field projects

1. **Public health data analysis**

   Australian vaccine preventable disease epidemiological review series: varicella-zoster virus infections, 1998–2015

2. **Field investigation of a public health problem**

Investigation into increased lymphogranuloma venereum amongst men who have sex with men – New South Wales, Australia 2016

3. **Public health surveillance system establishment and evaluation**

   An evaluation of an early warning alert and response system (EWARS in a Box) implemented after Cyclone Winston, Fiji 2016

4. **Epidemiological study**

Identifying residual transmission of lymphatic filariasis in post-mass drug administration surveillance phase: Comparing school-based versus community-based surveys – American Samoa, 2016

Additional non-coursework related requirements

1. **Literature reviews were completed for each field project.**

2. **Lay piece for a non-scientific audience**

   I prepared lay language pieces as part of community awareness activities for the lymphatic filariasis study, which were used for radio advertisements in American Samoa. To raise awareness about lymphatic filariasis and about study, I organised and participated in mass media activities through radio and television. These activities led to a noticeable increase in the recruitment of study participants.

3. **Publications (selected only)**

   Sheel M, Beard F, Dey A, Macartney K, McIntyre P. **"Do higher rates of herpes zoster hospitalisation among Indigenous Australians warrant consideration of vaccination at a younger age?"**. The Medical Journal of Australia. *Accepted 20 February 2017*

   Sheel M, Quinn H, Beard F, Dey A, Kirk M, Koehler A, Markey P, McIntyre P, Macartney K. **"Australian vaccine preventable disease epidemiological review series: varicella-zoster virus infections, 1998–2015"**. The Communicable Diseases Intelligence. *Submitted June 2017*

4. **Oral presentations (selected only)**

Sheel M, Sheridan S, Gass K, Won K, Fuimaono S, Kirk M, Graves P, Lau C. **Eliminating lymphatic filariasis: Comparing school-based Transmission Assessment Survey and a community-based survey, American Samoa, 2016.** Paper presented at the 2017 FETP International Night held during 66th Annual EIS Conference, Atlanta, Georgia, USA in April 2017.

Sheel M, Quinn M, Dey A, Kirk M, Beard F, Macartney K. **Hospitalisations and mortality associated with varicella and herpes zoster, Australia, 1999-2013.** Presented at the Communicable Diseases Control Conference hosted by the Communicable Diseases Network of Australia, Melbourne, Victoria, Australia in June 2017.

Sheel M, Beard F, Dey A, Macartney K, McIntyre P. **Higher zoster hospitalisations in Indigenous Australians: is vaccination at younger age warranted?** Presented at the Communicable Diseases Control Conference hosted by the Communicable Diseases Network of Australia, Melbourne, Victoria, Australia in June 2017.

Sheel M and Collin J. **Post-emergency surveillance in a box: Evaluation of the WHO's early warning and alert response system (EWARS in a Box) following Tropical Cyclone Winston, Fiji 2016.** Presented at the National Centre for Epidemiology and Population Health Seminar Series, Canberra, Australia in August 2017.

5. Teaching to first year MAEs

I coordinated MAE2016 cohort's teaching activities during the course block 3. In collaboration with fellow MAE Ms Alyson Wright (lead facilitator), Mr Samuel McEwen and Ms Mica Hartley, I contributed to the group teaching exercise on '***What's wrong with that?***'. The aim of the session was to develop critical thinking in participants when reviewing results and outcomes of studies. The objectives of the session were:

- To understand the importance of questioning data.
- To identify issues when interpreting data analysis.
- To apply critical thinking techniques/terms to data analysis.

6. Teaching lesson from the field

Conducing cross-sectional surveys in a resource limited setting. This session was taught via video-conference on 11 October 2017. The objectives of the session were:

- To understand the key logistical and ethical considerations when implementing a survey in low resource settings such as American Samoa.

- To estimate sampling and post-stratification weights required to undertake multi-stage cluster survey analyses.

Chapter 2: Public health data analysis

Australian vaccine preventable disease epidemiological review series: varicella-zoster virus infections, 1998–2015

Prologue

My role

One of the primary objectives of the National Centre for Immunisation Research and Surveillance (NCIRS) is to conduct surveillance for vaccine preventable diseases. As a part of their routine surveillance activities, NCIRS undertakes epidemiological reviews for vaccine preventable diseases for the Communicable Diseases Intelligence (CDI), the quarterly publication of the Office Health Protection, Commonwealth Department of Health, Australia.

For my data analysis project, I conducted an epidemiological review of varicella-zoster virus related conditions including varicella (chicken pox) and herpes zoster (shingles) in Australia for the years 1998 to 2015. I was provided with three data sets, notification from the National Notifiable Diseases Surveillance System (NNDSS), hospitalisations from the Australian Institute of Health and Welfare (AIHW) Hospital Morbidity Database and mortality data from the Australian Bureau of Statistics (ABS). I conducted data analyses using Stata13 and Microsoft Excel. With the support of my co-authors, findings from this data analyses were compiled for publication in CDI. The submitted manuscript is included in this chapter.

Lessons learned

This project was the first of four projects that I began working on during the MAE program, and was a steep learning experience. Previous to the MAE, I had no experience of working with administrative datasets containing routinely collected surveillance data. Understanding how the data was collected and working with these databases was a great learning experience and I am grateful to have acquired such a skill. Learning about the nuances of hospitalisation data was one of my most liked (yet hated) learning experiences. For example, 15 years of data was provided as four separate datasets, each of which had different coding for fields such Aboriginal status, date and time formats, age restrictions or checking data completeness for different fields. All of these had to be systematically recoded and appended in Stata. I undertook descriptive and analytical epidemiological review of varicella and herpes zoster for the study. I learnt about analysing count data and the use of different epidemiological tools including negative binomial and Poisson regression models. Traditionally, NCIRS utilises Poisson regression to analyse disease trends but following my experience we had several discussions around the use of different models for analyses of count data. I learnt about the role of epidemiological data analyses in influencing evidence based policy decisions and in identifying key public health messages.

Public health impact

Although this report was prepared for the CDI, findings from this work were timely for several other purposes. The varicella vaccine was funded under the National Immunisation Program for children aged 18 months in 2005. This was the first study to evaluate the population-wide impact of the national immunisation program on the epidemiology of both varicella and herpes zoster. Some of the most significant findings are summarised below.

A vaccine for herpes zoster for people aged 70-79 years was introduced in November 2016. We wanted to conduct a baseline epidemiological review for herpes zoster in order to monitor the impact of the national zoster immunisation program. An ancillary finding from this project was the higher hospitalisation rates of herpes zoster in Aboriginal and Torres Strait Islander people at a younger age (60 years). We undertook this analysis after concerns were raised by our Aboriginal and Torres Strait Islander stakeholders about inappropriately restrictive funding with regard to Aboriginal and Torres Strait Islander populations. The results from this study were accepted for publication in the Medical Journal of Australia (Appendix 2A). The findings were also submitted to the Australian Technical Advisory Group on Immunisation for policy review to fund the zoster vaccine for Aboriginal Australians at a younger age. Data from the epidemiological review were also presented by A/Prof Kristine Macartney to the Joint Committee on Vaccination and Immunisation, United Kingdom as part of their review process for funding of a national varicella immunisation program.

The findings from this work also highlighted the limitations of Australia's current surveillance systems, which may not be suitable for monitoring the changing epidemiology of herpes zoster. In this paper, we advocate for improved herpes zoster surveillance systems in order monitor the impact of the national zoster immunisation program.

I presented this work at the Communicable Diseases Conference hosted by the Communicable Diseases Network of Australia held in Melbourne, Australia in June 2017 and at the New Zealand Immunisation Conference held in Wellington, New Zealand in September 2017.

Acknowledgements

Thank you to all co-authors for providing input in to data analyses, interpretation of results and editing of the manuscript.

Thank you to all NCIRS colleagues who helped and supported while I undertook the analyses. In specific, I would like to thank Ms Han Wang for providing all the datasets and Ms Catherine King for guidance on MeSH terms and MEDLINE searches. Thank you to Ms Stephanie Knox, ex-NCIRS Stata guru for helping with understanding the logic behind writing a Stata code.

Thank you to Associate Professor Kristine for guiding me through the complex world of varicella and herpes zoster. Thank you to Professor Peter McIntyre for encouraging me to undertake herpes zoster analyses in Aboriginal and Torres Strait Islander populations and for asking ‘so what’ at every stage of my MAE.

Thank you to all my NCIRS supervisors, Dr Aditi Dey, Dr Helen Quinn and Dr Frank Beard for your guidance and support with the data analysis. I would also like to acknowledge my academic supervisor A/Prof Martyn Kirk, who patiently answered all my questions. Thank you for teaching me about regression analyses and encouraging me to undertake in-depth analysis just like ‘peeling an onion’.

Australian vaccine preventable disease epidemiological review series: varicella-zoster virus infections, 1998–2015

Meru Sheel[1,2], Helen Quinn[1, 31], Frank Beard[1, 3*], Aditi Dey[1, 3], Martyn Kirk[2], Ann Koehler[4], Peter Markey[5], Peter McIntyre[1,3], Kristine Macartney[1, 3]

[1]National Centre for Immunisation Research and Surveillance, Westmead, New South Wales

[2]National Centre for Epidemiology and Population Health, Australian National University, Acton, Australian Capital Territory

[3]University of Sydney, Sydney, New South Wales

[4]Communicable Disease Control Branch, South Australia Health, South Australia

[5]Centre for Disease Control, Department of Health, Northern Territory

Keywords: varicella zoster virus, varicella, herpes zoster, chickenpox, shingles, epidemiology, disease surveillance, immunisation, vaccine preventable disease

Corresponding author

Dr Meru Sheel

Masters of Philosophy (Applied Epidemiology) Scholar

National Centre for Immunisation Research and Surveillance

Email: Meru.Sheel@health.nsw.gov.au

Phone: 02-98451447

[1] Equal contribution

Author details

Dr Meru Sheel[1,2] – Masters of Philosophy in Applied Epidemiology (MAE) Scholar

Dr Helen Quinn[1,3] – Senior Research Fellow

Dr Frank Beard[1,3] – Staff Specialist, Public Health Physician

Dr Aditi Dey[1,3] – Manager, Surveillance, NCIRS

Associate Prof Martyn Kirk[2] – Convenor, Masters of Philosophy in Applied Epidemiology

Dr Ann Koehler[4] - Director

Dr Peter Markey[5] – Head, Disease Surveillance

Prof Peter McIntyre[1,3] – Director, NCIRS

Associate Prof Kristine Macartney[1,3] – Deputy Director, NCIRS

Abstract

Introduction: In 2005, the National Immunisation Program implemented a varicella vaccine for children aged 18 months, and in 2016, a herpes zoster (HZ) vaccine for adults aged 70-79 years. This epidemiological review analyses national trends in varicella and HZ for the years 1998-2015 to examine the impact of a funded varicella vaccine and provide a baseline for monitoring the impact of a funded HZ vaccine.

Methods: Varicella and HZ notifications (2002-2015), hospitalisations (1999-2013) and deaths (1998-2013) were sourced. We stratified analyses by age, sex and Indigenous status, and estimated rates and incidence rate ratios.

Results: Funded varicella vaccine led to a rapid decline in varicella notifications, hospitalisations and deaths. During the post-varicella vaccine period, hospitalisations declined in all age groups <40 years, with greatest reduction of 84% in children aged 18-59 months. Annual HZ hospitalisation rate was 10.8 per 100,000. HZ hospitalisation rates increased with age and were highest in persons aged ≥75 years (87.6 per 100,000). Post-herpetic neuralgia (PHN) was diagnosed in 32.5% HZ hospitalisations with highest hospitalisation rate in persons aged ≥75 years (32.1 per 100,000). Varicella and HZ hospitalisation rates were significantly higher among Indigenous Australians. Twenty one deaths were coded as due to varicella and 340 deaths were coded as due to HZ in persons aged <40 years and ≥40 years, respectively.

Conclusions: The national varicella immunisation program substantially reduced varicella associated morbidity and mortality. Burden of HZ and PHN is substantial, and timely and high quality surveillance will be crucial to assess the impact of the national HZ immunisation program.

Introduction

Varicella-zoster virus (VZV) is a herpes virus and is the aetiological agent for varicella (chickenpox) and herpes zoster (shingles).[1] Varicella is an acute and self-limiting disease with an average incubation period of 14-16 days (range from 10 to 21 days). The disease is highly contagious with a secondary attack rate of 90% in susceptible contacts of persons with varicella.[1, 2] Varicella typically presents as a vesicular rash accompanied by fever and malaise but can occasionally be asymptomatic or have atypical presentations. Complications include secondary skin infections, pneumonia, meningitis and encephalitis. Primary infection with VZV usually provides long lasting immunity and further episodes of clinical disease are rare in immunocompetent individuals.[2, 3]

VZV remains dormant for years in the dorsal root ganglia adjacent to the spinal cord: reactivation of the latent virus can lead to herpes zoster (HZ). Characteristics of HZ include a vesicular rash with a unilateral dermatomal distribution which is usually accompanied with acute pain. Post-herpetic neuralgia (PHN) is the most common complication of HZ, and is defined as pain persisting 90 days or more from the onset of the rash. PHN is often debilitating and refractory to treatment.[4-6]

In Australia, varicella vaccine was registered for use in 1999 and included on the National Immunisation Program (NIP) in November 2005 as a single dose at 18 months of age, along with a school-based single cohort catch-up program for 12-13 year olds.[7, 8] Uptake of varicella vaccine assessed at 2 years of age was 76.1% in 2007, and increased to 84.4% in 2012.[7, 9, 10] In July 2013, a combination vaccine (measles-mumps-rubella-varicella or MMRV) replaced the monovalent varicella vaccine at age 18 months; following which vaccine uptake increased to 89.6% in 2014.[11] A vaccine for HZ was registered in Australia in 2005, but was not widely available on private prescription or added onto the NIP until November 2016.[12] Although the vaccine is registered for use in people aged ≥50 years, it is funded on the NIP for people aged 70 years with a 5 year catch-up program for people aged 71-79 years.[12]

Early assessment of the impact of inclusion of varicella vaccine on the NIP demonstrated a decline in hospitalisations due to varicella, especially in children less than 4 years of age, along with a reduction in severe outcomes of varicella, including congenital and neonatal varicella.[9, 13, 14] Several studies have documented increasing incidence of HZ in Australia, both before and after the introduction of the varicella vaccine.[15, 16] Age-related increases in the risk of HZ are associated with a decline in cellular immunity to VZV, however, the underlying cause of the rising incidence (even after age adjustment) remains unclear.[16]

This study aims to review the epidemiology of varicella and HZ in Australia from 1998 to 2015, assess the impact of the national varicella immunisation program and provide a baseline for monitoring the impact of the national HZ immunisation program.

Methods

Data sources

Notification data

The National Notifiable Diseases Surveillance System (NNDSS) receives varicella and HZ notifications from all Australian states and territories (jurisdictions) except New South Wales (Table 1). Varicella and HZ became notifiable as early as 2002 in South Australia and as late as 2009 in Victoria.

Table 1: Proportions (varicella, herpes zoster or not elsewhere classified) of total varicella zoster virus (VZV) related conditions reported through the National Notifiable Diseases Surveillance System (NNDSS), by state or territory, Australia 2002-2015.

Jurisdiction (state or territory)	Year notification commenced	Notified by laboratory	Follow-up laboratory notification	VZV-related conditions (percentage of total notifications)		
				Varicella	Herpes zoster	Not elsewhere classified
New South Wales	N/A	N/A	N/A	N/A	N/A	N/A
Victoria	2009	Yes	No	13.2	19.8	66.9
Queensland	2006	Yes	No	7.1	3.8	89.1
South Australia	**2002**	**Yes**	**Yes**	**24.1**	**66.3**	**9.7**
Western Australia	2006	Yes	No	17.1	38.9	44
Tasmania	2006	Yes	No	11.4	63.8	24.8
Northern Territory	**2006**	**Yes**	**Yes**	**41.9**	**56.4**	**1.8**
Australian Capital Territory	2006	Yes	No	12.7	26.5	60.7
National	2006	-	-	14.1	26.3	59.6

National case definitions exist for varicella-zoster infection (chickenpox), varicella-zoster infection (shingles) and varicella-zoster infection (not elsewhere classified).[17] For chicken pox and shingles, both confirmed and probable cases are required to be notified. Confirmed cases of shingles (HZ) and chickenpox (varicella) require laboratory definitive evidence and clinical evidence. Laboratory confirmation requires detection of VZV from a skin or lesion swab, or VZV-specific IgM in an unvaccinated person (for varicella). In case of varicella, a case is considered confirmed if clinical and epidemiological evidence of disease is available. For

probable cases of chicken pox and shingles, clinical evidence of disease is sufficient. Varicella-zoster infection (not elsewhere classified) requires only laboratory confirmed definitive evidence of VZV. [17]

Notification data for the years 2006 to 2015 were sourced from the NNDSS database. South Australian notification data for the years 2002 to 2004 were sourced from the South Australian Department for Health and Ageing. Analysis of notification data was restricted to South Australia and Northern Territory, as these are the only jurisdictions that routinely follow up laboratory notifications of VZV infection for clinical and/ or epidemiological evidence and had a low proportion of 'not elsewhere classified' notifications (Table 1).

Hospitalisation data

We obtained national data from the Australian Institute of Health and Welfare (AIHW) National Hospital Morbidity Database. All hospital admissions (public and private) in Australia are captured through this administrative database which collects demographic and clinical details. All eligible hospitalisations between 1 January 1999 and 31 December 2013 were identified using the International Statistical Classification of Diseases, 10th Revision, Australian Modification (ICD-10-AM) codes B01.0-B01.9 (varicella or its complications), B02.0-B02.9 (HZ or its complications), where listed as the principal or other diagnosis. Cases of PHN were identified using ICD-10-AM codes B02.2 (PHN), G53.0 (PHN under cranial nerve disorders) and G53.1 (multiple cranial nerve palsies in infectious and parasitic diseases classified elsewhere).

Mortality data

Mortality data were obtained from the AIHW's National Mortality Database (1998-2005) and the Australian Coordinating Registry (2006-2013). We restricted analysis to underlying cause of death (UCOD), which was identified using ICD-10-AM codes B01.0-B01.9 (varicella) and B02.0-B02.9 (herpes zoster). Age-specific analyses were limited due to the small cell size rule applied by the data custodians. In addition, the positive predictive value for varicella coded deaths is known to be poor and due to issues of misclassification of HZ and varicella,[18] we restricted analyses to persons aged <40 and ≥40 years for varicella and HZ associated deaths, respectively.

Population estimates

National, jurisdictional and age-specific mid-year resident population estimates were obtained from the Australian Bureau of Statistics (ABS).

Data analysis

Annual crude and age-specific rates were calculated using ABS mid-year population estimates as the denominator and are expressed as rates per 100,000 total population or population in sex, geographical or Aboriginal and Torres Strait Islander (from here on referred to as Indigenous) subgroups as appropriate. Reported rates refer to hospitalisations where the relevant condition was coded as the principal diagnosis, unless otherwise stated.

We calculated varicella and HZ notification and hospitalisation rates for the period 1999 to 2015. To assess changes in disease epidemiology following introduction of the national varicella immunisation program, we undertook comparative analyses over two time periods: pre-vaccine (1999-2004) and post-vaccine (2007-2015). Analysis of HZ hospitalisation rates for older age groups was restricted to non-Indigenous populations as age-specific counts for Indigenous persons were unavailable for persons aged ≥75 years for the latter years of the study period.

Summary statistics including median and range were calculated for length of hospital stay. *P*-values were derived using the Wilcoxon-Mann-Whitney test. Incidence rates and 95% confidence intervals (CI) were calculated for the total population, non-Indigenous and Indigenous populations at the national level and relevant jurisdictional groupings, as indicated, assuming a negative binomial distribution. Negative binomial regression was used to analyse yearly trends in rates of hospitalisation and calculate the incidence rate ratios (IRR). All analyses were conducted using Microsoft Excel 2010 and STATA software (version 13.1; StataCorp, College Station, Texas USA).

Indigenous hospitalisation data

We restricted analyses to the four jurisdictions (Queensland, Western Australia, South Australia and Northern Territory) with adequate Indigenous data quality prior to 2007,[19] with supplementary analyses incorporating data from New South Wales and Victoria for the years 2007 to 2013. Hospitalisations with missing information on state of residence (<1% of total) were excluded.

Ethics approval was not required as de-identified aggregated population-based data were used for routine public health surveillance purposes only.

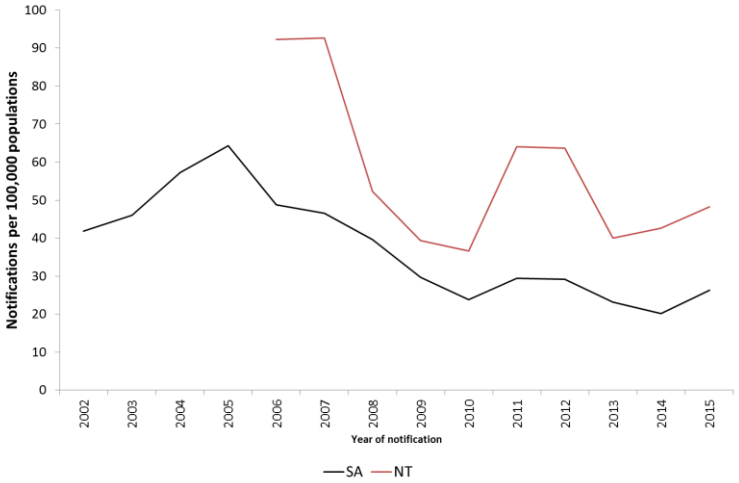
Results

Notifications of varicella and herpes zoster

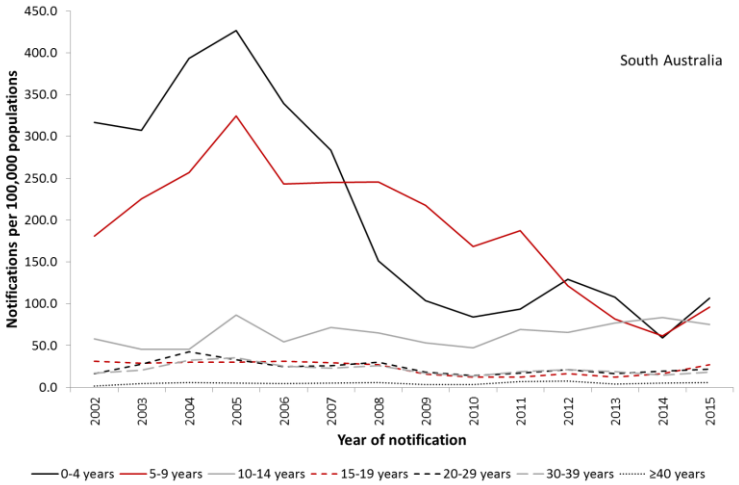
Varicella

Varicella notification rates in South Australia declined from 41.8 per 100,000 (95% CI 38.6–45.2) in 2002 to 26.3 per 100,000 (95% CI 23.4–28.9) in 2015 (Figure 1A). Varicella notification rates in the Northern Territory reduced from 92.3 per 100,000 (95% CI 79.8–106.3) in 2006 to 48.2 per 100,000 (95% CI 39.4–57.8) in 2015.

(A)



(B)



(C)

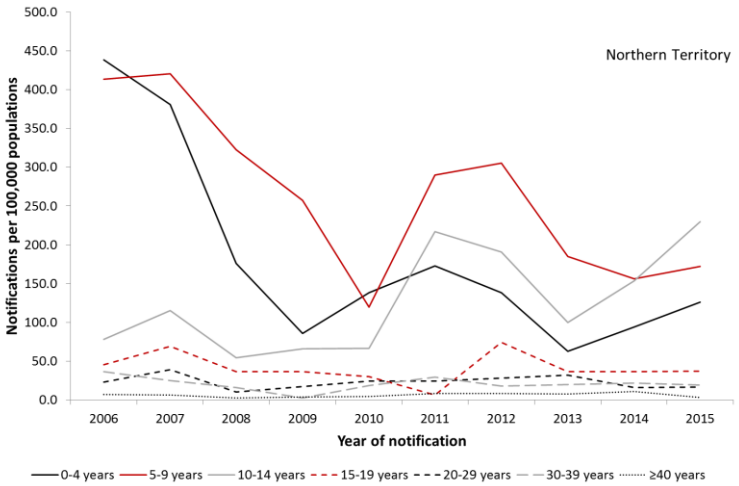


Figure 1: Notification rates for varicella by jurisdiction [South Australia (SA) and Northern Territory (NT)] (A) and age group (B and C), 2002- 2015

Declines in age-specific varicella notification rates were observed in both South Australia and the Northern Territory (Figures 1B and 1C). In South Australia, varicella notification rates in persons aged 0-4 years reduced by 63% during the post-vaccine (2007-2015) period (IRR 0.37; 95% CI 0.23-0.59). Reduced varicella notification rates were also observed in other age groups <40 years during the post-vaccine period (data not shown).

Herpes zoster

In contrast to varicella, HZ notification rates increased over time in both South Australia and in the Northern Territory (Figure 2A). In South Australia, HZ notification rates increased steadily from 23.1 per 100,000 (95% CI 20.7–25.6) in 2002 to 136.9 per 100,000 (95% CI 131.4–142.6) in 2015. In the Northern Territory, HZ notification rates increased from 38.2 per 100,000 (95%CI 30.3–47.6) in 2006 to 148.4 per 100,000 (95% CI 133.5–164.5) in 2015. Similar trends were also observed in age-specific rates with the highest incidence in persons aged ≥70 years, both in South Australia and the Northern Territory (Figures 2B and 2C). Fluctuations in notification rates in the Northern Territory are likely to be associated with its small population size, especially in older age groups.

Varicella and herpes zoster associated hospitalisations

Varicella

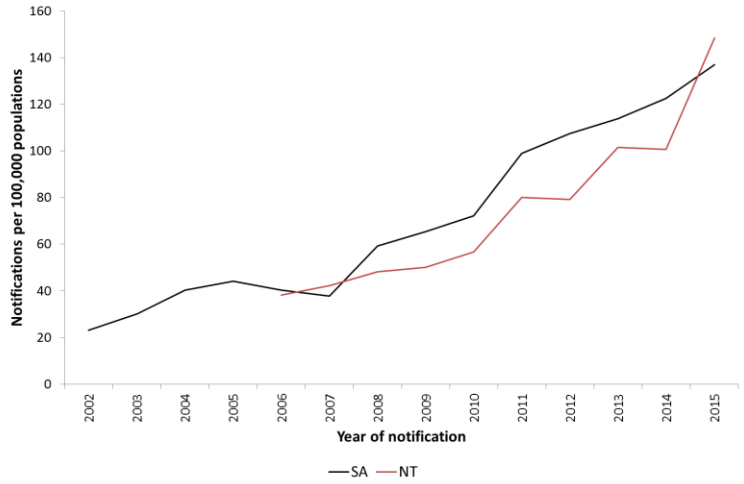
There were 18,615 episodes of varicella associated hospitalisation between January 1999 and December 2013, of which 12,824 (68.9%) had a principal diagnosis of varicella. The annual varicella hospitalisation rate reduced from 6.9 per 100,000 (95% CI 6.3–7.1) in 1999 to 2.1 per 100,000 (95% CI 1.9–2.3) in 2013.

The average annual hospitalisation rate for the period 1999-2013 was 4.2 per 100,000 (95% CI 3.4–5.3). Hospitalisation rates were similar in females (3.3 per 100,000; 95% CI 2.6-4.1) and males (4.5 per 100,000; 95% CI 3.5–5.6). There was a rapid decline in hospitalisation rates after the varicella vaccine was added onto the NIP in 2005 (Figure 3A). Hospitalisation rates were 41% lower in 2007 compared to 2005 (IRR 0.59; 95% CI 0.53–0.65).

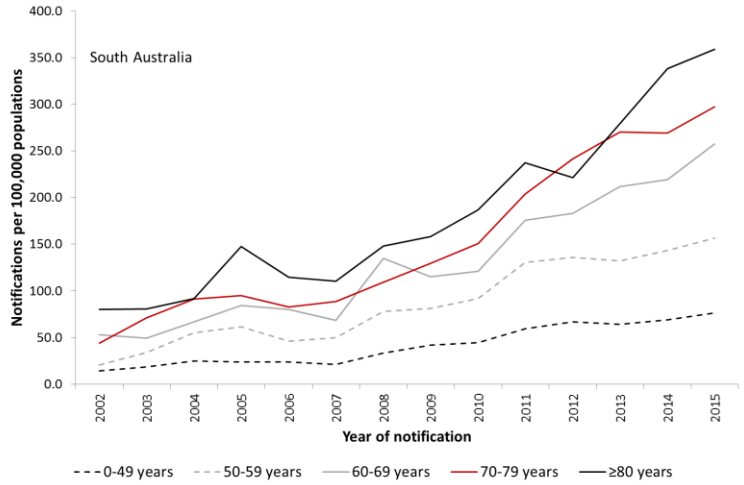
Age-specific trends in hospitalisation rates are presented in Figure 3B. During 1999-2013, hospitalisation rates were highest in children aged ≤17 months (30.3 per 100,000; 95% CI 23.0–40.0) and lowest in adults aged ≥40 years (1.5 per 100,000; 95% CI 1.4–1.6).

There were significant reductions in hospitalisation rates for all age groups <40 years during the post-vaccine period (2007-2013) compared to the pre-vaccine period (1999-2004) (Table 2). The largest decreases were seen in children aged 18-59 months (IRR 0.16; 95% CI 0.12–0.23), and in those aged ≤17 months (IRR 0.33; 95% CI 0.26–0.40). Despite the rapid decline during the first

(A)



(B)



(C)

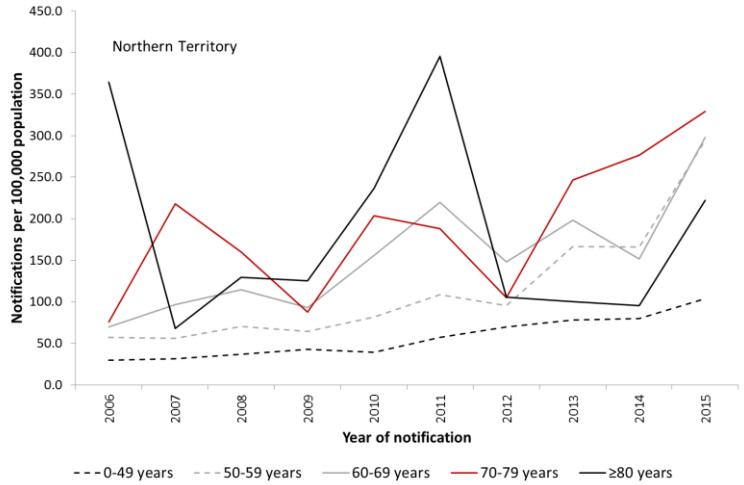
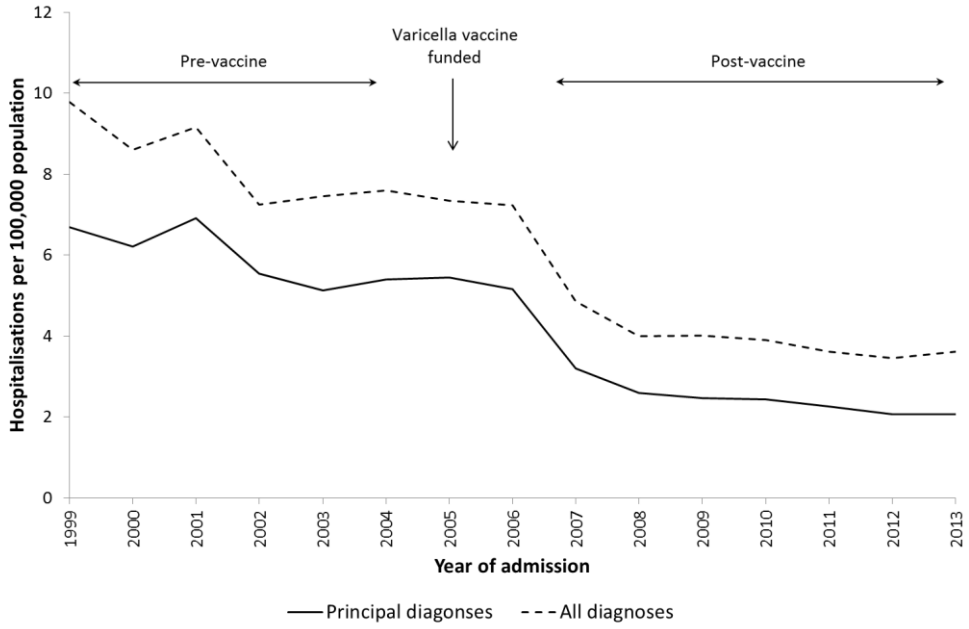


Figure 2: Notification rates for herpes zoster, by jurisdiction [South Australia (SA) and Northern Territory (NT)] (A) and age group (B and C), 2002- 2015

(A)



(B)

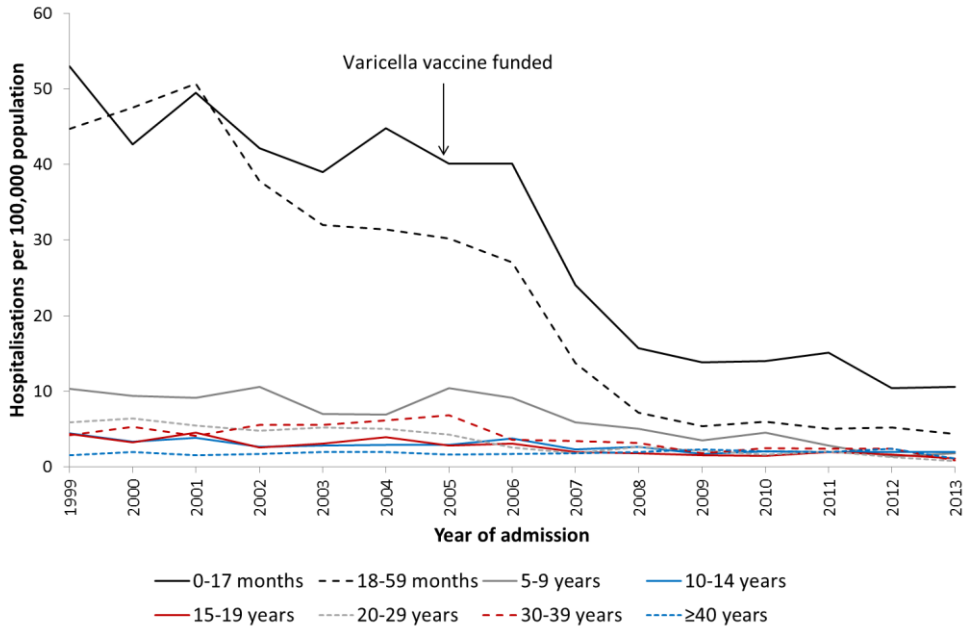


Figure 3: Varicella hospitalisation (principal diagnosis) rates (A) and by age group (B), Australia, 1999-2013

Table 2 Varicella associated hospitalisations, Australia, 1999-2013[2]

	Pre-varicella vaccine 1999-2004		Post-varicella vaccine 2007-2013		
Age group	**Hospitalisations (n)**	**Rate[3] (95% CI)**	**Hospitalisations (n)**	**Rate[‡] (95% CI)**	**IRR[4] (95% CI)**
Principal varicella in all Australians					
0-17 months	1020	45.2 (41.6-49.1)	454	14.8 (12.1-18.1)	0.33 (0.26-0.40)
18-59 months	2188	40.7 (35.1-47.2)	458	6.7 (5.0-8.9)	0.16 (0.12-0.23)
5-9 years	713	8.9 (7.82-10.2)	338	3.6 (2.5-5.0)	0.40 (0.27-0.58)
10-14 years	269	3.3 (2.9-3.9)	202	2.1 (1.8-2.4)	0.63 (0.52-0.76)
15-19 years	291	3.6 (3.1-4.2)	165	1.6 (1.4-1.9)	0.45 (0.36-0.56)
20-29 years	913	5.6 (5.2-6.1)	432	2.0 (1.6-2.3)	0.35 (0.29-0.41)
30-39 years	850	4.8 (4.4-5.3)	584	2.7 (2.3-3.2)	0.56 (0.46-0.68)
≥40 years	690	1.4 (1.3-1.5)	1105	1.6 (1.4-1.7)	1.15 (1.01-1.30)
All ages	6934	6.0 (5.5-6.5)	3738	2.4 (2.2-2.7)	0.41 (0.35-0.47)
All varicella in all Australians					
0-17 months	1421	62.9 (56.8-69.7)	592	19.3 (15.4-24.2)	0.31 (0.24-0.39)
18-59 months	2455	45.6 (40.1-52.0)	529	7.7 (5.5-10.1)	0.17 (0.12-0.25)
5-9 years	1129	14.1 (12.5-15.9)	525	5.5 (4.0-7.6)	0.39 (0.27-0.56)
10-14 years	420	5.2 (4.6-5.8)	302	3.1 (2.8-3.9)	0.60 (0.52-0.69)
15-19 years	409	5.1 (4.2-6.1)	228	2.2 (1.9-2.6)	0.44 (0.35-0.56)
20-29 years	1366	8.4 (7.6-9.3)	648	2.9 (2.4-3.5)	0.35 (0.28-0.43)
30-39 years	1205	6.8 (6.3-7.4)	821	3.8 (3.4-4.3)	0.55 (0.48-0.64)
≥40 years	1236	2.4 (2.3-2.6)	2369	3.4 (3.0-3.8)	1.37 (1.18-1.59)
All ages	9641	8.3 (7.6-9.1)	6014	3.9 (3.6-4.2)	0.47 (0.42-0.53)

[2] Age-specific hospitalisations identified using ICD-10-AM code B01.0-B01.9
[3] Average annual hospitalisation rate per 100,000 population
[4] Incidence rate ratio between hospitalisation rates during pre and post-varicella vaccine periods

five years after varicella vaccine was introduced under the NIP, limited additional decline in hospitalisation rates was observed in more recent years (Figure 3A and 3B). Similar findings were observed on analyses of hospitalisations where varicella was recorded in any diagnosis field (Table 2). Trends in hospitalisation rates by jurisdiction were broadly similar (Figure 4).

Between 1999 and 2013, there were 47,477 bed days recorded for hospitalisations coded as due to varicella. The overall median length of stay was 2 days with length of stay longest in those aged ≥40 years (5 days).

Herpes zoster

There were 80,960 episodes of HZ associated hospitalisations during 1999-2013. Of these, 33,549 (41.4%) episodes had a principal diagnosis of HZ. Over this period, the average annual HZ associated hospitalisation rate was 10.8 per 100,000 (95% CI 10.5–11.1). The HZ hospitalisation rate increased from 9.7 per 100,000 (95%CI 9.2–10.1) in 1999 to 11.4 per 100,000 (95% CI 11.0–11.9) in 2013 (Figure 5A), an average annual increase of 1% (IRR 1.01; 95% CI 1.01-1.02). Over this period, the HZ hospitalisation rate for females (30.0 per 100,000; 95% CI 28.7–31.3) was higher than for males (21.8 per 100,000; 95% CI 20.7–22.9). The difference was most pronounced in females ≥75 years with a hospitalisation rate of 95.1 per 100,000 (95% CI 92.6–97.6) compared to males (76.4 per 100,000; 95% CI 73.6–79.2).

HZ hospitalisation rates increased with age (Figure 5B). Hospitalisation rates were highest in persons aged ≥75 years (87.6 per 100,000; 95% CI 85.9–89.4), followed by those aged 70-74 years (37.4 per 100,000; 95% CI 35.8–39.0) and lowest in those aged 0-49 years (2.4 per 100,000; 95% CI 2.3–2.4). Amongst non-Indigenous populations, for whom data were available for older age groups (Figure 5C), people aged ≥85 years old had the highest hospitalisation rate of 129.0 per 100,000 (95% CI 124.3–134.0) (Table 3).

When we compared hospitalisation rates during the post-varicella vaccine period (2007-2013) to the pre-varicella vaccine period (1999-2004) in non-Indigenous people, the IRR was 1.08 (95% CI 1.03–1.13) for all ages, 0.94 (95% CI 0.88–1.02) for those aged 70-74 years, and 0.89 (95% CI 0.84–0.95) for those aged 75-79 years (Table 3).

Post-herpetic neuralgia (PHN)

Almost a third (32.5%) of all hospitalisations (principal) coded as HZ also had a diagnosis of PHN recorded in the diagnostic field (within the first 30 diagnostic fields). The overall rate of PHN hospitalisations remained stable (Figure 6A) for the years 1999-2013 (IRR 1.00; 95% CI 0.99-1.01), with the highest rate in those aged ≥75 years (32.1 per 100,000) followed by people aged 70-74 years (14.1 per 100,000). PHN-associated hospitalisations increased

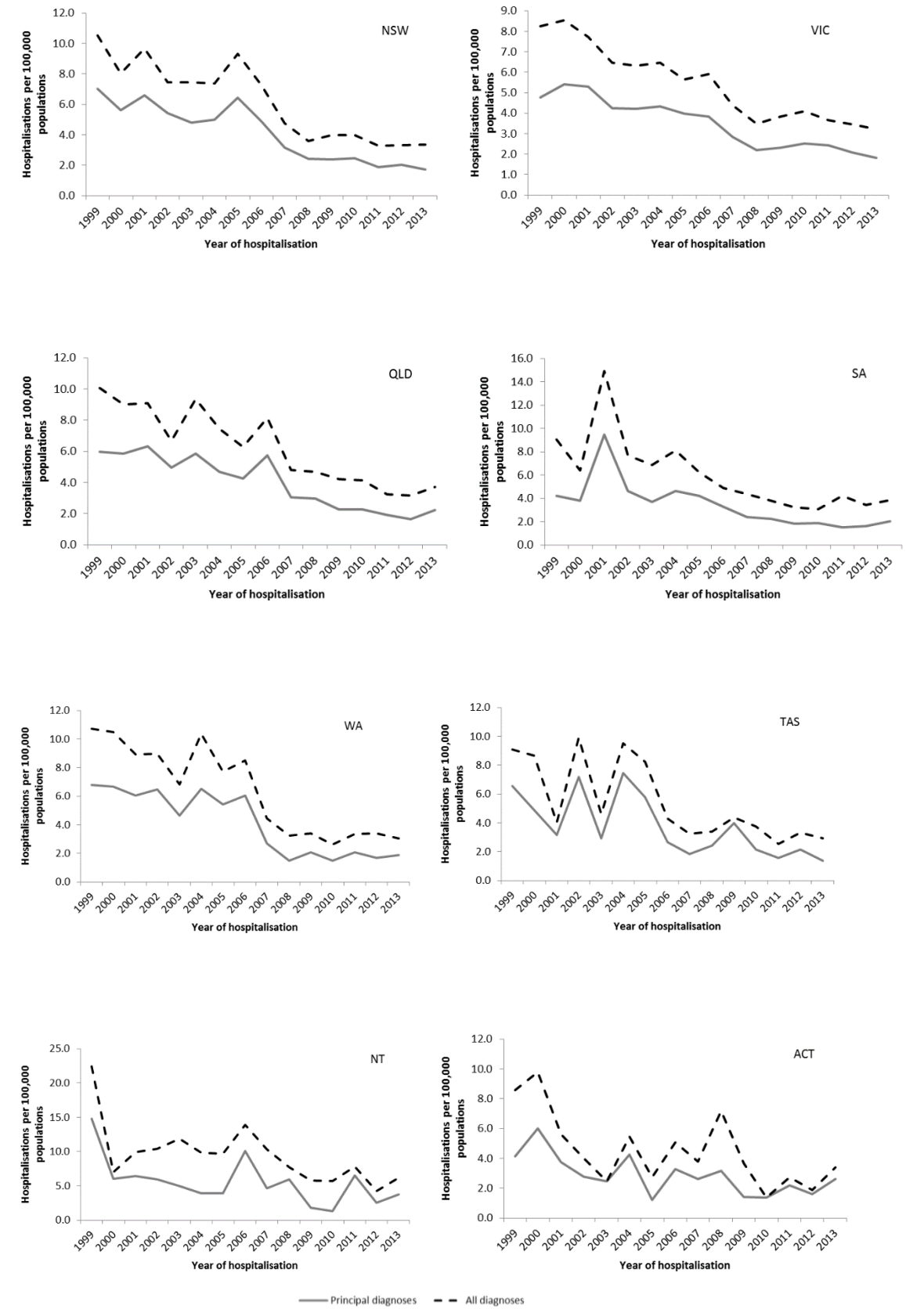


Figure 4: Varicella hospitalisation rates, by state or territory, Australia, 1999-2013

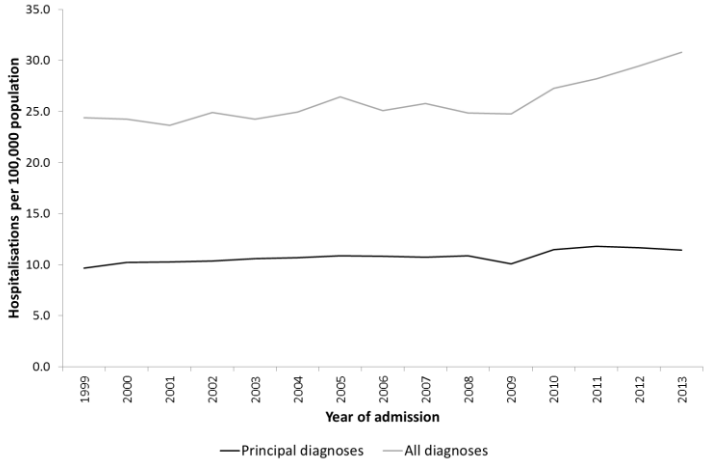
Table 3: Herpes zoster associated hospitalisations, Australia, 1999-2013[5]

	Study period 1999-2013		Pre-varicella vaccine 1999-2004		Post-varicella vaccine 2007-2013		
Age groups	**Hospitalisations (n)**	**Rate[6] (95% CI)**	**Hospitalisations (n)**	**Rate[††] (95% CI)**	**Hospitalisations (n)**	**Rate[††] (95% CI)**	**IRR[7] (95% CI)**
Principal herpes zoster in all Australians							
0-49 years	5103	2.4 (2.3-2.4)	1982	2.4 (2.3-2.6)	2458	2.3 (2.2-2.4)	0.97 (0.91-1.04)
50-59 years	3115	8.1 (7.7-8.5)	1084	7.8 (7.3-8.4)	1619	8.3 (7.7-9.0)	1.07 (0.96-1.20)
60-69 years	5079	18.6 (18.0-19.3)	1620	17.7 (16.7-18.9)	2828	19.3 (18.5-20.0)	1.09 (1.02-1.16)
70-74 years	3720	37.4 (35.8-39.0)	1438	38.2 (36.8-39.6)	1780	35.9 (33.4-38.6)	0.94 (0.86-1.02)
≥75 years	16532	87.6 (85.9-89.4)	5846	87.1 (84.9-89.4)	8492	87.9 (84.8-91.2)	1.01 (0.96-1.06)
All ages	33549	10.8 (10.5-11.1)	11970	10.3 (10.0-10.6)	17177	11.1 (10.7-11.6)	1.08 (1.03-1.14)
All herpes zoster in all Australians							
0-49 years	10009	4.6 (4.5-4.8)	3907	4.7 (4.6-4.9)	4771	4.5 (4.3-4.8)	0.96 (0.89-1.03)
50-59 years	6898	17.9 (17.2-18.6)	2463	17.7 (17.0-18.4)	3490	17.9 (16.7-19.3)	1.01 (0.93-1.10)
60-69 years	11852	43.2 (41.4-45.0)	3724	40.8 (38.7-43.0)	6656	45.3 (42.8-47.8)	1.11 (1.03-1.20)
70-74 years	9002	90.2 (86.3-94.3)	3478	92.4 (89.4-95.5)	4428	88.9 (81.6-96.9)	0.96 (0.87-1.06)
≥75 years	43199	228.1 (221.9-234.5)	14796	220.4 (216.9-224.0)	22788	235.5 (225.4-246.2)	1.07 (1.01-1.12)
All ages	80960	25.9 (25.0-27.0)	28368	24.4 (23.0-24.8)	42133	27.3 (25.8-28.9)	1.12 (1.05-1.19)
Principal herpes zoster in non-Indigenous Australians[8]							
70-74 years	3689	37.4 (35.8-39.0)	1427	38.2 (36.3-40.2)	1763	35.8 (33.3-38.6)	0.94 (0.88-1.02)
75-79 years	4787	59.4 (57.4-61.6)	1938	62.7 (60.0-65.6)	2181	56.1 (53.8-58.5)	0.89 (0.84-0.95)
80-84 years	5349	92.0 (89.0-95.1)	1886	94.0 (88.8-99.5)	2746	90.9 (86.6-95.4)	0.97 (0.90-1.04)
≥85 years	6340	129.0 (124.3-134.0)	2011	126.5 (118.5-135.1)	3528	130.8 (123.7-138.3)	1.03 (0.95-1.13)
All ages	33007	10.9 (10.6-11.2)	11805	10.4 (10.2-10.7)	16867	11.3 (10.9-11.7)	1.08 (1.03-1.13)
All herpes zoster in non-Indigenous Australians[§§]							

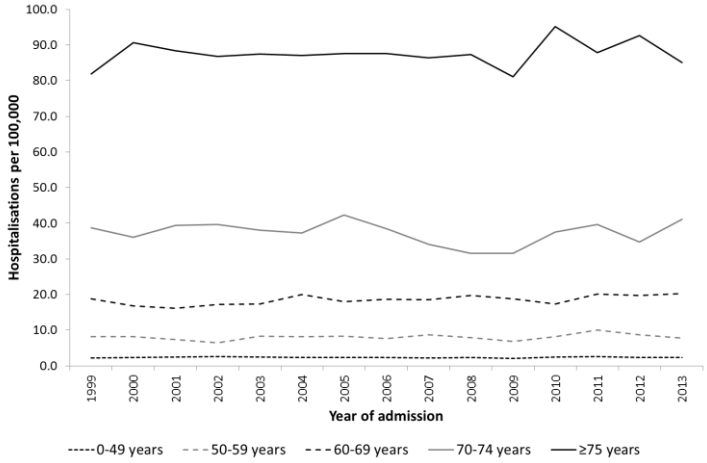
[5] Age-specific hospitalisations identified using ICD-10-AM code B02.0-02.9
[6] Average annual hospitalisation rate per 100,000 population
[7] Incidence rate ratio between hospitalisation rates during pre and post-varicella vaccine periods
[8] Hospitalisations for Indigenous Australians were excluded.

