The application of syndromic surveillance to public health practice

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Statement of originality

*The thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository**, subject to the provisions of the Copyright Act 1968.*

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Statement of authorship

I hereby certify that the work embodied in this thesis contains a published paper/s/scholarly work of which I am a joint author. I have included as part of the thesis a written statement, endorsed by my supervisor, attesting to my contribution to the joint publication/s/scholarly work.

Thesis by publication

I hereby certify that this thesis is in the form of a series of published papers of which I am a joint author. I have included as part of the thesis a written statement from each co-author, endorsed by the Faculty Assistant Dean (Research Training), attesting to my contribution to the joint publications.

Beverley J Paterson Date

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ABSTRACT

This *Thesis by Publication* is a series of eleven scientific papers and letters published in peer reviewed, professional journals which explore how syndromic surveillance has been applied to public health practice. At the time of submission, ten papers have been published in peer reviewed journals and one has been accepted for publication.

Chapter One, 'Overview', introduces the topic of syndromic surveillance. The separate papers are placed within the context of what is known about syndromic surveillance and public health.

Chapter Two, 'Literature Review', is a peer reviewed article '**The remarkable adaptability of syndromic surveillance to meet public health needs**' that examines the literature to determine how syndromic surveillance has been used as a tool in public health practice and how it has been adapted by practitioners over time to meet changing public health information needs. This scientific publication was published in the *Journal of Epidemiology and Global Health*.

Chapter Three, 'Gathering the evidence: syndromic data utilisation', includes four published papers and scientific letters that demonstrate how syndromic data sources can inform public health responses or provide additional information to help characterise a particular disease. The peer reviewed article '**Historical data and modern methods reveal insights in measles epidemiology: a retrospective closed cohort study'** was published in the journal *BMJ Open*. The scientific letter '**Influenza: H1N1 goes to school'** was published in in the journal *Science.* The scientific letter '**Use of workplace absenteeism surveillance data for outbreak detection**' was published in the journal *Emerging Infectious Diseases*. The peer reviewed article '**Changes in the severity of 2009 pandemic A/H1N1 influenza in England: a Bayesian evidence synthesis'** was published in the *British Medical Journal.*

Chapter Four, 'Implementing and evaluating the evidence: syndromic surveillance in practice', is a series of three published papers and scientific letters that establish the value and effectiveness of developing a syndromic surveillance system for a specific purpose. The peer reviewed article '**Pacific-wide simplified syndromic surveillance for early warning of outbreaks**' was published in the journal *Global Public Health.* The peer reviewed article '**Sustaining surveillance: evaluating syndromic surveillance in the Pacific'** was published in *Global Public Health.* The scientific letter '**Pandemic response in low-resource settings**

requires effective syndromic surveillance' was published in the journal *Influenza and other respiratory viruses*.

Chapter Five, 'Presenting the evidence: changing public health policy', includes two published papers and one published scientific letter which illustrate how syndromic surveillance can be used to inform public health policy. The peer reviewed article '**A review of the epidemiology and surveillance of viral zoonotic encephalitis and the impact on human health in Australia'** has been published in the journal *New South Wales Public Health Bulletin*. The peer reviewed article '**Review of Australia's polio surveillance'** has been accepted for publication in the journal *Communicable Disease Intelligence*. The scientific letter, '**Guillain-Barré Syndrome**' has been published in the *New England Journal of Medicine.*

The final chapter, 'Discussion and Conclusions', summarises the overall findings from the thesis, discusses public health outcomes resulting from the thesis, identifies gaps in the literature and limitations of the research, and discusses further areas for research.

As demonstrated throughout the thesis, syndromic surveillance is a broad term covering multiple divergent approaches to surveillance. This flexibility appears to be its strength, making it useful to address a range of public health needs.

LIST OF CITATIONS FOR PAPERS INCLUDED IN THIS THESIS

1. **Paterson BJ**, Durrheim DN: The remarkable adaptability of syndromic surveillance to meet public health needs. *Journal of Epidemiology and Global Health* 2013, 3(1):41-47
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8. **Paterson BJ,** Durrheim DN, Hardie K. Pandemic response in low-resource settings requires effective syndromic surveillance. *Influenza and other respiratory viruses* 2013, doi 10.1111/irv.12098.
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Paterson BJ, Kirk MD, Cameron AS, D'Este C, Durrheim DN: **Historical data and modern methods reveal insights in measles epidemiology: a retrospective closed cohort study**. *BMJ Open* 2013, **3**(1).

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Paterson B, Durrheim DN, Tuyl F: **Influenza: H1N1 goes to school**. *Science* 2009, **325**(5944):1071-1072.

Paterson B, Caddis R, Durrheim D: **Use of workplace absenteeism surveillance data for outbreak detection**. *Emerging Infectious Diseases* 2011, **17**(10):1963-1964.

Paterson BJ, Durrheim DN: **Guillain-Barre syndrome**. *New England Journal of Medicine* 2012, **367**(10):973.

Paterson BJ, Durrheim DN: **The remarkable adaptability of syndromic surveillance to meet public health needs**. *Journal of Epidemiology and Global Health* 2013, 3(1):41-47

Paterson BJ, Durrheim DN, Hardie K. **Pandemic response in low-resource settings requires effective syndromic surveillance.** *Influenza and other respiratory viruses* 2013, doi 10.1111/irv.12098.

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GLOSSARY OF TERMS AND ABBREVIATIONS

ABLV	Australian Bat Lyssavirus
AHPC	Australian Health Protection Committee
AFP	Acute Flaccid Paralysis
APSU	Australian Paediatric Surveillance Unit
AQIS	Australian Quarantine and Inspection Service
Bayesian	A method of statistical inference that begins with the state of knowledge, i.e., the facts, prior to an exposure or an intervention, and augments this with study data to yield the state of knowledge posterior to the study [1]
Case Fatality Rate	The number of deaths due to a specific disease as compared with the total number of cases of the disease [2]
CDNA	Communicable Disease Network of Australia
DAFF	Department of Agriculture, Fisheries and Forestry
DoHA	Department of Health and Ageing
ERLNA	Enterovirus Reference Laboratory Network of Australia
GBS	Guillain–Barré Syndrome
HeV	Hendra virus
IHR	International Health Regulations
ILI	Influenza-like-illness
IPV	Inactivated Poliomyelitis Vaccine
JEV	Japanese encephalitis virus
LDC	Least developed countries
MVEV	Murray Valley encephalitis virus
NCC	National Certification Committee
NERL	National Enterovirus Reference Laboratory
NPRL	National Polio Reference Laboratory
NOCS	Queensland Notifiable Conditions System
Outbreak	An epidemic limited to localized increase in the incidence of disease [1]
PAEDS	Paediatric Active Enhanced Disease Surveillance

Pandemic	An epidemic occurring worldwide, or over a very wide area, crossing international boundaries, and usually affecting a large number of people [1]
PEP	Polio Expert Panel
PICTs	Pacific Island Countries and Territories
Public health	Health of the whole population or community
OPV	Oral Poliomyelitis Vaccine
R	Effective reproduction number – average number of secondary infectious persons resulting from one infectious person in a given population in which some individuals may already be immune because of infection or vaccination [3]
R_0	Basic reproduction number – the average number of secondary infectious persons resulting from one infectious person following their introduction into a totally susceptible population [3]
SARS	Severe Acute Respiratory Syndrome
Sensitivity	The proportion of cases of a disease detected by the surveillance system or the ability of the system to detect outbreaks, including the ability to monitor changes in the number of cases over time [2]
Sensitivity analysis	A method to determine the robustness of an assessment by examining the extent to which results are affected by changes in methods, values of variable, or assumptions [1]
Serial interval	Time interval between successive infections in a chain of transmission [3]
SPC	Secretariat of the Pacific Community
SSBA	Security Sensitive Biological Agents
Surveillance	The ongoing, systematic collection, collation, analysis of data and the timely dissemination of those who need to know so that action can be taken [1]
Syndrome	A symptom complex in which the symptoms and/or signs coexist more frequently than would be expected by chance [1]

Syndromic surveillance	Surveillance system using a case definition based on symptoms or indicators, not requiring laboratory confirmation, which provides data for public health purposes
TGA	Therapeutic Goods Administration
Timeliness	Reflects the speed between the steps in a public health surveillance system [4]
Triangulation	The use of a variety of data in a study to validate the findings [5]
VAPP	Vaccine-Associated Paralytic Poliomyelitis
VIDRL	Victorian Infectious Diseases Reference Laboratory
WNV	West Nile virus
WHA	World Health Assembly
WHO	World Health Organization

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CHAPTER ONE: OVERVIEW

This *Thesis by Publication* is a series of eleven papers and scientific letters published in peer reviewed, professional journals which explore how syndromic surveillance has been applied to public health practice. The published research includes: interrogation of case definitions, syndromes, surveillance systems, implementation, data sources, data collection, different surveillance approaches and analyses, and system evaluation; with a particular focus on the application of syndromic surveillance to public health. Each paper includes reference to one or more of these generic aspects. Some papers address syndromic surveillance specific to priority public health diseases (such as measles and polio) or encephalitis, while other papers focus on specific public health requirements; particularly the detection of outbreaks or emergent diseases and the particular surveillance requirements during a pandemic.

The research objectives of the thesis are to determine:

- The roots, evolution and contemporary application of syndromic surveillance.
- The breadth, value and limitations of syndromic surveillance as applied to public health.
- The adequacy of current evaluation frameworks for evaluating syndromic surveillance.

DEFINING SYNDROMIC SURVEILLANCE

Last (2001) defines a syndrome as "A symptom complex in which the symptoms and/or signs coexist more frequently than would be expected by chance on the assumption of independence" [1]. He defines surveillance as the "systematic ongoing collection, collation, and analysis of data and the timely dissemination of information to those who need to know so that action can be taken" [1]. In surveillance terms, 'syndromic' relates to a specific set of symptoms not requiring laboratory confirmation for diagnosis, such as influenza-like-illness (ILI), or not able to be specifically tested by laboratory analysis. It can also refer to indicators, such as work-place absenteeism, that provide trends which can be monitored over time, even in near real-time. There are also systems, known by other terms, which could reasonably be classified as syndromic surveillance. Henning (2004) noted that the following terms have all been used: early warning system, prodrome surveillance, outbreak detection system, information system-based sentinel surveillance, biosurveillance system, health indicator surveillance and symptom-based surveillance [2]. Biosurveillance commonly refers to surveillance that looks for biological threats or risks, by "detecting aberrations in normal illness patterns" [3].

For the purpose of this thesis, syndromic surveillance refers to any surveillance system using a case definition based on symptoms or indicators, not requiring laboratory confirmation, which provides data for public health purposes.

Syndromic surveillance uses a spectrum of approaches ranging from fully automated systems applying sophisticated statistical algorithms, to simple manual systems where a select number of syndromes are noted in a patient log, tallied at the end of the week and responded to in a defined manner. Common examples of syndromes used for syndromic surveillance include 'acute flaccid paralysis' [4-9], a syndrome potentially indicative of poliomyelitis, or 'acute fever and rash' [8-10], a syndrome potentially indicative of measles. Other syndromes that have been utilised in public health, include diarrhoea [11-15], food-borne illness [16-20], gastroenteritis [21, 22], prolonged fever [9], dengue-like-illness [23, 24] and, probably the most common, ILI [9, 25-39].

SYNDROMIC DATA

Syndromic data can be collected in a variety of settings including sentinel general practices [40, 41], hospital emergency departments [32, 42], community health centres [43], and through web-based surveys [39, 44]. Syndromic surveillance may also include the collection of data through the use of non-specific indices which act as proxy measures for particular diseases [45]. Epidemiological indices include pharmaceutical sales [46, 47], school and workplace absenteeism [46, 48], call centre activity [49], visits to emergency departments [50-53], poisons centre calls [54], distribution of antivirals [55], ambulance dispatches [56-58], and free text emergency department (ED) chief complaints [47, 59]. In recent years, search volume data from internet-based search engines have also being used for syndromic surveillance purposes, most commonly to monitor ILI [25, 60-62]. Syndromic surveillance data may provide an early signal of an unusual disease pattern when compared to background activity.

Analysis of syndromic surveillance data is complex and uses a wide range of statistical methodologies to identify outbreaks; geographic, temporal or spatial clusters; exceedance of thresholds; spread of disease and seasonal patterns [63-67]. While the analysis depends on the surveillance system, four types of analysis are generally conducted – descriptive analysis (focussing on observed patterns of disease); inferential analysis (inferring patterns, predicates and outcomes of disease); aberration detection (real-time identification of clusters in space or time); and demographic analysis (to understand what is happening at the population level)[68]. A continuing challenge when analysing syndromic surveillance data is the difficulty in determining the denominator [63].

SYNDROMIC SURVEILLANCE AND INFECTIOUS DISEASE THREATS

Recent infectious disease threats, including severe acute respiratory syndrome (SARS), avian influenza (H5N1) and the influenza A(H1N1) pandemic of 2009 (pdm09) have all contributed to the recognition that countries need to be able to monitor the spread of infectious diseases within the region and across the globe. The advent of SARS in 2003 focused the world's attention on emerging infectious diseases [69] and the potential for an emerging infectious disease to cause "significant social and economic disruption" [70]. SARS was the first infectious disease event in modern times that illustrated how rapidly a deadly disease could spread across the globe and the subsequent cost to infected individuals and affected countries' economies [71]. Following SARS, the emergence of avian influenza (H5N1) led to the establishment of a global influenza surveillance programme based on syndromic surveillance for ILI [72]. The review of the International Health Regulations (IHR) in 2005 obligated countries to ensure that the IHR core capacity requirements for "surveillance, reporting, notification, verification, response and collaboration activities" [73] were in place. This encouraged establishment of a public health surveillance continuum from data collection to response in all countries.

An assessment of the real or potential threat of an emerging infectious disease, through surveillance, is required for several purposes including: understanding the impact of the disease at the individual and population levels; assisting in determining appropriate public health responses; assessing the effectiveness of interventions; and understanding the specific epidemiology of the disease. In response to the threat of emerging infectious disease, surveillance systems are required to: rapidly detect the condition; characterise the disease in terms of time, person and place; and assess the transmissibility and severity of the disease. Ideally, systems must be sensitive enough to detect an emerging infectious disease or unusual event but specific enough so that signals are not generated when an unusual event is not occurring. As the timing of emergence is unpredictable, ongoing surveillance is a core tool for detecting and understanding emerging infectious diseases [74]. Control of emerging infectious disease requires timely and responsive disease surveillance systems appropriate for both animal and human populations [75].

EVALUATING SYNDROMIC SURVEILLANCE SYSTEMS

Critical evaluations of public health surveillance systems ensure that they are working effectively and meeting their stated purpose and objectives. Such evaluations should generate recommendations to improve the surveillance system [76]. In syndromic surveillance, evaluation is generally used to assess the attributes of the system - simplicity, flexibility, acceptability, sensitivity, predictive value positive, representativeness, and timeliness [63], or to assess whether the syndrome is a useful tool to track a particular disease. A number of frameworks and guidelines have been developed as tools for syndromic surveillance evaluation. The key frameworks most commonly utilised are the Centers for Disease Control and Prevention (CDC) 2004 *Framework for evaluating public health surveillance systems for early detection of outbreaks* [77] and the World Health Organization (WHO) 2006 *Communicable disease surveillance and response systems: guide for monitoring and evaluating* [78].

Most syndromic surveillance evaluations have examined technical aspects or attributes of the system [79] with timeliness being the key assessed attribute [31-33, 38, 50, 77, 80-86]. While timeliness is extremely important for an early alert system, the balance between sensitivity and specificity is equally important. The specificity of a system refers to whether a null alert means that there is no disease. A system with high specificity will generate few false alerts, whereas a system with low specificity will generate many false alerts or 'noise'. If the generation of false alarms requires a resource intensive response then the system needs to have higher levels of specificity [87]. The potential for the generation of 'noise' due to low specificity is a limitation inherent to a syndromic surveillance system. It is equally important to ensure that if no alert is occurring that there are no outbreaks of disease [77].

If outbreaks of particular syndromes have potentially catastrophic consequences, for example threaten a global eradication programme or herald an infection with high transmissibility and case fatality, then measures will need to be introduced to increase sensitivity [87]. Because of these limitations, it is useful for syndromic surveillance systems to be implemented in conjunction with laboratory confirmation as the next step of the surveillance continuum. Laboratory confirmation can be used to determine if the detected syndrome is confirmed as the disease of interest and, hence, if a public health response is required.

Syndromic surveillance systems are potentially more sensitive and timely than traditional surveillance systems [88, 89] but have lower levels of specificity and positive predictive value [90]. Sensitivity and timeliness represent the likelihood that epidemics are detected at the

earliest possible stages [69] and positive predictive value the likelihood that a statistical alert signals an outbreak or a problem of public health importance [69]. Measurement of the sensitivity of a syndromic surveillance system can present difficulties as it "requires an alternative data source of high quality" [77], for "gold standard" comparison purposes, which can be very difficult – particularly in resource poor settings.

The CDC evaluation framework (2004) highlights the importance of data quality, which includes validity, representativeness and data completeness [77] – all important considerations for syndromic surveillance systems which may function with limited access to clinical or demographic data.

SYNDROMIC SURVEILLANCE AND PUBLIC HEALTH

Syndromic surveillance may serve a wide range of purposes applied to public health including: early detection of threats and hazards and a timelier public health response, particularly to bioterrorism events [3, 91-93]; identifying changes in the severity of a particular disease [39, 94-97]; identifying emergent infectious diseases [51, 98, 99]; detecting geographical clusters of infectious disease [33, 96, 100, 101]; developing a baseline or thresholds against which the statistical probability of excursions can be monitored [9, 25, 96]; and demonstrating the effectiveness of interventions [43]. Syndromic surveillance has also been used to monitor public health during, or following, natural disasters such as the Icelandic ash cloud [32], extreme storm events [102], mass gatherings [51, 54, 103], heat waves [104] or pandemics [50, 94, 105-108].

As syndromic surveillance is based on clinical syndromes rather than laboratory confirmation, it is also useful in settings where: there is limited timely access to laboratories, including many developing countries [8]; laboratory diagnoses are not available, including in the early stages of an emergent disease; or laboratories are overwhelmed with testing, as occurred during the 2009 influenza pandemic [109]. In situations where laboratory confirmation is readily available, the emphasis for syndromic surveillance is on the rapid early detection or suspicion of disease, followed by timely laboratory confirmation and public health response.

The following section describes the content of each of the Chapters, including published articles.

Chapter Two: Literature Review

Chapter Two addresses the first research objective of determining what has previously been published on the roots, evolution and contemporary application of syndromic surveillance, and the second research on the breadth, value and limitations of syndromic surveillance as applied to public health. Within this context, the chapter examines how public health practitioners have used syndromic surveillance to address a wide variety of health information needs. The scientific publication '**The remarkable adaptability of syndromic surveillance to meet public health needs**' [110] explores the value of syndromic surveillance as a tool for public health. The aim of this paper is to trace the development of syndromic surveillance over time and the different ways in which it has been applied to address public health needs. This peer reviewed article was published in the *Journal of Epidemiology and Global Health*.

Chapter Three: Gathering the evidence: syndromic surveillance data utilisation

Chapter Three partially addresses the second research objective to determine the breadth, value and limitations of syndromic surveillance as applied to public health. Within this context, the chapter has a particular focus on the application of syndromic surveillance in identifying the real or potential threat of an emerging infectious disease. The chapter explores how syndromic surveillance data have been collected and utilised over time and in very different contexts to address public health issues.

The scientific publication '**Historical data and modern methods reveal insights in measles epidemiology: a retrospective closed cohort study'** [111], is an historical analysis of syndromic measles data from the nineteenth century which addresses why measles arrived much later in Australia than most other infectious diseases. These same data were also used to provide new insights into the serial interval and reproductive number for measles, both of which are key parameters used in infectious disease modelling. This peer reviewed article was published in the journal *BMJ Open*.

The second area explored in this chapter is the use of syndromic and other surveillance data, collected during the 2009 influenza pandemic, to improve our understanding of the severity of the influenza pandemic. It also focuses on the development of new syndromic surveillance tools during a pandemic.

The scientific letter '**Influenza: H1N1 goes to school'** [112], published in *Science,* uses syndromic data from a school-based setting to calculate the effective reproduction number (*R*) of the novel influenza virus during the 2009 influenza pandemic.

The scientific letter '**Use of workplace absenteeism surveillance data for outbreak detection'** [48] establishes the value of syndromic work-place absenteeism data for surveillance during the 2009 influenza pandemic. This scientific letter was published in the journal *Emerging Infectious Diseases*.

The scientific publication '**Changes in the severity of 2009 pandemic A/H1N1 influenza in England: a Bayesian evidence synthesis'** [97] published in the journal *British Medical Journal,* retrospectively examined the severity of the 2009 influenza pandemic during the first and second waves of activity experienced by England in 2009-10.

These very different contexts, within which syndromic surveillance data have been used as evidence to support public health policy, demonstrate the breadth and value of syndromic surveillance.

Chapter Four: Implementing and evaluating the evidence: syndromic surveillance in practice

The fourth Chapter partially addresses the second research objective to determine the breadth, value and limitations of syndromic surveillance as applied to public health. Within this context, the chapter has a particular focus on the application of syndromic surveillance in identifying the real or potential threat of an emerging infectious disease, particularly in developing regions. It also examines the research objective of determining the adequacy of current evaluation frameworks for evaluating syndromic surveillance. The chapter focuses on the implementation and evaluation of a syndromic surveillance system in the South Pacific. The 2005 IHR revision required all countries to develop certain minimum core public health capacities, including the ability to detect and respond to communicable disease outbreaks, and the rapid reporting of outbreaks of international concern to the WHO [73]. In developing countries, where there are often long delays in laboratory confirmation, the implementation of simple syndromic surveillance systems may provide the opportunity to facilitate rapid, early warning and response capacity. The scientific publication '**Pacific-wide simplified syndromic surveillance for early warning of outbreaks**' [113], published in the journal *Global Public Health,* documents the reasoning behind the implementation of a simple yet sustainable syndromic surveillance system across all Pacific Island Countries and Territories (PICTs).

The scientific publication '**Sustaining surveillance: evaluating syndromic surveillance in the Pacific'** [114], published in *Global Public Health,* describes the findings from an in-country qualitative and quantitative evaluation conducted in five PICTs to identify strengths and

weaknesses of the syndromic surveillance system, determine ease of use, and make recommendations to improve the system.

The scientific letter '**Pandemic response in low-resource settings requires effective syndromic surveillance'** [115] further emphasizes the value of syndromic surveillance to pandemic planning in a developing setting. This scientific letter was published in *Influenza and other respiratory viruses*.

CHAPTER FIVE: PRESENTING THE EVIDENCE: CHANGING PUBLIC HEALTH POLICY

Chapter Five partially addresses the second research objective to determine the breadth, value and limitations of syndromic surveillance as applied to public health. Within this context, the chapter has a particular focus on the application of syndromic surveillance in identifying the real or potential threat of an emerging infectious disease or a disease on the verge of eradication. It also examines the research objective of determining the adequacy of current evaluation frameworks for evaluating syndromic surveillance. The chapter explores how syndromic surveillance can be used as an approach to address an identified public health issue. It also investigates how the evidence collected through a review of a syndromic surveillance system can be used to modify public health policy. The first scientific publication in this Chapter, '**A review of the epidemiology and surveillance of viral zoonotic encephalitis and the impact on human health in Australia'** [116], considers the impact on public health from the emergence in Australia of a number of highly pathogenic zoonotic viruses, including Hendra virus (HeV) and Australian Bat Lyssavirus (ABLV). Both of these pathogens present with an encephalitis syndrome in humans. This peer reviewed article has been published in the journal *New South Wales Public Health Bulletin*.

Polio eradication is an important international public health initiative, with substantial resources and investment at the global level and resulting opportunity costs. The scientific paper, '**Review of Australia's polio surveillance'**, accepted for publication in the journal *Communicable Disease Intelligence*, documents a 2012 review of current Australian polio surveillance activities. This review considers whether the current complementary strategies in Australia are the optimal surveillance system for a high income country, with sophisticated medical and laboratory infrastructure, and a long history of freedom from endemic polio circulation.

The scientific letter, '**Guillain- Barré Syndrome**' [117], published in the *New England Journal of Medicine,* emphasizes the important role of Guillain-Barré Syndrome (GBS) in surveillance for polio eradication.

Chapter Six: Discussion and conclusions

The concluding Chapter explores how syndromic surveillance has been applied to public health practice. It addresses the research objectives, identifies research limitations, gaps in the literature and makes recommendations for future research.

As demonstrated throughout the thesis, syndromic surveillance is a broad term covering multiple divergent approaches to surveillance. This flexibility appears to be its strength, making it useful to address a range of public health needs.

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CHAPTER TWO:
LITERATURE REVIEW

Syndromic surveillance and public health

This chapter examines the literature to address the following research objectives:

- To determine the roots, evolution and contemporary application of syndromic surveillance.
- To determine the breadth, value and limitations of syndromic surveillance as applied to public health.

Syndromic surveillance has played an increasingly important role in public health. The goal of syndromic surveillance is the earlier detection of epidemics and a timelier public health response than would be possible using traditional surveillance methods [2-4]. Syndromic surveillance has often been implemented as part of a broader surveillance strategy used to detect outbreaks of disease earlier than traditional surveillance sources [1]. While the main purpose of syndromic surveillance is generally to detect and respond to infectious disease outbreaks in a timely manner it also serves a number of additional purposes including: detection of threats and hazards, particularly bioterrorism [5-8]; identification of changes in severity of a particular disease [9-13]; characterisation of emerging infectious diseases [14-16]; identification of geographical clusters [17-20]; identification of historical trends; identification of risk groups for particular syndromes; detection of the start and end of a season, particularly for influenza; and assessment of the effectiveness and progress of interventions [21]. The application of syndromic surveillance methodologies has changed over time, with public health professionals adapting the methods to meet changing public health information requirements.

The scientific publication '**The remarkable adaptability of syndromic surveillance to meet public health needs**' [22] describes trends in the development of syndromic surveillance and the different ways in which it has been applied to address public health needs. These trends are identified from the literature, with Tag Clouds used to visually demonstrate the dynamic evolution of syndromic surveillance. The paper also discusses the wide variation in syndromic surveillance definitions and approaches. It highlights how this flexibility has made syndromic surveillance a valuable tool for public health epidemiology.

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Published articles included in this Chapter:

1. Paterson BJ, Durrheim DN. The remarkable adaptability of syndromic surveillance to meet public health needs. Journal of Epidemiology and Global Health 2013;3(1):41-47.

PAPER ONE: THE REMARKABLE ADAPTABILITY OF SYNDROMIC SURVEILLANCE TO MEET PUBLIC HEALTH NEEDS.

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The remarkable adaptability of syndromic surveillance to meet public health needs

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Abstract The goal of syndromic surveillance is the earlier detection of epidemics, allowing a timelier public health response than is possible using traditional surveillance methods. Syndromic surveillance application for public health purposes has changed over time and reflects a dynamic evolution from the collection, interpretation of data with dissemination of data to those who need to act, to a more holistic approach that incorporates response as a core component of the surveillance system. Recent infectious disease threats, such as severe acute respiratory syndrome (SARS), avian influenza (H5N1) and pandemic influenza (H1N1), have all highlighted the need for countries to be rapidly aware of the spread of infectious diseases within a region and across the globe. The International Health Regulations (IHR) obligation to report public health emergencies of international concern has raised the importance of early outbreak detection and response. The emphasis in syndromic surveillance is changing from automated, early alert and detection, to situational awareness and response. Published literature on syndromic surveillance reflects the changing nature of public health threats and responses. Syndromic surveillance has demonstrated a remarkable ability to adapt to rapidly shifting public health needs. This adaptability makes it a highly relevant public health tool.
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1. Introduction

Syndromic surveillance provides an indication of disease patterns, a method for detecting aberrations in health data, or a signal that an event of public health concern is occurring. Syndromic surveillance systems have been implemented since the 1990s, initially with a focus on bioterrorism event detection.

Last (2001) [1] defines a syndrome as: "A symptom complex in which the symptoms and/or signs coexist more frequently than would be expected

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by chance on the assumption of independence.'' In surveillance terms, 'syndromic' relates to a specific set of symptoms not requiring laboratory confirmation for diagnosis. Common examples of syndromes used for syndromic surveillance include: acute flaccid paralysis (AFP), a syndrome potentially indicative of poliomyelitis; influenza-like-illness (ILI); or acute fever and rash, a syndrome potentially indicative of measles.

Syndromic surveillance captures a spectrum of approaches ranging from fully automated systems, using sophisticated statistical algorithms, to simple manual systems. It includes very specific case definitions for syndromes such as AFP to the generic counting of over-the-counter medications for coughs and colds. As it is based on clinical syndromes rather than laboratory confirmation, it is also potentially useful in settings where there is limited timely access to laboratories, including many developing countries [2]. As an approach, syndromic surveillance incorporates elements of data collection and analysis of specific syndromes or indicators (to detect disease), verification (that disease actually exists), information sharing (to those who need to know in order to respond), feedback to those who collected the data (to confirm that an action is occurring), and, in many recent cases, response and control measures to mitigate global health security threats.

Recent infectious disease threats such as SARS, avian influenza (H5N1) and pandemic influenza (H1N1) have highlighted the need for governments and public health agencies to rapidly learn of potential infectious disease threats to facilitate timely and appropriate public health responses. The requirement for improved early warning and response systems may be 'reshaping' global health surveillance [3]. The published literature on syndromic surveillance reflects the changing nature of these threats and responses. Over time, syndromic surveillance has been applied to a remarkable range of public health issues using a wide variety of data sources. Not only has it been used to collect data on particular disease syndromes, but it has also been used to monitor the public's health following, or during, natural disasters, such as the Icelandic ash cloud, mass gatherings, heat waves, floods or pandemics.

This paper documents the evolution of syndromic surveillance from bioterrorist detection systems to those implemented for outbreak detection and response. By characterising the changing approaches used in syndromic surveillance, and the drivers for this change, it demonstrates the encouraging adaptability of syndromic surveillance and the important role it plays in public health.

2. Methodology

An analysis of published articles on syndromic surveillance was undertaken in published English-language literature to examine the evolution of syndromic surveillance. MEDLINE, EMBASE, Scopus and Web of Science databases were searched using the term ''syndromic surveillance'' for English language studies published prior to February 2012. After removing duplicates and non-English language articles, 415 records were obtained. Citations were downloaded into Endnote X4. Reference lists were then hand searched to obtain further relevant additional published articles and a total of 769 articles were thus included in the study.

To identify trends in the publication of syndromic surveillance articles, PubMed was searched for all articles with the term 'syndromic surveillance' in the title or abstract, as published in PubMed prior to 20 February, 2012; 214 articles were obtained and were downloaded into Endnote X4. This database was then searched to identify publication year for each article and the number of articles published each year. The database was further searched using the terms 'bioterrorism' and 'influenza' to identify articles published each year on these topics. Keywords assigned to these articles were extracted for the periods 2001–2004, 2005–2008, and 2009–2011, based on visual changes in the data, and these were imported into NVivo 9. Each of these time-periods was queried and a tag cloud created. Tag clouds represent by size the frequency of a particular word in a document, or in this case the frequency of keywords used in syndromic surveillance publications. The tag cloud used a Word search for the 100 most frequent words with the following characteristics: a minimum length of six characters; matching set to include stemmed words; and used the following Stop words – epidemiology, methods, statistics, and numerical – to reduce visual confusion in the tag cloud results.

3. Results and discussion

In this study, published literature was examined to assess the evolving usage of syndromic surveillance for public health purposes.

While generally acknowledged as a simplified view of the many approaches used in syndromic surveillance, predominantly two different approaches were commonly reported in the literature. The first is based on networked systems and encompasses the timely, automated extraction,

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using syndromic algorithms from an individual or multiple data sources, with alerts generated when there is an exceedance of a baseline threshold using statistical methods. The emphasis in this approach is on the timely, automated collection of data; the application of a syndromic algorithm to clinical or non-clinical data; the use of statistical methods to recognise that the data are exceeding a defined threshold or to monitor trends; and the generation of alerts to those who need to know so that a response can be implemented. This form of syndromic surveillance is traditionally associated with systems designed to rapidly detect bioterrorism events. An example is the Essence (Electronic Surveillance System for the Early Notification of Community-Based Epidemics), a biosurveillance system used in the United States which uses aberration detection algorithms of syndrome groups, extracted from ICD-9 classification groups, to detect whether the observed count is above or below the expected count [4].

The second approach involved the regular, timely reporting of syndromic activity, based on agreed case definitions, at sentinel sites; detection of outbreaks, either based on an exceedance of historical data, or the reporting of syndromic cases in excess of the number clinicians would usually expect (which may include the reporting of unusual medical events); proportionate investigation and response; and regular feedback to concerned parties. The emphasis here was on both detection and response, with low technological requirements making it suitable for use in developing regions. An example of this is the syndromic surveillance system established in the Pacific Island Countries and Territories (PICT) [5].

3.1. Early application of syndromic surveillance in public health

The different approaches reflect the flexibility of syndromic surveillance to adapt to changing public health requirements and, while not truly linear in time, noticeable trends or themes are apparent in the literature. An exploration of the literature revealed that while public health surveillance was being discussed and implemented from the early 1960s, based on the visionary work of Langmuir [6] and Raska [7], with many of the principles developed then still applicable, the term syndromic surveillance only regularly entered peer-reviewed literature at the beginning of the twentieth century.

In the 1980s, the goal of global eradication of polio resulted in acute flaccid paralysis (AFP) surveillance being implemented globally as the key surveillance measure for the eradication of polio [8]. T. Jacob John also established a novel, district-level disease surveillance system in Southern India [9], which sought to control and limit disease outbreaks through early detection (described by a standardised set of symptoms); regular reporting and response; and would be termed a syndromic surveillance system if implemented today. This model included elements of data collection, analysis, confirmation, feedback and response – all key elements of modern-day syndromic surveillance. This approach was later further adapted in a rural African setting with a focus on rural hospitals reporting presentations of nine core clinical syndromes, including cholera and meningitis-like disease [10].

In the 1990s, the STD and HIV literature documented the value of syndrome-based diagnosis and treatment for case management purposes [11,12]. There were also some early examples of outbreak surveillance systems based on syndromes in developed countries. Among other examples, New York City implemented a syndromic surveillance system to detect outbreaks of waterborne illness using surveillance for diarrhoeal illness, stool submissions in laboratories and over-the-counter (OTC) pharmacy sales [13]; and public health officials in England compared data collected through a call centre (NHS Direct), using an algorithm for influenza-like symptoms, to routinely available surveillance data to assess the usefulness of syndromic surveillance for influenza surveillance [14].

3.2. Syndromic surveillance application in response to the bioterrorism threat

In the literature there was an apparent surge in interest in syndromic surveillance following the terrorist events in the United States of America, the United Kingdom and Spain, as well as the 2001 anthrax outbreak [15]. The word syndromic was applied because the majority of such systems monitored syndromes which might herald the early stages of epidemics [16]. Fig. 1 presents a graphic representation of the adaptability of syndromic surveillance as public health requirements for information have changed. A review of the published literature on syndromic surveillance shows the rapid growth in publications following the terrorist attacks, with the number of publications published each year peaking in 2004, after the emergence of SARS. These events appear to have accelerated the development of syndromic surveillance as a tool for the early identification of unexpected biological events [17].

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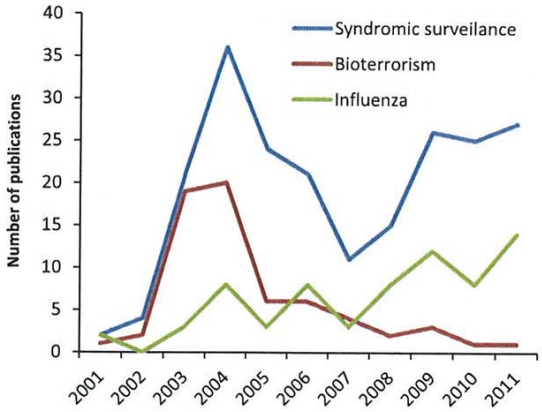

Figure 1 Trends in syndromic surveillance publications, 2001–2011.

3.3. Syndromic surveillance and emerging infectious disease threats

Fig. 1 demonstrates that from 2005 there was a decrease in the number of publications addressing bioterrorism and a shift in focus to emergent diseases and pandemics (with 'influenza' used here as a proxy indicator). A second wave of interest in syndromic surveillance is apparent from 2008 after the emergence of avian influenza and the 2009 influenza pandemic. Tag clouds, as shown in Fig. 2, highlight the predominance of bioterrorism as a keyword in syndromic surveillance publications from 2001 to 2004, and its lessening importance over time. In contrast, influenza and outbreaks increase in importance reflecting increasing public health activities in these two areas from 2005 to 2011.

