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Pandemic H1N1 influenza lessons from the southern hemisphere

M G Baker (michael.baker@otago.ac.nz)[1], H Kelly[2], N Wilson[1]
1. University of Otago, Wellington, New Zealand
2. Victoria Infectious Diseases Reference Laboratory, Melbourne, Australia

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Early in the 2009 H1N1 influenza pandemic, an editorial in *Eurosurveillance* noted the importance of observing experience with this novel virus in the southern hemisphere during their usual winter influenza season [1]. This special issue of Eurosurveillance is a timely response to that call. It contains reports from the island of Réunion, South Africa, South America (Brazil, Peru), and Australia (New South Wales and Victoria). It also includes an overview of the effect of the pandemic on indigenous people. This editorial summarises some of the key findings from these papers, reviews features of pandemic H1N1 influenza epidemiology in these countries, and lists some potential lessons for the northern hemisphere (and possible future waves in the southern hemisphere).

Important findings from the papers in this issue

Investigators from Réunion Island (located near Madagascar in the Indian Ocean) [2] used data from multiple surveillance systems, including influenza-like illness (ILI) reports by sentinel practitioners, virological surveillance, surveillance of hospital emergency departments and intensive care units (ICUs), and fatal cases attributed to influenza A(H1N1)v infection. The introduction of the pandemic virus happened later than in other southern hemisphere countries with community transmission not documented until 23 July 2009. The pandemic virus became the predominant circulating influenza virus on Réunion within four weeks following its first detection.

The paper from South Africa provides one of the first reports on the pandemic from an African country [3]. It is based on a descriptive analysis of the national epidemiology of the H1N1 influenza pandemic, focussing on laboratory-confirmed cases and deaths. Surveillance included multiple systems and an expected shift in focus as the pandemic progressed. The final analysis was based on a large number of laboratory-confirmed cases (12,331) including 91 deaths. Of particular note was the high proportion of fatal cases who were human immunodeficiency virus (HIV)-positive (53% based on 17/32 tested, against a background HIV prevalence of 18% in 15-49 year-old adults) and pregnant (56%, based on 25/45 women of reproductive age).

Assessment of the pandemic in Brazil [4] was based on surveillance of notified influenza cases and later ILI cases with severe acute respiratory infection (SARI). Reflecting its large population, Brazil reported 34,506 cases of ILI with SARI, although only 16.7% were laboratory-confirmed as pandemic influenza. There were 1,567 recorded deaths among SARI cases, including 645 with confirmed pandemic influenza. The age distribution of cases (peaks in the under five year-olds and in adults 20-29 years, with lower rates in the over 60 year-olds) was similar to that seen in higher income countries such as Australia and New Zealand. Severe illness was associated with pregnancy and a range of co-morbidities (notably chronic lower respiratory and metabolic diseases). The authors also noted marked geographic variations with cases concentred in southern and south-eastern Brazil, regions with more temperate climates bordering other affected South American countries.

Description of the pandemic in Peru [5] was based on established sentinel ILI and virological surveillance of influenza, surveillance of SARI, acute respiratory infection (ARI) and pneumonia, and additional case and cluster investigation. Peru reported 8,381 confirmed cases including 143 fatalities. Most fatal cases (75.5%) had an identified co-morbidity, notably metabolic, cardiovascular or respiratory disease.

This edition includes three separate reports from Australia. Investigators from New South Wales (NSW) [6] provide perhaps the most comprehensive description of the pandemic using multiple surveillance systems (including use of novel systems such as ambulance despatch data and web-based systems for capturing attendances at specialist influenza clinics and ICU utilisation). The pandemic there lasted 10 weeks and had a substantial impact on ICUs, with an increased risk of severe illness, including respiratory failure, in those aged between 35 and 60 years. As seen elsewhere, vulnerable groups included pregnant women, indigenous people (Aboriginal or Torres Strait Islanders), those with chronic respiratory disease, and those with morbid obesity. However, the general influenza-related mortality and overall mortality between April and September 2009 was lower than that seen during the same period in recent years.

Although commencing earlier, the pandemic in Victoria [7] followed a similar epidemic pattern to NSW, based on a general practitioner sentinel surveillance system and notifications of laboratory-confirmed influenza. Peak ILI rates were comparable in magnitude to several previous years. Understanding of the Victorian experience has been strengthened by an accompanying paper which estimates the reproduction number (R) during the epidemic in that state[8]. After accounting for undetected transmission, the authors estimate R at 1.6 (95% credible interval: 1.5-1.8).

The final paper is focussed on the impact of the pandemic on indigenous people, rather than on a specific geographic area [9]. From the southern hemisphere, this analysis included indigenous people in Brazil (Amerindians), Australia (Aborigines and Torres Straits Islanders), New Zealand (Māori and Pacific peoples), and the Pacific (Polynesians, Melanesians). It also included indigenous people in the northern hemisphere, notably in Canada and the United States. In all of these countries indigenous peoples experienced significantly elevated risks of serious infection, with

Table

Key epidemiological features of the H1N1 influenza pandemic 2009 reported by selected southern hemisphere countries

Country or state	First detection of influenza A(H1N1)v [date]	Established community transmission [date]	Pandemic peak [date]	Population [N]	Hospital admissions [N]	Cumulative incidence of hospitalisation [per 100,000]	Deaths [N]	Cumulative incidence of deaths [per million population]	Source
Africa and Indian Ocean									
Réunion Island	5 July	23 July	24-30 August	802,000	255	31.8	6	7.5	European Centre for Disease Prevention and Control Daily Update, 1 October 2009
South Africa	14 June	15 July	3-9 August	49,052,489	NA	NA	91	1.9	South African National Institute for Communicable Disease, 12 October 2009
South America									
Argentina	NA	NA	22-28 June	40,301,927	11,086	27.5	580	14.4	Influenza Pandemica (H1N1) 2009. Republica Argentina, 9 October 2009
Brazil	7 May	16 July	3 August	186,842,147	NA	NA	899	4.8	PAHO Regional Update Pandemic (H1N1) 2009, 9 October 2009
Chile	17 May	26 May	11 June (Los Lagos)	16,284,741	1,585	9.7	134	8.2	PAHO Regional Update Pandemic (H1N1) 2009, 9 October 2009
Paraguay	NA	NA	NA	6,349,000	128	2.0	42	6.6	PAHO Regional Update Pandemic (H1N1) 2009, 9 October 2009
Peru	9 May	NA	22 June (Lima y Callao)	29,546,963	NA	NA	153	5.2	PAHO Regional Update Pandemic (H1N1) 2009, 9 October 2009
Uruguay	NA	NA	NA	3,494,382	NA	NA	20	5.7	PAHO Regional Update Pandemic (H1N1) 2009, 9 October 2009
Oceania									
Australia	8 May	4 June	21 July	21,262,641	4,844	22.8	183	8.6	Australian Influenza Surveillance Report No. 21, 2 October 2009
• Victoria	20 May	4 June	28 June	5,402,600	513	9.5	24	4.4	Victorian Influenza Report No. 24, reference [8]
• NSW	21 May	15 June	17 July	7,017,100	1,267	18.1	51	7.3	NSW Health Influenza Epidemiology Report 1 May to 20 September 2009
Fiji	NA	NA	NA	849,000	NA	NA	0	0	Pacific Public Health Surveillance Network: Pandemic Influenza A / H1N1 2009 Surveillance, Report as of 21 October 2009
French Polynesia	NA	NA	NA	264,000	NA	NA	7	26.5	Pacific Public Health Surveillance Network: Pandemic Influenza A / H1N1 2009 Surveillance, Report as of 13 October 2009
New Caledonia	NA	NA	NA	249,000	NA	NA	9	36.1	European Centre for Disease Prevention and Control Daily Update, 1 October 2009
New Zealand	25 April	1-7 June	6-12 July	4,143,279	1,001	24.2	18	4.3	Influenza Weekly Update 28 September-4 October 2009
Samoa	NA	NA	NA	179,000	NA	NA	2	11.2	Pacific Public Health Surveillance Network: Pandemic Influenza A / H1N1 2009 Surveillance, Report as of 21 October 2009
Tonga	NA	NA	NA	104,000	NA	NA	1	9.6	Pacific Public Health Surveillance Network: Pandemic Influenza A / H1N1 2009 Surveillance, Report as of 21 October 2009

NA: not readily available

hospitalisation and mortality rates that were three to seven times higher than those reported for non-indigenous populations.

The time course and impact of the pandemic in southern hemisphere countries

The countries described in this issue of *Eurosurveillance* are located south of the equator and share the same winter season. Consequently the emergence of pandemic H1N1 influenza coincided with their peak period for seasonal influenza. Despite considerable geographical and demographical differences between them, the pandemic showed a surprisingly consistent pattern of infection across these countries. We have summarised some epidemiologic features of the H1N1 influenza pandemic in these countries (Table). For purposes of comparison, we have included data on several other large South American countries (Argentina, Chile, Paraguay, Uruguay,) and some of the larger Pacific Islands (New Caledonia, French Polynesia, Samoa, Fiji) for which data were readily available in the public domain.

Following its detection in Mexico in mid-March 2009, the epidemic spread rapidly to all southern hemisphere countries listed in the Table [10]. In these countries, the first reported identifications of introduced virus ranged from late April through to early July. Introduction of the virus was followed by a variable interval before local community transmission was confirmed (i.e. transmission from cases with no known history of overseas travel or contact with a person or group with a connection to an imported case). Community transmission was usually accompanied by a rapidly accelerating epidemic that peaked within two to six weeks. The pandemic virus swiftly replaced seasonal influenza viruses [11]. The epidemic decline, although rapid, was usually somewhat slower than the initial rise.

Rates of hospitalisations and deaths showed wide variability by country. Hospitalisation rates ranged from 2.0 to 31.8 per 100,000 population, and mortality rates ranged from 0 to 36.1 per million population.

Consistent features of the pandemic in southern hemisphere countries

Within larger countries there were often marked regional variations in influenza rates. Some regions lagged by a few days to a few weeks. At the end of the spread within the country, there were often large geographic variations in the reported incidence of infection and its outcomes (hospitalisation and mortality rates).

There were consistent patterns in those most likely to present with clinical illness, and particularly, those most likely to have poor outcomes of infection such as hospitalisation, ICU treatment, or death. Illness rates tended to be highest in children under the age of five years, sometimes with a second peak in young adults, with uniformly low rates in older populations (60+ years). The downward shift in age was well illustrated in South Africa where the median age of pandemic H1N1 influenza cases was 16 years, compared with 27 years for seasonal influenza A(H1N1) in 2008.

Indigenous people were vulnerable to poor outcome from pandemic H1N1 influenza infection [9]. Other vulnerable groups were pregnant women (with ICU admission rates in Australasia about nine times higher than expected [12]), severely obese people (with ICU admission rates in Australasia for those with a body mass index (BMI) of >35 about five times higher than expected [12]), and those with asthma or other chronic respiratory disease (with ICU admission rates in Australasia more than twice as high as would be expected [12]). HIV infection appeared more common in fatal cases in South Africa than expected based on prevalence in the population [3].

Mortality from the pandemic appeared to be relatively low. Most countries reported mortality rates of less than one per 100,000 population. There is evidence from New South Wales that excess

Box

Pandemic lessons from the southern hemisphere

1. *Remain cautious*. The 2009 H1N1 influenza pandemic demonstrated typical pandemic influenza behaviour in all southern hemisphere countries were it was detected, including relatively high infectiousness in some populations, rapid replacement of seasonal influenza viruses, and a downward shift in the age groups affected. A similar pattern can be expected during the northern hemisphere influenza season. This virus therefore deserves the caution due any new pandemic influenza virus that has capacity to evolve over time.
2. *Consider the relatively low severity of this pandemic*. The public health impact of this pandemic virus places it at the least severe end of the pandemic influenza scale (category 1 out of 5 on the Pandemic Severity Index [21]). The resources applied to the public health response, and messages from health authorities to the public, need to appropriately reflect this level of threat.
3. *Protect vulnerable groups*. Some groups have a much higher risk of poor outcomes, notably indigenous populations, pregnant women, and those with serious chronic health conditions (including respiratory and cardiovascular disease, diabetes, morbid obesity, and possibly HIV infection). Public health management should be focussed on protecting these groups.
4. *Consider the limited role for containment*. Containment measures now have only a limited role given the global distribution of pandemic H1N1 influenza. Border control measures could be considered for isolated populations, but even these are likely to be of limited value except in places with very low travel volumes [22].
5. *Consider cost-effective mitigation measures*. Public health measures to limit the spread of pandemic H1N1 influenza may have value in reducing the intensity of the pandemic peak once community transmission is established. Relatively low-cost measures such as promotion of hand and respiratory hygiene and home isolation of those who are ill, are likely to be the most defensible [23]. They may also provide co-benefits in terms of reducing transmission of other infectious diseases. More disruptive social distancing such as school closures seem difficult to justify unless the severity of this pandemic increases.
6. *Plan for the impact on health services*. Pandemic influenza may strain healthcare services, particularly ICUs and emergency departments. This pressure may be most intense during a relatively short epidemic peak.
7. *Optimise surveillance*. Some surveillance methods are better than others at characterising the pandemic at all stages. Systems that appeared particularly valuable were established sentinel surveillance systems that combined virological and epidemiological data, systems that could rapidly report hospitalisations and deaths from influenza, and well organised networks of clinicians (notably ICU specialists) who were able to characterise particularly important sub-populations of cases. There is potential for greater use of more novel approaches (cross sectional telephone surveys of ILI, sero-surveys, and even use of Google Flu Trends [24 25]).
8. *Plan research*. Northern hemisphere countries are well placed to plan and conduct research to investigate important questions about pandemic influenza epidemiology, prevention and control. In particular, there is still a high level of uncertainty about the effectiveness of both pharmaceutical and non-pharmaceutical interventions for reducing the spread and impact of such pandemics.

mortality from influenza and pneumonia over the period of the pandemic was less than in previous years [6]. These results suggest the case fatality ratio (CFR) was also low. The main limitation in estimating the CFR is uncertainty over the size of the infected denominator population [13]. A report from New Zealand estimated approximately 7.5% of the population had symptomatic illness, suggesting 10-15% may have been infected and a CFR of <0.01% [14]. Samoa provides a dramatic illustration of the impact of this pandemic compared to the 1918-19 pandemic. At that time the islands (then named "Western Samoa") had the highest death rate for any country or territory, losing 19-22% of its population [15]. In the current pandemic Samoa has recorded only two deaths, a mortality rate of 0.001% (Table).