	Study period 1999-2013		Pre-varicella vaccine 1999-2004		Post-varicella vaccine 2007-2013		
Age groups	**Hospitalisations (n)**	**Rate[6] (95% CI)**	**Hospitalisations (n)**	**Rate[††] (95% CI)**	**Hospitalisations (n)**	**Rate[††] (95% CI)**	**IRR[7] (95% CI)**
70-74 years	8931	90.2 (86.2-94.4)	3457	92.5 (89.5-95.7)	4386	88.9 (81.3-97.0)	0.96 (0.87-1.06)
75-79 years	12145	150.8 (146.3-155.3)	4808	155.7 (148.7-163.0)	5729	147.3 (142.0-152.9)	0.95 (0.89-1.00)
80-84 years	13759	236.4 (228.0-245.1)	4636	231.7 (220.0-243.9)	7204	238.3 (224.7-252.6)	1.03 (0.95-1.11)
≥85 years	17184	348.2 (338.1-358.6)	5330	335.8 (325.5-346.4)	9779	361.5 (347.8-375.7)	1.08 (1.02-1.14)
All ages	79874	26.4 (25.4-27.4)	28069	24.8 (24.5-25.2)	41487	27.7 (26.1-29.4)	1.12 (1.05-1.19)

(A)



(B)



(C)

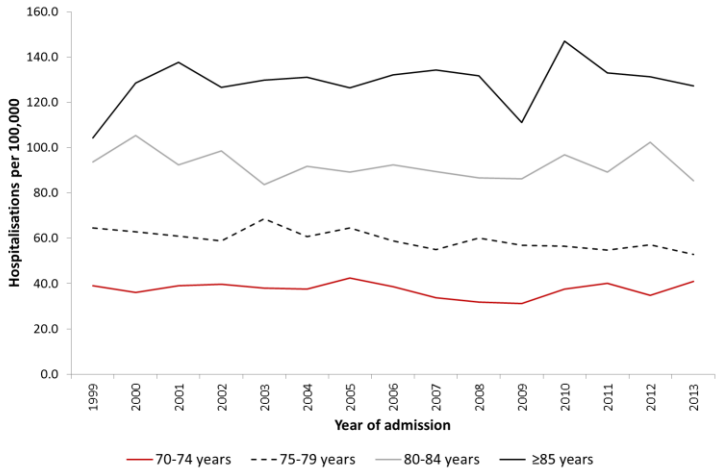
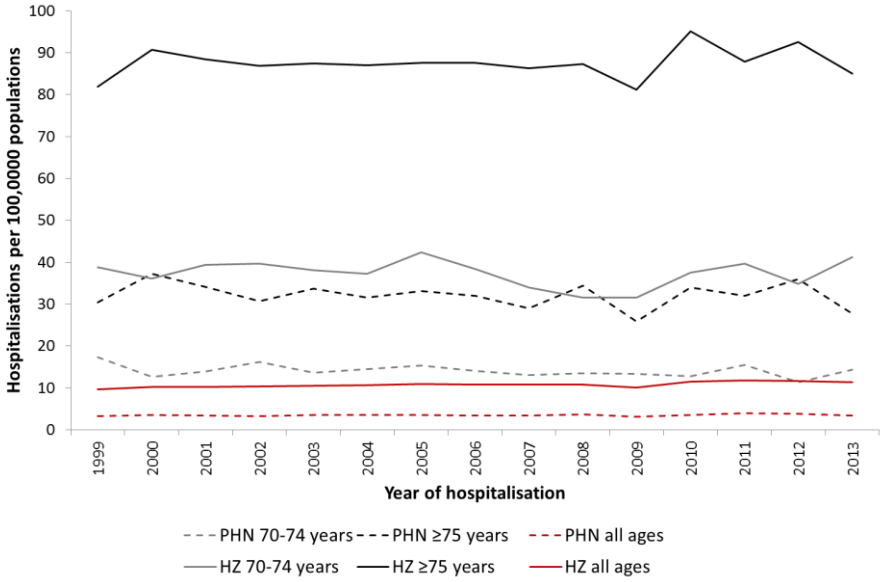


Figure 5: Herpes zoster hospitalisation rates (A), herpes zoster hospitalisation rates (principal diagnosis) by age group in all Australians (B) and in older non-Indigenous people (C), Australia, 1999-2013

(A)



(B)

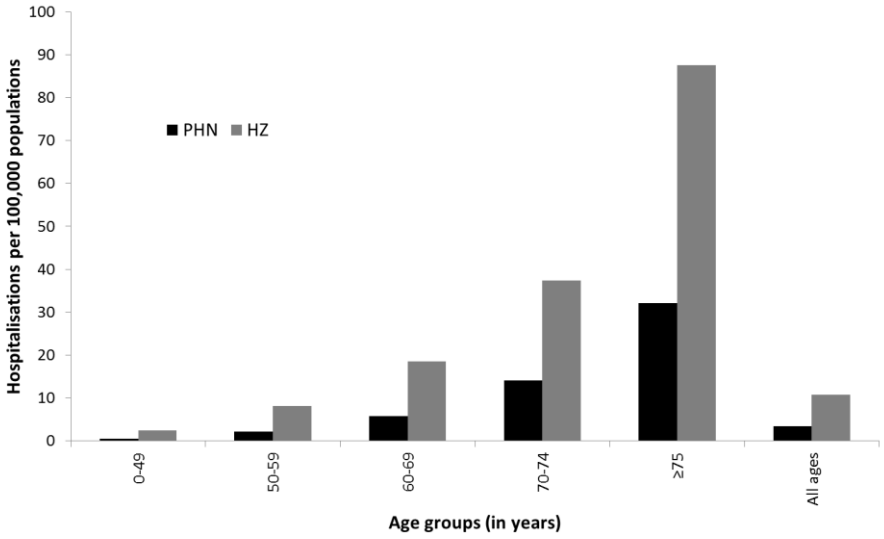


Figure 6: Hospitalisation rates for post-herpetic neuralgia [PHN] and herpes zoster [HZ] (A) and by age groups (B), Australia, 1999-2013[9]

[9] Analyses restricted to episodes where HZ was recorded as a principal diagnosis and PHN was recorded within the first 30 diagnostic fields. Principal HZ includes episodes of PHN.

disproportionately with age, where 26.7% HZ hospitalisations in those aged 50-59 years had an episode of PHN compared to 36.6% in those aged ≥75 years (Figure 6B).

Between 1999 and 2013, there were 226,276 bed days for hospitalisation coded as due to HZ. The overall median length of stay was 4 days with length of stay increasing with age. Median length of stay per admission was 4 days and 6 days for people aged 70-74 and ≥75 years, respectively. HZ hospitalisations in which a diagnosis for PHN was also recorded were associated with a higher median length of stay (5 days) compared to those not also recorded as having PHN (4 days) ($p<0.05$).

VZV associated hospitalisations in Indigenous Australians

Varicella

We compared varicella hospitalisation rates in Indigenous people over the pre- and post-vaccine periods using data from four jurisdictions (Queensland, Western Australia, Northern Territory and South Australia). We observed significant decreases in hospitalisation rates in all age groups, with the greatest reduction of 89% (IRR 0.11; 95% CI 0.06-0.22) in children aged 18-59 months (Table 4). Similar findings were observed when we compared varicella hospitalisation rates in children aged 18-59 months from the four jurisdictions for the pre-vaccine period (38.1 per 100,000; 95% CI 29.8-48.7) to hospitalisation rates in Queensland, Western Australia, South Australia, Northern Territory, New South Wales and Victoria for the post-vaccine period (6.3 per 100,000; 95% CI 3.1-12.3).

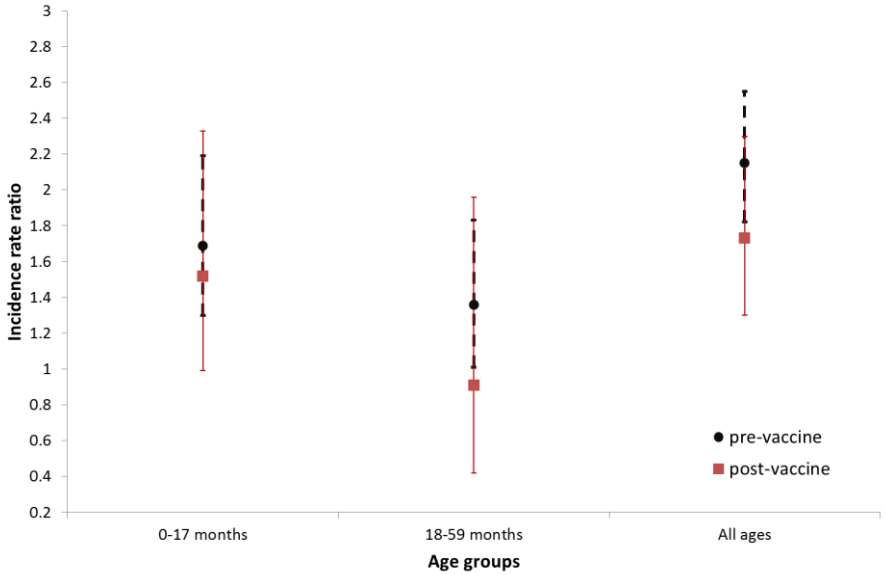
For Queensland, Western Australia, South Australia and the Northern Territory in the pre-vaccine period, the hospitalisation rate in Indigenous children aged 18-59 months was 36% higher compared to non-Indigenous children (IRR 1.36; 95% CI 1.01–1.83) but similar during the post-vaccine period (IRR 0.91; 95% CI 0.42–1.96). Similar trends were also observed in children aged 0-17 months, with the IRR for Indigenous versus non-Indigenous populations during the post-vaccine period 1.52 (95% CI 0.99-2.33), compared to 1.69 (95% CI 1.30-2.19) in the pre-vaccine period (Figure 7A). Indigenous Australians had higher varicella hospitalisation rates compared to non-Indigenous Australians in all other age groups (Tables 2 and 4).

Herpes zoster

When we analysed data from six jurisdictions (New South Wales, Victoria, Queensland, South Australia, Northern Territory and Western Australia) for the years 2007-2011, we found HZ hospitalisation rates in Indigenous people to be almost double those in non-Indigenous people

aged 50-59 years (IRR 1.87; 95% CI 1.29-2.71) and 60-69 years (IRR 1.77; 95% CI 1.27-2.48) (Figure 7B). However, no significant difference was observed in people aged 70-79 years (IRR 0.83; 95% CI 0.51-1.36).

(A)



(B)

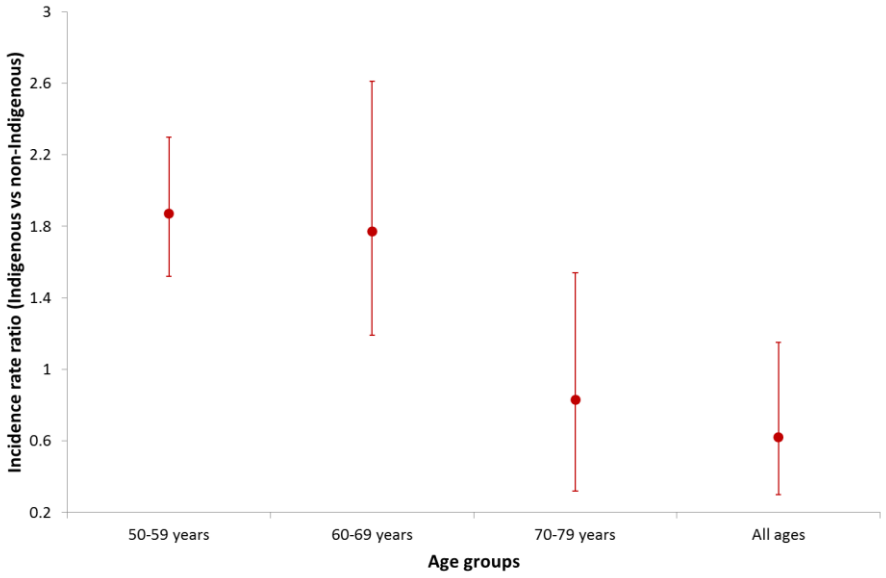


Figure 7: Incidence rate ratios for varicella (A) [10] and herpes zoster (B)[11] hospitalisation rates between Indigenous and non-Indigenous Australians by age groups, Australia, 1999- 2013

[10] Analyses restricted to Queensland, South Australia, Western Australia and the Northern Territory. Pre-varicella vaccine=1999-2004 and post-varicella vaccine=2007-2013.
[11] Analyses restricted to New South Wales, Victoria, Queensland, South Australia, Western Australia and the Northern Territory for the years 2007-2011.

Table 4: Varicella hospitalisations (principal diagnosis) by age groups and vaccine period in Indigenous populations, Australia, 1999- 2013[12,13]

	Pre-varicella vaccine 1999-2004		Post-varicella vaccine 2007-2013		
Age group	**Hospitalisations (n)**	**Rate[14] (95% CI)**	**Hospitalisations (n)**	**Rate‡‡‡ (95% CI)**	**IRR[15] (95% CI)**
0-17 months	69	73.0 (57.7-92.5)	25	21.1 (12.6-35.3)	**0.29 (0.18-0.46)**
18-59 months	64	38.1 (29.8-48.7)	9	4.3 (1.7-11.0)	**0.11 (0.06-0.22)**
5-9 years	38	15.6 (11.4-21.4)	11	3.5 (1.9-6.2)	0.22 (0.11-0.43)
10-14 years	9	4.2 (1.7-10.8)	19	6.2 (4.0-10.0)	1.49 (0.66-3.33)
15-19 years	4	2.2 (0-5.8)	7	2.5 (0-6.6)	1.17 (0.29-4.71)
20-29 years	13	4.3 (2.5-9.3)	6	1.4 (0-3.0)	0.32 (0.12-0.84)
30-39 years	7	2.6 (1.2-5.4)	10	2.9 (1.4-6.1)	1.12 (0.39-3.24)
≥40 years	8	2.9 (1.1-4.4)	12	2.0 (1.0-3.8)	0.90 (0.36-2.24)
All ages	212	11.5 (10.0-13.1)	99	3.8 (2.7-5.2)	0.33 (0.25-0.44)

[12] Analyses restricted to Queensland, South Australia, Western Australia and the Northern Territory

[13] Age-specific hospitalisations identified using ICD-10-AM code B02.0-02.9

[14] Average annual hospitalisation rate per 100,000 population

[15] Incidence rate ratio between hospitalisation rates during pre and post-varicella vaccine periods

Varicella and herpes zoster associated mortality

During the period 1998-2013, there were 21 deaths with varicella coded as the underlying cause of death (UCOD). In people aged <40 years the number of deaths was two-thirds lower in the post-vaccine period (2007-2013; 5 deaths) compared to the pre-vaccine period (1998-2004; 15 deaths). In children aged <10 years, the number of deaths reduced from 6 deaths in 1998-2004 to <4 deaths in 2007-2013.

During the same period, there were 340 deaths where HZ was coded as the UCOD with an overall crude mortality rate of 0.23 per 100,000 (95% CI 0.21-0.26) in those aged ≥40 years. Of these deaths, 5 (1.5%) were in people 40-59 years of age, 7 (2.1%) in those aged 60-69 years, 40 (11.8%) in those aged 70-79 years and 288 (84.7%) in those aged ≥80 years. The number of HZ-related deaths recorded for females (230, 67.6%) was twice that of males (110, 32.4%).

Discussion

Introduction of the national varicella immunisation program in 2005 for children aged 18 months was associated with a rapid and significant decline in varicella hospitalisation rates in Australia, particularly in children aged ≤10 years. While the varicella vaccine was available through the private market from 2000 and was recommended for use in 2003,[2] the vaccine did not have significant impact on hospitalisation rates until it was introduced under the NIP in 2005 as a single dose at 18 months of age with no formal catch-up program. Previously published data on varicella hospitalisations until 2010 reported 70% and 60% reductions in the age groups of 1-4 year olds and <1 year olds, respectively.[9] By December 2013, we found 84% reduction in hospitalisation rates in the post-varicella vaccine period in children aged 18-59 months, most of whom would have received the vaccine. Significant herd effect with 67% reduction in varicella hospitalisation rates was evident in children aged <18 months, who are not eligible for varicella immunisation. In the 20-29 years and 30-39 years age groups, varicella hospitalisation rates also reduced by 65% and 44%, respectively, suggesting that the herd protection effects of universal childhood immunisation also extend to adults of childrearing age, who are susceptible to more severe disease than children.[20-22] Similar impacts following one-dose varicella immunisation programs have been documented in other countries including the USA, Canada, Italy, Germany, Taiwan and Uruguay.[23] Hospitalisation rates in those aged ≥40 years did not decline during the post-vaccine period (IRR 1.15; 95% CI 1.01–1.30), most likely due to naturally acquired VZV-specific immunity in this age group and possible misclassification of HZ as varicella.[18, 24]

Despite the relatively high vaccine coverage and rapid initial decline in hospitalisation rates, little change in varicella hospitalisation rates was observed from 2010 onwards. Approximately 300 varicella hospitalisations continue to occur each year in those aged <40 years. Two recent Australian studies, one in Queensland and one nationally across all sentinel sites in the Paediatric Active Enhanced Disease Surveillance (PAEDS) network, have shown a single dose of varicella vaccine to have moderate effectiveness against varicella-associated hospitalisations of 81.9% and 64.6%, respectively.[25, 26] Further decreases in hospitalisation rates and interruption of community-wide transmission will likely require a second dose of vaccine.[27] In the USA, continuing varicella outbreaks and episodes of breakthrough disease were documented, despite high coverage attained under their one-dose varicella immunisation program, and prompted a switch to a two-dose program in 2006. [28-31] Introduction of a second dose led to a greater than 40% decline in hospitalisations during the years 2006-2010 compared to 2002-2005, as reported from two sentinel surveillance sites, and was accompanied by reduction in severe disease and outbreaks.[32-34] Similar to the USA, where overall deaths reduced by 66% in the first 6 years following the introduction of the one-dose program,[35] we found a 67% reduction in varicella-attributable deaths in people aged <40 years during the post-vaccine period. In 2007, addition of a second dose of varicella vaccine to the NIP was deemed not cost-effective by the Pharmaceutical Benefits Advisory Committee.[36] However, our findings suggest that it may be time to re-examine the potential for NIP funding of a second dose in the childhood schedule, if Australia is to achieve any further significant reductions in varicella-associated morbidity and mortality.[37]

A national HZ immunisation program, using the live attenuated zoster vaccine, was introduced in Australia in November 2016 for people aged 70-79 years. Our report focussed on HZ-related hospitalisations – although only around 3% of HZ cases are hospitalised,[38] hospitalisation rates are a measure of severe disease posing a significant economic burden on the health system.[39, 40] Consistent with other studies, our results demonstrate higher hospitalisation rates and mortality associated with HZ in older people (associated with immunosenescene) and in females (in whom a different response to latent VZV infection has been identified).[38, 41] We found similar HZ hospitalisation rates between the pre- and post-varicella vaccine periods, including in those aged 70-74 years (IRR 0.94; 95% CI 0.86–1.02) and ≥75 years (IRR 1.01; 95% CI 0.96–1.06), but an increasing trend in the HZ notification rate in South Australia and the Northern Territory. While this increase in notifications may be partly due to increased testing, similar to that seen with influenza and pertussis,[42] several studies have documented increases in community-based consultations and emergency department presentations for HZ, which may be due to a combination of ageing of the Australian population, greater use of immunosuppressive

medications and reduced natural boosting to VZV since the introduction of universal childhood varicella immunisation.[16, 43-45]

One third of all hospitalised cases in our study had PHN recorded in a diagnostic field, with the highest hospitalisation rate (32.1 per 100,000) in people aged ≥75 years. In Australia, the economic burden of HZ and PHN are significant, with an estimated total cost of 32.8 million Australian dollars each year to the health care system.[40] Pain associated with PHN is often refractory to treatment and can have substantial negative impact on the health-related quality of life.[12, 46, 47]

During the pre-vaccine period, Indigenous children aged 18-59 months had higher varicella hospitalisation rates compared to their non-Indigenous counterparts. Funded childhood varicella immunisation has contributed towards 'closing the gap'— during the post-vaccine period, Indigenous children aged 18-59 months had similar varicella hospitalisation rates compared to their non-Indigenous counterparts. However, Indigenous people overall continue to be hospitalised due to varicella and HZ at almost double the rate compared to non-Indigenous people. Our recent work demonstrated that Indigenous Australians aged 60-69 years had higher HZ hospitalisation rates compared to non-Indigenous Australians aged 70-79 years, who are currently eligible for funded HZ immunisation.[48]

High quality disease surveillance strategies are imperative for monitoring the population-wide impact of immunisation programs and driving evidence-based policies. Our study highlights a number of limitations of using notification and hospitalisation data for surveillance of varicella and HZ. While varicella and HZ are considered to be nationally notifiable diseases, differences in reporting mechanisms, the inherent challenges in reporting of these diseases (related to reliance on clinical/ epidemiological information rather than solely laboratory diagnosis) and absence of routine reporting from New South Wales to the NNDSS significantly limit interpretation of the data. South Australia and the Northern Territory are the only jurisdictions that routinely follow up laboratory notifications of VZV in order to be able to align cases with national case definitions. Both notification and hospitalisation data considerably underestimate the true burden of varicella and HZ, as both diseases are generally self-limiting and only a small proportion are likely to be tested for, notified and/or hospitalised. Notification data may be influenced by changes in testing practices over time. Surveillance using hospitalisation data is not timely and data may be influenced by access to hospitals over time, coding practices and misclassification between varicella and HZ.[18, 24, 49]

Other industrialised countries with national HZ immunisation programs have implemented a variety of surveillance systems targeted at capturing cases of HZ. In the UK, enhanced surveillance using sentinel GP clinics and pain clinics was established to monitor the effectiveness of their HZ immunisation program.[50, 51] Several other European countries conduct active surveillance for HZ including sentinel surveillance. [52] In the USA, active sentinel surveillance sites initially established for varicella surveillance were also successful at monitoring the epidemiology of HZ after the introduction of HZ vaccine in 2006.[53, 54]

In conclusion, introduction of a national varicella immunisation program in 2005 substantially reduced varicella associated morbidity and mortality in Australia. Minimal decline has been observed during recent years and further reductions in disease incidence will most likely require a second dose of varicella vaccine to be added on the NIP. A vaccine for HZ was introduced under the NIP in 2016. Timely and high quality surveillance, including data on HZ encounters at the primary health care level, will be crucial to evaluate the population-wide impact of this program.

Acknowledgements

We would like to acknowledge Allison Cairns, Vaccine Preventable Diseases Surveillance Section of Department of Health for providing useful comments on a late draft of the manuscript.

We thank the Australian Coordinating Registry, state and territory registries of births, deaths and marriages, state and territory coroners, and the National Coronial Information System, for providing access to cause of death data.

The National Centre for Immunisation Research and Surveillance is supported by the Australian Government Department of Health, the NSW Ministry of Health and The Children's Hospital at Westmead. The opinions expressed in this paper are those of the authors, and do not necessarily represent the views of these agencies.

References

1. Heymann DL. *Control of Communicable Diseases Manual, 20th Edition*. APHA Press, 2015.
2. Australian Technical Advisory Group on Immunisation (ATAGI). *The Australian immunisation handbook*. 10th ed. Canberra: Australian Government Department of Health and Ageing, 2015.
3. Macartney KK and Burgess MA. Varicella vaccination in Australia and New Zealand. *The Journal of infectious diseases*. 2008; 197 Suppl 2: S191-5.
4. Cunningham AL, Breuer J, Dwyer DE, et al. The prevention and management of herpes zoster. *The Medical journal of Australia*. 2008; 188: 171-6.
5. WHO. Varicella and herpes zoster vaccines: WHO position paper, June 2014. *Weekly epidemiological record*. 2014.http://www.who.int/wer/2014/wer8925.pdf?ua=112/01/2017.
6. Cohen JI. Clinical practice: Herpes zoster. *The New England journal of medicine*. 2013; 369: 255-63.
7. Ward K, Dey A, Hull B, Quinn HE, Macartney K and Menzies R. Evaluation of Australia's varicella vaccination program for children and adolescents. *Vaccine*. 2013; 31: 1413-9.
8. Department of Health. National Immunisation Program Schedule. 2016. Accessed 20 December 2016.http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/national-immunisation-program-schedule.
9. Heywood AE, Wang H, Macartney KK and McIntyre P. Varicella and herpes zoster hospitalizations before and after implementation of one-dose varicella vaccination in Australia: an ecological study. *Bulletin of the World Health Organization*. 2014; 92: 593-604.
10. Hull BP, Dey A, Menzies RI, Brotherton JM and McIntyre PB. Immunisation coverage, 2012. *Communicable diseases intelligence quarterly report*. 2014; 38: E208-31.
11. Hull BP, Dey A, Beard FH, Hendry A, Brotherton JM and McIntyre PB. Immunisation coverage annual report, 2014. *Commun Dis Intell*. 2017.
12. Department of Health. PBAC Public Summary Documents - November 2014. 2015. Accessed 12 December 2016.http://www.pbs.gov.au/pbs/industry/listing/elements/pbac-meetings/psd/11-2014.
13. Khandaker G, Marshall H, Peadon E, et al. Congenital and neonatal varicella: impact of the national varicella vaccination programme in Australia. *Archives of Disease in Childhood*. 2011; 96: 453-6.
14. Marshall HS, McIntyre P, Richmond P, et al. Changes in patterns of hospitalized children with varicella and of associated varicella genotypes after introduction of varicella vaccine in Australia. *Pediatric Infectious Disease Journal*. 2013; 32: 530-7.
15. Carville KS, Grant KA and Kelly HA. Herpes zoster in Australia. *Epidemiology and infection*. 2012; 140: 599-600; author reply -1.
16. MacIntyre R, Stein A, Harrison C, Britt H, Mahimbo A and Cunningham A. Increasing trends of herpes zoster in Australia. *PloS one*. 2015; 10: e0125025.
17. Communicable Diseases Network Australia. Surveillance case definitions for the Australian National Notifiable Diseases Surveillance System 2017. Accessed 29 March 2017.http://www.health.gov.au/casedefinitions.
18. Galil K, Pletcher MJ, Wallace BJ, et al. Tracking Varicella Deaths: Accuracy and Completeness of Death Certificates and Hospital Discharge Records, New York State, 1989–1995. *American Journal of Public Health*. 2002; 92: 1248-50.
19. Australian Institute of Health and Welfare. Indigenous identification in hospital separations data—quality report. Health Services Series no. 35. Cat. no. HSE 85. Canberra2010.http://www.aihw.gov.au/publication-detail/?id=6442468330
20. Waye A, Jacobs P and Tan B. The impact of the universal infant varicella immunization strategy on Canadian varicella-related hospitalization rates. *Vaccine*. 2013; 31: 4744-8.

21. Singleton RJ, Holman RC, Person MK, et al. Impact of Varicella Vaccination on Varicella-related Hospitalizations Among American Indian/Alaska Native People. *Pediatric Infectious Disease Journal*. 2014; 33: 276-9.
22. Davis MM, Patel MS and Gebremariam A. Decline in varicella-related hospitalizations and expenditures for children and adults after introduction of varicella vaccine in the United States. *Pediatrics*. 2004; 114: 786-92.
23. Varicella and herpes zoster vaccines: WHO position paper, June 2014. *Releve epidemiologique hebdomadaire / Section d'hygiene du Secr*. 2014; 89: 265-87.
24. Lin F and Hadler JL. Epidemiology of primary varicella and herpes zoster hospitalizations: the pre-varicella vaccine era. *The Journal of infectious diseases*. 2000; 181: 1897-905.
25. Sheridan SL, Quinn HE, Hull BP, Ware RS, Grimwood K and Lambert SB. Impact and effectiveness of childhood varicella vaccine program in Queensland, Australia. *Vaccine*. 2017; In press.
26. Quinn H, Gidding H, Macartney K, et al. Vaccine effectiveness against hospitalised varicella. *15th National Immunisation Conference*. Brisbane, Australia: Public Health Association, Australia, 2016.
27. Gao Z, Gidding HF, Wood JG and MacIntyre CR. Modelling the impact of one-dose vs. two-dose vaccination regimens on the epidemiology of varicella zoster virus in Australia. *Epidemiology and infection*. 2010; 138: 457-68.
28. Chaves SS, Zhang J, Civen R, et al. Varicella disease among vaccinated persons: clinical and epidemiological characteristics, 1997-2005. *Journal of Infectious Diseases*. 2008; 197 Suppl 2: S127-S31.
29. Marin M, Guris D, Chaves SS, et al. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports*. 2007; 56: 1-40.
30. Marin M, Marti M, Kambhampati A, Jeram SM and Seward JF. Global Varicella Vaccine Effectiveness: A Meta-analysis. *Pediatrics*. 2016; 137: e20153741.
31. Lopez AS, Guris D, Zimmerman L, et al. One dose of varicella vaccine does not prevent school outbreaks: is it time for a second dose? *Pediatrics*. 2006; 117: e1070-7.
32. Bialek SR, Perella D, Zhang J, et al. Impact of a routine two-dose varicella vaccination program on varicella epidemiology. *Pediatrics*. 2013; 132: e1134-40.
33. Lopez AS, Zhang J and Marin M. Epidemiology of Varicella During the 2-Dose Varicella Vaccination Program - United States, 2005-2014. *MMWR Morbidity and mortality weekly report*. 2016; 65: 902-5.
34. Leung J, Lopez AS, Blostein J, et al. Impact of the US Two-dose Varicella Vaccination Program on the Epidemiology of Varicella Outbreaks: Data from Nine States, 2005-2012. *The Pediatric infectious disease journal*. 2015; 34: 1105-9.
35. Marin M, Zhang JX and Seward JF. Near elimination of varicella deaths in the US after implementation of the vaccination program. *Pediatrics*. 2011; 128: 214-20.
36. Department of Health. PBAC Public Summary Documents - November 2007. 2007. Accessed 17 February 2017.http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2007-11/pbac-psd-measles-nov07.
37. Macartney K. Prevention of varicella: time for two-dose vaccination. *Lancet*. 2014; 383: 1276-7.
38. Liu B, Heywood AE, Reekie J, et al. Risk factors for herpes zoster in a large cohort of unvaccinated older adults: a prospective cohort study. *Epidemiology and infection*. 2015; 143: 2871-81.
39. Carapetis JR, Russell DM and Curtis N. The burden and cost of hospitalised varicella and zoster in Australian children. *Vaccine*. 2004; 23: 755-61.
40. Stein AN, Britt H, Harrison C, Conway EL, Cunningham A and Macintyre CR. Herpes zoster burden of illness and health care resource utilisation in the Australian population aged 50 years and older. *Vaccine*. 2009; 27: 520-9.

41. Opstelten W, Van Essen GA, Schellevis F, Verheij TJ and Moons KG. Gender as an independent risk factor for herpes zoster: a population-based prospective study. *Annals of epidemiology*. 2006; 16: 692-5.
42. Kaczmarek MC, Ware RS and Lambert SB. The contribution of PCR testing to influenza and pertussis notifications in Australia. *Epidemiology and infection*. 2016; 144: 306-14.
43. Carville KS, Riddell MA and Kelly HA. A decline in varicella but an uncertain impact on zoster following varicella vaccination in Victoria, Australia. *Vaccine*. 2010; 28: 2532-8.
44. Nelson MR, Britt HC and Harrison CM. Evidence of increasing frequency of herpes zoster management in Australian general practice since the introduction of a varicella vaccine. *Medical Journal of Australia*. 2010; 193: 110-3.
45. Jardine A, Conaty SJ and Vally H. Herpes zoster in Australia: evidence of increase in incidence in adults attributable to varicella immunization? *Epidemiology and infection*. 2011; 139: 658-65.
46. Serpell M, Gater A, Carroll S, Abetz-Webb L, Mannan A and Johnson R. Burden of post-herpetic neuralgia in a sample of UK residents aged 50 years or older: findings from the Zoster Quality of Life (ZQOL) study. *Health and quality of life outcomes*. 2014; 12: 92.
47. Drolet M, Brisson M, Schmader KE, et al. The impact of herpes zoster and postherpetic neuralgia on health-related quality of life: a prospective study. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*. 2010; 182: 1731-6.
48. Sheel M, Beard FH, Dey A, Macartney K and McIntyre P. Do higher rates of herpes zoster hospitalisation among Indigenous Australians warrant consideration of vaccination at a younger age? *Medical Journal of Australia*. 2017; In press.
49. Wormsbecker AE, Wang J, Rosella LC, et al. Twenty Years of Medically-Attended Pediatric Varicella and Herpes Zoster in Ontario, Canada: A Population-Based Study. *PloS one*. 2015; 10: e0129483.
50. Public Health England. Shingles: guidance and vaccination programme. 2013. Accessed 17 February 2017.https://www.gov.uk/government/collections/shingles-vaccination-programme.
51. Public Health England. Herpes zoster (shingles) immunisation programme 2013/14: Report for England. PHE publications gateway number: 20145632014.https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/383018/ShinglesReport2014.pdf
52. Statens Serum Institut. Surveillance of Varicella and Herpes Zoster in Europe. European Centre for Disease Control, 2010. Accessed 17 February 2017.http://ecdc.europa.eu/en/publications/Publications/varicella_zoster_report_2009_euvacnet.pdf.
53. Goldman GS and King PG. Review of the United States universal varicella vaccination program: Herpes zoster incidence rates, cost-effectiveness, and vaccine efficacy based primarily on the Antelope Valley Varicella Active Surveillance Project data. *Vaccine*. 2013; 31: 1680-94.
54. Tseng HF, Harpaz R, Luo Y, et al. Declining effectiveness of herpes zoster vaccine in adults 60 years and older. *The Journal of infectious diseases*. 2016.

Chapter 3: Field investigation of a public health problem

Investigation into increased lymphogranuloma venereum amongst men who have sex with men – New South Wales, Australia

Prologue

My role

In March 2017, I was nominated to lead an investigation into a potential outbreak of lymphogranuloma venereum (LGV) in New South Wales in 2016. LGV is a severe sexually transmitted infection caused by L1, L2 and L3 serovars of *Chlamydia trachomatis*. Rectal LGV is more commonly observed in men who have sex with men (MSM) and very few outbreaks have been reported in Australia. In 2016, 58 cases of LGV were reported compared to 17 cases in 2015. The last LGV in New South Wales (NSW) was reported in 2010. Large outbreaks of LGV have been recently reported in the United Kingdom and other parts of Europe. In order to investigate the outbreak, I was seconded to the Blood Borne Virus/ Sexually Transmitted Infections (BBV/STI) team within the Communicable Diseases Branch at Health Protection New South Wales (NSW).

The investigation was conducted under the leadership of Dr Christine Selvey, and I was assisted by the BBV/STI epidemiologist Ms Tove Fitzgerald (MAE2014). As this was not a 'regular' outbreak, my supervisors proposed that my role will be to first establish if the reported increase was a real outbreak and secondly, identify possible causes for the observed increase in LGV cases. The investigation was conducted over a six month period. I organised and visited the public health laboratory and the public health units. I communicated with all the stakeholders involved in this outbreak response. I led the design of the retrospective case series, the patient survey and drafted the final report enclosed in this chapter.

Lessons learned

One of the main lessons learned during this public health investigation was the political nature and sensitivities around working with STIs in Australia. HIV is co-infection is common in people with STIs including LGV. People with HIV often experience severe stigma and discrimination. Subsequently, the *NSW Pubic Health Act 2010* (the Act) has strict privacy provisions around the disclosure of HIV status. Therefore investigations of STIs have limited scope and are often 'unsuccessful'. For this reason, STI investigations are often also perceived as not important by other public health professionals. LGV and other rectal STIs are more common amongst a sub-group of MSM, who are involved in high risk activities such as group sex, sharing of group sex toys, fisting, and are involved in receptive anal intercourse, often under the influence of drugs and rarely use condoms. This is often perceived as personal choice and not truly 'high-risk'. Despite that, are we as public health professionals not ethically obliged

to care and to work towards disease prevention, even though it might be difficult? As part of this investigation, I learned how to interpret the Act, and how public health investigations are bound by the Act. I learned about the rising incidence of bacterial STIs as we improve our efforts at preventing STIs caused by blood-borne viruses including HIV and Hepatitis C.

As detailed in this chapter, one of the main challenges was communication with clinicians and their overall lack of support of public health response. This was particularly concerning when directors of publicly funded sexual health clinics were not supportive of the investigation. Other public health professionals who have worked on STIs shared similar thoughts around liaising with clinicians. STI investigations are faced with much greater resistance compared to other notifiable infectious diseases. While there are several possible reasons which may influence this including high work load, fear of 'breakdown' of doctor-patient relationships, sensitive nature of STIs, it also highlight a lack of coordination and collaboration between stakeholders. Similarly, there may have been occasions where the public health authorities did not provide feedback to data providers including clinicians and public health laboratories; hence not closing the 'surveillance feedback loop'.

Public health impact

One of the first steps of any outbreak investigation is 'confirm the existence of an outbreak'. In order to do, I visited the Centre for Infectious Diseases and Microbiology (CIDM), the public health laboratory in NSW responsible for testing of all LGV specimens. Although the aim of visit was to source the testing denominator data, I identified additional cases of LGV for previous years that were not recorded in the NSW Notifiable Conditions Information Management System (NCIMS). On further investigation, I found out that these cases were misclassified as chlamydia in NCIMS. Subsequently, the total number of case count for 2015 was 34. Since then, several other issues were identified with LGV surveillance, including how laboratories notify the public health units and the requesting clinician. These findings are expected to help strengthen the LGV surveillance system.

We were unable to obtain sufficient data to identify the exact causes of the increase in LGV, but did obtain evidence of infection in HIV-negative MSM using pre-exposure prophylaxis, and also identified one case of asymptomatic infection. Prior to this, Health protection NSW did not have any evidence of LGV amongst HIV-negative persons or asymptomatic LGV infections. It is hoped that this information will provide impetus for further investigation to understand the risk factors driving LGV transmission in NSW.

The enclosed chapter will be used as a report to Health Protection NSW. An abridged version of the report will be circulated to clinicians who participated in the investigation, community support groups (ACON and Positive Life), CIDM and to study participants.

Acknowledgements

Sincerest thanks to Dr Christine Selvey for her guidance and support in conducting this outbreak investigation. I have enjoyed learning about STIs and the burden they pose on the public health system. Thank you also for leading by example and teaching me about good public health practice.

Sincere thanks to Ms Tove Fitzgerald for incredible support and encouragement in undertaking this outbreak investigation. Thank you for all your help, sharing your knowledge and for all the laughs during my time at the Communicable Diseases Branch.

Thank you to many others within the BBV/STI and the Communicable Diseases Branch, including Dr Vicky Sheppeard, Ms Meeyin Lam and Dr Nick Rose for their assistance in conducting this investigation. Thank you to the collegiality of everyone at the Communicable Diseases Branch.

Thank you to all others were involved in this investigation including Ms Kelley-Anne Resler and Dr Mark Ferson from South-East Sydney Pubic Health Unit, and Mr Andrew Ingleton from Sydney Public Health Unit for exposing me to the 'practical and real' side of STI investigations. I appreciate the input and feedback of Mr Craig Cooper from ACON and Mr Nic Parkhill from Positive Life. Their support in conducting this investigation is sincerely appreciated. Thank you to Mr Danny Koh and Ms Linda Donovan of CIDM, for providing the laboratory data and information about LGV testing patterns.

Finally, thanks to my MAE supervisors, Dr Frank Beard and Associate Professor Martyn Kirk for the encouragement and acknowledging the challenges I faced. There were times when all the work felt like wasted effort and resources.

Although a challenging experience, the lessons learned will contribute towards my professional growth as I progress towards the next stage of my career in public health.

Investigation into increased lymphogranuloma venereum amongst men who have sex with men – New South Wales, Australia

Authors

Meru Sheel
Christine Selvey

Investigation team, Health Protection New South Wales

Meru Sheel
Tove Fitzgerald
Meeyin Lam
Christine Selvey

Collaborators

Sheena Adamson, Health Protection New South Wales
Craig Cooper, Positive Life New South Wales
Linda Donovan, Centre for Infectious Diseases and Microbiology, New South Wales
Mark Ferson, South Eastern Sydney Local Health District, New South Wales
Andrew Ingleton, Sydney Local Health District, New South Wales
Danny Ko, Centre for Infectious Diseases and Microbiology, New South Wales
Zeina Najjar, Sydney Local Health District, New South Wales
Nicolas Parkhill, ACON, New South Wales
Kelly-Anne Resler, South Eastern Sydney Local Health District, New South Wales

Frank Beard, National Centre for Immunisation Research and Surveillance, New South Wales
Martyn Kirk, National Centre for Epidemiology and Population Health, Australian National University, Australian Capital Territory

Abstract

Introduction: Lymphogranuloma venereum (LGV) is caused by *Chlamydia trachomatis* (Ct) serovars L1, L2 and L3. Common co-infections include human immunodeficiency virus (HIV), syphilis and other sexually transmissible infections (STIs). In men who have sex with men (MSM), rectal LGV can lead to severe clinical presentation and sequelae, enhanced HIV transmission and increases the risk of community-wide transmission. LGV is a laboratory notifiable condition in NSW. In 2016, Health Protection NSW reported a noticeable increase in the number of LGV cases compared to 2015. Following this, Health Protection NSW launched a public health investigation to identify the factors that were contributing to the increased LGV.

Methods: LGV notification data for the study period 1 January 2016 to 31 March 2017 were extracted from the NSW Notifiable Conditions Information Management System (NCIMS). In order to identify symptoms and risk-factors associated with this increase, we conducted a retrospective case series. For this, we designed an electronic questionnaire in NCIMS, which was administered to all cases diagnosed with LGV during the study period, and for whom contact details were available.

Results: During the study period, there were 66 LGV notifications for NSW residents. All notifications were in males, of which 22 (33.3%) were in those aged 30-39 years. Most cases (74.2%) resided in Sydney metropolitan region. Of the 66 cases, contact details were available for 20 patients. We administered the electronic questionnaire to all 20 cases, of which 11 responded. Ten participants completed the survey. All 10 cases were symptomatic, and reported participating in high-risk sexual activities including condomless anal intercourse with male sex partners. Five respondents self-reported their HIV status as negative and reported having used PrEP at the time of LGV diagnosis.

Conclusions: All survey participants engaged in high-risk sexual behaviour, but due to the overall poor response rate (15%), we were unable to identify the exact reasons for the increase in LGV. The investigation found LGV surveillance to be sub-optimal and identified inconsistencies with the surveillance process. This report summarises the key challenges encountered by the investigation team, lessons learnt and includes practical recommendations for improving future public health response to LGV.

Introduction

Lymphogranuloma venereum (LGV) is caused by *Chlamydia trachomatis* (Ct) serovars L1, L2 and L3. Common co-infections include human immunodeficiency virus (HIV), syphilis and other sexually transmissible infections (STIs) such as, gonorrhoea and chlamydia caused by non-LGV serovars.[1, 2] In heterosexual people, the most common initial clinical manifestation of LGV is unilateral tender inguinal and/or femoral lymphadenopathy.[2] A self-limited genital ulcer or papule sometimes occurs at the site of inoculation. In women with rectal exposure and men who have sex with men (MSM), rectal LGV classically presents as proctitis (stage I), which can progress to more severe sequelae including fluctuant bubo (localised enlargement of the lymph nodes in the groin area), lymphadenitis and intra-abdominal or retroperitoneal lymphadenopathy (stage II).[3] Recent studies have also reported asymptomatic rectal infection with LGV-causing Ct.[4] The infection can be treated with a 21 days course of doxycycline, however if left untreated can advance to chronic proctitis, fistulae, strictures and/or genital oedema.[5]

Traditionally, LGV was endemic in heterosexual people in parts of Africa, the Caribbean and Asia, but recent studies have reported increased LGV amongst MSM populations in industrialised nations including Australia,[6] Europe,[7-9] United States[10] and United Kingdom.[4, 11] In the UK, more than 2000 cases were reported during an LGV outbreak in 2003-2012.[12] No clear reasons have been identified for this recent emergence of LGV amongst MSM populations, but increasing incidence has been frequently associated with high-risk sexual activities amongst a subgroup of MSM, and declining use of condoms especially for anal intercourse.[6, 13] High-risk sexual behaviours include group sex, use of shared sex toys and fisting prior to receptive anal intercourse, often associated with the use of recreational drugs. The risk of transmission is particularly increased in HIV-positive MSM who have condomless anal intercourse with others who have the same HIV status (serosorting).[14] Efforts have been made to sequence and determine genetic variability in LGV-causing serovars, with L2b being the most commonly circulating serovar overseas[15] and in Australia.[16] Despite increasing incidence of LGV, there exist several gaps in our knowledge of risk factors associated with the increase in LGV and its transmission.

In Australia, LGV is not a nationally notifiable condition but is required to be notified to public health authorities in New South Wales (NSW), Queensland, Western Australia, the Northern Territory and Tasmania. In January 2017, Health Protection NSW reported a noticeable increase in the number of notifications of LGV during 2016. In 2016, there were 58 notifications compared to 17 notifications in 2015.[17] The observed increase was considered to be amongst MSM and most cases resided in metropolitan Sydney.[18] Increased notifications were observed

simultaneous with the implementation and expansion of a large-scale trial of pre-exposure prophylaxis (PrEP) [EPIC-NSW] for the prevention of HIV in persons at high risk of HIV infection. As of 26 March 2017, a total of 5320 participants were enrolled in EPIC-NSW. EPIC-NSW participants undergo three monthly screening for anal, rectal and pharyngeal chlamydia and gonorrhoea, syphilis and HIV. In NSW, increases were also observed in the number of notifications of other STIs including chlamydia, gonorrhoea and syphilis; however it was not clear whether the increase in STI notifications was due to increased screening or an increase in disease incidence. For these reasons, we wanted to examine 1) if this increase was a true increase in LGV or an artefact of increased STI screening amongst MSM populations; 2) if this increase was associated with the use of PrEP.

In December 2016, Health Protection NSW convened an expert group to discuss the increase in LGV. Experts included public health physicians, sexual health clinicians and epidemiologists. The expert group agreed to formally investigate the increase in LGV cases and explore ideal study designs. Following this meeting, NSW Health issued an alert for all NSW sexual health clinicians, s100 GPs and gastroenterologists noting an ongoing increase in LGV, requesting LGV testing in patients with proctitis and emphasising the need for testing of sexual contacts.[18]

Like any other outbreak investigation, active case-finding and identifying risk factors are important for STI control. NSW Health's Communicable Disease Branch has a responsibility to investigate sources of infection and control outbreaks of communicable diseases. As HIV co-infection is common in high-risk populations with STIs, especially bacterial STIs such as chlamydia, syphilis, gonorrhoea and LGV, gaining information on HIV status is critical to inform prevention and control strategies. Follow-up of LGV is particularly important because of its frequently severe clinical presentation and sequelae, the possible consequence of enhanced HIV and hepatitis C transmission in those with LGV and the risk of community-wide transmission.[1] However, section 56(3) of the NSW *Public Health Act* 2010 (the Act), prohibits medical practitioners from disclosing whether a patient has or has been tested for HIV. Although sub-section 4 specifies some circumstances under which such disclosure is allowed, this does not include disclosure to public health authorities.[19] Additionally, section 56(1) of the Act requires that HIV notifications are made only in a de-identified form, which means that Health Protection NSW is unable to determine the HIV status of people notified with an STI.

Historically, LGV was rare in NSW.[20] In 2010, NSW Health observed a dramatic increase in LGV notifications, following which enhanced surveillance was conducted from May 2010 to April 2012.[6] A public health investigation was launched, however due to the restrictions on disclosure of a person's HIV status as described above, and the need to collect information on

HIV status of people notified with LGV, ethics approval was considered necessary. Ethics approval was sought from the Illawarra Shoalhaven, South Eastern Sydney and Sydney Local Health Districts (LHDs) to obtain HIV status of LGV cases in a de-identified manner from the medical practitioners. However, obtaining HIV status from the clinicians was not approved by the ethics committees. Subsequently, enhanced surveillance consisting of doctor and patient interviews was conducted. Doctor and patient interviews were conducted to collect information on symptomatology and sexual risk factors, and patient interviews were specifically used for determining the HIV status. During the investigation period, 88 LGV notifications were received. As part of the enhanced surveillance, the investigation team were able to contact 37 doctors who had diagnosed 67 (76%) of the LGV infections. The doctors granted permission to contact 30 (45%) cases directly and of those, successful contact was made with 22 (73%) patients. Of the 22 cases, all reported participating in condomless anal intercourse in the months prior to being diagnosed with LGV and 18 (82%) self-reported they were HIV-positive.[6] The high proportion of HIV-positive people in the 2010 study emphasises the need to know the HIV status of an individual during a LGV investigation. The outbreak subsided without any targeted intervention, and no specific causes for the reported increase were identified.

The aim of this investigation was to determine if the 2016 LGV increase represented an outbreak and to identify factors contributing to increased notifications of LGV in NSW between 1st January 2016 and 31st March 2017.

Methods

LGV notification

In NSW, laboratories are required to notify a positive LGV test. As per the NSW Health case definition, a confirmed case requires demonstration of *Chlamydia trachomatis* serovars L1 to L3 in fluid aspirated from a fluctuant bubo or from a genital lesion by immunofluorescence (IF), enzyme immunoassay (EIA), DNA probe, polymerase chain reaction (PCR), culture or by specific micro-IF serological tests.[21]

After a LGV case is notified, follow-up of notifications by PHUs is not generally conducted. Laboratory confirmed LGV notifications are entered into the NSW Notifiable Conditions Information Management System (NCIMS), a confidential state-wide database. LGV notifications in NSW residents for the period 1 January 2010 to 31 March 2017 were extracted from NCIMS. In NSW, eight LHDs (Central Coast, Illawarra Shoalhaven, Nepean Blue Mountains, Northern Sydney, South Eastern Sydney, South Western Sydney, Sydney, Western Sydney) cover the Sydney metropolitan region and seven (Far West, Hunter New England, Mid

North Coast, Murrumbidgee, Northern NSW, Southern NSW, Western NSW) cover rural and regional NSW.

Laboratory testing

In NSW, all LGV testing is performed at the Centre for Infectious Diseases and Microbiology (CIDM), Westmead, Australia. The 2014 Sexually Transmissible Infections in Gay Men Action Group (STIGMA) guidelines recommend LGV testing for symptomatic individuals only. In NSW, there is no clear indication of LGV testing patterns. A small number of laboratories refer all chlamydia positive anal swabs to CIDM for LGV testing independent of clinician referral, while most seek LGV testing only when requested by the clinicians. To better understand LGV testing patterns, we sourced testing numerator and denominator data from CIDM. Percentage positive were calculated for each year as the number of LGV positive samples divided by total number of specimens tested for LGV.

LGV specimens are tested using an *in-house* validated real time (RT) PCR protocol based on previously published protocol.[22] Briefly, all specimens received by the CIDM public health laboratory are tested using a multiplex RT-PCR using consisting of degenerate primers which target the outer membrane protein-I (omp-I) gene for species-specific detection of Ct, in combination with primers targeting the polymorphic membrane protein H (pmp-H) gene for specific LGV detection. CIDM does not sequence-type LGV serovars as part of routine LGV testing.

Stakeholder engagement

During April-August 2017, we (Health Protection NSW) conducted this investigation in collaboration with Sydney and South Eastern Sydney PHUs, the LHDs with the majority of LGV cases. We also consulted with community support groups, Positive Life NSW and ACON prior to commencing the LGV investigation described below.