Many recent emergent pathogenic infectious diseases have signalled their emergence through cases presenting with particular syndromes, such as encephalitis, influenza-like-illness (ILI) or severe acute respiratory syndrome (SARS), emphasising the importance of surveillance for syndromes as a method of detecting emergent diseases. The highly pathogenic Nipah and Hendra viruses presented as an encephalitic syndrome with a high case fatality rate [18,19]. The arrival of SARS in 2003 focused the world's attention on emerging infectious diseases (EID) [16], the potential for an EID to cause ''significant social and economic disruption,'' and the need for early identification to limit further spread [20]. SARS was the first infectious disease event in modern times that confirmed how rapidly a deadly disease could spread across the globe and the subsequent cost to infected individuals and affected countries' economies [21]. More recently, a syndromic approach first signalled a disturbing, unusual event occurring in Jordan when an apparent cluster of cases and fatalities from an unknown disease presented as a SARS with renal complications. It was only when this disease was finally identified, in a later case, as a novel coronavirus that the mystery behind the unusual cluster was solved [22]. Enhanced syndromic surveillance for further SARS presentation due to this novel coronavirus has currently been recommended at the global level by the World Health Organization [23].

The advent of SARS in 2003 led public health officials in developed economies to appreciate the potential benefits of syndromic surveillance to public health beyond bioterrorism and the possibility that it could be used to detect unusual disease clusters [24,25]. The influenza pandemic (H1N1) in 2009 also highlighted the need for surveillance systems able to provide early detection of first cases through the identification of patients with an ILI syndrome [26]. It also had value later during the pandemic; Elliott (2009) noted that when countries changed phase to 'containment', and were no longer able to laboratory confirm each case, then ''syndromic surveillance takes precedence as the primary means of estimating the community burden of pandemic influenza infections [27].'' As a result of the pandemic, and in an effort to improve public health surveillance, the CDC stated that it was ''expanding and automating syndromic surveillance [28].''

3.4. Syndromic surveillance and the International Health Regulations

The 2005 IHR revision required all countries to develop certain minimum core public health capacities, including the ability to detect and respond to communicable disease outbreaks, and the rapid reporting of public health emergencies of international concern to the World Health Organization (WHO) [29]. Included in the IHR core capacity requirements are: ''surveillance, reporting, notification, verification, response and collaboration activities [29].'' The IHR obligation to report public health emergencies of international concern have raised the importance of early outbreak detection and response.

Standardised approaches to data collection, analysis, reporting, outbreak investigation and response are necessary for a surveillance system to effectively serve as an early warning system for biological, chemical or radiological threats. Evaluations of syndromic surveillance systems are necessary to confirm that they are able to meet public health requirements and obligations by adequately

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Figure 2 Tag clouds for keywords extracted from published literature on syndromic surveillance, 2001—2011.

identifying outbreaks when they are occurring and, when an outbreak is detected, that there is an appropriate public health response [30,31].

For developing countries, where there are often long delays in laboratory confirmation, the implementation of simple syndromic surveillance systems may provide the opportunity to ensure a country's early warning and response capacity [32]. The Pacific Island Countries and Territories (PICT) have developed a syndromic surveillance system to respond to an identified need for a functional surveillance system, capable of identifying and responding to outbreaks in a systematic manner, while taking account of limited local

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resources. In 2010, all PICTs agreed to implement a syndromic surveillance system to facilitate early warning and response, to meet these IHR obligations [33]. A further refinement was the development of 'response protocols' to standardise responses to outbreaks [34,35].

An evolving purpose of syndromic surveillance is to improve real-time 'situational awareness' which follows an outbreak from detection to response. Buehler et al. (2008) describe situational awareness as ''the ability to monitor the course of outbreaks regardless of how they are detected,'' and to ''track, characterise and monitor trends [36].'' The Centers for Disease Control and Prevention (CDC) (2010) describe the use of situational awareness for surveillance purposes as ''public health professionals processing innumerable bits of data, assigning meaning, ascertaining significance, determining implications, and acting and adjusting accordingly.'' Situational awareness reflects the notion that information for incremental decision-making does not just come from a single source and that syndromic surveillance can help to make sense of the ''epidemiological puzzle [37].''

4. Conclusions

Syndromic surveillance has many applications in the public health field particularly, in recent times, for health security and the early detection of emerging health threats. Syndromic surveillance application for public health purposes has changed over time and reflects a dynamic evolution from the collection, interpretation of data, and dissemination of data to those who need to act; to a more holistic approach that incorporates response as a core component of the surveillance system.

The IHR obligation to report public health emergencies of international concern have accentuated the importance of early outbreak detection and response. Syndromic surveillance evolution has not been completely linear, but rather approaches have co-existed and evolved over time. The use of a syndromic surveillance approach to detect outbreaks and unusual patterns is not without its critics. Henning (2004) suggested cautious use of syndromic surveillance, noting that it should not replace traditional systems or the reporting by clinicians of unusual events [17]. Other challenges include the availability of resources for follow-up, movement of persons after exposure and the difficulty of detecting unusual events during seasonal increases in disease [15].

Using published literature to demonstrate the evolution of syndromic surveillance has some limitations, as the literature may not be representative of what is actually being implemented in public health programs. Publication bias and a lack of publications from the developing countries may also limit the validity of this approach.

Syndromic surveillance as applied to infectious diseases serves a wide number of purposes, including: early detection of threats and hazards, and a timelier public health response, identifying changes in severity of a particular disease, identifying emergent diseases, developing baselines or thresholds so that unusual occurrences can be detected, and demonstrating the effectiveness and progress of interventions. A number of authors have suggested that syndromic surveillance is appropriate for developing regions [32,38,39] particularly in view of the difficulties these areas have in receiving laboratory confirmations in a timely manner. The recognition that decision-making and public health responses are based on information from a range of sources has highlighted the value of syndromic surveillance to improve situational awareness.

Syndromic surveillance has demonstrated a remarkable ability to adapt to rapidly shifting public health needs and the flexibility to utilise different approaches depending on the situation. This adaptability makes it a highly relevant public health tool. Central to this is the public health requirement for credible, rapidly available surveillance information to allow informed decisions on responding to and controlling emerging threats.

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CHAPTER THREE:
GATHERING THE EVIDENCE: SYNDROMIC SURVEILLANCE DATA UTILISATION

This chapter addresses the following thesis objectives:

- To determine the breadth, value and limitations of syndromic surveillance as applied to public health.

- To determine the breadth, value and limitations of syndromic surveillance as applied to public health.

Within this context, modern mathematical methodologies are applied to historical syndromic measles data to demonstrate the breadth, value and application of syndromic data. It also assesses the value and limitations of syndromic surveillance in identifying the real or potential threat of an emerging infectious disease, and the breadth of syndromic surveillance limitations.

Historical syndromic data

While surveillance using syndromic data is considered to be a relatively new tool, historical records show that data on disease syndromes have been collected by public health officials in many countries. These data have been used to firstly identify and then address public health needs. An important example was data collected by surgeon superintendents, meticulously recorded in log books, on all medical events that occurred on voyages from England to Australia. Major outbreaks of disease on the large clippers in the middle of the nineteenth century were documented in these log books. Following these outbreaks, a number of commissions into the health of emigrants resulted in smaller numbers of passengers (although still greater than those of the early part of the nineteenth century); improvements in hygiene; less confined living areas for passengers; and improved ventilation on the ships [1].

Historical syndromic data provide the opportunity to understand the characteristics of infectious disease outbreaks from the pre-vaccination era. These characteristics provide valuable information from which assumptions or parameters can be developed for use in infectious disease modelling – information which cannot be so readily collected in the post-vaccination era. The scientific publication '**Historical data and modern methods reveal insights in measles epidemiology: a retrospective closed cohort study'** [2] used syndromic measles data, collected almost two centuries ago, to estimate basic reproduction numbers (R_0), for outbreaks on board ships to Australia, thus establishing the plausibility that changing

societal and transport factors contributed significantly to the introduction of measles to Australia.

Ships surgeons' logbooks from historic archives, 1829–1882, were retrospectively reviewed for measles outbreak data. Serial intervals, R_0, proportion immune, outbreak generations, age-distribution, within-family transmission and outbreak lengths were calculated for these closed cohorts; providing new information on parameters for measles in closed environments. The concept for this work, data collection and analysis was originally undertaken during the Masters of Applied Epidemiology at the Australian National University. Further in-depth analysis, writing and preparation of the manuscript were undertaken during this PhD. Inclusion of this scientific publication is with the permission of the Dean, Graduate Studies, University of Newcastle.

Syndromic surveillance and pandemics

In April, 2009, a novel strain of influenza (H1N1) , was identified by existing surveillance systems and notified according to the protocols of the International Health Regulations, leading to the World Health Organization's Director-General declaring a pandemic (Phase 6) on 11 June 2009. The influenza pandemic (H1N1) in 2009 highlighted the need for surveillance programmes that were able to provide early detection of initial cases, allowing a comprehensive epidemiological assessment of these early cases, and monitoring of pandemic [3].

Early in the pandemic little was known about the specific pandemic virus strain including its transmissibility, severity and risk groups. The scientific letter '**Influenza: H1N1 goes to school'** [4], published in *Science,* reports on a secondary analysis of a large cluster of ILI, using the case definition of self-reported fever and either cough or sore throat, in a school based setting in the early stages of the 2009 influenza pandemic. The syndromic ILI data were used to calculate the effective reproduction number (R) of the novel influenza virus in a school-based setting. This research provided evidence that the 2009 H1N1 virus had a transmission rate comparable to the lower R_0 estimates of the 1918 pandemic and provided public health practitioners with information on the transmissibility of the pandemic. Early epidemiologic understanding of a novel virus is a key requirement for the development of appropriate public health responses. Surveillance information must be capable of being rapidly collected, analysed and disseminated to inform public health action.

The rapidly changing information requirements of the pandemic meant that existing surveillance systems were not always sufficient for public health purposes. Monitoring the pandemic (H1N1) 2009 influenza virus was achieved by extending existing seasonal influenza surveillance systems and introducing additional surveillance systems to determine the evolving detailed epidemiology, the spectrum and severity of clinical disease, and the transmission characteristics of the infection. New data sources, including syndromic data, were examined to establish if they provided timelier, useful or more cost effective surveillance solutions. In London, absenteeism data collected by Transport for London during the 2009 influenza pandemic were compared with routinely published ILI surveillance, for comparative weeks of the year, to establish their usefulness as a new syndromic surveillance system. The data were also examined for their ability to generate alerts when compared with historical baseline data. The results from this investigation were published in a scientific letter '**Use of workplace absenteeism surveillance data for outbreak detection'** [5] in the journal *Emerging Infectious Diseases*.

The first cases of novel influenza were identified in Mexico and the United States and assumptions on how the pandemic might spread were based on this international surveillance intelligence. Surveillance from Mexico suggested that the novel virus was relatively severe; however early data from the United States was indicative of a milder virus similar to seasonal influenza. These conflicting reports lead to some uncertainty around the severity of the disease. The scientific publication **'Changes in the severity of 2009 pandemic A/H1N1 influenza in England: a Bayesian evidence synthesis'** [6] published in the *British Medical Journal,* retrospectively examined the severity of the 2009 influenza pandemic during the first and second waves of pandemic activity experienced by England in 2009-10. Case severity, defined as the probability of infection leading to severe events, included case fatality ratios, case hospitalisation ratios and case intensive care admission ratios. An important factor in ensuring the robustness of this analysis was the triangulation of data from multiple surveillance systems, including syndromic surveillance data. Syndromic data collected from ILI consultations, through either primary care or the National Pandemic Flu Service, was one of the four data sources used in the analysis.

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Published articles included in this Chapter:

2. Paterson BJ, Kirk MD, Cameron AS, D'Este C, Durrheim DN. Historical data and modern methods reveal insights in measles epidemiology: a retrospective closed cohort study. BMJ Open 2013;3(1):doi:10.1136/bmjopen-2012-002033.
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PAPER TWO: HISTORICAL DATA AND MODERN METHODS REVEAL INSIGHTS IN MEASLES EPIDEMIOLOGY: A RETROSPECTIVE CLOSED COHORT STUDY.

Paterson BJ, Kirk MD, Cameron AS, D'Este C, Durrheim DN. Historical data and modern methods reveal insights in measles epidemiology: a retrospective closed cohort study. BMJ Open 2013;3(1):doi:10.1136/bmjopen-2012-002033.

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Historical data and modern methods reveal insights in measles epidemiology: a retrospective closed cohort study

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ABSTRACT

Objectives: Measles was endemic in England during the early 1800s; however, it did not arrive in Australia until 1850 whereas other infectious diseases were known to have arrived much earlier—many with the First Fleet in 1788—leading to the question of why there was a difference.

Design: Ships surgeons' logbooks from historical archives, 1829–1882, were retrospectively reviewed for measles outbreak data. Infectious disease modelling techniques were applied to determine whether ships would reach Australia with infectious measles cases.

Setting: Historical ship surgeon logbooks of measles outbreaks occurring on journeys from Britain to Australia were examined to provide new insights into measles epidemiology.

Primary and secondary outcome measures: Serial intervals and basic reproduction numbers (R_0), immunity, outbreak generations, age-distribution, within-family transmission and outbreak lengths for measles within these closed cohorts.

Results: Five measles outbreaks were identified (163 cases). The mean serial interval (101 cases) was 12.3 days (95% CI 12.1 to 12.5). Measles R_0 (95 cases) ranged from 7.7–10.9. Immunity to measles was lowest among children ≤10 years old (range 37–42%), whereas 94–97% of adults appeared immune. Outbreaks ranged from 4–6 generations and, before 1850, were 41 and 38 days in duration. Two outbreaks after 1850 lasted longer than 70 days and one lasted 32 days.

Conclusions: Measles syndrome reporting in a ship surgeon's logs provided remarkable detail on prevaccination measles epidemiology in the closed environment of ship voyages. This study found lower measles R_0 and a shorter mean clinical serial interval than is generally reported. Archival ship surgeon log books indicate it was unlikely that measles was introduced into Australia before 1850, owing to high levels of pre-existing immunity in ship passengers, low numbers of travelling children and the journey's length from England to Australia.

ARTICLE SUMMARY

Article focus

- Previously untapped archival material, meticulously recorded by Surgeon Superintendents on-board ships travelling from Britain to Australia in the 1800s, has been used to address the question of why measles did not reach Australia until 1850, when other infectious diseases were known to have arrived much earlier—many with the First Fleet in 1788.
- The characteristics of measles, particularly risk groups, transmission mechanism, reproductive number, length of incubation and period of communicability, resulted in measles only being introduced into Australia almost a century after European settlement.
- Political and social changes around 1850 allowed the introduction of measles into Australia.

Key messages

- Measles syndrome reporting in a ship surgeon's logs provided remarkable detail on prevaccination measles epidemiology in the closed environment of ship voyages.
- This study found lower measles R_0 and a shorter mean clinical serial interval than is generally reported.
- Archival ship surgeon log books indicate it was unlikely that measles was introduced into Australia before 1850, due to high levels of pre-existing immunity in ship passengers, low numbers of travelling children and the journey's length from England to Australia.

Strengths and limitations of this study

- This study is the first to use historical surgeon superintendent logbooks to retrospectively review the 163 measles cases on five ships bound for Australia between 1829 and 1882.
- The use of historical data for epidemiological analysis presents a number of challenges and there is no way to validate information recorded by individual surgeon superintendents.
- Novel historical outbreak data were used to improve our understanding of measles epidemiology; providing new insights into serial intervals and the basic reproduction number of measles.

INTRODUCTION

Measles was endemic in England during the early 1800s but Australian government

Measles on the high seas

records suggest that measles was only introduced after 1850 despite regular shipping contact between the two countries (figure 1).[1] The early absence of measles was remarkable as diphtheria, scarlet fever and whooping cough exacted a great toll on European settlers and Aboriginal Australians in early colonial times,[1 2] following the arrival of the first fleet to Australia in 1788. It has been suggested that Australia was initially protected against measles because of its high infectivity with outbreaks possibly burning out during the voyage to Australia, which could take up to 8 months.[1–3] To prevent outbreaks on voyages, passengers were subjected to a medical examination and not allowed to travel if they were deemed to be harbouring an infectious disease.[4 5] However, with Britain's Whig Government assuming power (1846–1852) with a strong mandate for Free Trade and the introduction of a *Bill to Repeal the Navigation Acts, 1849*, British shipping lines bought faster and larger American ships to carry passengers and cargo to Australia.[6] These fast clippers were introduced on the England to Australia route around 1850, shortening the journey from approximately 180 days to less than 100 days and they carried as many as 1000 passengers.[7] The discovery of the Great Circle Route in this period—a non-stop southerly route from England to Australia—further shortened the journey time, while the Australian gold rush during the early 1850s resulted in a large influx of immigrants (370 000in 1852 alone[8]). Previous limits on the number of children allowed to immigrate to Australia—a couple could not receive assisted passage if they had more than three children under 10 years of age and two under seven, were lifted in 1852.[9]

In the 1800s, surgeon superintendents on sea voyages to Australia recorded symptoms, treatments and outcomes of individuals by age and sex in logbooks. The sentinel features of the measles syndrome (rubeola) were well standardised in medical texts by the 1800s[10] allowing differentiation from other illnesses. In 1864, Dr Aitken accurately described measles: "The eruption in crops of a crimson rash, consisting of slightly elevated minute dots, disposed in irregular circular forms, or crescents; preceded by catarrhal symptoms for about four days, and accompanied with fever. It affects the system only once; and sometimes prevails as an epidemic. The eruption lasts six or seven days, and the whole duration of the disease is completed in from nine to twelve days".[11]

Disease infectivity is expressed by its basic reproduction number (R_0). Measles has an R_0 of 12–18.[12–15] Serial intervals are commonly used to estimate R_0[16] and, for measles, this ranges from 6–29 days[17] with 14 days commonly applied.[18] Outbreaks linked to a single index case occurring in closed cohorts, such as island settings,[18] or entirely susceptible populations have provided informative epidemiological data. A small number of historical prevaccination outbreaks provided measles parameter estimates[10 19–22] but ambiguity remains over incubation periods[23] and clinical serial intervals.[17] Surviving surgeon superintendents' logbooks from long voyages provide a unique historical record of medical events, effectively providing data on outbreaks in a closed cohort with a known number of susceptibles and a fixed population. These data were used to estimate measles parameters including serial intervals and basic R_0, age distributions, immunity and length and generations of outbreaks. The likelihood of measles reaching Australia before 1850 was also investigated.

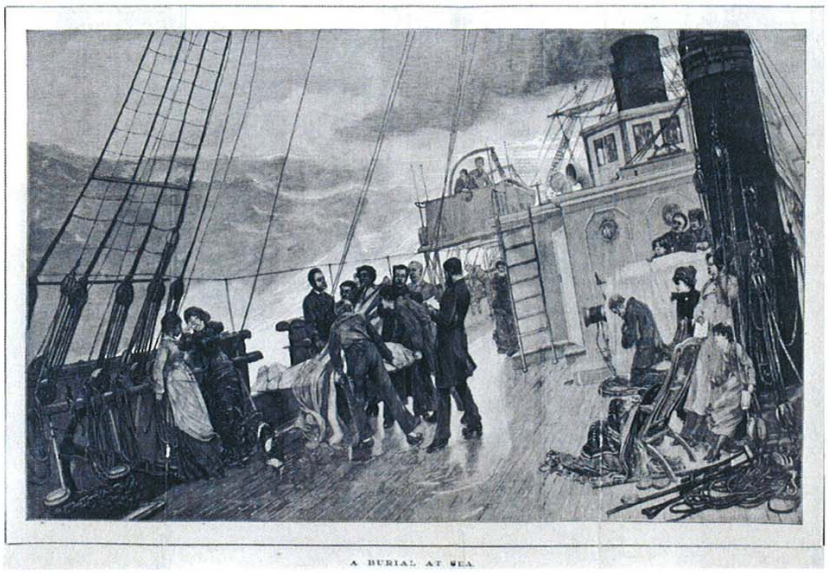

Figure 1 A burial at sea*.
*November 1880, The Illustrated Australian News. Used with permission of the State Library of Victoria, Australia.

Paterson BJ, Kirk MD, Cameron AS, *et al. BMJ Open* 2013;3:e002033. doi:10.1136/bmjopen-2012-002033

METHODS

We identified measles (rubeola) outbreaks in surgeon superintendents' logbooks for the period 1829–1882. Generally, disease cases were summarised by week of voyage, with the number and gender of passengers and crew, length of voyage and the number of children aged either less than 10 or 14 years of age. One author (BP) searched microfiche Admiralty records held under the Australian Joint Copying Project in the National Library of Australia,[24] Canberra; summaries of measles outbreaks in immigrant ships papers[25] held at the Adelaide Research Centre; and surgeons' reports[26] located at the Sydney Records Centre. References to measles outbreaks in other archival records, including other logbooks, diaries or outbreak inquiries, were also examined. The reports or log books were incomplete and represent only a small number of voyages to Australia, hence only a small subset of measles epidemics for this period have been able to be examined. Only measles outbreaks where detailed data were available were included in the analysis.

Microsoft Excel 2003, Microsoft Excel 2007 and Stata 11 were used to calculate immunity, age distribution, case death rates, serial intervals (time between the onset of measles syndrome symptoms in one generation to the onset of symptoms in the next generation, assuming that cases were assessed soon after symptom onset[17]), generations of outbreaks, length of outbreaks, immunity levels and basic R_0, separately for each cohort where a measles outbreak was identified and the required data were available.

Average serial intervals and 95% confidence levels were calculated using individual serial intervals between each generation which contained case level data. Stata 11 was used to calculate CIs. We defined a serial interval as the time between the onset of measles syndrome symptoms in one generation to the onset of symptoms in the next generation,[17] as recorded by the surgeon superintendents. It was assumed that cases were seen by the surgeon superintendent soon after onset of symptoms. Individual generations were identified by visually inspecting the data to identify separate 'waves of infection' and confirming that these were plausible by checking them to ensure that they were within the range of known measles serial intervals, which range between 6 and 29 days.[17] We assumed that passengers with the same names were members of the same family group and living in close contact. Where 'family members' were infected within one serial interval range of an infected 'family member', we assumed the family member was the source of infection and used their onset date to calculate the serial interval. Cases were assigned to a 'generation' based on these data and assumptions.

Outbreak length was considered as the time between measles clinical symptom onset in the first and last cases. Owing to measles' high infectivity and the confined ship environment, we assumed that all susceptible individuals became infected during an outbreak that is, the number of susceptibles at the beginning of the outbreak was equal to the total number of cases during the outbreak.[27]

The basic R_0 (average number of secondary cases generated by a primary case in a completely susceptible population)[12] was estimated based on the assumption that the number of susceptibles and population were known. The effective reproduction number (R) is the number of new infectious hosts in a combined population of people immune or susceptible. R is the product of R_0 times the proportion (x) of the contacts made with susceptibles: $R = R_0x$. If $R_0 = 18$ for measles and 85% of the population is immune and 15% are susceptible, then the effective reproduction number is $R=18\times0.15=2.7$. A case of measles would produce on average only 2.7 cases rather than 18 in this population. Using the *Solver* function in Excel and data from each outbreak, the basic R_0 was estimated by determining the values that maximised the likelihood of the entire outbreak (the product of the probabilities for each generation).

Using the outbreak data, and assuming random population mixing the probability of infection of susceptibles in each generation was estimated using the formula:

$$p(\text{infection}) = 1 - (1 - (R_0/P))^{ci}$$

where R_0=reproduction number, P=ship population, and ci=cases in each generation (Gay NJ. Personal Communication. London: UK Health Protection Agency, 2008). The probability of infection was the probability that a susceptible individual would become infected in each generation. The risk that a susceptible individual would become infectious between time t and t+1 was given by the Reed-Frost stochastic model formula[15]

$$\lambda_t = 1 - (1 - p)^{I_t}$$

where λ_t=the risk that a susceptible individual becomes infected in the next time interval, p= the probability that two specific individuals come into effective contact and I_t = the number of infectious individuals at timet. We assumed homogenous mixing of the ship population.

A Reed-Frost stochastic model, using the CRITBINOM and random number generation function in Excel, was used to establish the likelihood that infectious measles cases would be on a ship when it reached Australia. This model predicted the number of secondary cases in each generation and determined the likely length of each outbreak. The CRITBINOM function simulated a binomially distributed random number and introduced chance into the model.[15] Parameters used in this model were the number of index cases; number of susceptible individuals; expected basic R_0 (calculated in the previous step) and ship population. One thousand simulations of each outbreak were then run to determine the most likely number of generations of measles cases for these parameters. The simulation results were graphed as the probable distribution of outbreak generations relative to the voyage duration.

RESULTS

Twenty-nine surgeons' logbooks of emigrant voyages to Australia (1837–1847), 323 immigrant ship papers (1848–1885) and six reports by ships surgeons during immigrant voyages were identified and reviewed. In addition, 160 logbooks of convict ships from 1816–1849 were briefly examined, but as most passenger lists did not include children, they would not sustain outbreaks. Five ships with detailed measles syndrome outbreak data were identified during the period 1829–1885, with a total of 163 cases (table 1). None of these ships had ports of call after leaving the British Isles and before arriving in Australia. Four of these outbreaks occurred on emigrant ships: the 'Garrow',[28] the 'Roslin Castle',[29] the 'Trevelyan'[30] and the 'Duntrune,[31] and one on the convict ship 'America'.[32] The number of measles cases on each ship ranged from 6–52. Passenger and crew numbers ranged from 175–487, with voyages after 1850 having larger passenger numbers. The proportion of children on voyages ranged from 20–25%.

Infections by age group and sex

Surgeons' logbooks for three ships, 'America', 'Garrow' and 'Roslin Castle', were comprehensive enough to allow detailed outbreak description, with the median age of cases being 6 years (range <1–31). Epidemic curves of the outbreaks on the 'America' (figure 2), 'Garrow' (figure 3) and 'Roslin Castle' (figure 4) display distinctive clusters of measles cases. Three cases on the 'America' were children, but no information was available on the total number of children on board. Case fatality rates could only be estimated for the 'Garrow' outbreak, where 9% (4/43) of cases died.

Serial intervals and generations

Serial intervals on the 'America', 'Garrow' and 'Roslin Castle' ranged from 4–20 days, with a mean of 12.3 days (95%CI 12.1 to 12.5) (table 2). All outbreaks started with 2–3 coprimary cases rather than a single index case and lasted for 3–4 generations, with only three on the 'Roslin Castle', which had the most cases recorded (n=52). Based on the estimated outbreak length (70 +days) on the 'Trevelyan' and 'Duntrune' and estimated mean serial interval of 12.3 days, it is likely that there were five to six generations of measles infections during these outbreaks.

Immunity to infection by age group

Measles immunity estimates ranged from 81% to 97% among all passengers (table 1). On the 'Garrow' and the 'Roslin Castle', immunity was highest among adults with a range of 94–97%. In children, immunity estimates ranged from 37% (19/52) of children under 10 years of age on the 'Garrow' to 42% (31/74) of children under 14 years on the 'Roslin Castle'. Both the 'Trevelyan' and 'Duntrune' had measles cases peaking in the last week of the voyage and the 'Trevelyan' had measles cases on

Table 1 Summary of measles outbreaks on convict and emigrant ships on voyages to Australia, 1829–1882

Ship	Type	Year	Voyage	Voyage length (days)	Outbreak length (days)	Measles cases (total passengers)			Immunity (%)		
						Children	Adults	Total	Children	Adults	Total
'America'	Convict	1829	Unk	180	41	3 (Unk)	3 (Unk)	6 (175)	Unk	Unk	97
'Garrow'	Emigrant	1838	Belfast to Sydney	116	38	33 (52)*	10 (179)	43 (231)	37a	94	81
'Trevelyan'	Emigrant	1876	Plymouth to Adelaide	84	>70	Unk (77)†	Unk (269)	26 (346)	Unk	Unk	92
'Duntrune'	Emigrant	1876	Plymouth to Adelaide	84	>70	Unk (124)†	Unk (363)	36 (487)	Unk	Unk	93
'Roslin Castle'	Emigrant	1882	Plymouth to Sydney	91	32	43 (74)†	9 (289)	52 (363)	42b	97	85

Unk, unknown.
*Child defined as a person <10 years old.
†Child defined as a person <14 years old.

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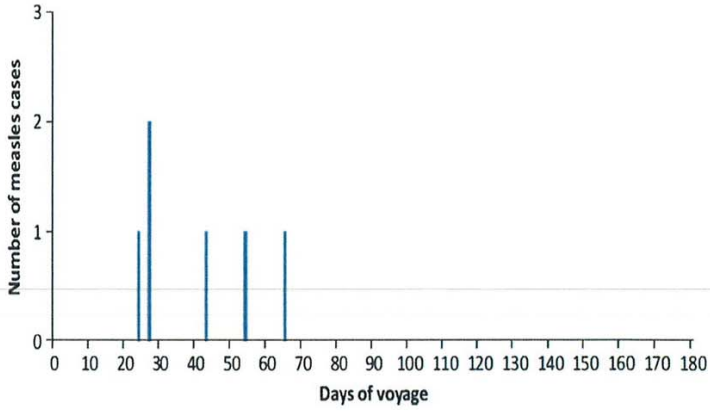

Figure 2 Measles outbreak on the ship 'America', by days of voyage, 1829.

arrival in Australia suggesting that susceptibles were not exhausted during the voyage.

Basic reproduction number

R_0 was calculated for the 'Garrow' and 'Roslin Castle' (table 2), being 8.7 and 10.9, respectively. It was not possible to estimate R_0 on the America because it is unknown whether the guard's children, accounting for half the cases, would have mixed with convicts hence not meeting our assumption of homogeneous mixing. Further, the R_0 on the 'Trevelyan' and 'Duntrune' could not be estimated.

Outbreak duration

Outbreaks before 1850 lasted for 38 and 41 days, whereas in the late 1800s one outbreak lasted 32 days, and two ('Trevelyan' and 'Duntrune') exceeded 70 days (with one likely continuing during quarantine in Australia). Voyages to Australia ranged from 84–180 days, with shorter journey times after 1850.

Stochastic measles outbreak modelling

Figures 5–7 shows the modelled, possible number of outbreak generations, following the initial introduction of measles cases, as occurred during the actual voyages, and compares these to the actual length of voyage (shaded section of figures 5–7). Figure 5 shows that following the introduction of three infectious cases into the susceptible population on the 'America' in 1829, 100% (n=1000) of probable outbreaks would be less than the journey length of 180 days. Figure 6 shows that following the introduction of three infectious cases into the susceptible population on the 'Garrow' in 1838, 92% (n=920) of probable outbreaks would be less than the journey length of 116 days. Following the introduction of two infectious cases into the susceptible population on the 'Roslin Castle' in 1882, 51.5% (n=515) of probable outbreaks would be less than the journey length of 91 days (figure 7).

DISCUSSION

Despite efforts to restrict individuals and families with infectious diseases travelling on ships from Britain to Australia in the 19th century, outbreaks of infectious

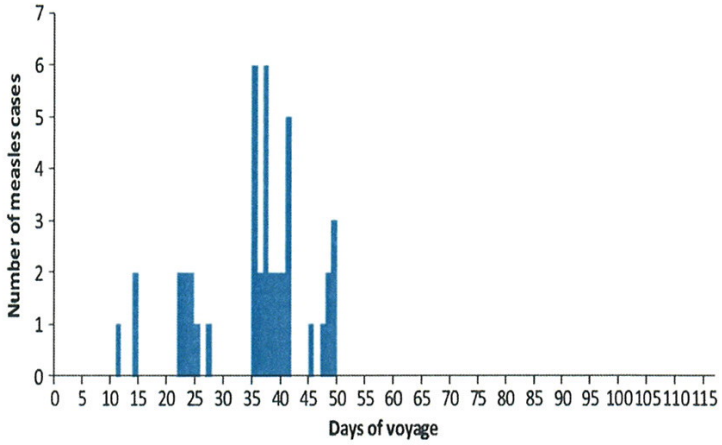

Figure 3 Measles outbreak on the ship 'Garrow', by days of voyage, 1838.

Measles on the high seas

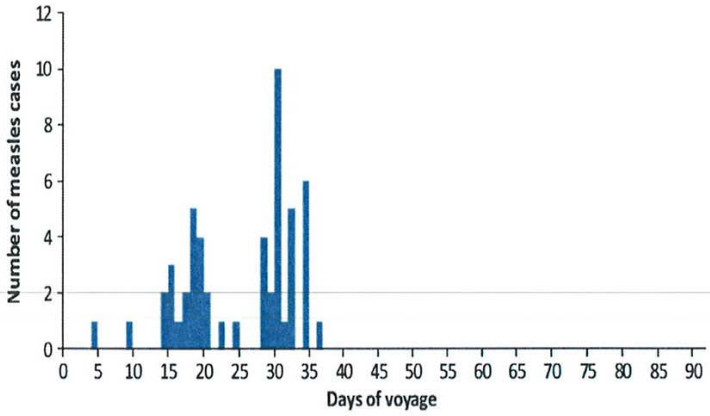

Figure 4 Measles outbreak on the ship 'Roslin Castle', by days of voyage, 1882.

diseases, including measles, occurred on some voyages. The introduction of fast clippers able to carry up to 1000 passengers coincides with the first recorded case of measles in Australia in 1850. Cumpston[1] notes extracts from the Quarantine Station in Sydney which record the increasing numbers of ships after this time who reached port with either measles cases or who had measles deaths during the quarantine period. It is likely that the briefer journey period and the greater number of passengers on board ship allowed the transmission of measles to continue throughout the journey, with some passengers continuing to be infectious on arrival in Australia. The increased numbers of child passengers following the removal of the restrictions on the number of children and the large influx of immigrants to the gold rush would also have contributed to the spread of measles.

Probability of measles reaching Australia before 1850

Cumpston[1] makes a compelling case that although measles was frequently recorded on ships before 1850, no infectious measles cases reached Australia. The possibility of an earlier epidemic in Sydney in 1834 and in Hobart in 1835 has been suggested by Donovan,[33] although there was dissension among medical practitioners at the time as to whether the disease in question was measles, scarlet fever or some other infection. Cumpston[1] notes that, from available references, there are many reports from officials documenting the lack of measles cases in the various Australian colonies. Once measles did reach Australia in 1850, the outbreaks were obvious and no longer disputed among the medical fraternity. Following its probable, initial introduction into Victoria, Australia in 1850, measles spread across the country and was recorded in New South Wales in 1853,

Table 2 Serial intervals, probability of infection, R_0 and R for measles infections on the ships 'America', 'Garrow' and 'Roslin Castle' travelling from England to Australia, 1838–1882

		Serial interval					
Ship	Generation	Days into voyage	Measles cases	Mean (95% CI)	Probability of infection	Basic reproductive number (R0) (outbreak)	Effective reproductive number (R) (outbreak)
America*	1	24–27	3		0.34	–	–
	2	43	1	17 (12.7 to 21.3)	0.13	–	–
	3	54	1	11	0.13	–	–
	4	65	1	11	0.13	–	–
Garrow	1	11–14	3	–	0.22	7.1	1.3
	2	22–28	8	12 (11.2 to 13.1)	0.22	–	–
	3	35–41	25	13 (12.7 to 13.5)	0.54	–	–
	4	45–49	27	10 (9.3–10.0)	0.2	–	–
Roslin Castle	1	4–9	2	–	0.05	10.9	1.6
	2	14–24	21	11 (10.3–12.5)	0.47	–	–
	3	28–36	29	13 (13.0–13.6)	0.59	–	–
Combined voyages	3–4	–	101	12.3 (12.1–12.5)	–	–	–

*The convict ship 'America' continued to take prisoners on board until day 27 of the voyage. The first three measles cases were put ashore at Woolwich, England on day 27.

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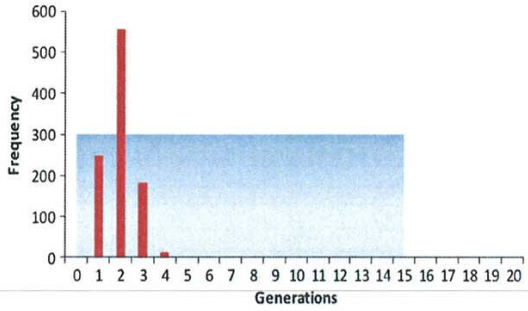

Figure 5 Simulated number of outbreaks based on the characteristics of the measles outbreaks on the ship 'America' 1829, by the number of outbreak generations. Shaded area is the actual duration of the ship voyage (180 days).