The pandemic appears not to have overwhelmed health services in the southern hemisphere countries reviewed in this issue, although some services were at their maximum capacity. In Australia and New Zealand, ICU admissions due to confirmed infection with pandemic influenza were carefully tracked and reached a maximum of 8.9 to 19.0% of ICU capacity during the most intense weeks of the pandemic [12]. However, a report from Argentina suggested that the pandemic can threaten to overwhelm healthcare systems unless the public is given very clear messages about the appropriate use of these services [16].

Pandemic containment measures were inconsistently used in southern hemisphere countries and their impact remains uncertain. Border and cluster controls were reported by Australia (NSW [6] and Victoria [7]), New Zealand [14], Réunion Island [2] and Peru[5]). Both New Zealand and Réunion reported delays of several weeks from the first detection of imported cases to the establishment of community transmission. By contrast, investigators in Victoria suggested that community transmission of the pandemic virus may have been established prior to the commencement of testing [7].

Southern hemisphere countries used data from a range of surveillance systems. The most comprehensive appeared able to provide timely and sensitive information on general practice consultations, emergency department attendances, hospitalisations, ICU utilisation, and deaths from influenza and related diseases. Countries with fewer resources had correspondingly fewer sources of information. Surveillance in these settings tended to be orientated toward meeting the more minimal surveillance requirements of the World Health Organization (WHO) [17], which focus on early detection and investigation, comprehensive assessment, and monitoring of the pandemic.

Areas of uncertainty and research needs

The infectiousness of the pandemic virus (as measured by the reproduction number) and existing immunity in the population have not been fully characterised. The analysis from Victoria presented here [8], may help to explain one of the paradoxical findings of the pandemic in southern hemisphere countries: the observation of a rapid rise in the epidemic curve would suggest a fairly infectious virus, whereas the proportion of the population apparently infected appears relatively small [14]. The estimated reproduction numbers of 1.6 for Victoria was within the range of 1.37 reported for Peru [18] to 1.96 for New Zealand [19]. As the analysis for Victoria suggests, a single estimate of R is inadequate to fully characterise the infectiousness of the virus. Their finding of higher infectiousness in children suggests an epidemic that was rapidly propagated in children, with some 'spillover' into adult populations. Combined with some pre-existing immunity in older age groups, this modelling would help to explain the observed epidemic pattern. Serological surveys will be useful to clarify these issues further.

It is too early to expect robust evaluations of the interventions used in southern hemisphere countries during the pandemic. The apparent success of border controls and cluster controls at delaying pandemic entry into some countries, such as New Zealand and Réunion, should be evaluated. The declining reproduction number observed in Victoria may reflect the effect of mitigation strategies such as reactive school closure, quarantine, antiviral treatment and prophylaxis and voluntary social distancing or may merely be a feature of the pandemic virus infecting an immunologically naïve population. Again, the effects of pharmaceutical treatment and social distancing measures need further evaluation. As has happened in Australia, we believe it is appropriate for national funding agencies to support both commissioned and investigator-led research, so that we can learn as much as possible from this pandemic [20].

There are lessons that European countries can potentially learn from the experience in the southern hemisphere with this pandemic (Box). High quality surveillance and research in the northern hemisphere also has the capacity to reduce the considerable uncertainty that remains around the behaviour of this new pandemic virus.

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Preliminary analysis of the pandemic H1N1 influenza on Réunion Island (Indian Ocean): surveillance trends (July to mid-September 2009)

F Thouillot1, C Do[1], E Balleydier[1], E Rachou[2], F Staikowsky[3], P Morbidelli[4], Y Jacques-Antoine[5], A Bourde[6], M Lagrange-Xélot[7], P Poubeau8, A Winer[9], B A Gauzere[10], A Michault[11], M C Jaffar-Bandjee[12], G Henrion[13], L Filleul[1], E D'Ortenzio (eric.dortenzio@sante.gouv.fr)[1]

1. Regional office (Cire) of the French Institute for Public Health Surveillance (Institut de veille sanitaire), Réunion, France
2. Regional Health Observatory (Observatoire régional de la santé), Réunion, France
3. Emergency Department (Service des urgences), Regional Hospital Centre of Saint-Pierre, Réunion, France
4. Emergency Department (Service des urgences), Hospital Centre of Saint-Paul, Réunion, France
5. Emergency Department (Service des urgences), Clinic of Saint-Benoît, Réunion, France
6. Emergency Department (Service des urgences), Regional Hospital Centre of Saint-Denis, Réunion, France
7. Infectious Diseases Unit (Unité des maladies infectieuses), Regional Hospital Centre of Saint-Denis, Réunion, France
8. Infectious Diseases Unit (Unité des maladies infectieuses), Regional Hospital Centre of Saint-Pierre, Réunion, France
9. Intensive Care Unit (Service de réanimation), Regional Hospital Centre of Saint-Pierre, Réunion, France
10. Intensive Care Unit (Service de réanimation), Regional Hospital Centre of Saint-Denis, Réunion, France
11. Laboratory for Bacteriology, Parasitology, Virology and Hospital Hygiene (Laboratoire de de bactériologie, parasitologie, virologie et hygiène hospitalière), Regional Hospital Centre of Saint-Pierre, Réunion, France
12. Laboratory for Microbiology, Regional Hospital Centre of Saint-Denis, Réunion, France
13. Hospital Based Mobile Emergency Unit (SAMU), Regional Hospital Centre of Saint-Denis, Réunion, France

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First infections with the 2009 pandemic H1N1 influenza virus were identified on Réunion Island in July 2009. By the end of July, sustained community transmission of the virus was established. Pandemic H1N1 influenza activity peaked during week 35 (24 to 30 August), five weeks after the beginning of the epidemic and has been declining since week 36. We report preliminary epidemiological characteristics of the pandemic on Réunion Island in 2009 until week 37 ending September 13.

Introduction

On 21 April 2009 (week 17), the United States Centers for Diseases Control and Prevention (US CDC) published a report about first cases of so-called 'swine influenza A(H1N1)' infection in two children in southern California [1]. On 24 April 2009 (week 17), the World Health Organization (WHO) informed about an epidemic caused by what was then called 'new swine-origin influenza A(H1N1) virus' originating from Mexico, and declared a public health emergency of international concern. In response to the threat of emergence and spread of the pandemic influenza A(H1N1)v virus, the Regional Office (Cire Réunion-Mayotte) of the French Institute for Public Health Surveillance (InVS) on Réunion Island implemented enhanced influenza surveillance in May 2009 to detect the introduction of the pandemic H1N1 influenza and monitor its spread and impact on public health [2]. On 5 July 2009 (week 27), while seasonal influenza was already reported on the island, the first imported case of pandemic H1N1 influenza was detected on Réunion Island in a traveller returning from Australia [3]. From 5 to 23 July, no evidence of local transmission of pandemic H1N1 influenza was detected, all laboratory-confirmed cases were considered as imported or having an epidemiological link with another imported laboratory-confirmed case. From 23 July (week 30), there was evidence of local transmission, and the individual surveillance was shifted to a population-based surveillance, according to French procedures [4]. In this preliminary analysis, we report the epidemiological characteristics of influenza on Réunion Island in 2009 until week 37 ending September 13.

Methods

On Réunion Island, enhanced influenza surveillance, set up in May 2009 and previously described [2], has been modified after evidence of local transmission and rapid spread of the 2009 pandemic H1N1 influenza virus. The objective of the previous surveillance was to detect and to confirm all infected travellers arriving from countries where autochthonous transmission of pandemic H1N1 influenza virus was known to occur while the aim of the ongoing surveillance is to describe the trends of the influenza epidemic in the population and to characterise the dynamics of virus spread on the island. On 23 July, the new surveillance procedure was introduced using a range of indicators available from surveillance systems implemented before the emergence of the epidemic.

These systems include (for details see reference [2]):

- Surveillance of influenza-like illness (ILI) by the network of sentinel practitioners' including 24 general practitioner and three paediatricians scattered across the island to collect and provide timely information on influenza activity and the rate of ILI among their patients; these physicians reported on a weekly basis the number of ILI and their total number of consultants.
- Virological surveillance, to collect and provide detailed and timely information on circulating influenza virus strains;
- Surveillance of the activity of hospital emergency departments to collect and provide information from the four emergency departments of the four hospitals of Réunion;
- Surveillance of severe and fatal cases related to the pandemic H1N1 influenza virus, to better monitor the severity of the pandemic, to detect changes in the population groups affected by severe outcomes that may justify more robust public health measures, and to monitor deaths. A severe case was defined as a person with a laboratory-confirmed pandemic H1N1 influenza infection and admitted to an intensive care unit.

Results

Surveillance of ILI by sentinel practitioners' network

Weekly ILI consultation rates in 2009 were compared with the rates observed in the same period in the previous five years (2004-2008). From week 23 (starting 1 June) to week 30 (starting 20 July) 2009, the weekly ILI consultation rates remained below the 2004-2008 mean for the same period. Starting with the end of July (week 31) the ILI rate exceeded the 2004-2008 mean and increased sharply until week 35 2009 (starting 24 August). During this peak week, the rate of ILI reported by sentinel practitioners represented 20.6% of their consultations. This rate was the highest observed in Réunion in the past five years of influenza surveillance (Figure 1). During this peak week, 65% of nasal swabs performed by sentinel network physicians were positive for influenza A(H1N1)v.

Virological surveillance

Influenza B virus was first detected in week 23 (starting 1 June) and was the only strain found during the following four weeks. Few influenza A(H3N2) viruses were detected during week 30 to 32. As already mentioned, influenza A(H1N1)v virus was first detected in week 27 (starting 29 June). In weeks 27 and 38 (starting 14 September), 716 influenza A(H1N1)v viruses were isolated. In week 31 (starting 27 July), the pandemic virus became the dominant circulating strain on the island and reached 95% of all influenza-positive strains on week 34 (Figure 2). Some of the influenza A viruses that have not yet been not subtyped by the local laboratories have been sent to the French National Reference Centre for Influenza for complementary analysis.

Surveillance of hospital emergency department activity

From week 27 to week 30, the number of emergency department visits, regardless of the diagnosis (including the number of consultations for ILI), remained stable. In week 31, the visits increased rapidly. The total number of visits to emergency departments reached the highest value in week 33, while the total number of emergency department visits for ILI reached a peak in week 35. Since week 36, emergency department visits for ILI symptoms have been decreasing (Figure 3).

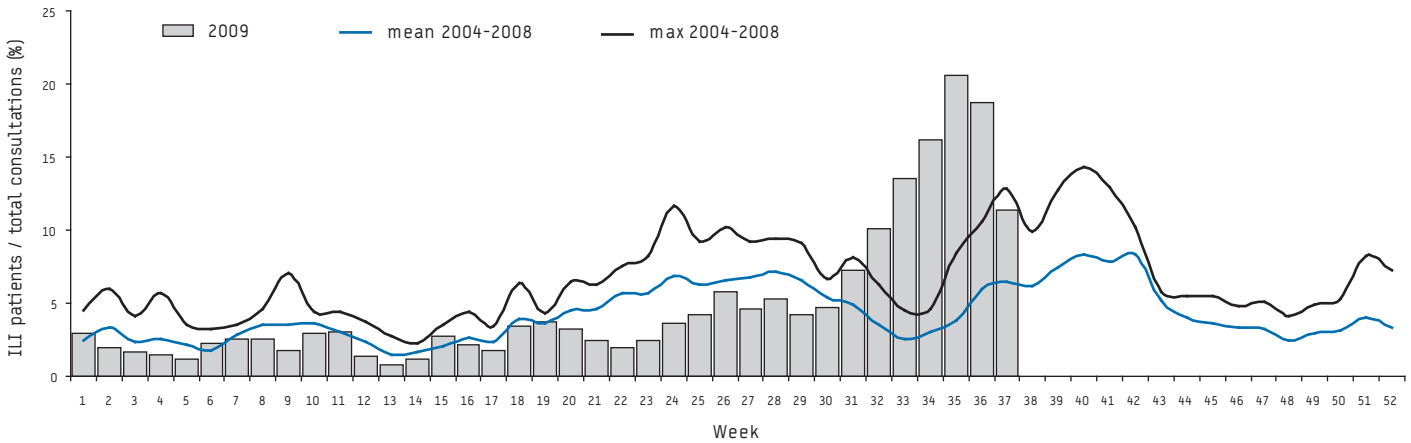
Surveillance of severe and fatal cases

Between 5 July and 13 September, 255 patients with laboratory-confirmed pandemic H1N1 influenza were hospitalised, including 119 who presented with a pre-existing comorbidity (Table). Nineteen of these 255 patients were hospitalised in an intensive care unit and were considered as severe cases (Figure 4).

On average, approximately 10 death certificates mentioning 'influenza' are received each year on Réunion. Between week 35 and 38, four women (5, 18, 28 and 78 years-old) and two men (32 and 69 years-old) infected with pandemic H1N1 influenza virus died. All of them had presented with comorbidity except for the 32 year-old man for whom only alcohol consumption without liver dysfunction was reported.

Figure 1

Consultation rates for influenza-like illness reported from the sentinel practitioner network, by week, Réunion Island, 2009



ILI: influenza-like illness.
Source: Observatoire régional de la Santé and réseau sentinelle, Réunion.

Discussion

First infections with the 2009 pandemic H1N1 influenza virus were identified on Réunion Island on July 2009. By the end of July, sustained community transmission of the virus was established. Pandemic H1N1 influenza activity peaked during week 35 (24 to 30 August), five weeks after the beginning of the epidemic and has been declining since week 36.

Data concerning comorbidities should be interpreted with caution, particularly for pregnant women. Indeed, healthcare providers might be more likely to admit a pregnant woman than a non-pregnant woman with similar findings, which could lead to an exaggerated percentage of pregnant women among hospitalised patients. We believe that mass media communication could have increased public anxiety and could have had an impact on the number of consultations for ILI, but this paper analysed only symptomatic cases reported through the sentinel network.

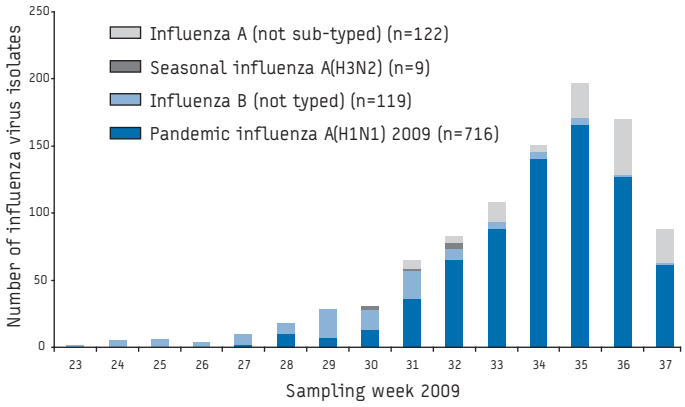
Like other countries in the southern hemisphere, the influenza season on Réunion began with cocirculation of the seasonal as well as the pandemic influenza A(H1N1) strain [5,6]. The pandemic virus became the predominant circulating influenza virus on Réunion within the four weeks following its first detection. A similar delay of four weeks was also observed in New Zealand [7]. Overall, the pandemic appears to have been remarkably similar in Australia, New Zealand and Réunion [5,6].