Patient questionnaire

As the privacy provision under the Act does not permit the diagnosing or treating doctors to disclose the HIV status of their patients,[19] we conducted a retrospective case series using patient questionnaire. We designed an electronic survey (Appendix 3A) in NCIMS, which was administered via text messages to mobile phones or via email, depending on the patient's preference. Survey design was based on previous questionnaires used during the 2010 LGV outbreak investigation. Feedback on survey questions and appropriate language use was sought from representatives from ACON and Positive Life NSW. We collected information on

demographic details, symptoms, history of PrEP use at the time of LGV diagnosis, and HIV status.

As the current notification form only contains a field for postal address, patient contact details (mobile phone number or email address), were requested from the diagnosing clinicians or directors of the health service. We requested diagnosing clinicians/ health services to also ensure that patients were aware of their diagnosis and inform them of this investigation.

Data analyses

We conducted descriptive epidemiology using notification data recorded on NCIMS including date of specimen collection, age, sex, postcode and site of infection. For the survey, crude numbers and proportions (where appropriate) were reported. All analyses were conducted in Microsoft Excel.

Ethics approval was not sought as the investigation was conducted by Health Protection NSW as a public health activity aligned with the objectives of the Act.

Results

LGV notifications

During our study period of 1 January 2016-31 March 2017, there were 66 notifications for LGV, of which 58 were reported during 2016.

In 2015, Health Protection NSW initially reported 17 cases of LGV. During the first month of this investigation, we visited the CIDM laboratory, where we identified an additional 17 cases of LGV in 2015 that were misclassified as non-LGV chlamydia in NCIMS, increasing the total count of LGV cases to 34. Figure 1 shows the updated epidemic curve for LGV for the years 2010 to Quarter 1, 2017.

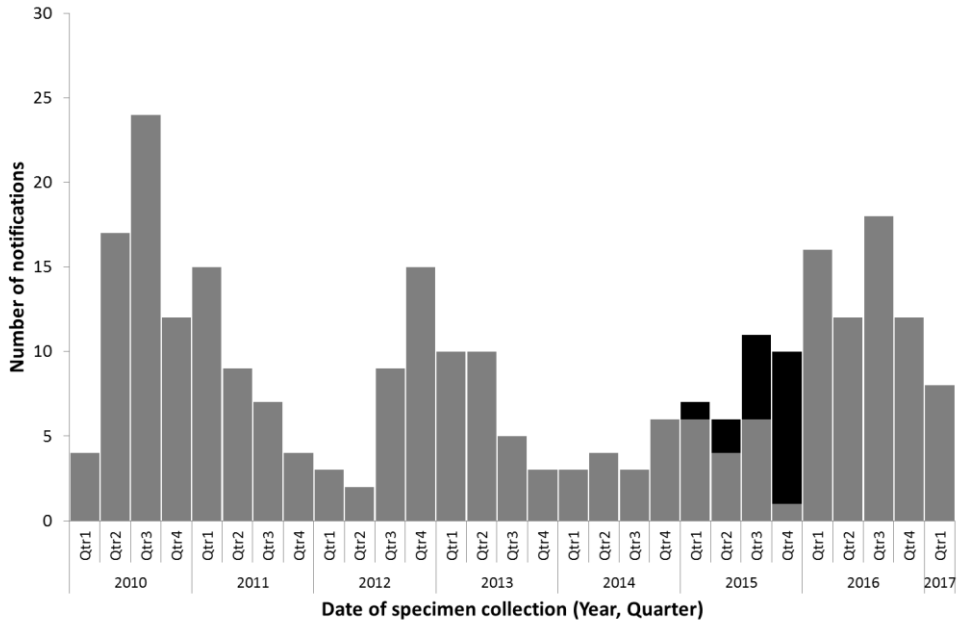


Figure 1: Number of LGV notifications by year and quarter, New South Wales, 2010-2017. Bars in black represent cases that were misclassified as non-LGV chlamydia. Data source: NSW Notifiable Conditions Information Management System (NCIMS).

During the study period, all (66) LGV notifications were in males, of which 22 (33.3%) were in those aged 30-39 years (Figure 2). The median age was 37 years (range 19-70 years). Of all LGV cases, 49 (74.2%) were residents of Sydney and South Eastern Sydney LHDs (Figure 3), with the remainder of cases residing in other NSW LHDs.

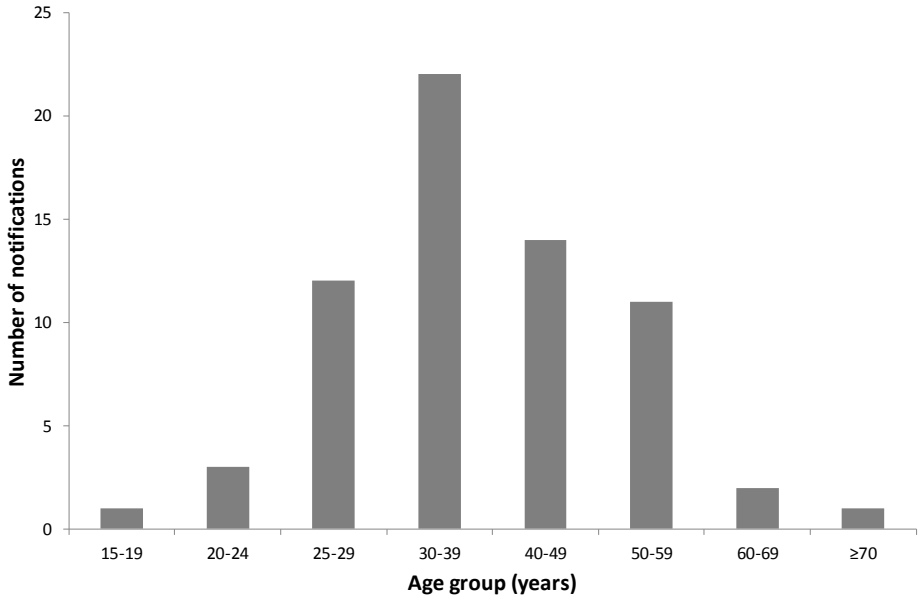


Figure 2: LGV notifications by age group and year, New South Wales, 1 January 2016-31 March 2017. Data source: NSW Notifiable Conditions Information Management System (NCIMS).

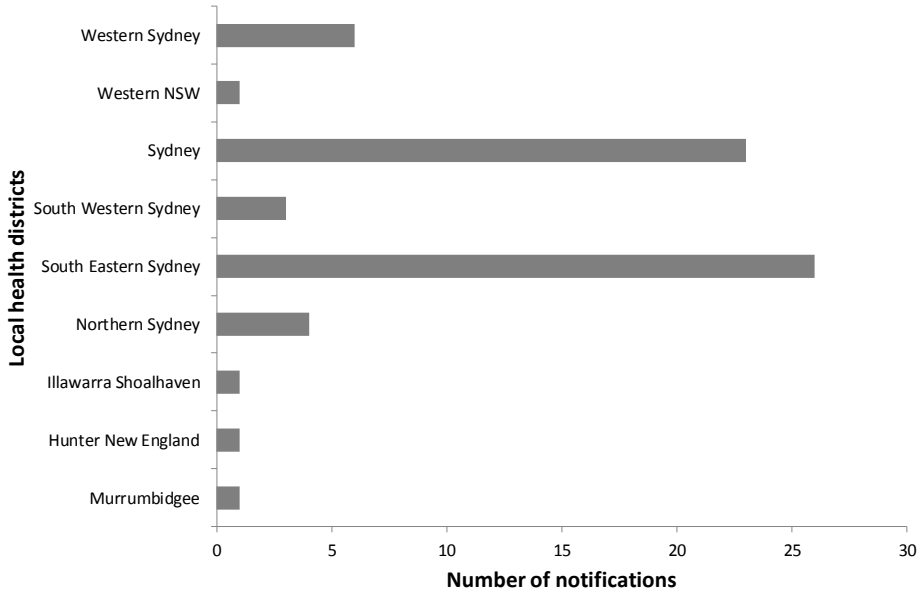


Figure 3: LGV notifications by local health districts (LHD), New South Wales, 1 January 2016-31 March 2017. Central Coast, Illawarra Shoalhaven, Nepean Blue Mountains, Northern Sydney, South Eastern Sydney, South Western Sydney, Sydney, Western Sydney cover the Sydney metropolitan region. Far West, Hunter New England, Mid North Coast, Murrumbidgee, Northern NSW, Southern NSW, Western NSW cover rural and regional NSW. Data source: NSW Notifiable Conditions Information Management System (NCIMS).

Laboratory results

Of the 66 notifications, 57 (86.4%) specimens were isolated from the anus and rectum, one (1.5%) from a bubo, four (6.1%) from the genitourinary tract and four (6.1%) whose specimen site was unknown.

In 2016, CIDM tested 614 specimens for LGV, of which 61 (9.9%) were confirmed for L1-L3 Ct (LGV positive), of which 58 notifications were for NSW residents. In 2015, CIDM tested 398 specimens for LGV, of which 37 (9.3%) were LGV positive. Of the 37 tests that were LGV positive, 34 notifications were for NSW residents. Percentage positivity remained the same between 2015 and 2016, but greater numbers of tests were performed during 2016. Percentage positivity reduced to 3.5% during January-June 2017 (data not shown).

In 2014, CIDM tested 1090 specimens for LGV, of which 20 (1.3%) were LGV positive. Prior to 2015 and prior to the revision of the STIGMA guidelines in 2014, South Eastern Area Laboratory Services (SEALS) requested LGV testing on all rectal specimens that tested positive for chlamydia. In 2014, SEALS requested 811 LGV tests compared to 47 in 2015. In 2015, with the revision of STIGMA guidelines, SEALS stopped routine referral of all chlamydia positive rectal specimens for LGV testing, which could explain the reduced number of LGV tests performed in 2015.

Survey results

We sourced details of the diagnosing clinicians from CIDM, as this information is not routinely entered into NCIMS. Of the 66 LGV cases, the majority were diagnosed at publicly funded sexual health clinics or private GPs known to have a high case load of MSM (Table 1). Over a period of four weeks, 10 of the 15 diagnosing health services provided contact details for some patients. These services had diagnosed/treated 35 (53%) of the 66 cases LGV. Permission was provided to contact 20 (30.3%) patients. Nine patients did not provide permission to be contacted and six could not be successfully contacted by the health services. Of the remaining five health services, which had diagnosed 31 cases, two responded to our initial request for assistance but only one agreed to contact patients to seek permission and provide us with patient contact details. This health service provided contact details approximately eight weeks after our initial request; and permission to contact was only granted for one out of the 15 cases diagnosed at this clinic. Due to this delay, we were unable to administer the survey to this patient. For the health services who did not respond to our request, we do not have information on whether these health services attempted to contact their patients.

Table 1: Summary of LGV cases by health service provider type, New South Wales, 1 January 2016 - 31 March 2017[16]

Prescriber type	Number of services	Number of responding services	Number of cases diagnosed	Number of cases for whom permission to contact was obtained
Publicly funded sexual health services	8	5	37	8
Private s100 clinics	3	2	25	11
Private hospitals	2	1[17]	2	1
Non s100 General Practice	2	2	2	0

We administered the electronic questionnaire (via text message/ email) to all 20 cases who granted permission to be contacted. Surveys were administered soon after we obtained consent. If a response was not received within 48-72 hours, cases were re-sent the survey. If no response was obtained within 48-72 hours after the second attempt, we attempted to call the patients for whom phone numbers were available. We received complete responses from 10 cases (50%), of whom one case preferred to be interviewed on the phone. The nine remaining cases completed the survey using the electronic questionnaire, two of whom responded after receiving the phone reminder. One case declined by directly responding to the text message. Key results are summarised in Table 2. All 10 participants identified as neither Aboriginal nor Torres Strait Islander and identified as males at the time of birth. All respondents reported participating in condomless intercourse and having multiple sexual partners (Table 2).

[16] Initial request for assistance was on 9 August 2017. Results are up to date as of 1 October 2017

[17] One case was referred for follow-up to a private s100 clinic.

Table 2: Summary data from of LGV survey participants (N=10), New South Wales, 1 January 2016-31 March 2017

Questionnaire variable	Number
Local Health District area	
Sydney	2
Northern Sydney	3
South Eastern Sydney	5
Country of birth	
Australia	6
Overseas	3
Unknown	1
Sexual identity	
Gay or homosexual	8
Bisexual	2
Intersex	
Yes	1
No	9
HIV status	
Positive	5[18]
Negative	5
Condom use for anal (or vaginal) sex with casual partner	
Never	2
Less than half the time	4
More than half the time	3
Always (not counting breakages)	1
Condom use for anal (or vaginal) sex with regular partner	
Never	4
Less than half the time	2
More than half the time	2
Always (not counting breakages)	2
Sex of partner	
Male	9
Male and Female	1
Number of sex partners	**Median (range)**
3 months	15 (2-60)
12 months	65 (7-600)

All 10 survey participants were symptomatic and proctitis was common. Symptoms of proctitis included rectal pain, tenesmus (continuous feeling of bowel movement), pain with bowel movement, rectal discharge and mucus discharge (Figure 3). We included a question to ask the participants their reason for visiting the doctor if they were asymptomatic. It's likely that this question was unclear to several participants, as four symptomatic survey participants answered the question. Of the four cases who responded to the question asking reasons for visiting the doctor, three indicated they attended their health service for routine sexual health screening (even though they were symptomatic), and one attended after being identified as a sexual contact of someone who had been diagnosed with LGV. Of the 10 participants, two reported having at least one STI including gonorrhoea and chlamydia at the time of LGV diagnosis. All

[18] One patient reported HIV diagnosis date as 4 months after LGV diagnosis

survey participants reported receiving treatment for LGV. Only five participants reported informing their sexual partners of their LGV diagnoses, using specialised partner notification text messaging services and in-person.

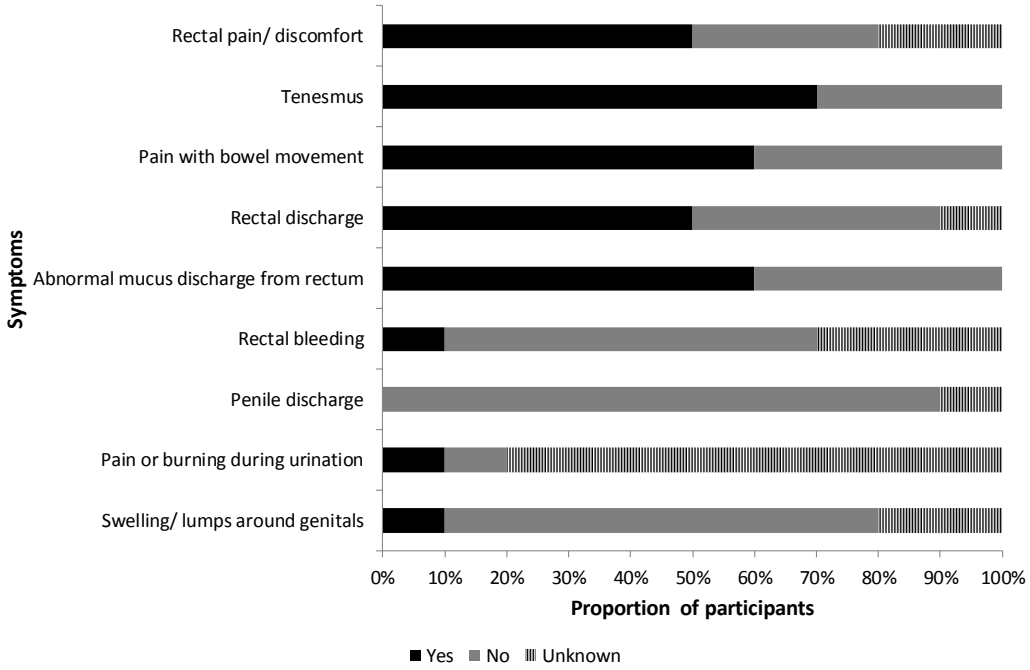


Figure 3: Presenting symptoms as reported by LGV survey participant (N=10), New South Wales, 1 January 2016-31 March 2017

Of the 10 survey participants, five cases reported being HIV-positive, one of whom was diagnosed with HIV approximately four months after the LGV diagnosis. This LGV case, who was later diagnosed with HIV, reported having used post-exposure prophylaxis (PEP) at the time of LGV diagnosis. At the time of LGV diagnosis, self-reported HIV status of five cases was negative. All five HIV-negative LGV cases reported having been using PrEP at the time of LGV diagnosis. One HIV-positive patient reported use of PEP, but we believe they may have confused this with antiretroviral therapy.

In order to obtain permission to contact the patients, we contacted health services either via email or via phone. In some cases, depending on availability, we were able to speak directly with the diagnosing doctor. Amongst those cases who did not agree to be contacted but whose doctors responded, two were symptomatic with proctitis and one was asymptomatic (as reported by diagnosing doctor). The asymptomatic case was identified through routine STI screening. The diagnosing doctor did not request a test for LGV, and reported not being notified of the diagnosis by the laboratory.

Discussion

NSW experienced an increase in LGV notifications during 2016. During the study period of 1 January 2016-31 March 2017, there were 66 LGV notifications, compared to 34 notifications in 2015. In order to gain an insight into factors contributing to this increase, we designed a survey to retrospectively collect information from cases. We were able to administer an electronic questionnaire to 20 cases. Of the 20 cases that were administered the questionnaire, 11 responded, of whom 10 completed the survey, resulting in an overall response rate of 15%. In addition, we obtained symptomatology information for another three cases from the diagnosing doctors.

Our findings from the survey should be considered in light of the overall poor response rate. Using the online survey, we identified five HIV-negative cases, all of whom were using PrEP at the time of LGV diagnosis. The remaining five cases were HIV-positive, of whom one was diagnosed with HIV four months after being diagnosed with LGV. Collectively, through the survey and on speaking with the diagnosing doctors, we identified a total of 12 symptomatic cases and one asymptomatic case. High risk behaviours including condomless anal intercourse with casual and regular partners, as well as having high numbers of sexual partners were commonly reported.

As this investigation was conducted retrospectively for all cases between 1 January 2016 and 31 March 2017, it was most likely affected by several biases. Recall bias around remembering LGV symptoms, number of sexual partners, and co-infection with other STIs after a prolonged period of time is possible. However, considering proctitis is highly uncomfortable, it is unlikely that patients would not recall symptoms associated with LGV. In addition, due to the risk of recall bias, we did not ask about the number of sexual partners at the time of LGV diagnosis, but asked about the number of sex partners in the previous three or 12 months as an indicator of sexual risk. The National Gay Periodic Survey uses >10 male sex partners in the previous six months as a key indicator in determining risk-behaviour.[23] Half of the survey participants reported not informing their sexual contacts of their LGV diagnosis (data not shown). Although this finding might be biased by recall and by the small sample size, it indicates that contact tracing might not always be undertaken. Contact tracing should be done comprehensively for all LGV cases. According to the current LGV guidelines, the treating doctor is responsible for contact tracing.[21] However, this is reliant on the patient providing details of sexual contacts to the treating doctor. Finally, the fact that five out of the ten survey respondents reported being HIV-negative, and due to the stigma associated with being HIV-positive, it is possible HIV-negative persons may have been exposed to selection bias. Consequently, HIV-negative persons

may have been more likely to respond to the request of the health service providers and to the survey.

We were unable to estimate the notification rates for LGV by sex, age group, and by LHD as correct information on denominator data is not available. For instance, we do not know the proportion of MSM living in each LHD or where infection was acquired, and as observed majority of cases geographically resided in metropolitan Sydney (Figure 3). Although population data for males in New South Wales could be used as denominator, we believe this may not be a correct representation of the results.

HIV co-infection is common amongst people with LGV, globally and in NSW. A systematic review of a small number of studies reported HIV prevalence of 67%-100% among LGV cases.[14] Furthermore, MSM with LGV had 8.19 times odds of acquiring HIV (95% CI 4.68-14.33) than those who had non-LGV chlamydia infections.[14] Although the LGV investigation conducted in response to the outbreak in NSW in 2010 was limited by its sample size and the poor response rate, it found 18 (82%) out of 22 LGV cases (from a total of 88 notifications) were HIV-positive.[6] In the UK, of the 434 confirmed LGV cases in 2014, 312 (74%) were HIV-positive, of which 313 (98%) were diagnosed with HIV before or at the same time as their LGV diagnosis.[24] Some biological association between HIV positivity and LGV infection has been suggested, but needs further research. Serosorting amongst HIV-positive MSM with high-risk sexual behaviours might contribute to high HIV prevalence amongst LGV positive persons.[14] However, the introduction of HIV prevention strategies such as PrEP may influence partner selection and risk behaviours based on a person's HIV status. In our study, despite the small numbers, the presence of LGV infection amongst HIV-negative people may indicate changing epidemiology. A meta-analysis showed the introduction of PrEP might have led to unintended increase in other STIs including chlamydia, gonorrhoea and syphilis in MSM using PrEP compared to those not using PrEP.[25] Similarly, increased notifications of STIs including LGV is most likely due to a combination of factors including reduced condom use and increased number of sexual partners among PrEP users. It is also likely to be influenced by increased detection of STIs in high-risk MSM who are HIV-negative and are on PrEP, who may not have previously sought quarterly clinical care or STI screening.

The investigation of laboratory data suggested that the number of specimens tested for LGV during 2016 was 1.5 times higher than in 2015, but the percentage positivity remained the same (~9%). Given that most labs do not routinely refer all chlamydia positive rectal specimens for LGV testing and all of the survey respondents were symptomatic, it is unlikely the reported

increase in LGV was associated with increased sexual health screening amongst MSM but may have been a real increase.

Our data do not provide any conclusive evidence on what may have led to the increase in LGV notifications, but it highlights the need for further public health investigation to inform future prevention and control strategies. We identified numerous reasons that are likely to have resulted in an overall low response rate. Key challenges and lessons learned are described below, so as to improve future outbreak investigations and public health response.

Challenges in designing the investigative approach

At the beginning of the investigation period, we explored several alternative approaches to conducting this investigation. The first of these was linking of LGV notification data with HIV notification data through the NSW Health's Communicable Diseases Register (CDR), maintained by the Centre for Epidemiology and Evidence, with the aim of identifying the proportion of LGV cases with diagnosed HIV infection. However, the data linkage could not be completed in the required time frame. Data linkage would provide de-identified data on HIV status of the 2016 LGV cases but would not have provided information on PrEP use or symptomatology in LGV patients.

We also explored whether diagnosing clinicians could be interviewed, as was done during the 2010 investigation.[6] As discussed above, due to the HIV privacy provision in the Act,[19] treating doctors would have been unable to disclose the HIV status of their patients, as only the cases can be directly questioned about their HIV status. In addition, PHUs indicated that it is difficult to engage with busy doctors, therefore requesting data from doctors might not be efficient, and would not align with the timelines of this investigation. We considered other methods to collect de-identified patient data, but due to the small number of LGV cases, ethics approval requirements and time limitations, these alternative approaches were not deemed practical. We were unable to identify a suitable alternative approach to the investigation, so in consultation with collaborators and stakeholders, a retrospective case series of all LGV cases was considered the most suitable study design. Considering the delays in designing a study and lack of clarity around acceptable public health investigation supports the need for review of STI outbreak investigation processes.

Challenges in conducting the investigation

Two key reasons are likely to have resulted in the overall poor response rate of 15%; 1) this investigation was conducted retrospectively for cases diagnosed in 2016 and in early 2017. Therefore people may perceive this as a 'research study' rather than a public health

investigation and are less likely to be motivated to participate. 2) Limited/ delayed information provided by health service providers, that was required to conduct this public health investigation. Of the 66 cases, we administered the survey to all 20 (30%) patients who agreed to be contacted. Nine patients were contacted by their doctor, but did not agree to be contacted by Health Protection NSW. We could not contact the remaining LGV cases as phone or email contact details were not available. Similar obstacles were experienced by PHU staff during the NSW 2010 LGV outbreak, wherein permission to contact patients directly was obtained for only 30 out of the 67 LGV cases (45%). Despite being conducted prospectively, of the 30 cases, 22 (73%) were successfully interviewed by the PHUs resulting in an overall response rate of 25%.[6]

At present, notification forms do not contain a field for mobile phone numbers, and hence providing that information is not mandatory for disease notification. As a result, NCIMS does not contain patients' phone or email contact details. Although postal address is required for disease notification, and under the Act, could have been obtained from the health services, sending letters via post would not have been ideal for timely public health response. Further this was not considered practical as people may no longer reside at their reported address.

During our investigation, we had to request health services to provide patients' mobile phone numbers. As reporting mobile phone numbers is not required as part of the notification process, health services were required to seek permission from their patient to provide their contact details to the health authorities. While the latter is applicable to most other notifiable conditions, obtaining mobile phone numbers of patients from doctors is usually not as prohibitive. The process of contacting patients is time consuming and onerous for already busy diagnosing doctors/ health services, resulting in non-provision of information and delays in timely public health response. This may also impact the doctor-patient relationship, which in the context of STIs can be particularly sensitive in nature.

If the notification process included reporting mobile phone numbers, public health authorities would not have to rely on health services for obtaining patients' contact details. In order to not adversely impact the relationship between a doctor and their patient, doctor's assent to contact their patient would still be recommended, but would not be a limiting a factor. As per the Act, this would allow public health authorities to directly contact the patient and seek information on risk factors, improving the timeliness of the public health response.

The above issues could be avoided if the Act was modified to provide an exemption that allowed diagnosing clinicians to disclose the HIV status of patient with a notifiable condition.

Such an exemption could only be authorised by the Chief Health Officer or NSW Health Secretary, during public health emergencies. If the above was permitted, then in instances such as the LGV outbreak, Health Protection NSW could obtain information on a patient's HIV status along with symptomatology and key risk factors, directly from the diagnosing doctor. This would then eliminate the need for Health Protection NSW to contact the patient.

It is also important to acknowledge the personal and sensitive nature of information sought in an STI investigation, which may have influenced the overall response rate. For example, a patient may not feel comfortable sharing the sex of their partners, the number of sexual partners, history of other STIs, HIV status etc.; particularly with public health authorities who are perceived as the 'government'. Although important for public health practice and permitted under the Act, requesting risk factor information from doctors might be perceived as breaching patient confidentiality and trust. This is in contrast to other outbreak investigations such as for gastroenteritis, where patients and doctors might be comfortable and motivated to provide information of dining venues or history of foods consumed, that can then help identify the source of the outbreak.

In order to minimise any further delays to the public health investigation that had already been delayed because of the time taken to consider the most feasible approach and consult with stakeholders, the survey was not piloted. The wording around some questions could have been improved, for example, we asked reasons for visiting the doctor if the participant was asymptomatic (Question 6.25). In retrospect, we should have asked reasons for visiting the doctor irrespective of the symptoms. We also identified technical issues with the survey design as this was the first time an electronic questionnaire was designed in NCIMS. The NCIMS online survey was not easy to design and was not very intuitive or interactive. For instance, we were unable to provide links to LGV fact sheets and sexual health information for those accessing the survey. We used electronic surveys in preference to phone interviews, as STI research suggests people are more likely to respond and provide more accurate data using electronic surveys.[26, 27] In our study, three participants completed the survey after receiving a reminder via a phone call. While electronic surveys might be preferred, people may forget receiving a text message resulting in poor response rate. Some of the survey non-responders accessed the survey but did not complete it, and may have later forgotten receiving the text. Furthermore the text messages/emails containing the survey link were accompanied by a generic NSW Health template and not a personalised message, which may have impacted the response rate. For future investigations, the current electronic survey should be re-designed using sophisticated platforms, which are easy to use, affordable and allow secure data storage (for

example Red Cap, Qualtrics and Secure Data Kit). In order to minimise the workload on public health professionals, automated but personalised reminders could be utilised.

Issues with LGV surveillance

As was identified during the first month of this investigation, surveillance for LGV was sub-optimal with 17 LGV cases diagnosed in 2015 misclassified on NCIMS as non-LGV chlamydia. In 2016, epidemiologists from Health Protection NSW coordinated the data entry process with CIDM and the PHUs to ensure all LGV notifications were entered into NCIMS. The laboratory testing patterns for LGV in 2014 were not clear, i.e. we were unable to exactly determine if some laboratories were routinely referring all chlamydia positive rectal specimens to CIDM for LGV testing. Prior to 2014, SEALS also conducted diagnostic testing for LGV. Collating the data for previous years was beyond the scope of this investigation. As a result, we were unable to validate the data prior to 2015.

These inaccuracies in reporting highlight the need for a standardised operating procedure for LGV surveillance. The protocol should identify reporting requirements for all those contributing to the surveillance system, including clinicians, public health laboratories and surveillance officers. A formal evaluation of the LGV surveillance system would be beneficial, and will help identify simple strategies for improved surveillance.

Testing guidelines

Current STIGMA guidelines do not recommend LGV testing as part of routine sexual screening or for asymptomatic cases.[28] During our investigation, we identified one asymptomatic case. During an outbreak investigation of LGV in Michigan USA, proctitis was found in 50% of LGV cases.[10] In a UK-based study, LGV was asymptomatic in 27% of cases, which included rectal, urethral and pharyngeal infections.[4] Asymptomatic carriage of LGV serovars has been observed in other industrialised countries including the Netherlands.[29, 30] Introducing LGV testing as part of routine STI screening might not be cost-effective, but detecting asymptomatic infection, particularly rectal infection may be warranted to prevent onward transmission. This is especially important as two of our cases reported being bisexual and one case was reported asymptomatic by their doctor.

Case definition

The current NSW Health case definition requires *Chlamydia trachomatis* serovars L1 to L3 in fluid aspirated from a fluctuant bubo or from a genital lesion.[21] The current case definition doesn't include rectal LGV and should be revised such that a confirmed case is laboratory

definitive evidence of *Chlamydia trachomatis* serovars L1 to L3 irrespective of the site of specimen collection.

Conclusions and future directions

The increase in LGV is most likely due to a combination of factors including increased use of PrEP, reduced condom use, increased numbers of sexual partners, and increases in other high-risk sexual behaviour. These risk factors are not mutually exclusive and have all been associated with increases in bacterial STIs globally.[14] Although the number of LGV notifications in 2017 has reduced, it continues to be higher than the numbers in 2014. Enhanced surveillance is critical to understand the risk factors and PrEP use amongst LGV cases. Determining the prevalence of asymptomatic LGV is important to understand the transmission dynamics and prevent ongoing transmission. LGV testing could be included in routine STI screening but will still require follow-up of laboratory notifications to obtain information on symptomatology. For the 2016 outbreak, whole genome sequencing (WGS) could be explored to identify any epidemiologically linked cases in order to better understand transmission of LGV in NSW, and differentiate locally and overseas acquired cases. WGS is increasingly utilised to identify epidemiological links between cases of foodborne illnesses and other communicable diseases such as Legionnaires' disease and tuberculosis, and could be useful for LGV.

Our experience should be communicated to other states and territories, especially where PrEP has been introduced, so timely public health response, health promotion messages around condom use and safe sex practices can be bolstered. For example, in Queensland, as of September 2017, 15 LGV notifications were received compared to the 2012-2016 year to date mean of 3.9.[31] The Queensland PrEP study (QPrEPd) has enrolled 800 participants. In Victoria, where another large PrEP trial (VicPrEP) is currently underway, LGV is not notifiable as a separate condition, and is only captured under chlamydia notifications. As LGV is not nationally notifiable, there are no standardised national guidelines for monitoring and responding to LGV. With travel and movement amongst MSM populations, spread of LGV is highly likely.

As LGV re-emerges as a disease of public health importance, improving preparedness for future STI outbreaks should be prioritised. In contrast to other transmissible communicable diseases, LGV affects a small number of people with high-risk sexual behaviour; however LGV holds the potential of causing a wide-spread outbreak amongst MSM, as has been observed in the UK and in parts of Europe.[24, 32] A multi-country evaluation of the European Surveillance of Sexually Transmitted Infections Network demonstrated varied levels of preparedness for responding to

STI outbreaks, and little experience was noted with managing STI outbreaks compared to threats like avian flu, SARS, or bioterrorism.[33] In addition to a standardised approach to surveillance and outbreak management, collaboration between public health authorities and health services, strategies for prompt treatment and continued promotion of safer sexual behaviour are needed. Finally, if we want to reduce the community-wide prevalence of STIs, we must continue to work towards reducing the stigma associated with being diagnosed with HIV or other STIs.

Recommendations for improving public health response to LGV in NSW

1. Revise current case definition for LGV.

2. Strengthen the existing LGV surveillance system by developing and implementing standard operating procedures. Standard operating procedures must indicate operational process and required actions for all those contributing to the LGV surveillance process.

3. Determine the prevalence of asymptomatic LGV infection. This will also assist with developing appropriate testing (STIGMA) guidelines.

4. Revise the NSW Health LGV control guidelines, and develop a preparedness plan for future LGV outbreaks, particularly in relation to identifying an investigative approach that can be implemented rapidly.

5. Consider enhanced surveillance using simple electronic tools so as to minimise the workload on staff in public health units. Enhanced surveillance will help understand the transmission of LGV, asymptomatic infection and risk factors associated with increased LGV; and assist with timely outbreak investigations.

Acknowledgements

We would like to thank all study participants who completed the LGV survey. Sincere thanks to health service providers who assisted us with this investigation.

References

1. White JA. Manifestations and management of lymphogranuloma venereum. *Current opinion in infectious diseases*. 2009; 22: 57-66.
2. Division of STD Prevention. Centres for Diseases Control and Prevention. Lymphogranuloma venereum (LGV). Accessed 21 September 2017.https://www.cdc.gov/std/tg2015/lgv.htm.
3. Stoner BP and Cohen SE. Lymphogranuloma Venereum 2015: Clinical Presentation, Diagnosis, and Treatment. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2015; 61 Suppl 8: S865-73.
4. Saxon C, Hughes G, Ison C and for the UKLGVC-FG. Asymptomatic Lymphogranuloma Venereum in Men who Have Sex with Men, United Kingdom. *Emerging infectious diseases*. 2016; 22: 112-6.
5. Ceovic R and Gulin SJ. Lymphogranuloma venereum: diagnostic and treatment challenges. *Infect Drug Resist*. 2015; 8: 39-47.
6. Templeton DJ, Ressler KA, Hope K and Poynten IM. Enhanced surveillance of a lymphogranuloma venereum outbreak in Sydney 2010-2012. *Australian and New Zealand journal of public health*. 2016; 40: 368-70.
7. Peuchant O, Touati A, Sperandio C, et al. Changing Pattern of Chlamydia trachomatis Strains in Lymphogranuloma Venereum Outbreak, France, 2010-2015. *Emerging infectious diseases*. 2016; 22: 1945-7.
8. Nieuwenhuis RF, Ossewaarde JM, Götz HM, et al. Resurgence of Lymphogranuloma Venereum in Western Europe: An Outbreak of Chlamydia trachomatis Serovar L2 Proctitis in The Netherlands among Men Who Have Sex with Men. *Clinical Infectious Diseases*. 2004; 39: 996-1003.
9. Petrovay F, Balla E and Erdosi T. Emergence of the lymphogranuloma venereum L2c genovariant, Hungary, 2012 to 2016. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*. 2017; 22.
10. de Voux A, Kent JB, Macomber K, et al. Notes from the Field: Cluster of Lymphogranuloma Venereum Cases Among Men Who Have Sex with Men - Michigan, August 2015-April 2016. *MMWR Morbidity and mortality weekly report*. 2016; 65: 920-1.
11. Hughes G, Alexander S and Simms I. Exponential growth of lymphogranuloma venereum diagnosis in the UK: investigation of the largest documented outbreak among men who have sex with men. *Sex Transm Infect*. 2011; 87.
12. Hughes G, Alexander S, Simms I, et al. Lymphogranuloma venereum diagnoses among men who have sex with men in the U.K.: interpreting a cross-sectional study using an epidemic phase-specific framework. *Sex Transm Infect*. 2013; 89: 542-7.
13. Macdonald N, Sullivan AK, French P, et al. Risk factors for rectal lymphogranuloma venereum in gay men: results of a multicentre case-control study in the UK. *Sexually Transmitted Infections*. 2014.
14. Ronn MM and Ward H. The association between lymphogranuloma venereum and HIV among men who have sex with men: systematic review and meta-analysis. *BMC Infect Dis*. 2011; 11: 70.
15. Latini A, Zaccarelli M, Paglia MG, et al. Inguinal and anorectal Lymphogranuloma Venereum: a case series from a sexually transmitted disease center in Rome, Italy. *BMC Infectious Diseases*. 2017; 17: 386.
16. Templeton DJ, Sharp N, Gryllis S, O'Connor CC and Dubedat SM. Prevalence and predictors of lymphogranuloma venereum among men who have sex with men at a Sydney metropolitan sexual health clinic. *Sexual health*. 2013; 10: 190-1.
17. NSW Ministry of Health. Communicable Diseases Weekly Report - Week 1, January 2017. 2017.

18. NSW Ministry of Health. Lyphogranuloma venereum (LGV) Alert. 2017. Accessed 9 August 2017.http://www.health.nsw.gov.au/Infectious/alerts/Documents/LGV-alert-jan-2017.pdf.
19. New South Wales Legislation. NSW Public Health Legislation. 2010. Accessed 21 September 2017.http://www.health.nsw.gov.au/phact/Pages/default.aspx.
20. Templeton DJ, Grulich AE, Yew J, et al. Lymphogranuloma venereum is rare in Australian community-based samples of men who have sex with men. *Sex Transm Dis*. 2011; 38: 48-9.
21. New South Wales Health. Lymphgranuloma Venereum control guidelines. *Control Guidelines*. 2014. Accessed 12 October 2017.http://www.health.nsw.gov.au/Infectious/controlguideline/Pages/lymphogranuloma.aspx.
22. Schaeffer A and Henrich B. Rapid detection of Chlamydia trachomatis and typing of the Lymphogranuloma venereum associated L-Serovars by TaqMan PCR. *BMC Infect Dis*. 2008; 8: 56.
23. Holt M, Mao L, Prestage G, Zablotska I and de Wit J. Gay Community Periodic Surveys: National Report 2010. . Sydney: National Centre in HIV Social Research, The University of New South Wales. , 2011.https://csrh.arts.unsw.edu.au/media/CSRHFile/GCPS_2010_National_report.pdf
24. Childs T, Simms I, Alexander S, Eastick K, Hughes G and Field N. Rapid increase in lymphogranuloma venereum in men who have sex with men, United Kingdom, 2003 to September 2015. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*. 2015; 20: 30076.
25. Kojima N, Davey DJ and Klausner JD. Pre-exposure prophylaxis for HIV infection and new sexually transmitted infections among men who have sex with men. *AIDS*. 2016; 30: 2251-2.
26. Gold J, Lim MS, Hocking JS, Keogh LA, Spelman T and Hellard ME. Determining the impact of text messaging for sexual health promotion to young people. *Sex Transm Dis*. 2011; 38: 247-52.
27. Hensel DJ, Fortenberry JD, Harezlak J and Craig D. The feasibility of cell phone based electronic diaries for STI/HIV research. *BMC medical research methodology*. 2012; 12: 75.
28. Australian Sexual Health Alliance. Australian STI Management Guidelines. The Australian Government Department of Health. Accessed 9 August 2017.http://www.sti.guidelines.org.au/sexually-transmissible-infections/lgv#cause.
29. Annan NT, Sullivan AK, Nori A, et al. Rectal chlamydia--a reservoir of undiagnosed infection in men who have sex with men. *Sex Transm Infect*. 2009; 85: 176-9.
30. Spaargaren J, Fennema HS, Morre SA, de Vries HJ and Coutinho RA. New lymphogranuloma venereum Chlamydia trachomatis variant, Amsterdam. *Emerging infectious diseases*. 2005; 11: 1090-2.
31. Queensland Health. Notifiable Conditions Weekly Totals. 2017. Accessed 18 September 2017.https://www.health.qld.gov.au/clinical-practice/guidelines-procedures/diseases-infection/surveillance/reports/notifiable/weekly.
32. European Centre for Disease Prevention and Control. Lymphogranuloma venereum - Annual Epidemiological Report 2016 [2014 data]. In: ECDC, (ed.). Stockholm, 2016. Accessed 19 September 2017.http://ecdc.europa.eu/en/healthtopics/chlamydia/lymphogranulomavenereum/Pages/AnnualEpidemiologicalReport2016.aspx.
33. Timen A, Hulscher ME, Vos D, et al. Control measures used during lymphogranuloma venereum outbreak, Europe. *Emerging infectious diseases*. 2008; 14: 573-8.

Chapter 4: Public health surveillance system establishment and evaluation

An evaluation of an early warning alert and response system (EWARS in a Box) implemented after Cyclone Winston, Fiji 2016

Prologue

My role

In April-May 2016, I was deployed as an epidemiologist with the Global Outbreak Alert and Response Network (GOARN) and the World Health Organization (WHO) Division of Pacific Technical Support (DPS) to provide technical support to the Fiji Centre for Communicable Diseases Control (FCCDC). With the help of WHO DPS, the Fiji Ministry of Health and Medical Services (MoHMS) implemented Early Warning, Alert and Response System EWARS in a Box and was an up-scaled version of the Fiji Syndromic Surveillance System. This was the first ever implementation of the system in a Pacific Island Country. EWARS in a Box (hereafter referred to as EWARS) is an automated 'field-ready' kit that includes the hardware and software required for rapid deployment of surveillance systems.

My primary responsibility was to support surveillance following Tropical Cyclone Winston. With the help of my supervisors, I proposed an evaluation of EWARS in a box. The evaluation was conducted in collaboration with Julie Collins (MAE Scholar at Hunter New England Population Health Unit), who arrived two weeks later.

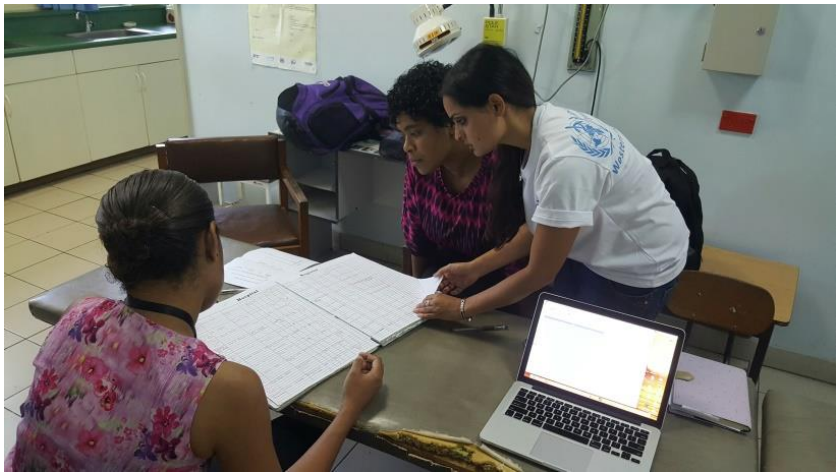
The MMWR guidelines on Evaluating Public Health Surveillance Systems have limited applicability for evaluating surveillance systems in developing countries particularly during humanitarian emergencies. Keeping this in mind, I designed the evaluation framework based on the MMWR guidelines as well as previously published evaluations of the Pacific and Fiji Syndromic Surveillance Systems, WHO guidelines on surveillance in health emergencies and the guidelines developed by European Centre for Disease Control. A final report containing evaluation outcomes and recommendations both for Fiji and for improvement of EWARS system were submitted to the Fiji MoHMS in July 2016.

Specifically, I drafted an initial evaluation proposal containing a framework for evaluating EWARS. I described the system and the surveillance process. I conducted stakeholder interviews, and evaluated timeliness, completeness, stability, representativeness, costs and Event Based Surveillance. Ms Julie Collins designed a cross-sectional survey of the focal points at health facilities and the surveillance officers; and evaluated some of the key attributes associated with the system experience (acceptability, usefulness, flexibility, data validity and simplicity). I led the drafting of the final report and collated comments from the Australian collaborators. I have compiled the key findings from the evaluation into a manuscript. Feedback

on an early draft was provided by Dr Eric Nilles. The manuscript is enclosed in the main body of this chapter along with the final report submitted to the Fiji MoHMS (Appendix 4A).

Ms Mere Taufa, Ms Julie Collins and Dr James Flint (left to right) conducting review of clinic registers during EWARS site visit, Fiji, May 2016

In addition to conducting EWARS related surveillance and the evaluation, I supported other surveillance activities, and assisted with an outbreak investigation of severe acute respiratory infection (SARI). My contributions to this work are summarised in Chapter 1.



EWARS surveillance officers, Ms Mere Taufa and Ms Emi Colaimima along with DR Meru Sheel, reviewing paediatric ICU registers, CWM Hospital, Fiji, May 2016

Lessons learned

Overall, this was a great opportunity where I learned about disease surveillance in a developing country following a natural disaster. The experience offered professional growth in several aspects including leadership, politics of public health and the role of diplomacy when working with national health authorities. I learned about navigating difficult situations in the field, managing personality clashes and keeping calm even when overworked and sleep deprived.

Some of my key professional lessons learned are summarised below:

1. Politicised nature of public health and its implication on public health activities: one of the first things that I learned was the political nature of public health, which often requires a strategic approach and diplomacy skills. For example, planning EWARS evaluation, in theory, sounded simple but I soon realised that going into another country, and suggesting an evaluation is not that straightforward. Even though WHO DPS was supportive, for the MoHMS an evaluation appeared like something might be 'wrong'. For that reason, it was important to identify the rationale and usefulness of the evaluation for Fiji MoHMS. I identified the needs of the MoHMS and the National Advisor for Communicable Diseases (Dr Mike Kama), and suggested the outcomes that would improve future implementation of EWARS in Fiji and globally. At meetings, I referred to the proposal as an assessment rather than an 'evaluation'. Slight change in approach and highlighting the benefits of an 'assessment' led to the National Advisor permitting the study as a joint collaboration between FCCDC and WHO DPS.

2. Leadership in public health is vital: I was sent on this mission within the first six weeks of the MAE. While I had previously worked in some challenging environments, this experience was very different, and initially I felt like a novice (imposter syndrome perhaps!). After arriving in Fiji, it was clear that if I was to conduct the evaluation, I was going to have to take charge and make it happen. I learned engaging everyone is crucial and can be highly beneficial (albeit creates more work, but is worthwhile!). I established an evaluation working party (based on the National Advisor's recommendations) and a project steering group. I designed the framework based on feedback received from members of the working party and the surveillance team. Some of the members were also involved in the governance and implementation of EWARS, and provided insight into some of the issues, and preempted some of the problems that we might encounter. The National Advisor was very supportive and provided leadership in conducting this evaluation. He directed his team to assist us with field visits and interviews, and his support set an example of effective public health leadership. Overall, it was clear that in-country

partners had the best working knowledge of the health systems, and working in collaboration was essential to navigate difficult channels and conduct the evaluation effectively.

Public health impact

1. At the request of the National Advisor for Communicable Diseases, preliminary findings and recommendations were presented at a meeting hosted by the MoHMS on 27 May 2016. The meeting was held at the WHO DPS office in Suva, Fiji and was attended by EWARS surveillance officers, MoHMS members and EWARS teams from Central, Western and Northern division. Prof John Aaskov (Queensland University of Technology) and Prof Kim Mullohand (Murdoch Children's Research Institute) were also present at the request of Dr Mike Kama. Both Prof Aaskov and Prof Mullohand are global health experts, and were delighted to learn about the potential of EWARS, and its potential to overcome some of the common challenges experienced by surveillance systems during humanitarian emergencies.

2. The final evaluation report was submitted to the MoHMS and WHO DPS in August 2016. The report contained recommendations that would enable Fiji to integrate EWARS into routine surveillance, and that would strengthen surveillance if the system was re-activated during another natural disaster. EWARS-specific recommendations were also provided to WHO DPS and WHO Geneva for system-specific improvements. Fiji MoHMS continues to use EWARS for routine surveillance, and the EWARS platform has been expanded to support the Pacific Syndromic Surveillance System. Based on these recommendations, several modifications have been made to improve the performance of EWARS, surveillance continues and EWARS has now been adopted into routine surveillance activities.

3. One of the incidental findings of the evaluation highlighted the contribution of the EWARS surveillance officers during the post-disaster surveillance process. The surveillance officers were critical in ensuring timely reporting and follow-up of alerts. Following our recommendations, the surveillance officers' continue to be employed and support surveillance through EWARS. The evaluation also demonstrated the capacity building offered by the in-coming WHO epidemiologists and recommendations were made for FCCDC to employ full-time epidemiologists.

4. In order to share the lessons learned with the global health community and public health practitioners working in humanitarian emergencies, I have adapted the final report into a manuscript.

Acknowledgements

There are many people who I would like to acknowledge for my wonderful experience and the success of this project. Firstly, thank you to all those have been listed as co-authors on the manuscript, and members of the EWARS working party. Thank you for your support and feedback.

In specific, I would like to thank Ms Julie Collins (fellow MAE, Hunter New England Population Health Unit) for sharing the Fiji experience and for collaborating on the evaluation; Dr Eric Nilles (Epidemiologist Emergency Surveillance and Response, WHO DPS) for his guidance and wisdom, offering great learning opportunities and for making the entire experience fun – I hope we continue to collaborate long term; Dr Angela Merianos (Team Leader, WHO DPS) for providing leadership and for the critical and honest feedback; Mr James Flint (Epidemiologist, Hunter New England Population Health) for his supervision and the calm presence during our deployment in Fiji. James assisted with the evaluation and led the case finding for the paediatric SARI investigation; Associate Professor Martyn Kirk (MAE academic supervisor) for encouraging me to persevere and complete the evaluation process; Dr Mike Kama (National Advisor, FCCDC) for the warm welcome, providing leadership, generosity and support with undertaking this evaluation; Dr Daniel Faktaufan (Senior Medical Officer, FCCDC) for his support in undertaking this evaluation, organising site visits and a fabulous Fiji style yum cha experience; Dr Devina Nand (Epidemiologist, MoHMS) for the warm welcome, support and guidance in jumping loop holes within MoHMS and Dr Christopher Haskew (Epidemiologist, WHO Geneva) for his sustained interest in the evaluation and for the technical support in undertaking this evaluation.

My sincere thanks to EWARS surveillance officers including Dr Sam Fullman (Event Based Surveillance), Mr Isireli Rabukawaqa (National), Ms Mere Taufa (Central Division), Ms Emi Colaimima (Eastern Division) for their hard work with EWARS and the evaluation.

All other WHO colleagues and friends including Dr Viema Biaukula, Mr Mark Jackson, Mr Peter Vanquaille, Mr Paul Jaskierniak, Ms Temalesi Vakaotia, Ms Losalini Vakasavuwaqa for all their assistance and for all the laughs! I hope to cross-paths with all of you again!

An evaluation of an early warning alert and response system (EWARS in a Box) implemented after Cyclone Winston, Fiji 2016

Abstract

Background: In February 2016, after Cyclone Winston affected Fiji, public health assessments recognised several epidemic-prone diseases capable of causing outbreaks. As part of the World Health Organization's core commitments an early warning and alert response system for outbreak detection was implemented two weeks after the cyclone. The system, EWARS in a Box (EWARS) is a smartphone-based automated system consisting of hardware and software required for rapid deployment during health emergencies. Fiji EWARS consisted of Indicator-based Surveillance (IBS) and Event-based Surveillance (EBS). We evaluated the system's performance during the post-disaster period of epidemiological weeks 10-21, with the aim of providing practical recommendations for future use.