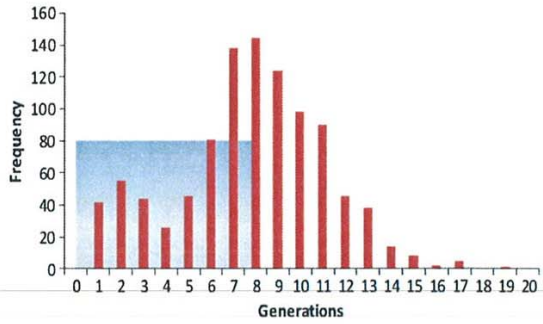

Figure 7 Simulated number of outbreaks based on the characteristics of the measles outbreaks on the ship 'Roslin Castle' 1882, by the number of outbreak generations. Shaded area is the actual duration of the ship voyage (91 days).

Tasmania in 1854, Queensland in 1857, South Australia in 1859 and Western Australia in 1860.[1] From 1860–1899, measles epidemics occurred simultaneously across Australia at periodic intervals which is the nature of measles epidemiology globally, once introduced into a susceptible population. These epidemics caused high death rates, particularly in the under-5-year age group. Death rates of 200–300/100 000 were common.[1]

The documented outbreaks of measles clinical syndrome on five ships bound for Australia between 1829 and 1882 support the hypothesis that it is unlikely that measles reached Australia before 1850. Two ships arriving post-1850 had documented cases in the final week of the voyage or on arrival, whereas none of the pre-1850 outbreaks lasted long enough to reach Australia. Stochastic modelling reveals that voyages before 1850 were highly unlikely to have reached Australia with infectious cases of measles on board, whereas the 1882 'Roslin Castle' outbreak would have had almost a 50% chance of arriving in Australia with infectious cases. On this ship, the hospital became full during the second generation of measles infections and further cases were treated in their own bunks. This may have resulted in a shortened outbreak with susceptibles being exposed to the infection in the living quarters. Although pre-1850 voyages occasionally docked at the Cape of Good Hope, an examination of the length of six voyages in the 1830s (not reported in this study), between England, South Africa and Australia indicated that the length of each individual leg makes it unlikely that measles outbreaks would have lasted long enough on the second part of the journey to reach Australia. Earlier ships had smaller numbers of passengers and crew, including fewer children, than later voyages. The characteristics of measles, particularly risk groups, transmission mechanism, reproductive number, length of incubation and period of communicability resulted in measles only being introduced into Australia almost a century after European settlement.

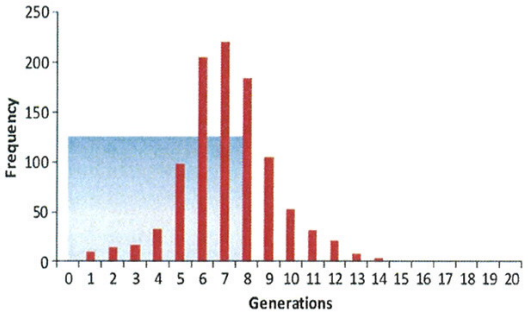

Figure 6 Simulated number of outbreaks based on the characteristics of the measles outbreaks on the ship 'Garrow' 1838, by the number of outbreak generations. Shaded area is the actual duration of the ship voyage (116 days).

Immunity

Measles virus is highly infectious, and before the availability of a measles vaccine, virtually all children were infected by the time they reached 10 years of age.[34] This study confirms that the burden of measles in the 19th-century outbreaks fell on children, with the average age of infection being 6 years. The oldest case was 31 years old, indicating high immunity levels among adults. On the 'Garrow' and 'Roslin Castle', adult measles cases were rare (3–6%), and all three adult cases (>14 years of age) on the 'Garrow' occurred in families with child cases, making within-family transmission likely.

Serial intervals

Although there is much published literature on measles, there is relatively little information available on serial intervals[17] which are a key measure used in determining R_0 and secondary attack rates for measles outbreaks. This study provides details of clinical onset serial intervals of a number of measles outbreaks in closed cohorts. Fine[17] notes that the parameter definitions for serial intervals in measles transmission differ between texts and that none of the references provide citable data on

which the estimates are based. Estimates generally range between 6–29 days[17] with 14 days in common usage. In this study, the mean serial interval was 12.3 days, less than the generally applied 14 days. Ideally, serial intervals are determined where there is a single index case, which was not the situation on these voyages. On the 'America', where the second and third generations infected only one further case, the serial interval was 11 days. These findings support the view that serial intervals are shorter where individuals are in close proximity and transmission may occur earlier.[17]

Basic reproductive number (R_0)

Measles has an estimated basic R_0 of 12–18(refs [13 15]) this compares with pertussis 10–18, polio 5–7, HIV 2–12 and chicken pox 7–11,[12] making it one of the most infectious diseases known. The R_0 estimated on the 'Garrow' was 7.1 and 10.9 on the 'Roslin Castle'. Lower R_0 have previously been reported by Anderson and May; R_0 of 5–6 for a Kansas outbreak,[35] attributed to lower population density.[36] In congested vessels, close proximity would likely facilitate measles transmission by aerosolised droplets, but pre-existing high levels of immunity and non-homogeneous mixing patterns could have resulted in lower R_0. Isolating infectious measles cases would reduce the contact rate between infectious individuals and susceptibles, resulting in a reduced reproduction number and making longer chains of transmission possible. Surgeon superintendents were obviously aware of measles infectivity, recording that measles cases were isolated from the rest of the ship population. This is noteworthy, given that germ theory was not accepted by the medical community until the mid-to-late 19th century.

Limitations

Using historical data for epidemiological analysis presents a number of challenges. Firstly historical records are held in a number of collections that may not be well catalogued, meaning that a comprehensive search is not possible. References to measles outbreaks were sought in a variety of archives. Reports and log books were incomplete and represent only a small number of voyages to Australia, making it difficult to generalise the results to other voyages in this time period. Some logbooks contained only summary accounts of measles outbreaks. There is no way to validate information recorded by individual surgeon superintendents. Although measles case definitions were available at the time, it is not possible to confirm consistent application by surgeons. Some measles cases may have been mild and not reported to the surgeon, or families may have deliberately hidden infectious cases. Some records were difficult to read making errors in the data possible. The precision of the R_0 calculation is affected by the accuracy of the assumed number of susceptibles on board.

CONCLUSIONS

Measles syndrome reporting in ship surgeon's logs provided remarkable detail on prevaccination measles epidemiology in the closed environment of ship voyages and indicate that it was unlikely that measles was introduced into Australia before 1850, due to the relatively high level of preexisting immunity in ship passengers and crew, low numbers of children travelling and particularly the journey's length from England to Australia. Following major outbreaks of disease, including measles, on the large clippers in the mid-19th century, commissions into the health of emigrants resulted in smaller passenger numbers, hygiene improvements, less-confined living areas, and improved ventilation on the ships.[37] These improvements would have reduced the measles R0, resulting in longer outbreaks. This is an early example of disease syndrome surveillance leading to improved public health measures.

In historical analysis, this is a good illustration of social and technological changes resulting in the emergence of an infectious disease. Regular and rapid air travel has had a similar impact in the modern era, resulting in the swift transmission of infectious diseases, including measles, around the world.[38]

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Contributors BP, MK and SC conceived and designed the study. BP collected the data. BP and CdE analysed the data. BP, MK, SC and DD drafted the manuscript. All authors critically revised the manuscript for important intellectual content. BP had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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Competing interests None.

Ethics approval As this is an historical analysis, ethics approval was not required for this project.

Access to the data All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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PAPER THREE: INFLUENZA: H1N1 GOES TO SCHOOL.

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LETTERS

edited by Jennifer Sills

Influenza: H1N1 Goes to School

A KEY DETERMINANT OF THE SUCCESS OF influenza containment is the transmission rate of the novel strain. C. Fraser *et al.* ["Pandemic potential of a strain of influenza A (H1N1): Early findings," Reports, 19 June, p. 1557] estimated the basic reproduction number (R_0) of the Mexican outbreak of influenza A (H1N1) to be in the range of 1.2 to 1.6. The value of R_0 is a key measure of transmissibility and estimates the number of secondary cases in a completely susceptible population. Their findings were comparable to lower estimates for the 1918 pandemic, where R_0 ranged from 2 to 3 (*1*).

To further investigate the transmissibility of this novel virus, we conducted a secondary analysis of the largest reported cluster of influenza A (H1N1) (*2*). We used survey data from students of the St. Francis Preparatory School outbreak in the United States to calculate the effective reproduction number (R) in a school-based setting. R is the average number of secondary cases generated by an infectious case during an epidemic and is usually comparable to R_0. This survey collected data on self-reported fever and either cough or sore throat between 8 and 28 April 2009.

We used the method proposed by Vynncky *et al.* (*3*) to calculate R from the growth rate of the epidemic. We based our parameter assumptions on estimates for seasonal influenza commonly reported in the literature, because such values are not yet available for H1N1. The parameters were as follows: incubation period of 2 days; infectious period of 3 days; and a calculated serial interval of 5 days. The serial interval is the time between the onset of symptoms for first and second generation cases. Using daily data from the outbreak growth phase, we calculated R to be 2.69 [95% confidence interval: 2.20 to 3.22; degrees of freedom (df) = 13]. Increasing the estimated infectious period to 5 days results in an R of 3.45 (95% confidence interval: 2.74 to 4.28; df = 13). The confidence interval for R was derived from a Monte Carlo simulation based on the uncertainty of the slope estimate. Estimates of R were relatively insensitive to the use of data from the growth phase or entire outbreak.

Our calculated R is specific to this school setting and, with the increased transmission potential of a close-contact setting such as a school, is likely to be higher than transmission rates in the community-wide Mexican outbreak. The use of parameters estimated from seasonal influenza will need confirmation for the 2009 influenza A H1N1 virus. Our analysis supports the findings from Fraser *et al.* that this H1N1 virus has a transmission rate comparable to the lower R_0 estimates of 2 for the 1918 pandemic (*1*).

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PAPER FOUR: USE OF WORKPLACE ABSENTEEISM SURVEILLANCE DATA FOR OUTBREAK DETECTION.

Paterson B, Caddis R, Durrheim D. Use of workplace absenteeism surveillance data for outbreak detection. Emerging Infectious Diseases 2011;17(10):1963-1964.

Use of Workplace Absenteeism Surveillance Data for Outbreak Detection

To the Editor: We applaud Mann et al. on their use of a school-based absenteeism surveillance system to compare daily all-causes absenteeism data against a historic baseline to detect outbreaks of influenza-like illness (ILI) as an adjunct to traditional disease reporting (*1*). The growing availability of electronic human resources systems has increased the potential to harness near real-time workplace absenteeism data to complement school absenteeism surveillance and other sources of traditional outbreak surveillance.

In London, United Kingdom, during the first wave of pandemic influenza A (H1N1) 2009, workplace absenteeism data from the Transport for London attendance/absence reporting system were compared with the historical baseline 3-year mean for comparative weeks of the year. The proportion of Transport for London employees absent because of self-reported or medically certified ILI, during June 28–October 17, 2010, generated surveillance alerts when compared with historical baseline data above the 95th and 99th percentile thresholds (SDs 1.96 and 2.58). For the same period, cause-specific workplace influenza absenteeism data were highly correlated with routinely published ILI surveillance, including the National Pandemic Flu Surveillance and sentinel General Practitioner systems (Figure) (*2*).

In Australia, workplace all-causes absenteeism for a major Australia-wide employer has been included as a nonspecific indicator of influenza surveillance by the Australian government for >15 years. A recent study during a severe influenza season in Australia confirmed that employee

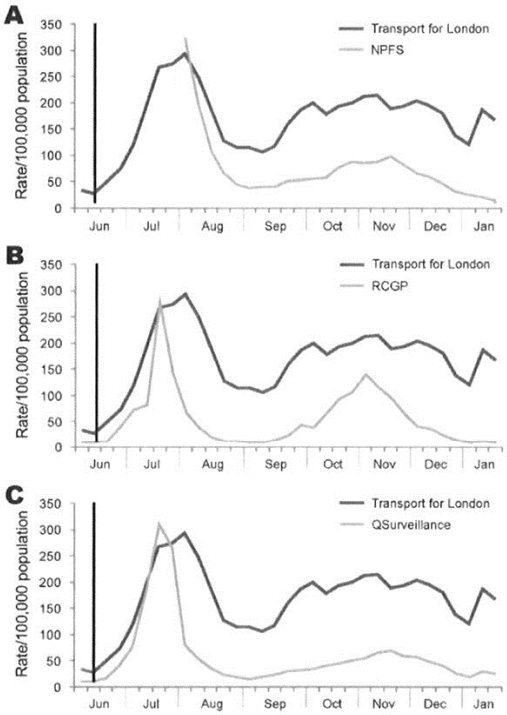

Figure. Comparison of transport for London absenteeism rates from influenza data to syndromic surveillance indicators of influenza-like illness rates, London, United Kingdom, 2009. A) National Pandemic Flu Service (NPFS); B) Royal College of General Practitioners (RCGP); and C) QSurveillance. Vertical black line indicates when the World Health Organization declared a pandemic on June 11, 2009. Source: Health Protection Agency, London, and Transport for London.

absenteeism was highly correlated with laboratory-confirmed influenza, and such information could be used to provide surveillance alerts up to 2 weeks before other traditional influenza surveillance data sources (*3*).

The use of workplace absenteeism data, particularly from large employers, has the potential for overcoming the major limitation of school-based absenteeism data in detecting outbreaks of ILI: the effects of school holidays and local planned school closures. Near real-time workplace absenteeism is an effective surveillance tool and should be more widely incorporated in influenza surveillance systems.

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PAPER FIVE: CHANGES IN SEVERITY OF 2009 PANDEMIC A/H1N1 INFLUENZA IN ENGLAND: A BAYESIAN EVIDENCE SYNTHESIS.

Presanis AM, Pebody RG, Paterson BJ, et al. Changes in severity of 2009 pandemic A/H1N1 influenza in England: a Bayesian evidence synthesis. British Medical Journal 2011;343:d5408.

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RESEARCH

Changes in severity of 2009 pandemic A/H1N1 influenza in England: a Bayesian evidence synthesis

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Abstract

Objective To assess the impact of the 2009 A/H1N1 influenza pandemic in England during the two waves of activity up to end of February 2010 by estimating the probabilities of cases leading to severe events and the proportion of the population infected.

Design A Bayesian evidence synthesis of all available relevant surveillance data in England to estimate severity of the pandemic.

Data sources All available surveillance systems relevant to the pandemic 2009 A/H1N1 influenza outbreak in England from June 2009 to February 2010. Pre-existing influenza surveillance systems, including estimated numbers of symptomatic cases based on consultations to the health service for influenza-like illness and cross sectional population serological surveys, as well as systems set up in response to the pandemic, including follow-up of laboratory confirmed cases up to end of June 2009 (FF100 and Fluzone databases), retrospective and prospective follow-up of confirmed hospitalised cases, and reported deaths associated with pandemic 2009 A/H1N1 influenza.

Main outcome measures Age specific and wave specific probabilities of infection and symptomatic infection resulting in hospitalisation, intensive care admission, and death, as well as infection attack rates (both symptomatic and total). The probabilities of intensive care admission and death given hospitalisation over time are also estimated to evaluate potential changes in severity across waves.

Results In the summer wave of A/H1N1 influenza, 0.54% (95% credible interval 0.33% to 0.82%) of the estimated 606 100 (419 300 to 886 300) symptomatic cases were hospitalised, 0.05% (0.03% to 0.08%) entered intensive care, and 0.015% (0.010% to 0.022%) died. These correspond to 3200 (2300 to 4700) hospital admissions, 310 (200 to 480) intensive care admissions, and 90 (80 to 110) deaths in the summer wave. In the second wave, 0.55% (0.28% to 0.89%) of the 1 352 000 (829 900 to 2 806 000) estimated symptomatic cases were hospitalised, 0.10% (0.05% to 0.16%) were admitted to intensive care, and 0.025% (0.013% to 0.040%) died. These correspond to 7500 (5900 to 9700) hospitalisations, 1340 (1030 to 1790) admissions to intensive care, and 240 (310 to 380) deaths. Just over a third (35% (26% to 45%)) of infections were estimated to be symptomatic. The estimated probabilities of infections resulting in severe events were therefore 0.19% (0.12% to 0.29%), 0.02% (0.01% to 0.03%), and 0.005% (0.004% to 0.008%) in the summer wave for hospitalisation, intensive care admission, and death respectively. The corresponding second wave probabilities are 0.19% (0.10% to 0.32%), 0.03% (0.02% to 0.06%), and 0.009% (0.004% to 0.014%). An estimated 30% (20% to 43%) of hospitalisations were detected in surveillance systems in the summer, compared with 20% (15% to 25%) in the second wave. Across the two waves, a mid-estimate of 11.2% (7.4% to 18.9%) of the population of England were infected, rising to 29.5% (16.9% to 64.1%) in 5-14 year olds. Sensitivity analyses to the evidence included suggest this infection attack rate could be as low as 5.9% (4.2% to 8.7%) or as high as 28.4% (26.0% to 30.8%). In terms of the probability that an infection leads to death in the second wave, these correspond, respectively, to a high estimate of 0.017% (0.011% to 0.024%) and a low estimate of 0.0027% (0.0024% to 0.0031%).

Conclusions This study suggests a mild pandemic, characterised by case and infection severity ratios increasing between waves. Results suggest low ascertainment rates, highlighting the importance of systems enabling early robust estimation of severity, to inform optimal public health responses, particularly in light of the apparent resurgence of the 2009 A/H1N1 strain in the 2010-11 influenza season.

Introduction

Since the first confirmed cases of pandemic influenza A/H1N1 were reported in April 2009, 18 449 deaths have been notified worldwide.[1] Reported numbers of laboratory confirmed cases and deaths are of limited value in determining the severity of a

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disease because of the difficulties in identifying, testing, confirming, and reporting cases, particularly during a pandemic.[2-8] For policy makers, however, understanding severity is crucial to determine appropriate public health responses. Severity estimates are needed early on in an outbreak, when timely (but perhaps not the most robust) estimates are required, but also when an epidemic has run its course, to quantify robustly both the severity and total burden of disease and to assess whether public health responses and surveillance systems were adequate in the midst of the epidemic. An assessment of severity is a key element in understanding the epidemiology of the 2009 pandemic and for planning for future pandemics, particularly if more severe or more transmissible influenza strains emerge. Furthermore, if unusual patterns of age specific mortality continue for several years, as has happened in past pandemics[9] and as seems to be the case with the 2009 pandemic,[10] knowledge of the severity and burden of the strain is important for planning healthcare resource allocation as well as for understanding if severity is changing over time.

A measure of the severity of an infection is its case severity, the probability that an infected individual develops severe disease. Specifically, the case fatality ratio (the probability that an infection leads to death, estimated by taking the ratio of deaths to cases) is often used, together with the case hospitalisation ratio and case intensive care admission ratio (table 1⇓). A case may be defined either as any infection or a symptomatic infection, meaning a febrile influenza-like illness. Although influenza typically causes symptomatic infection, a substantial proportion of infected individuals will be asymptomatic or have only mild symptoms. These individuals are unlikely to be identified unless serological testing is undertaken on a population basis.[11 12] Estimation is therefore required to obtain a quantification of severity. In this paper, we estimate the symptomatic case fatality, case intensive care admission, and case hospitalisation ratios (the probabilities of symptomatic infections leading to severe events (table 1⇓)) for pandemic A/H1N1 in England, from multiple sources of data available from various surveillance systems, and derive the corresponding infection severity ratios (the probabilities of all infections leading to severe events) using data from population sero-incidence surveys on the infection attack rate.[13]

Severity estimation is potentially complicated by two key problems affecting the observed numbers of severe events and cases—censoring and ascertainment bias.[2-4 6-8] Censoring happens in the midst of an epidemic, when some severe events resulting from infections to date have yet to occur, leading to underestimation of the number of severe events. Ascertainment bias refers more generally to undercounting of cases because of surveillance systems not capturing all cases for multiple reasons. To estimate case severity ratios correctly, methods accounting for these biases are required. Previous attempts to estimate the symptomatic case fatality ratio of pandemic A/H1N1 in England[3-15] have accounted for censoring but not all ascertainment biases and, in particular, have not accounted for all the uncertainty inherent in the data. Crucially, they have not used all the available information in the estimation process. To address these limitations, we adapted a Bayesian approach to severity estimation,[8] synthesising all available relevant data and prior information on biases to derive estimates of the infection and case severity ratios, the infection attack rate, and the symptomatic attack rate in England. For a retrospective analysis, as presented here, censoring is no longer an issue, so we did not need to account for it, but our analytical approach is easily adapted to a mid-pandemic situation where censoring does induce bias.[8] In accounting for ascertainment bias, we assessed the proportion of infections detected in both pre-existing surveillance systems monitoring seasonal influenza and systems specifically set up in response to the pandemic A/H1N1 outbreak.

As England experienced two waves of pandemic A/H1N1 infection in 2009-10, we investigated changes in severity across the waves, comparing the periods 1 June to 31 August 2009 (summer) and 1 September 2009 to 28 February 2010 (autumn-winter). In absolute terms, more deaths and hospitalisations were observed from September to November than in the three summer months: it is important to understand whether this reflects greater numbers of infections in the autumn, better ascertainment, or a real increase in severity. The answer has important implications for surveillance and public health responses in future pandemics.

Methods

Sources of information

Several influenza surveillance systems at the Health Protection Agency provide data on pandemic A/H1N1 cases.

Confirmed cases—The FF100[16] and FluZone[17] databases comprise detailed information on each of the first few thousand confirmed cases of pandemic A/H1N1 influenza, including dates of severe outcomes. From these, we estimated the delay from symptom onset to hospitalisation using a parametric mixture survival model,[18] giving an estimate (assumed unbiased) of the proportion of confirmed cases hospitalised, which we used indirectly in our Bayesian analysis. Since the survival model was fitted to data from early on in the epidemic, on confirmed cases that were followed up only until the end of June 2009, this is the only analysis where we have accounted for censoring.

Symptomatic cases—During the pandemic, the Health Protection Agency fitted a regression model to data on the number of consultations for influenza-like illness (in primary care and through the National Pandemic Flu Service) and to data on the positivity rate, to produce weekly age specific and region specific estimates[19 20] of the number of symptomatic cases accessing healthcare. These were divided by estimates of the proportion of influenza-like illness cases in patients who consulted healthcare services, to obtain estimates of the total number of symptomatic cases. These are thought to underestimate the true symptomatic attack rate, given other evidence on the infection attack rate.[13]

Seroincidence—Repeated cross sectional serological surveys were undertaken as part of the annual collection of residual sera for the Health Protection Agency sero-epidemiology programme from patients accessing healthcare in England. Data from these surveys, taken before the pandemic (a 2008 baseline), after the first wave of infections in August-September 2009,[13] and after the second wave[21] are published, providing evidence (though highly uncertain because of small sample sizes, low power, and potential biases in the sampled population) on the age specific infection attack rate during both waves.

Hospitalisation—A web based surveillance system in England was established by the Health Protection Agency and Department of Health after the end of the first wave in August 2009[22] to ascertain and collect data on all confirmed cases of pandemic A/H1N1 influenza hospitalised in acute NHS trusts in England. Of these, 970 cases, confirmed during the first wave, were retrospectively added to the database and 1306 cases were added prospectively during the second wave. Ascertainment of cases, however, was incomplete, with only 129 (77%) of the 168 acute NHS hospital trusts in England participating. This

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database provided information (from a line listing at 9 July 2010) on the number of hospitalisations of confirmed cases and on the ratios of intensive care admissions and deaths to hospitalisations. We considered the observed hospitalisations to reflect only a subset of all pandemic A/H1N1 hospitalisations but assumed the observed ratios of intensive care admission to hospitalisation and death to hospitalisation provided unbiased information on the probabilities of severe events given hospitalisation.[18]

Death—As at 9 July 2010, 380 deaths among people with confirmed pandemic A/H1N1 infection or mention of influenza on the death certificate had been reported to the Health Protection Agency or the chief medical officer.[14 15] Among individuals with symptom onset from 1 June to 31 August, 79 deaths were observed in the summer wave, and 301 deaths were observed in the second wave among individuals with symptom onset 1 September to 28 February. A capture-recapture analysis suggests that deaths were under-ascertained by approximately 10%.[23]

Estimation approach

We adapted a Bayesian approach to estimate the attack rates, infection severity ratio, and symptomatic case severity ratio.[8] We considered five severity levels (infection, symptomatic infection, hospitalisation, intensive care admission, and death (fig 1⇓)), denoted g=*INF*, *S*, *H*, *I*, and *D*; and seven age groups, <1, 1-4, 5-14, 15-24, 25-44, 45-64, and ≥65 years.

We defined $N_{a,t,g}$ to be the number of infections in age group *a*, wave *t*, and severity level *g* (table 2⇓), and defined $c_{a,t,g|k}$ to be the probability that pandemic A/H1N1 cases in age group *a* and wave *t* at severity level *k* progress to level *g* (namely, the ratio of cases at level *g* to those at level *k* if cases at *g* are a subset of those at *k* (such as if all deaths occur in hospital)). Then the infection and symptomatic case severity ratios were expressed as products of the component probabilities of progressing through each successive level of the severity pyramid (fig 1⇓, table 2⇓). For example, the case fatality ratio was defined as the product of the probability of hospitalised cases dying, the probability of symptomatic cases being hospitalised, and the probability of an infection being symptomatic: $c_{a,t,D|INF}=c_{a,t,D|H}c_{a,t,H|S}c_{a,t,S|INF}$. These components were estimated by synthesising the available information on infection at each severity level and on ascertainment probabilities, $d_{a,t,g}$, the probabilities that severe events were captured by surveillance systems (table 2⇓). Further combining with population sizes, we also obtained estimates of the infection and symptomatic attack rates.

To do this, we combined the observed surveillance data with our knowledge of each probability before observation, summarised by a "prior" distribution, to obtain an updated distribution (the "posterior") which formally summarised our final knowledge of the quantities of interest. This distribution, accounting for both imperfect detection and all uncertainty inherent in the data as well as uncertainty about some model assumptions through the introduction of informative prior distributions,[18] was summarised by its centiles—the median and the 2.5 and 97.5 centiles (denoted the 95% credible interval). The Bayesian analysis was carried out in OpenBUGS.[24]

Statistical model

Figure 2⇓ illustrates the relation between the data and the quantities to be estimated. Full model details are given by Presanis et al[18] but are briefly described here, with table 2⇓ summarising the model parameters. The Bayesian evidence synthesis combined both direct (solid lines, fig 2⇓) and indirect information on each parameter, where indirect evidence might take the form of data on other quantities indirectly influencing the parameter of interest (such as the number of deaths informing the number of hospitalisations) or model assumptions.

Data from the sero-incidence study[13] were used to inform the infection attack rate in the summer wave ($c_{a,Summer,INF|POP}$). We considered the Health Protection Agency estimates of symptomatic infection[19 20] to be biased downwards, providing information on a quantity ($N_{a,t,SB}$) that was a proportion of the true number of symptomatic cases ($N_{a,t,S}$, where $d_{a,t,S}$ denotes this proportion). This proportion was estimated in the first wave of influenza from the information on the infection attack rate in combination with prior information on the proportion ($c_{S|INF}$) of infections that are symptomatic (table 1⇓). This proportion symptomatic was assumed to be equal across age groups[25] and waves. By assuming the age specific bias in the Health Protection Agency estimates, $d_{a,t,S}$, was similar, but not necessarily equal, in the two waves (table 1⇓), we estimated the number of symptomatic infections $N_{a,t,S}$ in the autumn-winter period.[18] Combined again with the prior information on the proportion of infections which are symptomatic, we obtained an estimate of $N_{a,t,INF}$ in the autumn-winter wave.

The detected number of hospitalised cases[22] and deaths[14 15] were considered a subset of the true number of cases, $N_{a,t,g}$, for *g=H,D* respectively, with corresponding detection probability, $d_{t,g}$, assumed equal across age groups. Similarly, the observed number of intensive care admissions and deaths from the subset of hospitalisations with non-missing data on outcomes were a proportion of the observed number in the subset, denoted $c_{a,t,g|H}$ for *g=I,D*, respectively (table 2⇓).

Each age specific symptomatic case hospitalisation ratio, $c_{a,t,H|S}$, was constrained to be less than the corresponding age specific confirmed case hospitalisation ratio. These confirmed case hospitalisation ratios were themselves informed by the age specific estimates given by a parametric mixture survival model.[18] After accounting for censoring, the estimated confirmed case hospitalisation ratio averaged over age was 1.20% (95% confidence interval 0.97% to 1.49%).

Importantly, we assumed the detection probabilities to be less than 100% for both hospitalisations and deaths. We gave $d_{t,H}$ a vague prior distribution (table 2⇓) that accounts for under-ascertainment. We chose a prior distribution for $d_{t,D}$ with mean 90%, ranging between 80% and 97%, based on a capture-recapture study,[23] to reflect under-ascertainment due to test sensitivity or other reasons for failing to appear in surveillance systems. We allowed both $d_{t,H}$ and $d_{t,D}$ to vary by wave, but not age.

Results

Table 3⇓ shows that in the summer wave of influenza, 0.54% (95% credible interval 0.33% to 0.82%) of the estimated 606 100 (419 300 to 886 300) symptomatic cases were hospitalised, corresponding to 540 (330 to 820) out of every 100 000 symptomatic cases and to a total of 3200 (2300 to 4700) hospitalisations. Of the symptomatic cases in this first wave, 0.05% (0.03% to 0.08%) entered intensive care (corresponding to 310 (200 to 480) intensive care admissions) and 0.015% (0.010% to 0.022%) died (90 (80 to 110) deaths).

In the second wave, 0.55% (0.28% to 0.89%) of the 1 352 000 (829 900 to 2 806 000) estimated symptomatic cases were hospitalised, corresponding to 7500 (5900 to 9700) admissions. Of the symptomatic cases in the second wave, 0.10% (0.05% to 0.16%) entered intensive care (1340 (1030 to 1790)

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admissions) and 0.025% (0.013% to 0.040%) died (340 (310 to 380) deaths).

Just over a third (35% (26% to 45%)) of infections were estimated to be symptomatic. The estimated probabilities of infections resulting in severe events were therefore 0.19% (0.12% to 0.29%), 0.02% (0.01% to 0.03%), and 0.005% (0.004% to 0.008%) in the summer wave for hospitalisation, intensive care, and death, respectively. The corresponding second wave proportions were 0.19% (0.10% to 0.32%), 0.03% (0.02% to 0.06%), and 0.009% (0.004% to 0.014%) (table 3⇓). Age specific infection and case severity ratios are given in figure 3⇓. The case fatality ratios, for both symptomatic cases and all cases, differed substantially across waves (table 3⇓), with 93.5% posterior probability that these were greater in the autumn-winter wave than in the summer. The age specific differences over time were less pronounced (fig 3⇓). The probabilities of intensive care admission and death among hospitalised patients also increase over time (fig 4⇓). We estimated a cumulative infection attack rate across the two waves of 11.2% (7.4% to 18.9%), with age specific and wave specific estimates given in table 4⇓.

The observed number of hospitalisations in the autumn-winter wave was 1481, representing an estimated 20% (15% to 25%) of the estimated 7500 (5900 to 9700) hospitalised cases (table 3⇓), a substantial bias. Surveillance of suspected (rather than confirmed) cases of pandemic A/H1N1 influenza indicated that 17 519 of these were hospitalised in the autumn-winter wave[17]: comparison with our estimate of the number of hospitalised cases (table 3⇓) therefore suggests between 34% and 55% of suspected cases were true cases. An estimated 30% (20% to 43%) of hospitalisations were detected in surveillance systems in the summer, compared with 20% (15% to 25%) in the second wave. The bias in the Health Protection Agency case estimates, averaged across age, was substantial but uncertain, with the case estimates $N_{a,t,SB}$ representing 40% (24% to 59%) of the true number of symptomatic cases, $N_{a,t,S}$, in the summer and 36% (19% to 57%) of them in the autumn-winter.

Sensitivity analyses

Several sensitivity analyses to the choice of denominator data and to the prior distribution of the infection attack rate were performed to further assess the uncertainty in the attack rates.[18] Differences due to the choice of prior distribution of the infection attack rate were small relative to the differences due to choice of denominator data, so we concentrated on sensitivity to the denominator. Specifically, four models with different denominators were considered: (1) Health Protection Agency case estimates only, assumed unbiased; (2) the model presented in the main results section, with both the case estimates (assumed biased downwards) and the summer sero-incidence data, and the second wave attack rates obtained by assuming a similar bias in the Health Protection Agency case estimates in the two waves; (3) using the sero-incidence data from both waves,[13 21] assuming these are unbiased and that the Health Protection Agency case estimates are biased downwards; and (4) using the sero-incidence data from both waves,[13 21] assuming these are biased upwards and the Health Protection Agency case estimates are biased downwards.

The estimates of the infection attack rate in both waves across the four different choices of denominator may be as low as 5.9% (4.2% to 8.7%) (model 1) or as high as 28.4% (26.0% to 30.8%) (model 3), with the corresponding estimates for 5-14 year olds varying between 17.9% (11.5% to 28.4%) and 58.8% (52.8% to 64.5%). The estimates of the case fatality ratio in the second wave were therefore highest in model 1 at 0.017% (0.011% to 0.024%) and lowest in model 3 at 0.0027% (0.0024% to 0.0031%).

Discussion

This study suggests a mild pandemic, with case and infection severity ratios highest in children and older adults and increasing over time. Infection attack rates were highest among school age children. The results suggest under-ascertainment of severe cases through routine systems and considerable uncertainty in the denominators of symptomatic and all infection, highlighting the limits of current surveillance. Robust systems are essential for future early estimation of severity.

Variation by age and wave of influenza

The case severity ratio estimates show a clear U shape to the age distribution (fig 3⇓), in contrast to the estimated infection and symptomatic attack rates (table 4⇓), which have an inverted U shape, with the peak in school age children. These distributions indicate that proportionately fewer adults were infected than children, with 5-14 year olds having an infection attack rate of 29.5% (16.9% to 64.1%), whereas young and old cases were most likely to be severely affected. Among those hospitalised, the age distribution was again different, with the probability of severe outcomes increasing with age (fig 4⇓), possibly due to increased risk of comorbidities.[22] Although children and older adults were more likely than other adults to be admitted to hospital, once there, children were less likely than adults to enter intensive care or to die.

Our estimates of the number of hospitalisations and corresponding detection probability suggest a large bias in the observed hospitalisations due to under-ascertainment of confirmed cases. However, the estimated number was still substantially smaller than the observed suspected number of hospitalisations, suggesting between 34% and 55% of suspected hospitalisations in the autumn-winter wave were true pandemic A/H1N1 influenza cases. We estimated an increase in infection, case, and hospitalisation severity ratios between waves. The age specific increases were slightly less evident than the overall increases, because of the smaller sample sizes and hence greater uncertainty.

The higher severity among hospitalised cases older than 25 years estimated in the second wave (fig 4⇓) may indicate a change in healthcare seeking behaviour or hospital admission policy, or may represent a real increase in severity. Initially, when less was known about risk groups and outcomes, individuals may have been more likely to seek healthcare and hospitals more cautious in admitting suspected cases than during the second wave,[26 27] so that those observed in hospital in the second wave may have had more severe illness on average than those hospitalised in the first wave. The difference between waves was less pronounced in children and young adults, possibly because the same cautious hospital admission behaviour may have applied to this population throughout.

Uncertainties and assumptions

Although behaviour change might explain the increase in probabilities of severe outcomes after hospitalisation, it might not be the only contributory factor to the increase in symptomatic case severity ratios. It is possible that a true increase in severity may have played a part in the estimated increase if, for example, other effect modifying factors such as

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bacterial super-infection were more common in the autumn-winter wave than in the summer, as was observed.[28 29]

If behaviour change had played a large part in the estimated increase in severity, then we might not have accounted adequately for under-ascertainment in the denominator of symptomatic cases, despite finding a substantial though uncertain bias in the Health Protection Agency estimates, or we may have overestimated the case hospitalisation ratio in the second wave. Alternatively, the observed ratios of intensive care admission to hospitalisation and death to hospitalisation ratios (assumed to provide unbiased information) may actually have been biased.