Réunion Island is presumed to have a double exposure to seasonal influenza, one from the southern hemisphere and the other one from the northern hemisphere given the intense links with continental France. As the winter influenza season started in continental France in week 38, persistent influenza activity on Réunion cannot be excluded. Ongoing surveillance will detect a second wave of the epidemic and continue to monitor and characterise potential changes in the virus.

These findings demonstrate the value of using integrated epidemiological, virological and hospital surveillance in order to monitor the scope of an influenza epidemic, identify circulating strains and provide guidance to public health control measures.

Figure 2

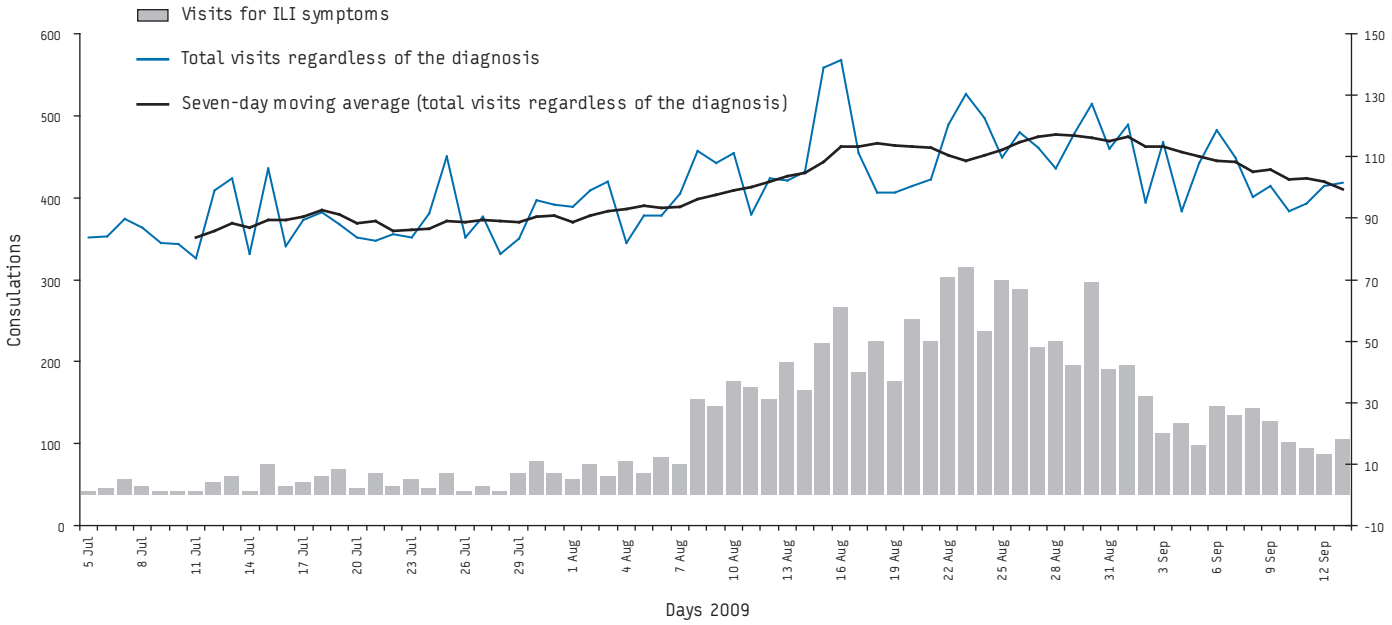
Isolated influenza viruses, Réunion Island, 5 July-13 September 2009 (n=966)



Source: Microbiology laboratories(Saint Denis Hospital, Saint-Pierre Hospital), Réunion.

Figure 3

Total consultations and consultations for symptoms of influenza-like illness in emergency departments, Réunion Island, 5 July-13 September 2009



ILI: Influenza-like illness
Source: Oscour® network

These preliminary results could provide relevant information for European countries regarding their own management of the ongoing epidemic and control measures. A complete epidemiological, clinical and virological analysis at the end of the epidemic should be available within a few weeks.

Acknowledgements

We are very grateful to all practitioners of the sentinel network for their collaboration in collecting and kindly providing data for this surveillance system. We thank all the clinicians for their participation in collecting clinical data.

Table

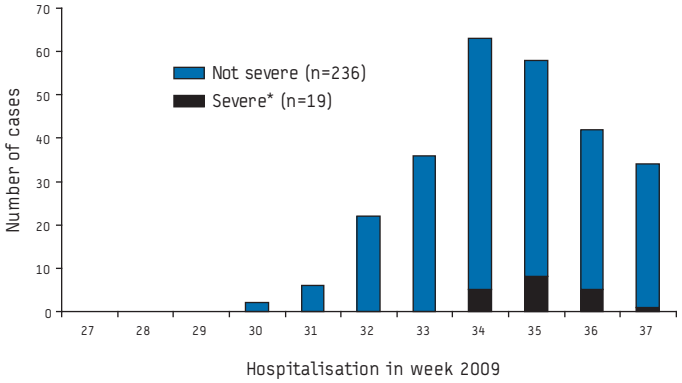
Frequency of risk factors in hospitalized patients infected with pandemic H1N1 influenza virus, Réunion Island, 2009 (n=119)

Comorbidities	n (%)*
Pregnancy	33 (28)
Children ≤ 1 year	30 (25)
Chronic respiratory disease	20 (17)
Diabetes	15 (13)
Cardiac insufficiency or severe valvulopathy	9 (7.6)
Congenital heart disorder	4 (3.4)
Immunodeficiency	4 (3.4)
Obesity	4 (3.4)
Long-lasting stay in a specialised establishment	3 (2.5)
Bronchopulmonary dysplasia	2 (1.7)
Sickle cell anaemia	2 (1.7)
Nephrotic syndrome	1 (0.8)
Cystic fibrosis	1 (0.8)
Child or teenager with long-lasting aspirin treatment	1 (0.8)

* Multiple answers were possible.

Figure 4

Hospitalisations of patients with laboratory-confirmed pandemic H1N1 influenza, Réunion Island, 5 July-13 September 2009 (n=255)



*A severe case was defined as a patient with laboratory-confirmed pandemic H1N1 influenza who was admitted to an intensive care unit or died.

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Interim report on pandemic H1N1 influenza virus infections in South Africa, April to October 2009: Epidemiology and factors associated with fatal cases

B N Archer (bretta@nicd.ac.za)[1,2], C Cohen[1,3], D Naidoo[1], J Thomas[1,3], C Makunga[1], L Blumberg[1,4], M Venter[1,5], G A Timothy[3], A Puren[1,4], J M McAnerney[1], A Cengimbo[1], B D Schoub[1,4]

1. National Institute for Communicable Diseases (NICD), a division of the National Health Laboratory Service (NHLS), Johannesburg, South Africa
2. School of Health Systems and Public Health, University of Pretoria, Pretoria, South Africa
3. School of Public Health, University of Witwatersrand, Johannesburg, South Africa
4. School of Pathology, University of Witwatersrand, Johannesburg, South Africa
5. Department of Medical Virology, University of Pretoria, Pretoria, South Africa

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We provide an interim report on pandemic H1N1 influenza activity in South Africa, with a focus on the epidemiology and factors associated with deaths. Following the importation of the virus on 14 July 2009, and the epidemic peak during the week starting 3 August, the incidence in South Africa has declined. A total of 12,331 cases and 91 deaths have been laboratory-confirmed as of 12 October 2009. Age distribution and risk groups were similar to those observed elsewhere. The median age of patients who died (33.5 years) was significantly higher than that of the non-fatal cases (15.0 years, p<0.01). The most common underlying conditions among fatal cases were infection with human immunodeficiency virus (17/32 tested) and pregnancy (25/45 women of reproductive age). Active tuberculosis coinfection was present in seven of 72 fatal cases. These findings should be taken into consideration when planning vaccination strategies for 2010.

Introduction

The first human cases of infection with the pandemic influenza A(H1N1)v virus were detected in the United States (US) and Mexico during April 2009 [1,2]. Following this, rapid global transmission was observed, prompting the World Health Organization (WHO) to raise the pandemic alert level to the highest phase-6 on 11 June 2009, while noting that the current pandemic may be characterised as moderate in severity [3]. As of 11 October 2009, the WHO has reported over 399,232 laboratory-confirmed cases of pandemic H1N1 influenza and more than 4,732 associated deaths worldwide [4]. Similarities with regards to the epidemiological behaviour of the influenza A(H1N1)v virus have been observed among populations of both the northern and southern hemispheres [5-12]. Further similarities have been observed globally in the risk factors contributing to severe disease and death, with underlying disease recorded in at least half of the fatal cases. Two risk factors appear to be of particular importance based on data already published: pregnancy (30% of the 20-39 year-old women who died) and metabolic diseases (especially severe obesity and diabetes, 30% of fatal cases) [12].

Although much has been published on the epidemiology of pandemic H1N1 influenza infections globally [1,2,5-12], there is little published data from the African continent. The epidemiology of pandemic influenza in South Africa might differ from that described elsewhere for numerous reasons. Firstly, the country is burdened with a high prevalence of other infectious diseases such as human immunodeficiency virus (HIV, approximately 5.2 million infected, 18.8% prevalence in adults 15-49 years of age, 28% antenatal prevalence in 2007 [14]) and tuberculosis (TB, approximately 1% prevalence in 2006 [15]). Secondly, there is a significant burden of non-communicable conditions such as obesity (24% of males and 27% of females in 2008) and diabetes (2.6% of males and 3.9% of females in 2008) [15]. Thirdly, there are large numbers of pregnant woman who may be at risk (total fertility rate 2.38 children per woman, general fertility rate 81 per 1,000 woman of reproductive age (15-49 years) in 2009) [16]. Finally, importation of the novel influenza virus into South Africa occurred during the winter months, when seasonal influenza epidemics are typically observed (South Africa experiences a temperate climate with the coldest months typically between May and September). The following report provides a preliminary analysis of the epidemiology of laboratory-confirmed pandemic H1N1 influenza cases and deaths in South Africa from 28 April to 12 October 2009.

Methods

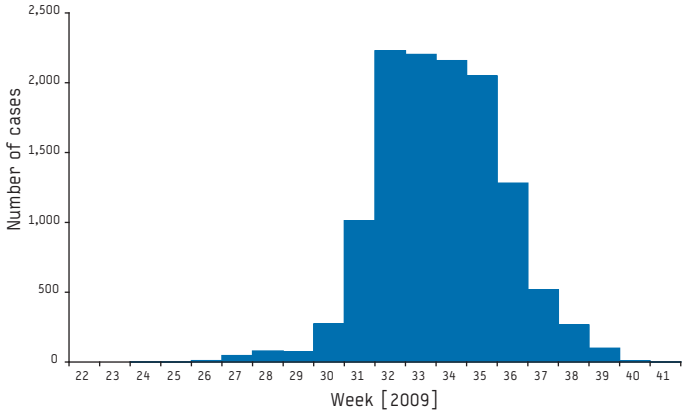
Methods for case finding, surveillance systems, laboratory testing and diagnostic strategies in South Africa have varied considerably with the evolution of the influenza pandemic over the period from April to October 2009. Following the first reports of transmission in the northern hemisphere, South Africa developed local case definitions and a procedure for active case-finding of possible imported cases, which were in place from 28 April 2009. These included the collection of nasal and throat swabs from all individuals who met the interim definition for a suspected-case of recent onset of influenza-like illness (ILI) and a history of travel to an area reporting a confirmed community-wide outbreak, or close contact with a suspected or confirmed case, within the seven days prior to onset of symptoms. Diagnostic testing was initially

done by the National Influenza Centre at the National Institute for Communicable Diseases (NICD), and testing was performed using the real-time PCR protocol distributed by the United States Centers for Disease Control and Prevention (US CDC) for the detection and characterisation of pandemic influenza A(H1N1)v virus.

With the spread of infection among local communities, a strategy of laboratory testing and diagnosis of all ILI cases became unsustainable and unnecessary. In accordance with the WHO recommendations to cease universal laboratory testing of all suspected cases once the 100 case mark had been reached (100 cases had been confirmed in South Africa on 15 July 2009), the country reverted to testing only selected cases where a clinical decision warranted laboratory investigations. The new recommendation provided to South African clinicians was to collect specimens only from patients with moderate to severe illness or in case of unusual events such as: cases of severe or fatal ILI, clusters of respiratory illness requiring hospitalisation, or unexplained or unusual clinical patterns associated with serious or fatal cases. Furthermore, in response to the critical situation regarding molecular diagnostics capacity with the increased demand for testing, there was an active effort from 15 July 2009 to decentralise laboratory testing from NICD and to include a network of private and public health diagnostic laboratories throughout the country. Systematic surveillance systems administered by the NICD for detection and characterisation of ILI and severe acute respiratory infections (SARI) were maintained and strengthened (data from the individual surveillance programmes will be reported elsewhere but are summarised on the NICD website: http://www.nicd.ac.za.