Methods: We conducted semi-structured stakeholder interviews and a cross-sectional survey of focal points at EWARS sites and surveillance officers to assess their experience of the system. We extracted data from the EWARS database to assess the system's performance during the study period.

Findings: EWARS-IBS recorded 34 113 cases for the nine syndromes under surveillance from 326 861 total consultations. Four confirmed outbreaks were detected through EWARS-EBS. Automated processes for collation, analysis and dissemination of data reduced the burden on surveillance teams and subsequently saved human resources, minimised human error and ensured EWARS surveillance teams focused on public health response. EWARS was acceptable by public health practitioners, and was perceived to be useful for timely monitoring of diseases trends and outbreak detection. The system was simple, stable and flexible meeting the core criteria for rapid deployment during health emergencies.

Conclusions: EWARS provides ready tools for standardised implementation and reporting of post-disaster early warning surveillance; and can improve the detection of outbreaks while minimising the reporting burden on the public health system.

Introduction

Humanitarian emergencies including conflicts and natural disasters increase the risk of communicable disease outbreaks. Effective and timely surveillance and response measures can mitigate risks,[1] but public health systems are frequently disrupted during humanitarian emergencies, particularly in developing countries where existing surveillance systems are fragile.[2] Early Warning and Alert Response Networks (EWARN) were designed to enhance surveillance and response capacities during complex humanitarian emergencies or after major disasters.

Acknowledging the importance of robust early warning surveillance and response mechanisms, the World Health Organization (WHO) developed EWARN Guidelines and supported the development and implementation of EWARN systems during humanitarian emergencies in a number of developing countries[3] including the Disease Early Warning System (DEWS) after the 2005 earthquake in Pakistan, Surveillance in Post Extreme Emergencies and Disasters (SPEED) following 2013 Typhoon Haiyan in the Philippines,[4] and after the 2013 tsunami in the Solomon Islands[5] and Cyclone Pam in 2015 in Vanuatu.[6]

Few developing countries have preparedness plans for enhanced surveillance following disasters or other humanitarian emergencies, and therefore most emergency surveillance systems are rapidly developed during crises and lack standardized data collection, management and analysis methods.[4] Further, the collection, analysis and reporting of large volumes of surveillance data is a burden to public health systems that are already struggling to address other urgent priorities.[5, 7-10] To address these challenges, WHO developed a tool kit known as 'EWARS in a Box' (hereafter EWARS) that includes the hardware and software necessary to rapidly deploy an early warning surveillance system during major humanitarian emergencies. EWARS was first implemented in South Sudan in 2015.[11]

In February 2016, Cyclone Winston, one of the most powerful storms recorded in the South Pacific made landfall in Fiji. The storm affected almost 400,000 people, damaged approximately 40,000 homes and displaced nearly 55,000 persons. As part of the public health response, the Fiji Ministry of Health and Medical Services (MoHMS) and WHO conducted a rapid public health risk assessment to identify key public health priorities.[12] The assessment identified multiple factors associated with increased risk of disease transmission and outbreaks including large numbers of displaced persons, overcrowded emergency shelters, limited access to clean water, disruption of hygiene and sanitation infrastructure, and increased potential exposure to mosquitos and other disease vectors. Several epidemic-prone diseases were recognised as moderate to high-risk for causing outbreaks, including leptospirosis, diarrhoea (including dysentery), typhoid, dengue, chikungunya, Zika virus and acute respiratory

infections.[12] Subsequently, the MoHMS with assistance from the WHO, implemented EWARS two weeks after the cyclone.

Prior to Cyclone Winston, Fiji's early-warning disease surveillance – the Fiji Syndromic Surveillance System (FSSS), reported five syndromes (diarrhea, influenza-like illness, prolonged fever, acute fever and rash, and dengue-like illness) on a weekly basis from 12 sentinel health facilities.[13] EWARS was implemented at 34 health facilities that reported nine diseases/syndromes, in addition to reporting *ad hoc* health events. EWARS sites were selected based on population density, proximity to severely affected areas and displaced persons, and access to transport and telecommunication; 11 of the 12 FSSS sites were used as EWARS sites. Figure 1 shows the path of Cyclone Winston, population density in each region and EWARS sites.

In addition to weekly reporting of cases meeting a specific case definitions (indicator-based surveillance or IBS), Fiji EWARS included a component of event-based surveillance (EBS). EBS is the structured reporting of events that may not meet the criteria for reporting through the IBS, but may have important medical and public health implications.[14] For example, a cluster of unusual neurological disease that does not meet any of the pre-specified case definitions or does not exceed a threshold in the IBS system (and therefore would not trigger an alert) may indicate the start of a serious outbreak and would typically be reported through EBS system. With a few exceptions, prior EWARN systems have primarily relied on IBS for the early detection of outbreaks.[14]

As EWARS is a novel concept and continues to evolve based on field-level feedback, we conducted a detailed evaluation of the Fiji EWARS system (Box 1). This paper describes the system's performance in Fiji. We summarize the findings and key lessons learnt (Box 2) with the aim of providing practical insight for improving the system, its implementation and operation for surveillance in humanitarian emergencies.

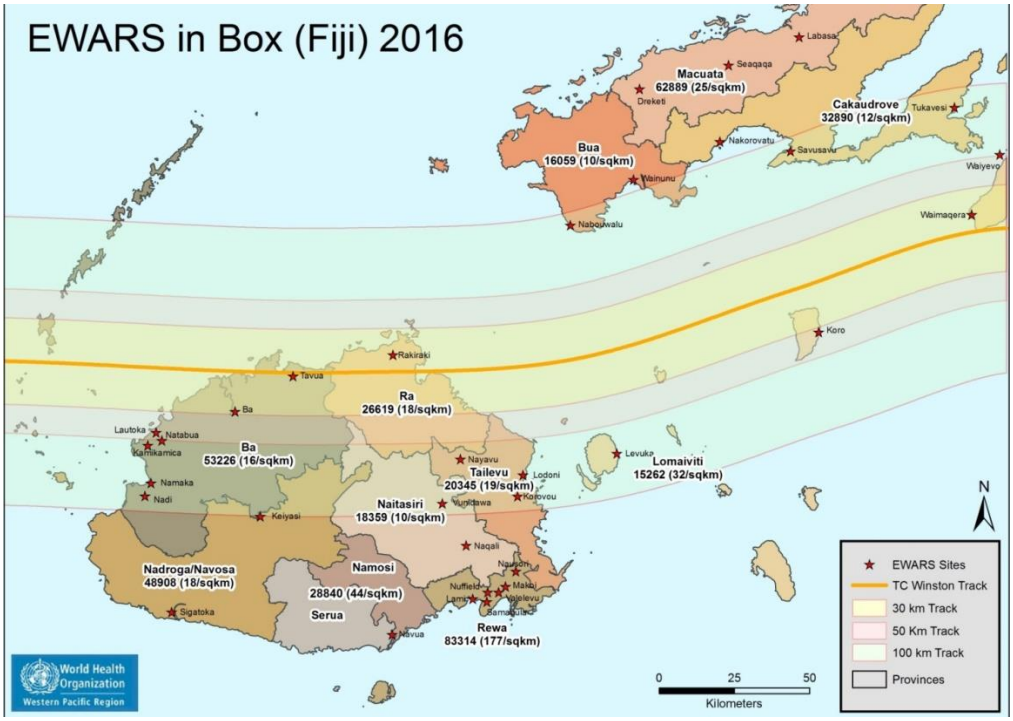


Figure 1: Path of Cyclone Winston, EWARS surveillance sites, total population and population density for each province in Fiji, 2016.[19][20]

[19] Projected population figures for 2016 were provided by the Fiji Ministry of Health and Medical Services (MoHMS), estimated using 2007 census conducted by Fiji Bureau of Statistics and MoHMS divisional boundaries.

[20] Image developed Paul Jaskierniak, World Health Organization Division of the Technical Pacific Support.

Box 1: Evaluation Aims and Objectives

The aim of this evaluation was to assess the overall performance of EWARS in a Box, following Cyclone Winston in Fiji in 2016.

Objectives of the evaluation were:

- Assess the ability of EWARS to monitor communicable diseases trends and signal early warnings for suspected outbreaks of epidemic-prone diseases to generate timely public health action.
- Identify current gaps in disease surveillance under EWARS.
- Assess the utility of data in influencing public health actions.
- Provide recommendations for strengthening of surveillance using EWARS.

Box 2: Key lessons learnt during surveillance using EWARS in a Box following Cyclone Winston in Fiji, 2016

- Improving the use of EWARS weekly bulletin by customizing the layout in a country-specific manner will assist in improved public health response.
- The syndromes under surveillance should be selected based on risk assessments conducted following a disaster. Where possible, thresholds should be set using baseline epidemiological data.
- Event Based Surveillance for outbreak detection, particularly for conditions not captured for Indicator Based Surveillance is encouraged.
- Building sustainable public health workforce and surge capacity, by providing ongoing technical support for focal points at health facilities and surveillance officers is highly recommended. Training should be conducted in 'train the trainer' format. Further emphasis should be laid upon conducting alert verification, understanding surveillance data and outbreak investigations.
- Enhanced crisis leadership during public health emergencies is critical. In order to achieve sustainable surveillance, greater interaction between all those involved in surveillance activities is encouraged.

System description

EWARS is a portable field-ready kit containing mobile phones, laptops, mobile (local) server and solar chargers, enabling the system to be self-powered for approximately 24 hours (http://ewars-project.org/).[11] During implementation, three joint MoHMS/ WHO teams consisting of one MoHMS surveillance officer and one WHO epidemiologist with expertise in EWARS, conducted standardized two-hour training workshops at each EWARS site. Smartphones with EWARS software application were provided to designated surveillance focal points at each EWARS site. Training included background on the importance of early outbreak detection and response, syndromes and diseases under surveillance, case definitions, use of the smartphone and EWARS application (including trouble shooting), and reporting times and protocols. Data could be entered into the EWARS application regardless of connectivity, but transmission to the central EWARS database required mobile or internet connection. Figure 2 describes in detail the operational process flow for EWARS (IBS and EBS).

For IBS, each EWARS site reported age-stratified case counts (<5 years and ≥5 years) weekly against nine syndromes or suspected diseases (acute fever and rash, prolonged fever, influenza-like illness, watery diarrhoea, bloody diarrhoea, acute jaundice syndrome, suspected dengue, suspected meningitis and zika-like illness). Standard case definitions were used (Table 1). Total weekly consultations were reported to determine proportional morbidity. Syndromes were monitored using thresholds that were initially established based on standard thresholds and subsequently calculated using aberration detection algorithms (Table 1).[13] EWARS sites also reported unusual public health events for example clusters of deaths, unusually severe disease, an animal, bird or fish die-off, etc.[14] These EBS events were immediately reported by phone or email to a dedicated surveillance officer, who could be contacted via a toll free number at any time. An "alert" was defined as (i) an increase in cases of a specific syndrome or suspected disease above the threshold for that site or (ii) any event perceived by health care worker at EWARS sites to have potential adverse public health implications and was reported through EBS. EWARS uses automated algorithms to compile and analyse data. If surveillance thresholds were exceeded or EBS reports received, alert verification was initiated and emails to the designated surveillance team members were auto-generated. Weekly epidemiological bulletins were automatically generated and emailed to pre-specified recipients. All data collected as part of EWARS is owned by the national health authorities and is stored in a secure database.

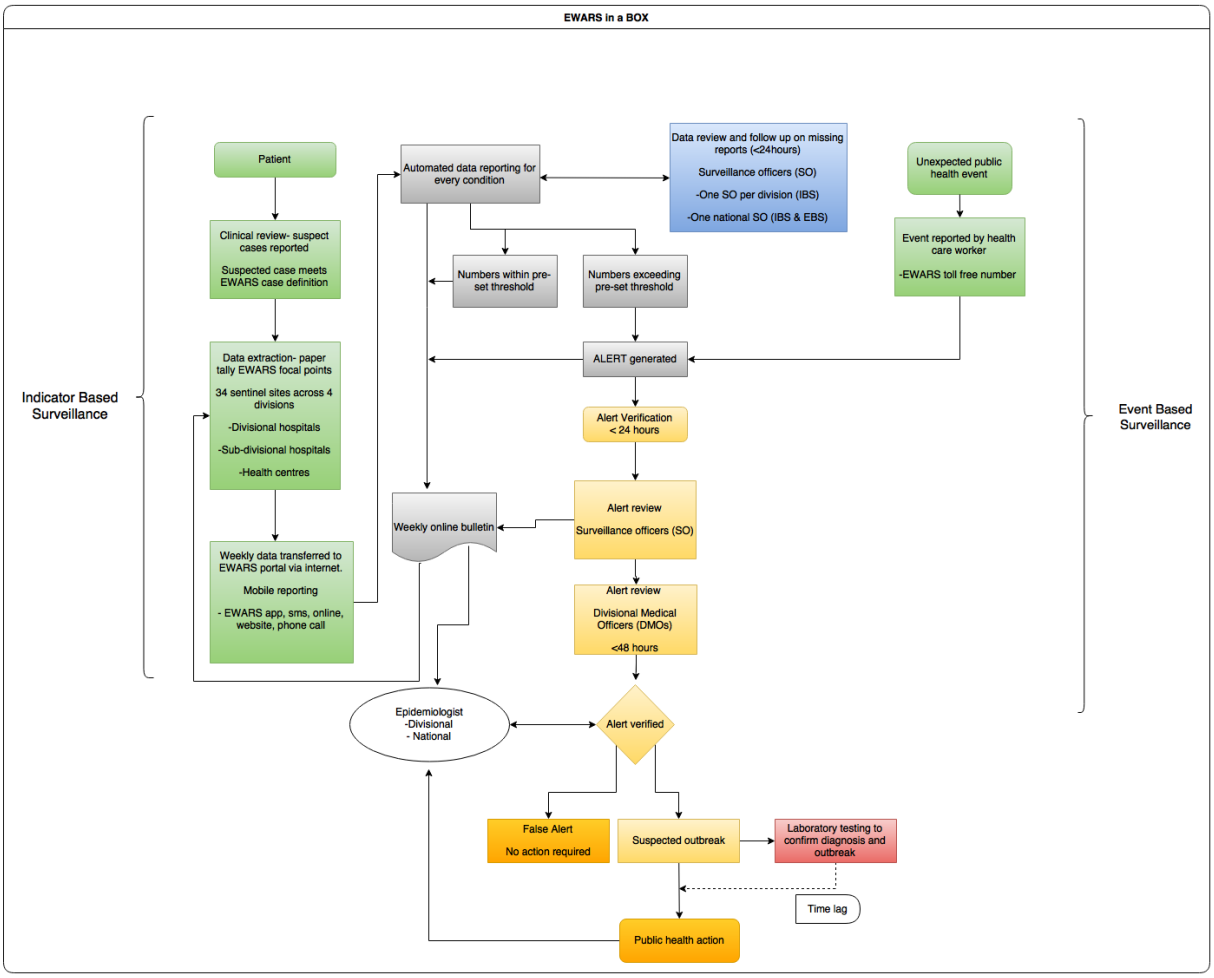


Figure 2: Operational flow of data for EWARS in a Box, Fiji 2016

Table 1: EWARS syndromes, case definitions, thresholds and surveillance outputs, epidemiological weeks 10-21, Fiji.

Syndrome	Case definition	Thresholds	Number of cases	Incidence = cases/ total consultations*100 (%)[21]
Acute fever and rash	Fever either reported or measured (>38°C) plus non-blistering rash	1 case	672	2
Prolonged fever	Any fever either reported or measured (>38°C) lasting three or more days	Twice the average number of cases seen in the previous 2 weeks	1461	4.3
Influenza-like illness	Fever either reported or measured (>38°C) plus cough and/or sore throat.	Twice the average number of cases seen in the previous 2 weeks	16426	48.2
Acute watery diarrhoea	Three or more loose or watery stools in 24hrs (non-bloody).	Twice the average number of cases seen in the previous 2 weeks	10054	29.8
Acute bloody diarrhoea	Any episode of acute bloody diarrhoea	3 cases in one location in 1 week or twice the average number of cases seen in the previous 2 weeks	293	0.7
Acute jaundice syndrome	Jaundice (yellow eyes or dark urine) and severe illness with or without fever.	3 cases	71	0.2
Suspected dengue	Fever for at least 2 days plus at least two of the following symptoms: nausea or vomiting; muscle or joint pain; severe headache or pain behind the eyes rash; bleeding	Twice the average number of cases seen in the previous 3 weeks	4,520	13.3
Suspected meningitis	Sudden onset of fever, plus one or more of the following: severe headache; neck stiffness; altered consciousness; petechial/puerperal rash.	1 case	33	0.1
Zika-like illness*	Generalized maculopapular rash plus two or more of the following: arthralgia or myalgia; red eyes or non-purulent conjunctivitis; oedema of hands or feet; low grade fever (< 38℃); pain behind the eyes	3 cases	583	1.7

[21] Total number of consultations for epidemiological weeks = 326 861

* Zika-like illness was added in during week 13.

Evaluation methodology

We designed an evaluation framework based on previously published evaluation methodologies [15-19] including evaluations of the Pacific Syndromic Surveillance System[13, 20-22], the FSSS and previously outlined EWARN guidelines.[14] Evaluation attributes along with their definitions and data sources are listed in Table 2.

Table 2: Attributes used to evaluate EWARS in a Box, Fiji 2016.

System attributes	Definition	Data sources
Timeliness[22]	Submission of data on time (Monday following week under surveillance)	EWARS database Cross-sectional Survey
Completeness[§]	Submission of data independent of the timeliness (Sunday following week under surveillance)	EWARS database Cross-sectional Survey
Data Validity[§]	Accuracy of data captured by the surveillance system	EWARS database Site visits and retrospective review of clinic records
Usefulness[§]	System's contribution in monitoring diseases trends and early detection of signals that might lead to potential disease clusters or outbreaks	Cross-sectional Survey
Flexibility[§]	Ability to adapt to changing information needs or operating conditions without significant time, staff contribution or funding	Cross-sectional Survey Stakeholder interviews
Simplicity[§]	Ease of operating the surveillance system	Cross-sectional Survey
Acceptability[§]	Willingness of users to participate in the surveillance process including data collection and analysis	Cross-sectional Survey
Stability	Reliability of the system and its resilience to change	EWARS database Cross-sectional Survey
Costs	Expenditure associated with equipment, and the implementation and operation of the system.	Fiji Ministry of Health and Medical Services Fiji Health Sector Support Program WHO Division of the Technical Pacific Support
Representativeness	Geographical appropriateness and coverage	Review of implementation protocol EWARS database Population data, Fiji Ministry of Health and Medical Services Stakeholder interviews

[22] These attributes were restricted to Indicator Based Surveillance.

Study period

EWARS was evaluated for the period coinciding with the National State of Emergency: 7 March 2016 to 29 May 2016 (epidemiological weeks 10 to 21).

Stakeholder engagement

Stakeholders were interviewed using semi-structured questionnaires to examine the significance, strengths and weaknesses of the system. Stakeholders included staff from the MoHMS, WHO headquarters, the WHO Division of Pacific Technical Support (DPS), and the Fiji Health Sector Support Program, i.e. organisations involved in the design and implementation of the system or with an overarching role in the governance and performance of EWARS. Stakeholders also included members from partner organisations including other United Nation agencies and Red Cross Fiji, who were not directly involved but utilised information generated through EWARS.

Data analyses

We reviewed standard operating protocols and documentation used by WHO and MoHMS. System performance was evaluated using data collected via the EWARS database. System experience was evaluated using a cross-sectional survey of EWARS users. "Users" were persons submitting data into the system (focal points or doctors in-charge of the reporting site) and those monitoring the reporting (surveillance officers). Two self-administered online surveys were designed in SurveyMonkey® and distributed via email. All five surveillance officer and 27/34 (79%) of focal points completed the survey. Unless otherwise specified, user survey results presented refer to responses of focal points at EWARS sites and summarised in Supplementary Table 1.

Site visits

We visited 11 EWARS sites across the Northern, Western and Central divisions of Fiji. Site selection was based on access and other logistical considerations. At each site, we reviewed the data collection and reporting processes and clinical records for epidemiological weeks 13 and 17. Data collected from clinic reviews were compared to data extracted from the EWARS database for the same period.

Ethics approval was obtained from the Fiji National Research Ethics Review Committee (2017.86.NW).

Results

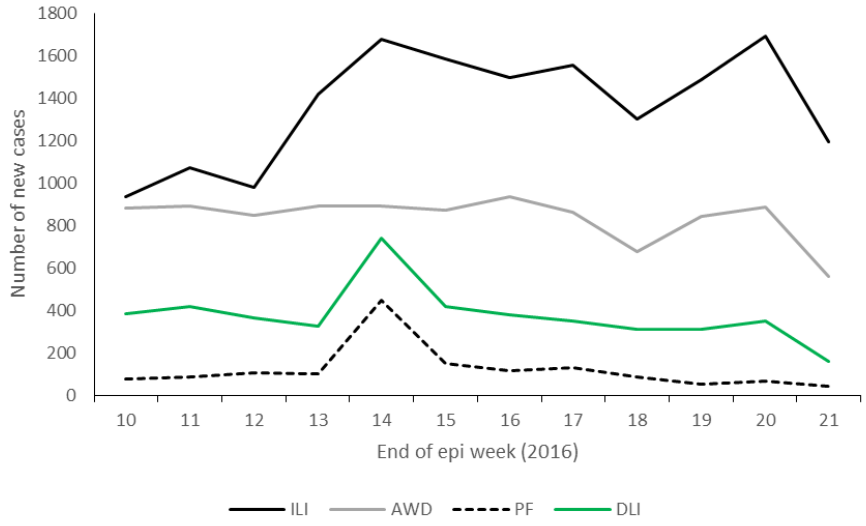
Indicator based surveillance

Surveillance outputs

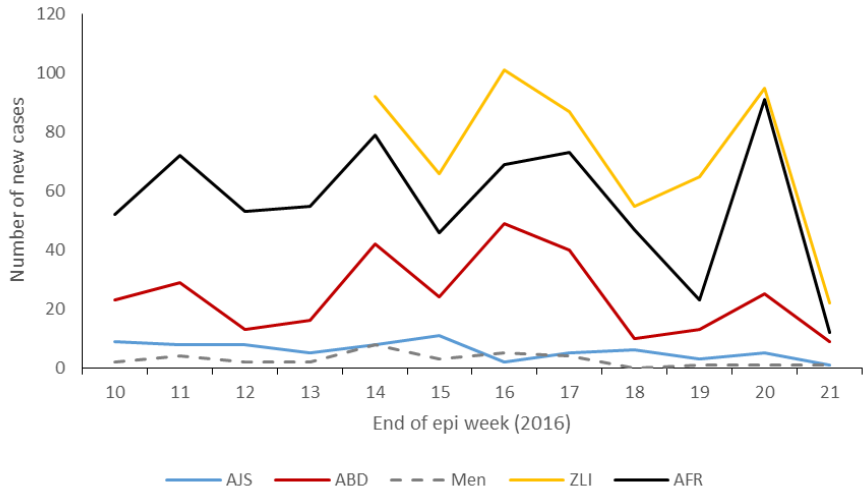
EWARS was implemented in epidemiological week 9 of 2016. Zika-like illness was added in week 13. During epidemiological weeks 10-21, 34 113 cases that met one of the case definitions were reported from 326 861 total consultations (Table 1). Counts and proportional morbidity (number of new cases/total number of weekly consultations) for each syndrome under surveillance are presented in Figure 3. Influenza-like illness (ILI) was the most commonly reported syndrome (48.2%) (Table 1). From epidemiological week 14 we observed increasing trends of ILI. This increase was concomitant with increased laboratory-confirmed influenza cases and cases of severe acute respiratory infections. An outbreak investigation of influenza was initiated by MoHMS with support from WHO DPS.

Except for the outbreak described above, IBS did not detect any major outbreaks. Several small clusters of watery diarrhoea and measles were identified, but weren't always reported back through the EWARS (personal communication with subdivisional medical officer). Stakeholders felt that automated alerts were better at generating an outbreak response at the divisional and sub-divisional levels, compared to previous national emergencies.

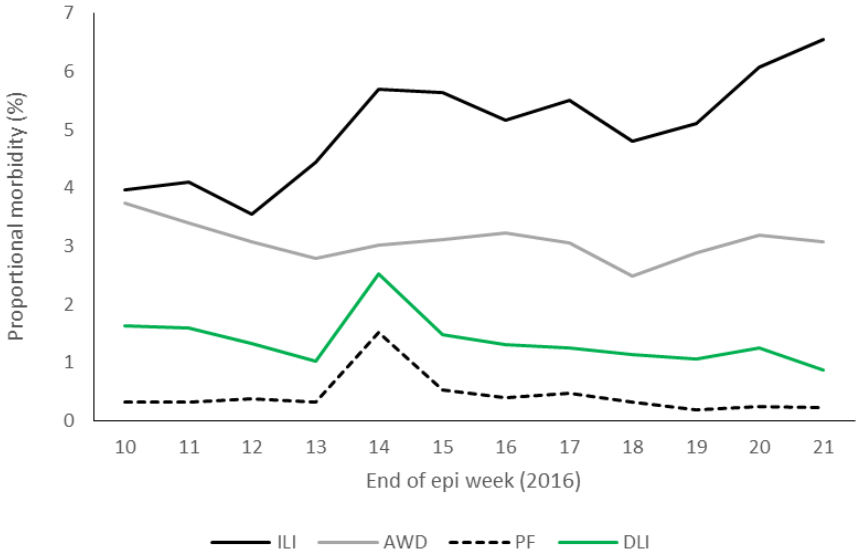
A)


1800
1600
1400
1200
1000
800
600
400
200
0
Number of new cases
10
11
12
13
14
15
16
17
18
19
20
21
End of epi week (2016)
ILI
AWD
PF
DLI

B)


120
100
80
60
40
20
0
Number of new cases
10
11
12
13
14
15
16
17
18
19
20
21
End of epi week (2016)
AJS
ABD
Men
ZLI
AFR

C)



D)

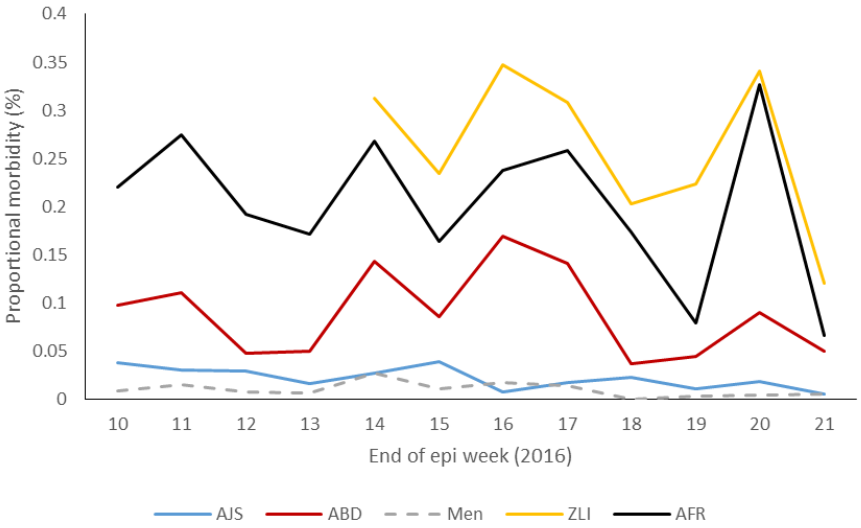


Figure 3: National trends [A and B] and proportional morbidity[23] [C and D] for influenza-like illness (ILI), acute watery diarrhoea (AWD), prolonged fever (PF) and dengue-like illness (DLI), acute jaundice syndrome (AJS), acute bloody diarrhoea (ABD), acute fever and rash (AFR), suspected meningitis (Men) and Zika-like illness (ZLI)[24]as reported through EWARS, Fiji during epidemiological weeks 10 – 21, 2016[25]

[23] Proportional morbidity = number of new cases / total number of weekly consultations *100
[24] Zika-like illness began reporting from epidemiological week 13.
[25] Data for week 21 may not be complete due to delayed reporting.

Timeliness and completeness

The national average for timeliness and completeness of reporting was 64% and 90%, respectively, but intra-division variations in reporting trends and practices were observed (Figure 4). Eighty-eight percent of Users (21/24) experienced situations where they were unable to report on time (Supplementary Table 1).

During the study period, 325 alerts were generated. On average, 88.2% (range 52-100%) alerts were verified. Three of the five surveillance officers indicated delays in alert verification were usually associated with the inability of surveillance officers to contact focal points.

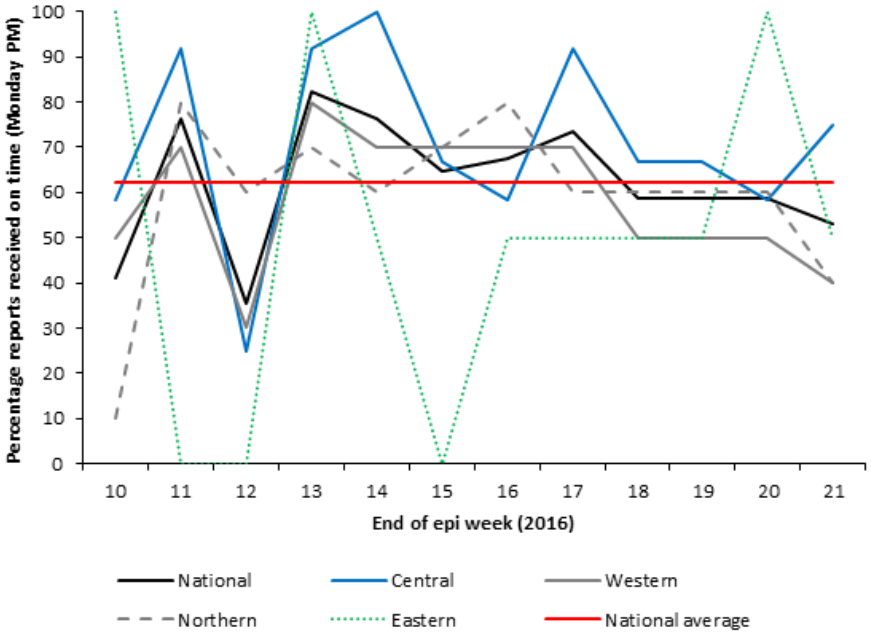
Data validity

Due to logistical reasons, complete case counts for epidemiological weeks 13 and 17 could be obtained from only three sites. Site reviews highlighted heterogeneity and discrepancy in reporting, most likely due to variation in data collection and reporting practices. Inconsistencies were more common at larger EWARS sites with more medical providers.

System usefulness

Most Stakeholders and Users (25/27, 93%) were confident that EWARS was an effective early warning system for disease outbreaks. Eighty-nine percent (24/27) of Users thought the total number of syndromes were appropriate to capture syndromes that could lead to outbreaks in Fiji. In general, Stakeholders and Users (21/27, 77%) agreed that the weekly EWARS epidemiological bulletin was useful. Similarly, national-level public health authorities reported that the bulletins were helpful for providing updates and coordinating public heath response measures. Further, the bulletins facilitated information sharing between public health personnel and EWARS sites.

A)



B)

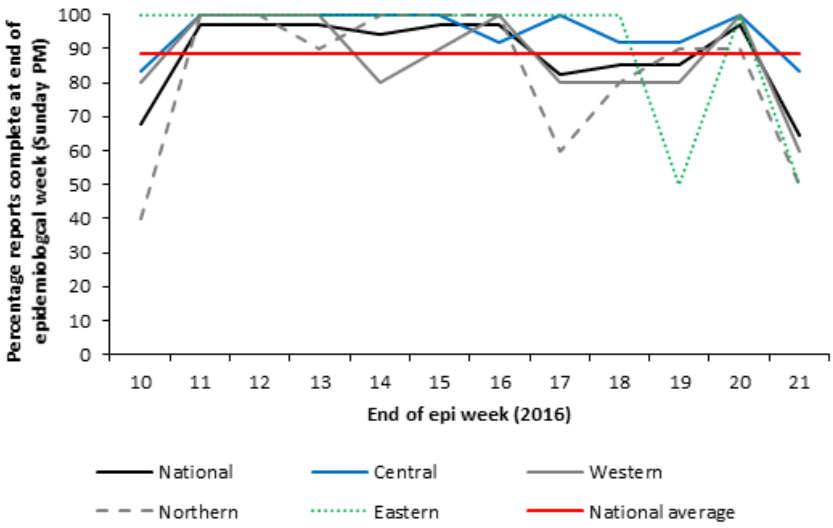


Figure 4: Timeliness [A] and completeness [B] of EWARS- IBS reporting at National and Divisional level through EWARS, Fiji, epidemiological weeks 10-21. Number of reporting sites (National= 34, Central = 12, Eastern = 2, Western = 12, Northern = 10)

Flexibility, simplicity and acceptability

Stakeholders and Users were asked if reporting and surveillance processes were easy to amend, for instance when Zika-like illness was added in week 13. System developers and all five surveillance officers reported that the system was easily modified and processes adaptable. Similarly, most Users (25/27, 93%) reported the surveillance process easy to amend. Two Users (7%) who did not find the process amenable struggled to correctly apply the case definition for Zika-like illness.

Reporting using the EWARS smartphone application was highly acceptable. Users (24/27, 89%) reported EWARS mobile application easy to use and preferred reporting with the EWARS application compared with email or telephone (24/26, 92%). Many Users (14/27, 52%) reported increased workload in addition to their routine activities, which contributed towards delayed reporting.

As feedback to those collecting and submitting the data is crucial for good quality surveillance, we asked Users if they received feedback on the data provided or alerts generated from their health facility. Most Users (22/27, 81%) received feedback after an alert was generated, and 19/27 (70%) received weekly bulletins. During the site visits, some Users expressed that aggregated data presented in the weekly bulletin was not easy to comprehend or not very useful. This was most likely due to limited understanding of epidemiological data. Four of the five surveillance officers found the EWARS website simple to navigate and easy to use. In general, focal points and surveillance officers were satisfied with the training and ongoing support provided by the EWARS team during the surveillance period.

System Stability

We assessed EWARS' requirements for upgrades and outages using server logs extracted from the host server at Amazon Web Services. At the server level, EWARS had a constant stream of activity with regular spikes in activity (data not shown). From a user perspective, 15/27 (55%) Users reported experiencing some difficulty in accessing EWARS via its mobile application or website. Most of these problems were in the early phase after EWARS was implemented and were resolved by the system developers soon after the problem was identified.

Representativeness

EWARS was implemented at 34 sentinel sites across all four divisions of Fiji (Figure 1). Overall the system was largely representative and included most of the severely affected population (Supplementary Table 2). Due to limited access, some of the small and geographically remote islands in the Eastern Division may have been under-represented.

Event Based Surveillance

Due to the immediate and *ad hoc* nature of EBS, we were unable to assess EBS using our evaluation framework, nonetheless it is important to acknowledge its impact. Ten alerts were triggered through EBS, all of which were verified. Of these, four were confirmed outbreaks, two of which were associated with large outbreaks of viral conjunctivitis (830 cases), one with typhoid and one with symptoms of prolonged fever but unknown aetiology. The time from reporting to initiating a public health response ranged from zero to four days.

All Stakeholders and Users felt that EBS was useful but was under-utilised. Sixteen (59%) focal points indicated that they would directly contact the divisional medical officers (the most senior MoHMS staff in the administrative unit) if they encountered an unusual public health event and three (11%) indicated they would report the event using the EWARS toll free number. The system under-utilisation was likely due to limited awareness and training on the EBS component of EWARS (versus IBS).

EWARS associated costs

During the study period, the total direct costs associated with implementation and operation of EWARS was approximately USD 185,000. This did not include the salaries of repurposed MoHMS staff (for example EWARS site focal points, who performed EWARS data collection and reporting, in addition to their routine activities) or repurposed WHO staff. The EWARS equipment was a relatively small proportion of the total costs: smart phones, USD 7500; laptops for surveillance officers, USD 13,450. Other expenditures (USD 70,400) included salary support for surveillance officers, travel during the implementation phase, contractual services and transport. The largest costs were associated with consultant epidemiologist flights, fees, and other expenses. Of the total expenditure, MoHMS and the Fiji Health Sector Services Program contributed 3.5% and 7.5%, respectively; WHO contributed the remainder.

Discussion

We report the findings of an assessment of the early warning disease surveillance system implemented after Cyclone Winston in Fiji in 2016. The system used, EWARS – is a low-cost tool kit developed by WHO that includes hardware and software for automated data collection, entry, analysis, alert generation, and reporting.[11]

Overall, EWARS was acceptable and simple to use by public health professionals, and was perceived to be useful for timely monitoring of diseases trends. The system was simple, stable and flexible meeting the core criteria for rapid deployment during health emergencies.

Surveillance using mobile phones has been used in a number of settings[23] including after natural disasters such as the 2008 Sichuan earthquake in China.[24] Highly automated surveillance systems in the context of natural disasters are relatively new and not routinely implemented.[25]

One of the most important features of EWARS that could not be quantified was its automated elements, including data analyses, alert generation and distribution of weekly bulletins. Several authors of this paper have implemented EWARN systems in a range of post-disaster settings, many of which relied on traditional excel-based, email and telephone data reporting, required manual data analysis and dissemination of information. The effort and energy invested in these activities by surveillance teams was substantial, consuming large amounts of time, leaving little time for alert verification, rapid risk assessments, and outbreak investigations. EWARS saved substantial human resources, minimised human error and ensured EWARS surveillance teams focused on data collection, and management and response to alerts.[4, 5]

Timely submission of surveillance data is crucial for timely outbreak detection and generating an appropriate public health response.[19] Minimal delays in reporting were observed, and were mostly associated with increased workload at EWARS sites. It is difficult to identify the exact reasons for variable reporting trends from some sites, but is most likely influenced by specific staff motivation, training, and supervision. This is further evident from fatigue in reporting towards the end of the study period. Some reporting delays were due to insufficient mobile phone credit, but these occurrences were rare and easily resolved. These issues highlight the need for ongoing technical support and timely 'feedback' for all those involved in surveillance activities.[19]

Whilst real-time surveillance is ideal, it is difficult to implement and most systems rely on weekly reporting.[13, 25] In Fiji, weekly (IBS) reporting was complemented by 'real-time' EBS. EBS is specifically designed for outbreak detection and not for monitoring disease trends.[26] It offered greater coverage and detected conditions not captured under IBS. Its capacity value was evident in its ability to detect an outbreak of conjunctivitis which would otherwise not have been captured by IBS-EWARS. The outbreak was verified by a designated medical surveillance officer with minimal delay (data not shown). Non-specific signals were further minimised by restricting the reporting to health care workers. Similar observations were made in Sierra Leone, where a community-based EBS established for Ebola virus disease in January 2015, detected low-level disease transmission at the village level.[27] Even though EBS was not used to its full potential, we believe that EBS, if recommended to countries will be highly beneficial for outbreak detection during health emergencies and during routine surveillance.[26]

Like other post-disaster systems, EWARS and our evaluation had some limitations. Implementation of EWARS relied on access to affected areas and telecommunication services. For example, some islands of the Eastern Division were inadequately captured, and some outbreaks may have been undetected. While some of these obstacles are difficult to overcome during after a disaster, a portable and rapidly deployable system such as EWARS is likely to be advantageous once connectivity is re-established.[24] We were unable to accurately measure the data quality, but several discrepancies around data reporting and case identification were identified through site reviews. Many of these issues are associated with syndromic surveillance and have been described previosuly.[4, 13, 21, 22] Continued efforts should be made towards addressing concerns around data reporting, refinement of sensitive case definitions, misclassification of cases; and improved links to other systems such as laboratory surveillance.[22, 28, 29] In order to improve the specificity of diagnosis and patient management, use of rapid tests or point-of-care tests is encouraged.[1] The surveys were designed and collected with the assistance of MoHMS surveillance officers, which may have influenced responses of the EWARS focal points. As the surveys collected de-identified data and were administered using SurveyMonkey®, we believe the reporting bias to be minimal[30].

Regardless of these limitations, our findings suggest surveillance using EWARS was feasible, robust and met its objectives. EWARS offers potential for strengthened surveillance during health emergencies. Epidemics of infectious diseases are at heightened risks during humanitarian emergencies when populations are displaced, and resources are exhausted.[31] Sustaining surveillance beyond emergencies is a common challenge owing to the complexity of health systems, lack of resources and response capacities[8] but the integration of automated aspects of EWARS into routine surveillance is expected to overcome some these difficulties.[32] After Fiji, EWARS was deployed in Nigeria and Ethiopia (Samara and Adama), and the platform was expanded to support the Pacific Syndromic Surveillance System.

The early detection of disease outbreaks can be difficult under the best of circumstances. During humanitarian emergencies, particularly in developing counties, the challenges are magnified several-fold. Tools to facilitate and standardise the implementation and reporting of post-disaster early warning surveillance, such as EWARS in a Box, can improve the detection of outbreaks while minimising the reporting burden on the public health system.

Acknowledgments

Evaluation of EWARs was jointly conducted by Fiji Centre for Communicable Disease Control and WHO DPS. We would like to acknowledge all those who were involved in post-Cyclone

Winston surveillance. In specific, our since thanks to the Divisional Medical Officers, Sub-divisional Medical Officers, EWARS surveillance officers, focal points at all EWARS sites and consultant epidemiologists for their hard work. Thank you to all support staff at the Fiji Centre for Communicable Disease Control, Ministry of Health and Medical Services, WHO Division of Pacific Technical Support in Fiji and Fiji Health Sector Support Services for their work during the post-disaster period.

Dr Meru Sheel and Ms Julie Collins are Field Epidemiology Training Program Fellows enrolled in the Masters of Philosophy in Applied Epidemiology (MAE) program at the Australian National University and are supported by the Australian Government Research Training Program (RTP) Scholarship. Dr Meru Sheel is supported by a scholarship from the National Centre for Immunisation Research. Ms Julie Collins is supported by a scholarship from the Hunter New England Population Health.

References

1. Connolly MA, Gayer M, Ryan MJ, Salama P, Spiegel P and Heymann DL. Communicable diseases in complex emergencies: impact and challenges. *Lancet (London, England)*. 2004; 364: 1974-83.
2. Gayer M, Legros D, Formenty P and Connolly MA. Conflict and emerging infectious diseases. *Emerging infectious diseases*. 2007; 13: 1625-31.
3. WHO. Emergency Response Framework (ERF). 2013.http://www.who.int/hac/about/erf/en/
4. WHO. Early warning surveillance and response in emergencies. Report of the second WHO technical workshop. 2011.http://apps.who.int/iris/bitstream/10665/70665/1/WHO_HSE_GAR_DCE_2011.2_eng.pdf 14/06/2016.
5. Bilve A, Nogareda F, Joshua C, et al. Establishing an early warning alert and response network following the Solomon Islands tsunami in 2013. *Bulletin of the World Health Organization*. 2014; 92: 844-8.
6. Worwor G, Harries AD, Merilles OE, Jr., et al. Syndromic surveillance in Vanuatu since Cyclone Pam: a descriptive study. *Western Pacific surveillance and response journal : WPSAR*. 2016; 7: 6-11.
7. Centers for Disease C and Prevention. Early warning disease surveillance after a flood emergency--Pakistan, 2010. *MMWR Morb Mortal Wkly Rep*. 2012; 61: 1002-7.
8. Mala P, Ghada M, Wasan A, et al. Establishment of EWARN system for the Syrian crisis: Experiences and challenges. *International Journal of Infectious Diseases*. 21: 280.
9. Pinto A, Saeed M, El Sakka H, et al. Setting up an early warning system for epidemic-prone diseases in Darfur: a participative approach. *Disasters*. 2005; 29: 310-22.
10. Valenciano M, Bergeri I, Jankovic D, Milic N, Parlic M and Coulombier D. Strengthening early warning function of surveillance in the Republic of Serbia: lessons learned after a year of implementation. *Euro Surveill*. 2004; 9: 24-6.
11. WHO. WHO launches new early warning system in a box to help 500 000 people for only $USD 15 000. 2015. Accessed 15/06/2016.http://www.afro.who.int/en/ssd/news/item/8231-who-launches-new-early-warning-system-in-a-box-to-help-500-000-people-for-only-$usd-15-000.html.
12. Fiji MoHMS. Rapid Public Health Risk Assessment Tropical Cyclone Winston Republic of Fiji. Fiji Minnistry of Health and Medical Services and World Health Organisation. 2016.http://www.health.gov.fj/wp-content/uploads/2016/03/20160315-Rapid-Health-Risk-Assessment-TC-Winston-Mar2016-for-editing_14-March-2016_final-2.pdf22/05/2017.
13. Craig AT, Kama M, Samo M, et al. Early warning epidemic surveillance in the Pacific island nations: an evaluation of the Pacific Syndromic Surveillance System. *Tropical medicine & international health : TM & IH*. 2016.
14. WHO. Early detection, assessment and response to acute public health events: Implementation of Early Warning and Response with a focus on Event-Based Surveillance. Interim ed. 2014.http://www.who.int/ihr/publications/WHO_HSE_GCR_LYO_2014.4/en/15/06/2016.
15. Buehler JW. Review of the 2003 National Syndromic Surveillance Conference--lessons learned and questions to be answered. *MMWR supplements*. 2004; 53: 18-22.
16. Buehler JW, Hopkins RS, Overhage JM, Sosin DM and Tong V. Framework for evaluating public health surveillance systems for early detection of outbreaks: recommendations from the CDC Working Group. *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports / Centers for Disease Control*. 2004; 53: 1-11.
17. Bravata DM, McDonald KM, Smith WM, et al. Systematic Review: Surveillance Systems for Early Detection of Bioterrorism-Related Diseases. *Annals of Internal Medicine*. 2004; 140: 910-22.

18. European Centre for Disease Prevention and Control. Data quality monitoring and surveillance system evaluation – A handbook of methods and applications. Stockholm: ECDC2014
19. WHO. Communicable disease surveillance and response systems: Guide to monitoring and evaluating. 2006.http://www.who.int/csr/resources/publications/surveillance/WHO_CDS_EPR_LYO_2006_2.pdf15/06/2016.
20. Craig A, Kool J and Nilles E. The Pacific experience: supporting small island countries and territories to meet their 2012 International Health Regulations (2005) commitments. *Western Pacific surveillance and response journal : WPSAR*. 2013; 4: 14-8.
21. Kool JL, Paterson B, Pavlin BI, Durrheim D, Musto J and Kolbe A. Pacific-wide simplified syndromic surveillance for early warning of outbreaks. *Global public health*. 2012; 7: 670-81.
22. Paterson BJ, Kool JL, Durrheim DN and Pavlin B. Sustaining surveillance: evaluating syndromic surveillance in the Pacific. *Global public health*. 2012; 7: 682-94.
23. Rosewell A, Ropa B, Randall H, et al. Mobile phone-based syndromic surveillance system, Papua New Guinea. *Emerging infectious diseases*. 2013; 19: 1811-8.
24. Yang C, Yang J, Luo X and Gong P. Use of mobile phones in an emergency reporting system for infectious disease surveillance after the Sichuan earthquake in China. *Bulletin of the World Health Organization*. 2009; 87: 619-23.
25. Checchi F, Warsame A, Treacy-Wong V, Polonsky J, van Ommeren M and Prudhon C. Public health information in crisis-affected populations: a review of methods and their use for advocacy and action. *Lancet (London, England)*. 2017.
26. Hartley D, Nelson N, Walters R, et al. Landscape of international event-based biosurveillance. *Emerging health threats journal*. 2010; 3: e3.
27. Stone E, Miller L, Jasperse J, et al. Community Event-Based Surveillance for Ebola Virus Disease in Sierra Leone: Implementation of a National-Level System During a Crisis. *PLoS currents*. 2016; 8.
28. Hope K, Durrheim DN, d'Espaignet ET and Dalton C. Syndromic Surveillance: is it a useful tool for local outbreak detection? *J Epidemiol Community Health*. 2006; 60: 374-5.
29. Dagina R, Murhekar M, Rosewell A and Pavlin BI. Event-based surveillance in Papua New Guinea: strengthening an International Health Regulations (2005) core capacity. *Western Pacific surveillance and response journal : WPSAR*. 2013; 4: 19-25.
30. Eysenbach G and Wyatt J. Using the Internet for surveys and health research. *J Med Internet Res*. 2002; 4: E13.
31. Watson JT, Gayer M and Connolly MA. Epidemics after natural disasters. *Emerging infectious diseases*. 2007; 13: 1-5.
32. Haskew C, Spiegel P, Tomczyk B, Cornier N and Hering H. A standardized health information system for refugee settings: rationale, challenges and the way forward. *Bulletin of the World Health Organization*. 2010; 88: 792-4.

Supplementary Table 1: Summarised results from cross-sectional survey of Focal Points, EWARS, Fiji 2016[26]

Q	EWARS site location	Number (% response rate)
	Central Eastern Northern Western *Total*	12 (100) 2 (100) 5 (50) 8 (80) *27 (79)*
Q	**What do you think is the purpose of EWARS?** *(>1 response per respondent)*	
	Theme: outbreak detection Theme: outbreak response Theme: general disease surveillance or monitoring	18 (67) 9 (33) 12 (44)
Q	**How well do you think EWARS is able to signal an early warning for potential disease outbreaks?**	
	Very well Somewhat well Not very well Not at all well	18 (67) 7 (26) 2 (7) 0 (0)
Q	**Do you think EWARS has had any impact on public health in Fiji?**	
	Yes No Unsure	20 (77) 0 (0) 6 (23)
Q	**In your opinion, how easy is it to use EWARS on the mobile phone?**	
	Very easy Somewhat easy Not very easy Very difficult	24 (89) 3 (11) 0 (0) 0 (0)
Q	**Have you ever had difficulty accessing EWARS on the mobile phone?** *Application not working*	
	Yes How often did you experience difficulty - Very often (most weeks) - Somewhat often (> once a month) - Not very often (≤ once a month) - Not often (≤2 during study period) No Unsure	15 (56) 2 (13) 6 (40) 3 (20) 4 (27) 12 (44) 0 (0)
Q	**At your health facility, what is the process used to record patients who meet the case definitions?**	
	Medical officers record cases directly on the EWARS tally sheet at the time a patient is seen Medical officers record cases on an EWARS line list Weekly review of register or logbook by Medical Officer or Nurse Not known Other	4 (20) 1 (5) 13 (65) 0 (0) 2 (10)

[26] For confidentiality reasons, qualitative data is not reported.