Other unaccounted factors might also have influenced apparent changes in severity, such as any potential shift in the age distribution of incident cases,[30] the use of antiviral drugs as prophylaxis or treatment, and the vaccination campaign. These last two factors might be postulated to reduce rather than increase severity.[17] However, vaccination uptake increased only towards the second half of the second wave,[17] so it might not have had a large effect on severity. Also, the per population rate of collection of antivirals via the National Pandemic Flu Service was lower in the second wave than in the first,[17] so if the attack rate was larger in the second than in the first wave, the effect of antivirals on reducing severity might have been greater in the first wave than in the second.

The estimated infection attack rate across all ages in the summer wave of 3.4% (2.4% to 4.8%), and the corresponding rate in 5-14 year olds of 10.0% (5.9% to 14.9%), are somewhat smaller than those estimated from the sero-incidence data alone in London and the West Midlands, but larger than those estimated from the sero-incidence data alone in other regions.[13] Thus there may have been regional differences[13] that were smoothed over by our estimates averaged across England. A regional analysis may be beneficial, although the consequent small sample sizes would entail large uncertainty in such estimates.

The differences also highlight the uncertainties surrounding the estimation of attack rates, as evidenced by the relatively wide credible intervals, particularly for the age specific rates (table 4⇓). Results from our sensitivity analyses show that the attack rate estimates are highly dependent on the model and data used, further emphasising the uncertainties surrounding the denominators. The sensitivity of results to data used to inform denominators[18] suggests further work is needed in synthesising all available data. It is clear that the evidence on denominators provided by the sero-incidence data and by the Health Protection Agency estimates conflict, the extent to which either source may be biased is less apparent.

The Health Protection Agency case estimates relied on broad assumptions about the proportion of individuals with influenza-like illness who contacted healthcare services,[20] without allowing for a likely substantial change in this proportion over the course of the epidemic.[31] Further, the Health Protection Agency case estimates represent numbers symptomatic where symptomatic is interpreted as presentation with febrile influenza-like illness due to pandemic A/H1N1, and may therefore miss individuals with milder symptoms due to pandemic A/H1N1.[20]

On the other hand, as Miller and colleagues[13] and Hardelid et al[21] point out, their cumulative incidence estimates rely on the definition of "positivity" used, as well as on an assumption that the study population is representative of the population of interest. There is concern that the serology samples taken during the pandemic might have come from a population at greater risk of infection than average, and therefore more likely to have been vaccinated in the second wave, possibly introducing bias.[13 21 32] The authors also point out that small sample sizes imply limited power to detect changes in prevalence, particularly in older age groups. Care should therefore be taken not to over-interpret the estimates from our sensitivity analyses.

The model on which our main results are based (model 2 in our sensitivity analyses) incorporates uncertainty in the estimates that approximately covers the range, by age group, of the uncertainty in the estimates from model 1 and model 3, the two models which assume unbiased Health Protection Agency case estimates and unbiased sero-incidence data, respectively. Our estimates of the proportion of cases that were symptomatic (ranging from 30% (21% to 40%) to 39% (30% to 49%) in the sensitivity analyses) are broadly comparable with estimates from studies of seasonal influenza[11 12] and other studies of pandemic A/H1N1.[25 33-35] A further sensitivity analysis[18] to the choice of prior information on the proportion of infections that are symptomatic (mean prior value 63% (95% credible interval 50% to 76%)[12]) gives a posterior estimate of 55% (40% to 69%), with estimates of symptomatic case severity and the infection attack rate mildly sensitive to this choice. However, the difference in estimates is outweighed by the uncertainties in the denominators of symptomatic infection and all infection.

Our estimates rely on some assumptions of representativeness, such as that observations from hospital surveillance are representative of all English hospitals, not just those participating in the scheme, and that reporting practices did not change between the two waves of influenza. Finally, by using the sero-incidence data to infer the infection attack rate, we are implicitly assuming that by "infection" we mean infection with detectable antibody response, since we did not adjust for test sensitivity. Given the small sample sizes, concerns about the representativeness of the serology data, and the uncertainty in the denominators, we believe any uncertainty due to test sensitivity will be relatively small.

Comparison with other studies

Our analysis gives definitive estimates of the case severity ratios in England, lying between the US estimates based on medical attendances in Milwaukee and hospitalisations in New York (approach 1 in paper by Presanis et al[8]; symptomatic case fatality ratio 0.048% (0.026% to 0.096%)) and the estimates based on self reported influenza-like illness in New York (approach 2 in paper by Presanis et al[8]; symptomatic case fatality ratio 0.007% (0.005% to 0.009%)). Our estimates are somewhat lower than the early estimates of the confirmed case fatality ratio provided by Garske et al,[3] which ranged from 0.11% to 1.47% overall and from 0.13% to 0.41% in the UK, accounting for censoring. These were based, however, only on confirmed cases as a denominator, so were expected to be larger. Nishiura et al[4] likewise considered confirmed cases as a denominator, accounting for censoring, and estimating between 0.16% and 4.48% of these in the US and Canada to be fatal.

Our estimates are more comparable with other estimates where infections or symptomatic infections were used as a denominator: Wilson and Baker[6] estimated a range for the case fatality ratio of 0.0004% to 0.06%, and Baker et al[7] estimated a symptomatic case fatality ratio of 0.005%, somewhat lower than ours. Hadler et al[36] estimated a range for the symptomatic case fatality ratio in New York between 0.0054% and 0.0086%, whereas Donaldson et al[14] reported a symptomatic case fatality ratio for England of 0.026% (range 0.011% to 0.066%), and Pebody et al[15] reported a ratio of 0.04% (range 0.02% to 0.10%).

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Wu et al[37] estimated a case fatality ratio of 0.0109% (0.0041% to 0.0377%).

Conclusions and policy implications

While we have been careful to outline underlying assumptions and possible uncertainties in our analysis, we have nevertheless estimated severity in a robust statistical framework, systematically accounting for possible biases. Identification of biases is possible only in an evidence synthesis framework, through the "triangulation" of multiple data sources: each source on its own provides a (potentially biased) view of only one aspect of the severity of an epidemic. The credible intervals reported fully reflect the uncertainty in the observed data, the estimation process, and some (though not all) model assumptions.

Finally, our study suggests a mild pandemic, characterised by case and infection severity ratios increasing between the two influenza waves, while the process of synthesis and reconciliation of the data available from different sources has highlighted the importance of transparent design of routine influenza surveillance to derive robust estimates of key measures of severity. Multiple information streams—and an established framework to interpret these data as quickly as possible—are critically important, particularly in light of the apparent resurgence[10] of the pandemic A/H1N1 strain in the 2010-11 influenza season.

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Contributors: AMP performed the main statistical analysis, developed the model, and wrote the paper. RGP, BJP, and AC collated the data, contributed to model development, and helped revise the paper. BDMT and PJB contributed to statistical analysis, to model development, and to critical revisions of the paper. ML and DDA conceived and planned the project and contributed to model development and to critical revisions of the paper. RGP, ML, and DDA are the guarantors for the study. All authors gave final approval of the published paper and had full access to the data used in the study.

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What is already known on this topic

Initial estimates of the severity of the 2009 A/H1N1 influenza pandemic were highly uncertain, with later estimates suggesting a relatively mild pandemic but with an age distribution of infections different from that for seasonal influenza

Previous studies of the severity of the 2009 A/H1N1 influenza pandemic in England have not fully accounted for biases, have not made comprehensive use of all available relevant evidence to quantify the uncertainty in these severity measures, and have not provided an assessment of changes in severity nor of the adequacy of routine surveillance systems

What this paper adds

This study is the first to provide a complete overview of the severity of the first two waves of the 2009 pandemic A/H1N1 influenza outbreak in England, synthesising all available relevant influenza surveillance data

The analysis fully accounts for biases and under-ascertainment of confirmed cases in each surveillance system and accounts robustly for uncertainty in the data

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Tables

Table 1 | **Measures of severity of influenza infection**

Quantity	Definition	Estimated by
Case fatality ratio	Probability that an infection leads to death	No of deaths/No of infections
Case intensive care admission ratio	Probability that an infection leads to intensive care admission	No of intensive care admissions/No of infections
Case hospitalisation ratio	Probability that an infection leads to hospital admission	No of hospital admissions/No of infections
Symptomatic case fatality ratio	Probability that a symptomatic infection leads to death	No of deaths/No of symptomatic infections
Symptomatic case intensive care admission ratio	Probability that a symptomatic infection leads to intensive care admission	No of intensive care admissions/No of symptomatic infections
Symptomatic case hospitalisation ratio	Probability that a symptomatic infection leads to hospital admission	No of hospital admissions/No of symptomatic infections
Infection attack rate	Proportion of the population cumulatively infected	No of infections/No of population
Symptomatic infection attack rate	Proportion of the population cumulatively infected with febrile influenza-like illness	No of symptomatic infections/No of population

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Table 2| **Details of model of severity of 2009 pandemic A/H1N1 influenza in England: model parameters; their prior distributions or functional forms; and evidence (direct or indirect) contributing to the parameter estimates**

Parameter (description)	Prior distribution or functional form	Rationale	Evidence	
			Direct	Indirect
Conditional probabilities				
$c_{a,I,In/I/Pop}$ (infection attack rate)	Dirichlet(1,1,1)	Vague prior assuming we know nothing a priori (that is, a flat prior covering the 0 to 1 range). Age specific	Serological data for summer wave (binomial likelihoods for observed baseline and pandemic number of positive samples, with the corresponding serial prevalences as the proportion and total numbers of samples as the size)	Assumption (see $d_{a,t,S}$ below) of a similar bias in the HPA case estimates in the two waves. The remaining data and model assumptions
$c_{S/I/In/I}$ (proportion symptomatic)	Beta(40,60)	Informative prior: mean 40% (95% prior probability of lying in 30% to 50%).[25] Assumed equal across age groups and waves	None	All the data and model assumptions
$c_{a,t,H/S}$ (symptomatic case hospitalisation ratio)	Uniform(0, $c_{a,H/C}$)	Informative prior constraining the symptomatic case hospitalisation ratio to lie between 0 and the confirmed case hospitalisation ratio. Age and wave specific	None	The observed number of hospitalisations. The remaining data and model assumptions
$c_{a,H/C}$ (confirmed case hospitalisation ratio)	Beta distributions, one for each age group	Informative priors, reflecting estimates of the confirmed case hospitalisation ratio obtained from a parametric mixture survival model[18] fitted to data on laboratory confirmed cases. Averaged across all age groups, this estimate is 1.2% (0.97% to 1.49%). Age specific	None	All the data and model assumptions
$c_{a,t,I/H}$ (probability of intensive care admission given hospitalisation)	Beta(1,1)	Vague prior assuming we know nothing a priori (that is, prior mean 50% with 95% of prior mass lying in 2.5% to 97.5%). Age and wave specific	Observed ratio of intensive care admissions to hospitalisations among confirmed cases with non-missing data (binomial likelihood for the number of intensive care admissions, with $c_{a,t,I/H}$ as the proportion and the number of hospitalisations as the size)	The remaining data and model assumptions
$c_{a,t,D/H}$ (probability of death given hospitalisation)	Beta(1,1)	Vague prior assuming we know nothing a priori (that is, prior mean 50% with 95% of prior mass lying in 2.5% to 97.5%). Age and wave specific	Observed ratio of deaths to hospitalisations among confirmed cases with non-missing data (binomial likelihood for the number of deaths, with $c_{a,t,D/H}$ as the proportion and the number of hospitalisations as the size)	The observed number of deaths. The remaining data and model assumptions
Detection probabilities				
$d_{a,t,S}$ (proportion of number symptomatic "observed" in the HPA case estimates)	Beta(1,1)	Vague prior assuming we know nothing a priori (that is, prior mean 50% with 95% of prior mass lying in 2.5% to 97.5%). This prior is assumed only for the summer wave. The odds ratio of this proportion in the autumn-winter wave relative to the summer wave is assumed to lie between 0.7 and 1.3. Age specific.	None	The HPA case estimates and the serological data. The remaining data and model assumptions
$d_{t,H}$ (proportion of number of hospitalisations that are observed)	Beta(1,1)	Vague prior assuming we know nothing a priori (that is, prior mean 50% with 95% of prior mass lying in 2.5% to 97.5%). Wave specific, but assumed equal across age groups.	None	The observed number of hospitalisations. The remaining data and model assumptions
$d_{t,D}$ (proportion of the number of deaths that are observed)	Beta(45,5)	Informative prior reflecting an estimate of this proportion taken from a capture-recapture study[23]: (mean 90% with 95% of prior probability lying in 80% to 97%). Wave specific, but assumed equal across age groups.	None	The observed number of deaths. The remaining data and model assumptions
Case severity ratios				
$c_{a,t,D/In/}$ (case fatality ratio)	$c_{a,t,D/In/}=c_{a,t,D/H}\times c_{a,t,H/S}\times c_{a,t,S/In/}$	Product of component conditional probabilities	None	All the data and model assumptions
$c_{a,t,D/S}$ (symptomatic case fatality ratio)	$c_{a,t,D/S}=c_{a,t,D/H}\times c_{a,t,H/S}$	Product of component conditional probabilities	None	All the data and model assumptions

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Table 2 (continued)

Parameter (description)	Prior distribution or functional form	Rationale	Evidence	
			Direct	Indirect
$c_{a,t,I\|Inf}$ (case intensive care ratio)	$c_{a,t,I\|Inf}=c_{a,t,I\|H}\times c_{a,t,H\|S}\times c_{a,t,S\|Inf}$	Product of component conditional probabilities	None	All the data and model assumptions
$c_{a,t,I\|S}$ (symptomatic case intensive care ratio)	$c_{a,t,I\|S}=c_{a,t,I\|H}\times c_{a,t,H\|S}$	Product of component conditional probabilities	None	All the data and model assumptions
Number of individuals at each severity level				
$N_{a,Pop}$ (population size of England in age group a)	N/A	Assumed constant, taken from ONS 2008 population estimates	ONS 2008 population estimates	None
$N_{a,t,Inf}$ (number of infections)	$N_{a,t,Inf}=c_{a,t,Inf\|Pop}\times N_{a,Pop}$	Product of infection attack rate and population size	None	All the data and model assumptions
$N_{a,t,S}$ (number of symptomatic infections)	$N_{a,t,S}=c_{S\|Inf}\times N_{a,t,Inf}$	Product of proportion symptomatic and number of infections	None	All the data and model assumptions
$N_{a,t,SB}$ (number of symptomatic infections as estimated by HPA, assumed biased downwards)	$N_{a,t,SB}=d_{a,t,S}\times N_{a,t,S}$	Product of bias in HPA case estimates and number of symptomatic infections	HPA case estimates (normal likelihood for the middle estimate, with lower and upper estimates assumed to be 3 standard deviations away from the mid-estimate).	The remaining data and model assumptions
$N_{a,t,H}$ (number of hospitalisations)	$N_{a,t,H}=c_{a,t,H\|S}\times N_{a,t,S}$	Product of symptomatic case hospitalisation ratio and number of symptomatic infections	Observed number of hospitalisations (binomial likelihood for the observed hospitalisations with the detection probability $d_{t,H}$ as the proportion and the "true" number of hospitalisations $N_{a,t,H}$ as the size)	The remaining data and model assumptions
$N_{a,t,I}$ (number of intensive care admissions)	$N_{a,t,I}=c_{a,t,I\|H}\times N_{a,t,H}$	Product of intensive care admission to hospitalisation ratio and number of hospitalisations	None	All the data and model assumptions
$N_{a,t,D}$ (number of deaths)	$N_{a,t,D}=c_{a,t,D\|H}\times N_{a,t,H}$	Product of death to hospitalisation ratio and number of hospitalisations	Observed number of deaths (binomial likelihood with the detection probability $d_{t,D}$ as the proportion and the "true" number of deaths $N_{a,t,D}$ as the size)	The remaining data and model assumptions

HPA=Health Protection Agency. ONS=Office for National Statistics

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Table 3| **Posterior summaries of severity of 2009 pandemic A/H1N1 influenza in England. Values are posterior median estimates (95% credible intervals) for all ages**

Parameter	Wave of influenza	
	June–August	September–February
Symptomatic case severity ratio (%):		
Hospitalisation (sCHR)	0.54 (0.33 to 0.82)	0.55 (0.28 to 0.89)
Intensive care admission (sCIR)	0.05 (0.03 to 0.08)	0.10 (0.05 to 0.16)
Fatality (sCFR)	0.015 (0.010 to 0.022)	0.025 (0.013 to 0.040)
Infection severity ratio (%):		
Hospitalisation (CHR)	0.19 (0.12 to 0.29)	0.19 (0.10 to 0.32)
Intensive care admission (CIR)	0.02 (0.01 to 0.03)	0.03 (0.02 to 0.06)
Fatality (CFR)	0.005 (0.004 to 0.008)	0.009 (0.004 to 0.014)
Numbers infected, by severity*:		
Total (N_{Inf})	1 750 000 (1 235 000 to 2 470 000)	3 909 000 (2 316 000 to 8 223 000)
Symptomatic (N_S)	606 100 (419 300 to 886 300)	1 352 000 (829 900 to 2 806 000)
Hospitalisation (N_H)	3 200 (2 300 to 4 700)	7 500 (5 900 to 9 700)
Intensive care admission (N_I)	310 (200 to 480)	1 340 (1 030 to 1 790)
Fatality (N_D)	90 (80 to 110)	340 (310 to 380)
Attack rates (%):		
Infection (IAR)	3.4 (2.4 to 4.8)	7.7 (4.6 to 15.0)
Symptomatic (SAR)	1.2 (0.8 to 1.7)	2.7 (1.7 to 5.3)
Proportion of infections that are symptomatic ($c_{S|Inf}$) (%)	35 (26 to 45)	35 (26 to 45)
Detection probability (%):		
Symptomatic (d_S)	40 (24 to 59)	36 (19 to 57)
Hospitalisation (d_H)	30 (20 to 43)	20 (15 to 25)
Fatality (d_D)	88 (78 to 95)	90 (80 to 96)

*Numbers rounded to the nearest 100 for infections, symptomatic infections, and hospitalisations, and to the nearest 10 for intensive care admissions and deaths. See table 2 for list of abbreviations and meanings.

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Table 4| **Posterior summaries of infection attack rates in 2009 pandemic A/H1N1 influenza in England, by age and wave of influenza. Values are posterior median estimates (95% credible intervals)**

	Infection attack rate (%)		
Age (years)	**June–August wave**	**September–February wave**	**Total**
<1	8.0 (3.3 to 15.7)	6.1 (2.4 to 18.4)	14.5 (6.6 to 31.5)
1–4	7.2 (3.3 to 13.3)	15.0 (5.3 to 53.1)	22.7 (9.9 to 62.3)
5–14	10.0 (5.9 to 14.9)	19.3 (9.1 to 52.4)	29.5 (16.9 to 64.1)
15–24	3.7 (1.8 to 7.3)	7.0 (3.4 to 22.3)	10.9 (6.3 to 27.1)
25–44	2.8 (1.1 to 6.9)	5.2 (2.1 to 19.4)	8.2 (3.7 to 24.7)
45–64	1.4 (0.5 to 3.4)	5.0 (1.5 to 20.5)	6.4 (2.3 to 22.9)
≥65	0.3 (0.1 to 1.4)	0.5 (0.1 to 3.7)	0.8 (0.2 to 4.9)
Total	3.4 (2.4 to 4.8)	7.7 (4.6 to 15.0)	11.2 (7.4 to 18.9)

BMJ 2011;343:d5408 doi: 10.1136/bmj.d5408

Figures

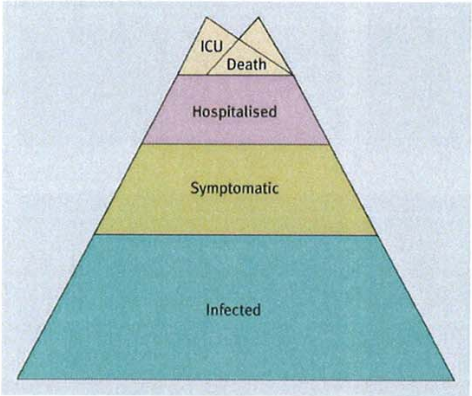

Fig 1 Severity levels for infection with pandemic A/H1N1 influenza. Each level is assumed to be a subset of the level below, with admission to intensive care (ICU) and death assumed to be overlapping subsets of hospitalisation. We therefore assume that no pandemic A/H1N1 deaths occurred outside hospital

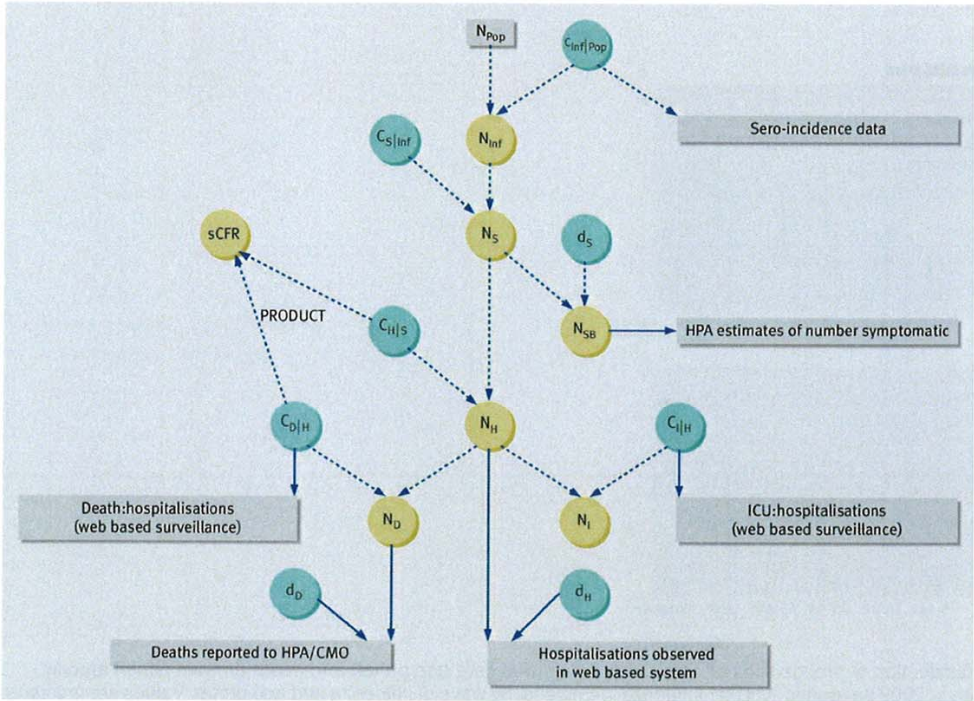

Fig 2 Schematic illustration of relation between data (rectangles) and the quantities of interest (parameters, in circles) in model of severity of 2009 pandemic A/H1N1 influenza in England (see table 2 for descriptions of the parameters). The data and parameters shown are for one age group in the summer wave of influenza, and the age and time period indices are not shown for conciseness. N_{pop} (population size of England in age group) is an (observed) constant, blue circles represent parameters on which we placed prior distributions (reflecting our knowledge about these before the analysis) whether informative or not. Solid lines represent direct evidence, and broken lines represent functional relationships: information flows from the data directly through the solid lines to the parameters, then indirectly through the broken lines to other parameters. Only the symptomatic case fatality ratio (sCFR) is shown, with the other infection and case severity ratios left out for conciseness. (See table 2⇓ for full list of abbreviations)

BMJ 2011;343:d5408 doi: 10.1136/bmj.d5408

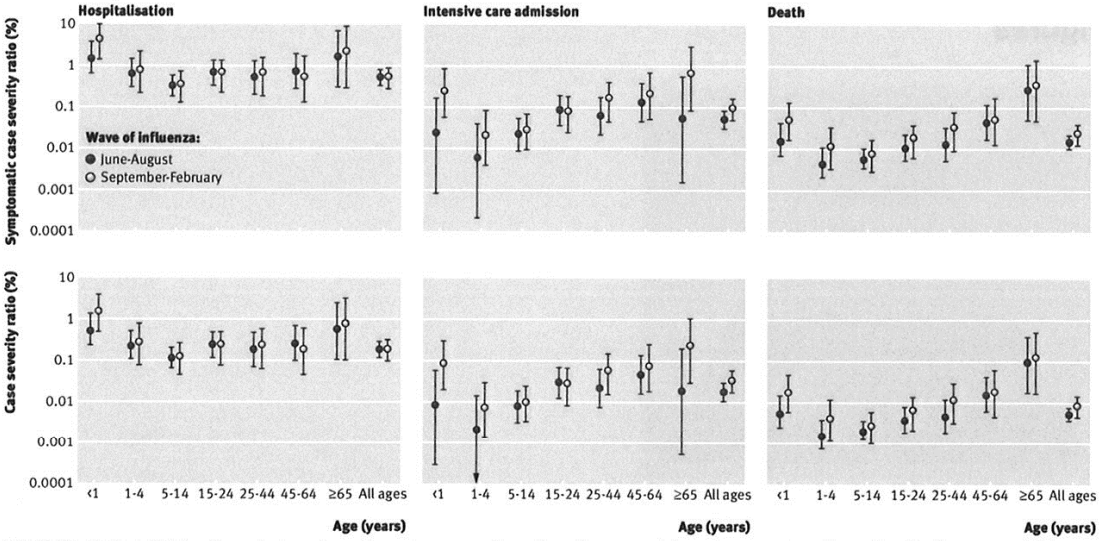

Fig 3 Posterior distribution of symptomatic case severity ratios (top panels) and case severity ratios (bottom panels) in 2009 pandemic A/H1N1 influenza in England, by wave of influenza and age group. Values are medians (95% credible intervals) on a log scale

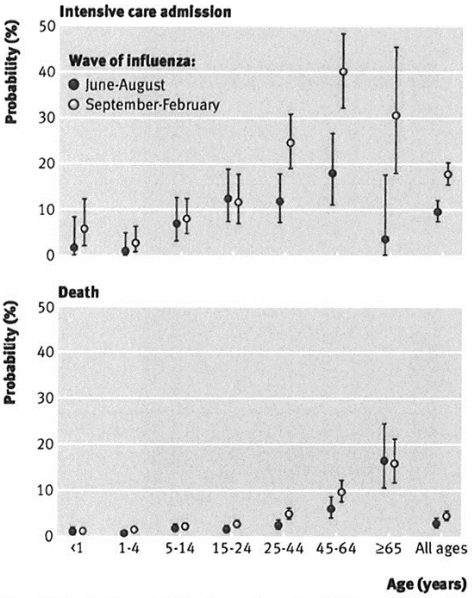

Fig 4 Posterior distribution of probabilities of admission to intensive care (top panel) and death (bottom panel) among hospitalised cases in 2009 pandemic A/H1N1 influenza in England, by wave of influenza and age group. Values are medians (95% credible intervals)

CHAPTER FOUR:
IMPLEMENTING AND EVALUATING THE EVIDENCE: SYNDROMIC SURVEILLANCE IN PRACTICE

This chapter addresses the following research objectives:

- To determine the breadth, value and limitations of syndromic surveillance as applied to public health.

- To determine the adequacy of current evaluation frameworks for evaluating syndromic surveillance.

Within this context, the chapter has a particular focus on the application of syndromic surveillance in identifying the real or potential threat of an emerging infectious disease, particularly in developing regions, and the strengths and weaknesses of current evaluation frameworks.

Syndromic surveillance in the Pacific Island Countries and Territories

Prior to the 2009 (H1N1) influenza pandemic the Pacific Island Countries and Territories (PICTs) had recognised the considerable challenge posed by infectious disease outbreaks in terms of detection and response [1, 2] and the potential impact of emerging infectious diseases [3, 4]. The 2009 influenza pandemic acted as a catalyst for rapidly establishing syndromic surveillance systems, specifically for ILI, using a standardised approach across countries. In March 2010, all PICTs agreed to build upon this simple system and expand it to include the timely reporting of four core syndromes (Acute Fever and Rash; Diarrhoea; ILI; and Prolonged Fever) using common case definitions, for the purpose of early warning and response to meet their IHR obligations [5]. The development and implementation of this syndromic surveillance system is described in the scientific publication '**Pacific-wide simplified syndromic surveillance for early warning of outbreaks'** [6].

This is an example of a syndromic surveillance system being developed to respond to an identified need for a functional surveillance system, capable of identifying and responding to outbreaks in a systematic manner, while taking account of limited local resources.

Towards the end of the first year of implementation of the new system a formative evaluation was conducted. The objective of this study was to evaluate the implementation of the PICTs syndromic surveillance system in terms of adoption of the system, data quality, timeliness of reporting and level of compliance. The study examined whether the system was meeting its objective of serving as an early warning system. As the system extends beyond outbreak detection, the evaluation also explored the capacity of the system to investigate and respond

to outbreaks. The questions addressed were: (i) has the syndromic surveillance system been successfully implemented across the PICTs?; and (ii) is the surveillance system effective in allowing local health authorities to detect unusual cases and clusters of disease early; and to respond rapidly to limit the impact of outbreaks?

Data were collected using: semi-structured key informant interviews with selected PICTs who were involved in the system; observational techniques including field inspections of raw data and data collection methods; analysis of syndromic data reported to WHO; and the reporting of alerts and outbreaks were compared pre and post implementation. In-country evaluations of participating PICTs were chosen based on their participation in the system for a reasonable length of time; implementation approach; and time and resources for the evaluator to travel to participating PICTs. System components and attributes were explicitly identified and timeliness, compliance and proportion of sites reporting were analysed. Success of the system was determined by positive or negative feedback about the system from users, number of countries participating in the system, and the capacity of the system to detect and respond to outbreaks. The results of this study were published in the peer reviewed article '**Sustaining surveillance: evaluating syndromic surveillance in the Pacific'** [7], which is a companion article to the previously mentioned '**Pacific-wide simplified syndromic surveillance for early warning of outbreaks'** [6].

The number of PICTs participating in the system increased from 6 to 20 (of a possible 22) between 2010 November and 2011 September. Respondents were extremely positive about the system's ability to detect outbreaks with informants noting that, because the system was based on syndromes (identified immediately clinically) rather than on laboratory confirmation (which could take weeks), the identification of outbreaks was more rapid than in previous years. In-country key informants universally agreed that the syndromic surveillance system was valuable and a marked improvement over previous systems in allowing early detection and response to outbreaks.

The scientific letter '**Pandemic response in low-resource settings requires effective syndromic surveillance'** [8] comments on how syndromic surveillance can be applied in a developing setting to assist in pandemic planning. This was prompted by Starbuck et al (2012) commenting that there was a significant gap in future responses to severe influenza pandemics in low-resource settings [9]

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Published articles included in this Chapter:

6. Kool JL, Paterson B, Pavlin BI, Durrheim D, Musto J, Kolbe A. Pacific-wide simplified syndromic surveillance for early warning of outbreaks. Global Public Health 2012;7(7):670-681.
7. Paterson BJ, Kool JL, Durrheim DN, Pavlin B. Sustaining surveillance: evaluating syndromic surveillance in the Pacific. Global Public Health 2012;7(7):682-694.
8. Paterson BJ, Durrheim DN, Hardie K. Pandemic response in low-resource settings requires effective syndromic surveillance. Influenza and Other Respiratory Viruses 2013;doi:10.1111/irv.12098.

PAPER SIX: PACIFIC-WIDE SIMPLIFIED SYNDROMIC SURVEILLANCE FOR EARLY WARNING OF OUTBREAKS.

Kool JL, Paterson B, Pavlin BI, Durrheim D, Musto J, Kolbe A. Pacific-wide simplified syndromic surveillance for early warning of outbreaks. Global Public Health 2012;7(7):670-681.

Global Public Health
2012, 1–12, iFirst article

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Pacific-wide simplified syndromic surveillance for early warning of outbreaks

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The International Health Regulations require timely detection and response to outbreaks. Many attempts to set up an outbreak early warning system in Pacific island countries and territories (PICTs) have failed. Most were modelled on systems from large countries; large amounts of data often overwhelmed small public health teams. Many conditions required overseas laboratory confirmation, further reducing timeliness and completeness. To improve timeliness and reduce the data burden, simplified surveillance was proposed, with case definitions based on clinical signs and symptoms without the need for laboratory confirmation or information on symptoms, location, sex and age. After trials in three PICTs, this system was implemented throughout the Pacific. Enthusiastic adoption by public health staff resulted in 20 of 22 PICTs reporting weekly to the World Health Organization within 12 months of starting to use the system. In the first year, the system has detected many infectious disease outbreaks and facilitated timely implementation of control measures. For several Pacific countries and territories, this is the first functional and timely infectious disease surveillance system. When outbreak detection is the principal objective, simplification of surveillance should be a priority in countries with a limited public health system capacity.

Keywords: early warning; syndromic surveillance; Pacific; infectious diseases; outbreak detection; outbreak response

Background

The International Health Regulations (IHR), updated in 2005 and adopted by all World Health Organization (WHO) member states, require that countries have the capacity to detect, assess, notify and report public health events of potential international concern, including infectious disease outbreaks, in a timely fashion (World Health Organization 2008a). The feasibility of all countries acquiring the surveillance capacity to comply with this requirement has been questioned (Fidler and Gostin 2006). The 2009 influenza pandemic confirmed the limited capacity of

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many countries to meet IHR requirements, particularly with regard to surveillance and response (Wilson *et al.* 2010).

A combination of surveillance methods has been suggested as part of IHR implementation, including rumour surveillance, event-based surveillance and indicator-based surveillance. The latter category includes 'classic' notification of numbers of cases of disease or syndromes (World Health Organization 2008a). For a discussion of the different types of surveillance systems, see, for example, the textbook by Teutsch and Churchill (2000).

The Pacific Ocean covers approximately a third of the earth's surface. It contains about 3000 islands in 22 countries and territories, including several of the world's smallest independent countries: seven Pacific island countries and territories (PICTs) have fewer than 25,000 residents (World Health Organization 2010, Secretariat of the Pacific Community 2011b). Some of the remotest areas in the world are in the Pacific. The PICTs are culturally and ethnically diverse, and at vastly different levels of development. Not including New Zealand, the Pacific islands region was estimated in June 2011 to have a population of 10 million, 6.7 of whom lived in Papua New Guinea (Secretariat of the Pacific Community 2011b).

Rates of infectious diseases are high in the Pacific (Singh *et al.* 2001, World Health Organization 2008b, Gani 2009, Johnson *et al.* 2010, UNESCAP 2011). The impact of infectious disease epidemics in the Pacific is exacerbated by a limited health infrastructure, geographic isolation, infrequent transportation and an inadequate communication infrastructure (Nelesone *et al.* 2006). In addition, populations are sometimes immunologically naive to imported diseases, leading to higher attack rates and increased severity (Morens *et al.* 2004, Duffy *et al.* 2009). Rates of non-communicable diseases, such as diabetes and heart disease, are among the highest in the world as well, increasing the vulnerability to infectious diseases. Historically, epidemics have impacted the Pacific severely. The first introduction of measles resulted in 40% mortality in Fiji in 1875 (Morens *et al.* 2004) and the 1918 'Spanish Flu' caused up to 25% mortality on some islands (McLeod *et al.* 2008). Notable recent epidemics include cholera, typhoid fever, dengue and influenza.

Outbreak detection and response in PICTs are constrained by the limited availability of trained public health workers who have to divide their time between many priorities. In the past, Pacific small island nations have tried to implement ambitious disease notification systems, based on the routine notifiable disease systems that have been in use by most larger countries of the world since the first half of the twentieth century. These 'classic' surveillance systems rely on clinicians making or suspecting a diagnosis, confirming this suspicion by laboratory diagnosis and then notifying health authorities when the condition is on a predefined list. The number of notifiable conditions in Pacific island countries typically varied from 20 to over 60. Many of these conditions required overseas laboratory confirmation, and, in practice, were rarely reported. In addition, many systems required a detailed breakdown of age groups, sex, and other parameters. As an example, one PICT used a form with over 430 fields to be filled in monthly by all clinics. These large amounts of data overwhelmed national surveillance units (often just one person). Another problem noted frequently is that clinicians often are reluctant to report a suspected diagnosis before it has been confirmed by an overseas laboratory. The resulting poor sustainability, timeliness, and completeness made these systems ineffective for outbreak detection.

Syndromic surveillance has been implemented in a limited number of developing countries in Africa and Asia (Durrheim *et al.* 2001, John *et al.* 2004). Case definitions are based on clinical signs and symptoms rather than laboratory confirmation, making it particularly useful in settings with limited access to laboratories, a common feature in most PICTs. The gain in timeliness provided by a syndromic system is substantial (Nelesone *et al.* 2006).

To address the need for improved early warning, we proposed to simplify surveillance as much as possible with as little data as possible to be collected for the early warning of the most common outbreak-prone diseases.