Figure 1

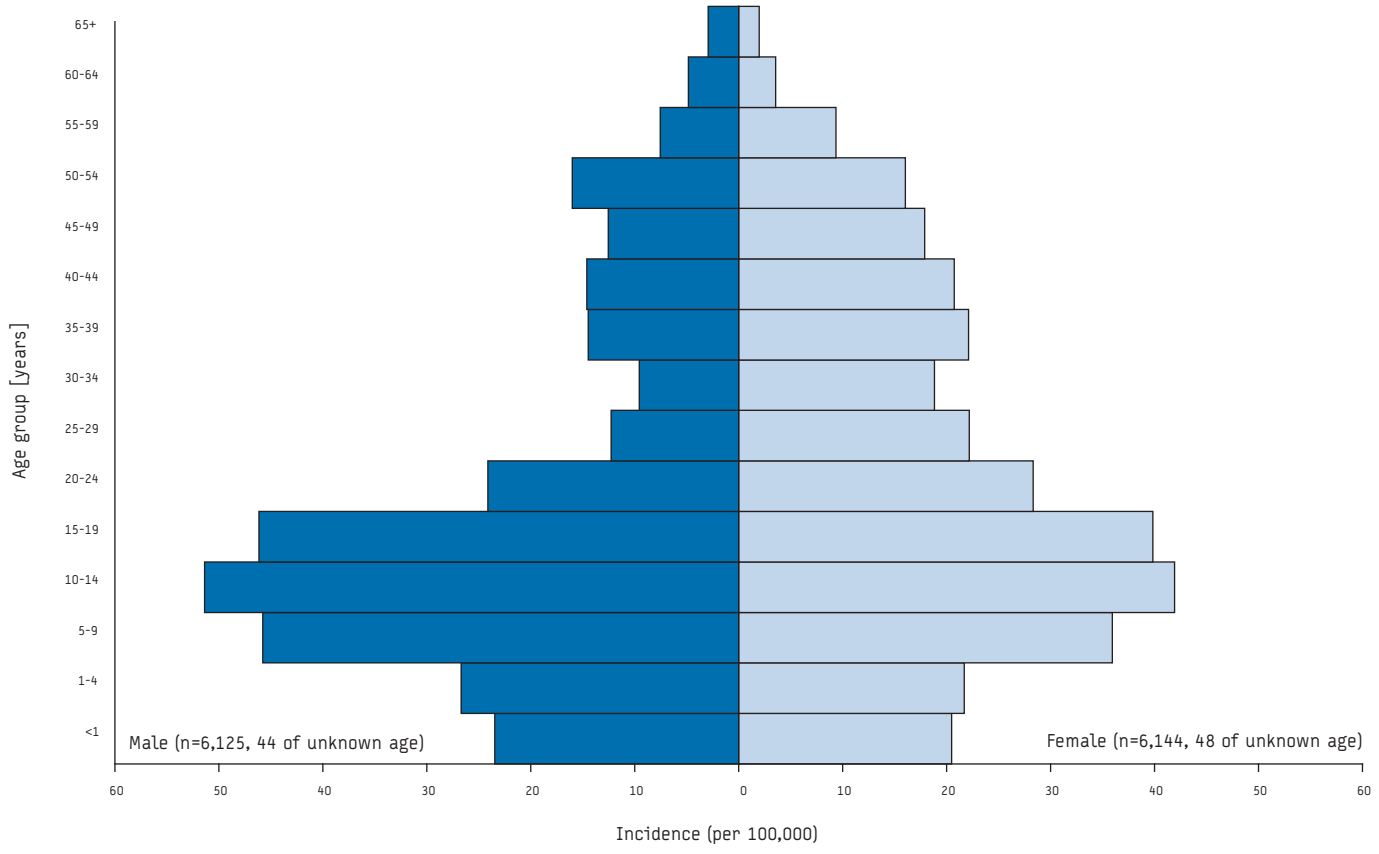
Laboratory-confirmed cases of pandemic H1N1 influenza by week*, South Africa, 28 April - 12 October 2009 (n=12,331, of which 25 with unknown date)



* Week calculated from date of onset or, if onset was unknown, from date of specimen collection.

Figure 2

Incidence of laboratory-confirmed pandemic H1N1 influenza cases by age-group and gender, South Africa, 28 April - 12 October 2009 (n=12,331, of which 113 of unknown age and 62 of unknown gender)



In response to the pandemic, the NICD has maintained an ongoing collective national database of all pandemic H1N1 influenza cases confirmed within the country by the various private and public diagnostic laboratories. This database contains basic demographic, spatial and temporal data about each case. Clinical data were not available. Although routine testing of mild cases was discouraged following 16 July 2009, it can be assumed that the cumulative data collated within this national dataset and reported here includes a mixture of ILI and SARI clinical presentations. Further investigations of all pandemic H1N1 influenza-associated deaths were conducted using a standardised case investigation form to collect detailed information on the patients' past medical history, clinical presentation and development of complications from the attending physicians. A pandemic H1N1 influenza-related death was defined as any person for whom H1N1 influenza infection was confirmed in an ante mortem or post mortem specimen, and who died from a clinically compatible illness or complications attributable to that infection, with no period of complete recovery between illness and death and no alternative cause of death. Case investigations into all confirmed deaths are ongoing, with information on underlying risk factors currently available for 76 patients who died; however, basic demographic data are available for all 91 deaths.

For the purposes of this paper, incidence rates were defined as the total number of new laboratory-confirmed pandemic H1N1 influenza cases detected in South Africa from 28 April to 12 October 2009 per 100,000 persons within the same population group, calculated utilising the 2009 mid-year population estimates published by Statistics South Africa [16]. Sub-population estimates for 2008 were substituted where 2009 estimates were unavailable. Sustained local transmission was defined as the detection of four or more laboratory-confirmed cases without epidemiological links to a confirmed case or a history of international travel. Underlying factors and comorbidities (diabetes mellitus; obesity, cardiovascular disease (excluding hypertension) or active TB (including pulmonary and extrapulmonary TB)) were defined as presence or absence of the condition as diagnosed and reported by the attending clinician. HIV infection was defined as documented evidence of a laboratory-confirmed HIV-positive or negative status. We note that HIV testing was not mandatory and was likely conducted based on clinical indications of HIV infection (if conducted during the acute phase of influenza infection). Documentations of HIV results conducted prior to influenza infection were also included. Pregnancy and puerperium included patients within 42 days post delivery.

Univariate analysis was performed using the Fisher's exact test or the Mantel-Haenszel test for categorical variables, and the Kruskal-Wallis test for continuous variables. Analysis was performed with EpiInfo 2000 (version 3.5.4) software. Two-sided p-values of <0.05 were considered as significant throughout.

Results

The first pandemic H1N1 influenza virus infection in South Africa was confirmed on 14 June 2009. Over a period of the next

Figure 3

Map of South Africa showing the incidence of laboratory-confirmed pandemic H1N1 influenza cases by province, 28 April - 12 October 2009 (n=12,331, of which 43 of unknown province)

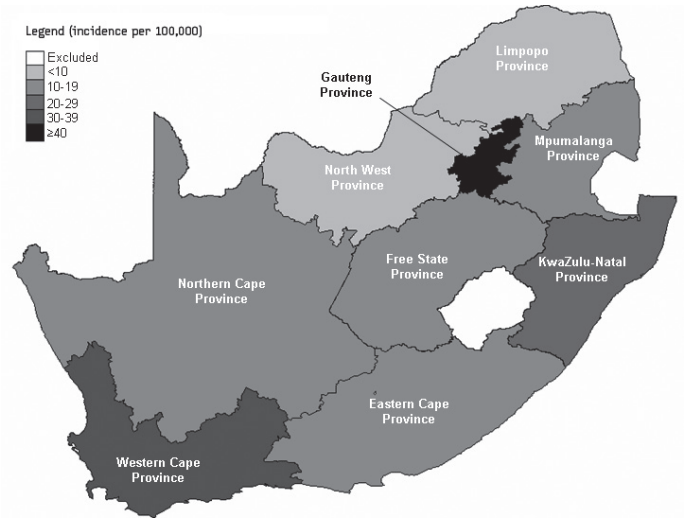
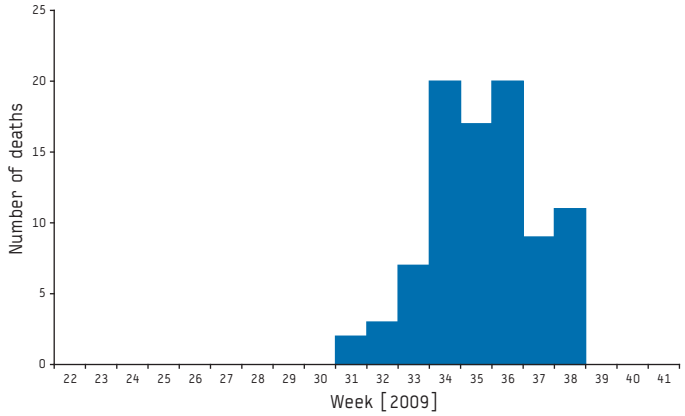


Figure 4

Deaths associated with laboratory-confirmed pandemic H1N1 influenza by week*, South Africa, 28 April - 12 October 2009 (n=91, of which three with unknown date)



* Week calculated from date of death.

Table

Selected clinical characteristics of pandemic H1N1 influenza-associated deaths, South Africa, 28 April - 12 October 2009 (n=91*)

Factor	Frequency of factor / Number of cases withdata available	%
HIV infection	17 / 32	53
Pregnancy or puerperium	25 / 88	28
Obesity	16 / 73	22
No co-morbidities identified	16 / 76	21
Diabetes	11 / 72	15
Cardiac disease†	9 / 71	13
Active tuberculosis (TB)	7 / 72	10

† Cardiac disease includes: previous stents, mitral stenosis, cardiomyopathy, congestive cardiac failure, previous valvular replacement, recent myocardial infarction, and previous cardiac bypass surgery; excludes hypertension.
* Patients may have had multiple factors.
HIV: human immunodeficiency virus.

one month (until 15 July), the number of confirmed cases rose to over 100, a large proportion of whom were associated with a history of international travel within the seven days before onset of symptoms (42 of the first 100 cases). The establishment of sustained local transmission within this same period resulted in a rapid increase in the reported number of cases (Figure 1), with the epidemic peaking during week 32 (the week starting 3 August) with 2,229 new confirmed cases reported. A case frequency of over 2,000 cases per week was maintained for a period of four weeks (week 32 starting 3 August to week 35 ending 30 August), and was followed by a rapid decrease in the number of newly reported cases.

By 12 October 2009, a total of 12,331 laboratory-confirmed cases of pandemic H1N1 influenza had been recorded in South Africa, an incidence rate of 25 per 100,000 population. Overall, males and females were equally affected, with 6,125 male and 6,144 female cases among the 12,269 cases with known age, Figure 2). The age of all confirmed cases ranged from under one month to 90 years, with a median of 15.5 years. Sixty-four percent of cases (7,759/12,213) were under 20 years-old. The incidence of confirmed pandemic H1N1 influenza infections varied by geographical administrative region, with the provinces Gauteng (52 per 100,000) and Western Cape (38 per 100,000) reporting the highest rates (Figure 3).

A total of 91 pandemic H1N1influenza-associated deaths were confirmed between the beginning of the outbreak and 12 October 2009. The frequency of deaths over time follows a similar pattern to that observed for cases (Figure 4).

The age distribution of fatal cases ranged from three days to 70 years, with a median of 33.5 years. This is significantly older than for the non-fatal cases that had a median of 15.0 years (range under one month to 90 years, p-value<0.01). Fifty-nine percent (54/91) of fatal cases were female. HIV infection (17 HIV-positive of 32 tested) and pregnancy (25 of the 88 pregnant or puerperal woman and of the 45 women of reproductive age who died) were the most frequently reported underlying factors among patients who died (Table). Twenty-five of the 76 fatal cases were reported as having no underlying disease or risk factors, and seven of 72 were reported as having an active TB coinfection. Among the 21 deaths associated with pregnancy with data available for the stage of pregnancy, 18 were within the third trimester, one was in the second trimester, and two in the puerperium. Ten of 14 tested pregnant or puerperal woman had an HIV infection, and four of 21 had active pulmonary TB.

Discussion and conclusions

Laboratory-based surveillance for pandemic H1N1 influenza in South Africa has recorded a total of 12,331 confirmed cases to 12 October 2009. The first reported cases were associated with travel; however, the virus quickly established itself locally with sustained transmission occurring within one month of the first case, which was followed by an exponential increase in case numbers. While the establishment of a network of both public and private sector laboratories was critical in providing data on laboratory-confirmed cases, the frequencies of new cases per week reported through these systems were likely affected by a time lag in the implementation of testing, followed by a high demand for testing that stretched both sectors to capacity. These factors, combined with the change to a strategy testing only the more severe cases, implemented from the middle of the epidemic until its end, may have resulted in the plateaued epidemic curve presented here (see Figure 1). Although sporadic cases of confirmed influenza A(H1N1)v virus infection continue to be reported in South Africa, all testing laboratories are currently reporting a significant decline in the number of new positives, coinciding with the change from winter to spring in South Africa.

Infections have primarily been detected among younger age groups. The median age of cases was 15.5 years, which appears to be younger than the median age of seasonal influenza A(H1N1) cases recorded in 2008 (median age 27 years, range one month to 73 years [17]). Relatively higher incidence rates were noted in provinces containing the three largest metropolitan areas, and the highest incidence was noted in Gauteng Province. This province includes the primary hub for international travel to and from South Africa and has the highest population density of the country. In addition, patients in large metropolitan areas are more likely to access healthcare and be tested for influenza.

The median age of patients who died (33 years) was higher than that of non-fatal cases (15.0 years), suggesting that adults appear to be at higher risk of death associated with pandemic influenza virus infection as compared to children or teenagers. The high prevalence of HIV infection (53% of those tested), pregnancy (56% of woman of reproductive age), and TB (10% of deaths and 19% of pregnancy-associated fatal cases), in comparison to the overall prevalence of these conditions observed in South Africa, suggests that these comorbidities are possible risk factors associated with fatal pandemic influenza infections. Other comorbidities such as metabolic conditions were also identified.

Although there was a significant underestimation of the incidence of disease and the true number of deaths, laboratory-based surveillance became critical during the outbreak to allow counting of cases and collection of epidemiological information to describe the outbreak. Limitations of the data presented here include the possible introduction of bias due to: differences in laboratory testing practices between subpopulations, changes in the surveillance and recommended testing strategy during the pandemic, and the addition of laboratories offering testing with commercially available kits that had varying policies on testing. Information on underlying factors associated with fatal cases may also be biased by currently missing data. The prevalence of HIV among deaths is also limited in that only 32 of the 91 fatal cases are currently recorded to be tested, and furthermore the practice of HIV testing is known to be more likely in individuals with clinical evidence of HIV infection. Data are currently pending on important factors including: outstanding HIV status, level of immunosuppression and antiretroviral treatment history in HIV infected patients, as well as details of concurrent TB and anti-TB treatment. Such information will be important in gaining insight into possible interactions between pandemic influenza and HIV or TB.

Many important questions remain unanswered for South Africa and the southern hemisphere. For example: whether the pandemic will recur during the summer, or what the risk factors are for severe disease and death in developing and middle income countries on the African continent. The epidemiology of pandemic influenza documented here is similar to that observed elsewhere [1,2,5-12]; however, our data suggests that common infectious conditions such as HIV and TB may be associated with increased mortality risk. Even if this elevated risk is found to be relatively small, with the large numbers of HIV and TB infected people in sub-Saharan Africa, this

may translate into a substantial public health impact. Nonetheless, further studies that utilise a representative comparison group are required to explore these hypothesised risks. With limited resources to conduct vaccinations in 2010, emerging data on risk groups for severe illness in South Africa and other countries will be critical for planning targeted campaigns.