Q	**How do you send / transmit the EWARS weekly reports? (***Tick all that apply)*	
	EWARS mobile phone application EWARS website (using computer) Email Telephone call SMS Other	25 (93) 1 (4) 4 (15) 8 (30) 6 (22) 3 (11)
Q	**What is your preferred reporting method? *(Ranked as first preference)***	
	EWARS mobile phone application EWARS website (using computer) Email Telephone call SMS	24 (92) 0 (0) 0 (0) 2 (8) 0 (0)
Q	**Have there been situations where you could not submit the EWARS weekly report on time (before Monday 6pm)?**	
	Yes No Unsure	21 (88) 3 (13) 0 (0)
Q	**What are the most common challenges for timely reporting? (***Tick all that apply)*	
	Tally sheet not received on time from other staff No access to internet (no credit) No access to internet (no signal) No access to phone Not enough time / workload too busy Unsure Other	11 (46) 4 (17) 11 (46) 2 (8) 14 (58) 0 (0) 4 (17)
Q	**Are you aware of the EWARS case definitions?**	
	Yes No Unsure	27 (100) 0 (0) 0 (0)
Q	**How easy is it to classify cases into the syndrome categories?**	
	Very easy Somewhat easy Not very easy Very difficult	11(41) 16 (59) 0 (0) 0 (0)
Q	**How easy was it to amend the reporting process when an additional syndrome (Zika-like illness) was added to EWARS?**	
	Very easy Somewhat easy Not very easy *Reasons for difficulty* *Theme: similar case definitions and patient presentation* Not at all easy (very difficult)	12 (44) 13 (48) 2 (7) 2 (100) 0 (0)
Q	**Have you received any feedback when an EWARS alert has been generated for your health facility?**	
	Yes No Unsure N/A	22 (81) 3 (11) 1 (4) 1 (4)

Q	**Do you receive the EWARS weekly bulletin?**	
	Yes No Unsure	19 (70) 7 (26) 1 (4)
Q	**How useful is the information in the EWARS weekly bulletin for your health facility?**	
	Very useful Somewhat useful Not very useful Not at all useful	9 (33) 12 (44) 3 (11)
Q	**How have you used the information in the EWARS weekly bulletin?**	
	Theme: information sharing Theme: to compare with other reporting areas Theme: to initiate preventive or responsive public health actions	6 (32) 5 (26) 5 (26)
Q	**How could the EWARS weekly bulletin be improved?**	
	Theme: include health facility specific surveillance data Theme: include outcome of previous week's case investigations Theme: increase access to other staff members at health facility	3 (16) 1 (5) 2 (11)
Q	**Do you ever distribute the information in the weekly bulletin to other persons or organisations?**	
	Yes No Unsure	9 (35) 16 (62) 1 (4)
Q	**Who do you distribute the information to?**	
	Theme: health facility colleagues Theme: community health care workers Theme: regional public health staff	8 (89) 3 (33) 1 (11)
Q	**How satisfied do you feel with the training that you received when EWARS was implemented?**	
	Very satisfied Somewhat satisfied Not very satisfied Not at all satisfied	11 (41) 12 (44) 3 (11) 1 (4)
Q	**How supported do you feel to be able to carry out your EWARS responsibilities?**	
	Very supported Somewhat supported Not very supported Not at all supported	13 (48) 14 (52) 0 (0) 0 (0)
Q	**Overall, how satisfied are you with EWARS?**	
	Very satisfied Somewhat satisfied Not very satisfied Not at all satisfied	16 (59) 11 (41) 0 (0) 0 (0)

Supplementary Table 2: Population size and EWARS surveillance site coverage by Division, Fiji, 2016. [27]

Divisional region	Population (%)	Number of EWARS sites (%)	Number of health facilities	Percentage of health facilities captured by EWARS
Central	361895 (41.6)	12 (35.3)	52	23.1
Eastern	36870 (4.2)	2 (5.9)	52	3.8
Western	344663 (39.6)	10 (29.4)	61	16.4
Northern	127556 (14.6)	10 (29.4)	45	22.2
National	870984 (100)	34 (100)	210	16.2

[27] **Projected population figures for 2016 were provided by the Fiji Ministry of Health and Medical Services (MoHMS), estimated using 2007 census conducted by Fiji Bureau of Statistics and MoHMS divisional boundaries.**

Chapter 5: Epidemiological study

Identifying residual transmission of lymphatic filariasis in post-mass drug administration surveillance phase: Comparing school-based versus community-based surveys – American Samoa, 2016

Prologue

My role

In September 2016, I was deployed to American Samoa as a field epidemiologist as part of an operational research project - Transmission Assessment Survey (TAS) Strengthening in American Samoa. The aim of this project was to compare the effectiveness for two survey designs for epidemiological assessment of transmission of lymphatic filariasis following mass drug administration (MDAs).

This project was a joint collaboration between the Research School of Population Health, Australian National University (ANU), the Taskforce for Global Health (TFGH), the Centers for Disease Control and Prevention (CDC), and the American Samoa Community College.

I was the co-lead for the fieldwork component of this study. I spent a total of eight weeks in American Samoa, conducting the school and community-based surveys. My role in the field include coordinating a school and a community based survey, which involved interviewing study participants and collecting finger prick blood samples to test for circulating filarial antigen (CFA). The interviews were conducted using electronic questionnaires using mobile phones. We collected information on geospatial coordinates, demographics and risk factors. We also established follow-up clinics for treatment of study participants who had a positive test. I trained field and lab teams; managed the logistics and budgets including paying field teams; and participated in community activities including presenting at local symposiums and judging high school science competition, conducting TV and radio interviews. My role and reflections from the field are detailed in part one of this chapter. The field experience will be submitted to PLOS Blogs for publication.

The main study components are summarised below:

1. School-based survey – targeting school children aged 6-7 years

2. Household members of antigen positive school children – follow-up of children from part 1.

3. Community-based survey of persons aged ≥8 years

a) 30 randomly selected villages

b) ‘Hotspot’ villages – two purposively selected villages, which were not randomly selected but were previously known to be foci of residual transmission

For the analyses, I conducted the final cleaning and appending of all data sets. I performed multiple analyses including descriptive epidemiology, univariate logistic regressions and multi-stage cluster survey analyses. Only the results comparing the school and community survey are enclosed in this chapter (primary hypothesis). I led the analyses and drafting of the manuscript enclosed in the second part of this chapter. I collated comments from supervisors Dr Colleen Lau, Professor Patricia Graves and Associate Professor Martyn Kirk.

Lessons learned

This project was an amazing learning, challenging and fun experience. While there are many aspects that helped me develop personally and professionally, my key lessons learnt are summarized below:

1. Implementing cross-sectional surveys in a resource limited setting. I was involved in this project from the start of its implementation until the end. I learnt about planning and organization activities involved in surveys, shipment, employing and training staff in a developing country environment, and about how to effectively engage people. I learnt how to set-up follow up clinics in a resource limited setting, communicating with study participants and ensuring that they are comfortable with the information provided.

2. Statistical analyses-While I was not involved in the original study design; I learnt how to design multi-stage cross-sectional surveys. I learnt how to conduct cluster survey analyses for multi- stage surveys

3. Collaboration-All collaborators were excellent at information sharing, and it was evident that open and honest collaboration is the key to success public health programs.

4. Leadership and project management – As the fieldwork leader, I learnt how to effectively lead in a resource limited setting. This was one of my favourite aspects of the work, as I was not only responsible for everyday coordination and logistics, but also supervision of local teams.

Public health impact

The main purpose of our study was to compare the two surveys and identify the strengths and weaknesses of each for post-MDA for lymphatic filariasis. We found the community survey was more reliable and provided in depth information on high risk groups and was better at identifying ongoing transmission. These findings will help inform future WHO recommendations for post-MDA surveillance for lymphatic filariasis under the Global Programme.

The key findings are summarized in a manuscript (enclosed in this chapter), and were presented to the TFGH and CDC, and to the Department of Health in American Samoa. Following on from that, discussions have begun between country partners to discuss the next steps in LF elimination.

Additional recommendations specific to American Samoa and those aimed at improving post-MDA surveillance have been discussed, and being implemented slowly. The project led to local capacity building – local staff members were trained and will be good human resources for future surveys. I worked with many of the staff, training and educating them on significance of good public health and concepts of public health.

Although reporting on cases of LF-related morbidity was not a part of my role, I documented all cases of lymphoedema or elephantiasis that I witnessed. These observations were presented in a report to the TFGH and WHO, which initiated the development of a morbidity management program for American Samoa. We raised local awareness about LF through presentations and discussions with local clinicians, public health practitioners, and laboratory managers.

We experienced several challenges with the rapid diagnostic tests (Filarial Test Strips). These issues were documented into a quality control report submitted to the TFGH and the kit manufacturer Alere^{TM}. These findings are expected to assist in improving the design and utility of the test kits in the field.

Presentations

I presented the results at the annual FETP International Night hosted by TEPHINET in Atlanta, Georgia USA in April 2017, at the PHAA Communicable Diseases Conference, Melbourne, June 2017 and the Australasian Tropical Health Conference, Cairns, September 2017; and several other local seminars in Sydney and Canberra.

Dr Colleen Lau presented the preliminary results at the weekly meeting of the Department of Health in American Samoa and the WHO consultation meeting on post-elimination surveillance of neglected tropical diseases in Cambodia.

Acknowledgements

Sincere thanks to Dr Colleen Lau for her supervision and mentorship. She was also a very personable leader (particularly when I was bitten by a dog!). Thank you also to Professor Patricia Graves and Dr Sarah Sheridan for their guidance in undertaking the fieldwork and epidemiological methods – and to have shared a passion for global health with them! Thanks to my ANU supervisor, Associate Professor Martyn Kirk, for creating this opportunity and for supporting me through the data analysis process. I am also grateful to Professor Cate D'Este, who patiently guided me through survey analyses, answering my 'silly' questions but also for encouraging me to perform in-depth analyses. While not of all the analyses have gone into the enclosed manuscript, I have learnt a lot about conducting survey analyses, and different elements that should be kept in mind.

Special thanks to all the study participants and to everyone I met during my stay in American Samoa. Samoan people are kind, generous and warm-hearted. While I may not be able to mention each one of them here, I must acknowledge their warm and gracious nature, and for being extremely supportive of our work.

Thanks to Dr Mark Schamedick for stimulating conversations, providing insight in to working in American Samoa, culture and assistance with logistics. Deepest gratitude and thanks to Dr Saipale Fuimaono. Dr Sai is an incredible doctor with immense experience – a 'mover and shaker', and was instrumental to the success of the fieldwork. He was extremely welcoming and encouraged me to participate in local Department of Health activities such as attending weekly meetings. He patiently listened to my stories from the field and encouraged me to 'keep going' every time I experiences an obstacle.

Thank you to the fabulous field team members, Ms Pae Tufono, Ms Meliame Tufono, Ms Susana Lin, Ms Fitilagi Tagioloa and Ms Donna Pule; and lab team members Ms Mary Matai'a, Ms Cathy Montabalo, Ms Nalini Lata, Ms Kima Savusa and Mr Jason Tufele. The fieldwork would not have been possible without your hard work and persistence. We had many long tiring days, walking in the heat and hiking up mountains. Thank you also to the Department of Health, Department of Education, village chiefs and mayors, school teachers and principals.

Leadership lessons from the field

In September 2016, I was deployed to American Samoa to co-lead a field team in a cross-sectional survey that was part of an operational research project – Transmission Assessment Survey (TAS) Strengthening in American Samoa. The project was collaboration between the Australian National University (ANU), the Taskforce for Global Health (TFGH), the Centers for Disease Control and Prevention (CDC), and the American Samoa Community College.

American Samoa is a chain of several small islands in the South Pacific Sea and has a tropical climate. It is comprised of a large main island known as Tutuila, the adjacent island of Aunu'u and a remote chain of islands known as the Manu'a islands. Pago Pago, the capital of American Samoa can only be accessed from Samoa and Hawaii. The total population of American Samoa is approximately 57,000 people who live in approximately 70 villages. The majority of the population lives on Tutuila and Aunu'u, which is where this study was conducted. People are mostly of Samoan origin, with a few Filipinos, Tongan, American and other Pacific Islander people. Despite being an unincorporated territory of the United States and having a strong American influence (especially American fast food), the culture continues to be mainly Samoan.

Polynesian Airlines carrier connects Samoa to Pago Pago, the capital of American Samoa [left]. View of Pago Pago Harbour and the Rainmaker Mountain from Mt Alava [right].

Typical Samoan house called fale (top row), fresh coconut being prepared for cooking at Tisa's Barefoot Bar, a Samoan fish curry and locally grown bananas ripening in a participant's house [from left to right].

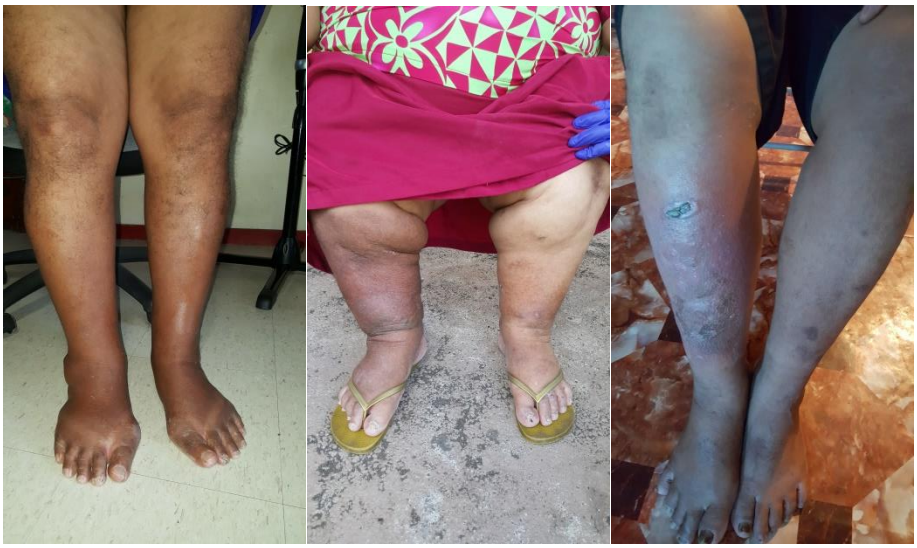
On my arrival, I was greeted by Dr Colleen Lau (principal investigator) and other Australian collaborators Drs Patricia (Tricia) Graves and Sarah Sheridan. They designed the study and had been in American Samoa for the previous week piloting the survey and training local fieldwork teams. I spent the first week familiarising myself with island life (which included driving on the other side of the road!), meeting the field team, and getting up to speed with the survey methodology before my colleagues returned to Australia. Field epidemiology is not only about the data, but is also about the people, the culture, logistics and coordination and understanding the disease context. Below are some reflections of my experience in this leadership role and lessons learned.

Study background

The World Health Organization (WHO) launched the Global Programme for Elimination of Lymphatic Filariaisis in 2000. The Programme aims to eliminate lymphatic filariasis by 2020, firstly by stopping the spread of infection via mass drug administration or MDA, which involves

large-scale preventative treatment in communities with endemic disease; and secondly, by supporting those living with disability. In American Samoa, the Department of Health conducted several rounds of MDA between the years 2000 and 2006. WHO recommends conducting surveillance surveys after MDAs have been completed to confirm there is no ongoing disease transmission. Our study was designed to compare two survey (school and community) methodologies for surveillance of lymphatic filariasis. The survey involved interviewing study participants, collecting few drops of blood to test for filarial antigen and providing treatment to anyone who had a positive test.

Lymphatic filariasis (LF), known as "mūmū tupa" in Samoan, is a mosquito-borne disease caused by the helminth worm, *Wuchereria bancrofti*. Repeated bites with infected mosquitos (*Aedes sp.*) can lead to elephantiasis or hydrocele, and are a major cause of permanent disability. Severe elephantiasis or hydrocele are not as common as they used to be, however people living with mild lymphedema or swelling of the leg can still be found.



Study participants with lymphoedema in American Samoa.

Project management in a resource limited setting

My primary role was to coordinate the school and community survey. For both surveys, I would organise the visits a week in advance, with the aim of visiting at least one school and one village every day, Monday to Friday, and a remote village on Saturdays.

We surveyed students from grades 1 and 2 from all elementary schools on the two main islands of American Samoa. For school surveys, I liaised with school principals to arrange the distribution and collection of consent forms, and arranged for us to visit the school to test the

children. Most school principals were extremely understanding and helpful. Some of the larger schools (with approximately 100-200 grade 1 and 2 students) required persistence, and took longer to coordinate and to recruit sufficient number of study participants. School children in American Samoa were extremely resilient to pain and only a handful of children were fearful of having a finger prick test. The students were also familiar with school-based vaccination programs, and would often excitedly chant "shots shots shots". In one school, we recruited greater than 95% of the eligible students. Later I found out that the teacher showed pictures of elephantiasis to her students, and explained the advantage of early testing. She assured the students that finger pricks don't hurt, and in order to make sure that the students weren't scared, she mimicked a finer prick by poking the students' finger with the pointed end of a pencil. Collectively, this might be why most of the students brought back signed consent forms and resulted in a high response rate.

School students line up to get tested for lymphatic filariasis in American Samoa. School surveys, although logistically simple, recruitment can be difficult, and rely on coordination by the school teachers and principals.

The community surveys were logistically more challenging. There are approximately 70 villages on the two main islands, of which we visited 32 villages. American Samoa has a Paramount Chief, and each village has a mayor who is responsible for operational affairs of the village. As they are prominent community leaders, we obtained their permission prior to conducting the study. The visit to each village was organised in coordination with the village mayor (this was usually done by one of our senior field workers). While some mayors were

quite generous with their time and would walk around the village with us, others were happy for us to carry-on our work without them.

With field team in one of the households while conducting community survey in Futiga, American Samoa.

Our daily visits to the villages occurred between 3-8pm on weekdays and on Saturday mornings. At the start, we would have a quick de-brief, following which we would split into two teams, each of which were assigned a set of selected houses, which were marked on fieldwork maps. Each team comprised of a bilingual interviewer and a phlebotomist. I would alternate between the two teams, guiding and supporting them as and when needed. At each house, we would provide participants with information about the study, seek consent and test them. Sometimes we would spend extra time talking to participants and addressing their concerns; especially in instances where a family member was hesitant to allow the rest of their family or children to be tested. At the end of each day, I would count the number of samples, cross-check the data that was recorded with the paper consent forms, and correct any errors.

Curious villagers surround the field team as they conduct interview and test participants.

In the mornings, I would visit our laboratory at the American Samoa Community College. This was a small room, on loan from one of the project collaborators, an American entomologist who has worked on the Island for over 15 years. At the lab, I would deliver the blood samples collected the day before, meet with the lab assistant and ensure everything was running smoothly. We were using a new rapid diagnostic kit (Filariasis Test Strips), which were easy to use but required regular monitoring for any irregularities and performance issues. I was required to conduct regular quality checks and monitor any operational challenges. I would undertake a quick stock-take of supplies and re-stock our field kits before heading out on another school and village visit. Despite all the planning – *en route* to school or village, we occasionally had to make a pit stop to buy gloves, Band-Aids, snacks or water.

Phlebotomist kit used during field work [left] and lab technician testing blood specimens at our temporary laboratory at the American Samoa Community College.

As the fieldwork leader, I managed all expenditures, was in charge of paying weekly salaries for field and lab workers, which meant constantly being on top of all the administrative paperwork. American Samoa is largely a cash-based economy but every cash withdrawal machine at all the banks in the country were broken. In order to pay the field workers, I would do up four to five rounds of cash withdrawal from different ATM machines around the Island. It is these simple things that we often take for granted at home, and can make everyday life and field work logistics difficult.

Local capacity building

One of my other key responsibilities was to provide ongoing training and support, and managing the field and lab teams. Mentoring and providing knowledge and skills to the local staff is an important element of field epidemiology and international development. It is also very gratifying and one thing I absolutely love about being a field epidemiologist. At the CDC conference in Melbourne, I had the privilege of sharing my experiences with an inspiring field epidemiologist, who at the end of our conversation said "it is our life's aim to become redundant". I could not agree more!

I learnt how to effectively lead, without being annoyed; to manage conflicts and strategic ways to manage time. In a resource limited setting, where both time and funding are limited, optimal use of of time is important as it directly impacts the operation of the project.

With the field teams, I realised that educating them on why it was important to collect good quality data, and how it impacted the study and the health of those living in American Samoa, streamlined our data collection process. With time, the teams felt more confident at recruiting families, worked more efficiently subsequently improving the data quality. I used my previous

laboratory experience to train the lab assistants and provide them with troubleshooting tips. It was great to see the lab assistants become excited about the data, and taking responsibility of their work. I engaged in local community activities and contributed to additional capacity building, by presenting at seminars or judging high school science competitions.

Building relationships and trust within the community

Within a few days of being on the Island, it was evident that most people had a family member or a friend or a distant relative who had suffered with LF, and perhaps even died because of severe elephantiasis or hydrocoele. Therefore it was no surprise that most community members were very supportive of the study and were happy to be tested. Many were grateful that we were there to test their children and grandchildren. In some instances, such as in the more 'urban' villages, we experienced mild skepticism – however over time the teams improved at approaching participants and educating those who were unaware. At the schools, I found building a relationship with the principals and teachers, and winning their vote of confidence improved the recruitment process.

In order to further engage the community and to improve our recruitment rates, I appeared on the radio and the local television news, where I talked about our study, its public health significance, confidentiality of the data and results, and about the treatment process. In the end, we tested 4000 participants and treated anyone who had a positive test.

Working in cross-cultural settings is fun but can be challenging. The communities in American Samoa are traditional and religious, with many traditional practices. Cultural events such as White Sunday, Halloween and even the presidential election slowed the recruitment process. Sometimes there were other competing urgencies, for example with the ongoing Zika outbreak and associated media scare, many people were concerned about Zika, and weren't as concerned about testing for LF. Everyday island life can be slow, meetings can run late or even be cancelled last minute. Sundays are a religious and family day, and it is culturally inappropriate to work, and access to villages/ beaches is restricted. Our project time lines were strict – most of the work had to be completed before the onset of the wet season, which would make certain parts of the island inaccessible. To overcome these, one must respect the culture and engage with the community leaders. It was important to not get frustrated, acknowledge the limitations, and adopt a flexible, opportunistic and spontaneous approach to working in this setting.

***En route* to neighboring island of Aunu'u on Halloween with team members.**

Finally, I am extremely grateful for the generosity and kindness of all the Samoan people, and for all the experiences - the field work and super long days in the hot and humid weather, the amazing science, not to mention the Samoan food, Samoan dancing and fresh Pina Coladas. Warmest thanks to our field and lab team members, study participants and local community champions, particularly those from the American Samoa Department of Health who were instrumental to the success of the fieldwork, and is a highly respected and accomplished community leader. I am also thankful to all my supervisors and collaborators for their mentorship and guidance in undertaking this project. American Samoa is a beautiful part of the world, and I hope to go back someday. Fa'afetai lava!

Dr Meru Sheel is Field Epidemiology Training Program Fellow in the Masters of Philosophy in Applied Epidemiology at the Australian National University. *Dr Sheel is supported by scholarships from the Australian Government Research Training Program and the National Centre for Immunisation Research and Surveillance, Australia. All photographs were taken by the author and verbal consent for use was obtained at the time.*

Identifying residual transmission of lymphatic filariasis in post-mass drug administration surveillance phase: Comparing school-based versus community-based surveys – American Samoa, 2016

Meru Sheel[1,2], Sarah L. Sheridan[3], Martyn Kirk[1], Patricia M. Graves[4], Colleen L. Lau[3] *et al*. (authors to be finalised)

[1] National Centre for Epidemiology and Population Health, Australian National University, Acton, Australian Capital Territory, Australia

[2] National Centre for Immunisation Research and Surveillance, Westmead, New South Wales, Australia

[3] Department of Global Health, Research School of Population Health, Australian National University, Acton, Australian Capital Territory, Australia

[4] College of Public Health, Medical and Veterinary Sciences, James Cook University, Cairns, Queensland, Australia

Abstract

Introduction: Under the Global Programme for Elimination of Lymphatic Filariasis (LF), American Samoa conducted seven rounds of mass drug administration (MDA) from 2000-2006. The World Health Organization recommends systematic post-MDA surveillance using Transmission Assessment Surveys (TAS) for epidemiological assessment of recent LF transmission. We compared the effectiveness of two survey designs for post-MDA surveillance: a school-based survey of children aged 6-7 years, and a community-based survey targeting people aged ≥8 years.

Methods: In 2016, we conducted a systematic school-based TAS in all elementary schools (n=29) and a cluster survey in 30 randomly selected villages on the two main islands of American Samoa. We collected information on school/ household locations, demographics, and risk factors using electronic questionnaires. Blood samples were collected to test for circulating filarial antigen (CFA) using the Alere™ Filariasis Test Strip. For those who tested positive, we prepared slides for microscopic examination of microfilaria. Descriptive statistics were performed for questionnaire variables. Data were weighted to account for sampling design, and for sex and age (community survey only). CFA prevalence was estimated using the complex survey design in Stata13.

Results: The school-based TAS (n=1143) identified nine antigen-positive children, and found an overall adjusted (survey design and sex) CFA prevalence of 0.7% (95% CI: 0.3-1.8). Of the nine positive children, we identified one microfilariaemic 7 year old child.

The community-based survey (n=2507, 711 households) identified 102 antigen positive people, and estimated an overall adjusted (survey design, age and sex) CFA prevalence of 6.2% (95% CI: 4.5-8.6). Adjusted village-level prevalence ranged from 0-47.1%. CFA prevalence increased with age and was higher in males. In the community survey, 22 out of 86 (25.6%) antigen positive people were microfilaraemic.

Conclusions: American Samoa failed school-based TAS, and the community-based survey identified higher than expected numbers of antigen-positive people. School-based TAS was logistically simpler and allowed sampling of a larger proportion of the target population, but results did not reflect the overall CFA prevalence in the population. The community-based survey, although operationally more challenging, identified CFA-positive individuals of all ages, and areas of high prevalence. Both surveys confirmed the presence of ongoing LF transmission.

Introduction

Lymphatic filariasis (LF) is a neglected tropical disease caused by *Wuchereria* and *Brugia* species of helminth worms. The disease is transmitted by mosquito vectors including *Aedes, Anopheles, Culex* and *Mansonia* species. Globally, an estimated 68 million people are infected; with 36 million microfilaemic people and 36 million people who are disabled or disfigured because of complications including lymphoedema, elephantiasis and scrotal hydrocoeles.[1] In 2000, the World Health Organization (WHO) launched the Global Programme to Eliminate Lymphatic Filariasis (GPELF), which aims to eliminate LF as a public health problem by 2020. The GPELF uses two strategies, (i) interrupt transmission of LF by conducting mass drug administration (MDA) in all disease endemic regions, and (ii) morbidity management and disability prevention for infected people.[2] The GPELF is estimated to have delivered 6.2 billion treatments to over 820 million people since its inception.[3] Under the GPELF, the Pacific Programme to Eliminate LF was formed in 1999 to support 22 Pacific Island Countries in the Western Pacific Region.[4] As of 2017, Cook Islands, Niue, the Marshall Islands, Tonga and Vanuatu have successfully achieved the GPELF's elimination targets.[5]

The GPELF recommends conducting Transmission Assessment Surveys (TAS) in children aged 6-7 years for epidemiological assessment of transmission.[2] The target population for the TAS is children 6-7 years because they were born during or after MDA, and any infection in this population would most likely be recently acquired compared to infections in older children or adults. Minimum of two TAS are recommended at 2-3 year intervals, until the absence of transmission can be verified. Transmission is considered to have ceased when mean antigen prevalence in an evaluation unit drops below the critical cut-off value. Critical cut-off values are thresholds below which transmission is considered not viable, and depend on the filarial parasite and vector. In regions with endemic *Wuchereria bancrofti* and where transmission is dominated by *Aedes*, TAS threshold is based on an antigen prevalence of 1%. Critical cut-off values are calculated so that the likelihood of an evaluation unit passing is at least 75% if true antigen prevalence is 0.5%, and no more than 5% if the true antigen prevalence is ≥1%.[2] Recent studies have highlighted the limitations of relying solely on TAS as a post-MDA surveillance tool, especially as prevalence reduces to low levels, and detecting any residual transmission becomes increasingly challenging. For example, in Sri Lanka, TAS of children aged 6-7 years were less sensitive at detecting low-level transmission compared to antibody detection in school children aged 6-7 years, xenomonitoring and community-based surveys of people aged ≥10 years.[6]

In American Samoa, where LF is endemic, *W. bancrofti* is the only known species of filarial worm, and is transmitted by both day and night biting *Aedes sp.* mosquitos. *Ae. polynesiensis* is the dominant and efficient day biting vector.[7] In 1999, the antigen prevalence using rapid immunochromatographic test (ICT) was estimated to be 16.5%.[8, 9] Under the Pacific Programme, the American Samoa Department of Health delivered seven rounds of MDA during 2000-2006. In 2007, ICT prevalence reduced to 2.3% with microfilaria prevalence of 0.5%.[8, 9] Another round of MDA was recommended, but was not conducted at large-scale due to logistical reasons.[8]

School-based TAS are recommended in regions (e.g. American Samoa) where net-school enrolment is ≥75%.[2] In 2011-2012, school-based TAS identified two antigen-positive children, and in 2015, one antigen-positive child was identified. Antigen-positive children identified during 2011-2012 and 2015 TAS all attended the same school. As the number of antigen-positive children identified was below the critical cut-off of six antigen-positive children, the country passed TAS in 2011-2012[10] and in 2015.[11]

Despite passing TAS in 2011-2012 and 2015, community-based human prevalence studies and molecular xenomonitoring studies of infected mosquitoes in American Samoa provided evidence of low-level ongoing transmission.[12, 13] In a retrospective study of serum samples collected in 2010, antigen (Og4C3) positive samples were identified from participants living across the main island of Tutuila, with higher antigen prevalence around the area (Ili'ili) where the antigen-positive children were identified during 2011-2012 and 2015 TAS.[12] A 2014 study conducted using a convenience sample of 1078 people from different regions of American Samoa and aged 9 to 73 years, demonstrated antigenaemia of 2.7% (95% CI 1.8-3.8). In a sub-group of 283 children aged <13 years who attended the same school as the antigen-positive children from the previous TAS, antigenaemia was 1.1% (95% CI 0.2-3.1).[11] This study identified foci (hotspots) of transmission around two villages, Fagali'i and Ili'ili. [11, 12]

The sample size and threshold for TAS are designed to report numbers of positives within a designated evaluation unit, which in the case of American Samoa was the whole country. Thus TAS may not be able to detect residual clusters of transmission, particularly if there is significant spatial variation in prevalence within an evaluation unit. In addition, the age group (6-7 years) tested in TAS may have low infection rate due to slow acquisition of infection, even if residual endemicity exists.

Although American Samoa had passed school-based TAS in 2011-2012 and in 2015, the 2010 and 2014 community-based studies, both suggested ongoing transmission on LF in American

Samoa. This raised concerns around the suitability of TAS of young children as a tool for post-MDA surveillance, not just in American Samoa but globally. As GPELF approaches the elimination target, WHO recommends developing post-MDA surveillance strategies that are cost-efficient and can be integrated into routine surveillance activities.[2, 11] In 2016, we investigated the effectiveness of two survey designs for post-MDA surveillance: a school-based TAS in children aged 6-7 years and a community-based survey in individuals aged ≥8 years. American Samoa was an optimal study site for two reasons: (i) there have been no MDA since 2007 and hence any infection in children aged ≤9 years is most likely to have been locally acquired (ii) recent evidence of ongoing LF transmission increases the likelihood of detecting any recent infections that were locally acquired.[11-13] The study was designed to survey the two populations (school children aged 6-7 years and community members aged ≥8 years) independent of each other. In this paper, we report our keys findings and discuss implications for strengthening of TAS for post-MDA surveillance.

Methods

Study location

American Samoa is a chain of seven South Pacific islands with a population of ~55,519 persons living in ~70 villages.[14] Over 90% of the population resides on the main island of Tutuila, and the adjacent island of Aunu'u. The remote Manu'a islands were not included in this study as previous seroprevalence studies did not provide any evidence of residual LF transmission.[12]

Target population and survey design

This study had two components A) a school-based survey and B) a community-based survey. Each of the survey designs and sampling methods are described below.

School-based survey

Based on WHO TAS guidelines, a systematic school-based survey was designed for children aged 6-7 years.[2, 10] All elementary schools (N=29) were included in the study. Attendance at Grade 1 and 2 in primary school was used as proxy for being 6-7 years old. Assuming 1% antigen prevalence, the target sample size was calculated using the *Survey Sample Builder*,[15] and was estimated to be 1,014 children. Based on this, the critical cut-off value was estimated to be six antigen-positive children.

Community-based survey

In parallel with the school-based survey, a multi-stage equal probability cluster survey based on WHO guidelines was conducted.[2] Of the 70 villages/ village segments (larger villages were

divided into village segments of <2000 residents and very small adjacent villages were grouped), we randomly selected 30 villages/ village segments (referred to as villages).

Using *Survey Sample Builder*, the sample size required to detect antigen prevalence of 1% was estimated to be 4,620 for persons aged ≥8 years. We assumed a target population of ~55,000 persons, and accounted for an additional 1.5 times within household clustering of participants.

The total numbers of households in the selected villages were estimated based on the census population size and we assumed that an average of seven persons lived in each household. Target number of households was estimated using the target sample size of persons required by the household size of 7 persons and accounted for a 15% non-response/ absentee rate. Sampling fraction was calculated as the proportion of households that needed to be sampled to achieve the target sample size. In each village, 29% households were selected (sampling fraction of 0.29).

Within each village, households were randomly selected from a line list of geo-referenced buildings obtained from the American Samoa Department of Commerce.[16] Detailed village maps showing locations and codes of selected households were prepared and printed prior to field work, and were used during village visits. Destroyed, abandoned or not currently occupied household were substituted with the next closest household. Within each household, all members aged ≥8 years were invited to participate. A household member was defined as an individual who considered the selected house as their principal place of residence or who slept in that house the previous night.

For both school and community-based surveys, participants were eligible irrespective of previous participation in MDA, duration of school attendance or length of residence in the villages.

Data and sample collection

School-based survey

At each school, we recorded the geographic positioning system (GPS) coordinates for the location of the school, total number of children enrolled in Grades 1 and 2, and the school attendance for the day. For each participant, we collected demographic information using electronic questionnaires based on information provided by the consenting parent/ guardian.

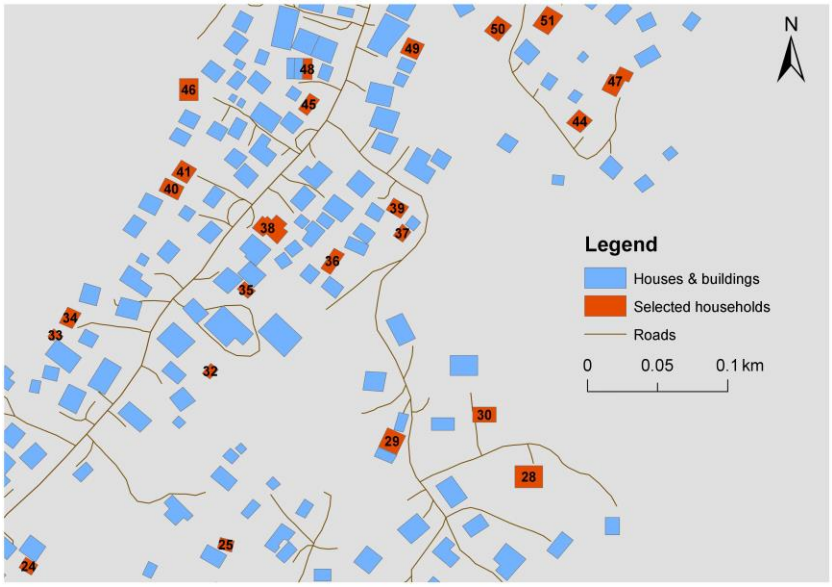
Community-based survey

Selected households were identified using fieldwork maps as described above (Figure 1A). GPS locations of households were recorded at the time of visit. If GPS satellite signal was not

available or a household was substituted, the location was marked on a map, and reconciled manually using the geographic information systems software (ArcGIS). On every occasion that we visited a village, we attempted to revisit households with previously-absent members to maximise participation rates.

Electronic questionnaires were administered by bilingual field research assistants. Questionnaires included demographics, occupation, number of household members aged ≥8 years, country of birth, duration lived in American Samoa, travel history and prior treatment for LF with albendazole and diethylcarbamazine (DEC) during MDA. Data were recorded using smart phones utilising the LINKS electronic database system developed by the Task Force for Global Health.[17]

(A)



(B)

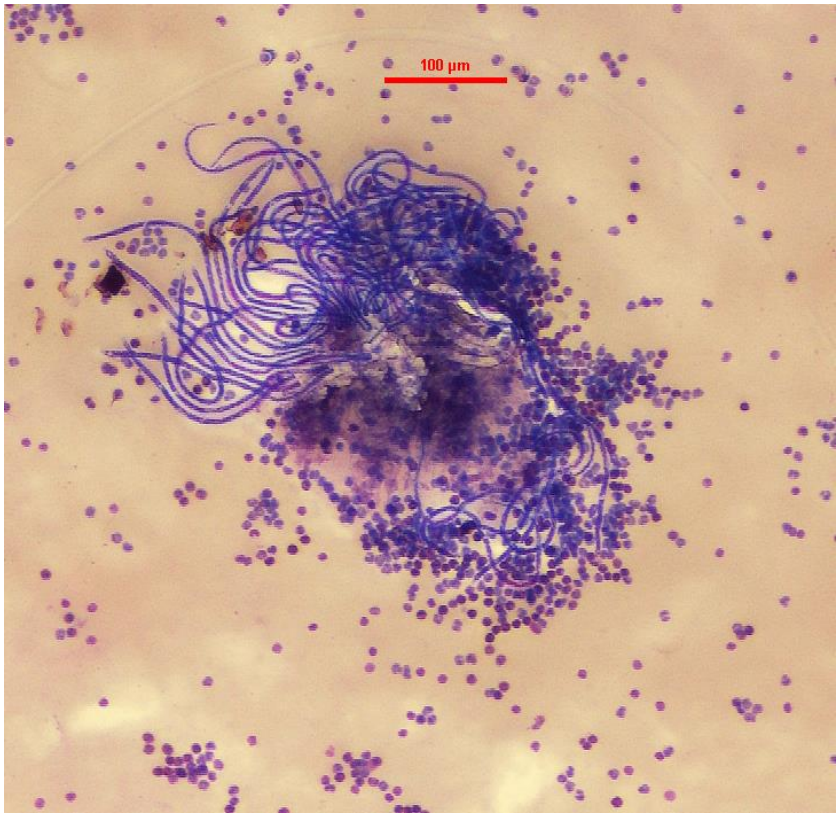


Figure 1: Sample village map used to identify selected households during fieldwork [A]; Blood film with medusa hair clump of filarial worms found in a study participant [B], American Samoa, 2016

Specimen collection and testing

For each participant, we collected 200µl of finger prick blood sample into heparinised microtainers. The blood samples were kept cool after collection, and were tested on the same or following day in a controlled field laboratory environment. Blood samples were tested for circulating filarial antigen (CFA) using the Alere™ Filariasis Test Strip (FTS).[18-20]

All FTS-positive school children were followed-up at home, unless the child's household was already selected for the community-based survey. All FTS-positive community participants were invited to a follow-up clinic, where they were given treatment (excluding pregnant women) with 400mg Albendazole and 6mg/kg DEC according to WHO guidelines.[2] To ensure compliance, participants were encouraged to consume medications in the presence of a field team member. All minors aged <18 years were given treatment following parental/ guardian consent.

During follow-up of FTS-positive people, we collected venous blood samples (~8ml) to repeat the FTS and prepare slides for microscopic examination of microfilaria (Mf) as described previously.[11] Briefly, we prepared three sets of slides per person, by applying 3 lines of 20µl of blood to each slide. Once completely dried, the slides were de-haemoglobinized, fixed with methanol and stained with 2% Giemsa stain for 50 minutes. Each set of slides were examined by two or three experienced parasitologists. A slide was considered Mf positive if ≥1 microfilaria were identified by at least one parasitologist (Figure 1B). Average of counts reported by all parasitologists was used to calculate the final density in Mf/ml.

Data analyses

The outcome measure was a positive FTS test. We undertook descriptive analyses for questionnaire variables and compared simple proportions using Pearson's chi square tests or Fisher exact tests. We estimated crude CFA prevalence and 95% confidence intervals (CI) using binomial exact methods.

We accounted for the multi-stage cluster sampling design of the survey using the 'svyset' command in Stata 13 (StataCorp, 24 College Station, TX). As American Samoa is considered a single evaluation unit for WHO's LF elimination programme,[10] specifying a strata level was not necessary. For the school-based survey, we calculated sampling weight for each participant by adjusting for response rates by schools, and applied post-stratification weights for sex to the entire sample.

For the community-based survey, we calculated a sampling weight for an individual as the inverse product of the probability of selection of the village (primary sampling unit, PSU), household and individual. We weighted for absentees within households and for coverage within each village to account for those households which could not be surveyed either due to logistical reasons, non-response or were vacant at the time of field teams' visit. As 30 out of the 70 eligible PSUs were selected, and selection was done without replacement, we applied a finite population correction (FPC) factor of 30/70.[21, 22] To estimate the country- and village-level CFA prevalence for people aged ≥8 years, we applied post-stratification weights for age and sex based on American Samoa's demographic distribution using information available from the 2014 Statistical Yearbook.[14]

Population estimates for American Samoa were sourced from the American Samoa Statistical Yearbook and were based on the 2010 census.[14]

All analyses were performed using Stata 13 or Microsoft Excel. *P* values of <0.05 were considered statistically significant.

Informed consent and ethics approvals

Ethics approvals for the study were granted by American Samoa Institutional Review Board and the Human Research Ethics Committee at the Australian National University (protocol number 2016/482). The study was conducted in collaboration with the American Samoa Department of Health and the American Samoa Community College. Official permissions for school and village visits were granted by the Department of Education and the Department of Samoa Affairs, respectively.

For the school-based survey, along with signed consent from a parent/ guardian, assent was sought from all participants. For the community-based survey, signed informed consent was obtained from adult participants or from parents/ guardians of those aged <18 years along with verbal assent from minors. All field activities were carried out in a culturally appropriate and sensitive manner with bi-lingual local field teams, and with verbal approval sought from village chiefs/ mayors prior to surveying.

Results

We recruited 1143 and 2750 persons from the school-based and community-based surveys respectively (Table 1).

Table 1: Summary of TAS Strengthening in American Samoa, 2016

Survey demographics	Number recruited	Number of valid FTS[28] (%)	Number FTS positive	Crude CFA prevalence (%)	Adjusted CFA prevalence (95% CI)	Number of Microfilariae slides collected[29]	Number of Microfilariae positive individuals (%)
A. School-based survey	1143	1143 (100)	9	0.8	0.7 (0.3-1.8)[30]	9	1 (11.1)
B. Community-based survey of 30 randomly selected villages/ village segments	2507	2496 (99.6)	102	4.1	6.2 (4.5-8.6)[31]	86	22 (25.6)
All participants	3650	3639 (99.7)	111	3.1	-	95	23 (24.2)

[28] FTS were classified as invalid if the test was invalid or due to insufficient sample.

[29] Excludes FTS-positive individuals who were lost to follow-up or did not want to be bled at time of follow-up.

[30] Adjusted for survey design and sex using SVYSET in Stata13

[31] Adjusted for survey design, age and sex using SVYSET in Stata13

School-based TAS of Grade 1 and 2 children

We sampled all elementary schools (N=29) on the two main islands of American Samoa. All Grade 1 and 2 students were invited to participate (N=2180). Of these, 1143 (52.4%) students returned signed consent forms and all were included in the study. The average participation rate by school was 57% (range 18.2-91.7%).

Table 2 summarises characteristics of participants identified though the school-based TAS. Of the 1143 students, we identified nine FTS-positive children with a crude CFA prevalence of 0.8% (95% CI: 0.4-1.5). As the critical cut-off for passing TAS was six, American Samoa failed school-based TAS.

Estimated overall CFA prevalence after adjusting for participation rates by school, and sex was 0.7% (95% CI: 0.3-1.8). The design effect for the school-based survey was 1.9. Adjusted CFA prevalence in males was 0.5% (95% CI: 0.1-1.9) and in females was 0.9% (95% CI: 0.4-2.4).

Of the nine FTS-positive children, four (44.4%) attended the same school in Pago Pago, and two (22.2%) attended the same school in Nua. FTS-positive children from Nua lived in Fagali'i, a suspected hotspot for transmission. The majority (7/9, 77.8%) of FTS-positive children were born in American Samoa and reported to have lived there for their entire life. Two (22.2%) FTS-positive children were born in Western Samoa, but this difference was not statistically significant compared to those born in American Samoa.

Of the nine FTS-positive children, one (11.1%) was microfilaraemic with Mf density of 1075 Mf/mm^3. The child was a 7 year old male who lived in Vaitogi (a village with evidence of ongoing transmission) and attended the school in Ili'ili.

Community-based survey of randomly selected villages

We visited 30 villages, and sampled 2507 persons from 711 households. The average household size was 6 (range 1-25) persons aged ≥8 years per household. We recruited participants from 77.6% of the selected households, and 83.2% (range 14.3-100%) of eligible household members (aged ≥8 years) participated in the study. Within household non-response was mostly associated with household members being absent at the time of visit, rather than refusal to participate. We recruited 1,140 (45.5%) males and 1,367 (54.5%) females (Table 3). Of the 2507 participants tested, 11 (0.4%) had invalid tests and were excluded from analyses (Tables 1 & 3). Of the 2496 participants with valid tests, 102 were FTS-positive, equivalent to an overall crude CFA prevalence of 4.1%. Of the 102 FTS-positive persons, 79 were male (crude CFA prevalence

7.0%) and 23 were female (crude CFA prevalence 1.7%). Crude CFA prevalence in males was significantly higher than females ($p<0.001$).

The original target sample size for the community-based survey, calculated based on an expected CFA prevalence of 1%, was 4620. Within the first two weeks of recruitment, the observed CFA prevalence (4.1%) was significantly higher than anticipated, and it was agreed that smaller target sample size of 2981 would provide adequate statistical power (Table 4).

Table 2: Summary of participants in the school survey, American Samoa, 2016

Questionnaire variables	Number tested (% of total tested)	Number FTS positive (Crude CFA prevalence)	*p* value[32]
Total	1143 (100)	9 (0.8)	
Age (years)			
5	62 (5.4)	0 (0)	0.74
6	524 (45.8)	3 (0.6)	
7	510 (44.6)	5 (1.0)	
8	39 (3.4)	1 (2.6)	
9	6 (0.5)	0	
10	2 (0.2)	0	
Sex			
Male	550 (48.1)	3 (0.5)	0.373
Female	593 (51.2)	6 (1.0)	
Location of school			
Nua	44 (3.9)	2 (4.5)	**<0.001**
Pago Pago	82 (7.2)	4 (4.9)	
Ili'ili	94 (8.2)	1 (1.1)	
Nu'uuli	93 (8.1)	1 (1.1)	
Faga'alu	44 (3.9)	1 (2.3)	
Others	786 (68.8)	0 (0)	
Place of birth			
American Samoa	1000 (87.5)	7 (0.7)	0.083
Western Samoa	54 (4.7)	2 (3.7)	
Other	83 (7.3)	0 (0)	
Unknown	6 (0.5)	0 (0)	
Village of residence			
Faga'alu	16 (1.4)	1 (6.3)	**<0.001**
Fagali'i	7 (0.6)	2 (28.6)	
Fagatogo	37 (3.2)	2 (5.4)	
Pago Pago	73 (6.4)	2 (2.7)	
Tafuna	157 (13.7)	1 (0.6)	
Vaitogi	55 (4.8)	1 (1.8)	
All other villages	798 (69.8)	0 (0)	
Duration lived in the village			
Less than 1 year	61 (5.3)	1 (1.6)	0.723
1-2 years	79 (6.9)	1 (1.3)	
3-5 years	154 (13.5)	0 (0)	
≥6 years	845 (73.9)	7 (0.8)	
Unknown	4 (0.4)	0 (0)	

[32] *P* value estimated using Chi-square or Fisher exact for significance of difference in crude CFA prevalence. Statistically significant results are highlighted in bold.

Table 3: Summary of participants in the community survey, American Samoa, 2016

Questionnaire variables	Number tested (%)	Number FTS positive (Crude CFA prevalence)	*p* value [33]
Total	2496 (100.0)	102 (4.1)	
Age group (years)			
8 to 9	147 (5.9)	4 (2.7)	**<0.001**
10 to 19	732 (29.2)	6 (0.8)	
20 to 29	363 (14.5)	8 (2.2)	
30 to 39	315 (12.6)	18 (5.7)	
40 to 49	340 (13.6)	22 (6.5)	
50 to 59	309 (12.4)	25 (8.1)	
60 to 69	183 (7.3)	9 (4.9)	
≥70	107 (4.3)	10 (9.3)	
Sex			
Male	1130 (45.3)	79 (7.0)	**<0.001**
Female	1366 (54.7)	23 (1.7)	
Household size (≥8 years old)			
≤2	218 (8.7)	9 (4.1)	0.176
3-6	1376 (55.1)	47 (3.4)	
7-9	551 (22.1)	31 (5.6)	
≥10	351 (14.1)	15 (4.3)	
Years lived in the village			
< 1 year	191 (7.7)	12 (6.3)	**<0.001**
1-2 years	123 (4.9)	10 (8.1)	
3-4 years	140 (5.6)	3 (2.1)	
5-10 years	175 (7)	7 (4.0)	
>10 years	676 (27.1)	44 (6.5)	
Whole life	1191 (47.7)	26 (2.2)	
Taken MDA in the past			
Yes	1015 (40.7)	54 (5.3)	**0.029**
No	1420 (56.9)	45 (3.2)	
Unsure	61 (2.4)	3 (4.9)	
Occupation groups			
Indoor	686 (27.5)	31 (4.5)	**<0.001**
Outdoor	28 (1.1)	5 (17.9)	
Fish cannery worker/ Fish cleaner	128 (5.1)	12 (9.4)	
Mixed indoor/outdoor	329 (13.2)	13 (4.0)	
Student	874 (35.0)	11 (1.3)	
Unemployed	318 (12.7)	20 (6.3)	
Other	133 (5.3)	10 (7.5)	
Travel outside of American Samoa in the previous 12 months			
Yes	751 (30.1)	29 (3.9)	0.71
No	1745 (69.9)	73 (4.2)	

[33] *P* value estimated using Chi-square or Fisher exact for significance of difference in crude CFA prevalence. Statistically significant results are highlighted in bold.

The age and sex distribution of the community-based survey participants and the general population of American Samoa is presented in Figure 2. After adjusting for the survey design, and age and sex distribution of American Samoa, the adjusted CFA prevalence was 6.2% (95% CI: 4.5-8.6). The design effect for the community-based survey was 4.2.