Methods

Pilot projects

We conducted a literature review and consulted with technical experts (national counterparts, Secretariat of the Pacific Community (SPC), WHO Regional Office, regional academic institutions, and the US Centers for Disease Control and Prevention). A functional model for syndromic surveillance of outbreak-prone conditions with its core components was first trialled successfully in India and in a southern African rural setting (Durrheim *et al.* 2001, John *et al.* 2004).

The core theoretical components of these systems were adapted and trialled in Tuvalu to validate their application in a remote Pacific Island setting (Nelesone *et al.* 2006). A similar system was also trialled in Niue and Nauru. Guam and French Polynesia had independently implemented reporting systems that included disease syndromes.

During the 2009 influenza pandemic, a Pacific regional surveillance system was implemented by the WHO in collaboration with all PICTs and the SPC. This consisted of reporting of syndromic influenza-like illness (ILI) cases as well as laboratory-confirmed influenza (Musto *et al.* 2010).

At a meeting in Madang in 2009, Pacific Ministers of Health reviewed the experience with simplified syndromic surveillance and requested that the WHO and the SPC further develop a standardised simplified syndromic surveillance system (SSS) for the Pacific based on the experiences in Tuvalu, Niue, Nauru, French Polynesia and Guam.

Decision-making process

A meeting was organised in March 2010 for IHR national focal points and surveillance coordinators from all PICTs. After extensive discussions, participants selected a core set of four syndromes, agreed on procedures and timelines for reporting, and determined appropriate responses to each syndrome. It was agreed that each Pacific jurisdiction would implement the system within 12 months and that an evaluation would be conducted after one year.

Case definitions used

The agreed standardised Pacific SSS focuses on the reporting of four core syndromes: acute fever and rash, diarrhoea, ILI, and prolonged fever; all using standard case definitions (Table 1). The syndromes were selected to cover major outbreak-prone

Table 1. Case definitions for the four core syndromes.

Syndrome	Case definition	Important diseases to consider
Acute fever and rash	Sudden onset of fever,[a] with acute non-blistering rash	Measles, dengue, rubella, meningitis, leptospirosis
Diarrhoea	Three or more loose or watery stools in 24 hours	Viral and bacterial gastroenteritis including cholera, food poisoning, ciguatera fish poisoning
Influenza-like illness (ILI)	Sudden onset of fever,[a] with cough and/or sore throat	Influenza, other viral or bacterial respiratory infections
Prolonged fever	Any fever[a] lasting 3 or more days	Typhoid fever, dengue, leptospirosis, malaria, other communicable diseases

[a]Fever is defined as 38°C/100.4°F or higher. If no thermometer is available, fever or chills reported by the patient or the caregiver are also acceptable.

infectious diseases that are important for the Pacific, and which can be recognised with reasonable sensitivity and specificity by using a limited number of easy to assess signs and symptoms (Pavlin *et al.* 2010). All case definitions were based on existing internationally accepted standards and examples. An effort was made to keep the definitions practical and simple.

Integration with existing surveillance systems

The system complements existing surveillance systems and, where possible, builds on existing data-collection mechanisms, reporting pathways and response procedures. It does not replace the need for laboratories to report confirmed cases of important outbreak-prone diseases, such as leptospirosis, influenza, dengue and typhoid fever. It does, however, replace the routine collection of large quantities of data about individual patients in situations where such data would not be used for early warning purposes (World Health Organization and Secretariat of the Pacific Community 2010a).

Flexibility of implementation

To avoid overwhelming the national data management capacity, most countries chose to initially introduce the SSS at one or a few sentinel sites, usually the largest hospitals, and not to attempt population-wide coverage. The rationale was that significant outbreaks would result in increased cases presenting at the major health-care sites. The number of sentinel sites varies by PICT, from 1 to 25 (Paterson *et al.* 2012).

Data collection methodology also allowed some flexibility. Some countries rely on data extraction from outpatient department logbooks; others use a form with two to five questions posed to a patient by a triage nurse when the patient presents. Doctors and nurses interviewing and examining patients were trained on the case definitions and encouraged to note these on specific forms or in specific columns in logbooks. New Caledonia, Guam and French Polynesia already had well-functioning weekly surveillance systems and decided to retrieve the case numbers from these systems. The Cook Islands were able to add a simple entry screen to their electronic

medical records system, and two countries (Fiji and Papua New Guinea) have implemented reporting using mobile phones.

Reporting pathways, feedback reporting and timing

At the beginning of each week, sentinel sites report their tallies from the previous week to the national level. National surveillance coordinators review this data and note any unexpected increase in cases. National coordinators report the numbers weekly to the WHO Pacific Support Division in Fiji, and they are actively reminded if the report is not received on time. National coordinators are also encouraged to produce a one-page surveillance bulletin every four weeks for feedback to their reporting sites and other stakeholders. Each Thursday the WHO posts information generated from the SSS on the 'PacNet' email list server (Pacific Public Health Surveillance Network 2011) and on the Internet (Secretariat of the Pacific Community 2011a, World Health Organization 2011), so that PICTs are informed about communicable disease activity in nearby jurisdictions, and to allow regional trends to be identified. An automated system has been developed using Microsoft Excel, with plans to migrate to Microsoft Access. A report table lists the number of cases of the four syndromes by PICT for the week concerned, highlighting numbers that exceed 90% of numbers reported by that country in all previous weeks (Figure 1). A set of 20 small charts shows the trend of cases of diarrhoea, ILI and prolonged fever for the last 26 weeks (i.e., half a year) in each participating PICT (Figure 2).

Pacific Syndromic Surveillance -- weekly report

Year: 2011 Week: 47 ending on 27 November 2011

Country / Area	Last update received	Sites reporting	Acute fever and rash Sudden onset of fever with acute nonblistering	Diarrhoea 3 or more loose or watery stools in 24 hrs	Influenza-like illness Sudden onset of fever, plus: cough and/or sore	Prolonged fever Any fever lasting 3 days or longer
American Samoa	29 Nov 2011	3	0	26	54	1
Cook Islands	29 Nov 2011	12	0	7	0	0
Federated States of Micronesia	30 Nov 2011	4	1	16	25	2
Fiji	30 Nov 2011	7	13	173	596	24
French Polynesia	30 Nov 2011	15		45	21	1
Guam	29 Nov 2011	1		1	1	
Kiribati	30 Nov 2011	2	1	54	105	17
Marshall Islands	1 Dec 2011	2	16	16	56	95
Nauru	1 Dec 2011	1	0	13	0	0
New Caledonia	30 Nov 2011	8		2	0	27
New Zealand	30 Nov 2011	21			34	
Niue	29 Nov 2011	1	1	6	16	1
Northern Mariana Islands	30 Nov 2011	2	0	6	25	1
Palau	29 Nov 2011	1	0	25	34	2
Papua New Guinea	30 Nov 2011	1	0	0	0	0
Pitcairn Islands	1 Dec 2011	0	0	0	0	
Samoa	30 Nov 2011	2	1	13	87	0
Solomon Islands	30 Nov 2011	4	6	27	44	13
Tokelau	29 Nov 2011	1	0	6	10	0
Tonga	30 Nov 2011	1	0	20	30	0
Tuvalu	1 Dec 2011	1	0	0	7	0
Vanuatu						
Wallis & Futuna	27 Nov 2011	1	0	6	8	0

Figure 1. Syndromic Surveillance weekly summary table for week 47, 2011, as distributed through the PacNet email list server. The table is generated by a Microsoft Excel spreadsheet, automatically highlighting case numbers that exceed 90% of historical values. The high numbers of cases in the Marshall Islands were caused by an epidemic of dengue.

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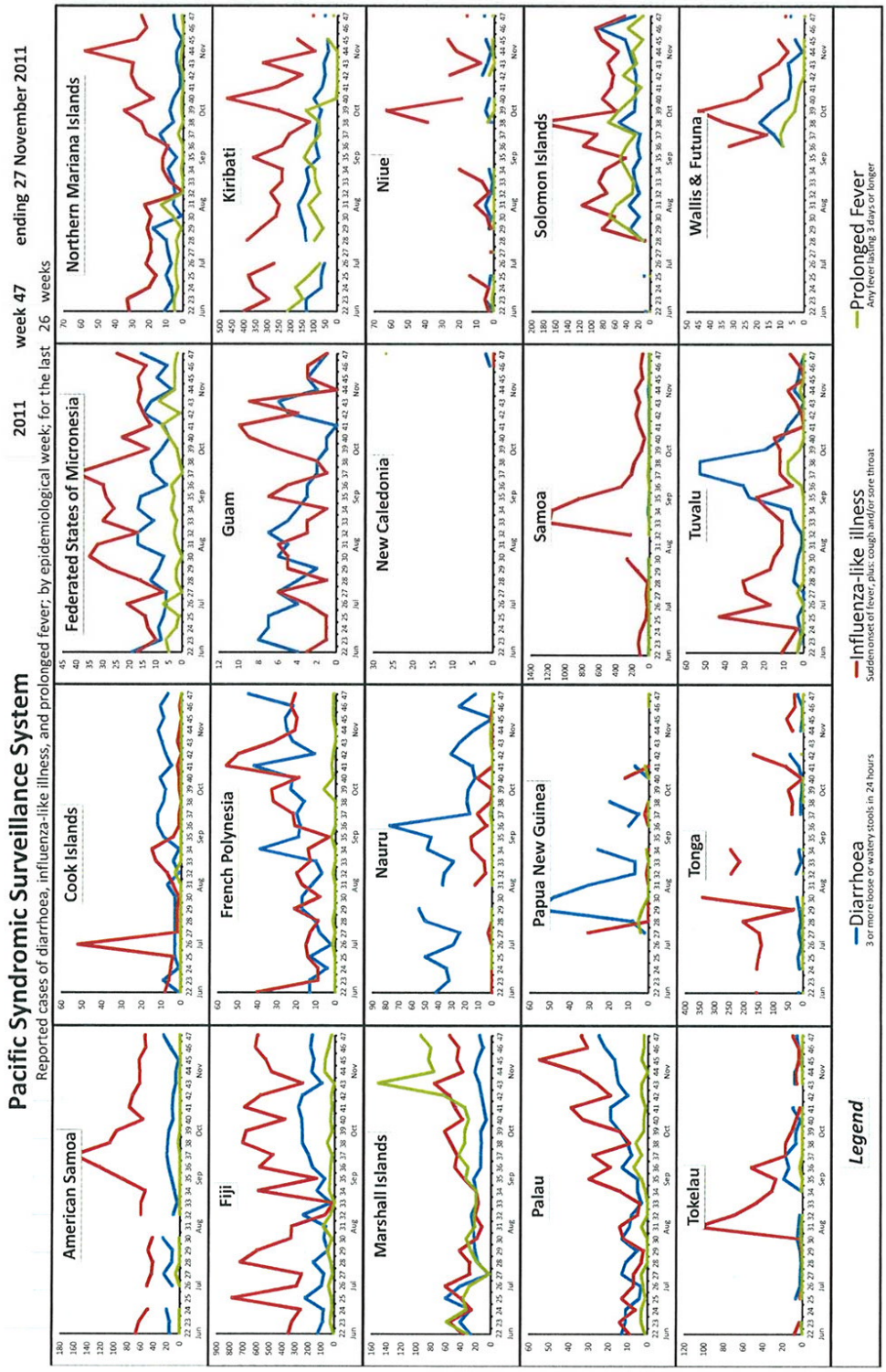

Figure 2. Pacific Syndromic Surveillance weekly summary charts for week 47, 2011, as distributed through the PacNet email list server. Influenza-like illness outbreaks are visible in Cook Islands, American Samoa, Samoa, Solomon Islands, Tokelau, Tuvalu, and Niue. Several of these were later confirmed as influenza by laboratory, and some were found to be caused by identical strains. Diarrhoeal disease outbreaks are visible in Tuvalu and Tokelau: these were related to a drought. The high numbers of prolonged fever and ILI in the Marshall Islands were associated with a dengue outbreak.

In addition, a weekly narrative is included in the email body, providing more information on current outbreaks and other public health events of concern, as provided by the national health authorities and other sources.

Implementation support

Each PICT received on-site support from the SPC or WHO to implement the system. PICTs have further been supported by remote consultation with the two agencies; for example in the establishment of thresholds or through the provision of advice for the investigation of potential outbreaks. To further facilitate the implementation and troubleshooting of the Pacific SSS, the 'Practical Guide for Implementing Syndromic Surveillance in PICTs (World Health Organization and Secretariat of the Pacific Community 2010a) was developed by the WHO and SPC and made freely available to the PICTs. A 'Pacific Outbreak Manual' (World Health Organization and Secretariat of the Pacific Community 2010b) was also developed by the two agencies in consultation with PICT representatives. This manual provides advice on dealing with outbreaks of each of the four syndromes (including differential diagnosis, confirmation strategies and control methods).

Results

Outbreak identification

When a graphic representation is used to highlight the trends, it is easy to recognise unusual increases in reported cases (Figures 2–5). After several months of data had been collected, several PICTs established thresholds based on historical averages and standard deviations, using simple formulae in computer spreadsheets. As data become available for multiple years, it will be possible to establish thresholds that take seasonal variations into account.

Three examples from Fiji, Nauru and Tuvalu illustrate the usefulness of the SSS. Two peaks in ILI cases in Fiji were later confirmed in the laboratory as influenza. The Fiji example also shows a way to account for variations in the number of reporting sites, as employed by several PICTs (Figure 3). A large outbreak of diarrhoea in Nauru at the beginning of 2011, caused by a breakdown of drinking-water disinfection, was identified by the surveillance system (Figure 4). The rapid detection enabled a timely response: the public was warned and additional chlorine was added to the reticulation system, resulting in rapid interruption of the outbreak. Figure 5 shows reported cases of ILI and diarrhoea in Tuvalu from November 2010 to September 2011. At least two peaks of ILI are visible, in weeks 6 and 19. The peak in week 6 was later confirmed as an outbreak of influenza A/H1N1; the week 19 peak was later confirmed as an outbreak of influenza B. A sharp rise in cases of diarrhoea is visible more recently and is associated with a severe drought. In all three outbreaks in Tuvalu the syndromic surveillance resulted in a timely recognition so that control measures could be implemented.

Discussion

For many PICTs, the Pacific SSS provides for the first time a well-functioning and timely reporting system that enables them to achieve some of the key capacities

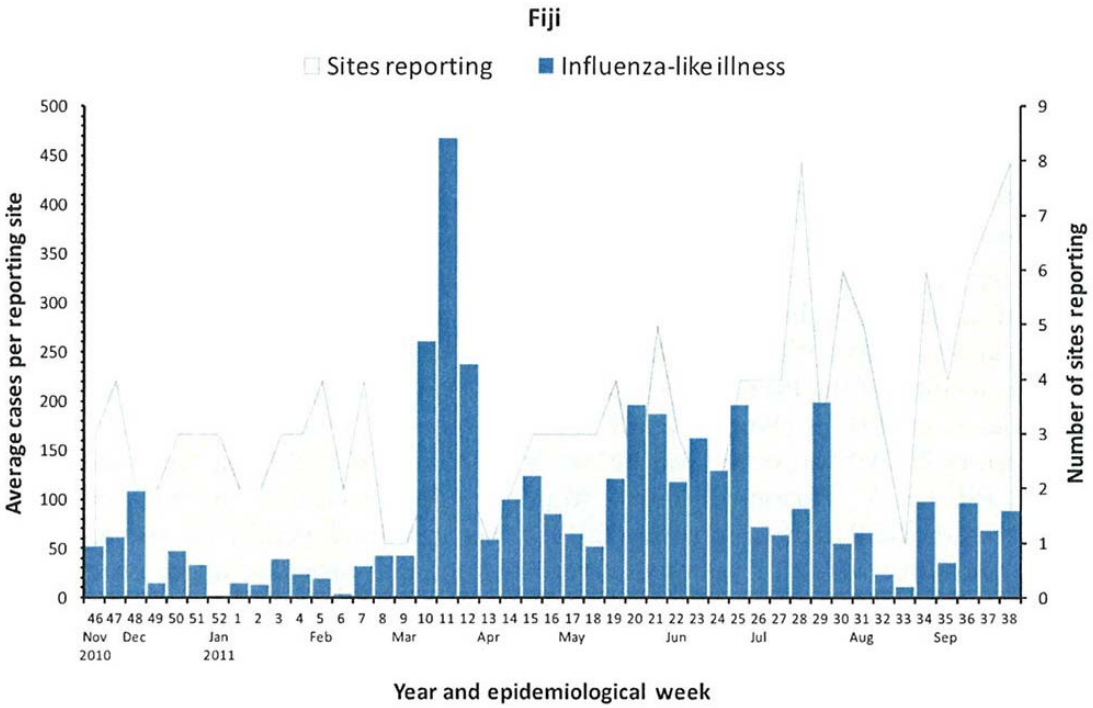

Figure 3. Cases of influenza-like illness and number of sites reporting in Fiji, from November 2010 to September 2011, by year, month, and epidemiological week. The number of sites that were reporting varied substantially, and this affected the numbers of reported cases; to adjust for this, the average number of cases per site per week is shown. An outbreak of influenza A caused the peak in week 11; the cluster between weeks 19 and 25 was caused by influenza B. (Laboratory information is courtesy of the Fiji Ministry of Health).

required under the IHR. Attaining these capacities can be challenging for countries with limited public health resources (Fidler and Gostin 2006, Wilson *et al.* 2010). Important factors in the success of the Pacific SSS are the low data burden; strong support at all levels of health ministries and departments; the piloting of SSS by a number of PICTs; flexibility of implementation; and active participation in decisions on case definitions and procedures, the latter assuring ownership by PICT health authorities.

A stand-out feature of this system, when compared to previous systems, is its simplicity and the focus on a limited number of syndromes that are relevant to the region and can be assessed easily through the use of practical case definitions. In the past, Pacific small island nations have had complicated disease notification systems that were difficult to sustain and may not have been a priority for busy public health workers. In addition, many important diseases could only be confirmed in overseas laboratories. As a result, many surveillance systems suffered long delays before the reported information was analysed and reported, significantly weakening their early warning and response functionality.

Limitations of the system are mostly related to the simplification and data-burden reduction. The exclusive reporting of syndromes means that a diagnosis will not be available at the time when an increase in cases is first noticed and reported. The omission of sex and age information, geographic location, and symptoms means that an additional investigation will be required whenever an outbreak is suspected.

In most cases, such an investigation can be straightforward and rapid, such as reviewing some patient information and discussing the cases with attending clinicians, but in some cases a full-fledged investigation with line lists, epidemic curves and specimen collection may be necessary.

Most PICTs chose to implement a sentinel surveillance model, so that only trends can be detected, but no population-based incidence rates or total number of cases estimated. If such information is needed, then this, too, will require additional surveys and investigations. Comparison of case numbers or rates between countries is not possible, because of differences in data collection methods and the absence of accurate denominator data. In PICTs with more than a few reporting sites, the number of sites reporting can vary substantially per week. To achieve good reporting completeness, active follow-up and reminders by the national surveillance coordinator is required. Some degree of adjustment for the variation in the number of reporting sites can be attempted, for example, by calculating the average number of cases per reporting site, as shown in Figure 3.

Experience with syndromic surveillance in a number of low- and middle-income countries in different regions, including Asia, Africa, and now the Pacific, has clearly demonstrated its usefulness across different epidemiological, ethno-cultural and socio-economic contexts. The generic attributes are clearly translatable and flexible to local adaptation.

In a region where infectious disease outbreaks and epidemics are not uncommon, the ability to detect outbreaks is of high public health importance. In its first year of

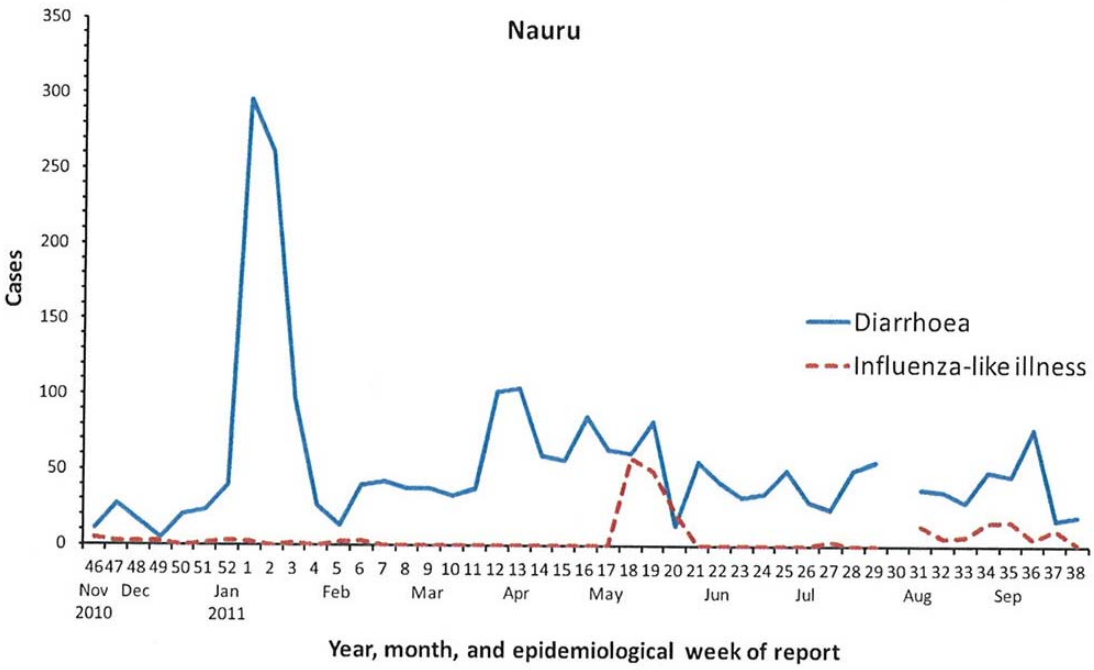

Figure 4. Cases of diarrhoea and influenza-like illness in Nauru, reported through the syndromic surveillance system. The outbreak in diarrhoeal illness in January 2011 was caused by a breakdown in water disinfection. After the health authorities were alerted by the syndromic surveillance data, they were able to quickly interrupt the outbreak by adding chlorine to the drinking water. No data was reported to WHO in week 30. (Outbreak information is courtesy of Drs Soakai, Tangitau and Soe, Nauru Ministry of Health).

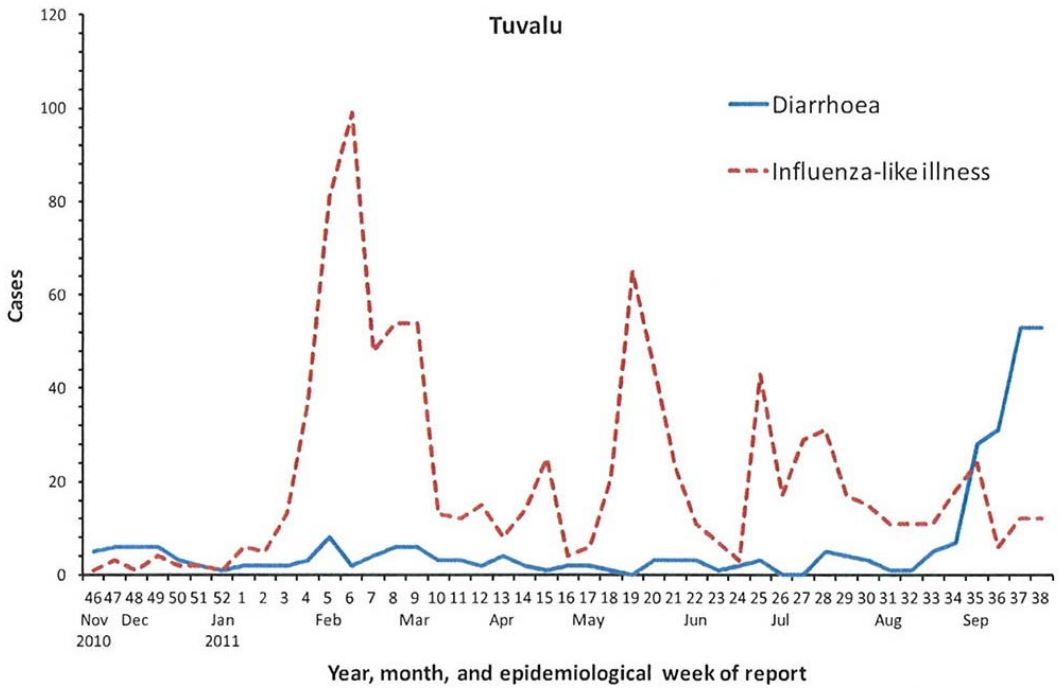

Figure 5. Reported cases in Tuvalu of influenza-like illness (ILI) and diarrhoea, November 2010 to September 2011. It clearly shows several peaks of influenza-like illness. Two of these were confirmed by laboratory as caused by the influenza virus. The outbreak of diarrhoea starting in week 35 was associated with a prolonged drought, with a resulting water shortage. (Outbreak information is courtesy of Dr Stephen Homasi, Tuvalu Ministry of Health).

implementation, the Pacific SSS has convincingly identified a number of outbreaks, enabling rapid public health responses. In addition, the system has greatly improved communication across borders on infectious disease events. The strengthened regional outbreak detection and response capacity will help reduce the impact and spread of infectious diseases within and between countries and territories in the Pacific. This system is likely to be easily adaptable to other resource-limited areas looking to improve their outbreak detection capacities.

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PAPER SEVEN: SUSTAINING SURVEILLANCE: EVALUATING SYNDROMIC SURVEILLANCE IN THE PACIFIC.

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Sustaining surveillance: Evaluating syndromic surveillance in the Pacific

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Prior to the 2009 H1N1 pandemic, the Pacific Island Countries and Territories (PICTs) had agreed to develop a standardised, simple syndromic surveillance system to ensure compliance with International Health Regulations requirements (rapid outbreak detection, information sharing and response to outbreaks). In October 2010, the new system was introduced and over the next 12 months implemented in 20 of 22 PICTs. An evaluation was conducted to identify strengths and weaknesses of the system, ease of use and possible points for improvement. An in-country quantitative and qualitative evaluation in five PICTs identified that the most important determinants of the system's success were: simplicity of the system; support from all levels of government; clearly defined roles and responsibilities; feedback to those who collect the data; harmonisation of case definitions; integration of data collection tools into existing health information systems; and availability of clinical and epidemiological advice from external agencies such as the World Health Organization and the Secretariat of the Pacific Community. Regional reporting of alerts, outbreaks and outbreak updates has dramatically increased since implementation of the system. This syndromic system will assist PICTs to detect future influenza pandemics and other emerging infectious diseases and to rapidly contain outbreaks in the Pacific.

Keywords: syndromic surveillance; Pacific; evaluation; early warning system; infectious diseases

Introduction

In 2010, in recognition of the challenges posed by recent infectious disease outbreaks (Duffy *et al.* 2009, Thein *et al.* 2010) and the potential impact of emerging infectious diseases (Morens *et al.* 2004), Pacific Island Countries and Territories (PICTs) commenced implementing a standardised, simple syndromic surveillance system (Kool *et al.* 2012). This system was built on the introduction of influenza-like-illness (ILI) surveillance by all PICTs during the 2009 influenza pandemic. Further details on the history, functionality and implementation of this system are reported elsewhere (Kool *et al.* 2012).

Critics have questioned the value and sustainability of syndromic surveillance when public health resources are scarce (Reingold 2003, Koo 2005). Both formative and summative evaluations of syndromic surveillance systems are essential to explore

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determinants of successful system implementation and to allow adjustment during system expansion. Evaluation also ensures that opportunity costs associated with system development are justified by improved outbreak detection and response (Sosin 2003).

Towards the end of the first year of system implementation, a formative study was conducted to evaluate the implementation of the Pacific syndromic surveillance system, with a focus on degree of adoption, data quality, reporting timeliness and compliance and to ensure that required changes were identified early in the life of the system. The study examined the system's ability to act as an early warning system for detecting, investigating and responding to outbreaks, and explored factors that appeared to contribute to successful syndromic surveillance system functioning in low-resource settings.

Methods

The syndromic surveillance system evaluation was undertaken by an independent, external epidemiologist (BP) engaged by the World Health Organization (WHO), between May 2011 and September 2011, using: semi-structured key informant interviews during in-country visits in five PICTs; observational techniques including field inspections of raw data and data collection methods; and analysis of syndromic data reported to WHO by all participating PICTs. In-country evaluations of participating PICTs were chosen based on their participation in the system for a reasonable length of time; implementation approach; and time and resources for the evaluator to travel to participating PICTs. The evaluation was adapted from the Centers for Disease Control and Prevention (CDC) framework for evaluating syndromic surveillance systems (Buehler *et al.* 2004), the WHO guide for monitoring and evaluating surveillance and response systems for communicable diseases (World Health Organization 2006), and formative evaluation techniques commonly used in public health evaluations (Patton 2002, Braun and Clarke 2006). Immediate feedback was provided during in-country visits on how system performance could be improved. To limit possible withholding of relevant information, informants were notified that responses would be anonymised. Country level reports of in-country visits were provided to individual PICTs by the evaluator for confirmation and follow-up.

Key informants included national syndromic surveillance coordinators, senior Health Ministry staff, Directors of Public Health, doctors, nurses and clerks in hospitals and health clinics, statisticians or health information officials and other public health officials, including an expatriate epidemiologist. Additional interviews were conducted with WHO and Secretariat of the Pacific Community (SPC) staff. Interview guides were pre-prepared for different categories of informants, and interviews were recorded for transcription and thematic analysis (Braun and Clarke 2006). Where possible, collection points were visually inspected and data entry demonstrations observed. The reliability of identified themes was tested with public health officials from six other PICTs, who were interviewed by phone or completed a semi-structured questionnaire by email.

Quantitative data from participating PICTs from November 2010 to September 2011 were analysed in Excel 2007 for timeliness (percentage of participating PICTs reporting prior to the WHO weekly deadline) and compliance (percentage of participating PICT reporting to WHO each week and percentage of sites reporting from each PICT). Data quality was assessed during in-country visits by observing data collection practices and comparing patient-level data with data captured in the syndromic surveillance system.

Markers of system performance included the perceptions of key informants, the country participation and compliance rates and the capacity of the system to detect and respond to outbreaks, as recollected by key informants and contrasted with reports to WHO. The reporting of alerts, outbreaks and outbreak updates to the PacNet listserver, which has been established for longer than a decade for the rapid communication of epidemic threats in the region, were also examined and counted for the years 2010 and 2011 (before and after the implementation of the system). This count does not include reports duplicated in French. Regional alerts for PICTs and New Zealand were included in the count. Where alerts for a syndrome across multiple PICTs were notified in the same report, this was counted as a single alert.

Results

Six PICTs were approached for in-country interviewing with one refusal. Forty-three key informants were interviewed in-country: Cook Islands ($n = 10$), Fiji ($n = 12$), Kiribati ($n = 4$), Nauru ($n = 8$) and Tuvalu ($n = 9$). A small number (7) of more remote informants were interviewed by phone or email: American Samoa ($n = 1$), Guam ($n = 1$), Palau ($n = 1$), Papua and New Guinea ($n = 1$), Solomon Islands ($n = 2$) and Tonga ($n = 1$).

System components and attributes

The purpose of the system is 'To develop a simple, sustainable system that allows local health authorities to detect unusual cases and clusters of disease early, in order to respond rapidly to limit the impact of outbreaks' (World Health Organization and Secretariat of the Pacific Community 2010). The system is based on the weekly reporting of four core syndromes (ILI, diarrhoea, prolonged fever and acute fever with rash), using common case definitions, to improve rapid outbreak detection, information sharing, response to outbreaks, and hence ensure compliance with International Health Regulation (IHR) requirements (Fidler and Gostin 2006, World Health Organization 2008). System components and attributes are described in Table 1.

Acceptability and timeliness

The number of PICTs participating in the system increased from 6 to 20 of a possible 22 between November 2010 and September 2011 (Figure 1). During this period, 631 country reports were submitted to WHO. Ninety-one percent (575/631) of reports were received on time and this has steadily improved (Figure 1). After a significant decrease in 1 week (Week 9, 2011), it was recognised that reminders and

Table 1. Pacific syndromic surveillance system: system components and attributes.

	System components
System structure	Supported by WHO and SPC (including training); support at all levels of government; implementation manual 'Practical guide for implementing syndromic surveillance in Pacific Island Countries and Territories 2010' (World Health Organization and Secretariat of the Pacific Community 2010); sentinel sites generally based at major hospitals or health clinics; national focal-point for syndromic surveillance (responsible for tallying, analysing data, identifying outbreaks, initiating outbreak investigation and reporting).
Case ascertainment	Standardised case definitions of four core syndromes (influenza-like-illness – ILI, diarrhoea, prolonged fever and acute fever with rash); a fifth 'syndrome' is for unusual events; optional addition of syndromes at the local level; cases generally identified by doctor but occasionally by nurses or health information clerks.
Data collection and analysis	Paper-based (encounter forms, patient registers and logbooks) or electronic reporting mechanisms; guidance provided on analysis; threshold identification.
Reporting	Weekly reporting to WHO (including zero reports); unusual events reported immediately; regular feedback at the local level to surveillance sites and in-country stakeholders; weekly consolidated Pacific syndromic surveillance report sent to stakeholders via PacNet listserv (also made available on SPC and WHO websites).
Outbreak investigation and response	Thresholds for investigation; outbreak responses generally based on 'Pacific outbreak manual' (World Health Organization and Secretariat of the Pacific Community n.d.) or customised local outbreak manual; standard outbreak investigation steps; further detail on cases collected in the event of an outbreak; rapid local responses but provision of accessible public health advice or assistance from WHO and/or SPC on request.
	System attributes
Simplicity	Based on the tallying and reporting of cases that meet four syndromic case definitions; does not require laboratory confirmation; high training needs due to staff turnover; perceived as a simple system by users.
Flexibility	Range of approaches implemented by PICTs; adapted from early pandemic influenza surveillance system and other earlier systems; includes a 'fifth syndrome' which captures unusual events; PICTs are able to include additional syndromes based on local needs.
Acceptability	Participants increased from 6/22 to 20/22 during the period November 2010 and September 2011; informants agreed that the system was useful and an improvement on previous systems; 84% of sites reported during the review period; assists PICTs in meeting their International Health Regulations (IHR) obligations.

Table 1 (*Continued*)

	System attributes
Data quality	Variable data quality with some discrepancies between clinical diagnostic data and captured syndromic data; no regular data quality checks; training in the use of thresholds to be implemented in the next training round; high visibility case definitions improved case ascertainment accuracy.
Sensitivity	In areas where sentinel sites had been implemented, the system is sensitive enough to detect outbreaks; in remote areas or areas without sentinel sites, outbreaks could be missed.
Timeliness	Ninety one percent (575/631) of reports were received on time (weekly); rapid identification of increases in cases as based on syndromes rather than laboratory confirmation.

encouragement by the central information unit at WHO was an important factor in ensuring on time reporting. From that date, WHO adopted standard operating procedures which included contacting non-responders at least twice by email or phone to remind them of the weekly reporting deadline. Informants noted that because the system was based on syndromes (identified immediately) rather than on laboratory confirmation (which could take weeks), the identification of outbreaks

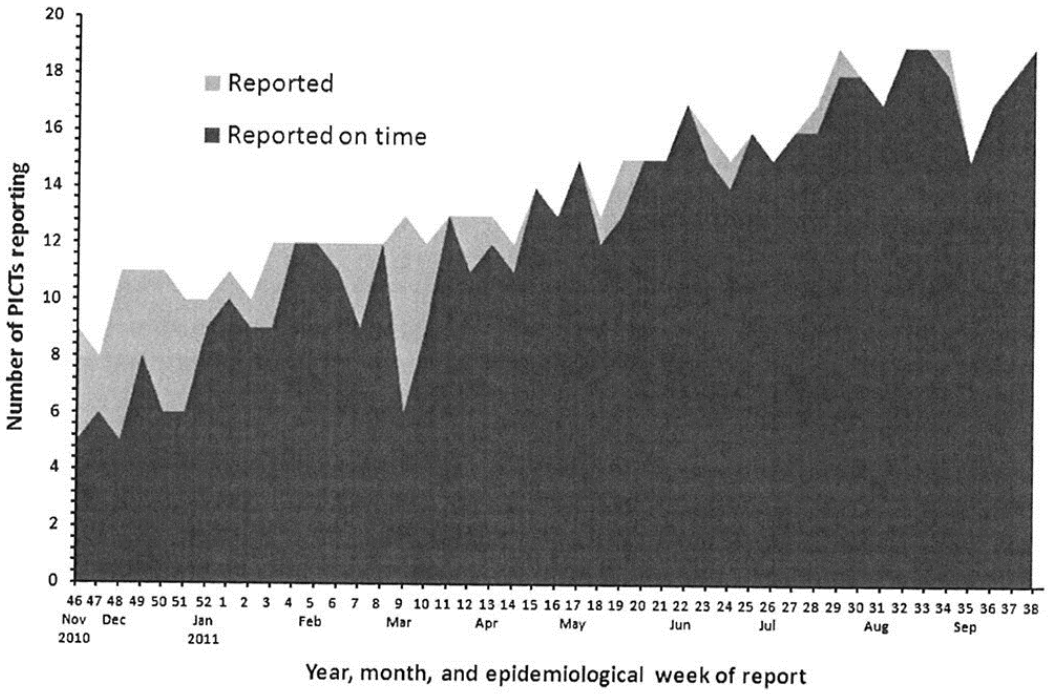

Figure 1. Number of Pacific Island Countries and Territories (PICTs) reporting and number reporting on time (i.e., by Wednesday each week) to the WHO syndromic surveillance hub. Note: There are 22 PICTs (not counting New Zealand), of which 20 participated in the system as of 30 September 2011. The month shown on the horizontal axis is the month containing the last day of the epidemiological week.

was more rapid than in previous years. There was great variability in the number of in-country reporting sites, ranging from 1 to 25, usually depending on population size, with some variation over time. On average 84% of participating in-country sites reported during the review period.