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Pandemic H1N1 influenza in Brazil: Analysis of the first 34,506 notified cases of influenza-like illness with severe acute respiratory infection (SARI)

W K Oliveira (wanderson.kleber@saude.gov.br)[1,2], E H Carmo*[1], G O Penna[1,3], R S Kuchenbecker[2], H B Santos[2], W N Araujo[1], R Malaguti[1], B B Duncan[2], M I Schmidt[2], on behalf of the Surveillance Team for the pandemic influenza A(H1N1) 2009 in the Ministry of Health[4]

1. Secretariat of Health Surveillance, Brazilian Ministry of Health, Brasília, Brazil
2. Graduate Studies Program in Epidemiology, and Hospital de Clinicas de Porto Alegre, Federal University of Rio Grande do Sul, Porto Alegre, Brazil
3. Tropical Medicine Centre, Univesity of Brasília, Brasilia, Brazil
4. The members of the group are listed at the end of this article

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Recently, the brunt of the current influenza pandemic has been felt in the southern hemisphere. We report an analysis of the first 34,506 cases of influenza-like illness with severe acute respiratory infection (SARI) notified in Brazil during the epidemiological weeks 16 to 33. The 5,747 confirmed cases of pandemic H1N1 influenza showed two incidence peaks across the age span: one in children up to the age of five years (3.8/100,000) and one in individuals aged 20 to 29 years (4.6/100,000). People over the age of 60 had the lowest incidence (1.1/100,000 inhabitants). The epidemic peaked rapidly. Ninety-four percent of cases were concentrated in two of Brazil's five geographic regions – the south and southeast, regions that have a more temperate climate and thus colder winters. Case-fatality of pandemic H1N1 influenza presenting with SARI was 11.2% (95% confidence interval (CI): 10.4%-12.1%). People with a reported comorbidity had approximately twice the risk of those without (relative risk=1.89; 95%CI: 1.64-2.18).

Introduction

Brazil is second in the Americas and fifth in the world in population, and, as of 14 September, one of the countries most affected by the H1N1 influenza pandemic . The first laboratory-confirmed case of pandemic H1N1 influenza was detected in Brazil on 7 May 2009, during the epidemiological week 17 (EW17, ending 2 May). Until early July, most cases detected in Brazil through a surveillance system specifically set up for pandemic H1N1 influenza, were associated with recent travel to North America (Canada, Mexico and the United States) or Argentina, or had been in contact with suspected and confirmed cases with recent travel to affected areas. On 16 July (EW28), Brazil acknowledged its first case due to sustained transmission. Thereafter, notification of cases without link with international travel increased steadily, and cases spread across the country. As of 21 August 2009 (EW 33), 110,113 confirmed cases had been notified in all 35 countries in the Americas, with 1,876 deaths, 82% (1,876/2,185) of the total deaths worldwide [1,2].

The present paper describes the epidemiological profile of influenza-like illness (ILI) with severe acute respiratory infection (SARI), occurred during EW16 to 33 in Brazil. Case-fatality by sex and presence of comorbidity is also presented.

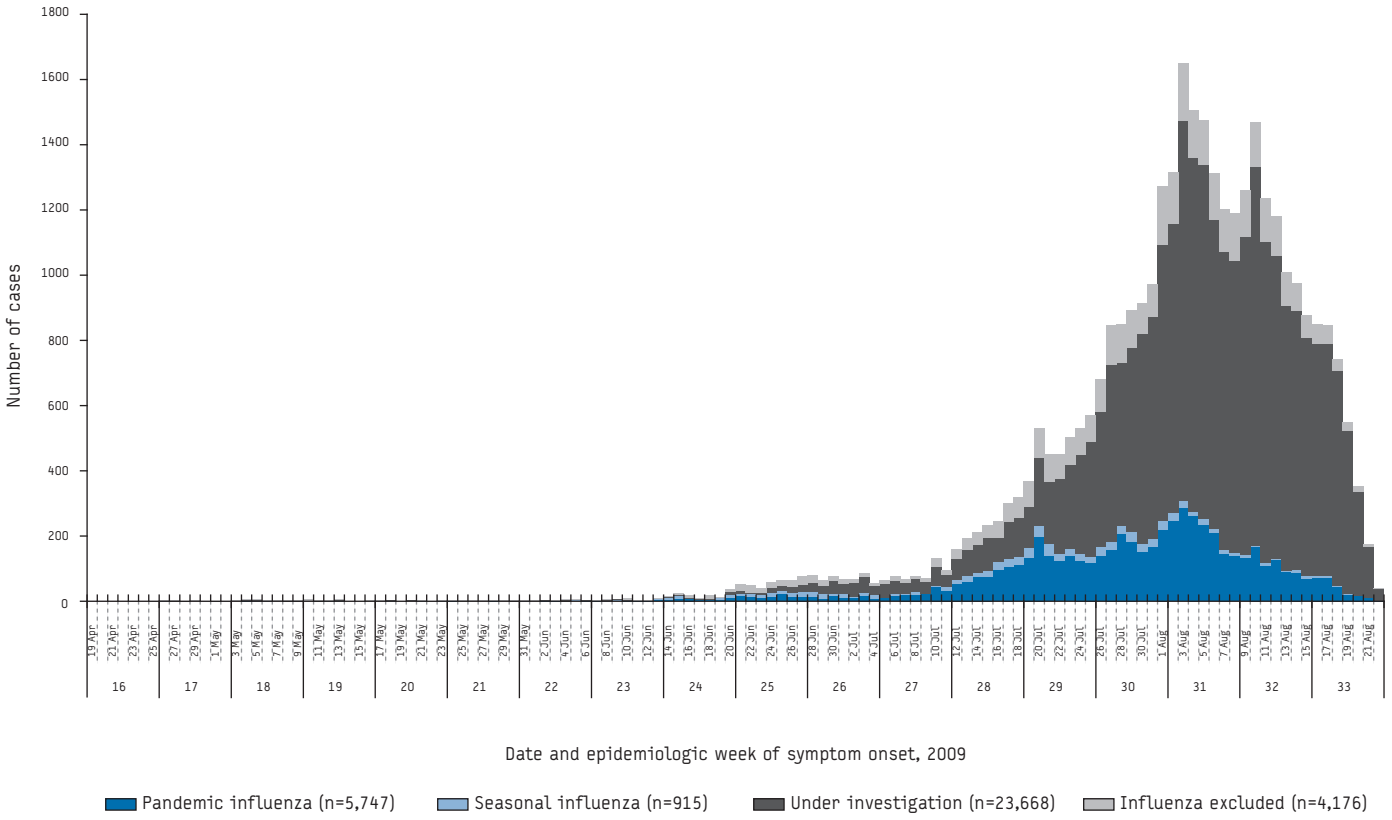
Methods

We obtained data from Brazil's case notification system for influenza-like illness by the pandemic influenza A(H1N1)v virus. Seasonal influenza case notification is not mandatory in Brazil, unless a novel strain is detected or there is a severe seasonal outbreak [3]. In Brazil, such notification is implemented through our national surveillance information system of notifiable diseases (SINAN). For pandemic influenza, an online form is utilised which gathers, among other things, information on demographics, presence of pregnancy, clinical findings, risk factors (including comorbidity) and outcome [4]. Comorbidities that historically represent an increased risk of poor outcome, such as chronic cardiovascular, respiratory, metabolic or renal conditions, haemoglobinopathies and immunodepression, are entered through check-boxes. An open field allows entering of additional information about specific clinic-related conditions.

Brazil initially adopted a case definition of influenza A(H1N1) v that included the following: fever >38ºC, cough, and close contact with an infected person or a travel history to countries with documented cases in the last 10 days. Additional symptoms could include headache and muscle or joint pain. That case definition, which served during the containment phase of the epidemic in Brazil, lasted until epidemic week 28. After EW28, given evidence of sustained influenza transmission within the country, the Brazilian Ministry of Health changed the definition for mandatory notification of suspected influenza cases to fever >38ºC, cough, and dyspnoea or death, i.e. the case definition was limited to cases of SARI. Laboratory investigation was also restricted to SARI cases. The presence of SARI, during both phases, was captured through the above-mentioned surveillance information system; these online records are updated whenever necessary, including outcome.

Figure 1

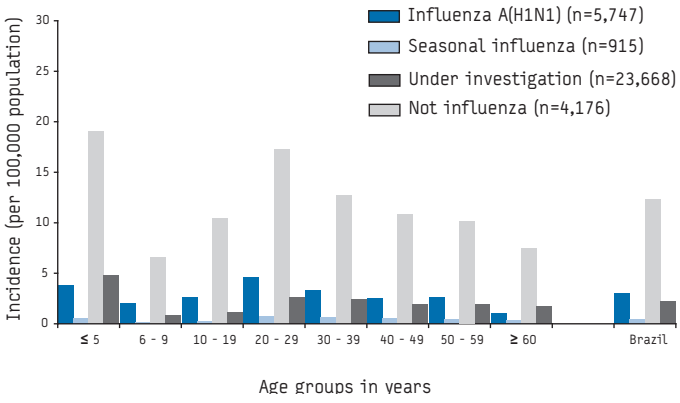
Number of notified cases of influenza-like illness with severe acute respiratory infection by date and week of symptom onset, Brazil, epidemiological weeks 16 to 33, 2009 (n=34,506)



Source: SINAN/MoH Brazil

Figure 2

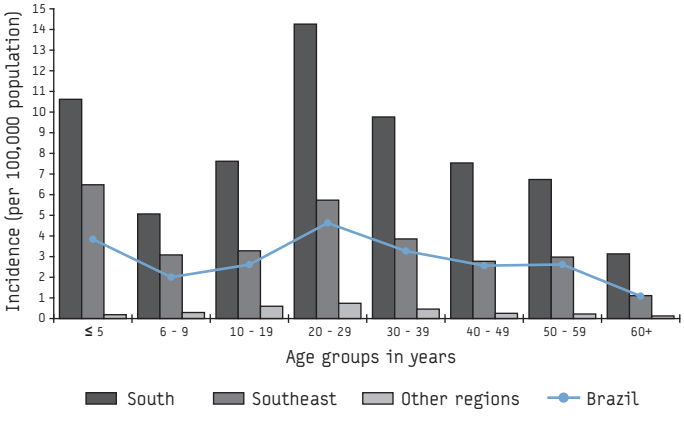
Incidence of notified cases of influenza-like illness with severe acute respiratory infection by age group, Brazil, epidemiological weeks 16 to 33, 2009 (n=34,506)



Source: SINAN/MoH Brazil

Figure 3

Incidence of laboratory-confirmed cases of pandemic H1N1 influenza 2009 with severe acute respiratory infection by age and geographical region, Brazil, epidemiological weeks 16 to 33, 2009 (n=5,745)



Source: SINAN/MoH Brazil

Laboratory diagnosis of influenza and the causative influenza virus strain was confirmed in respiratory samples (nasopharyngeal and pharyngeal swabs) with real-time RT-PCR with specific primers for pandemic H1N1 influenza, performed at reference laboratories of the Brazilian National Health System throughout the country. This report analyses data obtained until the end of EW34.

We describe the incidence of cases of ILI with SARI by age and geographic distribution of the cases as well as by calendar and epidemiologic weeks, the latter as defined by the Pan American Health Organization (PAHO) and the World Health Organization (WHO) [5], We also describe the frequency of and case-fatality by sex, pregnancy and the presence of reported comorbidities, presenting relative risks with 95% confidence intervals.

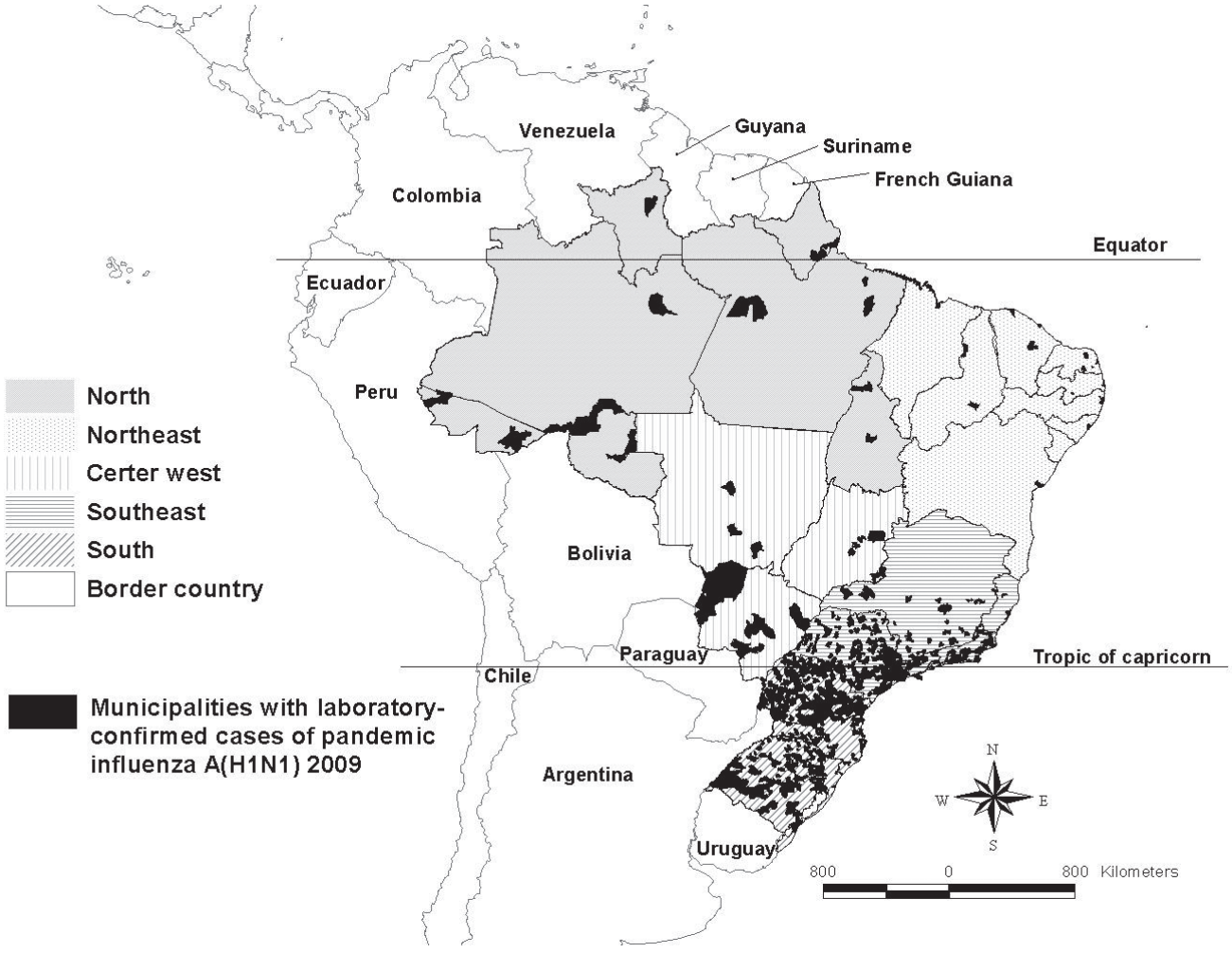
Results

During EW16-33, a total of 34,506 cases of influenza-like illness with SARI were reported in Brazil (Figure 1). From mid-July, the number of cases increased considerably. A total of 5,747 (16.7%) cases were laboratory-confirmed as pandemic H1N1 influenza. Of the remaining SARI cases, 915 (2.7%) were confirmed to be seasonal influenza, for 4,176 (12.1%) influenza was excluded as a cause, and the remaining 23,668 (68.6%) were either still under investigation at the end of EW34, when we closed our database for analysis (approximately 50% of those remaining), or were without specimen for investigation.