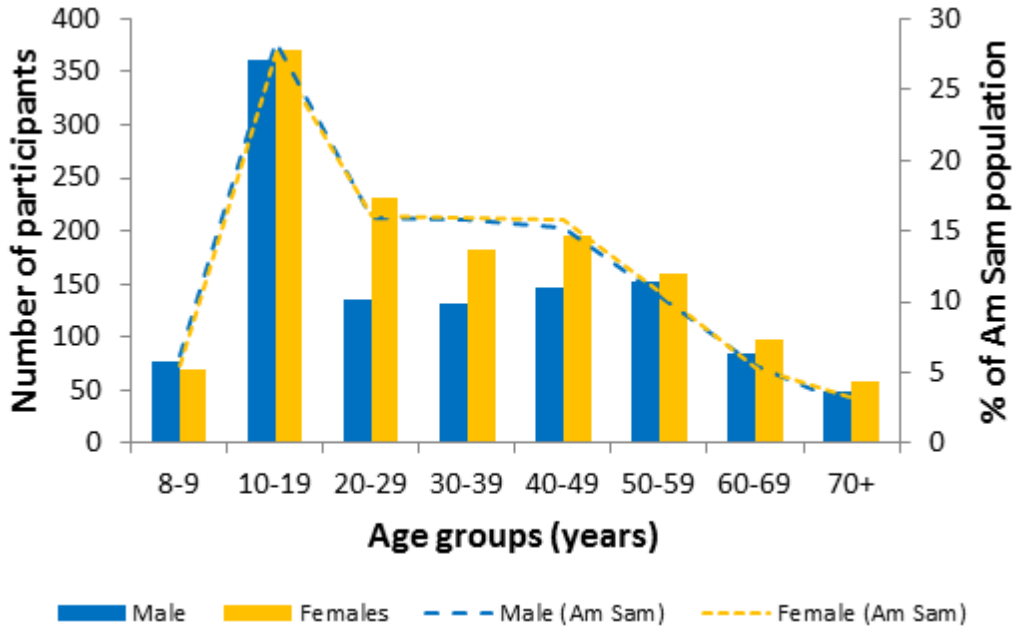


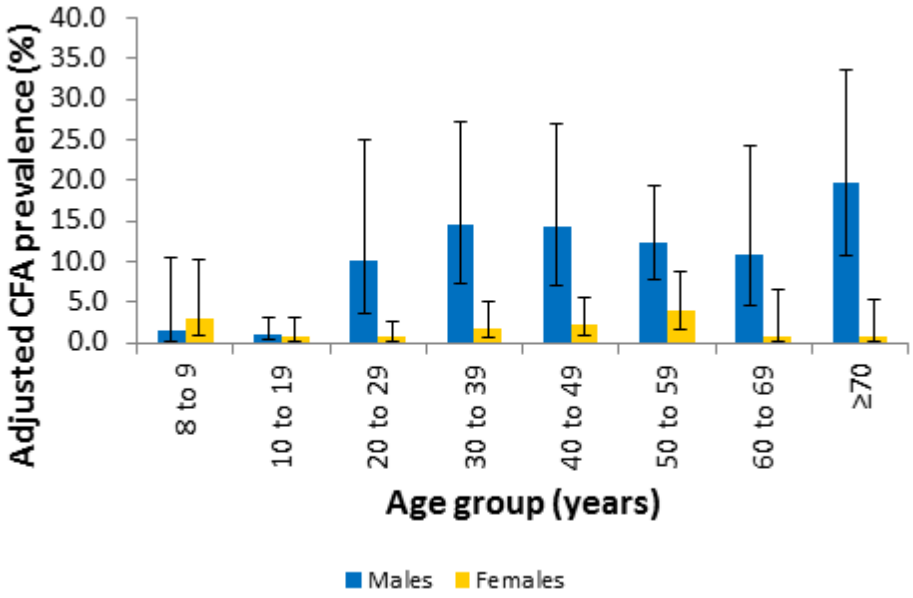
Figure 2: Age and sex distribution of participants (bars) from community survey and general population (dotted lines) living in American Samoa, 2016. Population estimates based on American Samoa 2014 Statistical Yearbook (American Samoa Department of Commerce)

After accounting for the survey design, adjusted CFA prevalence by age and sex in the randomly selected villages are presented in Figure 3A. In children aged 8-9 years, who were born after the MDA had stopped, the adjusted CFA prevalence was 2.2% (95% CI: 0.8-6.1).

Of the 102 FTS-positive individuals, we were able to prepare slides for 86 (84.3%) participants. Of these, 22 (25.6%) were microfilaraemic individuals of whom 19 (86.4%) were male (Figure 3B). The mean Mf density was 186.5 Mf/mm^3 (range 5.6-916.7 Mf/mm^3).

We estimated village-level CFA prevalence by adjusting for the survey design and for age and sex distribution. Adjusted village-level CFA prevalence varied from 0% to 47.1% (Table 4 and Figure 4). Notably, only 6/30 (20%) villages had zero FTS-positive individuals. Microfilaraemic people were dispersed throughout the island and lived in 10 of 30 randomly selected villages. Six (27.3%) microfilaraemic people lived in Vaitogi, the same village as the Mf-positive school child.

(A)



(B)

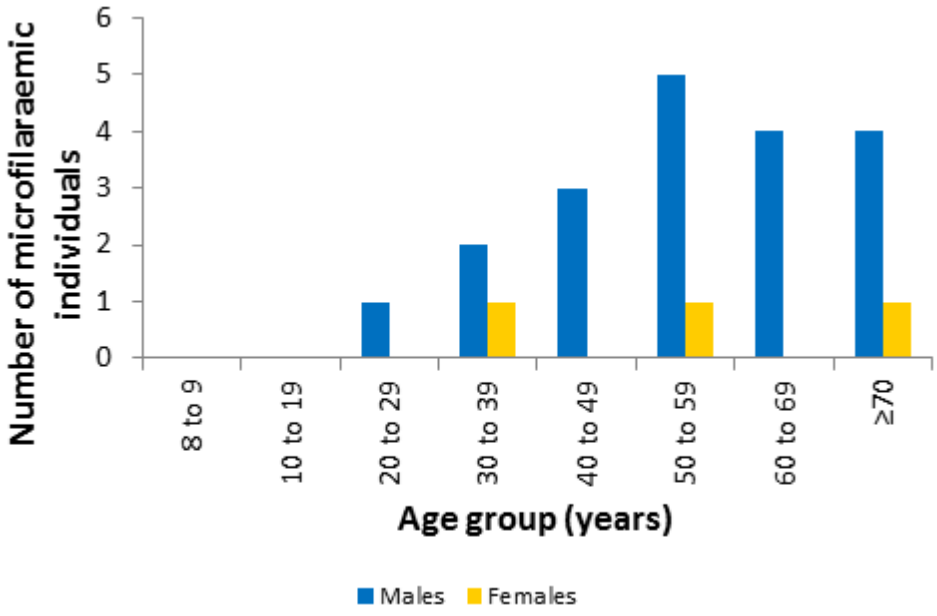


Figure 3: Adjusted* circulating filarial antigen (CFA) prevalence with 95% CIs [A] and microfilaraemic individuals by age and sex in community survey [B], American Samoa 2016. *Adjusted for survey design

Table 4: Summary of sampling and recruitment for community survey; and prevalence of circulating filarial antigen (CFA) for randomly selected villages, American Samoa 2016

Village	Total number of residents[34]	Estimated number of total households	Target number of households	Number of households sampled (% of target)	Target population aged ≥8 years	Number recruited (% of target)	Number FTS-positive	Crude CFA prevalence (%)	Adjusted CFA prevalence (95% CI)[35]
Village 1(Afono)	524	75	22	21 (95.5)	69	71 (82.3)	3	4.2	4.0 (1.7-9.3)
Village 2 (Alao)	495	71	20	12 (60)	65	44 (54)	0	0	-
Village 3 (Amaua)	96	14	4	5 (125)	13	19 (120.2)	1	5.3	4.9 (1.4-16.3)
Village 4 (Amouli)	920	131	38	33 (86.8)	121	111 (73.3)	2	1.8	2.7 (1-7)
Village 5 (Asili)	224	32	9	9 (100)	30	28 (75.9)	4	14.3	19.6 (9.7-35.6)
Village 6 (Auma)	254	36	10	9 (90)	33	39 (93.2)	2	5.1	8.3 (3.2-19.7)
Village 7 (Aumi)	186	27	8	6 (75)	25	23 (75.1)	0	0	-
Village 8 (Fagamalo)	47	7	2	3 (150)	6	13 (168)	4	30.8	47.1 (16.9-79.6)
Village 9 (Faganeanea)	150	21	6	5 (83.3)	20	23 (93.1)	0	0	-
Village 10 (Fagatogo)	1737	248	72	55 (76.4)	229	212 (74.1)	5	2.4	2.7 (1.4-5.2)
Village 11 (Fatumafuti)	113	16	5	3 (60)	15	5 (26.9)	1	20.0	44.8 (10-85.5)
Village 12 (Ili'ili)[36]	3195	456	132	87 (65.9)	421	308 (58.5)	15	4.9	4.9 (3.2-7.5)
Village 13 (Lauli'i)	892	127	37	27 (73)	118	104 (70.8)	1	1.0	1.1 (0.3-4)
Village 14 (Leloaloa)	448	64	18	15 (83.3)	59	40 (54.2)	7	17.9	25.8 (16.1-38.4)
Village 15 (Malaeimi)	1182	169	49	36 (73.5)	156	120 (61.6)	5	4.2	10.9 (5-22.2)
Village 16 (Malaeloa/Aitulagi)	698	100	29	20 (69)	92	90 (78.3)	4	4.4	8.1 (3.3-18.6)
Village 17 (Masausi)	164	23	7	7 (100)	22	24 (88.9)	0	0	-
Village 18 (Nua)	141	20	6	3 (50)	19	17 (73.2)	0	0	-
Village 19 (Pago Pago)[37]	1828	261	75	62 (82.7)	241	228 (75.7)	4	1.8	2.3 (1.2-4.5)

[34] Population estimates based on American Samoa 2014 Statistical Yearbook (American Samoa Department of Commerce). 80% of the population is estimated to be aged ≥8 years.

[35] Adjusted for survey design, and post-stratified for age and sex using SVYSET in Stata13.

[36] Village 12 and 20 were split into two segments for random selection of villages. Both segments of both villages were randomly selected. Data presented here are pooled for both segments for each of the villages.

Village	Total number of residents[34]	Estimated number of total households	Target number of households	Number of households sampled (% of target)	Target population aged ≥8 years	Number recruited (% of target)	Number FTS-positive	Crude CFA prevalence (%)	Adjusted CFA prevalence (95% CI)[35]
Village 20 (Pava'ia'i)	2450	350	101	73 (72.3)	323	255 (63.2)	3	1.2	2.5 (0.8-7.5)
Village 21 (Satala-Anua-Atuu)	674	96	28	22 (78.6)	89	81 (73)	7	8.8	9.0 (4.3-17.7)
Village 22 (Se'etaga)	299	43	12	13 (108.3)	39	49 (99.5)	2	4.1	3.4 (1.3-8.5)
Village 23 (Tafuna)[38]	2000	286	82	56 (68.3)	263	187 (56.8)	5	2.7	3.3 (1.4-7.6)
Village 24 (Taputimu)	841	120	35	29 (82.9)	111	88 (63.5)	0	0.0	-
Village 25 (Tula)	405	58	17	14 (82.4)	53	52 (78)	4	7.7	14.5 (5.9-31.5)
Village 26 (Utumea West)	53	8	2	3 (150)	7	12 (137.5)	1	8.3	12.7 (3.2-39.4)
Village 27 (Vaitogi)	1959	280	81	64 (79)	258	212 (65.7)	18	8.5	11.8 (7.9-17.4)
Village 28 (Vatia)	640	91	26	19 (73.1)	84	52 (49.3)	4	7.8	21.8 (9.8-41.6)
Total	**22601**	**3230**	**933**	**711 (76.2)**	**2981**	**2507 (84.1)**	**102**	**4.1**	**6.2 (4.5-8.6)**

[37] One of two segments of Pago Pago was randomly selected; number of residents shown here is half of the total population of Pago Pago.

[38] One of four segments of Village 23 was randomly selected; number of residents shown here is quarter of the total population of Tafuna.

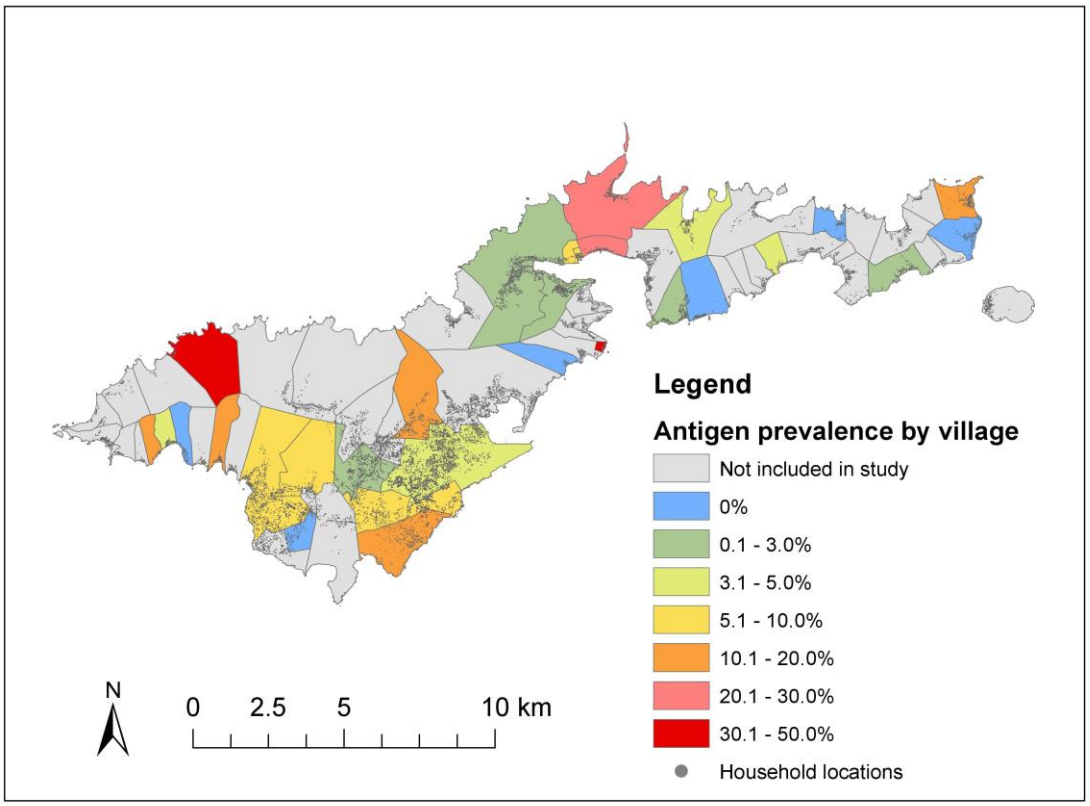


Figure 4: Location of villages (N=30) and adjusted* circulating filarial antigen (CFA) prevalence, American Samoa, 2016. *Adjusted for survey design, age and sex distribution of American Samoa.

Discussion

Our study confirmed ongoing transmission of LF in American Samoa. We identified 111 antigen-positive persons with an overall crude CFA prevalence of 3.1%. Of the 95 antigen-positive persons for whom slides were available, 23 (24.2%) were microfilaraemic including a 7 year old child. American Samoa failed school-based TAS in 2016, and the community-based survey identified higher than expected numbers of antigen-positive people. The school-based survey was logistically easier, cheaper and less time consuming, but the community-based survey provided detailed information on estimates of community-level CFA prevalence, areas of high prevalence and helped identify antigen and microfilariae positive people who are capable of perpetuating transmission.

The adjusted CFA prevalence in the school-based survey of children aged 6-7 years (0.7%) was significantly lower than the community-based survey of people aged ≥8 years (6.2%). Although antigen-positive people aged ≥8 years may not have been as recently infected as the 6-7 year old children, it is important to identify them in the post-MDA setting as they may serve as a

reservoir of parasites and maintain residual transmission.[23] The capacity of the community survey to detect residual transmission is also evident from its ability to identify antigen positive children aged 8-9 years (adjusted CFA prevalence of 2.2%, 95% CI 0.8-6.1), who were either born after the MDA or were too young to receive treatment, and would not have been otherwise identified through school-based TAS. Our findings indicate that prevalence estimated by TAS of young children may not be sufficiently sensitive to identify areas where antigen positive people aged ≥8 years live (i.e. areas of residual transmission).

The school-based TAS and the community-based survey had several advantages and limitations. The key comparisons between the two survey designs are summarised below. In our study, the school-based TAS was highly representative of the target population (6-7 years) and included 52.4% of Grade 1 and 2 children from all elementary schools. The school-based survey in 2016 identified two FTS-positive children living in Fagali'i, an area of known high LF transmission.[11] It also identified four FTS-positive children from another school, who lived in Fagatogo and Pago Pago. Both of these villages had estimated CFA prevalence of 2.7% and 2.3%, respectively, below the overall estimated CFA prevalence of 6.2%. Significantly higher CFA prevalence in children attending certain schools indicates that transmission might be occurring in and around schools. A study conducted in Samoa, where *Ae. polynesiensis* is an efficient day biting mosquito, observed spatial clustering of infected children aged ≤10 years in a few selected schools and provided suggestive evidence of transmission at the school-level.[24]

The school-based TAS provided limited information on risk factors including age and sex. No differences were observed in CFA prevalence between male and female children, most likely due to similar duration of time spent outdoors by children of both sexes. In contrast, the community-based survey indicated that males (particularly in persons aged ≥20 years) had higher CFA prevalence and greater proportion had detectable microfilaria. Adult males are most likely at higher risk due to the longer periods of time spent outdoors, increasing the likelihood of mosquito bites.[12, 25] Hormonal and pregnancy-mediated regulation of the immune system may also contribute to lower infection rates in female, particularly during the reproductive years.[26] The age differential between children and adults also supports modelling studies which suggested that testing of adults were more efficient at detecting transmission in low prevalence settings compared to testing children aged 6-7 years.[23]

The school-based survey was a systematic survey where all elementary schools on the two main islands were surveyed. The community-based survey was a modified WHO cluster survey, which is recommended for surveying large populations in resource-limited settings. By correcting for clustering during analyses,[22, 27] we believe our results are an accurate estimate of

the country-wide CFA prevalence. As only 30 of the 70 villages were sampled, the school and community-based surveys were not geographically aligned. Consequently, some children tested in the school-based survey lived in villages that were not selected for the community-based survey. However, as we surveyed a large proportion of the selected villages, and that many villages are contiguous along the limited number of roads in American Samoa, geographical concordance is unlikely to be as issue.

The reasons for persistence of high LF prevalence in American Samoa remain unclear, and could be associated with a multitude of factors including poor-coverage or systematic non-compliance during MDAs,[28, 29] migration and travel of people from other regions in the Pacific where LF transmission is ongoing[12, 25, 29] and the presence of efficient day and night biting mosquitoes.[13] However, as American Samoa failed TAS in 2016, one year after passing TAS in 2015; it raises several questions about the utility of TAS of young children for conducting post-MDA surveillance. It is unclear if there has been a resurgence of LF within one year or whether the 2015 TAS may have missed antigen-positive children, even though >90% schools were surveyed. As LF has a long incubation period, and microfilaremia and antigenemia develop over months to years after exposure,[30] it is unlikely that all the antigen-positive people of all ages identified in our study acquired infection during the period between 2015 TAS and 2016 TAS. Likely persistence of transmission was evident from the community-based human research studies conducted in 2010 and in 2014, which identified foci of residual transmission in certain parts of American Samoa and high antigen prevalence amongst migrant workers.[11, 12] As the previous TAS failed to detect these hotspots, it is possible that people living in high prevalence areas may have served as reservoirs and perpetuated LF transmission. Hypothetically, if at the time of 2011-2012 and 2015 TAS, post-MDA surveillance extended to testing of older persons, programme implementers may have identified infected individuals. This most likely would have provided evidence ongoing transmission and identified foci of residual transmission. Subsequently, disease resurgence could have been avoided or control measures such as territory-wide or targeted MDA could have been implemented earlier.

While further studies to understand the transmission dynamics and risk-factors influencing LF resurgence are underway, our data strongly suggests that current design of school-based TAS of children aged 6-7 years is not sufficiently sensitive for post-MDA surveillance . Considering the wide-spread transmission across American Samoa and the unexpectedly higher CFA prevalence, further MDA or other intervention such as test and treat will be required. Post-MDA surveillance strategies should be enhanced and focus on identification of infected persons.[2] Although community-based surveys are operationally challenging, surveillance activities should

focus on opportunistic and cost-effective methodologies targeting community members.[11, 23] For example, testing high-risk occupation groups at workplace clinics, pregnant women while attending routine antenatal appointments, community members at the time of routine health check-ups for chronic illnesses, high-school students at the time of vaccination campaigns and household members of antigen-positive people. Collectively, our findings call for careful planning and implementation of MDAs, and sensitive and sustainable post-MDA surveillance in order to achieve elimination goals of the global programme by 2020.

Acknowledgements

This study was funded by the Taskforce for Global Health. Dr Meru Sheel is Field Epidemiology Training Program Fellow in the Masters of Philosophy in Applied Epidemiology at the Australian National University, and is supported by scholarships from the Australian Government Research Training Program and the National Centre for Immunisation Research and Surveillance, Australia. Dr Colleen Lau holds an Australian National Health and Medical Research Council Fellowship (1109035).

We would like to acknowledge the hard work of all our field team members, particularly Ms Paeae Tufono, Ms Ledonna Pule, Ms Fitilagi Tagiola, Ms Susana Lin, Ms Meliame Tufono, Ms Nalini Lata, Mr Jason Tufele and Ms Catherine Montablo. We would also like to thank Ms Mary Matai'a of the American Samoa Department of Health for her assistance with logistics and laboratory testing of specimens. We also thank Dr Mark Schmaedick at the American Samoa Community College for his assistance with project logistics, and allowing us to use his laboratories. We are also grateful to all the school principals and teachers, and village mayors and chiefs for their assistance in conducting the fieldwork. Thank you to the NIH/NIAID Filariasis Research Reagent Resource Center (www.filariasiscenter.org) for providing the FTS positive control. DEC and Albendazole were supplied by WHO. Statistical advice for survey data analyses was provided by Professor Catherine D'Este (Australian National University, Australia).

References

1. Ramaiah KD and Ottesen EA. Progress and impact of 13 years of the global programme to eliminate lymphatic filariasis on reducing the burden of filarial disease. *PLoS Negl Trop Dis*. 2014; 8: e3319.
2. World Health Organization. Monitoring and epidemiological assessment of mass drug administration in the global programme to eliminate lymphatic filariasis: a manual for national elimination programmes. 2011.
3. World Health Organization. Global programme to eliminate lymphatic filariasis: progress report, 2015. *Weekly epidemiological record,*. 2016; 91: 441-60.
4. Ichimori K and Crump A. Pacific collaboration to eliminate lymphatic filariasis. *Trends Parasitol*. 2005; 21: 441-4.
5. WHO Western Pacific Region. Congratulations, Tonga! Pacific island state eliminates lymphatic filariasis as a public health problem. World Health Organization, 2017. Accessed 7 September 2017.http://www.wpro.who.int/mediacentre/releases/2017/20170731/en/.
6. Rao RU, Nagodavithana KC, Samarasekera SD, et al. A comprehensive assessment of lymphatic filariasis in Sri Lanka six years after cessation of mass drug administration. *PLoS Negl Trop Dis*. 2014; 8: e3281.
7. Schmaedick MA, Koppel AL, Pilotte N, et al. Molecular xenomonitoring using mosquitoes to map lymphatic filariasis after mass drug administration in American Samoa. *PLoS Negl Trop Dis*. 2014; 8: e3087.
8. Coutts SP, King JD, Pa'au M, et al. Prevalence and risk factors associated with lymphatic filariasis in American Samoa after mass drug administration. *Tropical medicine and health*. 2017; 45: 22.
9. Pacific Programme to Eliminate Lymphatic Filariasis. Country Programmes, American Samoa, National activities carried out to date. Division of Pacific Technical Support, WHO Western Pacific Region. Accessed 18 August 2017
10. Chu BK, Deming M, Biritwum NK, et al. Transmission assessment surveys (TAS) to define endpoints for lymphatic filariasis mass drug administration: a multicenter evaluation. *PLoS Negl Trop Dis*. 2013; 7: e2584.
11. Lau CL, Sheridan S, Ryan S, et al. Detecting and confirming residual hotspots of lymphatic filariasis transmission in American Samoa 8 years after stopping mass drug administration. *PLoS Negl Trop Dis*. 2017; 11: e0005914.
12. Lau CL, Won KY, Becker L, et al. Seroprevalence and spatial epidemiology of Lymphatic Filariasis in American Samoa after successful mass drug administration. *PLoS Negl Trop Dis*. 2014; 8: e3297.
13. Lau CL, Won KY, Lammie PJ and Graves PM. Lymphatic Filariasis Elimination in American Samoa: Evaluation of Molecular Xenomonitoring as a Surveillance Tool in the Endgame. *PLoS Negl Trop Dis*. 2016; 10: e0005108.
14. American Samoa Department of Commerce. 2014 Statistical Yearbook. 2014. Accessed.http://doc.as.gov/wp-content/uploads/2016/06/2014-Statistical-Yearbook.pdf.
15. Neglected Tropical Disease Support Centre. TAS-STH Survey Sample Builder Tool. Accessed.http://www.ntdsupport.org/resources/tas-sth-survey-sample-builder-tool.
16. American Samoa GIS User Group. American Samoa Government - Department of Commerce. Accessed.http://doc.as.gov/resource-management/ascmp/gis/user-group/.
17. Pavluck A, Chu B, Mann Flueckiger R and Ottesen E. Electronic data capture tools for global health programs: evolution of LINKS, an Android-, web-based system. *PLoS Negl Trop Dis*. 2014; 8: e2654.
18. Weil GJ, Curtis KC, Fakoli L, et al. Laboratory and field evaluation of a new rapid test for detecting Wuchereria bancrofti antigen in human blood. *Am J Trop Med Hyg*. 2013; 89: 11-5.
19. World Health Organization. Global programme to eliminate lymphatic filariasis: progress report, 2014. *Weekly epidemiological record,*. 2015; 90: 489-504.

20. Yahathugoda TC, Supali T, Rao RU, et al. A comparison of two tests for filarial antigenemia in areas in Sri Lanka and Indonesia with low-level persistence of lymphatic filariasis following mass drug administration. *Parasites & vectors*. 2015; 8: 369.
21. World Health Organization. Vaccination Coverage Cluster Surveys: Reference Manual Annexes. 2015.
22. World Health Organization. Vaccination Coverage Cluster Surveys: Reference Manual. 2015.
23. Harris JR and Wiegand RE. Detecting infection hotspots: Modeling the surveillance challenge for elimination of lymphatic filariasis. *PLoS Negl Trop Dis*. 2017; 11: e0005610.
24. Joseph H, Moloney J, Maiava F, McClintock S, Lammie P and Melrose W. First evidence of spatial clustering of lymphatic filariasis in an Aedes polynesiensis endemic area. *Acta tropica*. 2011; 120: S39-S47.
25. Liang JL, King JD, Ichimori K, Handzel T, Pa'au M and Lammie PJ. Impact of five annual rounds of mass drug administration with diethylcarbamazine and albendazole on Wuchereria bancrofti infection in American Samoa. *Am J Trop Med Hyg*. 2008; 78: 924-8.
26. Brabin L. Sex differentials in susceptibility to lymphatic filariasis and implications for maternal child immunity. *Epidemiol Infect*. 1990; 105: 335-53.
27. Carlin JB and Hocking J. Design of cross-sectional surveys using cluster sampling: an overview with Australian case studies. *Australian and New Zealand Journal of Public Health*. 1999; 23: 546-51.
28. Boyd A, Won KY, McClintock SK, et al. A community-based study of factors associated with continuing transmission of lymphatic filariasis in Leogane, Haiti. *PLoS Negl Trop Dis*. 2010; 4: e640.
29. King JD, Zielinski-Gutierrez E, Pa'au M and Lammie P. Improving community participation to eliminate lymphatic filariasis in American Samoa. *Acta tropica*. 2011; 120 Suppl 1: S48-54.
30. Witt C and Ottesen EA. Lymphatic filariasis: an infection of childhood. *Tropical medicine & international health : TM & IH*. 2001; 6: 582-606.

Appendices

Appendix 2A: Short report on herpes zoster in Indigenous Australians

Research letter

Rates of hospitalisation for herpes zoster may warrant vaccinating Indigenous Australians under 70

Meru Sheel[1,2], Frank H Beard[1,3], Aditi Dey[1,3], Kristine Macartney[1,3], Peter B McIntyre[1,3]

Herpes zoster (HZ) is caused by reactivation of latent varicella zoster virus infection. The most common complication of HZ is post-herpetic neuralgia (PHN), which is often debilitating and refractory to treatment.[1] The incidence of both HZ and PHN increases markedly with age.[2] In November 2016, a vaccine for HZ was included in Australia's National Immunisation Program (NIP) for all people aged 70, together with a 5-year catch-up program for those aged 71–79 years.[3] The vaccine is cost-effective for people aged 70–79, but is registered for vaccinating people from age 50.[3]

Concerns have been raised by clinicians in Aboriginal and Torres Strait Islander (Indigenous) health care that the NIP age criterion does not take into account the special circumstances of Indigenous Australians. First, fewer than 2% of Indigenous Australians are 70 years or older, compared with 10% of the non-Indigenous population (Box). Second, vaccines for pneumococcal disease and influenza are funded for Indigenous people from a younger age (50 and 15 years respectively) than for non-Indigenous Australians (65 years).[4]

There are few published data on the incidence of HZ among Indigenous Australians; in particular, analyses of HZ-related general practice encounters have not reported Indigenous-specific data.[2] We therefore compared data from the Australian Institute of Health and Welfare (AIHW) National Hospital Morbidity Database on the rates of HZ-related hospitalisations of Indigenous and non-Indigenous Australians during 2007–2011. We excluded Tasmanian and Australian Capital Territory data, as recommended by the AIHW for this period.[5] Hospitalisations associated with HZ were identified by International Classification of Diseases, revision 10, Australian modification (ICD-10-AM) codes B02.0–B02.9, and classified as principal diagnoses if recorded in the primary diagnostic field. Mid-year population estimates were obtained from the Australian Bureau of Statistics. Age-specific hospitalisation rates, incidence rate ratios (IRRs), and 95% confidence intervals (CIs) were estimated by negative binomial regression in Stata 13.1 (StataCorp).

We identified 214 HZ-related (principal) hospitalisations of Indigenous people and 11 252 of non-Indigenous people (Box). Hospitalisation rates were similar for Indigenous and non-Indigenous people aged 70–79 years or over 80, but were significantly higher among Indigenous people in younger age groups. For people aged 60–69 years, the IRR was 1.77 (95% CI, 1.27–2.48); further, the confidence interval for the hospitalisation rate of Indigenous people aged 60–69 years (34 [95% CI, 22–50] per 100 000 population) overlapped that of the rate for non-Indigenous people aged 70–79 years (44.8 [95% CI, 43.1–46.5] per 100 000 population). The results were similar when hospitalisations for which HZ was recorded in any diagnostic field were analysed (data not shown).

Patients hospitalised for HZ are at the severe end of the disease spectrum, accounting for only 3% of all HZ cases.[2,6] Nevertheless, our findings suggest that the burden of severe HZ among Indigenous Australians in their 60s is higher than for non-Indigenous Australians. This higher disease burden adds to other considerations that support reviewing the age criteria for funded zoster vaccination of Indigenous Australians.

Acknowledgements: This work was supported by the National Centre for Immunisation Research and Surveillance. Meru Sheel is a scholar in the Master of Philosophy in Applied Epidemiology program at the Australian National University.

Competing interests: No relevant disclosures. ■

Hospitalisations for herpes zoster (principal diagnosis) of Indigenous and non-Indigenous Australians, 2007–2011

	Indigenous Australians			Non-Indigenous Australians			
Age group	Number, 2007–2011*	5-year population (% of Indigenous population)	Average annual hospitalisations per 100 000 population (95% CI)	Number, 2007–2011*	5 year population (% of non-Indigenous population)	Average annual hospitalisations per 100 000 population (95% CI)	Incidence rate ratio† (95% CI)
0–49 years	110	2 687 761 (87.6%)	4.1 (3.3–5.1)	1553	68 660 660 (68.1%)	2.3 (2.1–2.5)	1.81 (1.46–2.24)
50–59 years	34	218 589 (7.1%)	16 (11–22)	1071	12 819 945 (12.7%)	8.3 (7.4–9.4)	1.87 (1.29–2.71)
60–69 years	35	104 776 (3.4%)	34 (22–50)	1804	9 581 725 (9.5%)	18.8 (17.9–19.8)	1.77 (1.27–2.48)
70–79 years	16	42 995 (1.4%)	37 (18–79)	2631	5 877 963 (5.8%)	44.8 (43.1–46.5)	0.83 (0.51–1.36)
≥ 80 years	19	14 315 (0.5%)	132 (67–262)	3390	3 825 213 (3.8%)	89.8 (48.7–166)	1.47 (0.57–3.78)
All ages	214	3 068 436	7.0 (5.5–8.8)	11 252	100 765 506	11.2 (10.6–11.7)	0.62 (0.53–0.73)

* Age-specific hospitalisations (ICD-10-AM codes B02.0–B02.9) in New South Wales, Victoria, Queensland, Western Australia, South Australia and the Northern Territory. † Ratio of hospitalisation rates for Indigenous *v* non-Indigenous Australians. ◆

[1]National Centre for Immunisation Research and Surveillance, the Children's Hospital at Westmead, Sydney, NSW. [2]National Centre for Epidemiology and Population Health, Australian National University, Canberra, ACT. [3]University of Sydney, Sydney, NSW. meru.sheel@health.nsw.gov.au • doi: 10.5694/mja16.01468

1 Cunningham AL, Breuer J, Dwyer DE, et al. The prevention and management of herpes zoster. *Med J Aust* 2008; 188: 171-176. https://www.mja.com.au/journal/2008/188/3/prevention-and-management-herpes-zoster

2 MacIntyre R, Stein A, Harrison C, et al. Increasing trends of herpes zoster in Australia. *PLoS One* 2015; 10: e0125025.

3 Australian Government Department of Health. Zoster virus vaccine live; 0.65 mL injection, prefilled syringe; Zostavax® [Pharmaceutical Benefits Advisory Committee public summary document]. Nov 2014. http://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2014-11/files/zoster-vaccine-psd-11-2014.pdf (accessed Dec 2016).

4 Department of Health. National Immunisation Program Schedule (from 20 April 2015). Nov 2016. http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/national-immunisation-program-schedule (accessed Dec 2016).

5 Australian Institute of Health and Welfare. Indigenous identification in hospital separations data: quality report (AIHW Cat. No. HSE 85; Health Services Series No. 35). Canberra: AIHW, 2010.

6 Liu B, Heywood AE, Reekie J, et al. Risk factors for herpes zoster in a large cohort of unvaccinated older adults: a prospective cohort study. *Epidemiol Infect* 2015; 143: 2871-2881. ■

Appendix 3A: LGV questionnaire

Created in and extracted from the NSW Notifiable Conditions Information Management System (NCIMS)

1	During 2015-2016, NSW Health observed increased cases of lymphogranuloma venereum (LGV) in New South Wales. We are currently interviewing people who were diagnosed with LGV during this period. LGV is a severe strain of chlamydia.	
2	LGV is one the conditions that doctors and laboratories are required to report to NSW Health. We have been informed that you were diagnosed with LGV. Your doctor felt it would be okay for us to contact you.	
3	In order for us to prevent the spread of LGV, it is important to collect information on what may have led to this increase.	
4	If you agree to participate, the information provided will be kept confidential and you will remain anonymous. The survey takes approximately 10 mins.	
5	Alternatively, if you feel uncomfortable completing this questionnaire, and would like to be contacted through a phone call or require peer-support to complete this questionnaire, please select 'unknown' in the consent box below.	
6	Are you happy to participate in this survey?	[ ] Yes [ ] No [ ] Unknown

6.1	Date Answer only if (6) is 'Yes'	__/__/____
6.2	Would you like to be contacted via phone? Answer only if (6) is 'Unknown'	[ ] Yes [ ] No
6.2.1	Please enter the best number to contact you on, and someone from NSW Health will contact you soon. Answer only if (6.2) is 'Yes'	_____
6.3	Thank you for your time. Please contact the NSW Sexual Health Info Line 1800 451 624 in case you want to ask any questions Answer only if (6) is 'No'	_____
6.4	Please enter your initials Answer only if (6) is 'Yes'	_____
6.5	Please enter your date of birth Answer only if (6) is 'Yes'	__/__/____
6.6	Please enter your Postcode Answer only if (6) is 'Yes'	_____
6.7	Country of Birth Answer only if (6) is 'Yes'	_____
6.8	Language spoken at home Answer only if (6) is 'Yes'	_____
6.9	Occupation Answer only if (6) is 'Yes'	_____
6.10	Do you identify as Answer only if (6) is 'Yes'	[ ] Neither Aboriginal nor Torres Strait Islander [ ] Aboriginal but not Torres Strait Islander [ ] Torres Strait Islander but not Aboriginal [ ] Both Aboriginal or Torres Strait Islander.
6.11	What gender were you assigned at birth? Answer only if (6) is 'Yes'	[ ] Male [ ] Female
6.12	What is your current gender identity? Answer only if (6) is 'Yes'	[ ] Male [ ] Female [ ] Non-binary [ ] Different identity
6.12.1	Please state your identity Answer only if (6.12) is 'Different identity'	_____
6.13	Do you consider yourself to be Answer only if (6) is 'Yes'	[ ] Gay or homosexual [ ] Bisexual [ ] Heterosexual or Straight [ ] Queer [ ] Different identity

6.13.1	Please state your identity Answer only if (6.13) is 'Different identity'	
6.14	Are you intersex? Answer only if (6) is 'Yes'	[ ] Yes [ ] No [ ] Unknown
6.15	At the time of diagnoses with LGV, did you have proctitis or rectal pain/ discomfort? Answer only if (6) is 'Yes'	[ ] Yes [ ] No [ ] Unknown
6.16	At the time of diagnoses with LGV, did you have frequent or continuous feeling that you need to open your bowels but couldn't? Answer only if (6) is 'Yes'	[ ] Yes [ ] No [ ] Unknown
6.17	At the time of diagnoses with LGV, did you have discomfort/ pain with bowel movements? Answer only if (6) is 'Yes'	[ ] Yes [ ] No [ ] Unknown
6.18	At the time of diagnoses with LGV, did you have rectal discharge? Answer only if (6) is 'Yes'	[ ] Yes [ ] No [ ] Unknown
6.19	At the time of diagnoses with LGV, did you have abnormal mucus discharge from your rectum? Answer only if (6) is 'Yes'	[ ] Yes [ ] No [ ] Unknown
6.20	At the time of diagnoses with LGV, did you have rectal bleeding? Answer only if (6) is 'Yes'	[ ] Yes [ ] No [ ] Unknown
6.21	At the time of diagnoses with LGV, did you have penile discharge? Answer only if (6) is 'Yes'	[ ] Yes [ ] No [ ] Unknown
6.22	At the time of diagnoses with LGV, did you have pain/discomfort or burning during urination? Answer only if (6) is 'Yes'	[ ] Yes [ ] No [ ] Unknown
6.23	At the time of diagnoses with LGV, did you have abnormal lumps around genitals (groins)? Answer only if (6) is 'Yes'	[ ] Yes [ ] No [ ] Unknown
6.24	At the time of diagnoses	

	with LGV, did you have any other symptoms?	
	Answer only if (6) is 'Yes'	
6.25	If you answered no to the above and had no symptoms, why did you go to the doctor?	[ ] Follow-up after sexual contact with someone who had LGV [ ] Follow-up after sexual contact with someone who had another STI [ ] Routine sexual health screen [ ] Not applicable
	Answer only if (6) is 'Yes'	
6.26	Did you receive treatment for LGV?	[ ] Yes [ ] No [ ] Unknown
	Answer only if (6) is 'Yes'	
6.27	At the time of LGV diagnosis, were you diagnosed with any other STI	[ ] Yes [ ] No
	Answer only if (6) is 'Yes'	
6.27.1	Gonorrhoea	[ ] Yes [ ] No [ ] Unknown
	Answer only if (6.27) is 'Yes'	
6.27.2	Chlamydia	[ ] Yes [ ] No [ ] Unknown
	Answer only if (6.27) is 'Yes'	
6.27.3	Syphilis	[ ] Yes [ ] No [ ] Unknown
	Answer only if (6.27) is 'Yes'	
6.27.4	Hepatitis B	[ ] Yes [ ] No [ ] Unknown
	Answer only if (6.27) is 'Yes'	
6.27.5	Hepatitis C	[ ] Yes [ ] No [ ] Unknown
	Answer only if (6.27) is 'Yes'	
6.28	What is your HIV status	[ ] HIV positive [ ] HIV negative [ ] HIV unknown [ ] Prefer not to say
	Answer only if (6) is 'Yes'	
6.28.1	When were you diagnosed (Month, Year)	
	Answer only if (6.28) is 'HIV positive'	
6.28.2	When did you last test for HIV?	
	Answer only if (6.28) is 'HIV negative'	
6.29	At the time of LGV diagnosis, were you taking any HIV prevention medication to protect yourself?	[ ] Yes [ ] No
	Answer only if (6) is 'Yes'	
6.29.1	What were you taking (click all that apply)	[ ] Pre-Exposure Prophylaxis or PreP [ ] Post-Exposure Prophylaxis or PEP
	(Select all that apply)	
	Answer only if (6.29) is 'Yes'	
6.30	How many sexual partners have you had	

	in the last 3 months? (includes vaginal, anal or oral sex)	
	Answer only if (6) is 'Yes'	
6.31	How many sexual partners have you had in the last 12 months? (includes vaginal, anal or oral sex)	
	Answer only if (6) is 'Yes'	
6.32	Who do you have sex with?	[ ] Men [ ] Women [ ] Both
	Answer only if (6) is 'Yes'	
6.33	How often have you used condoms for anal (or vaginal, if applicable) sex with a regular partner?	[ ] Always (not counting breakages) [ ] More than half the time [ ] Less than half the time [ ] Never [ ] I haven't had anal or vaginal sex
	Answer only if (6) is 'Yes'	
6.34	How often have you used condoms for anal (or vaginal, if applicable) sex with a casual partner?	[ ] Always (not counting breakages) [ ] More than half the time [ ] Less than half the time [ ] Never [ ] I haven't had anal or vaginal sex [ ] I do not have casual sex partners
	Answer only if (6) is 'Yes'	
6.35	Did you inform your sexual partners of the LGV diagnosis	[ ] Yes [ ] No
	Answer only if (6) is 'Yes'	
6.35.1	How did you inform them of the LGV diagnosis (tick all that apply)	[ ] In person [ ] Phone call [ ] Text [ ] Email [ ] Anonymous text messaging services [ ] Someone else notified them
	(Select all that apply)	
	Answer only if (6.35) is 'Yes'	
6.36	Would you like any further information or support in relation to LGV?	[ ] Yes [ ] No
	Answer only if (6) is 'Yes'	
6.36.1	How would you like to be contacted	[ ] Phone [ ] By post [ ] Email [ ] Peer-support ACON [ ] Peer-support Positive Life NSW
	Answer only if (6.36) is 'Yes'	
6.36.1.1	Please provide your contact details	
	Answer only if (6.36.1) is 'Phone', ' By post', ' Email', ' Peer-support ACON' or ' Peer-support Positive Life NSW'	
6.37	Do you have any questions or would like to give any feedback?	
	Answer only if (6) is	

	'Yes'	
6.38	Thank you for your time. Please contact the NSW Sexual Health Info Line 1800451624, if you want to ask any questions. Answer only if (6) is 'Yes'	_____

Appendix 4A: Evaluation of Post-Cyclone Winston Early Warning Alert and Response System (EWARS in a Box), Fiji 2016

A joint collaboration between the Fiji Centre for Communicable Diseases Control, Ministry of Health and Medical Services and the WHO Division of Pacific Technical Support, Fiji.

Final Report

August 2016

Acknowledgements

This evaluation was conducted by Dr Meru Sheel (National Centre for Immunisation Research and Surveillance & the Australian National University, Australia) and Ms Julie Collins (Hunter New England Population Health & the Australian National University, Australia) with support from the EWARS Evaluation Working Party and the Project Steering Committee.

Special acknowledgement and thank-you to the EWARS surveillance officers, focal points and consulting epidemiologists for supporting EWARS, providing valuable information and assisting with this evaluation.

EWARS Evaluation Working Party

Dr Mike Kama, National Advisor Communicable Diseases, MOHMS

Dr Devina Nand, Head Epidemiologist, MOHMS

Dr Josaia Samuela, Eastern DMO, MOHMS

Dr Eric Nilles, WHO DPS

Ms Julie Collins, HNE Population Health & ANU

Dr Meru Sheel, NCIRS & ANU

Project Steering Committee

Fiji Ministry of Health and Medical Services

Dr Mike Kama

Dr Devina Nand

Mr Vimal Deo

Dr Daniel Faktaufan

Dr Sam Fullman

Divisional Medical Officers, Fiji Ministry of Health and Medical Services

Dr Susana Nakalevu

Dr Tevita Qoriniyasi

Dr Josaia Samuela

Dr Dave Wippy

World Health Organization

Dr Viema Biaukula

Dr Christopher Haskew

Dr Angela Merianos

Dr Eric Nilles

Hunter New England Population Health

Mr James Flint

Australian National University

Associate Prof Martyn Kirk

Dr Katrina Roper

Executive Summary

Fiji established the Early Warning Alert and Response System (EWARS in a Box) in March 2016 in order to monitor communicable disease trends and detect early warning signals for potential outbreaks following the devastation caused by Tropical Cyclone Winston. Eight syndromes of epidemic concern were identified by the Ministry of Health and Medical Services and incorporated into the mobile-phone based syndromic surveillance system. An additional syndrome (Zika-like illness) was added two weeks after the system's implementation. EWARS enables front line health care workers to report data via a mobile phone application, which then transmits the data to a 'cloud-based' EWARS database. The system utilises two types of reporting systems- Indicator Based Surveillance (IBS) and Event Based Surveillance (EBS), both of which are integrated into a single web-based platform.

The purpose of this evaluation was to report on the performance of EWARS in a Box (EWARS) over the first three months of implementation in Fiji (Epidemiological weeks 10 to 21, 2016) and provide recommendations for future use in post-disaster settings, as well as for possible integration into Fiji's routine public health surveillance system.

Both quantitative and qualitative methods were utilised to evaluate the system attributes of EWARS. Reporting performance was assessed through a quantitative analysis of reported data, whilst the experience of using the system was explored through an online cross-sectional survey of EWARS users, along with site visits to reporting health facilities. EWARS actors (stakeholders) were consulted at multiple levels using semi-structured interviews.

The system recorded a total of 34,113 cases for the nine syndromes between 7 March 2016 and 29 May 2016. A total of 325 alerts were generated through IBS and 10 through EBS. No major public health events were detected during the post-disaster phase, however a number of small investigations were initiated based on surveillance data generated through EWARS.

The evaluation found that EWARS was generally well accepted by users and that there was a high level of confidence in the system's ability to monitor communicable disease trends and detect early warnings for potential disease outbreaks. Information provided via weekly epidemiological bulletins was considered useful by both system users and stakeholders, however recommendations were made for further utilisation. Completeness of reporting to EWARS was high throughout the period under evaluation, yet a number of barriers to timeliness were identified, particularly in relation to the workload burden on focal points. The system was found to be highly stable, flexible and portable, demonstrating its suitability for post-disaster settings.

Key recommendations include:

- Increasing engagement with EWARS reporting sites through regular site visits by surveillance officers;
- Strengthening Event Based Surveillance (EBS) reporting by increasing awareness among health care workers and outbreak response teams;
- Enhancing the usefulness of the EWARS weekly bulletin by improving the layout and including further interpretation;
- Developing standard operating procedures to assist surveillance officers in the verification of alerts and for guidance with specimen collection for laboratory confirmation of suspected cases;
- Providing epidemiological training for surveillance officers in outbreak identification, investigation and response. In addition, the inclusion of a 'train-the-trainer' format would enable knowledge transfer to focal points;

- Streamlining data collection and reporting processes at health facilities to improve timeliness and data quality; and
- Integration of the system into Fiji's routine syndromic surveillance would require further consideration around maintenance and storage of the data, infrastructure, cost and the representativeness of sites.

Based on EWARS' strong performance in Fiji, transitioning elements into Fiji's routine surveillance system may help to strengthen surveillance and public health in Fiji overall.

Abbreviations

ANU	Australian National University
DMO	Divisional Medical Officer
DPS	Division of Pacific Technical Support
EBS	Event Based Surveillance
Epi Week	Epidemiological Week
EWARN	Early Warning Alert and Response Network
EWARS	Early Warning Alert and Response System (EWARS in a Box)
FCCDC	Fiji Centre for Communicable Disease Control
FSSS	Fiji Syndromic Surveillance System
HNE	Hunter New England
IBS	Indicator Based Surveillance
IHR	International Health Regulations
MOHMS	Ministry of Health and Medical Services
NCIRS	National Centre for Immunisation Research and Surveillance
NDMO	National Disaster Management Office
PIC	Pacific Island Country
PSSS	Pacific Syndromic Surveillance System
SDMO	Sub-divisional Medical Officer
SO	Surveillance Officer
WHO	World Health Organization

List of Annexes

Introduction

Tropical Cyclone Winston made landfall in Fiji on February 20, 2016 causing widespread damage, destroying homes and schools, bringing down trees and powerlines, and flooding rivers. This category 5 tropical cyclone was the strongest in recorded history to hit Fiji. A National State of Emergency was declared on 21 February 2016 and remained in place for 60 days. The cyclone caused severe damage to infrastructure and crops in all four health divisions of Fiji. Areas most affected included:

- Savusavu, Nabouwalu, Taveuni (Northern Division);
- Lomaiviti group including Levuka, Koro Island, and Batiki Island (Eastern Division);
- Tailevu North, Rakiraki (Central Division); and
- Ba and other areas (Western Division).

As of 24 February 2016, 43 fatalities were confirmed by the Fiji government and an estimated 54,615 persons were residing in 899 evacuation centres (109 were schools) [report 29/02/16 from NDMO (http://www.newswire.com.fj)]. A rapid public health risk assessment conducted by the Fiji MOHMS and WHO identified a number of water-borne and vector-borne diseases that posed a medium to high risk for substantial outbreaks. Of particular concern were leptospirosis, diarrhoea (including dysentery), typhoid, and mosquito borne disease outbreaks including dengue, chikungunya and Zika virus [99]. An increased risk of respiratory infections due to overcrowding and decreased hand hygiene was also identified. Based on the findings from the public health risk assessment, the establishment of a post-disaster Early Warning and Alert Response Network (EWARN) was recommended. Under the WHO's core commitments and IHR obligations, an EWARN was established within 14 days of the disaster [90].

Different types of EWARN systems have been implemented previously following disasters such as the Disease Early Warning System (DEWS) in Pakistan, Surveillance in Post Extreme Emergencies and Disasters (SPEED) in the Philippines [91] and Solomon Islands [92]. More recently, the WHO Intelligence, Information and Monitoring unit (IIM) developed a web-based EWARN system using smartphones to capture and transmit surveillance data. This system, known as 'EWARS in a Box', was first implemented in South Sudan in 2015 [98]. EWARS in a Box was adapted and implemented in Fiji post-cyclone Winston.