In-country key informants universally agreed that the syndromic surveillance system was valuable and a marked improvement over previous systems in allowing early detection and response to outbreaks. One informant commented: 'this system . . . really everyone's taken to it; everyone feels like they own it, that it's useful'.

Implementation

Country-specific system review found that specific implementation elements varied between PICTs depending on available personnel, medical informatics systems and health system structure. A national surveillance coordinator, based within the Health Ministry, was generally assigned responsibility for system management and weekly reporting to WHO. System features common to all PICTs included: case ascertainment, case counting, outbreak detection, outbreak investigation, outbreak response, reporting and feedback. Some PICTs chose to collect data on other syndromes of local public health importance (e.g., conjunctivitis, dengue-like illness), in addition to the four core syndromes.

There was a wide variation in the type of technology employed to implement the systems. Technology included: automated, web-based mobile phone messaging systems; automatic extraction of the syndrome counts from the electronic medical records system; and paper-based recording and tallying. The use of sophisticated systems was often problematic due to variable Internet connectivity and technical failures. One clinician, when commenting on a highly technical system, noted, 'it's a great system when it works'.

When commenting on how implementation could be improved and what contributed to system success, key factors identified by respondents included simplicity of the system; support at all levels of government; clearly defined roles and responsibilities; feedback, particularly to those who collected the data; harmonisation of case definitions across different in-country health information systems; integration of data collection tools into existing health information systems; and the availability of clinical and epidemiological advice from an external agency such as WHO or SPC.

Data quality

Data quality varied across the implementing PICTs. In-country data review revealed occasional discrepancies between clinical diagnostic data and captured syndromic counts. No regular data quality checks or protocols were identified during the in-country visits. Case ascertainment had generally improved over the first year, with a common feature being periods of improved data collection following training visits by WHO or SPC. It was noted that data collection could deteriorate when new untrained doctors or nurses were appointed in the surveillance sites. Despite data quality variability, increases in syndrome counts routinely triggered outbreak investigations; however, inconsistent data quality hampered preparation and understanding of trends. None of the PICTs visited had defined outbreak thresholds, in part, due to the

limited available historical data and recognised variable data quality. WHO officials noted that threshold development was scheduled to occur during the next system training round. Follow-up interviews identified that thresholds are used in some other PICTs. An epidemiologist commented that 'the system has benefited us by establishing thresholds for these syndromes so it can tell us if we are seeing something unusual'.

Application of case definitions varied, with some obvious confusion in certain PICTs where duplicate health information systems existed to capture syndromes for polio, measles and tetanus elimination programmes, using similar but not identical case definitions (e.g., elimination surveillance uses an age cut-off in its definition of 'acute fever and rash', which is primarily used to identify measles; the syndromic system, in order to be more sensitive, uses no age cut-off for this syndrome). Case definition awareness was highest where syndromes were integrated into the manual patient register or electronic health records system. High visibility case definitions in consulting rooms appeared to assist in achieving case ascertainment accuracy.

Improved outbreak communication and political acceptance

A common response from key informants was that the syndromic surveillance system had improved communication during outbreaks; often expressed as a 'positive spin-off of the system'. This improved communication and openness was reported to have extended beyond outbreak responses. Respondents described how data sharing had improved, and noted that routine reporting of syndromic counts and outbreaks had decreased concerns about the political implications of outbreak reporting. 'People are more comfortable sharing information because they feel that there is no shame and none of the repercussions that they used to fear' (WHO staff member). The reporting of alerts, outbreaks and outbreak updates for the region through the PacNet listserver substantially increased from 29 in 2010 to 224 in 2011 (Figure 2). Informants also discussed how it was easier to share information about outbreaks

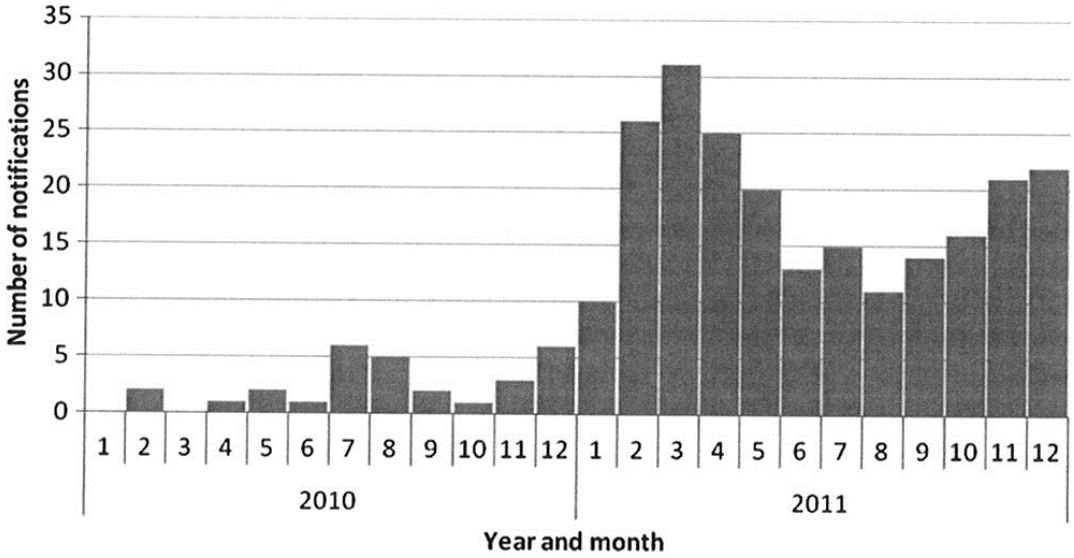

Figure 2. The reporting of alerts, outbreaks and outbreak updates for the region notified through the PacNet listserver, by month, 2010–2011.

once there were a larger number of PICTs participating in the system, as the regular reporting by many PICTs demonstrated that outbreaks were not uncommon and their PICT would not be singled out. Some concern was expressed by the Director of Health Services from one PICT, who noted negative trade ramifications following a media report implicating his country as the source of an influenza outbreak.

Clinicians consistently mentioned that regular information about outbreaks in the region improved their motivation to participate in the system. A senior medical officer reported: 'It's useful so that we can alert our doctors and we can know if someone is coming from these countries then we can know they might have this [disease]'.

Requirement for system support

Interviewees commented that the clinical and epidemiological support provided by WHO and SPC was integral to system success. The agencies had collaborated to provide in-country training at system introduction, and respondents reported regularly seeking advice on appropriate responses to outbreaks, particularly for uncommon diseases. Senior in-country key informants remarked positively on the unified approach that had established system credibility and the high-level support (provided by the Pacific Health Ministers at their biennial Meeting) that had confirmed the international importance of the regional early warning system. High-level support was also considered a key requirement for success: '. . . the doctors are very responsive to authority; we need high level written support from the Minister either directing them or pleading with them [to motivate them to report]' (Surveillance Coordinator).

Strengthened outbreak detection

Outbreaks were readily identified by the system, although in some smaller PICTs they were contemporaneously identified by outpatient clinicians. The value of the system was apparent to key respondents who reported that the only areas where outbreaks were initially identified through the media or by word of mouth were those where no sentinel reporting site existed, indicating that the system was sensitive enough to identify outbreaks. Respondents were extremely positive about the system's ability to detect outbreaks: 'Late last year we had an epidemic of diarrhoea and gastroenteritis and we really picked it up from the surveillance system' (Director of Medical Services). One outbreak was even identified during the initial weeks of system development. Interviewees also commented that it was easier to detect and respond to outbreaks earlier: '. . . we are now able to detect and respond to outbreaks earlier as the reporting from sentinel sites is based on symptoms rather than diseases which may take time to establish and report' (country Head of Communicable Disease).

Simplicity – an improvement on earlier systems

The system was reported as an improvement on previous surveillance systems, which often included many more conditions, some of which were considered irrelevant to respondents: 'Previously there were as many as 65 conditions – including overly common diseases like scabies and diseases that are almost impossible to confirm

locally, like plague or smallpox – things that weren't useful for detecting outbreaks' (WHO staff member). Clinicians also noted that it was easier to make a clinical diagnosis using the clearly defined case definitions in preference to laboratory confirmation which, because of the remoteness of many islands and the time taken for confirmation, limited its value for initiating an outbreak response.

Success of introducing the system for pandemic preparedness and meeting IHR requirements

A number of key informants commented on the implementation of regional ILI surveillance during the pandemic, and how with that structure in place, it was fairly simple to extend it to include the additional syndromes: 'We learned from that experience [the pandemic] and we're just hoping that we can keep that structure and improve that structure' (Health Protection Manager). Respondents provided examples of how they were updating their pandemic preparedness or disaster management plans, and the integration of the syndromic surveillance system into these plans: '. . . this is part and parcel of our disaster management plan. In fact, the surveillance system prompted the review' (Director of Public Health). A number of key informants also mentioned the relationship between the system and IHR obligations, though not all were clear on whether they had met their IHR obligations: 'IHR is one of the issues. We would like to know in detail what our IHR obligations are, so that we can see what we've done, what we need to improve and what we haven't done' (Director of Public Health).

System quality improvement

A structural element that appeared important to timely outbreak investigation was the location of a surveillance officer within health programmes rather than in a statistical or health information area. Respondents remarked that this facilitated analysis of data and timelier outbreak responses. Key informants noted the importance of having clearly defined roles and responsibilities for each player to ensure an efficient outbreak response: 'We should strengthen it by better supervision, by making sure the roles and responsibilities are clear' (WHO staff member). There was some concern noted about the sustainability of the system and acknowledgement that there was still scope for further improving implementation in some PICTs. The requirement for regular training, particularly in PICTs with a high turnover of clinical staff, was raised by a number of country respondents: 'My real concern is the sustainability . . . this is an issue that I've grappled with from day one . . . all my doctors are expatriates, all my clinical support are expatriates . . . I can't build capacity on the expatriates alone' (Secretary of Health).

Discussion

The syndromic surveillance system has expanded from 6 to 20 participating PICTs within a year, indicating that there is a high level of system acceptance. The participating PICTs include a number of low-income countries, suggesting that there may be a similar syndromic surveillance system applied in developing countries in other parts of the world that are struggling to meet their IHR requirements.

Encouragingly, there is overwhelming agreement that the system is effectively acting as an early warning system and, while data quality and analysis are still variable, this has not lessened the ability of the system to identify outbreaks. Effective outbreak response is the critical ethical and functional element of any early warning system (Carrel and Rennie 2008). Consistent collection and examination of data and standardised approaches to reporting, outbreak investigation and response are necessary for a surveillance system to effectively serve as an early warning system. Regional reporting of alerts, outbreaks and outbreak updates has dramatically increased since implementation of the system. Improvements in case ascertainment, data quality and training will further enhance the system.

Support for the system at all levels of government is a key determinant of successful system implementation. Interestingly, the availability of clinical and epidemiological advice from an external agency such as WHO or SPC was considered equally important by respondents. Dedicated support and training from WHO and SPC, and local political support, appeared critical to initial implementation and sustainable functioning. This could have future implications for the sustainability of the system if this support is withdrawn. Pressure to conform to social norms may have assisted in catalysing participation as the system gained wider acceptance; several respondents cited the need to be seen actively collaborating in this IHR-related system.

One of the beneficial, and perhaps unintended, consequences of the syndromic surveillance system was a general improvement in communication and data sharing within the clinical setting, the broader health system, between different government departments and, externally, with regional neighbours and agencies. While the regular reporting of syndromes by a large number of PICTs appears to be mitigating the fear of political reprisal for outbreak reporting, which was identified as a barrier to reporting in some countries during the 2009 pandemic (Briand *et al.* 2011), the potential for political reprisal remains a possibility.

The inter-country variation in specific system characteristics appeared to be a positive attribute in a region with variable socio-economic and health system development. Despite marked differences in technology, personnel, health system resources and medical informatics, PICTs productively participated and contributed to the regional early warning system. Simple, manual systems were often more robust than sophisticated, automated systems, indicating that sophistication is not a requirement for participation. Harmonisation of the syndromic surveillance system and pre-existing local systems are issues that need to be addressed in some PICTs. Expansion with additional case definitions that can help detect important outbreak-prone diseases important in the Pacific, such as 'dengue-like illness', should be considered. However, the added disease detection capability should be weighed carefully against the increase of the reporting burden. Improving the visibility of case definitions could help improve system performance. High turnover of clinical staff in the Pacific region is a particular challenge and regular training is of major importance.

Although only key informants from five PICTs were interviewed in-country, the consistency of the derived themes was confirmed during interviews with key informants from five additional PICTs. A clear limitation is that the experience of PICTs during early system implementation cannot confirm sustainability and future

success of the system. The WHO engaged an independent evaluator, and observations and reported data were compared with interview data to address the possibility that health officials might exaggerate the success of their country's implementation. A range of local respondents were interviewed to ensure a valid understanding of the local system. These comparisons confirmed that the systems were, in fact, functioning as described. Further evaluation of the system as it matures is recommended to provide longitudinal information.

There have only been a limited number of published evaluations of syndromic surveillance systems in developing settings (La Ruche *et al.* 2000, Durrheim *et al.* 2001, Nelesone *et al.* 2006, Jefferson *et al.* 2008, Meynard *et al.* 2008), although a number of authors have suggested that syndromic surveillance is appropriate for developing regions (Durrheim *et al.* 2001, Chretien *et al.* 2008, May *et al.* 2009, 2011). While the use of 'low technology' for syndromic surveillance has been recognised as having value in some developing settings (Chretien *et al.* 2008, Happel Lewis and Chretien 2008, May *et al.* 2009, 2011), there continues to be an emphasis on the technical aspects of syndromic surveillance systems and less emphasis on the importance of establishing a standardised process or framework (customised to each individual setting) for outbreak detection. The present evaluation demonstrates that technical capacity is only one component of a successful syndromic surveillance system and reliance on technology can be detrimental to a system when the technology fails, a not uncommon occurrence in developing countries.

While PICTs had agreed to establish a syndromic surveillance system prior to the 2009 pandemic, the need for systematic reporting of ILI cases during the pandemic encouraged countries to rapidly implement a system for collecting and transmitting syndromic data. The limited availability of laboratories for promptly confirming influenza demonstrated the usefulness of good case definitions to support clinical and public health interpretation and action. In the absence of this powerful incentive there may not have been the political will to implement the system so rapidly. The use of the system to assist countries in meeting their IHR obligations is another major incentive for implementation, though it is of concern that some PICTs reported not understanding if they were meeting their IHR obligations. These foundations made implementation of an expanded syndromic surveillance system an achievable aspiration. Detection of future influenza pandemics or other emerging infectious disease outbreaks in the Pacific will be greatly assisted by this syndromic surveillance system.

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PAPER EIGHT: PANDEMIC RESPONSE IN LOW-RESOURCE SETTINGS REQUIRES EFFECTIVE SYNDROMIC SURVEILLANCE.

Paterson BJ, Durrheim DN, Hardie K. Pandemic response in low-resource settings requires effective syndromic surveillance. Influenza and Other Respiratory Viruses 2013;doi:10.1111/irv.12098.

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Letter to the Editor

Pandemic response in low-resource settings requires effective syndromic surveillance

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To the editor:

Starbuck *et al.* have identified a significant gap in any future global response to a severe influenza pandemic.[1] The threat of inadequate preparedness and limited public health responses in low-resource settings, leading to uncontrolled transmission is a real and unwelcome possibility during a pandemic. The authors recommend that detailed authoritative guidance should be developed for low-resource settings and that support should be given to governments in these settings to adapt and implement these guidelines.

However, an appropriate public health response and effective management of cases depend primarily on early detection of suspected cases. This remains a major challenge in many developing countries, but syndromic surveillance offers a potential solution in these settings. A novel and visionary system, using a simple but standardised set of symptoms, was first developed by T. Jacob John in the early 1980s in Southern India.[2] The system utilised a district-level disease surveillance system in a low-resource setting, to control and limit disease outbreaks through early detection. This approach was further adapted in a rural African setting with a focus on rural hospitals reporting presentations of nine core clinical syndromes, including cholera and meningitis-like disease to ensure early identification of infectious disease outbreaks.[3]

A similar syndromic surveillance system for outbreak detection and response has recently been implemented in Pacific Island Countries and Territories (PICTs). In 2010, PICTS agreed to develop a regional standardised, simple and sustainable event-based syndromic surveillance system to ensure compliance with IHR requirements (rapid outbreak detection, information sharing and response to outbreaks).[3] Health resources vary across the region that includes a number of countries that are categorised as least developed countries (LDC).

The system is based on the early detection and reporting of four core syndromes (influenza-like illness, diarrhoea, prolonged fever and acute fever with rash) and the immediate reporting of unusual events. The system uses standardised case definitions and processes rather than focussing on a technology platform used to collect or analyse the data. A Pacific Outbreak Manual has been developed as an integral component of the system; to ensure that health workers have rapid access to robust and practical guidelines on the clinical and public health management of infectious disease outbreaks, including influenza-like illness, and triggers for action.[4] This provides PICTs with authoritative guidance on appropriate response measures during a severe influenza pandemic.

A recent evaluation highlighted the need for standardised surveillance to help meet IHR obligations and to ensure early warning of infectious disease outbreaks across the Pacific.[5] While there is variation in system implementation, it is apparent that this is a strength in a region that includes low-resource communities. Despite differences in personnel resources, medical informatics systems and processes, PICTs have productively participated in and contributed to a regional early warning system. The syndromic surveillance system expanded from six to twenty participating PICTs within 1 year, indicating a high level of acceptance of the system. While there are remaining challenges in ensuring uniform data quality, the system has proven effective in detecting outbreaks, its simplicity and the standardisation of both case definitions and responses are key elements in its usefulness. Detection of future influenza pandemics or other emerging infectious disease outbreaks in the South Pacific should be greatly assisted by this syndromic surveillance system.

Syndromic surveillance is particularly useful in settings where access to laboratory diagnosis is not timely, allowing containment measures to be implemented prior to having a definitive diagnosis. However, there are inherent limitations in a system based purely on syndromes due to the broad range of diseases that may cause certain syndromes, including influenza-like illness. To avoid exhausting public health

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resources on 'syndrome noise', it is important to select syndromes carefully for their relative public health importance and to establish local thresholds for response. It is important to reach prior agreement on the number of specimens that need to be sent from a particular area for laboratory confirmation at reference laboratories, to allow syndromic surveillance to serve as an efficient early warning system for a severe influenza pandemic.

Simplified syndromic surveillance should be a priority in countries with limited public health system or technological capacity.

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CHAPTER FIVE:
PRESENTING THE EVIDENCE: CHANGING PUBLIC HEALTH POLICY

This chapter addresses the following research objectives:

- To determine the breadth, value and limitations of syndromic surveillance as applied to public health.

- To determine the adequacy of current evaluation frameworks for evaluating syndromic surveillance.

Within this context, the chapter has a particular focus on the application of syndromic surveillance in identifying the real or potential threat of an emerging infectious disease or a disease on the verge of eradication. It also considers the adequacy of current evaluation frameworks.

Viral zoonotic encephalitis, surveillance and public health

With the emergence in Australia of a number of highly pathogenic zoonotic viruses in recent decades, including Hendra virus and Australian Bat Lyssavirus, which present with an encephalitic syndrome in humans, an improved understanding of encephalitis is required. While these viruses are known, other novel or undiscovered emerging infectious disease agents may exist in Australia. Human encephalitis in Australia causes substantial mortality and morbidity, with frequent severe neurological sequelae and long term cognitive impairment leading to a disproportionate impact on public health. Significant proportions of encephalitic conditions are of unknown aetiology and may point to the existence of one or more unidentified emerging infectious diseases [1]. Over a thousand (1,118) recorded adult encephalitis associated deaths occurred between 1979 and 2008, and an increasing proportion of these encephalitis deaths were due to “unknown” causes - from 47% between 1979-1992 to 57% from 1993-2006 [2]. While herpes simplex virus is the most commonly identified causative pathogen amongst adults hospitalised with encephalitis, the overwhelming majority (70%, range 62-79%) of hospitalised cases have no specific pathogen identified [1].

Encephalitis surveillance currently focuses on the use of sentinel animal monitoring or definitive diagnosis of notifiable conditions that may present as encephalitis. This is inadequate for detecting newly emerged encephalatides. As most encephalitis cases in adults are referred to specialists for assessment, hospital-based surveillance may aid in identifying increases in known pathogens or emergence of new pathogens that require a prompt public health response. The scientific publication ‘**A review of the epidemiology and surveillance of**

viral zoonotic encephalitis and the impact on human health in Australia' [3] reviews recently emerged or resurging viral zoonoses that may lead to encephalitis and considers whether hospital-based sentinel surveillance for an encephalitis syndrome would aid in identifying increases in known or emergent pathogens requiring a public health response.

Polio surveillance

In the 1980s, the goal of global eradication of polio resulted in acute flaccid paralysis (AFP) surveillance being implemented globally as the key surveillance measure for the eradication of polio [4]. Once an AFP case has been detected by the surveillance system, laboratory confirmation for poliomyelitis is required. In countries where polio continues to be endemic, detection of polio cases through AFP surveillance requires careful examination of the data by small geographical units to identify potential polio clusters. As part of the certification process to declare Regions polio-free, WHO recommends implementation of AFP surveillance in all member countries to detect wild poliovirus circulation and to document the absence of poliovirus circulation [5]. Globally, the incidence of polio is at its lowest level, yet the goal of eradication remains elusive with the last cases proving particularly difficult to eradicate. Since Western Pacific regional certification, one adult polio case was detected in Australia in 2007 and no paediatric cases have been identified. Polio surveillance will become more important if eradication is not able to be achieved and there is a rebound in global cases.

The scientific publication '**Review of Australia's polio surveillance'**, examines the various polio surveillance strategies currently utilised in Australia, including AFP surveillance, virological, laboratory and environmental surveillance. Document review and semi-structured key informant interviews were used to collect data necessary for this evaluation. Key informants were identified in consultation with the National Certification Committee (NCC) for the Eradication of Polio. Interviews were recorded, transcribed and thematically analysed. The reliability of identified themes was tested during subsequent interviews and data collected during the desktop review. This study was an iterative process with feedback on the findings sought from interviewees.

The review discusses the roles of the different organisations directly involved in surveillance, polio-related committees, and the purpose of polio surveillance and perceptions of risk relating to polio. These views are then balanced by consideration of Australia's obligations to report against polio surveillance measures to the WHO; information required to certify

Australia's polio free status; and the need to appropriately respond to any polio incursions [6]. Findings from the review resulted in ten policy recommendations being made to the NCC.

Guillain- Barré Syndrome (GBS) is the most common cause of AFP, which in turn is a marker syndrome for poliomyelitis. Identification of all AFP cases prevents paralytic polio being missed and adequate investigation, including the timely collection of two stool samples, ensures that polio has been excluded as a diagnosis [7]. The scientific letter '**Guillain- Barré Syndrome**' [8], emphasises the important role of GBS in polio surveillance, something that was missed in an otherwise comprehensive review of this condition [9].

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9. Paterson BJ, Mackenzie JS, Durrheim DN, Smith D. A review of the epidemiology and surveillance of viral zoonotic encephalitis and the impact on human health in Australia. New South Wales Public Health Bulletin 2011;22(5-6):99-104.
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PAPER NINE: A REVIEW OF THE EPIDEMIOLOGY AND SURVEILLANCE OF VIRAL ZOONOTIC ENCEPHALITIS AND THE IMPACT ON HUMAN HEALTH IN AUSTRALIA.

Paterson BJ, Mackenzie JS, Durrheim DN, Smith D. A review of the epidemiology and surveillance of viral zoonotic encephalitis and the impact on human health in Australia. New South Wales Public Health Bulletin 2011;22(5-6):99-104.

A review of the epidemiology and surveillance of viral zoonotic encephalitis and the impact on human health in Australia

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Abstract: Human encephalitis in Australia causes substantial mortality and morbidity, with frequent severe neurological sequelae and long-term cognitive impairment. This review discusses a number of highly pathogenic zoonotic viruses which have recently emerged in Australia, including Hendra virus and Australian bat lyssavirus which present with an encephalitic syndrome in humans. Encephalitis surveillance currently focuses on animals at sentinel sites and animal disease or definitive diagnosis of notifiable conditions that may present with encephalitis. This is inadequate for detecting newly emerged viral encephalatides. Hospital-based sentinel surveillance may aid in identifying increases in known pathogens or emergence of new pathogens that require a prompt public health response.

Human encephalitis causes substantial morbidity and mortality in Australia, frequently resulting in severe neurological sequelae and long-term cognitive impairment. While herpes simplex virus is the most commonly identified causative pathogen, the majority of adult encephalitis hospitalisations (70%, range 62–79%) have no specific pathogen identified[1] and an increasing proportion of encephalitis deaths are due to 'unknown' causes – from 47% between 1979 and 1992 to 57% between 1993 and 2006.[2] Recently emerged or resurging pathogens in Australia, including Murray Valley encephalitis virus, West Nile virus (Kunjin clade), Japanese encephalitis virus, Hendra virus and Australian bat lyssavirus, cause a human encephalitis syndrome; consequently, encephalitis surveillance may be useful for signalling the emergence of novel infectious diseases, particularly viral zoonoses that may impact on human health.

Emerging infectious diseases pose a substantial threat in Australia and globally due to increased urbanisation, climate change, new farming practices, virus re-assortment and changes in human behaviours.[3–5] The close interaction between animals and humans has provided opportunities for viruses to jump between species with 60% of known human infectious diseases and 75% of emerging infectious diseases being of animal origin.[5,6] A One Health approach, which recognises the interdependence of human and animal health and the environment, is required to improve the surveillance of and response to Australian emerging infectious diseases.

Surveillance for viral zoonotic encephalitis

Surveillance for human viral zoonotic encephalitis in Australia depends on four different systems: notifications of specific infections to state and Commonwealth governments under public health legislation; serological surveillance of sentinel animals for flaviviruses; confirmatory testing of bats submitted after human contact for Australian bat lyssavirus; and mosquito surveillance for flaviviruses.

Although the encephalitis syndrome *per se* is not notifiable in Australia, specific diagnosis of a number of viral zoonotic encephalitides (Murray Valley encephalitis virus, West Nile virus (Kunjin clade), Japanese encephalitis virus, other flavivirus encephalitides and Australian bat lyssavirus) are notifiable by all states and territories, using common case definitions, to the Australian Government Department of Health and Ageing National Notifiable Diseases Surveillance System.[7] Human Hendra virus infection is only notifiable in Queensland, although equine infections have occurred in both Queensland and northern New South Wales (NSW).[8] Unfortunately, mandatory notification does not guarantee comprehensive reporting as it is based on detection of a causative organism. Therefore encephalitis due to rare or emerging pathogens may go unrecognised, which has led to proposals for systematic surveillance of the encephalitis syndrome.[2,9]

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Zoonotic encephalitis viruses

Zoonotic encephalitis viruses fall into two groups, each with their own particular wildlife hosts, transmission mechanisms and ecologies. The first are the vectorborne and transmitted flaviviruses: Japanese encephalitis virus, Murray Valley encephalitis virus and West Nile virus (Kunjin clade). The second are the batborne viruses where bats act as the reservoir host: Hendra virus and Australian bat lyssavirus.

Vectorborne flaviviruses

The three flaviviruses Japanese encephalitis virus, Murray Valley encephalitis virus and West Nile virus (Kunjin clade) are closely related members of the Japanese encephalitis serological complex. Their maintenance hosts are ardeid waterbirds and their vectors are *Culex* spp. mosquitoes.

Japanese encephalitis virus (JEV)

JEV is the major cause of childhood viral encephalitis and associated disability in Asia.[10,11] Only 1:25–1:300 infections result in clinical disease[12,13] but 25% of clinical cases are fatal and 50% of affected humans experience neurological sequelae. Transmission cycles involve *Culex* spp. mosquitoes (especially *Cx. tritaeniorhynchus*), ardeid birds, such as black-crowned night herons (*Nycticorax nycticorax*), and pigs as vertebrate amplifying hosts.[14] Humans become infected by a bite from an infected mosquito but they are incidental, dead-end hosts. It is worth noting that JEV also causes encephalitis in horses, and they too are incidental, dead-end hosts.

JEV emerged unexpectedly in the Torres Strait in 1995 (probably following importation from Papua New Guinea), causing three human cases of encephalitis in Badu, two of whom died. A further case occurred in Badu in 1998, as well as the first human JEV case on mainland Australia near the mouth of the Mitchell River, Cape York.[15] Virus activity has been detected in the Torres Strait in almost all years since 1995, and in Cape York on the Australian mainland in 1998 and 2004.

Sentinel pig herds were kept on various Torres Strait islands and locations in northern Cape York for serological surveillance but, as these sites were usually close to human habitation and pigs are major virus amplifiers, the sentinel pig program was discontinued except for a single site on Cape York. Sporadic opportunistic mosquito collections are made by Queensland Health for virus isolation. Future JEV activity surveillance may be incorporated in the National Arbovirus Monitoring Program of Animal Health Australia, as cattle are safe animals for surveillance.[16]

A safe and effective inactivated, cell culture propagated JEV vaccine is available for those living or travelling in endemic areas,[17] and several newer vaccines with potentially greater efficacy and safety are undergoing clinical trial.

Murray Valley encephalitis virus (MVEV)

Encephalitis outbreaks due to MVEV were first detected on Australia's east coast in the early 20th century, and then re-emerged as epidemics in the Murray-Darling River basin in 1951 and 1974.[18] MVEV is now considered enzootic in the Kimberley and possibly the adjacent areas of the Northern Territory. The virus is maintained in a cycle primarily involving *Cx. annulirostris* and ardeid waterbirds, and variable activity occurs every year in these areas.[18] Virus activity outside these enzootic areas generally follows heavy rainfall and flooding within normally arid areas of northern and central Australia, as infected waterbirds migrate across the flooded areas.[19,20] This may explain the reappearance of MVEV encephalitis in central Australia and western NSW in 2000–2001.[21] It now appears that low level MVEV activity may occur occasionally in NSW, and may have resulted in a locally acquired human infection in 2008.[22] MVEV throughout Australia is predominantly genetically homogeneous, consistent with a single major enzootic source.[23,24]

Clinical MVEV encephalitis cases are uncommon in Australia with an average of 2–3 cases each year since the late 1970s. The incubation period ranges from 1 day to 4 weeks, and most infections are either asymptomatic or the patient only develops a self-limiting febrile illness with or without headache. Encephalitis occurs in only 1:500–1:1000 infected individuals with a mortality rate of 20%; about half of all survivors have significant residual neurological deficits, with worse outcomes in the very young and elderly.

Infection risk depends on the degree of mosquito exposure during a period of MVEV activity. Generally, all residents and travellers are susceptible, with cases in all ages, except amongst Indigenous communities where there is regular virus activity, with infection more likely in young Indigenous children due to protective immunity in older children and adults.[25,26]

Currently, there is neither a vaccine nor any specific antiviral therapy for MVEV. Sero-surveillance is carried out using sentinel chicken flocks in Western Australia, the Northern Territory, NSW and Victoria,[27] and by opportunistic mosquito sampling for virus isolation.

West Nile virus (Kunjin clade) (WNV-KUN)

WNV-KUN was first detected in northern Queensland in 1960 and is widely dispersed across tropical northern Queensland, the Northern Territory and Western Australia, being maintained in enzootic cycles similar to MVEV between *Culex* spp. mosquitoes and ardeid waterbirds. WNV-KUN activity is regularly detected in south-eastern Australia, but usually without recognised human cases.

WNV-KUN is believed to have caused 11% of encephalitis cases in the 1974 Murray Valley outbreak.[28] During the following three decades, three encephalitis cases caused by WNV-KUN were reported (all non-fatal), while 68 MVEV encephalitis cases were confirmed. The incubation period appears similar to MVEV infection but the encephalitic illness is more benign with complete or near complete recovery.[29]

Currently, there is neither a vaccine nor any specific antiviral therapy for WNV-KUN infection. MVEV sentinel chicken flocks are also tested for WNV-KUN infection.

Batborne viruses

Hendra virus (HeV)

HeV was first described in 1994 during an outbreak of severe respiratory disease amongst racehorses and humans in Brisbane.[30,31] A second outbreak occurred at the same time but was unrecognised for a further 13 months. A Mackay farmer, infected while assisting with an equine autopsy, suffered mild meningitis and recovered, but 13 months later relapsed with fatal encephalitis.[32] There have been 12 further outbreaks;[33,34] 11 in Queensland and one near Murwillumbah in NSW. There have been seven confirmed human HeV infections, with four deaths. Flying foxes of the genus *Pteropus* are the reservoir host,[35] but all human infections to date have been epidemiologically linked to horses, the major spill-over host. Horses are believed to become infected after grazing on pastures contaminated with bat urine, birthing fluids or spats (fibrous plant material remaining after mastication by bats). Humans become infected by the virus entering through cuts or grazes after exposure to equine bodily fluids, but humans are dead-end hosts and there is no evidence of human-to-human infection.

HeV is one of two members of the genus Henipavirus, the other being Nipah virus, the cause of fatal encephalitis affecting pigs and humans in Malaysia in 1999.[33] Nipah virus, like HeV, is a virus of Pteropid bats, but with pigs as the spill-over hosts. Very recent studies have indicated that pigs could also potentially act as spill-over hosts for HeV.[36] Human-to-human transmission with Nipah virus resulting in cases of clinical disease has been documented, with some of the cases probably being due to ingestion of bat-contaminated palm juice, whereas others may be due to other routes of infection.[33,37] Human-to-human transmission of HeV has not been reported. Over the past decade, sero-epidemiological studies have shown that HeV and Nipah virus, or closely related viruses, are widely distributed over the range of Pteropid bats.[33,34,38]

There is no active surveillance for HeV in Australia, in either humans or animals, and spill-over infections are uncovered when there is clinical evidence of infection in horses. Veterinarians and others likely to be exposed to infected bats or horses should take appropriate personal protection measures. It is not practical to prevent all interactions between flying foxes and horses, and no vaccines are available, although post-exposure prophylaxis is currently being investigated and shows promise.

Australian bat lyssavirus (ABLV)

ABLV was first isolated in 1996 in NSW from the brain of a black flying fox (*Pteropus alecto*) which was behaving strangely.[39] It is closely related to rabies virus,[40] but is distinguishable genetically and thus classified as lyssavirus serotype 1, genotype 7.[34,41] ABLV has been found in all four species of Australian flying fox (genus *Pteropus*) throughout their geographic range, and in at least one species of insectivorous microbat, the yellow-bellied sheath-tailed bat (*Saccolaimus flaviventris*), in Queensland.[34,42] Serological evidence of infection has also been found in a number of other genera, and the ecology and diversity of this virus is yet to be fully understood. Less than 1% of flying foxes in the wild are infected with ABLV, but this increases to as many as 15% of sick or injured flying foxes and about 3% of yellow-bellied sheath-tailed bats.[43] Limited studies to infect terrestrial wildlife have failed, although experimental exposure of domestic cats and dogs can produce mild signs and seroconversion but with no evidence of viral persistence.[44]

ABLV has caused two human deaths in Australia. The first was a bat carer who had been scratched by a yellow-bellied sheath-tailed bat 5 weeks earlier[45,46] and the second, a woman bitten 2 years prior by a flying fox.[47] In both patients the disease was similar to classical rabies, with non-suppurative encephalitis accompanied by hypersalivation, aggression and agitation. Currently available cell-culture derived vaccines appear efficacious in protecting against ABLV infection in exposed humans.[48,49] Bat carers and others at risk of ABLV exposure are offered pre-exposure vaccination and those exposed are given standard preparations of vaccine and the rabies immune globulin.[17,43] It is important that, wherever possible, the bat responsible for the potential exposure is sent for testing.