Of the 5,747 confirmed cases of pandemic influenza, 3,249 (56.5%) were women. The median age of all confirmed cases was 26 years (range: 0-90 years). The majority of cases (56%) were between 20 and 49 years-old. In addition to SARI-defining symptoms, the most frequent symptoms reported among the confirmed cases were myalgia (62.2%), rhinorrhoea (54%) and chills (53.4%).

Figure 4

Laboratory-confirmed cases of pandemic H1N1 influenza 2009 with severe acute respiratory infection by municipality. Brazil, epidemiological weeks 16 to 33, 2009 (n=5,747)



Data Source: SINAN (Brazilian Information System of Compulsory Notification); Shape File: IBGE (Brazilian Institute of Geography and Statistics).

Figure 2 shows the incidence of influenza-like illness with SARI during the study period according to the aforementioned diagnostic categories and age groups. The incidence was 3.0/100,000 inhabitants with two peaks – one in the group of up to five year-olds (3.8/100,000) and one in the group of 20-29 year-olds (4.6 per 100,000).

The spatial distribution of overall influenza-like cases amongst the five Brazilian regions is shown in Figures 3 and 4. Brazil's southeastern and southern regions were most affected, with incidences of 3.7/100,000 inhabitants and 8.6/100,000 inhabitants, respectively. Incidence was highest in municipalities bordering Argentina, Uruguay and Paraguay, and in temperate zone states with a more rigorous winter season. The other regions (North, Northeast and Center West) jointly contributed only with 6% of total cases.

Among the 2,256 women of childbearing age (15-49 years), 525 (23.3%) were pregnant (Table 1). Table 1 also presents the frequency of comorbidity in cases of SARI, and among those with confirmed pandemic influenza. For 33.3% of all SARI cases, at least one comorbidity was noted, chronic lower respiratory disease being the most frequently reported (27.2%), followed by chronic metabolic diseases (16.2%).

A total of 1,567 deaths occurred among cases of ILI with SARI, 645 of which were confirmed for pandemic influenza (Table 2). The case fatality rate was 4.5% among all ILI with SARI cases and 11.2% among those with confirmed pandemic influenza. Case fatality varied little between men and women (11.4% versus 11.1% for SARI due to pandemic influenza and 4.9% versus 4.3% for SARI overall). Confirmed cases for whom a comorbidity was reported had

Table 1

Frequency of characteristics among cases of influenza-like illness with severe acute respiratory infection, Brazil, epidemiological weeks 16 to 33, 2009 (n=34,506 including 5,747 confirmed pandemic H1N1 influenza cases)

Characteristics	Pandemic influenza A (H1N1) (n=5,747)		All SARI cases (n=34,506)	
	N	%	N	%
Sex				
Female	3,249	56.5	19,850	57.5
Male	2,498	43.5	14,656	42.4
Pregnancy (among women aged 15-49 years)				
No	1,323	58.6	8,276	61.7
Yes	525	23.3	2,789	20.8
1st trimester	86	3.8	544	4.1
2nd trimester	192	8.5	1,093	8.1
3rd trimester	225	10.0	1,046	7.8
Unknown gestational age	22	1.0	106	0.8
Unknown	408	18.1	2,353	17.5
Comorbidity*				
No comorbidity	3,763	65.5	23,012	66.7
One or more comorbidities	1,984	34.5	11,494	33.3
Chronic lower respiratory disease	564	28.4	3,125	27.2
Metabolic disorders	341	17.2	1,857	16.2
Diabetes mellitus	87	4.4	544	4.7
Obesity	105	5.3	514	4.5
Morbid obesity	17	0.9	69	0.6
Cardiovascular disease	271	13.7	1,886	16.4
Immunosuppression	254	12.8	1,446	12.6
HIV/AIDS	25	1.3	155	1.3
Kidney diseases	86	4.3	486	4.2
Haemoglobinopathies	43	2.2	278	2.4
Others	865	15.1	4,809	13.9

*Multiple answers for comorbidities were possible.
AIDS: acquired immunodeficiency syndrome; HIV: human immunodeficiency virus; SARI: severe acute respiratory infection.

greater case fatality, both for SARI (relative risk (RR)=2.16; 95% confidence interval (CI): 1.96-2.38) and for pandemic influenza (RR=1.89; 95% CI: 1.64-2.18).

Case fatality among pregnant women and non-pregnant women of childbearing age with pandemic influenza were similar, respectively 12.6% (66/525) and 11.7% (155/1,323) (RR=1.07; 95% CI: 0.82-1.41). When pregnancy was associated with at least one comorbidity, case fatality differed slightly between pregnant women with and without reported comorbidity, respectively 16.1% versus. 10.5%; (RR=1.54; 95% CI: 0.98-2.41).

Discussion

The H1N1 influenza pandemic was expected to extend to the countries in the southern hemisphere during the recent winter season (June to September). In addition to low temperatures and rainfall which encourage gathering in closed public areas, the vacation season in July increased international travel and thus virus transmissibility [6].

Brazil was seriously affected by the pandemic H1N1 influenza: 34,506 influenza-like SARI cases had occurred by EW33, of which 5,747 were confirmed as pandemic influenza, as reported by EW34. Men and women were similarly affected, although a large fraction of SARI cases among women of childbearing age were pregnant. The incidence showed two peaks across the age span, one in children until the age of five years (3.8/100,000) and one, slightly higher, in the age group of the 20-29 year-olds (4.6/100,000). Interestingly, those aged 60 years and older had the lowest incidence. Of note, most of the cases (94%) concentrated in two of Brazil's five geographic regions, the south and southeast, which have a more temperate climate and thus colder winters. Although in absolute numbers Brazil has, as of EW34, had the largest number of deaths (645) worldwide due to pandemic influenza, the mortality rate in the population was 0.39/100,000, compared with 1.26/100,000 in Argentina, 0.80/100,000 in Chile and 0.22/100,000 in Canada [1]. The epidemic peaked rapidly and then, by EW 32, the number of cases started to decline, assuming no important delays in reporting. In Brazil, the epidemic peak was seen in EW31, about four weeks after the peak in Argentina, Chile and Uruguay [7-9].

Within Brazil, the pandemic showed characteristics similar to those reported in other countries. The age distribution of incidence was quite different from that of seasonal influenza, with young adults bearing the heaviest burden and older people not very strongly affected. The distribution of comorbidities between the cases of SARI also showed a similar pattern to that found in other countries [7-9]. Though deaths were frequent in individuals with no known underlying disease, the presence of a comorbidity posed a greater risk of death [11].

Although a spatial and temporal analysis within the countries in the region has not been performed, most of the cases detected in the beginning of the epidemic in Brazil were associated with recent travel to Argentina, Chile and Uruguay, especially in municipalities bordering these countries. The most affected regions have long stretches of border with Argentina, Uruguay and Paraguay, with several points of heavy traffic and many additional, minimally monitored points of crossing.

The epidemiological characteristics of the pandemic – with the first cases identified near the border between Mexico and the United States [10], and the path of the epidemic within the Southern Cone of South America sweeping across land frontiers – indicate the need to develop a surveillance plan for land frontiers and to establish actions across countries to ensure travellers' and migrants' health. In addition to national surveillance systems, better sharing of information between bordering countries may help timely decision making in such highly contagious epidemics.

Our study has some limitations. We analysed influenza secondary data from the Brazilian national surveillance notification system, which has been used on a large scale for the first time during this epidemic. The simplicity and wide availability of direct online notification certainly stimulated a greater use of the surveillance

Table 2

Case fatality reported among cases of influenza-like illness with severe acute respiratory infection, Brazil, epidemiological weeks 16 to 33, 2009 (n=34,506)

		Number of deaths	Total	Case fatality (%)	RR (95% CI)	*P* value
SARI						
Comorbidity	Yes	813	11,494	7.1	2.16 (1.96-2.38)	<.001
	No	754	23,012	3.3		
Total		**1,567**	**34,506**	**4.5**		
Pandemic influenza A(H1N1)						
Comorbidity	Yes	322	1,984	16.2	1.89 (1.64-2.18)	<.001
	No	323	3,763	8.6		
Total		**645**	**5,747**	**11.2**		
Pandemic influenza during pregnancy						
Comorbidity	Yes	31	192	16.1	1.54 (0.98-2.41)	.06
	No	35	333	10.5		
Total		**66**	**525**	**12.6**		

CI: confidence interval; RR: relative risk.

system. That this report encompasses only influenza-like illness with SARI, generally treated in reference hospitals within the public system, in the context of heightened general concern about the pandemic, strengthens our belief that such reporting, at least for these seriously ill cases, was relatively complete. The comprehensiveness of reporting and of the information undoubtedly varied across healthcare settings. The option of marking check-boxes as well as spontaneously providing additional information regarding comorbidity in an open field added to this variability. In addition, as the number of confirmatory tests needed exceeded the capacity of the Brazilian laboratories network, which consists mainly of the National Influenza Centers, only a fraction of the reported SARI cases had laboratory classification at the time of this report. Considering that laboratory confirmation of severe cases was given priority and that most cases for which no specimen was received were probably milder ones, the case fatality rate for confirmed cases of influenza is likely to be overestimated. With the increase in the number of public health diagnostic laboratories now performing these tests, the interval between the date of collection and the result will be considerably reduced in the future. It is also possible that deaths that were not due to laboratory-confirmed pandemic influenza were notified and updated less frequently than those due to pandemic influenza. This could explain part of the lower case-fatality seen for total SARI cases. Finally, although there may be regional variation in the completeness of reporting, it is unlikely that the observed differences in incidence across the regions are due to differences in reporting. The health system is well organised in all regions of the country and historically, influenza peaks in the more temperate regions during the winter season. In fact, large areas of Brazil had very limited sustained pandemic influenza transmission during the period analysed here, similar to the experience of other countries of similar latitude.

In conclusion, although predominantly a tropical country, Brazil was seriously affected by pandemic influenza. Most of the cases occurred during the winter season in southern and southeastern Brazil, regions with temperate climate situated next to other heavily affected Latin American countries. Additional observational studies are currently underway to further characterise the epidemic in these regions. The intensification of regional collaborative initiatives within Latin America, especially in the Southern Cone, may enhance each country's capacity to respond to future influenza epidemics.

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Members of the Brazilian Ministry of Health epidemiology working group pandemic influenza A(H1N1) 2009: list of contributors (in alphabetical order):

Almeida WAF, Barrado JCS, Barros ENC, Barros FR, Carvalho ML, Cerroni MP, Costa LMC, Costa VM, Daufenbach LZ, Dimech GS, Domingues CM, Fragoso MAC, Guedes DGM, Simczak DR, Nunes E, Oliveira WA

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Pandemic influenza in a southern hemisphere setting: the experience in Peru from May to September, 2009

J Gómez (jgomez@dge.gob.pe)[1], C V Munayco[1], J C Arrasco[1], L Suarez[1], V A Laguna-Torres[2], P V Aguilar[2], G Chowell[3,4], T J Kochel[2]

1. Dirección General de Epidemiología (General Directorate of Epidemiology), Peru Ministry of Health, Lima, Peru
2. United States Naval Medical Research Center Detachment, Lima, Peru
3. Mathematical and Computational Modeling Sciences Center, School of Human Evolution and Social Change, Arizona State University, Tempe, Arizona, United States
4. Division of Population Studies, Fogarty International Center, National Institutes of Health, Bethesda

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This paper presents a description of Peru's experience with pandemic H1N1 influenza 2009. It is based on data from four main surveillance systems: a) ongoing sentinel surveillance of influenza-like illness cases with virological surveillance of influenza and other respiratory viruses; b) sentinel surveillance of severe acute respiratory infections and associated deaths; c) surveillance of acute respiratory infections in children under the age of five years and pneumonia in all age groups; and d) case and cluster surveillance. On 9 May 2009, the first confirmed case of pandemic H1N1 influenza in Peru was diagnosed in a Peruvian citizen returning from New York with a respiratory illness. By July, community transmission of influenza had been identified and until 27 September 2009, a total of 8,381 cases were confirmed. The incidence rate per 10,000 persons was 4.4 (in the 0–9 year-olds) and 4.1 (in the 10–19 year-olds). During epidemiological weeks (EW)* 26 to 37, a total of 143 fatal cases were notified (a case fatality of 1.71%, based on confirmed cases). The maximum peak in the number of cases was reached in EW 30 with 37 deaths. Currently, the impact of the pandemic in the Peruvian population has not been too severe, and fortunately, healthcare centres have not been overwhelmed. However, the future of this pandemic is uncertain and despite the fact that our country has not been seriously affected, we should be prepared for upcoming pandemic waves.

Introduction

Peru is a South American country that is divided by the Andes Mountains into three distinct natural regions (coastal desert, highlands and jungle region) all extending the entire length of the country. The coastal desert has limited rainfall (<20 cm per year) with temperatures ranging between 15 and 30°C, and Lima, the main and capital city, is located in the central part of this region. The highlands that include cities located over 2,000 m above sea level experience high levels of rainfall and temperatures ranging between -2 and 15°C. Finally, in the jungle region rainfall exceeds 200 cm per year, and cities are located close to sea level with temperature ranging from 18 to 32°C [1].

Since 1998, the Ministry of Health (MoH) of Peru has conducted virological surveillance of influenza and other respiratory viruses, and in 1999 surveillance of acute respiratory infections (ARI) and pneumonia cases and associated deaths was implemented. In 2006, the MoH established a sentinel surveillance system of influenza-like illness (ILI) cases in all the three regions of the country, in order to strengthen the National Surveillance Network [2]. Through these systems, influenza circulation in Peru has been detected throughout the year in coastal and jungle regions, and seasonal circulation during winter time has been identified in the highland region [3]. As a response of the World Health Organisation's (WHO) global pandemic alert, the MoH established two additional surveillance systems: a case and cluster surveillance, and surveillance for severe acute respiratory infection (SARI) and SARI deaths.

On 9 May 2009, the first confirmed case of pandemic H1N1 influenza in Peru was diagnosed in a Peruvian citizen returning from New York with a respiratory illness. Since then, the influenza A(H1N1)v virus has spread rapidly throughout the country [4]. In this context of preparation and response, this paper presents a description of Peru's experience with the H1N1 influenza pandemic using data from the different surveillance systems in Peru.