The following syndromes were reported through EWARS in a Box (Fiji):

<u>Weekly reporting (Indicator Based Surveillance or IBS)</u>

1. Acute fever and rash
2. Prolonged fever
3. Influenza-like illness
4. Watery diarrhoea
5. Bloody diarrhoea
6. Acute jaundice syndrome
7. Suspected dengue
8. Suspected meningitis
9. Zika-like illness

<u>Immediate reporting (Event Based Surveillance or EBS)</u>

- Any unexpected deaths or public health events that were potentially related to infectious, chemical or environmental causes.

Prior to Tropical Cyclone Winston, the Fiji Syndromic Surveillance System (FSSS) reported weekly on 5 syndromes (acute fever and rash, influenza-like illness, diarrhoea, prolonged fever and dengue-like illness) from 12 sentinel health facilities (hospitals and clinics) located across all four divisions of Fiji. EWARS in a Box was implemented in 34 health facilities across the four divisions (Central, Eastern, Western and Northern). EWARS in a Box is scaled-up version of the FSSS. Eleven of the 34 EWARS sites previously reported syndromic surveillance data through FSSS. The additional sites were selected based on their likelihood of experiencing an epidemic, population density, proximity to areas worst affected by the cyclone and location of internally displaced persons. In addition, telecommunication access was taken into account in site selection due to the reliance of EWARS in a Box on phone and internet access.

Rationale for EWARS in a Box

The objectives of EWARS in a Box (Fiji) align with that of other EWARN systems and centre on having an effective surveillance system that will allow monitoring of communicable diseases during the post-disaster phase. Humanitarian emergencies and natural disasters are often accompanied by communicable disease outbreaks leading to severe mortality and morbidity, which can largely be reduced by implementing timely and effective surveillance [88]. In the absence or breakdown of pre-existing surveillance systems, EWARS can monitor changing disease dynamics and generate early signals of potential communicable disease outbreaks.

The implementation of EWARS post-Cyclone Winston was necessary to supplement existing systems to ensure that MOHMS was able to adequately monitor burden of communicable diseases and detect potential disease outbreaks in a timely fashion.

In addition, EWARS was preferred as it is an automated EWARN system (detailed later), and hence served as a suitable surveillance system compared with previously implemented EWARNs reducing the time and human resources required for everyday surveillance including data collection, analysis and dissemination.

System description

'EWARS in a Box' (http://ewars-project.org/) is an EWARN, specifically designed for post-disaster emergencies in difficult-to-access locations [91, 101]. For the purposes of this report, 'EWARS in a Box' will be referred to as EWARS. EWARS comes as a field-ready box containing smartphones for data collection and reporting that only requires mobile coverage (no internet or electricity needed). This makes it a particularly useful surveillance system for post-disaster settings. One standard 'Box' contains 50 mobile phones that can support up to 50 health facilities covering up to 500,000 people. The kit also consists of a local server for data hosting and a solar power generators and chargers.

EWARS was implemented within two weeks of Cyclone Winston (by the end of epidemiological week 9) at 34 sites including health centres, sub-divisional and divisional hospitals across the four divisions (Annex A). EWARS enables front line health care workers to report data via a mobile phone application, which then transmits the data to a 'cloud-based' EWARS database. The EWARS database is hosted by the Amazon Web Services and is currently maintained by the WHO headquarters in Geneva. Figure 1 describes the operational process flow for EWARS for both IBS and EBS.

IBS predominantly relies on patients presenting to a health facility with one of the nine syndromes monitored by EWARS. Standard case definitions for each syndrome are used (Annex B) and numbers are recorded using a paper-based tally sheet (Annex C). At the end of an epidemiological week (Monday to Sunday), each site uses the EWARS mobile phone application to report the total number of cases per syndrome and total consultations for persons aged under 5 years and 5 years and over. In total, each site is expected to report 36 values including zero reporting.[39]

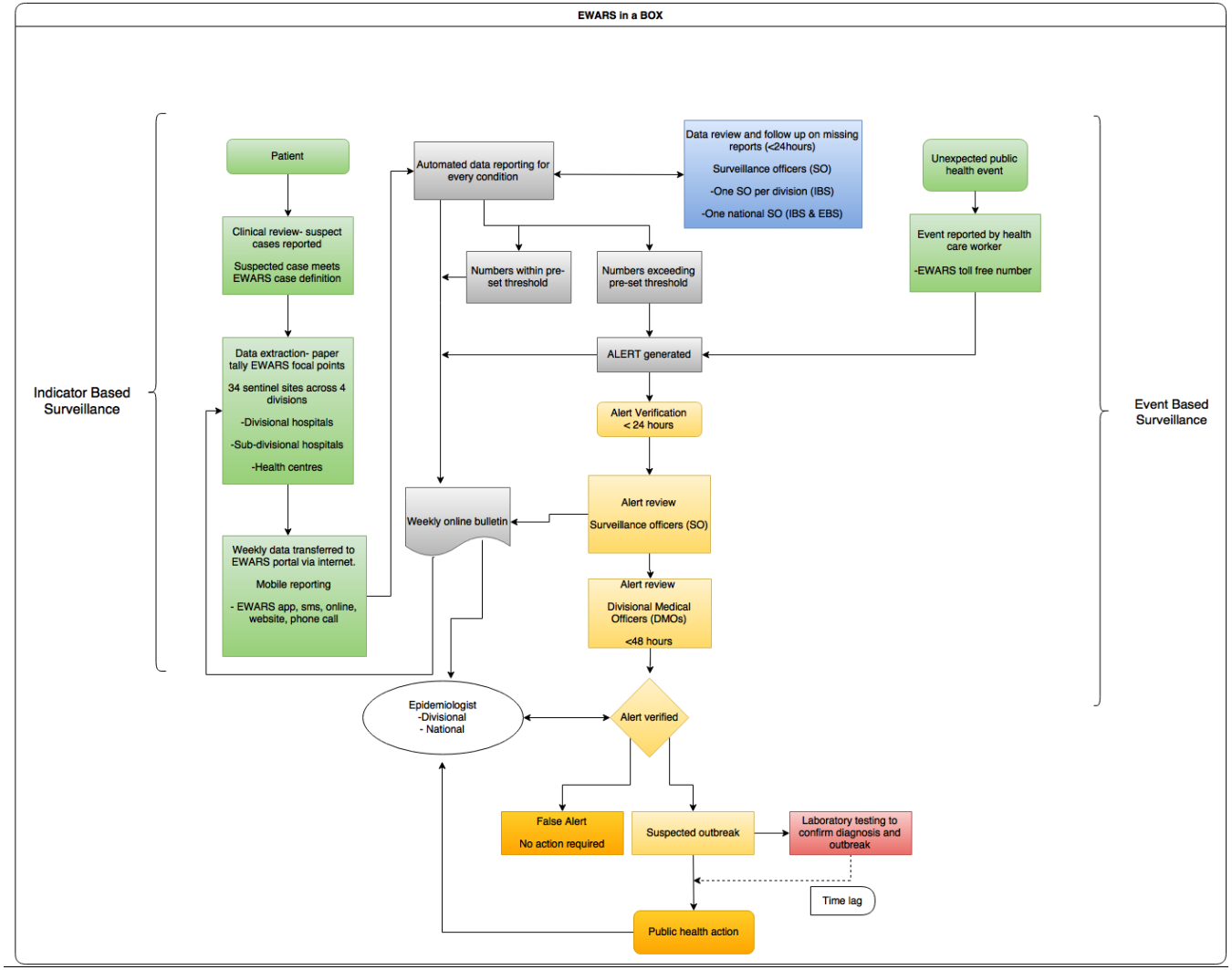
Like other syndromic surveillance systems, EWARS relies on pre-set thresholds for epidemic detection (Annex B). Once the data are entered via the mobile phones, an online system analyses the data and generates an 'alert' if the threshold is exceeded. Each alert triggers a chain of public health responses (as detailed in Figure 1). An alert is investigated by the relevant divisional surveillance officer, who conducts a rapid risk assessment to verify the alert (e.g. ruling out surveillance artefacts) and determine the reasons for the increase in the number of cases. The rapid risk assessment usually involves a telephone conversation with the EWARS focal point at the concerned health facility. The final decision on whether an alert is a 'false' or 'true' event is then decided by the divisional medical officer (DMOs) or consulting epidemiologist.

In contrast, EBS relies on health care workers reporting any unexpected or unusual public health event of an infectious, chemical or environmental nature, using the EWARS website or by calling the toll-free number listed on the EWARS posters and tally sheets that were provided to each site during the implementation of the system. In contrast to IBS, every submitted report generates an alert which then undergoes a risk-assessment by the national EBS surveillance officer. All verification and public health actions are recorded in EWARS in the same way as IBS reports. EWARS is the first ever early warning system to integrate IBS and EBS using a common platform for reporting and verification. Although IBS and EBS were traditionally considered independent surveillance systems, they have complimentary roles to play in communicable disease surveillance following a disaster and should be aligned to ensure comprehensive surveillance of public health events [101].

The surveillance data are automatically compiled at the end of each epidemiological week (epi week) into an epidemiological bulletin (Annex D). The system is automated with in-built algorithms so it can estimate the number of cases, proportional morbidity, performance indicators such as timeliness and completeness, numbers of alerts verified at divisional and national level. The weekly bulletin reports on both IBS and EBS, and contains information on trends on all 9 syndromes. The EWARS Weekly Bulletin is used to monitor disease trends by public health staff as well as divisional and national coordinators at FCCDC and MOHMS.

[39] Zero reporting requires health facilities to include a zero when there have been no cases of a particular syndrome, rather than leaving that field blank.

Figure 1: Operational flow of data for Early Warning and Response System in a Box, Fiji 2016.

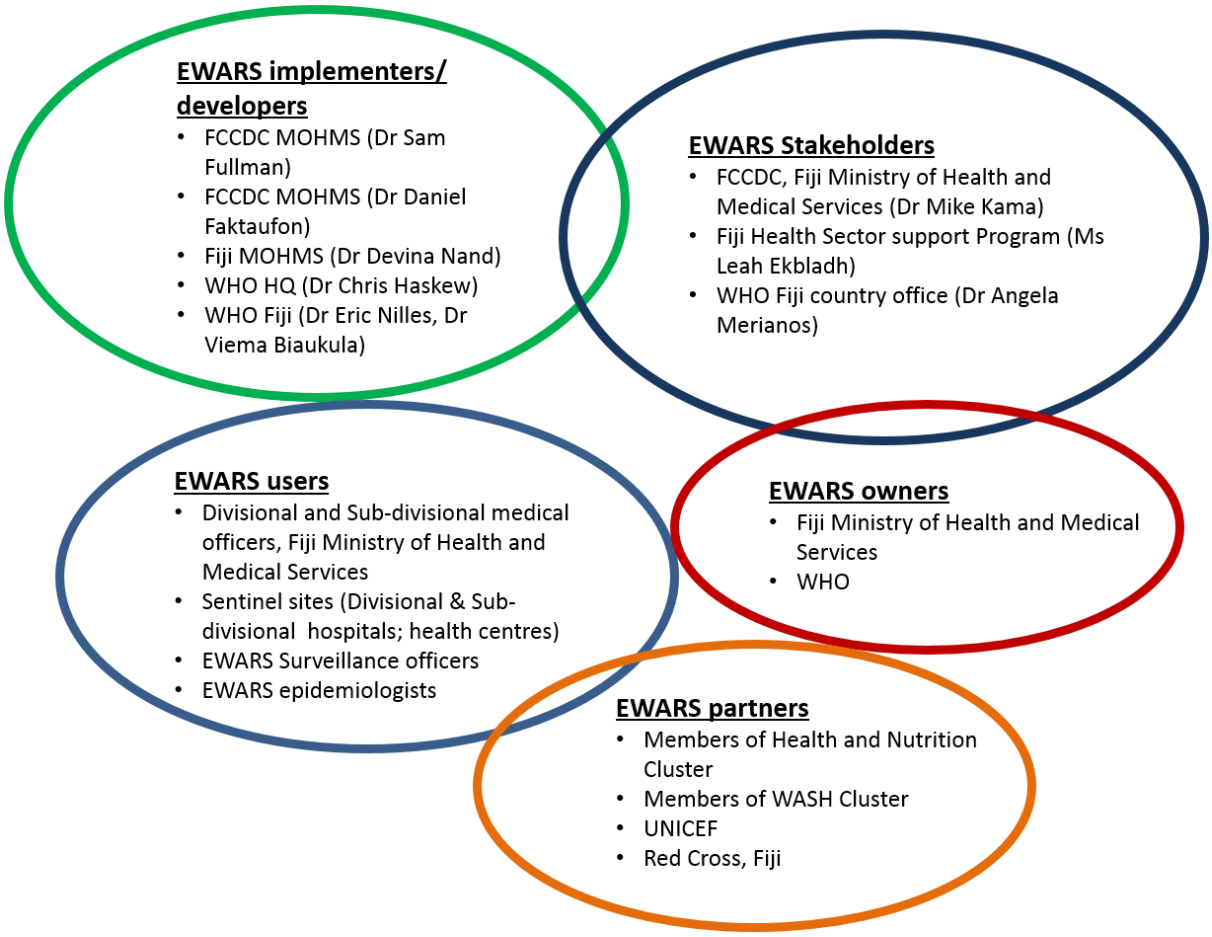


EWARS (System) actors

The EWARS actors in Fiji following cyclone Winston are depicted in Figure 2. For the purposes of the evaluation, the following definitions were applied:

- EWARS developers are those who were involved in the development and implementation of the system.
- EWARS stakeholders are those who had an overarching role in the performance of EWARS and its impact on public health in Fiji, and have some vested financial interest in the system.
- EWARS owners are those who own the system and the data stored within the system.
- EWARS users are those who were involved in collection, analysis, dissemination of information and were ultimately responsible for implementing public health response.
- EWARS partners are those who were not directly associated with EWARS but may have utilised the information generated via EWARS for other health related responses.

Figure 2: EWARS actors associated with EWARS in Fiji post cyclone Winston, 2016.[40]



[40] Roles and responsibilities of EWARS users are detailed in Annex G

Evaluation of EWARS in a Box (Fiji)

This evaluation of EWARS was a joint collaboration between the Fiji Centre for Communicable Diseases Control (FCCDC), Ministry of Health and Medical Services (MOHMS) and the WHO Division of Pacific Technical Services, Fiji. The evaluation involved a detailed review of EWARS in order to understand its performance after Cyclone Winston and endeavours to strengthen communicable diseases surveillance in Fiji. The evaluation was undertaken over a period of 6 weeks from May- June 2016.

The objectives of the evaluation were as follows:

Primary objective

- To assess the overall performance of EWARS during the post-cyclone Winston emergency phase.
- To evaluate the ability of EWARS to monitor communicable diseases trends and signal early warnings for suspected outbreaks and clusters of epidemic-prone diseases for timely public health action.

Secondary objectives

- To identify the current gaps in disease surveillance under EWARS
- To assess the impact of EWARS on strengthening the public health surveillance system in Fiji
- To assess the utility of data in influencing public health actions undertaken by EWARS partners
- To make practical recommendations to improve EWARS' performance for future use in other post-disaster settings
- To make recommendations for the incorporation of EWARS reporting into Fiji's routine communicable diseases surveillance system

Methods

The evaluation framework (Table 1) was structured based on recommendations from previously published evaluation methodologies [102-106] and evaluations of the Pacific Syndromic Surveillance System (PSSS) [100, 107-109] and the Fiji Syndromic Surveillance System (FSSS) (report under review).

Attributes were assessed using both quantitative and qualitative methods. All data analysis was conducted using Microsoft Excel 2010, unless otherwise specified. Key activities undertaken for the evaluation are outlined below:

- Interviewing of key informants including EWARS developers, stakeholders and partners to gain an understanding of the significance, strength and weaknesses of EWARS post-cyclone Winston. The same questionnaire was used regardless of the mechanism of delivery.

- Quantitative analysis of data was conducted using data stored within the EWARS database from epidemiological weeks 10 (week beginning 7 March 2016) up to 21 (week ending 29 May 2016)[41].
- The system was evaluated using attributes listed in table 1.
- Timeliness and completeness of reporting using IBS- EWARS over the 12 week period was assessed.
- Timeliness and impact of event based surveillance was assessed using the EWARS database. The assessment was restricted due to the availability of limited data since the implementation of EWARS.
- Visits to health facilities were undertaken to understand the process of data reporting and collection, and validate the quality of data reported.
- A cross sectional survey of EWARS users was conducted to assess the experience of the system. Users were identified at two levels: those who report to the system (focal points) and those who monitor the reporting (surveillance officers). Two self-administered online surveys were designed in SurveyMonkey® and distributed via email. Responses were collected through SurveyMonkey® and analysed in Microsoft Excel 2010 and Nvivo 11. A mixed-methods approach to data analysis was employed in order to analyse both quantitative and qualitative data provided through the survey. Response rates were high with 79% (27/34) of focal points and 100% (5/5) of surveillance officers completing the survey (detailed results in Annex E and F).

Table 1: Attributes used to evaluate EWARS

EWARS evaluation components	
System attributes	**Data sources**
Surveillance outputs	EWARS database
Timeliness and completeness (IBS only)	EWARS database; Survey
Data Validity (IBS only)	EWARS database; Site visits to understand data collection practices and retrospective review of clinical records
Usefulness	Survey
Flexibility	Survey; Interviews
Acceptability	Survey
Simplicity	Survey
Stability	EWARS database; Survey
Representativeness	EWARS database, MOHMS population data, Interviews
Costs	System owners and review of budgets
Portability	Interviews
Impact of Event Based Surveillance	EWARS database; Survey; Interviews

[41] Data extracted on 31/05/2016

Results

Surveillance outputs

A total of 34,113 cases were recorded from 326, 861 consultations between 7th March 2016 and 29th May 2016. Influenza-like illness had the highest incidence (16426 cases, 48.2%), followed by watery diarrhoea (10,054 cases, 29.8%), dengue-like illness (4,520, 13.3%), prolonged fever (1461 cases, 4.3%), acute fever and rash (672 cases, 2%), zika-like illness (583 cases, 1.7%), bloody diarrhoea (293 cases, 0.9%), acute jaundice syndrome (71 cases, 0.2%) and suspected meningitis (33 cases, 0.1%).

Figures 3 and 4 represent trends in syndromes, and figures 3A and 4A represent proportional morbidity for syndromes under surveillance through EWARS over the 12 week period. Proportional morbidity is expressed as a percentage of total weekly consultations. For simplicity reasons, only national level analysis is presented here. In conjunction with ILI- being the most commonly reported syndrome, increasing trends in ILI were observed from epi-week 14 onwards. The increase in ILI could be associated with overcrowding and displacement of people during Cyclone Winston (epi-week 8) and Cyclone Zena (epi-week 14). A retrospective analysis of laboratory data conducted by the FCCDC indicated that these early signals in trends of ILI corresponded with an increase in the number of laboratory confirmed cases of influenza. The increase in ILI was also accompanied by an increase in ICU admissions of patients with influenza-associated Severe Acute Respiratory Illness (SARI). However, in this circumstance, public health action was prompted by concerned hospital staff rather than through EWARS. The evaluation demonstrated that EWARS data were not always well understood and utilised to estimate the burden of disease and predict transmission, and hence generate a public health response.

Figure 3: National trends for influenza-like illness (ILI), acute watery diarrhoea (AWD), prolonged fever (PF) and dengue-like illness (DLI) as reported through EWARS, Fiji, Epidemiological weeks 10 – 21, 2016

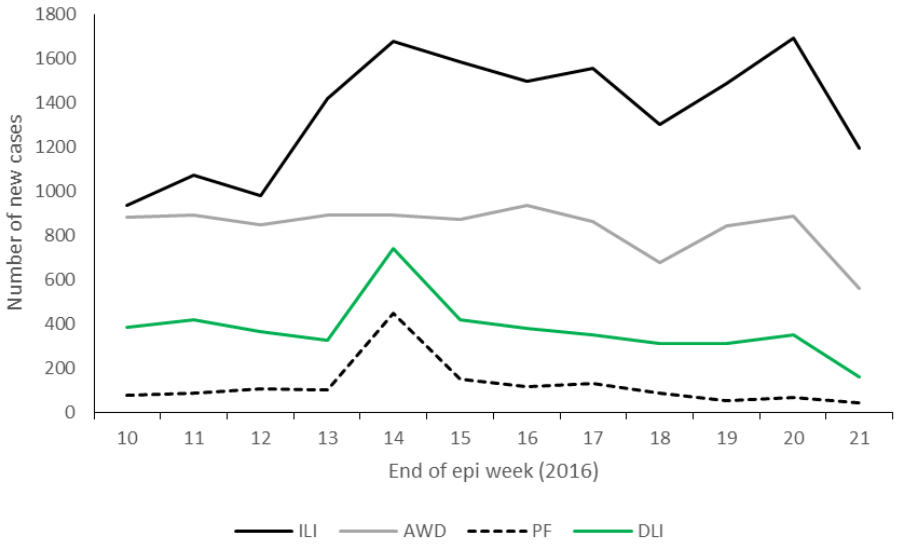


Figure 3A: Proportional morbidity [42] for influenza-like illness (ILI), acute watery diarrhoea (AWD), prolonged fever (PF) and dengue-like illness (DLI) as reported through EWARS, Fiji, Epidemiological weeks 10 – 21, 2016

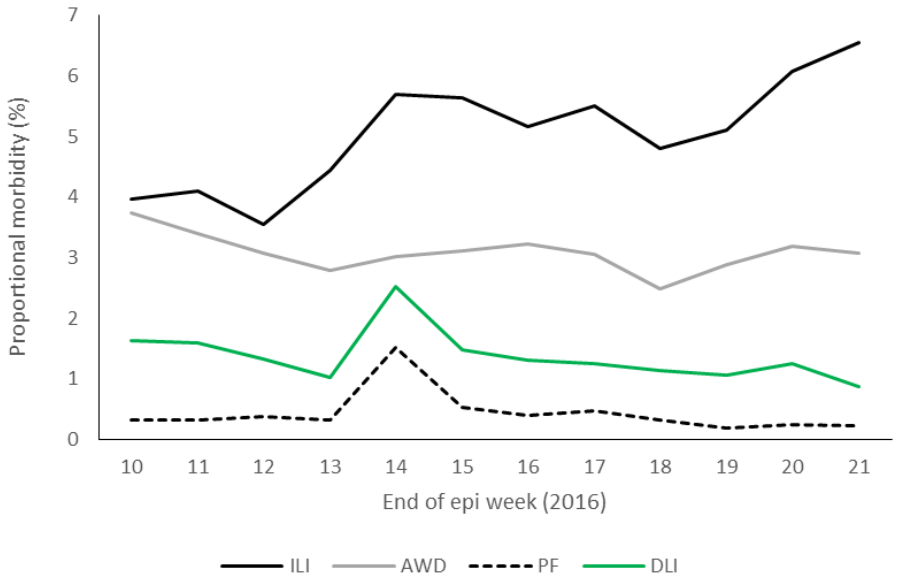
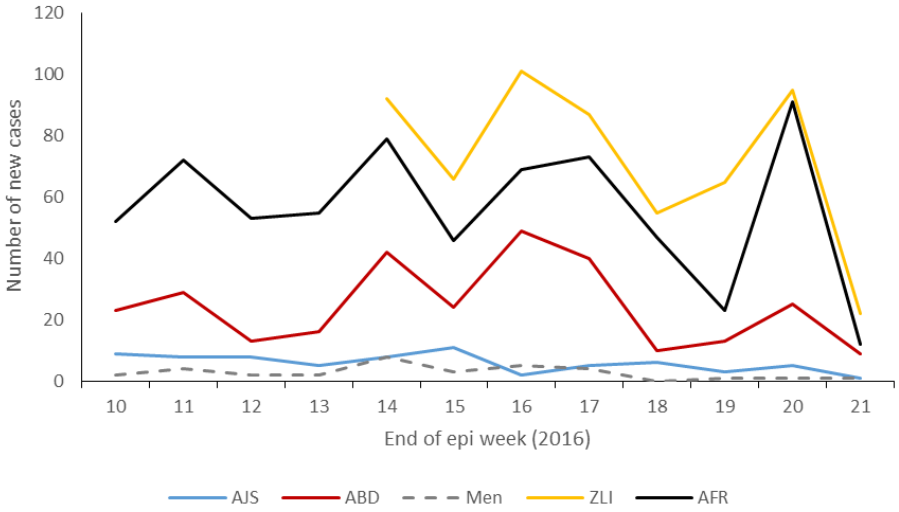
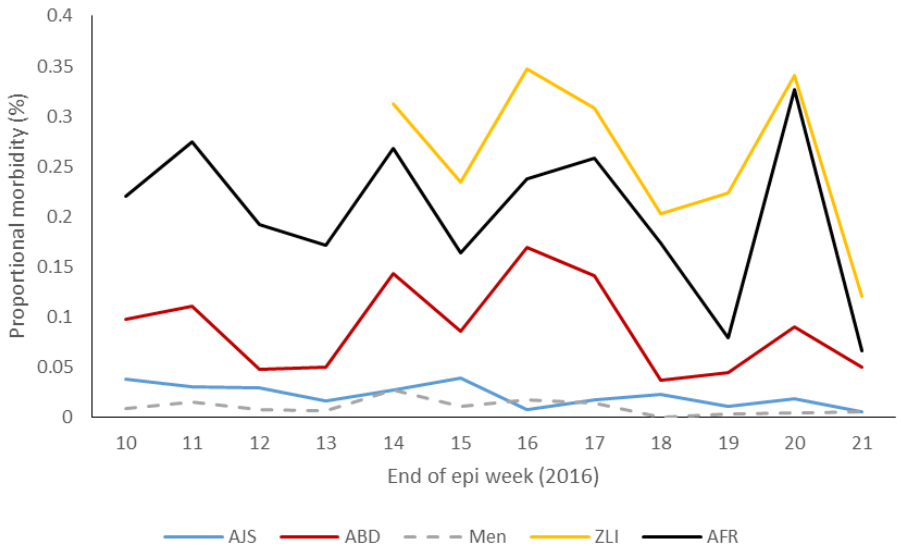


Figure 4: National trends for acute jaundice syndrome (AJS), acute bloody diarrhoea (ABD), suspected meningitis (Men), acute fever and rash (AFR) and Zika-like illness (ZLI)[43] as reported through EWARS, Fiji, Epidemiological weeks 10 – 21, 2016



[42] Morbidity = number of cases / total number of weekly consultations
[43] Zika-like illness was added during epi-week 13.

Figure 4A: Proportional morbidity[44] for acute jaundice syndrome (AJS), acute bloody diarrhoea (ABD), suspected meningitis (Men) and Zika-like illness (ZLI)[45] as reported through EWARS, Fiji, Epidemiological weeks 10 – 21, 2016



The system utilised sensitive case definitions and low thresholds to ensure that no potential disease outbreak signals were missed. Every time a reported event (# of cases) exceeded the threshold, an alert was automatically generated within EWARS. The alert log in figure 5 shows trends at an EWARS site for prolonged fever over time, along with the corresponding moving threshold in blue.

Figure 5: Snapshot of an alert log for prolonged fever from EWARS dashboard

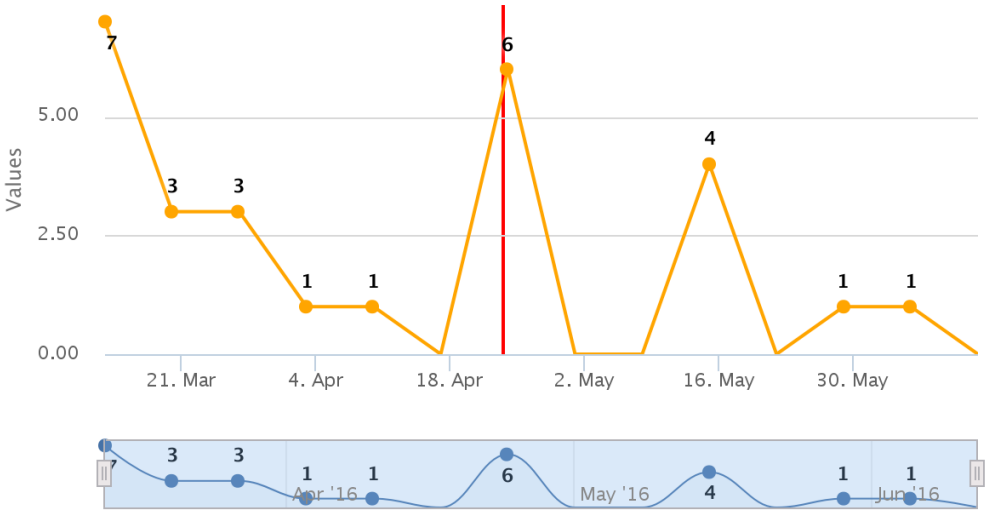


Table 2 summarises the number of alerts generated nationally over the 12 week period and the number of alerts verified. A total of 325 alerts were generated through IBS and 10 through EBS.

[44] Morbidity = number of cases / total number of weekly consultations
[45] Zike-like illness was added during epi-week 13.

Although a large number of IBS alerts were verified (suppressed or actioned), the evaluation highlighted that responses to alerts were often focussed on verifying the alert quickly and did not always include a rapid risk assessment. Consulting EWARS epidemiologists undertook in-country assessments of EWARS and, in conjunction with EWARS surveillance officers, established risk assessment protocols for alert verification.

Table 2: Number of alerts generated through EWARS, Fiji 2016.

Epi-week	# alerts generated	# (%) alerts verified	# alerts generated	# (%) alerts verified
	IBS		**EBS**	
10	9	9 (100)	0	0
11	14	14 (100)	3	1 (33)
12	16	16 (100)	3	1 (33)
13	31	31 (100)	1	1 (100)
14	43	42 (98)	1	0
15	32	31 (97)	0	0
16	41	41 (100)	1	0
17	34	30 (91)	0	0
18	15	14 (93)	0	0
19	30	18 (60)	0	0
20	39	20 (67)	0	0
21	21	11 (52)	1	1 (100)

Although no major outbreaks were detected through IBS during the post-disaster phase, the system triggered several investigations of small outbreaks of watery diarrhoea and measles[46]. EWARS actors felt that the automated alert system was more effective at mobilising the divisional outbreak response teams (DORT) and sub-divisional outbreak response teams (SORT) during post-Cyclone Winston disaster phase compared with previous national emergencies. However, further guidelines and training modules should be developed to better align the rapid response process with EWARS. For instance consultations with focal points and surveillance officers found that EWARS users lacked clarity on when specimens should be collected. Often focal points collected and shipped specimens from all cases, which significantly increased the volume and costs for laboratory testing during the post-cyclone response. Developing standard operating protocols recommending a minimum number and type of specimens for each syndrome are recommended. This will guide the EWARS sites and streamline the process of laboratory testing to confirm diagnosis of suspected cases.

Timeliness and completeness (Indicator Based Surveillance)

Timeliness refers to whether data are submitted on time to for any public health response and completeness refers to whether data are submitted independent of the time [106]. In order to

[46] personal communication with Suva SDMO

generate a timely public health response, it is of paramount importance for data to be submitted on time [106]. Although real time monitoring of syndromic surveillance is ideal, it is often difficult in the context of post-disaster emergencies and Pacific Island Countries.

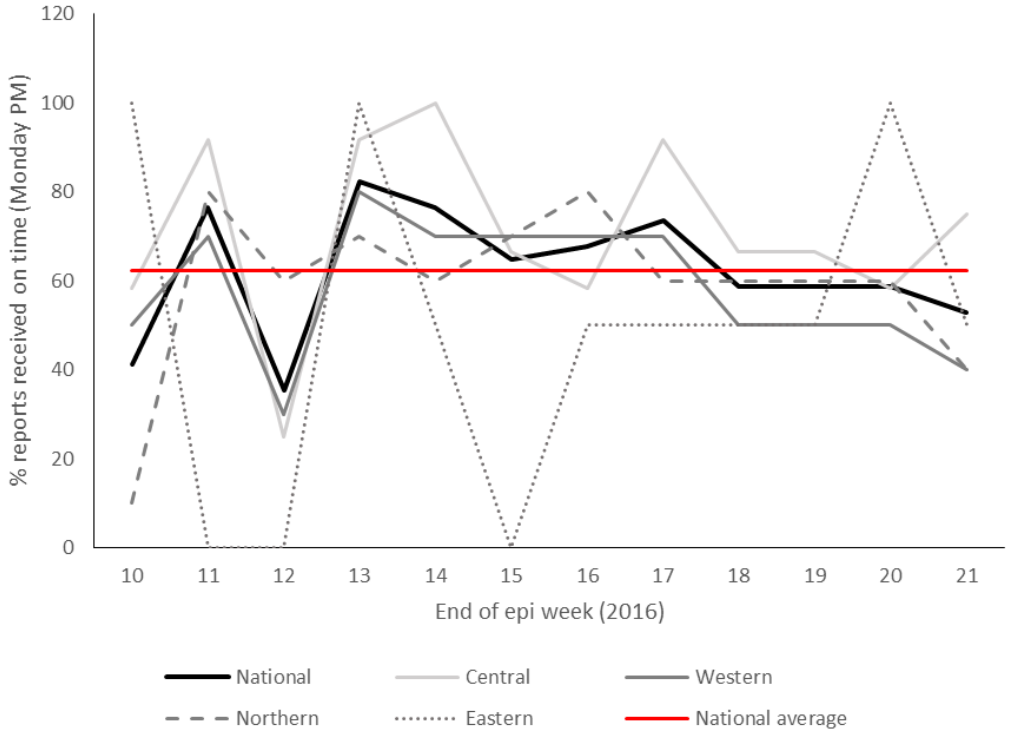
In relation to EWARS, timeliness of reporting was defined as the number of reports that were received by 6pm on the Monday (day 1) of the following epi-week. Table 3 represents the matrix used for calculating timeliness and completeness. Figure 6 shows national and divisional trends in reporting of data over the 12 week period. The national average for timeliness was 64%. Timeliness steadily improved over time, possibly due to a combination of factors including improved understanding of EWARS, enhanced data collection practices and relationship building between the surveillance officers and the focal points. In this context, it is important to note that divisional surveillance officers were actively involved and spent a significant amount of their time following up on report submissions to ensure timeliness of reporting.

> "Reporting on disease risk has been timely and consistent throughout the response. Health has been among the most active clusters in formulating public information campaigns about risks identified."
>
> - *EWARS partner*

Another measure of timeliness is the time taken to respond to an alert and initiate public health action. Quantitative analysis of the time taken to respond to an alert was not possible during the course of the evaluation. The majority of alerts were verified (Table 2), and most delays in the verification process appeared to be due to surveillance officers' being unable to access the focal points to review the cases[47].

[47] Survey and personal communication with EWARS surveillance officers

Figure 6: Timeliness of IBS reporting at National and Divisional level through EWARS, Fiji, epidemiological weeks 10-21. Expected number of reporting sites (National= 34, Central = 12, Eastern = 2, Western = 12, Northern = 10)

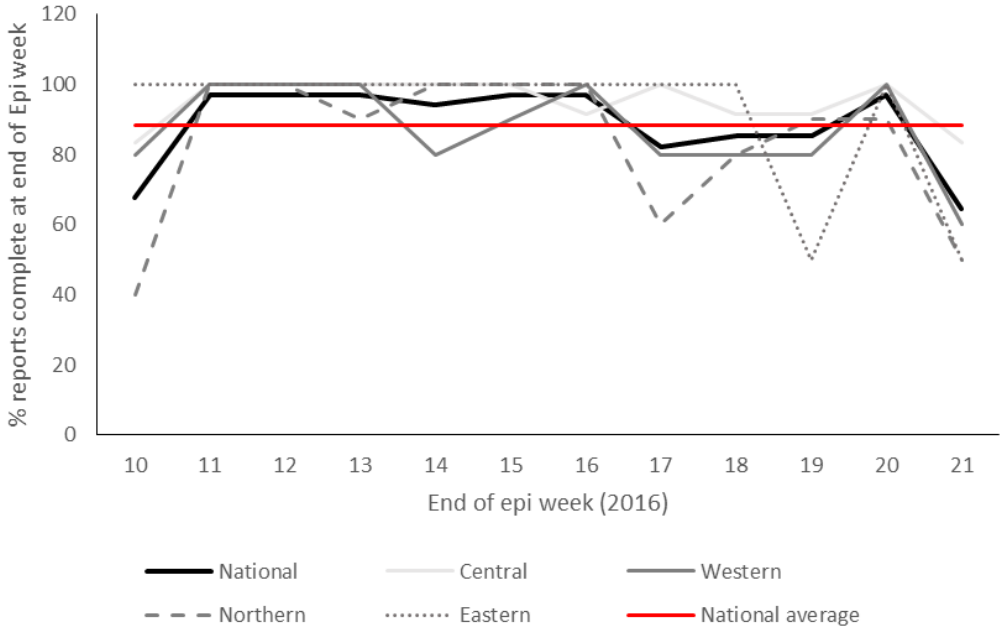


Completeness of reporting refers to the proportion of sites that submitted the data independent of the time of submission [106]. In this context, completeness is reported as the percentage of reports received by Sunday of the following epi-week (i.e. a report was considered incomplete if it was delayed by more than 7 days). Figure 7 shows national and divisional trends in the percentage of reports received by the end of each epi-week. The national average for completeness of reporting was 90%.

Both timeliness and completeness are indicators of the quality of surveillance data. Figures 5 and 6 showed most EWARS sites were in general reporting well although not always on time (by 6pm Monday). A timeliness and completeness target of 80% is recommended to ensure timely public health action is able to be taken. However, in order to improve the quality of data reporting, it is important to understand the barriers to reporting to improve system performance.

Important to note the timeliness and completeness of reporting appeared to be on downward trend after epidemiological week 20 (Figures 6 and 7). The percentage of IBS alerts verified dropped from 93% in week 18 to 50% in week 21 (Table 2). This could be indicative of fatigue in the surveillance system. Fiji has reported data on syndromic surveillance for several years where in frequency of reporting and data were found to be incomplete and not always on time [108].

Figure 7: Completeness of IBS reporting at National and Divisional level through EWARS, Fiji, epidemiological weeks 10-21. Expected number of reporting sites (National= 34, Central = 12, Eastern = 2, Western = 10, Northern = 10)[48]



Survey results showed the majority of focal points (21/24, 88%)[49] experienced situations where they were unable to report on time. The main challenge for timely reporting was the workload on focal points (14/24, 56%). Delays in some situations were attributed to other staff members not completing and handing in their tally sheets on time (11/24, 46%). Since EWARS sites may have several clinicians, focal points are often required to follow up multiple staff members in order to collate and submit the weekly reports. This was highlighted as an issue during site visit discussions, particularly in larger hospitals with a high number of reporting officers. The challenges for timely reporting highlight the need to streamline EWARS reporting processes within health facilities and to the need to align them with other already established surveillance systems.

Lack of internet signal was also highlighted as a challenge for timely reporting (11/24, 46%), and in some cases focal points were unable to report due to a lack of mobile phone credit (4/24, 17%). Albeit rare, the use of EWARS mobile phone credit for personal or other use by focal points has been highlighted as a concern by surveillance officers.[50] Systems to limit or monitor personal mobile phone use may be helpful to reduce this occurrence.

[48] Data updated on 31/05/2016
[49] 3 respondents did not answer this question.
[50] Consultation with surveillance officers.

Table 3: Timeliness and completeness of IBS reporting through EWARS in Fiji, epidemiological week 10- 21.

Information item	Epidemiological weeks												Total
	10	11	12	13	14	15	16	17	18	19	20	21	
Number of EWARS sentinel sites	34	34	34	34	34	34	34	34	34	34	34	34	34
Number of reports expected	34	34	34	34	34	34	34	34	34	34	34	34	306
Total number of reports received	23	33	33	33	32	33	33	28	29	29	33	22	277
Total number of reports received by Day 1 of Epi week (Monday)	14	26	12	28	26	22	23	25	20	20	20	18	196
Timeliness of reporting % reports received by Monday	41.2	76.5	35.3	82.4	76.5	64.7	67.6	73.5	58.8	58.8	58.8	52.9	64.1
Completeness of reporting % reports received by end of epi week	67.6	97.1	97.1	97.1	94.1	97.1	97.1	82.4	85.3	85.3	97.1	64.7	90.5

Data validity (Indicator Based Surveillance)

Data validity refers to the accuracy of information that is captured by the surveillance system [103, 106]. Teams consisting of EWARS epidemiologists and divisional surveillance officers visited a total of 11 EWARS sites across the Central, Northern and Western divisions in order to assess data validity. A retrospective review of clinic registers was undertaken by the surveying teams. Epidemiological weeks 13 and 17 were selected to assess quality of reporting in the earlier and later weeks of surveillance through EWARS. Ideally, the number of cases identified through the review would be comparable to the number of cases reported to EWARS.

There were a number of limitations in the assessment of data validity. Access to clinic registers was not always possible as they were often being used by medical practitioners. Therefore, complete case counts for both epidemiological weeks were obtained from 3 sites only. The total numbers of outpatient consultations for each epidemiological week were not available for two of the three sites, restricting the comparison to case counts.

The comparison of case counts captured by EWARS with the retrospective review data demonstrated a certain level of discrepancy (Annex H). The reported discrepancies were not necessarily indicative of data inaccuracy, but highlighted variability in reporting practices and the difficulty in replicating data collection processes at sentinel sites. In another instance, site 3 reported 29 cases of bloody diarrhoea to EWARS in epidemiological week 17, whilst the register review identified 23 cases of watery diarrhoea (Annex H). The error was clarified and amended by surveillance officers after an alert was generated, demonstrating the strength of EWARS' verification process and its contribution to data validity. Heterogeneity and complexity in data collection processes should be minimised to enhance data validity for improved outbreak detection.

In addition to reviewing the clinical records, the teams met with EWARS focal points and discussed site specific data collection practices. A number of challenges in applying case definitions were identified during the site visits and though the cross-sectional survey, including overlap between syndromes, patients meeting more than once case definition, and a lack of clarity and specificity surrounding case definitions. Discussions with focal points suggested that clinical history was sometimes applied to the identification of cases by clinical staff, regardless of symptoms recorded in the patient register. This may lead to misclassification when other health facility staff are involved in tallying cases. Ideally, patient registers should reflect the information being provided to EWARS.

Timely detection of an outbreak relies on data validity, however the accuracy of case counts is less critical during post-disaster settings where identifying 'hot-spots' rapidly is crucial. In these situations, data validity can be supported through strong verification processes as has been demonstrated by EWARS.

Usefulness

Usefulness refers to the system's contribution in monitoring diseases trends and early detection of signals that might lead to potential disease clusters or outbreaks [102]. Surveyed users were confident in the ability of EWARS to detect early warnings for potential disease outbreaks (its primary purpose). Sixty-nine percent of respondents (n=32) thought the system could detect early warnings very well and a further 25% thought that it could detect early warnings somewhat well.

The information provided by EWARS in the weekly bulletin was considered very useful (11/24, 46%) and somewhat useful (13/24, 54%) by users. Table 4 outlines the main uses of information among focal points who received the bulletin.

Table 4: Use of information in the EWARS Weekly Bulletin by focal points, cross-sectional survey, (n=19)[51]

Use of information	Focal points (%)
Information sharing amongst colleagues at the health facility and within the community	32%
Compare data trends of different reporting areas	26%
Initiate preventive or responsive health action	26%

Recommended improvements to the bulletin included more detail to support interpretation. For example, the inclusion of thresholds on graphs would support surveillance officers in monitoring trends and provide visual support for response activities. In addition, showing cases aged under 5yrs and over 5yrs (rather than combining these groups) would provide greater demographic detail to support targeted public health action. Discussions with focal points and surveillance officers during site visits indicated that health facility specific summaries would benefit disease monitoring at the local level, and details on the outcome of previous weeks' case investigations would assist medical officers in tracking cases.

Along with increased awareness and understanding of surveillance among health care workers, the cross-sectional survey revealed some improvements in clinical management as a result of EWARS.

> *EWARS was very helpful in making us vigilant with variety of cases that were flocking in after the cyclone. It enabled us to label cases appropriately and treat them appropriately as well."*
>
> *"[EWARS] made me understand each and every case definition their managements and proper investigations."*
> *-EWARS Focal points*

EWARS actors felt that EWARS had strengthened the communicable diseases surveillance in Fiji and, if re-activated during another disaster or integrated long term, it would be highly beneficial in improving Fiji's public health system.

> *"Best ever public health action in Fiji"*
> *- EWARS implementer*

Flexibility

A flexible surveillance system is able to adapt to changing information needs or operating conditions without significant time, staff contribution or funding [102]. In the context of this evaluation, flexibility refers to the adaptability of syndromes reported and modifications in the reporting process. Zika-like illness was included as a ninth syndrome three weeks after implementation. In order to assess the system's flexibility, EWARS users (focal points and

[51] 8 focal points indicated that they did not receive the EWARS Weekly Bulletin

surveillance officers) were asked how easy it was to amend their reporting and surveillance processes after Zika-like illness was added. Forty-four percent of focal points (n=27) indicated that it was very easy to amend the reporting process when an additional syndrome was introduced, and 48% indicated that it was somewhat easy. All surveillance officers indicated that it was very easy to amend the surveillance process when Zika-like illness was introduced.

Furthermore, discussions with EWARS developers revealed that modifying the online system was a relatively simple process. This was also true for ongoing changes made to the EWARS website and dashboard, and the alert management process. Adding an additional reporting site was also considered to be relatively simple. Koro Island health centre, which was in one of the worst affected regions, was included as an EWARS sentinel site in epi-week 13. The delay in implementation was associated with access to the island. EWARS was implemented with relative ease once infrastructure had been sufficiently restored, and the site could be accessed.

The flexibility of EWARS is an important attribute in the context of Fiji and for the implementation of EWARS in other post-disaster settings. As is expected from an early warning system, EWARS was found to require minimal resources and change in practices to scale-up or scale-down the number of syndromes or sites.

Acceptability

Acceptability refers to the willingness of users to participate in the surveillance process including data collection and analysis [102]. Accurate, timely and complete information for public health action relies on significant support for the system at the user level. Acceptability can be influenced by a number of factors such as the ease of reporting, the burden on time, feedback received on the information reported, and the level of training and support provided.

Although mobile phone reporting of surveillance data has been previously utilised in Fiji, reporting via smartphones using a web based application was a novel approach introduced in Fiji post-cyclone Winston. The cross-sectional survey revealed there was high acceptability among focal points in relation to using the EWARS application (Table 5). Similarly, most surveillance officers (4/5, 80%) indicated that it was very easy to use the EWARS website.

Table 5: Attitudes of EWARS focal points toward using mobile phones for EWARS reporting, cross-sectional survey (n=27)

Smart phone use for EWARS reporting	Focal points (%)
Using the EWARS mobile phone to transmit weekly reports	93%
Found mobile phones very easy to use for reporting	89%
Preferred method of reporting is through EWARS mobile phones	89%

A common theme identified through discussions at site visits was that reporting introduced a significant time burden on focal points. High workload was also recognised as a contributor to delayed reporting in the cross-sectional survey (14/27, 52%).

Focal points were generally positive about the feedback received both from surveillance officers and through the EWARS weekly bulletin. However, 26% of respondents (7/27) indicated that they had not received the bulletin and were not receiving feedback on the information reported to the system. In order to maintain acceptability of the system, it is important that focal points receive timely and useful feedback.

The majority of EWARS users were satisfied with the training and support they received during the implementation phase, and were satisfied with the system overall (Table 6).

Table 6: EWARS user satisfaction, cross-sectional survey, Fiji, 2016 (n=32)

EWARS user satisfaction	Very satisfied or somewhat satisfied (%)
Initial training for EWARS	88%
Ongoing support to conduct EWARS activities	100%
Overall satisfaction with the system	97%

Simplicity

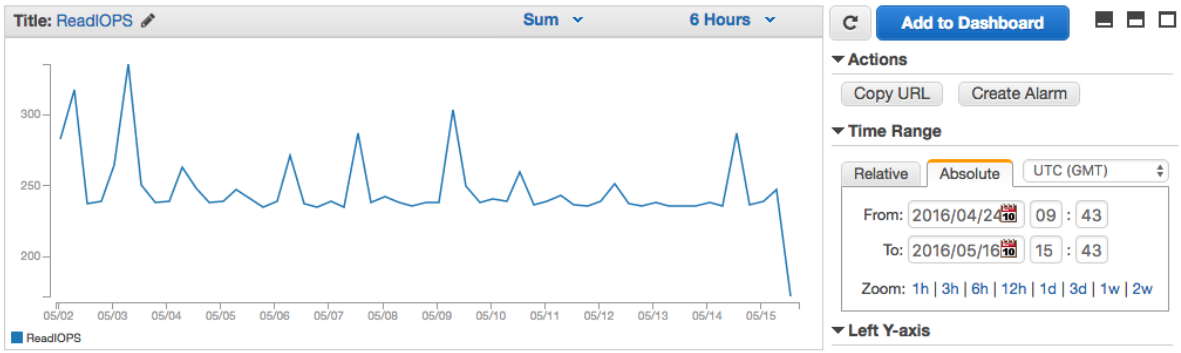
Simplicity refers to the ease of operation of the system and is highly related to acceptability and timeliness. EWARS introduced nine syndromes for weekly reporting, which is higher than that of previous syndromic surveillance systems in Fiji.[52] However, users did not indicate that the number of syndromes adversely affected the operation of the system (90% of users felt that the number of syndromes were appropriate).

> *"Mobile phones make it exciting to report data"*
> *"More time for training of focal points. Too much information and not enough time"*
> *- System implementer*

Stability

Stability refers to the reliability of the system and its resilience to change [103]. EWARS in a Box is highly technologically dependent and therefore it is critical that the system does not experience outages or require frequent upgrades. In order to assess the stability of the system, server logs were extracted from the host server at Amazon Web Services (AWS) (Figure 8). The graph shows a constant stream of activity with regular positive spikes (indicative of peaks in activity) from February to May 2016. An activity level of zero would suggest that the application was not functional. Based on this indicator, EWARS application had a very high level of stability.

Figure 8: EWARS server log from February – May 2016[53]



To further assess the stability of the system from users' perspective, focal points and surveillance officers were asked if they had ever experienced difficulty accessing the EWARS application or website. Of focal points who responded, 55% (15/27) indicated that they had some difficulty accessing the EWARS application on the mobile phone. The frequency with

[52] Five syndromes reported under the FSSS.
[53] Graph shows activity until 15/05/2016.

which focal points had difficulty accessing the application varied among respondents and between divisions. While the response was variable, 30% (8/27) of users reported they had difficulty more than once a month. The stability and accessibility of the system could further influence timely reporting of data. The EWARS website (www.ewars.ws) is currently undergoing a platform upgrade to improve its accessibility and support the increasing number of users globally, as well as users in remote locations where mobile connectivity and internet access can be limited.