Discussion

Globally, many of the recently emerged Australian zoonotic viruses have presented with an encephalitic syndrome in humans,[6,50] including the highly pathogenic HeV and ABLV.[51,52] Other zoonotic viral encephalitides have appeared in new Australian regions, including JEV, MVEV and WNV-KUN.[53] Current Australian surveillance, which focuses on seroconversion in sentinel animals in a limited number of sentinel sites (pigs for JEV and chickens for MVEV and WNV-KUN), definitive diagnosis in reservoir hosts (culled bats that have had potential transmission contact with humans for ABLV or horses for HeV), or definitive diagnosis in humans, has the

potential to miss encephalitis cases caused by notifiable conditions, and is particularly inadequate for detecting newly emerged viral encephalitides.[2] A recent study examining the diagnostic assessment of encephalitis in three Regional Referral Hospitals in NSW determined that only 15% of encephalitis patients were tested for flaviviruses and 0–7% were tested for specific zoonotic encephalitis viruses.[54]

Conclusion

Given that viral encephalitis generally causes relatively serious illness resulting in hospitalisation,[55] the utility of hospital sentinel surveillance of adults or paediatric medicine inpatients deserves prompt investigation, as does the use of a standardised diagnostic and testing algorithm which includes viral zoonotic encephalitides. Improvements in encephalitis surveillance at the animal, human, environment interface would aid in earlier identification of known pathogens and in alerting authorities to the emergence of new pathogens or outbreaks that may require public health investigation and action.

Editor's note

During 2011 there has been a resurgence in MVE across Australian states with 14 confirmed cases notified in the National Notifiable Diseases Surveillance System, including one in NSW, and two deaths. Canadian authorities also confirmed the additional death of a Canadian tourist who was infected in the Northern Territory.[56–59]

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PAPER TEN: REVIEW OF AUSTRALIA'S POLIO SURVEILLANCE

Paterson BJ, Durrheim, DN: Review of Australia's polio surveillance. *Communicable Disease Intelligence* (accepted for publication)

Review of Australia's polio surveillance

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Key words: Polio, surveillance, evaluation, epidemiology, acute flaccid paralysis

Abstract

With eradication almost within reach, the importance of detecting every poliomyelitis case has taken on additional significance and the selected surveillance strategy must be effective and efficient. A review of polio surveillance in Australia was conducted to consider whether current strategies were optimal.

Document review and semi-structured key informant interviews were used to conduct the review. Interviews were recorded, transcribed and thematically analysed. The review was an iterative process with feedback on the findings sought from interviewees.

Since Western Pacific Regional polio-free verification, one adult case was detected in 2007 and no Australian paediatric cases have been identified. Respondents reported that: it was not possible to prevent importations; paediatric cases were more likely to be identified than adult cases; and there may be a low level of suspicion among clinicians.

Case detection and outbreak mitigation were considered key reasons to undertake polio surveillance, while non-achievement of some WHO surveillance targets did not compromise Australia's polio-free status.

Identified issues were: potential for an importation with high attendant investigation and containment costs; low stool sample collection rates; and the opportunity to improve safeguards around the importation and laboratory storage of biological samples containing poliovirus.

The review found strong support for ongoing polio surveillance, particularly to detect imported cases and to demonstrate commitment to maintaining a polio-free Region. Existing polio strategies were considered appropriate for Australia.

Introduction

Global polio occurrence is at its lowest level, yet the goal of eradication is elusive with three countries, Pakistan, Afghanistan and Nigeria remaining endemic and cases also reported in Chad during 2012.[1] Under the International Health Regulations (2005), poliomyelitis caused by wild poliovirus is one of four specific diseases that must be notified to the World Health Organization (WHO) on detection.[2]

In the 1980s acute flaccid paralysis (AFP) surveillance was implemented globally as the key surveillance strategy for validating the eradication of polio.[3] AFP is a marker syndrome for poliomyelitis and a number of other conditions including Guillain-Barré Syndrome (GBS), the most common cause of AFP.[4] Identification of all AFP cases prevents paralytic polio being missed and adequate investigation, including the timely collection of two stool samples, ensures that polio has been excluded as a diagnosis.[5] As part of the certification process to declare WHO Regions polio-free, WHO recommended implementation of AFP surveillance in all member countries.[6]

Australia is one of a decreasing number of developed countries to maintain AFP surveillance. Over the past five years Australia has consistently achieved the non-polio AFP surveillance target, of one case per 100,000 children aged less than 15 years, but stool collection surveillance targets, of two stool specimens collected from 80% of cases classified as non-polio AFP, have never been met.

Poliomyelitis has been a notifiable condition in Australia since 1922.[7] Queensland is the only state where AFP is notifiable. Australia has high immunisation rates, with a 92.3% national average coverage rate at 12 months with three doses of polio containing vaccine,[8] and has experienced no community polio outbreaks since the 1970s. The Western Pacific Region, which includes Australia, was declared polio free in 2000.[9] In 2007, one imported polio case was detected in a Melbourne student returning from a visit to Pakistan, without further known local transmission.[10, 11]

A number of Western Pacific countries, including Papua New Guinea, remain classified as 'high risk' for polio outbreaks by the World Health Organization [Personal communication, Dr Sigrun Roesel, World Health Organization]. Australia is currently classified as 'low risk', but continues to receive a large number of short term arrivals, students, migrants and refugees from countries classified as endemic or 'high risk' or that continue to use oral poliomyelitis vaccine (OPV).[12]

To confirm ongoing eradication in Australia from 2000 a range of surveillance strategies were implemented to document the absence of circulating wild poliovirus, detect AFP cases, and monitor for vaccine-associated paralytic poliomyelitis (VAPP) while oral polio vaccine was still included in the immunisation schedule.[13] A response plan for polio importations and potential outbreaks has also been developed. Australia has two peak polio committees, the NCC and the Polio Expert Panel (PEP). Australia hosts a WHO accredited national enterovirus reference laboratory (NERL) at the Victorian Infectious Diseases Reference Laboratory (VIDRL).

A review of current Australian polio surveillance activities was undertaken to ensure that the current suite of strategies provide optimal surveillance for a high income country, with sophisticated medical and laboratory infrastructure, and a long history of freedom from endemic polio circulation. The review specifically examined whether: Australia was able to detect an imported case of poliomyelitis; surveillance helped to mitigate the risk of an outbreak; and there was sufficient evidence to demonstrate that Australia was free of circulating wild poliovirus.

Methods

The polio surveillance review was conducted by an independent epidemiologist from the Hunter Medical Research Institute, University of Newcastle, engaged by Australia's NCC, between April and November 2012.

The review framework was adapted from the CDC framework for evaluating surveillance systems,[14] the WHO guide for monitoring and evaluating surveillance and response systems for communicable diseases,[15] and techniques commonly used in public health evaluations.[16, 17] Generous timeframes and small numbers of interviewees permitted the use of semi-structured face-to-face interviews that enabled an in-depth investigation of respondents' views of the surveillance system. Interview guides were prepared and tailored to expert informants' roles. A desktop review of relevant documents was also conducted including: published articles, unpublished government reports and other grey literature.

Concepts and issues identified were explored and validated in subsequent interviews. Expert informants were chosen, in consultation with the NCC, based on their knowledge, roles or involvement with the surveillance system. Interviewees included laboratory personnel, paediatricians, policy makers, surveillance system administrators, research nurses, academics and members of polio peak committees. Twenty seven key informants were interviewed face to face, in Western Australia, Victoria, New South Wales and Queensland, and a further nine

by phone or email. During interviews, interviewees were encouraged to identify other key informants. One hundred percent of approached informants participated in the interviews. Interviews were recorded and transcribed.[16] Thematic analysis was applied to transcriptions using NVivo software. Situational analyses have been undertaken where appropriate.

The review was iterative, with feedback sought from key informants on identified issues, gaps in understanding and draft recommendations. The reliability of identified themes was tested during subsequent interviews and the document review.

Findings from the interviews and draft recommendations were presented to the NCC, for discussion and comment, prior to preparation of the final report.

Results

System description

The stated objective of Australian poliovirus surveillance is to conduct surveillance for poliovirus in Australia to detect imported cases, mitigate the risk of an outbreak and provide additional virological evidence that Australia continues to be free of circulating wild poliovirus [Personal communication, Nicolee Martin, Department of Health and Ageing]. Poliomyelitis surveillance system components include AFP surveillance, virological, laboratory and environmental surveillance (Table 1). The Victorian Infectious Diseases Reference Laboratory (VIDRL) coordinates most polio surveillance activities in Australia, including:

1) The National Enterovirus Reference Laboratory (NERL)
2) National AFP surveillance system
3) The Enterovirus Reference Laboratory Network of Australia (ERLNA)
4) Environmental surveillance

AFP surveillance focuses on children less than 15 years of age. There is no active surveillance system to detect polio specifically in adults except notification to the National Notifiable Diseases Surveillance System (NNDSS).

AFP case detection in Australia occurs actively through two systems, the Australian Paediatric Surveillance Unit (APSU) monthly reporting system and Paediatric Active Enhanced Disease Surveillance (PAEDS). Samples from AFP cases are forwarded to the NERL, a WHO-accredited polio reference laboratory. De-identified AFP case information is reviewed by the Polio Expert Panel two-monthly for classification.

Environmental surveillance for enteroviruses is currently implemented at three sentinel sites in Australia. No polioviruses were detected through environmental surveillance in 2010, 2011 or 2012, but other enteroviruses were successfully detected. Stool samples from the AFP surveillance system and adults where polio is suspected, and sewerage samples from the sentinel environmental sites are tested for poliovirus and other enteroviruses at the NERL.

Australia reports key polio surveillance indicators to the WHO and also provides an annual report to the Regional Certification Committee with evidence to verify that Australia continues to remain polio-free.

System performance

Following the introduction of the PAEDS system in 2007, Australia has met the non-polio AFP rate for children <15 years of age for the years 2008—2011. Prior to this the surveillance target was only achieved sporadically, in 2000, 2001, 2004 and 2006.[18] Australia however has never achieved the WHO criterion for stool sample collection rates. In 2011, 34% of non-polio AFP cases had adequate stool samples collected. Western Australia was the only jurisdiction able to achieve adequate stool samples (88%) in 2011.[19] Identified factors to improve stool sample collection rates included: active, daily visits with ward staff; monitoring whether stool samples had been submitted; and regular feedback and engagement of clinicians.

Surveillance objective 1. Is Australia able to detect an imported case of poliomyelitis?

Since the Western Pacific Region was declared polio-free in 2000, one imported case in an adult was detected in Australia in 2007. No paediatric cases have been identified.

"We are actually a well-protected country at threat of importation."

Respondents unanimously agreed that it was not possible to prevent importations but had mixed views on whether every imported case would be detected. Most felt that undetected importations were likely to have occurred in Australia. Reasons given were that most poliovirus infections are asymptomatic and would not present to a hospital; clinicians may have missed cases because of a low level of suspicion; or the case would have presented in a non-classical manner (without paralysis). One respondent observed, "We're looking for a needle in a haystack really."

Most thought that a paediatric flaccid paralysis case would be detected because of AFP surveillance but that an adult case might be missed. The risk of outbreaks was mitigated by

high vaccination coverage. Systematic environmental sampling for polioviruses was viewed as complementing AFP surveillance although detection would only be limited to areas under surveillance.[20]

Surveillance objective 2. Does surveillance help to mitigate the risk of an outbreak?

Respondents commented that the early detection of a poliomyelitis case was one of the main reasons to undertake surveillance. Early detection and a rapid public health response should mitigate the risk of further community transmission. They noted that the NERL had the capacity to rapidly surge virological testing in the event of an outbreak, and this had been successfully demonstrated during the 2007 polio importation. Virological surveillance amongst contacts and exposed high risk groups would help to determine whether an outbreak had been controlled. In particular, environmental surveillance conducted locally in the outbreak region, could help in assessing whether community transmission had occurred and would serve to demonstrate that an outbreak had been contained.

> *"It's nice to have as a surveillance strategy in your back pocket if you're going to invest heavily in a community response."*

Respondents noted that there was a response plan that would be activated in the event of detection of a single polio case to limit further transmission of poliovirus.[21] A number of respondents commented on the public health and economic imperative for containing an outbreak as early as possible. The costs associated with the importation of a single polio case were substantial however a larger outbreak could have a profound economic impact. Effective surveillance (including virological and environmental), early detection and immediate response was considered necessary to mitigate the risk of any future outbreak.

Surveillance objective 3. Is there sufficient evidence to demonstrate that Australia is free of circulating wild poliovirus?

Respondents were unanimous that there was sufficient evidence to demonstrate that Australia continues to be free of circulating wild poliovirus, as ratified annually since 2000 by the RCC. They indicated that AFP surveillance helped to demonstrate that Australia remains polio free and should continue in its current form.

While Australia did not achieve all the required WHO polio surveillance indicators, respondents considered that there was still sufficient evidence, with adequate AFP detection and accessibility to high quality laboratory services, that Australia remained polio-free. The

supplemental surveillance systems (environmental and enterovirus) were viewed as providing additional evidence that there was no circulating wild poliovirus. Prior to certification, WHO recognised that countries, including Australia, may have difficulty meeting all the reporting requirements, and that supplemental surveillance could be used to provide assurance that the country remained polio-free.

Identified gaps and issues

The major surveillance gaps identified were: detection of adult cases; ensuring that clinicians would recognise a poliomyelitis case; risk of importations; the need to improve stool sample collection rates; and the opportunity to improve safeguards around the importation and laboratory storage of biological samples containing poliovirus.

In general, respondents thought there was a low level of clinical suspicion. It was acknowledged that this is because the disease is rare and it is unlikely that most clinicians have seen a case of poliomyelitis. Detection of cases is generally considered to rely on astute clinicians considering poliomyelitis as a possible diagnosis in AFP cases.

There was some frustration that PAEDS had only demonstrated limited success in improving stool sample collection rates. Respondents recommended that active engagement of clinicians by the research nurses, or identifying a local clinical champion may improve clinician participation in stool sample collection. Respondents thought that Australia should be aiming for the highest possible stool collection in patients in which there was no obvious diagnosis. Stool sample collection should be based on the clinical imperative to test stool samples for diagnostic purposes.

> *"I think there is reluctance among clinicians to do unnecessary investigations."*

The possible inclusion of additional surveillance systems was mentioned by respondents; these included AFP being made notifiable nationally and the Australian and New Zealand Paediatric Intensive Care (ANZPIC) registry but they had not demonstrated success in Queensland or the required timeliness, respectively.

While respondents considered that individuals infected with poliovirus could have entered Australia without detection, they did not feel that this was of major concern as it was obvious that there had been no detected poliomyelitis outbreaks (and that none was likely to occur because of Australia's high vaccination coverage.) The majority of respondents believed that any broader community outbreak would have been detected by the system. Respondents

commented that there are a number of groups that pose a higher risk of poliovirus importation into Australia, particularly from endemic countries. They suggested that it would be useful to explore whether the current policies around vaccination of immigrants, refugees and travellers to and from endemic areas were adequate to address importation risks.

Many respondents mentioned their concerns about the lack of safeguards around the importation of biological samples that might contain poliovirus. They felt that it was of concern that a stool specimen containing poliovirus could be imported into Australia with relative ease. They noted that laboratories importing biological materials need to obtain an import permit for handling of these materials but, as poliovirus is currently designated as a Risk Level 2 organism (moderate individual risk, low community risk),[6] the controls around importation were limited. Respondents felt that it was critical that Australia should know where all poliovirus specimens were held, that they were secure and that importation of specimens potentially containing poliovirus were strictly controlled.

The future

Most respondents thought that if global polio eradication was achieved Australia should maintain the current AFP and other surveillance strategies for at least three years post-eradication. Enterovirus surveillance should, however, continue indefinitely post eradication to improve the epidemiological understanding of other important enteroviruses in Australia, including EV71. Respondents commented that surveillance may need to be enhanced if eradication was not achieved.

Discussion

The thematic analysis of responses by enterovirus and public health surveillance experts, and document review, found that Australia meets some but not all of its polio surveillance objectives, with room for improvement. Table 2 documents the recommendations arising from the polio surveillance review.

There is strong support for the continuation of polio surveillance, particularly to detect imported cases and to demonstrate solidarity with maintaining a polio-free status in the Region. While recognising that the polio surveillance system has developed in a relatively ad-hoc manner and that there are some remaining gaps, the existing polio strategies were considered appropriate for Australia. The established AFP surveillance system is a relatively small economic investment and was considered likely to successfully identify symptomatic,

paralytic polio in children. PAEDS is becoming the most important surveillance mechanism for detecting AFP cases; however APSU, in addition to detecting AFP cases, serves a supplementary function as an important mechanism for communicating with all Australian paediatricians. Enterovirus and environmental surveillance were considered important supplementary surveillance systems, with complementary strengths, and the NERL was recognised as being a highly credible organisation playing an integral role in national and regional polio surveillance.

There were ongoing concerns about potential importation of poliovirus without adequate controls. The potential to apply the new Biosecurity legislation (Biosecurity Bill 2012)[22] to address risks associated with the importation of biological samples containing poliovirus should be explored.

Respondents believed that Australia had a responsibility to meet World Health Assembly (WHA) member requirements to maintain surveillance of such quality that Australia would be able to detect cases and respond to them.

Polio eradication is a global public health emergency[23] and every effort should be made to complete this task. Australia should continue to maintain high immunisation coverage, support global eradication efforts financially, and sustain current polio surveillance to ensure that this public health goal is achieved.

Acknowledgements

The authors would like to acknowledge the help and assistance from all who so generously gave their time to be interviewed during this review. With special thanks to: National Certification Committee and Polio Expert Panel members; Bruce Thorley, NERL; Nicolee Martin, DoHA; and Sigrun Roesel, WHO. The authors would also like to acknowledge the helpful comments from reviewers.

Table 1: Australia's polio surveillance system, 2012

Surveillance System	System component	Description	Findings
Acute Flaccid Paralysis (AFP)	Australian Paediatric Surveillance Unit (APSU)	Commenced in 1995. Approximately 90% (~ 1360) of paediatric clinicians submit a monthly report card to the APSU. It includes request for the collection and testing of two stool samples and the completion of a clinical questionnaire.	The system may not be timely. Provides the only method to access regional and non-tertiary hospital AFP cases. Important mechanism for communicating with paediatricians. Low workload for respondents. Clinicians may not report AFP cases through the APSU system at PAEDS hospitals.
	Paediatric Active Enhanced Disease Surveillance (PAEDS)	Commenced in 2007. Four tertiary paediatric hospitals – Perth, Adelaide, Melbourne, Sydney. Brisbane is expected to commence in 2013. Uses hospital-based research nurses to actively identify cases of AFP, seek consent and ensure the collection of two stool samples. AFP is one of four conditions collected through the system.	Becoming the most important system for AFP surveillance. Some frustration that stool collection rates have not improved uniformly since implementation of the system. Some challenges in ensuring clinician engagement.
	Mandatory notification in Queensland	AFP is notifiable under the Queensland Public Health Act 2005 (PHA) by a clinician on the basis of clinical or provisional diagnosis.	AFP should not be made nationally notifiable.
Virological and enterovirus	National Enterovirus Reference Laboratory (NERL)	WHO-accredited polio reference laboratory. Receives samples from AFP surveillance.	Effective mechanism for enterovirus (including poliovirus) surveillance. Provides enterovirus testing in the Region.
	Enterovirus Reference Laboratory Network of Australia (ERLNA)	Established in 2008. Coordinated by the NERL. Sends untyped enterovirus samples for testing to the NERL. In 2011, 331 enteroviruses were typed by members of the ERLNA.	Provides epidemiological data on enteroviruses in Australia.
Environmental	Three sentinel sites in Newcastle, Byron Bay and Armidale	Implemented in 2010. Sites were chosen based on local public health support. Population size served and areas with large overseas student populations from endemic areas (Newcastle and Armidale) or relatively	Successful implementation of sentinel sites. Useful to trial a site at a major metropolitan location. Demonstrates that an outbreak is contained rather than used for case detection. Retention of

		low immunization coverage and regular international visitors (Byron Bay). Sewerage samples from the sentinel environmental sites are tested for poliovirus and other enteroviruses at the NERL	sentinel sites maintains skills and capacity.
National Notifiable Diseases Surveillance System (NNDSS)	National notification	Notifiable since 1922. Poliomyelitis (paralytic infection) and Poliovirus (non-paralytic infection) are currently notifiable. Includes wild poliovirus infection, Vaccine-associated paralytic poliomyelitis (VAPP) and Vaccine derived poliovirus (VDPV) infection.	Passive notification of poliomyelitis and poliovirus. One adult case notified in 2007.

Table 2: Recommendations arising from the review of Australia's polio surveillance system, 2012

	Recommendations
1.	Australia should continue to undertake active polio surveillance
2.	Existing polio surveillance strategies should occur for three years post-eradication and enterovirus surveillance should continue post-eradication. If eradication is not achieved, surveillance will need to be re-evaluated and may need to be enhanced
3.	The consolidated purpose, objectives and activities of the Australian polio surveillance system, including Australia's commitment to the WHO Global Polio Eradication Initiative, should be documented by the Department of Health and Ageing (DoHA)
4.	Acute flaccid paralysis (AFP) surveillance should continue in its current form through Australian Paediatric Surveillance Unit (APSU) and the Paediatric Active Enhanced Disease Surveillance system (PAEDS) with regular case review by Polio Expert Panel and reporting of classified cases to the WHO
5.	All attempts to improve stool collection rates should be made including through enhancing the effectiveness of the PAEDS program
6.	Polio should remain a nationally notifiable condition but AFP should not be nationally notifiable
7.	Sentinel environmental surveillance sites to supplement AFP surveillance should be maintained and sentinel environmental surveillance should be trialed in a major metropolitan area
8.	Enhanced communications to raise awareness of the importance of completing global poliovirus eradication and highlight the need for clinicians to remain vigilant for cases of poliomyelitis should be developed by DoHA
9.	The DoHA should review current policies relating to vaccination of immigrants, refugees and travellers to and from endemic countries to determine if these policies are adequate to address risks of importation
10.	A review of biosecurity arrangements for the laboratory containment of polioviruses should be conducted in collaboration with accountable individuals

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PAPER ELEVEN: GUILLAIN-BARRÉ SYNDROME.

Paterson BJ, Durrheim DN. Guillain- Barré syndrome. New England Journal of Medicine 2012;367(10):973.

CORRESPONDENCE

Guillain–Barré Syndrome

TO THE EDITOR: We are concerned that Yuki and Hartung (June 14 issue),[1] in their otherwise comprehensive review of the Guillain–Barré syndrome, have overlooked the importance of public health efforts in the surveillance of acute flaccid paralysis to the eradication of polio. Surveillance of acute flaccid paralysis, and hence Guillain–Barré syndrome, which the authors describe as the "most frequent cause of acute flaccid paralysis worldwide," is a key strategy in global efforts aimed at its eradication.[2] The recent declaration by the World Health Assembly that poliovirus eradication is a programmatic emergency for global public health[3] should convince clinicians around the world of the pivotal role they should continue to play in detecting and reporting cases of the Guillain–Barré syndrome to public health authorities. Despite heroic efforts, polio remains endemic in three countries (Pakistan, Afghanistan, and Nigeria) and has reemerged in a small number of additional countries. The recent importation of polio into China after more than a decade of absence throughout the Western Pacific region is a stark reminder of the necessity of continued vigilance during the polio endgame.[4,5]

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CHAPTER SIX:
DISCUSSION AND CONCLUSIONS

The aim of this thesis was to explore how syndromic surveillance has been applied to public health practice. Studies were conducted to demonstrate the value of syndromic surveillance, highlight the breadth of syndromic approaches and applications, and also document its limitations. The practical applications of syndromic surveillance in a variety of settings and across time were examined. The scope of the thesis included consideration of syndromic case definitions, implementation of novel syndromic surveillance systems, data collection, epidemiological analysis, disease characterisation, comparative analysis of different systems, evaluation and review of syndromic surveillance systems, and recommending changes to public health policy based on the research findings.

The objectives of the thesis were to explore and determine:

- The roots, evolution and contemporary application of syndromic surveillance.
- The breadth, value and limitations of syndromic surveillance as applied to public health.
- The adequacy of current evaluation frameworks for evaluating syndromic surveillance.

These objectives have been met by:

- examining the literature to determine the roots and evolution of syndromic surveillance and the contemporary application of syndromic surveillance to public health practice
- applying modern mathematical methodologies to historical syndromic measles data to demonstrate the breadth, value and application of syndromic data
- utilising syndromic data collected during the 2009 influenza pandemic to further characterise the epidemiology and severity of the pandemic to inform public health responses; thus helping to determine the application, value and limitations of syndromic data
- exploring the breadth of novel syndromic data sources to assess their value for syndromic surveillance during the 2009 influenza pandemic
- evaluating the implementation of a novel syndromic surveillance system across the Pacific Island Countries and Territories; thus assisting in the determining the application, breadth, value and limitations of syndromic surveillance and the adequacy of current evaluation frameworks

- considering the public health implications of emergent infectious diseases and assessing how syndromic surveillance systems can assist in improving the understanding of the overall epidemiology of the disease, and whether changes should be made to public health policy to ensure that emergent diseases are able to be detected; thus helping to determine the application, value and limitations of syndromic surveillance
- reviewing polio surveillance in Australia to determine whether the current surveillance strategies are optimal for a disease approaching eradication and to make recommendations on the future of the system; thus examining the breadth, value and limitations of syndromic surveillance and the adequacy of current evaluation frameworks.

Findings and outcomes

The scientific publication '**The remarkable adaptability of syndromic surveillance to meet public health needs**' [1] established that the role of syndromic surveillance has changed over time, from systems primarily established for bioterrorism purposes to systems able to address IHR requirements for detecting and responding to emergent disease threats. The research found that definitions for public health surveillance and syndromic surveillance have also changed, reflecting a dynamic evolution from the collection, interpretation and dissemination of data to inform public health needs; to a more holistic approach that emphasizes response as a core component of the surveillance system. Syndromic surveillance approaches are broad and can include highly automated technology-based systems or simple paper-based registers. Data may be collected on individual syndromes, such as ILI, or indicators, such as work-based absenteeism. The robust application of case definitions is a core requirement of syndromic surveillance. The lack of a requirement for laboratory confirmation means that syndromic surveillance is useful in settings with limited laboratory capacity. The study demonstrated that the need for credible, rapidly available information to inform public health decision-making has resulted in syndromic surveillance becoming a valuable public health tool.

Prior to the introduction of modern laboratory diagnostic techniques, diagnoses were based on the clinical assessment of symptoms against known syndromes. The application of modern mathematical methodologies to historical syndromic measles data provided a novel approach to answer the question of "When was it likely that measles arrived in Australia?"; to investigate prior hypotheses relating to plausible reasons for the late arrival of measles in Australia; and to develop parameters for serial intervals and reproductive numbers that can be used for infectious disease modelling. The scientific publication '**Historical data and modern**

methods reveal insights in measles epidemiology: a retrospective closed cohort study' [2] sought to establish why measles, which was endemic in England during the early 1800's, was not introduced into Australia until 1850, despite regular shipping contact. This study was the first to use historical surgeon superintendent logbooks to retrospectively review 163 measles cases on five ships bound for Australia between 1829 and 1882. An overestimation of measles cases may have occurred in the study as the syndrome 'fever and rash' could also describe other diseases including rubella. This study found lower measles R_0 (range 7·7–10·9) and a shorter mean clinical serial interval of 12·3 days (95%CI 12·1–12·5) than is generally reported. In over-crowded vessels close proximity would likely facilitate measles transmission by aerosolised droplets, but pre-existing high levels of immunity and non-homogenous mixing patterns could have resulted in a lower R_0. These findings support the view that serial intervals are shorter where individuals are in close proximity and transmission may occur earlier [3]. The analysis supports the hypothesis that it is unlikely that measles reached Australia prior to 1850; probably due to the relatively high levels of pre-existing immunity in ship passengers and crew, low numbers of travelling children and the journey's length from England to Australia; which meant that any measles outbreak would burn out prior to arrival in Australia. The study also provided new information on the measles basic reproduction number and serial intervals, both key parameters used in modeling measles outbreaks.

The influenza pandemic (H1N1) in 2009 underlined the need for surveillance systems that are able to provide early detection of initial cases, allowing a comprehensive epidemiological assessment of these early cases, and monitoring of pandemic progress. This thesis explored the utility of syndromic data, collected during the 2009 influenza pandemic, to characterise the epidemiology and severity of the pandemic and inform public health responses. Novel syndromic data sources were also assessed to determine their value for syndromic surveillance during the 2009 influenza pandemic. The scientific letter '**Influenza: H1N1 goes to school'** [4] reports on a secondary analysis of ILI syndromic data from a large cluster of pandemic (H1N1) influenza 2009 cases identified early in the recent pandemic. The analysis indicated that the effective reproduction number (R), in this school-based setting, was 2.69 (95%CI: 2.20-3.22). This is comparable to the lower R_0 estimate of the 1918 influenza pandemic. This parameter can assist public health policy practitioners in determining the severity of a pandemic and, hence, guide appropriate public health responses. As noted in the letter **'Influenza: H1N1 goes to school'**, transmission in schools is likely to be higher than in the general community, a finding supported by later estimates. A study of camp participants aged < 18 years found a comparable R_0 estimate of 2.7 (1.7-4.1)[5], whereas other studies of the general population

found lower R_0 estimates of 1.2 to 1.8[6]. It would be useful to undertake further research to assess how (*R*) changes over the course of a pandemic and whether the use or availability of different surveillance data impacts on the calculation of (*R*).

The scientific letter '**Use of workplace absenteeism surveillance data for outbreak detection'** [7] reported on a comparison of a novel syndromic data source with traditional surveillance sources collected during the 2009 influenza pandemic, to assess its value for surveillance purposes. The analysis confirmed that the use of workplace absenteeism data, particularly from large employers, is an effective surveillance tool and should be more widely incorporated into influenza surveillance. The scientific publication '**Changes in the severity of 2009 pandemic A/H1N1 influenza in England: a Bayesian evidence synthesis'** [8] confirmed that syndromic surveillance data are particularly useful when attempting to validate findings from multiple data sources. The study revealed that data on confirmed cases, based on numbers of confirmed cases, hospitalised confirmed cases and sero-incidence studies, provided conflicting information on the severity of the pandemic. The additional syndromic data sources (consultations for ILI in primary care and the National Pandemic Flu Service) were able to provide a clearer picture of disease severity, thus highlighting the benefits of syndromic surveillance. Results suggested low ascertainment rates, highlighting the importance of systems enabling early robust severity estimation, to inform the optimal public health response. The findings from this study suggested a mild pandemic, characterised by case and infection severity ratios that increased between successive waves. These studies verified the critical requirement for multiple information streams throughout a pandemic and reinforced the need to treat early findings during an emergency, such as an influenza pandemic, with caution.

Evaluations of syndromic surveillance systems are necessary to confirm that they are able to adequately identify outbreaks in a timely manner to enable appropriate public health responses. The scientific publications '**Pacific-wide simplified syndromic surveillance for early warning of outbreaks**' [9] and '**Sustaining surveillance: evaluating syndromic surveillance in the Pacific'** [10] and the scientific letter '**Pandemic response in low-resource settings requires effective syndromic surveillance'** [3] reflect on the implementation and evaluation of a simple syndromic surveillance system established in the South Pacific. The establishment of this system resulted in comprehensive surveillance and response to outbreaks across the PICTs. Regional reporting of alerts, outbreaks and outbreak updates has dramatically increased since implementation of the system. This system will assist PICTs to detect future influenza

pandemics and other emerging infectious disease outbreaks permitting rapid public health interventions.

The evaluation of the South Pacific syndromic surveillance system found that the most important determinants of the system's success were: simplicity of the system; support from government; clearly defined roles and responsibilities; feedback to those who collect the data; harmonisation of case definitions; integration of data collection tools into existing health information systems; and availability of clinical and epidemiological advice from external agencies such as World Health Organization and the Secretariat of the Pacific Community. These findings illustrate that a larger syndromic surveillance system can involve multiple smaller systems, based on common case definitions and standardised reporting, without the requirement for a common data collection method. It would be useful to further explore whether the technological platforms used in this developing setting were responsible for differences in the effectiveness of the system, including early detection of unusual events and public health control measures. Further evaluation of the system as it matures is recommended to provide longitudinal information.

Results from the South Pacific syndromic surveillance system evaluation were reported to the 'Meeting on International Health Regulations, the Asia Pacific Strategy for Emerging Diseases and the Pacific Public Health Surveillance Network', Nadi, Fiji and the International Conference on Emerging Infectious Diseases, in Atlanta, USA. Following the syndromic surveillance system evaluation, in partnership with the World Health Organization and the Secretariat of the Pacific Community, a proposal, *RAPID: Response and Analysis for Pacific Infectious Diseases,* was submitted to AusAID to address identified gaps in the surveillance system. This grant application was successful and the *RAPID* project will be undertaken from July 2013 – June 2016; with work primarily focused on building greater capacity in surveillance, epidemiology and outbreak response across the PICTs.

The thesis considered how syndromic surveillance systems can assist in improving the understanding of the overall epidemiology of emergent infectious diseases, and whether public health policy changes are necessary to ensure that emergent diseases are able to be detected. The scientific publication '**A review of the epidemiology and surveillance of viral zoonotic encephalitis and the impact on human health in Australia'** [9] identified the emergence in Australia of a number of highly pathogenic zoonotic viruses, including Hendra virus and Australian Bat Lyssavirus. These viruses present with an encephalitic syndrome in humans and are having an unknown impact on public health. An improved understanding of

the epidemiology of encephalitis is required to inform public health responses. One of the conclusions from the publication was the recommendation to implement a hospital-based sentinel encephalitis surveillance system. This would aid in identifying increases in known or emergent pathogens and improve what is known about the epidemiology of encephalitis in Australia. A 'One Health' approach, which recognises the interdependence of human and animal health, and the environment, is likely to be required to improve surveillance and response to Australian emerging infectious disease.

Findings from this study were presented to the European Society for Clinical Microbiology and Infectious Diseases, Grenoble, France. Following this study, a grant application was successfully submitted to the Hunter Medical Research Institute grants program to establish a pilot hospital-based encephalitis surveillance system. During 2012-2013, this pilot surveillance system was established at the John Hunter Hospital, Newcastle. Data collection for the pilot study has been completed.

As polio approaches eradication, the imperative to detect every case becomes increasingly important. The scientific publication '**Review of Australia's polio surveillance'** (accepted for publication in *Communicable Disease Intelligence,* ref Appendix C) documents the findings from a review of polio surveillance in Australia. The review was undertaken to determine whether the current surveillance strategies, which are primarily focussed on surveillance for the AFP syndrome, are optimal for a developed country and to make recommendations on the future of the system. Many other developed countries do not undertake or report AFP surveillance to WHO including, among others, the United Kingdom, the United States of America, Japan and Germany. For these reasons a critical examination of the value and effectiveness of polio surveillance in Australia was required.

Expert respondents reported that: it was not possible to prevent importations of poliovirus; paediatric polio cases would be more likely to be identified due to current surveillance than adult polio cases; and there may be a low level of suspicion among clinicians. The risk for community transmission of polio infections in Australia is considered low because of high immunisation rates. Other identified issues included: the importance of supplemental environmental and enterovirus surveillance systems; potential high costs resulting from an importation; continued importation risks; low stool sample collection rates; possible biosecurity inadequacy for imported samples; and opportunities for improved legislative controls around polio. AFP surveillance, currently undertaken through the Paediatric Active Enhanced Disease Surveillance (PAEDS) system and the Australian Paediatric Surveillance Unit

(APSU) helped demonstrate that Australia remains polio free and should continue in its current format. While the costs associated with the importation of a single polio case are substantial, a larger outbreak could have an even more profound economic impact. Effective surveillance (including virological and environmental), early detection and immediate response should mitigate the risk of an ongoing outbreak.

The review found that experts strongly supported the continuation of polio surveillance, including AFP surveillance; particularly to detect imported cases and demonstrate commitment to maintaining the Region's polio-free status.

Outcomes and policy recommendations from this work were presented to the: Australian National Certification Committee for the eradication of poliomyelitis; the 18th Meeting of the Regional Commission for the Certification of Poliomyelitis Eradication in the Western Pacific Region in Bejing; the International Meeting on Emerging Diseases and Surveillance, Vienna; the Communicable Diseases Network of Australia (CDNA); and the Communicable Disease Control Conference in Canberra. Immediate feedback provided during the evaluation highlighted a number of issues that were addressed by informants during the course of the review. Findings from the review are being used by a CDNA working group to improve stool collection rates for AFP cases. As a result of this study, the NCC has also raised the issue of effective laboratory containment of poliovirus with the Department of Health and Ageing.