Methods

The pandemic was described using data from four different surveillance systems, which are summarised below. All four systems report their data to the MoH. Case and cluster investigation was temporarily carried out at the beginning of the epidemic.

Sentinel surveillance of influenza-like illness cases and virological surveillance

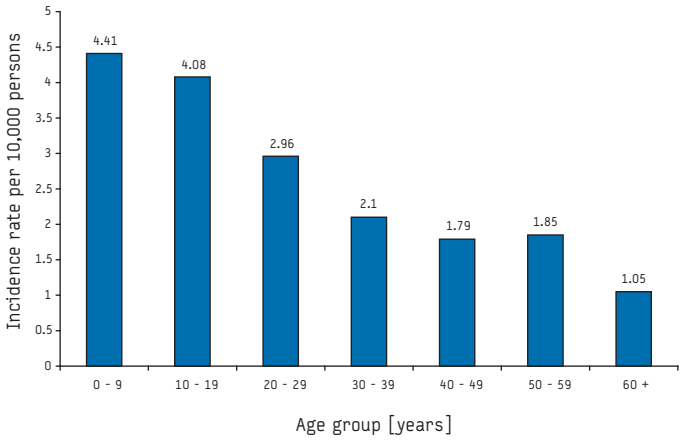
Sentinel surveillance has been implemented in 50 health centres in the country. Nasal or pharyngeal swabs were processed at the Instituto Nacional de Salud (National Institute of Health, INS) and the Naval Medical Research Center Detachment (NMRCD) as previously described [3].

Case and cluster investigation

On 9 May 2009, after the WHO issued a global pandemic alert, a surveillance system base on the case definition for pandemic H1N1 influenza was established by the MoH to define the procedures of

Figure 1

Incidence of confirmed cases of pandemic H1N1 influenza, by age group, Peru, 9 May-27 September 2009



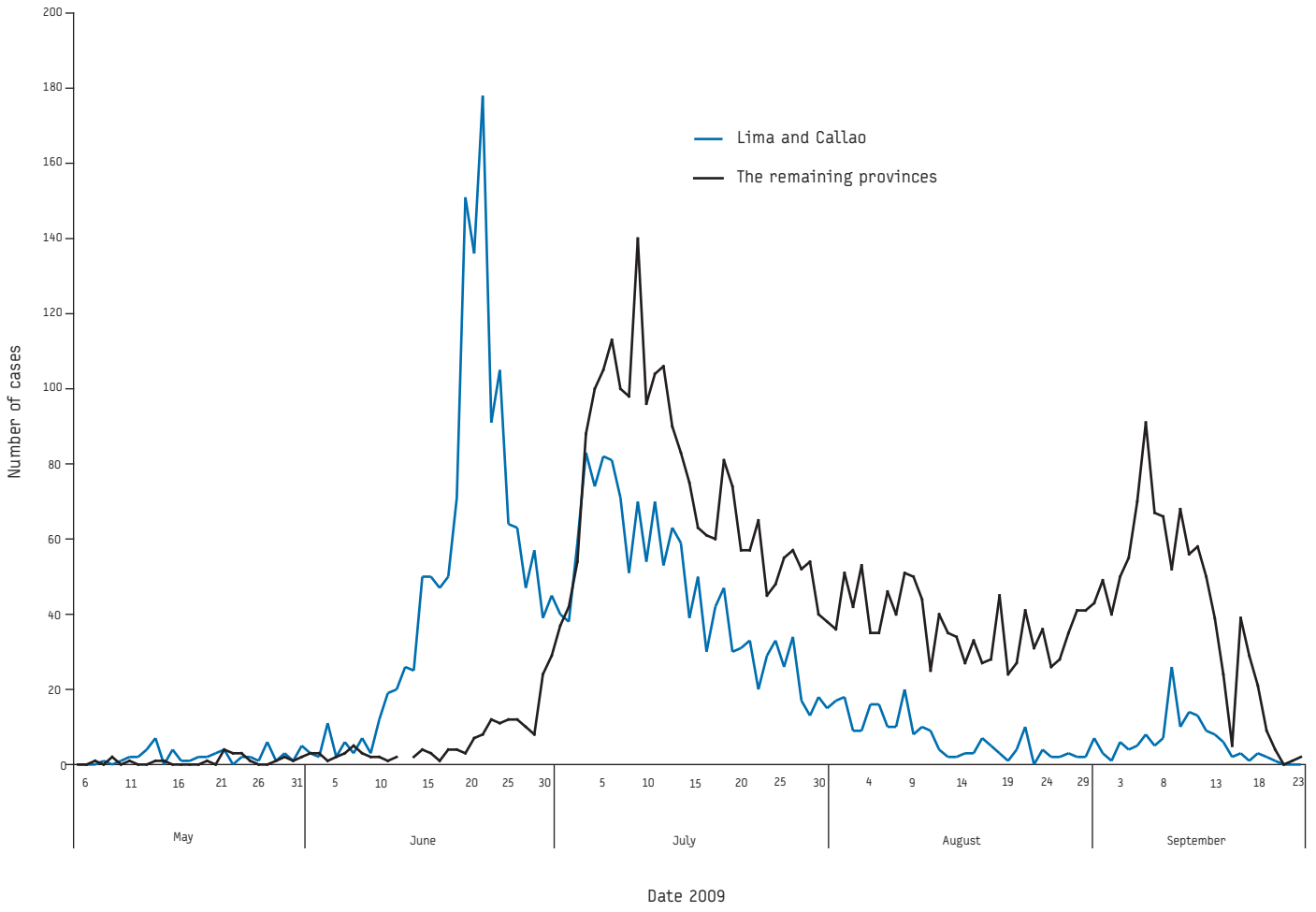
detection, notification, investigation, follow-up and epidemiological control of the H1N1 influenza in Peru [5,6]. A suspected case was defined as any person with a sudden onset of fever (>38ºC) and at least one of the following symptoms: cough or sore throat within seven days of symptoms onset, in an area where confirmed pandemic H1N1 influenza cases were reported or epidemiologically linked to a close contact of a confirmed case. A confirmed case was defined as any person with a positive result in the RT-PCR for influenza A(H1N1)v virus. This system was stopped on 7 July with the change to the mitigation phase.

Surveillance for severe acute respiratory infections and associated deaths

In July 2009, when community transmission of influenza was identified, the MoH of Peru intensified surveillance efforts to reinforce the sentinel surveillance of SARI [7]. SARI was defined as any patient, with sudden fever >38ºC, together with cough or sore throat and respiratory distress who needed medical care in a hospital. Hospitalisation was defined as a patient spending at least one night in a hospital or healthcare center. An online platform with

Figure 2

Confirmed pandemic H1N1 influenza cases by onset of symptoms, Peru, 6 May-25 September 2009 (n=7,886)



* for whom date of onset was available.

information of hospitalisation, comorbidities, outcomes, treatment and other variables was established.

Acute respiratory infections, pneumonia and pneumonia deaths surveillance

This system was optimised to follow up the spread of the pandemic. ARI included all children under the age of five years, while pneumonia cases and deaths were reported for all age groups.

Laboratory analysis

From nasal and/or oropharyngeal swabs, RT-PCR assays for the detection of influenza A(H1N1)v virus were performed at the INS and NMRCD as described by United States Centers for Disease Control and Prevention [8]. At NMRCD in Lima, the specimens were stored at -70ºC, and later inoculated for virus isolation and identification [3] . An online official system (NETLAB-INS) was established to access the results.

Control measures

When the active surveillance system was in place, case clusters were identified by sampling symptomatic cases. Control measures included the use of respiratory masks, increased hygiene (hand washing) and administration of antiviral drugs (oseltamivir) to all suspected and confirmed cases and their contacts during this containment phase [4]. Following the WHO pandemic alert, travel restrictions to Mexico were put in place on 30 April and measures were taken to increase awareness of travellers of the new influenza virus. Furthermore, active surveillance of febrile patients was established in all airports, and a telephone hotline was established to receive reports from the population on respiratory disease and house identification of cases and contacts [4]. During the subsequent mitigation phase, antiviral treatment was established on 21 July and it was focused on the high-risk group (pregnant women, cases under five years or over 60 years of age, or patients with SARI or a risk comorbidity) [4].

The clinical-epidemiological forms of the cases were entered into a database (NMRCD) or directly into an online platform on a website of the Dirección General de Epidemiología (General Directorate of Epidemiology, DGE).

Results

Sentinel surveillance of influenza-like illness cases and virological surveillance

We have previously reported the results of the sentinel surveillance system in Peru from June 2006 to May 2008 [3]. Until 27 September, approximately 1,122 cases of pandemic H1N1 influenza (13.4% of the confirmed cases) were identified by this system. During the pandemic, the implementation of this surveillance system allowed us to identify the first outbreak of community transmission (18 May) with 11 confirmed cases in one of the surveillance sites (Huanuco province) located in the highland region of Peru.

Figure 3

Cases of severe acute respiratory infections, Peru, EW22-EW37, 2009 (n=1,458)

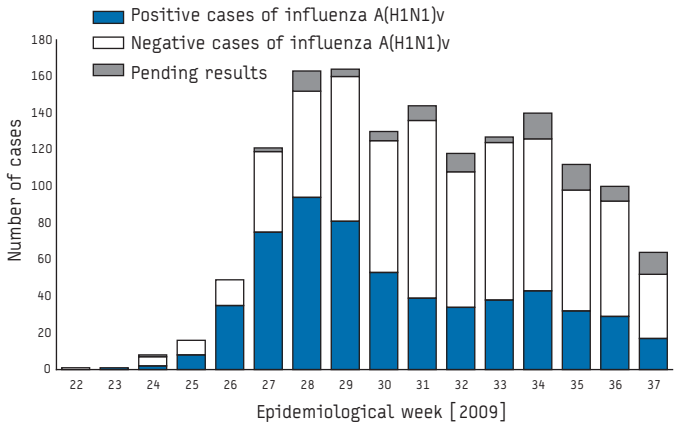
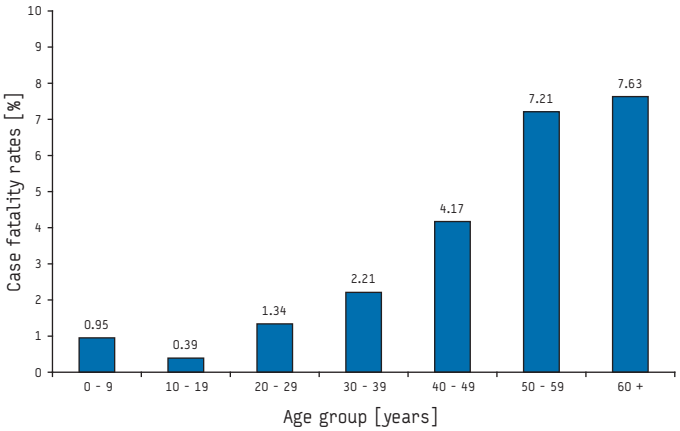


Figure 4

Case fatality rate per 100 cases by age group among patients infected during the influenza pandemic, Peru 2009, 9 May-19 September 2009 (n=143)



Table

Comorbidities and/or risk conditions detected in pandemic H1N1 influenza cases with fatal outcome, Peru, 9 May-19 September 2009 (n=143*)

Comorbidity and/or risk condition (N=143)	n (%)
No comorbidity or risk condition	35 (24.5)
Comorbidity and/or risk condition	108 (75.5)
Metabolic	36 (25.2)
Cardiovascular	30 (21.0)
Respiratory	16 (11.2)
Neurological	14 (9.8)
Renal	13 (9.1)
Genetic	13 (9.1)
Other	10 (7.0)
Pregnancy and puerperium	6 (4.2)
Rheumatologic	6 (4.2)
Infectious	5 (3.5)
Digestive	4 (2.8)
Cancer	3 (2.1)

* Multiple answers were possible

Case and cluster investigation

Description of cases

Until 27 September 2009, a total of 8,381 cases of pandemic H1N1 influenza have been confirmed, including 143 deaths. A total of 4,263 confirmed cases (52%) were males. The subjects' age ranged from ≤1 year to 80 years, with a median age of 19 years. Seventy-five percent of the cases were under 30 years-old and only 3.15% were older than 60 years. ILI cases were notified in all departments (administrative regions) of Peru, but Lima and Callao together notified almost 40% of the cases.

The risk of infection was greater in those younger than 20 years, probably associated with sustained transmission within schools. The incidence rates per 10,000 persons were 4.4 and 4.1 among the 0-9 year-olds and the 10-19 year-olds, respectively (Figure 1). During the containment phase, the large number of suspected cases that were detected (close to 400 per day) led to a delay in the generation of laboratory results by INS and NMRCD. When the containment phase ceased on 7 July, laboratory testing was focused on SARI patients.

After 13 June (epidemiological week EW 23), an increase in the daily number of ILI cases was identified with a peak on 22 June (EW 25), as shown in Figure 2. This was followed by a consistent decrease in the number of cases especially in Lima and Callao. Further, the percentage of positive samples increased from 10% (EW23) to 70% (EW 25) and then started to decrease.

While the first epidemic peak occurred in Lima and Callao, secondary peaks in the epidemic curve correspond to the epidemic wave in the rest of Peru. The aggregated epidemic curve is multimodal due to the sum of local epidemics at different spatial locations where the novel influenza virus arrived at different times.