Representativeness

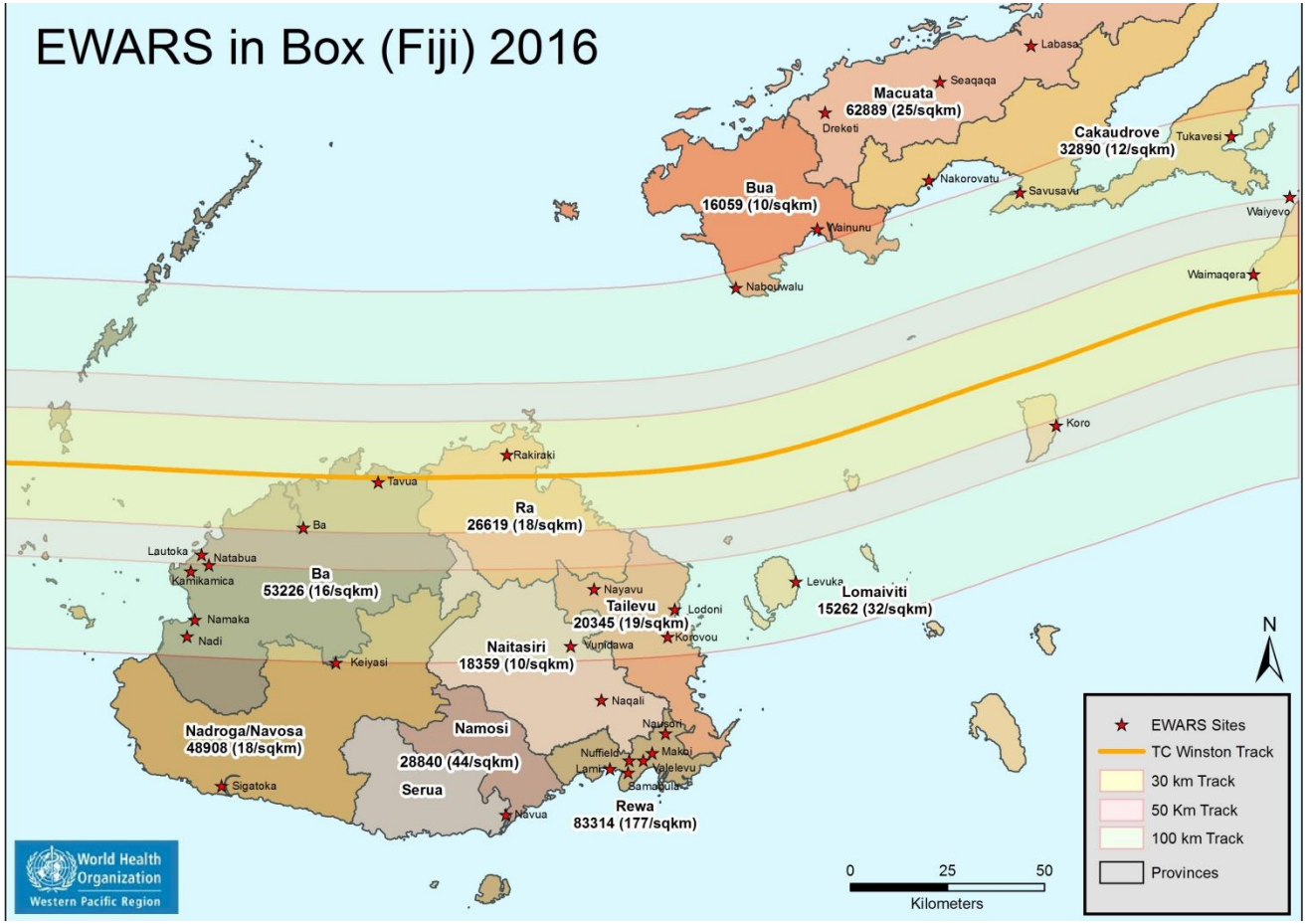
Representativeness in this context refers to the geographical appropriateness of the EWARS sites during the post-cyclone Winston emergency phase [103]. EWARN site selection after a natural disaster is often difficult due to the logistical challenges associated with collapsed infrastructure and access to health care facilities [92]. Sites were selected based on the following factors[54]:

- 11/12 sites already reporting to FSSS were captured
- Sites where both road and telecommunication infrastructure were somewhat intact
- Sites that were severely affected by Cyclone Winston and hence were at greater risk of experiencing a communicable disease outbreak (based on the rapid public health risk assessment) [99].
- Based on the population density in Fiji

The map in Figure 8 shows an overlay of the path of the cyclone and EWARS sites. Most EWARS sites were those lying within 100kms from the path of the cyclone. EWARS sites within the 50km band were most severely affected sites. Although most EWARS sites were fairly representative of the post-disaster phase, some areas were not captured due to limitations in access and damage to infrastructure (parts of Eastern division). This might have led to some localised outbreaks being missed by the surveillance system.

[54] Personal communication with EWARS developers

Figure 8: Map representing path of tropical cyclone Winston, EWARS surveillance sites, total population and population density for each province in Fiji, 2016. [55]



[55] Based on projected population estimates for 2016 as provided by Fiji MOHMS and are calculated based upon 2007 census conducted by Fiji Bureau of Statistics and using MOHMS divisional boundaries. Image courtesy of Paul Jaskierniak, WHO DPS

Table 7 lists the number of EWARS sites per division and the percentage of all health centres represented by EWARS sites. If EWARS (or a modification of it) was integrated into ongoing surveillance, site selection should be reviewed to assess coverage across all divisions.

Table 7: Population size and EWARS surveillance site coverage by Division, Fiji, 2016

	Population[56]	**% of total population**	**# EWARS sites**	**# health facilities**	**% of total EWARS sites**	**% of health facilities captured by EWARS**
Central	361894.6	41.6	12	52	35.3	23.1
Eastern	36869.9	4.2	2	52	5.9	3.8
Western	344663.3	39.6	10	61	29.4	16.4
Northern	127556.1	14.6	10	45	29.4	22.2
TOTAL	870983.9	100.0	34	210		

Cost

Cost of the surveillance system is an important factor in assessing the public health importance of the system itself [103]. Conducting a detailed cost-effectiveness analysis was beyond the scope of this evaluation, however, direct costs associated with EWARS were estimated (Table 8). Costing data was provided by the Fiji MOHMS, Fiji Health Sector Support Program (FHSSP) and WHO DPS in Fiji.

> "Good investment for the MOHMS"
> *- EWARS stakeholder*

The total cost of implementing and running EWARS in a Box for three months was approximately US$190,000. The costing does not include in-direct costs of MOHMS and WHO staff who contributed their time during this period, along with staffing costs of WHO consulting epidemiologists. The largest expenditure (~US$135, 000) was associated with supporting consultant EWARS epidemiologists in Fiji for the implementation and ongoing support of EWARS related activities. If EWARS was to be re-activated during another humanitarian disaster in Fiji, or was integrated into Fiji's existing syndromic surveillance, retention and continued up-skilling of trained surveillance officers, medical officers and focal points is highly recommended. Increased capacity building within the MOHMS staff will not only reduce the associated costs but also lead to long term development of a strong public health system in Fiji.

Table 8: Direct costs associated with EWARS in a Box; February – May 2016[57]

[56] Projected population estimates for 2016. Figures provided by Fiji MOHMS and are calculated based upon 2007 census conducted by Fiji Bureau of Statistics and MOHMS divisional boundaries.

Funding body	Item	Cost in USD
Fiji Ministry of Health and Medical Services (MOHMS)	Travel costs during implementation of EWARS in a Box	6, 578
Fiji Health Sector Support Program (FHSSP)	Salary support for surveillance officers	13, 882
World Health Organization (WHO)	EWARS in a Box (mobile handsets)	7, 477
	Mobile phone credit and data (Digicel)	1, 925
	Laptops for surveillance officers	13, 450
	Contractual services general	42, 405
	Consultant travel costs	92, 550
	Car rentals	5, 606
Total		**183, 873**

A complete cost-effectiveness analysis is recommended to assess the economic burden of responding to a large scale outbreak which could be averted, or the overall impact reduced, by using a functional early warning surveillance system.

Portability

Portability of the system refers to the possible use or duplication of the system in another circumstance or location [103]. EWARS in a Box is essentially a kit containing 50 mobile phones along with a two laptops that can be deployed within 48 hours of an humanitarian emergency [98]. Like any other surveillance system, the system is limited by its dependence on communication (road and telecommunication) being intact during the disaster phase. In Fiji, implementation of EWARS in a Box was undertaken within 14 days post-cyclone, soon after infrastructure had been restored and other key necessities such as shelter, food, safe drinking water and sanitation had been provided to those severely affected [99]. All stakeholders and developers felt that the implementation of EWARS in a Box was timely and relatively simple post-cyclone Winston. However, establishing guidelines and standard operating procedures, and documenting 'lessons learnt' for implementation and for future use of EWARS in a Box is recommended to facilitate the deployment of the system in future disaster settings.

Event based surveillance

Event Based Surveillance or EBS through EWARS is reliant on health care workers reporting any unusual public health events or unexpected deaths (Figure 1). As EBS is an immediate reporting system, it is difficult to assess the timeliness of EBS in a similar manner to IBS. For these reasons, its impact and effectiveness was measured by the time taken to respond to an alert (verification) and by the number of cases that were impacted by each investigation. Table 9 shows the time taken to respond to and verify alerts indicating potential outbreaks under EBS. The alerts were investigated by outbreak response teams. Of the 4 confirmed outbreaks, 2 were associated with conjunctivitis, 1 was associated with typhoid and the cause of 1 remained unknown. These data suggest that EBS was useful for outbreak detection during the post-cyclone response, and the impact of timely public health response can be broad. Table 2 also shows the number of EBS alerts that were verified.

[57] Costing information as of 19/05/2016

Table 9: Time taken to verify and confirm potential outbreaks when reported through EBS between epidemiological weeks 10-21, 2016

	Number of outbreaks	Time taken to generate a public health response (in days)[58]	Impact of outbreak	
			# of cases	# of deaths
Confirmed outbreaks	1	0	830	0
	1	1	50	0
	1	2	4	0
	1	4	12	1
Non-confirmed outbreaks	1	Unknown	13	0
	1	Unknown	1	0
	1	3	5	3
	1	6	31	0
	1	8	0	0
	1	21	4	3

Both surveys and stakeholder interviews suggested that EBS was not well adopted and required work to strengthen implementation. When focal points were asked *"What would you do if you saw an unusual public health event?"* the majority of respondents (16/27, 59%) indicated that they would directly contact and seek guidance from their SDMO or DMOs. Only 7/27 indicated that they would contact the FCCDC and 3/27 indicated they would use the toll free number to report the event. Importantly, the national coordinator for EBS felt that the reason the system was not performing well (personal communication) was due to the lack of training and awareness among health care workers.

All stakeholders felt that EBS had not performed well during the post-cyclone Winston phase, and believed EBS was important and should be strengthened.

> *"Don't think it has worked well at all; needs more awareness and training".*
> *-System implementer*

Several clusters or outbreaks were recently detected in Fiji, most of which were identified through non-IBS reporting, signifying the role of EBS during post-disaster emergencies. Further training to improve EBS reporting, risk assessment and verification process is recommended.

Conclusions

EWARS in a Box was implemented in Fiji after large-scale damage was caused by Tropical Cyclone Winston. WHO recommends a formal evaluation of an EWARN 3-6 months after its implementation [91]. This rapid evaluation assessed the performance of EWARS during the first three months of implementation in Fiji.

EWARS in a Box is a field-ready surveillance system that utilises smartphones and a web based application to collect and transmit surveillance data on nine syndromes. Although the system is specifically designed for post-disaster emergencies, the role of early warning systems for outbreak detection extends beyond the disaster phase and should be highlighted.

[58] Calculated as final date of verification minus the date of report

The evaluation demonstrated that EWARS had satisfied its primary purpose of monitoring communicable disease trends over time. In the absence of a large-scale outbreak, it was difficult to assess the system's sensitivity to detect outbreaks for reasons highlighted previously [100, 104].

Reporting through EWARS was complete and relatively timely. EWARS in a Box was considered simple, acceptable and generally useful by all those involved in the surveillance. The system was found to be portable and stable, making it ideal for use in low-resource and remote post-disaster settings. Importantly, EWARS in a Box was successful in overcoming several issues highlighted during a recent evaluation of the Fiji Syndromic Surveillance System (FSSS). Key factors contributing to the success of EWARS in Fiji after cyclone Winston are listed below:

- The system was easy to implement.
- Automated reporting, analysis and dissemination of surveillance data provided near- real time monitoring of communicable disease trends.
- In contrast to the FSSS where all activities were coordinated by a national surveillance officer, the divisional surveillance officers recruited specifically for EWARS were instrumental in ensuring that all reports were received on time and alerts were verified as quickly as possible. The role of the surveillance officers should be acknowledged and highlighted during future implementation of EWARS in other settings.

Like many other surveillance systems EWARS in a Box is limited by its reliance on access to telecommunication (mobile coverage) and access to sites. Another limitation was the lack of baseline data and hence the use of generalised thresholds for detecting outbreaks. Although the system was fairly representative of Fiji, some areas might have been missed due to limited access immediately after the cyclone.

Some issues pertaining to the quality of data and application of case definitions continue to exist, and improvement of these aspects should be considered. Some divisions performed better than others in relation to timeliness of reporting. This could be associated the with varying burden of disease and population density between the different divisions, however continued troubleshooting and engagement is recommended to ensure that reports are received on time. Increased dissemination and discussion of surveillance data should be undertaken in conjunction with subdivisional and divisional outbreak response teams in order to achieve effective and well-coordinated public health responses.

Substantial infrastructure, human resources and financial resources were used in the implementation of EWARS in a Box in Fiji. Based on EWARS' performance in Fiji, transitioning elements of EWARS into Fiji's routine surveillance system can provide as an opportunity to strengthen the surveillance system and the public health system in Fiji overall.

Recommendations to improve and strengthen EWARS in a Box

EWARS epidemiological bulletin

One of the key strengths of EWARS in a Box is its ability to automatically generate a bulletin at the end of each epidemiological week. The automated bulletins are highly beneficial during acute emergencies and minimise manual data recording, analysing, collating and dissemination of information. Automation of the bulletins reduces human error in reporting and significantly reduces the burden on human resources. In addition, the surveillance outputs and EWARS bulletin are flexible and should be adapted for each disaster setting. Key recommendations to improve the utility of the EWARS bulletin are below:

- Improving the layout and design of EWARS bulletin has been discussed with EWARS developers and is currently being reviewed by a consultant EWARS epidemiologist.

  -Consideration should be given to including further interpretation within each bulletin, inclusion of alert thresholds on graphs for further clarity and site-specific feedback. Although this might not be critical during an emergency phase as most responses are required to be coordinated at a national level.
- Ensure all EWARS actors receive the weekly bulletin. One of the keys to improving surveillance over time is to provide feedback to those who are responsible for collecting data. Empowering focal points with this information will improve long term engagement with the system.

Strengthen Event Based Surveillance reporting through EWARS

Increasing awareness on the public health importance of EBS and providing training to health care workers and outbreak response teams is recommended. Based on the findings from the survey, review of the current EBS reporting should be undertaken, where in all health care workers, SDMOs and DMOs should be encouraged to report any unusual public health events through EWARS. Timely EBS reporting and risk assessments can prevent or reduce the impact of large-scale outbreaks compared with indicator based surveillance.

Greater engagement with EWARS sites

Site visits conducted with the surveillance officers as part of the EWARS evaluation proved to be extremely useful in strengthening relationships with data providers, providing ad-hoc training, identifying issues and troubleshooting. If EWARS (or a modification of it) is continued in Fiji, regular visits to the surveillance sites by the Surveillance Officers would be very beneficial. A structured checklist could be developed to allow the Surveillance Officers to systematically review, assess, validate and strengthen surveillance.

Develop standard guidelines and training modules

- This is the first time EWARS in a Box has been implemented in a Pacific Island Country. Protocols detailing the operation of the system and the verification process should be documented for future deployment of EWARS.
- Rapid risk assessment guidelines should be implemented and training provided to assist with alert response. The evaluation found that the surveillance officers were clear on alert thresholds but were less confident around when an outbreak response should be initiated (response thresholds).
- Laboratory and other surveillance systems should be better aligned with EWARS. Standard protocols recommending a minimum number and type of specimens for each syndrome are suggested. This will guide the EWARS sites and streamline the process of laboratory testing to confirm diagnosis of suspected cases. In addition, the use of rapid diagnostics tests and/ or point of care testing should be explored to improve the data quality, improve the positive predictive value of the surveillance system and reduce the burden of laboratory surveillance.
- Lessons learnt from the Fiji experience of EWARS should be documented for use in other Pacific Island Countries and countries experiencing humanitarian disasters.

Recommendations for integration of EWARS into Fiji's existing surveillance system

Human capacity building at Divisional and National levels

Building human capacity is paramount for sustaining good public health surveillance. Building national capacity will also reduce costs associated re-activation of EWARS during another post-disaster emergency.

- Basic epidemiological training should be considered for all public health staff undertaking surveillance activities. Epidemiological training focused on outbreak identification, investigation and response is recommended for surveillance officers.
- Weekly meetings with the EWARS surveillance team (surveillance officers, SDMOs and DMOs) are recommended wherein bulletins (and other EWARS related issues) are reviewed in depth. This will ensure timely and effective public health response.
- Regular 'on-the-job' training for EWARS focal points should be considered. This training could be conducted in a 'train-the-trainer' format to allow focal point to readily transfer knowledge and skills to others involved in surveillance within their respective facilities. Retention of all trained staff involved in EWARS should be prioritised.

Case classification

The evaluation identified a number of issues around case classification, which affects the quality of data reported to the system. In order for effective identification and response to potential outbreaks, quality of data should be considered a priority. However, this needs to be weighed against the burden of reporting. The evaluation identified the following areas where case classification could be improved:

- Recording and monitoring of case classification issues by surveillance officers is recommended. These issues can be discussed and solutions sought during weekly surveillance meetings.

  In particular, a clarification on how 'fever' is defined in all case definitions is recommended (e.g. fever >38◦C or self-reported fever without a measured fever). Inclusion of self-reported fever greater 2 days, regardless of measured temperature on day of presentation, might also be considered.

- Encouraging the recording of syndromes directly into the clinic registers is highly recommended. To facilitate this process, case definitions could be provided in a laminated A5 format that can be kept in each clinic register for easy reference; inclusion of standard abbreviations for each syndrome (e.g. AFR, PF, ILI, WD, etc) would make recording in registers consistent. A longer term option would be to include an extra column in the clinic register for "Syndrome." Additionally, consideration could be given to adding "fever y/n", "length of fever (days)" and "recorded temp" columns into the register.

Representativeness of EWARS

The number of syndromes and sites represented by EWARS should be re-assessed prior to transitioning EWARS to Fiji's routine syndromic surveillance system. Current EWARS sites target areas that were severely affected by cyclone Winston. Similarly, the syndromes were chosen based on post-disaster epidemic risk assessment. Once the disaster phase is over, site selection should be reviewed. A communicable diseases risk assessment should be undertaken to determine the appropriateness of syndromes moving forward.

Data management

All syndromic surveillance data is currently stored in a cloud based EWARS server. All stakeholders should be consulted to discuss the migration and long term maintenance of the

database and the online system. It is recommended that the MOHMS seek WHO's guidance on this issue based on previous models where EWARS has been absorbed into countries' existing surveillance systems. Consideration should be given to a 'full cloud' and/ or 'hybrid cloud' model which allows automated updates to the software (maintained by WHO) while ensuring data security and encryption as per the MOHMS requirements.

Telecommunication

EWARS reporting is dependent of use of mobile data. The system has performed well overall, with some issues around access to mobile data and network coverage. MOHMS should seek guidance from both the Fiji Ministry of Information and WHO on improving mobile phone coverage and access to internet in remote settings.

Strengthening communication at all levels

Based consultations with EWARS actors, enhanced communication and dissemination of surveillance data between all those involved in post-disaster response is recommended during future emergencies.

References

1. Fiji MoHMS. Rapid Public Health Risk Assessment Tropical Cyclone Winston Republic of Fiji. Fiji Minnistry of Health and Medical Services and World Health Organisation. 2016.http://www.health.gov.fj/wp-content/uploads/2016/03/20160315-Rapid-Health-Risk-Assessment-TC-Winston-Mar2016-for-editing_14-March-2016_final-2.pdf22/05/2017
2. WHO. Emergency Response Framework (ERF). 2013.http://www.who.int/hac/about/erf/en/
3. WHO. Early warning surveillance and response in emergencies. Report of the second WHO technical workshop. 2011.http://apps.who.int/iris/bitstream/10665/70665/1/WHO_HSE_GAR_DCE_2011.2_eng.pdf 14/06/2016
4. Bilve A, Nogareda F, Joshua C, et al. Establishing an early warning alert and response network following the Solomon Islands tsunami in 2013. *Bulletin of the World Health Organization*. 2014; 92: 844-8.
5. WHO. WHO launches new early warning system in a box to help 500 000 people for only $USD 15 000. 2015.http://www.afro.who.int/en/ssd/news/item/8231-who-launches-new-early-warning-system-in-a-box-to-help-500-000-people-for-only-$usd-15-000.html
6. Connolly MA, Gayer M, Ryan MJ, Salama P, Spiegel P and Heymann DL. Communicable diseases in complex emergencies: impact and challenges. *Lancet (London, England)*. 2004; 364: 1974-83.
7. WHO. Early detection, assessment and response to acute public health events: Implementation of Early Warning and Response with a focus on Event-Based Surveillance. Interim ed. 2014.http://www.who.int/ihr/publications/WHO_HSE_GCR_LYO_2014.4/en/15/06/2016
8. European Centre for Disease Prevention and Control. Data quality monitoring and surveillance system evaluation – A handbook of methods and applications. Stockholm: ECDC2014
9. Buehler JW. Review of the 2003 National Syndromic Surveillance Conference--lessons learned and questions to be answered. *MMWR supplements*. 2004; 53: 18-22.
10. Buehler JW, Hopkins RS, Overhage JM, Sosin DM and Tong V. Framework for evaluating public health surveillance systems for early detection of outbreaks: recommendations from the CDC Working Group. *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports / Centers for Disease Control*. 2004; 53: 1-11.
11. WHO. Communicable disease surveillance and response systems: Guide to monitoring and evaluating. 2006.http://www.who.int/csr/resources/publications/surveillance/WHO_CDS_EPR_LYO_2006_2.pdf15/06/2016
12. Bravata DM, McDonald KM, Smith WM, et al. Systematic Review: Surveillance Systems for Early Detection of Bioterrorism-Related Diseases. *Annals of Internal Medicine*. 2004; 140: 910-22.
13. Craig A, Kool J and Nilles E. The Pacific experience: supporting small island countries and territories to meet their 2012 International Health Regulations (2005) commitments. *Western Pacific surveillance and response journal : WPSAR*. 2013; 4: 14-8.
14. Craig AT, Kama M, Samo M, et al. Early warning epidemic surveillance in the Pacific island nations: an evaluation of the Pacific Syndromic Surveillance System. *Tropical medicine & international health : TM & IH*. 2016.
15. Kool JL, Paterson B, Pavlin BI, Durrheim D, Musto J and Kolbe A. Pacific-wide simplified syndromic surveillance for early warning of outbreaks. *Global public health*. 2012; 7: 670-81.
16. Paterson BJ, Kool JL, Durrheim DN and Pavlin B. Sustaining surveillance: evaluating syndromic surveillance in the Pacific. *Global public health*. 2012; 7: 682-94.

Annexes

Annex A: List of EWARS reporting sites by Division and Sub-division

#	Division	Sub-division	Health facility	Name
1	Central Division	Tailevu Subdivision	Nayavu	Nayavu
2	Central Division	Suva Subdivision	Lami HC	Lami
3	Central Division	Suva Subdivision	Valelevu HC	Valelevu
4	Central Division	Suva Subdivision	Makoi HC	Makoi
5	Central Division	Suva Subdivision	Samabula HC	Samabula
6	Central Division	Suva Subdivision	Nuffield HC	Nuffield
7	Central Division	Serua/Namosi Subdivision	Navua Subdivisional Hospital	Navua
8	Central Division	Rewa Subdivision	Nausori Subdivisional Hospital	Nausori
9	Central Division	Tailevu Subdivision	Korovou Subdivisional Hospital	Korovou
10	Central Division	Tailevu Subdivision	Lodoni HC	Lodoni
11	Central Division	Naitasiri Subdivision	Vunidawa Subdivisional Hospital	Vunidawa
12	Central Division	Naitasiri Subdivision	Naqali HC	Naqali
13	Western Division	Nadroga/Navosa Subdivision	Sigatoka Subdivisional Hospital	Sigatoka
14	Western Division	Nadroga/Navosa Subdivision	Keiyasi	Keiyasi
15	Western Division	Nadi Subdivision	Nadi Subdivisional Hospital	Nadi
16	Western Division	Nadi Subdivision	Namaka HC	Namaka
17	Western Division	Lautoka Subdivision	Lautoka Subdivision Hospital	Lautoka
18	Western Division	Lautoka Subdivision	Kamikamica HC	Kamikamica
19	Western Division	Lautoka Subdivision	Natabua HC	Natabua
20	Western Division	Ba Subdivision	Ba Subdivisional Hospital	Ba
21	Western Division	Tavua Subdivision	Tavua Subdivisional Hospital	Tavua
22	Western Division	Ra Subdivision	Rakiraki Subdivisional Hospital	Rakiraki
23	Northern Division	Cakaudrove Subdivision	Savusavu Subdivisional Hospital	Savusavu
24	Northern Division	Cakaudrove Subdivision	Tukavesi HC	Tukavesi
25	Northern Division	Cakaudrove Subdivision	Nakorovatu HC	Nakorovatu
26	Northern Division	Bua Subdivision	Nabouwalu Subdivisional Hospital	Nabouwalu
27	Northern Division	Bua Subdivision	Wainunu HC	Wainunu
28	Northern Division	Macuata Subdivision	Labasa Divisional Hospital	Labasa
29	Northern Division	Macuata Subdivision	Dreketi HC	Dreketi
30	Northern Division	Macuata Subdivision	Seaqaqa HC	Seaqaqa
31	Northern Division	Taveuni Subdivision	Waiyevo Subdivisional Hospital	Waiyevo
32	Northern Division	Taveuni Subdivision	Waimaqera HC	Waimaqera
33	Eastern Division	Lomaiviti Subdivision	Levuka Subdivisional Hospital	Levuka
34	Eastern Division	Lomaiviti Subdivision	Koro HC	Koro

Annex B: List of EWARS syndromes, case definitions and thresholds

Syndrome	Case definition	Thresholds
Acute fever and rash	Fever either reported or measured (>38°C) PLUS non-blistering rash	1 case
Prolonged fever	Any fever either reported or measured (>38°C) lasting three or more days	Twice the average number of cases seen in the previous 2 weeks
Influenza-like illness	Fever either reported or measured (>38°C) PLUS cough and/or sore throat.	Twice the average number of cases seen in the previous 2 weeks
Acute watery diarrhoea	Three or more loose or watery stools in 24hrs (non-bloody).	Twice the average number of cases seen in the previous 2 weeks
Acute bloody diarrhoea	Any episode of acute bloody diarrhoea	3 cases in one location in 1 week or twice the average number of cases seen in the previous 2 weeks
Acute jaundice syndrome	Jaundice (yellow eyes or dark urine) AND severe illness with or without fever.	3 cases
Suspected dengue	Fever for at least 2 days PLUS at least two of the following:- nausea or vomiting; - muscle or joint pain; - severe headache or pain behind the eyes; - rash; - bleeding.	Twice the average number of cases seen in the previous 3 weeks
Suspected meningitis	Sudden onset of fever, PLUS one or more of the following:- severe headache;- neck stiffness;- altered consciousness; - petechial/puerperal rash.	1 case
Zika-like illness	Generalized maculopapular rash plus two or more of the following: Arthralgia or myalgia; Red eyes or non-purulent conjunctivitis; Oedema of hands or feet; Low grade fever (< 38℃), Pain behind the eyes	3 cases

Annex C: Tally sheet for EWARS reporting

Early Warning Epidemic Surveillance Reporting Form – Cyclone Winston

Ministry of Health and Medical Services, Fiji, 2016

*Health Facility:*_____ *Date of week beginning:*_____/_____/_____ *Date of week ending:*_____/_____/_____

	< 5 Years	5 + Years	TOTAL
Total number of consultations*			
Acute fever and rash *Case definition: Fever plus rash*			
Prolonged fever *Fever for 3 days or more*			
Influenza-like illness *Fever plus cough or sore throat*			
Watery diarrhea *3 or more loose or watery stools in 24 hours (non-bloody)*			
Bloody diarrhea *Any episode of acute bloody diarrhea*			
Acute jaundice syndrome *Jaundice (yellow eyes or dark urine) AND severe illness with or without fever*			
Suspected dengue *Fever for at least 2 days PLUS at least two of the following:* *(i) Nausea or vomiting; (ii) Muscle or joint pain; (iii)* *Severe headache or pain behind the eyes; (iv) Rash; (v)* *Bleeding*			
Suspected meningitis *Sudden onset of fever (>38°C) PLUS one or more of the following:* *Sudden onset of fever, PLUS one or more of:* *(i) severe headache; (ii) neck stiffness; (iii) altered consciousness; (v) petechial/purpural rash.*			
Zika like illness *Generalized maculopapular rash AND two or more of the following:* • *arthralgia or myalgia* • *red eyes or non-purulent conjunctivitis* • *pain behind the eyes* • *oedema of hands or feet* • *low grade fever (<38°C)*			

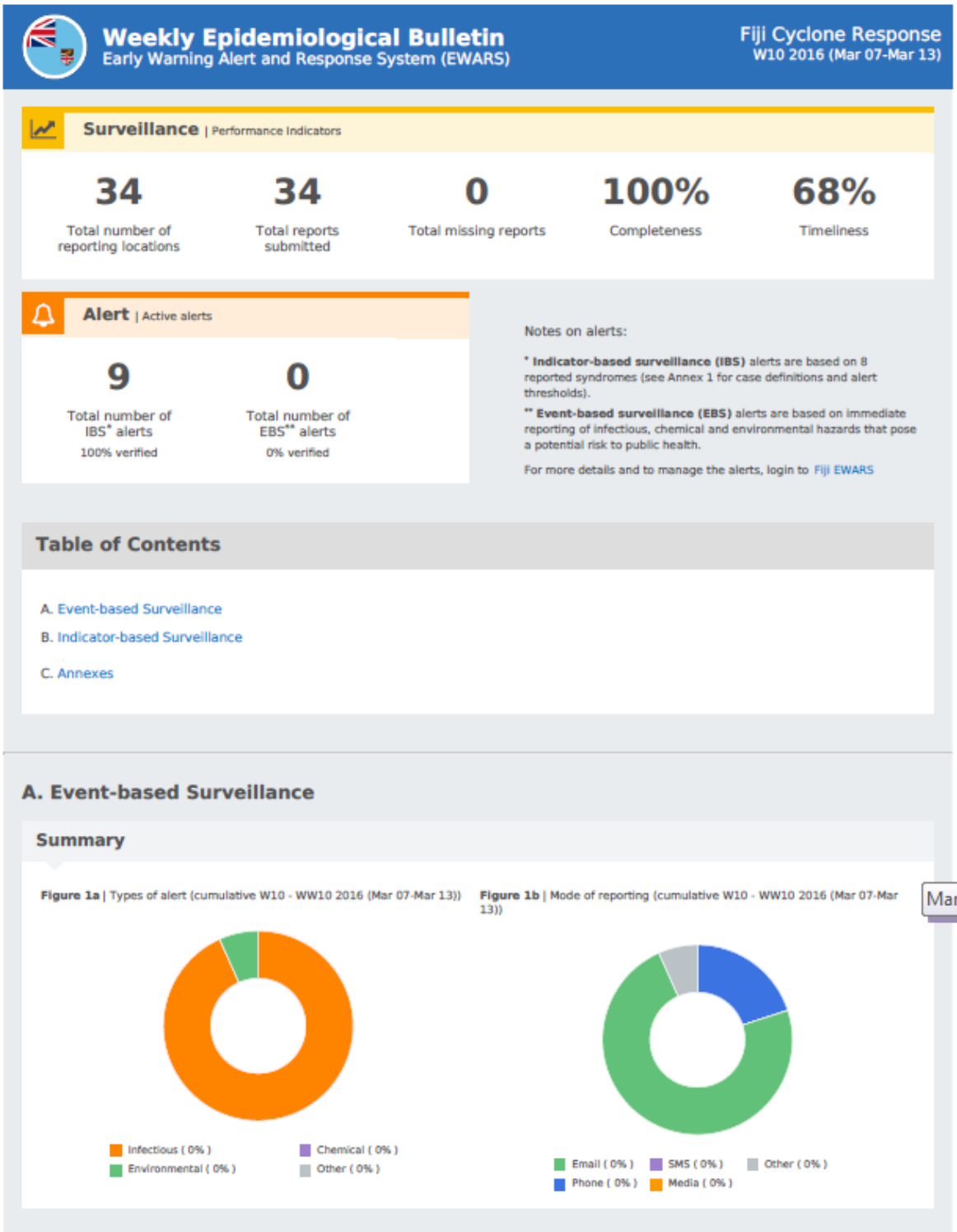
1 patient = 1 diagnosis

Unexpected events:_____ *(deaths, cluster of illness, bird or animal die off, etc)*

*DATE*____/____/_____ *NAME:*_____ *SIGNATURE:*_____

** Should include new visits only. Do not include repeat visits for a diagnosis that has already been seen |For immediate reporting contact Dr Sam Fullman (phone: 7600864, email: fullmans@who.int)*

Annex D: Snapshot of EWARS bulletin for epidemiological week 10



Weekly Epidemiological Bulletin
Early Warning Alert and Response System (EWARS)

Fiji Cyclone Response
W10 2016 (Mar 07-Mar 13)

Surveillance | Performance Indicators

34	34	0	100%	68%
Total number of reporting locations	Total reports submitted	Total missing reports	Completeness	Timeliness

Alert | Active alerts

9	0
Total number of IBS* alerts	Total number of EBS** alerts
100% verified	0% verified

Notes on alerts:

* **Indicator-based surveillance (IBS)** alerts are based on 8 reported syndromes (see Annex 1 for case definitions and alert thresholds).

** **Event-based surveillance (EBS)** alerts are based on immediate reporting of infectious, chemical and environmental hazards that pose a potential risk to public health.

For more details and to manage the alerts, login to Fiji EWARS

Table of Contents

A. Event-based Surveillance
B. Indicator-based Surveillance
C. Annexes

A. Event-based Surveillance

Summary

Figure 1a | Types of alert (cumulative W10 - WW10 2016 (Mar 07-Mar 13))

Figure 1b | Mode of reporting (cumulative W10 - WW10 2016 (Mar 07-Mar 13))

Annex E: EWARS Cross-Sectional Survey (Focal Points) Summary[59]

1	**Division**	**Number**	**(% response rate)**
	Central	12/12	100%
	Eastern	2/2	100%
	Northern	5/10	50%
	Western	8/10	80%
	Total	*27/34*	*79%*
2	**Position**	**Number (n=27)**	**(% total respondents)**
	Subdivisional medical officer	5	19%
	Medical officer	15	56%
	Nurse*	6	22%
	Other	1	4%
3	**What do you think is the purpose of EWARS?**	**Number (n=27)**	**(% total respondents)**
	Theme: outbreak detection	18	67%
	Theme: outbreak response	9	33%
	Theme: general disease surveillance or monitoring	12	44%
4	**Do you think EWARS has had any impact on public health in Fiji?**	**Number (n=26)**	**(% total respondents)**
	Yes	20	77%
	No	0	0%
	Unsure	6	23%
5	**In your opinion, how easy is it to use EWARS on the mobile phone?**	**Number (n=27)**	**(% total respondents)**
	Very easy	24	89%
	Somewhat easy	3	11%
	Not very easy	0	-
	Not at all easy (very difficult)	0	0%
6.1	**Have you ever had difficulty accessing EWARS on the mobile phone?** *Application not working*	**Number (n=27)**	**(% total respondents)**
	Yes	15	56%
	No	12	44%
	Unsure	0	-
6.2	**How often has this occurred?**	**Number (n=15)**	**(% total respondents)**
	Very often (most weeks)	2	13%
	Somewhat often (more than once a month)	6	40%
	Not very often (once or less than once a month)	3	20%
	Not at all often (twice or less)	4	27%
7.1	**Are you aware of the EWARS case definitions?**	**Number (n=27)**	**(% total respondents)**
	Yes	27	100%
	No	0	-
	Unsure	0	-
7.2	**How easy is it to classify cases into the syndrome categories?**	**Number (n=27)**	**(% total respondents)**
	Very easy	11	41%
	Somewhat easy	16	59%
	Not very easy	0	-
	Not at all easy (very difficult)	0	-
8	**At your health facility, what is the process used to record patients who meet the case definitions?**	**Number (n=20)**	**(% total respondents)**
	Medical officers record cases directly on the EWARS tally sheet at the time a patient is seen	4	20%
	Medical officers record cases on an EWARS line list	1	5%
	Weekly review of register or logbook by Medical Officer or Nurse	13	65%
	Not known	0	-
	Other	2	10%
9	**How do you send / transmit the EWARS weekly reports?** *Tick all that apply*	**Number (n=20)**	**(% total respondents)**
	EWARS mobile phone application	25	93%
	EWARS website (using computer)	1	4%
	Email	4	15%
	Telephone call	8	30%
	SMS	6	22%
	Other	3	11%
10	**What is your preferred reporting method?** *Ranked as first preference*	**Number (n=26)**	**(% total respondents)**
	EWARS mobile phone application	24	92%
	EWARS website (using computer)	0	-
	Email	0	-
	Telephone call	2	8%
	SMS	0	-

[59] For privacy reasons, qualitative data has not been included in the summary.

11.1	**Have there been situations where you could not submit the EWARS weekly report on time (before Monday 6pm)?**	**Number (n=24)**	**(% total respondents)**
	Yes	21	88%
	No	3	13%
	Unsure	0	-
11.2	**What are the most common challenges for timely reporting?** *Tick all that apply*	**Number (n=24)**	**(% total respondents)**
	Tally sheet not received on time from other staff	11	46%
	No access to internet (no credit)	4	17%
	No access to internet (no signal)	11	46%
	No access to phone	2	8%
	Not enough time / workload too busy	14	58%
	Unsure	0	-
	Other	4	17%
12	**What would you do if you identified an unusual public health event?** *Unexpected deaths, cluster of illness, animal die off, environmental hazard etc.*	**Number (n=27)**	**(% total respondents)**
	Theme: contact SDMO / DMO	16	59%
	Theme: contact EWARS surveillance officer	7	26%
	Theme: contact FCCDC (Mataika House)	7	26%
	Theme: use toll-free number to report event	3	11%
13	**Do you think the number of syndromes reported to EWARS is appropriate?**	**Number (n=27)**	**(% total respondents)**
	Yes	24	89%
	No - too many syndromes	1	4%
	No - too few syndromes	1	4%
	Unsure	1	4%
14.1	**How easy was it to amend the reporting process when an additional syndrome (Zika-like illness) was added to EWARS?**	**Number (n=27)**	**(% total respondents)**
	Very easy	12	44%
	Somewhat easy	13	48%
	Not very easy	2	7%
	Not at all easy (very difficult)	0	-
14.2	**Why was it difficult to amend the reporting process?**	**Number (n=2)**	
	Theme: similar case definitions and patient presentation	2	-
15	**How well do you think EWARS is able to signal an early warning for potential disease outbreaks?**	**Number (n=27)**	**(% total respondents)**
	Very well	18	67%
	Somewhat well	7	26%
	Not very well	2	7%
	Not at all well	0	-
16	**Have you received any feedback when an EWARS alert has been generated for your health facility?**	**Number (n=27)**	**(% total respondents)**
	Yes	22	81%
	No	3	11%
	Unsure	1	4%
	N/A	1	4%
17.1	**Do you receive the EWARS weekly bulletin?**	**Number (n=27)**	**(% total respondents)**
	Yes	19	70%
	No	7	26%
	Unsure	1	4%
17.2	**How useful is the information in the EWARS weekly bulletin for your health facility?**	**Number (n=27)**	**(% total respondents)**
	Very useful	9	33%
	Somewhat useful	12	44%
	Not very useful	3	11%
	Not at all useful	3	11%
17.3	**How have you used the information in the EWARS weekly bulletin?**	**Number (n=19)**	**(% total respondents)**
	Theme: information sharing	6	32%
	Theme: to compare with other reporting areas	5	26%
	Theme: to initiate preventive or responsive public health actions	5	26%
17.4	**How could the EWARS weekly bulletin be improved?**	**Number (n=19)**	**(% total respondents)**
	Theme: include health facility specific surveillance data	3	16%
	Theme: include outcome of previous week's case investigations	1	5%
	Theme: increase access to other staff members at health facility	2	11%
17.5	**Do you ever distribute the information in the weekly bulletin to other persons or organisations?**	**Number (n=26)**	**(% total respondents)**
	Yes	9	35%
	No	16	62%
	Unsure	1	4%
17.6	**Who do you distribute the information to?**	**Number (n=9)**	**(% total respondents)**
	Theme: health facility colleagues	8	89%
	Theme: community health care workers	3	33%
	Theme: regional public health staff	1	11%
18	**How satisfied do you feel with the training that you received when**	**Number (n=27)**	**(% total respondents)**

	EWARS was implemented?		
	Very satisfied	11	41%
	Somewhat satisfied	12	44%
	Not very satisfied	3	11%
	Not at all satisfied	1	4%
19	**How supported do you feel to be able to carry out your EWARS responsibilities?**	**Number (n=27)**	**(% total respondents)**
	Very supported	13	48%
	Somewhat supported	14	52%
	Not very supported	0	-
	Not at all supported	0	-
20	**Overall, how satisfied are you with EWARS?**	**Number (n=27)**	**(% total respondents)**
	Very satisfied	16	59%
	Somewhat satisfied	11	41%
	Not very satisfied	0	-
	Not at all satisfied	0	-

* Including the titles of Nurse Practitioner and Sister.

Annex F: EWARS Cross-Sectional Survey (Surveillance Officers) Summary[60]

1	**What do you think is the purpose of EWARS?**	**Number (n=5)**	**(% total respondents)**
	Theme: outbreak detection	3	60%
	Theme: outbreak response	3	60%
2	**Do you think EWARS has had any impact on public health in Fiji?**	**Number (n=5)**	**(% total respondents)**
	Yes	5	100%
	No	0	-
	Unsure	0	-
3	**In your opinion, how easy is it to use EWARS?**	**Number (n=5)**	**(% total respondents)**
	Very easy	4	80%
	Somewhat easy	0	-
	Not very easy	1	20%
	Not at all easy (very difficult)	0	-
4.1	**Have you ever had difficulty accessing the EWARS website?**	**Number (n=5)**	**(% total respondents)**
	Yes	1	20%
	No	4	80%
	Unsure	0	-
4.2	**How often has this occurred?**	**Number (n=1)**	**(% total respondents)**
	Very often (most weeks)	0	-
	Somewhat often (more than once a month)	0	-
	Not very often (once or less than once a month)	0	-
	Not at all often (twice or less)	1	-
5	**In your opinion, how timely are the reports submitted from health facilities in your division/s?**	**Number (n=5)**	**(% total respondents)**
	Very timely	0	-
	Somewhat timely	5	100%
	Not very timely	0	-
	Not at all timely	0	-
6	**How often do you correct errors in the reports submitted by the health facilities in your division/s?**	**Number (n=5)**	**(% total respondents)**
	Very often (most weeks)	0	-
	Somewhat often (more than once a month)	0	-
	Not very often (once or less than once a month)	3	60%
	Not at all often (twice or less)	0	-
	N/A	2	40%
7	**In your opinion, how accurately are the case definitions applied at the health facilities in your division/s?**	**Number (n=5)**	**(% total respondents)**
	Very accurately	1	20%
	Somewhat accurately	4	80%
	Not very accurately	0	-
	Not at all accurately	0	-
	Unsure	0	-
8	**In your opinion, what are the most common challenges for timely reporting?**	**Number (n=5)**	**(% total respondents)**
	Unable to speak with treating Medical Officer in a timely manner	3	60%
	Unable to speak with Divisional Medical Officer in a timely manner	1	20%
9	**Do you think the number of syndromes reported to EWARS is appropriate?**	**Number (n=5)**	**(% total respondents)**
	Yes	5	100%
	No - too many syndromes	0	-
	No - too few syndromes	0	-
	Unsure	0	-
10	**How easy was it to amend the surveillance process when an additional syndrome (Zika-like illness) was added to EWARS?**	**Number (n=5)**	**(% total respondents)**
	Very easy	4	80%
	Somewhat easy	1	20%
	Not very easy	0	-
	Not at all easy (very difficult)	0	-
11	**How well do you think Event Based Surveillance has been integrated into EWARS?**	**Number (n=5)**	**(% total respondents)**
	Very well	2	40%
	Somewhat well	2	40%
	Not very well	1	20%
	Not at all well	0	-
12	**How well do you think EWARS is able to signal an early warning for potential disease outbreaks?**	**Number (n=5)**	**(% total respondents)**
	Very well	3	60%
	Somewhat well	1	20%
	Not very well	1	20%

[60] For privacy reasons, qualitative data has not been included in the summary.

	Not at all well	0	-
13.1	**Do you receive the EWARS weekly bulletin?**	**Number (n=5)**	**(% total respondents)**
	Yes	5	100%
	No	0	-
	Unsure	0	-
13.2	**How useful is the information in the EWARS weekly bulletin in assisting you in your role?**	**Number (n=5)**	**(% total respondents)**
	Very useful	2	40%
	Somewhat useful	3	60%
	Not very useful	0	-
	Not at all useful	0	-
13.3	**How have you used the information in the EWARS weekly bulletin?**	**Number (n=5)**	**(% total respondents)**
	Theme: identify disease trends in reporting areas	1	20%
	Theme: compare trends between divisions	2	40%
13.4	**How could the EWARS weekly bulletin be improved?**	**Number (n=5)**	**(% total respondents)**
	Theme: include syndrome thresholds in graphs	2	40%
	Theme: separate data for <5yrs and >5yrs categories	1	20%
	Theme: link with laboratory data	1	20%
13.5	**Do you ever distribute the information in the weekly bulletin to other persons or organisations?**	**Number (n=5)**	**(% total respondents)**
	Yes	4	80%
	No	1	20%
	Unsure	0	-
13.6	**Who do you distribute the information to?**	**Number (n=5)**	**(% total respondents)**
	Theme: focal points, health inspectors and medical officers	3	60%
	Theme: national public health colleagues	1	20%
14	**How satisfied do you feel with the training that you received when EWARS was implemented?**	**Number (n=5)**	**(% total respondents)**
	Very satisfied	2	40%
	Somewhat satisfied	3	60%
	Not very satisfied	0	-
	Not at all satisfied	0	-
15	**How supported do you feel to be able to carry out your EWARS responsibilities?**	**Number (n=5)**	**(% total respondents)**
	Very supported	4	80%
	Somewhat supported	1	20%
	Not very supported	0	-
	Not at all supported	0	-
16	**Overall, how satisfied are you with EWARS?**	**Number (n=5)**	**(% total respondents)**
	Very satisfied	4	80%
	Somewhat satisfied	1	20%
	Not very satisfied	0	-
	Not at all satisfied	0	-

Annex G. EWARS Roles and Responsibilities

System contributors	Key roles and responsibilities	
	Information contributed to the system	**Information received by the system**
Divisional Medical Officers (DMOs)	• Provide guidance to SOs on the verification and action of alerts • Mobilise sub-divisional and divisional outbreak response teams where appropriate • Monitor surveillance activity compliance	• Receive the EWARS weekly bulletin • Receive detailed information from SOs on syndrome alerts
Focal points (MOs and nurses)	• Ensure MOs and other practitioners are aware of their surveillance responsibilities and have the required forms and case definitions • Monitor compliance with surveillance responsibilities within the health facility • Collate site data and report it to EWARS on a weekly basis • Act as the primary liaison between the health facility and national or divisional surveillance activities	• Receive the EWARS weekly bulletin • Review report information and screen for potential outbreak signals • In conjunction with SOs/SDMOs/DMOs, instigate public health responses where necessary
Medical Officers (MOs) / other clinicians	• See patients and apply the surveillance case definitions • Complete the EWARS tally sheet for each reporting period	• Receive the EWARS weekly bulletin and use the information to inform clinical practice, including situational awareness of potential outbreak prone disease risks
National surveillance coordinator	• Overall responsibility for system functioning, including overarching coordination, training and development	• Receive the EWARS weekly bulletin • Disseminate the EWARS weekly bulletin to EWARS actors • Regularly review EWARS data to identify potential outbreaks • Participate in risk assessment activities • Monitor and/or coordinate surveillance activities, as directed by the National Communicable Disease Coordinator
National Advisor Communicable Diseases	• Overall responsibility for the implementation of EWARS • Supervision of the National Surveillance Coordinator	• Receive the EWARS weekly bulletin • Regularly review EWARS data to identify potential outbreaks • Participate in risk assessment activities, as required • Advise national, divisional or subdivisional response teams, as required
Senior Officers within		• Receive the EWARS weekly

the MOHMS		bulletin • Advise response to public health events of concern, as required
Surveillance Officers (SOs)	• Ensure EWARS weekly reports are received by sentinel sites, follow up sites as required • Troubleshoot reporting and other problems encountered by sentinel sites • Verify alerts generated by EWARS through discussions with the site concerned, along with the DMO • Suppress or action alerts where required • Act as the primary liaison between the focal points and divisional/national MOHMS staff	• Receive the EWARS weekly bulletin • Regularly review EWARS data to identify potential outbreaks • Participate in risk assessment activities, as required • Participate in public health response activities, where required

Annex H: Comparison between cases identified through EWARS and retrospective review of clinic records for epidemiological weeks 13 and 17 across three EWARS sites, Fiji 2016

Epidemiological Week 13						
	Site 1		**Site 2**		**Site 3**	
	Register	**EWARS**	**Register**	**EWARS**	**Register**	**EWARS**
Acute fever and rash	0	0	2	1	0	0
Prolonged fever	0	0	4	5	0	0
Influenza-like illness	33	67	39	17	7	10
Watery diarrhoea	9	28	48	25	6	6
Bloody diarrhoea	1	0	1	2	0	0
Acute jaundice syndrome	0	0	0	0	0	0
Suspected meningitis	0	0	0	0	0	0
Suspected dengue	0	4	1	2	0	0
Zika-like illness	-	-	0	0	0	0
Epidemiological Week 17						
	Site 1		**Site 2**		**Site 3**	
	Register	**EWARS**	**Register**	**EWARS**	**Register**	**EWARS**
Acute fever and rash	0	0	0	0	0	48
Prolonged fever	0	0	2	2	0	0
Influenza-like illness	39	29	40	8	10	3
Watery diarrhoea	11	24	19	8	23	0
Bloody diarrhoea	0	0	0	1	0	29
Acute jaundice syndrome	0	0	0	0	0	0
Suspected meningitis	0	0	0	1	0	0
Suspected dengue	1	4	0	2	0	0
Zika-like illness	0	1	0	0	1	0