The scientific letter, '**Guillain- Barré Syndrome**' [10] promoted the value of GBS surveillance to polio eradication and reinforced the need for continued vigilance in the polio endgame.

SYNDROMIC SURVEILLANCE LIMITATIONS

The use of a syndromic surveillance approach to detect outbreaks and unusual patterns is not without its critics. Henning (2004) suggested cautious use of syndromic disease surveillance, noting that it should not replace traditional systems or the reporting by clinicians of unusual events [13]. Others question whether it is a useful tool to detect focal outbreaks too small to trigger statistical alerts or detection thresholds [14-18]. The availability of resources for follow up, migration of persons after exposure, and the difficulty of detecting unusual events during seasonal increases in disease have also been noted as important constraints [19]. Determining whether syndromic surveillance is fit for purpose, for particular diseases, needs to be explicitly addressed when undertaking evaluations of syndromic surveillance systems. For specific diseases, such as botulism, it may be more appropriate to utilise clinical diagnosis alone, particularly when differential diagnoses are limited.

The research undertaken for this thesis identified that syndromes need to be selected carefully for their public health importance and to limit syndromic 'noise'. Local thresholds should be established to ensure responses appropriate to threat and available resources. When data are extracted from a sentinel syndromic system, it can be difficult to generalise findings to the broader system. Data quality issues from individual syndromic surveillance systems need to be understood when considering public health responses. Use of data from syndromic surveillance systems, particularly during emergencies, can be difficult to validate and may indicate changes in health-care seeking behaviour, hospital admission criteria or reporting practices rather than changes in the pathogen or its occurrence.

There is a lack of clarity about what is meant by the term 'syndromic surveillance', making it difficult to extrapolate results from one syndromic surveillance system to another. It is clear from published literature that variations in the definition for 'syndromic surveillance' exist, and that attempts have been made to clarify these differences. The use of published literature to demonstrate the effectiveness of syndromic surveillance presents a number of challenges as the literature may not be representative of public health programme implementation. Publication bias and a relative lack of publications from the developing countries may also limit the interpretation and extrapolation of published results.

If an unusual event or outbreak is identified by a syndromic surveillance system, there needs to be a functional response to the detected event. Syndromic surveillance in itself is not sufficient. It is the first step in the public health response and is generally followed by laboratory confirmation. The benefits of early detection are diminished if response is not considered part of the system. The lack of specificity of syndromic surveillance could mislead public health officials who may ignore minor aberrations in the data, waiting instead for further confirmation through other data sources.

The accuracy of syndromic surveillance evaluations and reviews are dependent on the information provided by the informants. Informants may not be aware of issues in the systems or might exaggerate the success of the system. The consistency of the derived themes needs to be confirmed with the informants, and observations and reported data need to be compared with interview data to confirm the validity of the collected information. A clear limitation is that apparent early success of a syndromic surveillance system cannot confirm sustainability and future success of the system.

FUTURE DIRECTIONS

As syndromic surveillance evolves, questions remain unanswered over definitions, the full scope of potential applications of syndromic surveillance in public health and appropriate evaluation techniques. The key unresolved question requiring common agreement by the public health community is "What is syndromic surveillance?" As syndromic surveillance matures, this definition and the understanding of the role of syndromic surveillance in public health will change. Based on the findings from this thesis a definition for syndromic surveillance, requiring critical peer review, could be:

> Syndromic surveillance is the verifiable ongoing, systematic collection, collation, analysis, interpretation and dissemination of syndromic or indicator-based data to improve public health situational awareness and response.

A number of frameworks and guidelines have been developed as tools for syndromic surveillance evaluation however, given the rapidly evolving syndromic surveillance paradigm, these may no longer be fit for purpose [18, 20-23]. The IHR obligation to report outbreaks or events of international concern [24] has elevated the importance of early outbreak detection and response. In response to these events, the emphasis in syndromic surveillance is changing from automated, early alert and detection to situational awareness and response, particularly in developing countries. However, commonly used evaluation frameworks do not always adequately measure these characteristics. Appropriate indicators of surveillance system performance are dependent on the type of system [25] and, while it may be possible to measure the timeliness of a public health response, neither of the commonly used CDC [26] or WHO evaluation guidelines [27] suggest ways of measuring the effectiveness of the response, whether the response was proportionate and the return on investment i.e. mortality, morbidity or economic losses averted. The development of new evaluation frameworks that encompass these characteristics may be appropriate. There would be value in conducting cost effectiveness analyses of syndromic surveillance systems in comparison to traditional surveillance systems. The question that arises here is "What is the most appropriate framework to evaluate syndromic surveillance systems?"

There are a broad and diverse range of traditional and non-traditional data sources potentially available for syndromic surveillance, limited only by the imagination. Hospital-based data may play an important role in providing economical and novel data for syndromic surveillance [28,29]. Looking forward, the use of 'Big Data' for digital disease detection is a developing and innovative approach that uses a wide variety of electronic data sources to detect, identify and

respond to public health threats. 'Big Data' includes data accessed from mobile phones, social media including Facebook™ and Twitter™, blogging, email, online news data or internet searches; offering new data streams that can be monitored and mined for relevant public health information [30-34]. The emergent field of 'infoveillance' [33], focussing on crowdsourcing and user-generated content, where small amounts of data are contributed by a large number of voluntary participants, are proving their value in emergency situations, such as the 2010 earthquake and subsequent *Vibrio cholerae* outbreak in Haiti [34], or to explore public perceptions during the 2009 H1N1 influenza pandemic [32, 33, 34]. Geo-sentinel data, flight traffic movements, human resource data and genomic information can offer additional information on the likely transmission and direction of disease spread, virulence, and pathogen shift and evolution.

Probable challenges with these new data sources are numerous and include: overwhelming amounts of data; integration of data from multiple sources; issues around free-text or unstructured data; interpretation of user-generated data; assessments of the validity of the data; privacy and ethical constraints; geographic biases; and the requirement for new methodologies to deal with the scale and complexity of the new data [35-38]. Nonetheless, despite these challenges, the potential benefits to public health practice are vast, and relatively untapped, offering exciting opportunities to augment traditional surveillance systems.

Conclusions

Syndromic surveillance is not easily defined and there are a wide range of syndromic approaches that have been applied to address public health issues, making it difficult to answer the question "What is syndromic surveillance?" Like any surveillance system, the purpose and effectiveness of syndromic surveillance needs to be critically examined, particularly as public health requirements change. Appropriate public health responses rely on credible and timely information; information from multiple sources to provide validation of the data; and an understanding of the limitations of data sources. Syndromic surveillance is well suited to fulfil public health information requirements by: improving situational awareness of a disease; offering data validation; and recording early detection of disease emergence or spread. Syndromic surveillance is perhaps most useful when implemented to complement other diagnostic strategies including laboratory confirmation. It should be considered as the first step in the public health surveillance continuum from detection to appropriate public health responses. The collection, analysis and dissemination of syndromic data are no longer sufficient; ensuring appropriate responses should be an integral part of any syndromic

surveillance system. What is certain is that syndromic surveillance, in its many forms, is a useful tool when applied to public health practice.

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APPENDICES

APPENDIX A: PACIFIC SYNDROMIC SURVEILLANCE EVALUATION QUESTIONNAIRE GUIDE

Review of Syndromic Surveillance: PICTS

Questions: Suva Office, World Health Organization

Implementation

- List of countries implementing the system, current implementation stage
    1. Fully implemented
    2. Partial implementation
    3. Planning to implement
    4. Not planning to implement. Reasons for non-implementation of the system?
- Dates of implementation in each country
- Number of reporting sites in each country (table)
- How are the users or providers trained in the system?
- Proportion of population covered?
- Is the system simple to implement?

System

- What is the aim of the system? What objectives are trying to be achieved?
- Flow of information in the system (describe)
    1. How is data collected and who collects it?
    2. How is it recorded in the system (by country, region)
    3. What happens to the reports? Who receives the reports?
    4. How are the reports used to trigger action?
- What were the previous systems?
- Are any of these systems still in place?
- Does it complement other surveillance systems?
- Is this system an improvement on previous systems?
- What benefits have been seen in the system (training, improved lab turn-around, political will etc)
- What are the improvements, what are the limitations or downsides?
- Is the system simple to maintain? Is the system stable?
- Is the system proving to be sustainable? (review reports over time)

Stakeholders

- Who are the stakeholders in the system? What role does each of the stakeholders play?
- What is the role of the WHO and SPC in the system?
- From the perspective as a stakeholder, is the system meeting its' objectives?
- Other key informants who should be interviewed? (List - Ministry of Health, key focal points, clinicians, surveillance officers) others?

International obligations

- IHR notifications
    1. How many IHR notifications have been notified since the surveillance system was implemented?
    2. Was there immediate notification of the event of public health importance?
    3. Were the notifications a result of information received through the syndromic surveillance system?
    4. if no, how was the information received?

Reporting

- Number/proportion of weekly reports received since operational (table – countries vs proportion reporting weekly)
    1. ILI
    2. Diarrhoea
    3. Fever and rash
    4. Prolonged fever
- Is zero reporting occurring?
- Were the reports provided within the expected timeframes? (Timeliness)
- Known barriers to reporting? (Why isn't is working in particular countries) (Acceptability)
- Known enablers for reporting? (Why is it working in particular countries?)
- What happens to the reports? Who has access to the reports? Are the reports published in the media etc or used for league tabling?
- Is feedback provided to those who prepare the reports? What is the nature of the feedback?
- Were any unusual events reported outside of the weekly reporting?

- Was the data shared by WHO with SPC and other partner agencies? In a timely manner?

Outbreaks

- What outbreaks are you aware of that have occurred since the system was implemented? Were these picked up by the Syndromic surveillance system or through other means? (list - time, place, numbers, disease, severity, response, notification)
- List outbreaks by:
    1. Outbreak alert for syndrome generated, outbreak confirmed
    2. Outbreak alert for syndrome generated, no outbreak confirmed
    3. Outbreak of syndrome, no alert generated, syndrome case definition not sensitive to identify outbreak
    4. Outbreak of non-syndrome disease, no alert generated
- Timeliness of outbreak detection
- If outbreaks were missed by the system, then why do you think they were missed?
- How were the outbreaks confirmed? Did they need to be confirmed?
- What could be done to improve outbreak detection?
- How were outbreaks detected prior to the implementation of the system?
- Does the system meet the minimum IHR requirements for serving as an early warning system?

Unusual events

- Were any unusual events reported? List

Syndromes/thresholds

1. Are the core syndromes sensitive enough to identify outbreaks? Are there other systems available to check the sensitivity of the system against? (Sensitivity)
2. Do the core syndromes need any adjustment? If so, why?
3. If so, what should be changed?
4. Are the case definitions being used when reporting occurs?
5. Are there thresholds for every syndrome?
6. Are the thresholds being used as the basis for initiating action once a threshold is exceeded?

7. Are there any core syndromes that should be removed from the syndromes?
8. Are there any core syndromes that should be added to the system?
9. Rank the top three syndromes that could be added to the system

Response

1. Were outbreaks responded to rapidly to limit the impact of the outbreaks?
2. Did the responses follow the guidelines?
3. Describe some outbreaks, and how they progressed through the system including the response?

Other

- Are there any other public health benefits generated or enabled by the system? (Communication, information sharing more generally?)
- Is the system meeting its' aims? Anything else?

Questions: Ministries of Health

Today I'll be talking to you about the Pacific Syndromic surveillance system. This is a new system and we want to understand whether it's meeting its objectives – that is, helping with the detection and responses to outbreaks of infectious diseases. We'd also like to know about what is currently working, any problems you've encountered and what improvements could be made to the system.

Firstly, I'd like to talk to you about how the system has been implemented in your country and who the stakeholders are; I'd then like to talk to you about outbreaks and the reporting of outbreaks; what you think about the syndromes currently used by the system; and finally any issues you might have had and improvements you'd like to see.

Implementation

- Has this country implemented the Syndromic surveillance system (fully, partially, planning to, non-implementation)
- If no, what are the reasons for non-implementation?
- Dates of implementation
- Did you use the implementation guide to assist in implementation, was it useful?
- Number and type of reporting sites?
- Proportion of population covered?
- Is the system simple to implement?
- What other surveillance systems are used in this country?
- Does it complement other existing surveillance systems?

System

- Flow of information in the system (describe)
    1. How is data collected and who collects it?
    2. How is it recorded in the system
    3. What happens to the reports? Who receives the reports?
- Is the information useful to you at a government level?
- What do you see as the benefits to the system (training, improved lab turn-around, political will etc.)
- How are the reports used to trigger action?
- Any known downsides to the system?

- Is the system simple to maintain?
- Is the system stable (does it always work, if not do you know what happened?

Stakeholders

- Who are the stakeholders in the system in this country?
- What role does each of the stakeholders play?
- From your perspective as a stakeholder, is the system meeting its' objectives?
- Are there any other people who should be interviewed?

Reporting

- Is your country reporting within the expected timeframes?
- What helps with reporting in the expected timeframes?
- Are there any issues around providing reports within the expected timeframes?
- Are there any known barriers to reporting? (Why isn't is working)
- What happens to the reports? Who has access to the reports? Are the reports published in the media etc or used for league tabling?
- Are you fed back information about outbreaks occurring in other countries?
- Were any unusual events reported outside of the weekly reporting?

Outbreaks

- What outbreaks are you aware of that have occurred in your country since the system was implemented? Were these picked up by the syndromic surveillance system or through other means? (list - time, place, numbers, disease, severity, response, notification, confirmation of outbreak, timeliness of outbreak notification)
- If outbreaks were missed by the system, then why do you think they were missed?
- How were outbreaks detected prior to the implementation of the system?
- What could be done to improve outbreak detection?

Syndromes/thresholds

- Were the core syndromes adequate to detect serious outbreaks?
- Do the core syndromes need any adjustment? If so, why?
- If so, what should be changed?

- Are the case definitions being used when reporting occurs?
- Are there thresholds for each of the syndromes?
- Are the thresholds being used as the basis for initiating action once a threshold is exceeded?
- Are there any syndromes that should be removed from the list of core syndromes? (Any that aren't really useful)
- Are there any additional syndromes that should be added to the system?
- Rank the top three syndromes that could be added to the system

Responses

- Describe some outbreaks, and how they progressed through the system including the response? Do you know if the responses followed the guidelines, were these helpful?

Conclusion

- Overall, do you feel that Syndromic surveillance system is working? Is it helping to identify infectious disease outbreaks?
- Why do you think the system is working?
- Are there any issues or problems with the system that you can identify?
- What do you think could be improved? What would you change?
- Do you think that this system is better than the one previously used?
- Are there any other public health benefits generated or enabled by the system? (Communication, information sharing more generally?)
- Do you have any other comments?

Questions: surveillance officers (entering data into the system)

Today I'll be talking to you about the Pacific Syndromic surveillance system. This is a new system and we want to understand whether it's meeting its objectives – that is, helping with the detection and responses to outbreaks of infectious diseases. We'd also like to know about what is currently working, any problems you've encountered and what improvements could be made to the system.

As someone who collects the data and is so central to the system, I'd like to talk to you about how you collect and report the data; what you think happens to the data after it's been reported; any outbreaks that have happened since the system was implemented; what you think about the core syndromes; what works with the system; any issues or problems you might have encountered; and finally any improvements or changes you'd like to see.

Data

- Firstly, can you describe how data are collected in the system?
  - What data do you collect?
  - Do you use the case definitions for the core syndromes? What happens if you think something is important but it doesn't meet the case definition?
  - Who collects the data?
  - How often is it collected?
  - How do you record and report the data? How often do you report the data?
  - Does it ever happen that the data aren't able to be reported within the suggested timeframes? Are there any particular reasons that stand out that might make this occur (people away sick or on leave, too busy)
  - Is it easy to collect and report the data? What makes it easy, what makes it hard?
  - What happens to the reports? Who receives the reports?
  - Were you trained in how to report the data? If so, who did the training? Are the other people who do the reporting trained?

Outbreaks

- Do you use thresholds for each of the syndromes?
- Do you know how these thresholds were determined?
- What happens if there is a threshold alert? Is there someone that you notify?

- Are you aware of any outbreaks that have occurred in your country since the system was implemented? Describe the outbreaks?
- Do you know if these outbreaks were picked up by the syndromic surveillance system?
- If outbreaks were missed by the system, then why do you think they were missed?
- What could be done to improve the detection of outbreaks?

Unusual events

- Did any other unusual events, apart from the outbreaks described above, occur? Were these reported?

Syndromes/thresholds

- Were the core syndromes useful to detect serious outbreaks?
- Do the core syndromes need any adjustment? If so, why?
- If so, what should be changed?
- Are there any syndromes that should be removed from the list of core syndromes? (Any that aren't really useful)
- Are there any additional syndromes that should be added to the system?
- Rank the top three syndromes that could be added to the system

Conclusion

- Overall, do you feel that Syndromic surveillance system is working? Is it helping to identify infectious disease outbreaks?
- Why do you think the system is working?
- Have you encountered any issues or problems?
- What do you think could be improved? What would you change?
- Do you think that this system is better than the one previously used?
- Are there any other public health benefits generated or enabled by the system? (Communication, information sharing more generally?)
- Do you have any other comments?

Questions: Clinicians

Today I'll be talking to you about the Pacific Syndromic surveillance system. This is a new system and we want to understand whether it's meeting its objectives – that is, helping with the detection and responses to outbreaks of infectious diseases. We'd also like to know about what is currently working, any problems you've encountered and what improvements could be made to the system.

- What's your involvement with the Syndromic surveillance system? Describe.
- Have you had any training in using the system? What did that involve?

Outbreaks:

- How do you get information from the surveillance system?
- Have you heard about any outbreaks through the surveillance system?
- If you heard about an outbreak, how did you respond?
- Do you think that you receive the information in a timely enough manner to respond to an outbreak?
- Are you aware of any outbreaks that weren't identified by the system? Do you know of reasons why these weren't identified through the system?
- Do you know of any outbreaks that were identified early because of the system being in place?
- If you heard about an outbreak in another Pacific country would it change anything in your work practices?
- How did you used to find out about outbreaks? Is the current system an improvement?
- How could we improve outbreak detection?

Core syndromes:

- Do you think that the core syndromes are adequate to detect serious outbreaks?
- Do the core syndromes need any adjustment?
- If so, why and what should be changed?
- Do you know whether the case definitions are being used for the reporting?
- Are there any syndromes that should be removed from the list of core syndromes? (Any that aren't really useful)

- Are there any additional syndromes that should be added to the system?
- Rank the top three syndromes that could be added to the system

Conclusions:

- Overall, do you feel that Syndromic surveillance system is working? Is it helpful in identifying infectious disease outbreaks? Does it improve the responses to outbreaks?
- Why do you think the system is working?
- Have you encountered any issues or problems?
- What do you think could be improved? What would you change?
- Do you think that this system is better than the one previously used?
- Are there any other public health benefits generated or enabled by the system? (Communication, information sharing more generally?)
- Do you have any other comments?

APPENDIX B: REVIEW OF AUSTRALIA'S OF POLIO SURVEILLANCE QUESTIONNAIRE GUIDE

Draft Interview Question Guides

A review of current Australian polio surveillance activities is being undertaken to ensure that these optimally meet Australia's polio surveillance objectives. The review will consider whether current complementary strategies are the optimal surveillance system for a high income country, with sophisticated medical and laboratory infrastructure, and a long history of freedom from endemic polio circulation.

Surveillance components to be reviewed include: clinical, virological and environmental systems. The methodology includes: semi-structured expert informant interviews and observational techniques, including field inspections of raw data and data collection methods.

Semi-structured interview guides have been pre-prepared for the following interviews:

- National Enterovirus Reference Laboratory
- Enterovirus Reference Laboratory Network
- Members of the National Certification Committee
- Members of the Polio Expert Panel
- Directors of APSU and PAEDS
- Research Nurses
- National Focal Point for polio
- State government representatives
- Emergency Department Physicians/Paediatricians

National Enterovirus Reference Laboratory

- What is your role?
- What do you believe is the purpose of polio surveillance in Australia?
- Who are the key stakeholders in polio surveillance?
- What is the role of virological surveillance in Australia's polio surveillance?
- What is the role of the National Enterovirus Reference Laboratory? Has this role changed?
- What is the role of the Enterovirus Reference Laboratory Network?
- If there was a polio outbreak (multiple cases), how would the reference laboratory respond?
- How is the laboratory funded?

Linkages with stakeholders

- What are the linkages between the National Enterovirus Reference Laboratory and the Enterovirus Reference Laboratory Network?
- What are the linkages between the laboratory and the APSU and PAEDS systems?
- What relationship does the laboratory have with the Polio Expert Panel? What information do they require?
- What relationship does the laboratory have with the National Certification Committee? What information do they require?
- What relationship does the laboratory have with the Commonwealth Department of Health and Ageing and the CDNA? What information do they require?
- What is the role of the laboratory in relation to the polio response plan?

Virological surveillance

- How does virological surveillance for polio work?
- Are there any issues around the timing of laboratory samples (length of time required for cell culture testing of virological samples)?
- Sensitivity and specificity of the test?
- Does the laboratory ever get samples for children outside of the PAEDS or APSU system?

- How do you know if a case is a duplicate case?
- What are 'ineligible notifications of AFP cases'?
- What is 'Sufficient clinical information"?
- The laboratory does follow-up for stool samples – are there any issues around this?
- How many tests per year would you conduct each year to rule out polio? How many of these are for adult cases?
- Do labs ever send you samples to check for polio that were not originally requested by the clinician?
- Do you have any sense of the level of suspicion that a clinician would have for polio?
- Do you think that AFP surveillance is acceptable to clinicians?
- Do you have access to the clinical questionnaire completed by the clinicians? Do clinicians find the clinical questionnaire acceptable – do they complete – any issues/any changes?

AFP surveillance

- Why do we undertake AFP surveillance in Australia?
- Would a paediatric polio case be detected in Australia using existing surveillance systems?
- If there was no AFP surveillance would a paediatric polio case be able to be detected?
- Does AFP surveillance provide any additional benefits to Australia's health system?
- In this era of polio eradication, is Australia's surveillance system sensitive enough to capture all AFP cases?
- Why is it difficult to achieve the WHO indicators for stool collection?
- Are there any improvements that should be made to AFP surveillance?
- What are the barriers to AFP surveillance? What measures can be taken to address barriers?
- How successful has the Australian Paediatric Surveillance Unit (APSU) been in assisting Australia to achieve WHO AFP surveillance performance indicators?
- How successful has the Paediatric Active Enhanced Disease Surveillance (PAEDS) system been in assisting Australia to achieve WHO AFP surveillance performance indicators?
- What are the implications of having AFP as a notifiable condition?
- Does AFP surveillance provide any additional benefits to Australia's health system?

Laboratory containment

- Does current surveillance allow us to be confident that laboratory containment of potentially infectious polio materials been achieved?
- In the 2000 survey of laboratories possibly storing wild poliovirus or potentially infectious materials only 4 of 18 laboratories provided a final inventory of the materials. How do we know that some of these laboratories do not continue to have wild poliovirus or potentially infectious materials?
- What happened to the sample from the 2007 case?

Detection of adult cases of polio

- Would an adult polio case be detected in Australia using existing surveillance systems?

Environmental surveillance

- Why do we undertake environmental surveillance in Australia?
- How does environmental surveillance work?
- Is there any benefit to have a sentinel environmental surveillance system? What does it cost? Should there be more/less sites?
- Would environmental surveillance detect cases of polio? What would happen if polio was detected through this system?

Data Linkage

- What could be the role of the Australian and New Zealand Paediatric Intensive Care Registry and National AFP Surveillance Database Linkage Study in polio surveillance?
- Could the data be provided in a timely enough manner to be useful for polio surveillance?

Data

- Availability of data over time, by hospital, key demographics.

Conclusion

- Australia consistently does not meet the WHO indicators for stool sample collection, and has only recently been consistently meeting the non-polio AFP rate of 1 per 100,000 <15yrs. Do you believe that these indicators have relevance in a high income country, with sophisticated medical and laboratory infrastructure, and a long history of freedom from endemic polio circulation?
- Can you suggest any alternatives to the current system? What might be some issues around alternative systems?
- In this era of approaching polio eradication, how much of a priority do you think should be made of polio surveillance? How would this change post eradication?
- Have you identified any gaps, barriers or changes that you would like to see for polio surveillance?
- On a scale of 1 to 10, with 10 being a perfect score, how would you rate the effectiveness of current strategies in Australia for polio surveillance, in terms of being able to detect and respond to a polio case?

Enterovirus Reference Laboratory Network

- What is the role of virological surveillance in Australia's polio surveillance?
- What role does the Enterovirus Reference Laboratory Network play in polio surveillance?
- What is the relationship between the Enterovirus Reference Laboratory Network and the National Enterovirus Reference Laboratory?
- What data do you collect and who is it reported to?
- What would happen if there was an outbreak of polio?
- Do you hold any samples of potentially infectious polio virus? Do any laboratories hold samples of potentially infectious polio virus? What quality checks are in place to make certain of this?

Members of the National Certification Committee

- As a member of the National Certification Committee what do you believe is the purpose of polio surveillance in Australia?
- What is your role?

Detection

- Do the current surveillance strategies provide you with enough information to determine with confidence that Australia is polio free?
- Are there any issues that you have identified that could improve your ability to make this determination?
- Do you believe that we have the systems in place so that a paediatric polio case can be detected in Australia using existing surveillance systems?
- Do you believe that we have the systems in place so that an adult polio case can be detected in Australia using existing surveillance systems?
- If we miss non-clinical cases that do not cause an outbreak does it matter?
- Does not meeting the WHO indicators for stool collection have any implications for maintaining Australia's 'polio free' status?

Conclusion

- Australia consistently does not meet the WHO indicators for stool sample collection, and has only recently been consistently meeting the non-polio AFP rate of 1 per 100,000 <15yrs. Do you believe that these indicators have relevance in a high income country, with sophisticated medical and laboratory infrastructure, and a long history of freedom from endemic polio circulation?
- Can you suggest any alternatives to the current system? What might be some issues around alternative systems?
- In this era of approaching polio eradication, how much of a priority do you think should be made of polio surveillance? How would this change post eradication?
- Have you identified any gaps, barriers or changes that you would like to see for polio surveillance?

- On a scale of 1 to 10, with 10 being a perfect score, how would you rate the effectiveness of current strategies in Australia for polio surveillance, in terms of being able to detect and respond to a polio case?

Members of the Polio Expert Panel

- As a member of the Polio Expert Panel what do you believe is the purpose of polio surveillance in Australia?
- What is your role?

Detection

- What is the process for determining whether a case is polio or not? Who do you report to?
- Do the current surveillance strategies provide you with enough information to determine with confidence whether a case is polio or not?
- Are there any issues that you have identified that could improve your ability to make a determination?
- Do you believe that we have the systems in place so that a paediatric polio case can be detected in Australia using existing surveillance systems?
- Do you believe that we have the systems in place so that an adult polio case can be detected in Australia using existing surveillance systems?
- If we miss non-clinical cases that do not cause an outbreak does it matter?

Conclusion

- Australia consistently does not meet the WHO indicators for stool sample collection, and has only recently been consistently meeting the non-polio AFP rate of 1 per 100,000 <15yrs. Do you believe that these indicators have relevance in a high income country, with sophisticated medical and laboratory infrastructure, and a long history of freedom from endemic polio circulation?
- Can you suggest any alternatives to the current system? What might be some issues around alternative systems?
- In this era of approaching polio eradication, how much of a priority do you think should be made of polio surveillance? How would this change post eradication?
- Have you identified any gaps, barriers or changes that you would like to see for polio surveillance?

- On a scale of 1 to 10, with 10 being a perfect score, how would you rate the effectiveness of current strategies in Australia for polio surveillance, in terms of being able to detect and respond to a polio case?

Directors of APSU and PAEDS

- What is your role?
- As the Director of APSU/PAEDS what do you believe is the purpose of polio surveillance in Australia?
- What is the role of the APSU/PAEDS in polio surveillance? Who are the key stakeholders?
- How successful has the APSU/PAEDS been in assisting Australia to achieve WHO AFP surveillance performance indicators?
- Does AFP surveillance provide any additional benefits to Australia's health system?

Systems

- What are the overlaps between APSU and PAEDS? Are there any gaps between these surveillance systems?
- What is the National Enterovirus Reference Laboratory's role in AFP surveillance? Are there any issues? Are there any changes that you would like to see?
- Do clinicians find the clinical questionnaire acceptable – do they complete – any issues/any changes?
- Why is it difficult to achieve the WHO indicators for stool collection?
- What are the barriers to AFP surveillance? What measures can be taken to address barriers? Are there any improvements that should be made to AFP surveillance?
- What are the implications of having AFP as a notifiable condition?

Detection

- Would a paediatric polio case be detected in Australia using existing surveillance systems?
- If there was no AFP surveillance would a paediatric polio case be detected?
- In this era of polio eradication, is Australia's surveillance system sensitive enough to capture all AFP cases?

Conclusion

- Australia consistently does not meet the WHO indicators for stool sample collection, and has only recently been consistently meeting the non-polio AFP rate of 1 per 100,000 <15yrs. Do you believe that these indicators have relevance in a high income country, with sophisticated medical and laboratory infrastructure, and a long history of freedom from endemic polio circulation?
- Can you suggest any alternatives to the current system? What might be some issues around alternative systems?
- In this era of approaching polio eradication, how much of a priority do you think should be made of polio surveillance? How would this change post eradication?
- Have you identified any gaps, barriers or changes that you would like to see for polio surveillance?
- On a scale of 1 to 10, with 10 being a perfect score, how would you rate the effectiveness of current strategies in Australia for polio surveillance, in terms of being able to detect and respond to a polio case?

Research Nurses

- What is your role?
- Who are your main contacts in this role?
- What is the purpose of AFP surveillance?
- What data do you collect, how is it collected and how is it used?
- What's the process for getting the two stool samples?
- Do you do follow-up with the ward nurses about the stool samples?
- Do you ever get refusals from the parents?
- Are you in touch with the polio reference laboratory? How does that process work?
- Do you believe that the clinicians understand why you are collecting information on AFP cases? Are they cooperative? Do you think they would recognise a case of polio?
- Do clinicians find the clinical questionnaire acceptable – do they complete – any issues/any changes?
- Do you provide feedback to the clinicians?
- How do you know that you're capturing all the AFP cases? What quality checks are in place to ensure that you are capturing all AFP cases?
- What is the purpose of AFP surveillance in Australia?
- Australia consistently does not meet the WHO indicators for stool sample collection, do you have any thoughts on why this is so and any changes that could be made to improve this?

Conclusion

- On a scale of 1 to 10, with 10 being a perfect score, how would you rate the effectiveness of current strategies in Australia for AFP surveillance?
- Do you believe that we have the systems in place so that a paediatric AFP case can be detected in Australia using existing surveillance systems?
- Have you identified any gaps, barriers or changes that you would like to see for polio surveillance?

National Focal Point for polio

- What is the role of the National Focal Point for polio?
- From a Commonwealth Government perspective what is the purpose of polio surveillance in Australia?
- Who do you consider to be the key stakeholders for polio surveillance in Australia?
- What are Australia's obligations for polio surveillance?
- What are your requirements from polio surveillance?
- What are the links between Australia's polio surveillance system, the response system, and certifying Australia as polio free?
- In this era of approaching polio eradication, how much of a priority do you think should be made of polio surveillance? How would this change post eradication?
- What would be the implications if Australia did not attempt to meet the WHO indicators for polio surveillance? How would this impact on certification?

Notifiables

- What role does the NNDSS play in polio surveillance?
- AFP is only notifiable in Qld, would it make any difference if it was notifiable nationally?
- The case definition was recently changed – have there been any implications from this?

Detection

- How do we know that Australia remains polio free? If we miss non-clinical cases that do not cause an outbreak does it matter?
- Do you believe that we have the systems in place so that an adult polio case can be detected in Australia using existing surveillance systems?
- Do you believe that we have the systems in place so that a paediatric polio case can be detected in Australia using existing surveillance systems?
- Do you believe that the systems that are in place provide timely enough information in the event of an outbreak?

- New Guinea has been identified as a high risk country for polio – how has that risk been responded to?

Laboratory containment

- How confident are you that laboratory containment of potentially infectious polio materials been achieved?

Surveillance costs

- What does AFP surveillance cost? (Paeds and APSU and VIDRL)
- What does virological surveillance cost?
- What does environmental surveillance cost?

Conclusion

- Australia consistently does not meet the WHO indicators for stool sample collection, and has only recently been consistently meeting the non-polio AFP rate of 1 per 100,000 <15yrs. Do you believe that these indicators have relevance in a high income country, with sophisticated medical and laboratory infrastructure, and a long history of freedom from endemic polio circulation?
- On a scale of 1 to 10, with 10 being a perfect score, how would you rate the effectiveness of current strategies in Australia for polio surveillance?
- Have you identified any gaps, barriers or changes that you would like to see for polio surveillance?

State government representatives

- What is your role?
- From a State Government perspective what is the purpose of polio surveillance in Australia?
- Who do you consider to be the key stakeholders for polio surveillance in your state and Australia?

Detection

- How do we know that Australia remains polio free? What is the process for detecting polio cases in this state (both AFP and adult cases)?
- If we miss non-clinical cases that do not cause an outbreak does it matter?
- Do you believe that we have the systems in place so that an adult polio case can be detected in Australia using existing surveillance systems?
- Do you believe that we have the systems in place so that a paediatric polio case can be detected in Australia using existing surveillance systems?

Laboratory containment

- Does your state hold any stocks of polio materials in any laboratories? How do you know this?

Conclusion

- In this era of approaching polio eradication, how much of a priority do you think should be made of polio surveillance? How would this change post eradication?
- Australia consistently does not meet the WHO indicators for stool sample collection, do you have any thoughts on why this is so and any changes that could be made to improve this?
- Australia consistently does not meet the WHO indicators for stool sample collection, and has only recently been consistently meeting the non-polio AFP rate of 1 per 100,000 <15yrs. Do you believe that these indicators have relevance in a high income country, with sophisticated medical and laboratory infrastructure, and a long history of freedom from endemic polio circulation?

- On a scale of 1 to 10, with 10 being a perfect score, how would you rate the effectiveness of current strategies in Australia for polio surveillance?
- Have you identified any gaps, barriers or changes that you would like to see for polio surveillance?

Qld only

- AFP is only notifiable in Qld, why was it made notifiable in Qld?
- Are there any advantages or disadvantages to having AFP notifiable?
- New Guinea has been identified as a high risk country for polio – how has that risk been responded to?

Emergency Department Physicians/Paediatricians

- What is your role?

Clinical suspicion

- Have you ever had an AFP case or a case that you suspected might be polio?
- What actions did you take?
- Are you aware of which countries might be considered to be at highest risk for polio?

AFP surveillance

- What is the purpose of AFP surveillance in Australia?
- Have you ever filled in the clinical questionnaire for PAEDS? Were there any issues or changes you'd like to see?
- Have you ever filled in a monthly report form to APSU that included an AFP case? Did anyone contact you about this?

Conclusion

- In this era of approaching polio eradication, how much of a priority do you think should be made of polio surveillance? How would this change post eradication?
- Do you believe that we have the systems in place so that a paediatric or adult polio case can be detected in Australia using existing surveillance systems?
- Australia consistently does not meet the WHO indicators for stool sample collection, do you have any thoughts on why this is so and any changes that could be made to improve this?
- Have you identified any gaps, barriers or changes that you would like to see for polio surveillance?

APPENDIX C: PUBLICATION ACCEPTANCE NOTIFICATION FROM THE JOURNAL COMMUNICABLE DISEASE INTELLIGENCE

From: Leroy.Trapani@health.gov.au on behalf of CDI.EDITOR@health.gov.au Sent: Fri 3/05/2013 5:25 PM
To: Beverley Paterson
Cc:
Subject: Article accepted for CDI publication [SEC=UNCLASSIFIED]

Message standard copyright form.doc (31 KB)
Paterson - Polio - editorial comments (track changes) (D13-476318).DOCX (2 MB)

Dear Beverley

I am pleased to inform you that the report **'Review of Australia's polio surveillance'** has been accepted for publication in the next issue of *Communicable Diseases Intelligence*

Please find attached further editorial comments and copyright form, which is required to be signed by all authors and returned to us at your earliest convenience.

Yours sincerely

Leroy Trapani

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