Description of clusters

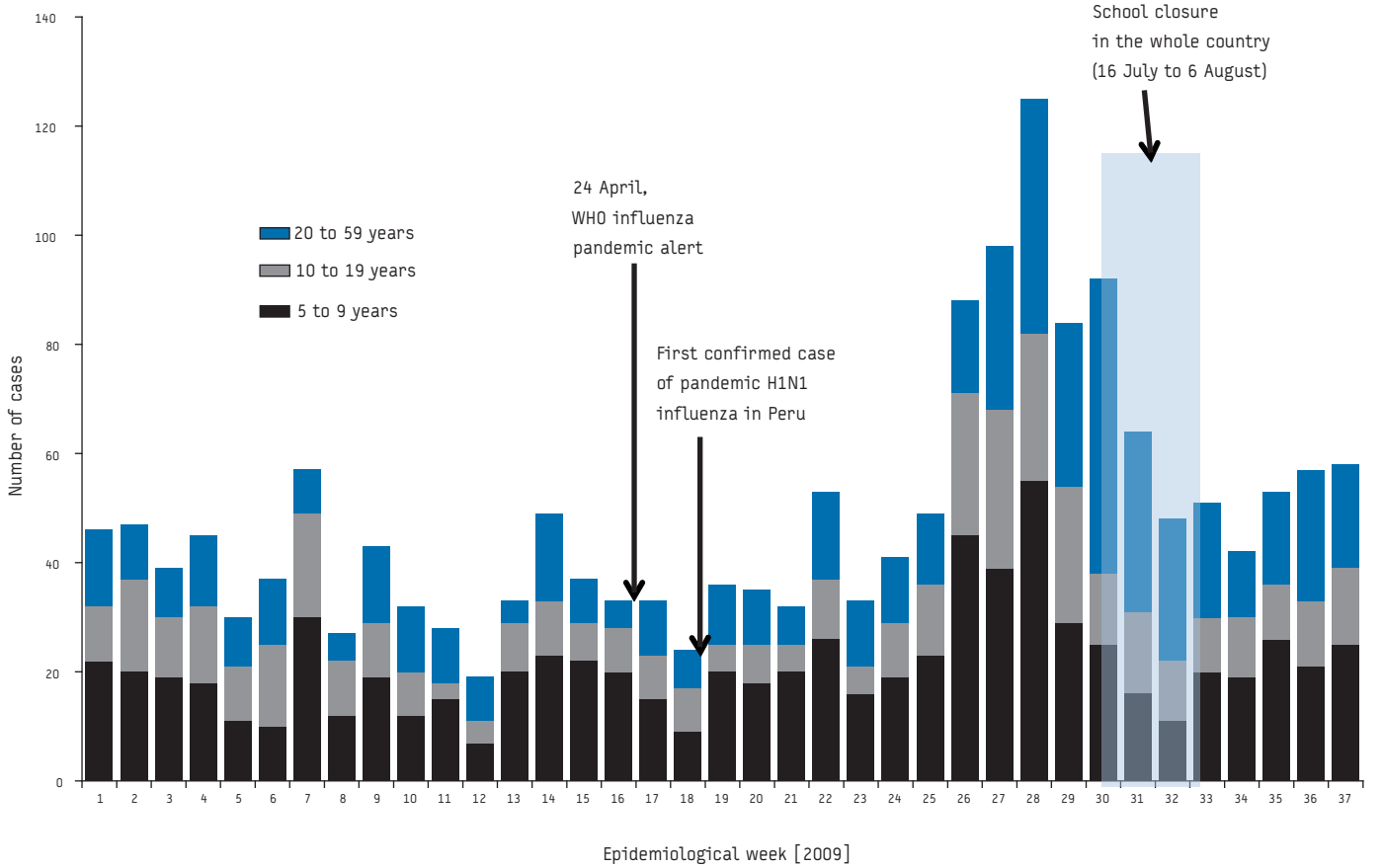
The onset of symptoms of the first case was on 9 May 2009. Following the index case, our surveillance system detected many isolated imported cases that generated clusters of different size. We detected and investigated six clusters associated with persons returning from countries with or without demonstrated transmission at the time. These countries included the Dominican Republic, Mexico, Argentina and the US. Two of these clusters led to community transmission in Peru. These clusters will be described in depth elsewhere.

Surveillance for severe acute respiratory infections and associated deaths surveillance

After the switch of the surveillance strategy from the containment to the mitigation phase (7 July) as described above, the epidemic trend was monitored through the detection of SARI cases. At the time of writing this report, the trend of SARI cases for the whole

FIGURE 5

Cases of pneumonia among 5-59 year-old patients from Lima and Callao, 2009 (n=1,798)



of Peru is slowly decreasing. In Peru, the peak was reached during EW 28, followed by a decrease in SARI cases (Figure 3). In the northern regions of the country, the peak was reached during EW 34, and in the southern regions a bimodal curve was observed with two peaks at EWs 28 and 34 (data not shown).

SARI deaths

During EWs 26-37, a total of 143 deaths associated with SARI were notified in 14 out of the 24 departments comprising Peru, a case fatality percentage of 1.63%, based on confirmed cases. Almost half of the deaths were recorded in the city of Lima and the port of Callao. The maximum peak was reached at EW 30 with 37 deaths. After that, the number of fatalities decreased to two cases in EW 37.

The median age of deaths was 39 years (range: 0-85 years) and 54% were women. The fatality rate was greater (7.63%) in persons over the age of 59 years, whereas the rate in the younger age groups (under 19 years of age) was lower than 1 (Figure 4).

In 32 of the deaths (24%), there were no recorded underlying conditions. Six of the deaths (4.5%) were in pregnant women or women in puerperium; six deaths were in cases with Down syndrome; 23 in cases with obesity; nine in cases with diabetes mellitus type 2 (three of them associated with obesity) (Table).

Acute respiratory infections, pneumonia and pneumonia fatalities surveillance

The epidemic curve of pneumonia cases among 5-59 year-olds in Lima and Callao increased in EW 26, reached the peak in EW 28 when schools were temporarily closed for three weeks. Following this measure, the number of cases decreased as shown in Figure 5.

Control measures

Between 24 April and 4 July 2009, no cases were identified in nearly 500,000 screened travellers, and hence the screening system at airports was deemed ineffective and was suspended. The first imported cases in travellers were identified who reported to the telephone hotline centre implemented by the MoH.

Discussion

Surveillance of pandemic H1N1 influenza in Peru provided valuable information about the behaviour of the pandemic in a developing southern hemisphere country. Lessons can be learned regarding the public health impact, prevention and control, impact on health services, and effective surveillance.

Public health impact of the pandemic

Lima, the largest city with a population of eight million, has the main international airport and was the first city in Peru affected by the new influenza virus. In addition, all laboratory testing for the country is centralised in this city. These factors could explain the fact that almost 30% of the initial confirmed cases of pandemic H1N1 influenza were located in Lima.

Until September 2009, Peru identified over 8,000 confirmed cases, but this is only the tip of the iceberg. The pattern of dissemination of this pandemic in Peru is associated with people' mobility and population density, and more populated areas tend to be affected earlier than smaller populations. Access to laboratory resources across Peru is not uniform and could have affected this transmission pattern. Moreover, distant and geographically isolated locations may have not reported cases before the appearance of severe cases who require mechanical ventilation in hospital settings.

We observed that while a great number of people under the age of 24 years were infected, this group had a lower probability of dying from influenza. The lower frequency of pandemic H1N1 influenza cases among those over 59 years of age supports the hypothesis that people who were exposed to influenza A(H1N1) during childhood before the 1957 have a certain extent of immunological protection to the influenza A(H1N1)v virus [9]. Such a consistent pattern has been reported in other regions including Mexico, the US, Europe, Australia and New Zealand [10-11]. When infected, however, these older patients had a high risk of fatality, in our country as reported in other regions [12].

Cases of pandemic H1N1 influenza in Peru presented predominantly mild and self-limiting illness, and although fever and cough were the most common clinical manifestations, many subclinical or asymptomatic cases should have circulated in the country. The majority deaths related to pandemic H1N1 influenza (75.5%) had a reported underlying medical condition. In fact, almost half of the deaths had conditions classified as high risk in other countries [13]. The fact that 25% of the cases did not have high risk conditions suggest that additional factors such as immunological status or access to healthcare could have contributed to the fatal outcome.

Our case definitions were very specific, but allowed us to develop interventions and to sample suspected cases to help us identify clusters and follow virus dissemination patterns throughout the country.

Control measures and limitations of the study

Initial control measures established by the MoH of Peru included travel restrictions and quarantine of suspected travellers following WHO recommendations [14]. However, these actions were not effective and did not significantly delay the spread of the virus into other nations including Peru. Also, many travellers could have enter the country during the incubation period, as detected in other countries [15]. The telephone hotline was found to be useful in identifying case clusters of suspected and confirmed cases and following the dissemination of the virus throughout the country [16]. House identification of cases and contacts and follow-up procedures involved a great deal of human resources. As a result, those activities were discontinued.

We believe that the epidemiological surveillance system recommended by WHO, i.e. early case detection and investigation, comprehensive assessment and pandemic monitoring [17], was essential for the development of adequate control measures. At the beginning of the pandemic, it is possible that our surveillance systems failed to detect many cases, especially those with mild disease. Many patients may not have visited a health centre or may not have had access to laboratory services. ARI surveillance was not as helpful as we expected, due to the limitations in detecting cases among outpatients. The SARI surveillance system, however, was useful because it allowed us to monitor the pandemic trends in all age groups and among the more severe cases. It also allowed us to evaluate the impact of the pandemic.

Conclusion

It is well known that previous pandemics have presented a second or third wave of morbidity and mortality. These multiple wave

profiles could be associated with spatial, seasonal, hemispheric (north, south, tropics) or climatic (humidity, temperature) factors [18,19]. Currently, the impact of the pandemic in the Peruvian population has not been severe, and fortunately healthcare centres have not been overwhelmed. However, the future of this pandemic is uncertain and despite the fact that our country has not been seriously affected, we should be prepared for upcoming pandemic waves.

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Disclaimers

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Ministry of Health of Peru and the Department of the Navy, Department of Defense, nor the U.S. Government.

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*Editor's note: Weeks in this article are numbered as epidemiological weeks as defined by the Pan American Health Organization (PAHO) and the World Health Organization (WHO): http://amro.who.int/english/sha/be993calend.htm

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Progression and impact of the first winter wave of the 2009 pandemic H1N1 influenza in New South Wales, Australia

New South Wales public health network (mcret@doh.health.nsw.gov.au)[1]
1. Individual contributors listed as the writing committee at the end of the article

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A range of surveillance systems were used to assess the progression and impact of the first wave of pandemic H1N1 influenza in New South Wales, Australia during the southern hemisphere winter. Surveillance methods included laboratory notifications, near real-time emergency department syndromic surveillance, ambulance despatch surveillance, death certificate surveillance and purpose-built web-based data systems to capture influenza clinic and intensive care unit activity. The epidemic lasted 10 weeks. By 31 August 2009, 1,214 people with pandemic H1N1 influenza infection were hospitalised (17.2 per 100,000 population), 225 were admitted to intensive care (3.2 per 100,000), and 48 died (0.7 per 100,000). Children aged 0-4 years had the highest hospitalisation rates, while adults aged 50-54 had the highest rates of intensive care admission. During the epidemic period, overall presentations to emergency departments were 6% higher than in 2008, while presentations for influenza-like illness were 736% higher. At the peak, confirmed cases of pandemic H1N1 influenza consumed 15% of intensive care capacity. Excess mortality from influenza and pneumonia was lower than in recent influenza seasons. Health services, particularly emergency departments and intensive care units, were substantially affected by the epidemic. Mortality from influenza was comparable with previous seasons.

Introduction

A pandemic influenza A(H1N1)v – previously called human swine influenza – virus was identified in April 2009 in Mexico and the United States. Since then, widespread community transmission of the virus has been confirmed on all continents, and the World Health Organization has announced a global influenza pandemic [1]. This paper focuses on the pandemic experience of New South Wales (NSW), Australia's most populous state (7.0 million people), which includes Australia's largest city and primary entry port - Sydney (4.4 million people).

The first case of pandemic H1N1 influenza was confirmed in Australia on 8 May 2009. A shift in public health response strategy from 'delay' to 'contain' was announced on 22 May, when local community transmission was identified [2]. On 17 June, Australia moved to the 'protect' phase of the response, in recognition of the generally mild clinical characteristics of the virus, and the widespread community transmission in Victoria [3]. This phase focused efforts on early detection and treatment of influenza-like illness in those considered at risk of severe illness. The change to the 'protect' phase saw a shift in laboratory testing from people with appropriate symptoms and potential exposure to the virus to people at greater risk of severe illness, particularly those hospitalised with an influenza-like illness. This shift in testing policy meant that non-laboratory-based surveillance systems became more important in assessing the population and health service impact of the pandemic.

In this report, we provide an overview of the progression and impact of the first winter wave of the 2009 pandemic H1N1 influenza in the Australian context, using data from a range of surveillance systems.

Methods

We used existing and new surveillance systems to monitor the progress and impact of the pandemic influenza virus. Existing systems included laboratory notifications, the hospital emergency department (ED) [4] and ambulance despatch surveillance system, and death certificate surveillance [5].

Laboratory notifications and hospital admissions

Public health staff entered information on suspected and confirmed cases and their contacts (including hospital admission status) into an open source, web-based outbreak database system (NetEpi) [6]. All laboratory notifications of confirmed influenza A(H1N1)v were entered centrally into the same database. In addition, eight large public laboratories submitted aggregate information on the number and results of respiratory virus testing performed each week.

Influenza clinics presentations and intensive care unit admissions

Two simple internet-accessible form-based databases were rapidly developed – one for recording daily aggregate influenza clinic activity, and the other for recording daily aggregate influenza-related intensive care unit activity (total number of suspected or confirmed influenza cases in adults, children and neonates; total number of pregnant patients with suspected or confirmed influenza, and total number of patients requiring treatment with extracorporeal membrane oxygenation [ECMO] for any reason). A separate internet-accessible register was used to collect clinical information on individual patients with confirmed influenza A infection admitted to intensive care [7,8].

Emergency department presentations

The ED surveillance system allowed a daily assessment of the number of ED presentations with assigned diagnoses of general respiratory illness, fever, unspecified infections, influenza-like illness and pneumonia. These figures may include some influenza clinic presentations because some hospitals recorded this information in their ED information systems. This was the first time that specialised influenza clinics were provided across the NSW Health service.

The ED surveillance system uses data routinely recorded in ED information systems and transmitted by real-time electronic messaging or frequent batch files to a surveillance database at the NSW Department of Health. This system currently includes 52 public hospital EDs in NSW and covers much of the state's population (72% of the state's 2.4 million annual ED presentations). ED diagnoses saved as International Classification of Diseases versions 9 or 10 [9] or the Systematized Nomenclature of Medicine-Clinical Terms (SNOMED-CT) [10], are used to group ED presentations into 'syndromes', such as influenza-like illness or pneumonia.

Ambulance service activity

The ambulance surveillance system currently covers the Sydney operations region and uses data recorded by emergency telephone operators who interact with a computer-aided ambulance despatch system. Additions to the despatch database are automatically transmitted in batch files hourly to the Department of Health surveillance database. Ambulance despatches are categorised according to the problem assigned during the emergency call, such as 'breathing problems'.

Deaths

Death certificate surveillance uses time-series of medical certificate cause of death information from the NSW Registry of Births, Deaths and Marriages to assess all-cause mortality and excess pneumonia and influenza deaths due to circulating influenza viruses.

Risk factors for ICU admission and death included pregnancy and weight status. Pregnancy was defined as any stage of pregnancy and the immediate post-partum period (up to 28 days post-delivery). Obesity was defined as a BMI ≥30 kg/m^2. Morbid obesity was defined as a BMI ≥40kg/m^2. The week commencing 15 June 2009 was considered the first week of the epidemic, as this corresponded to the first identification of community transmission in NSW. Data was correct and up-to-date as of 29 September 2009.

Results

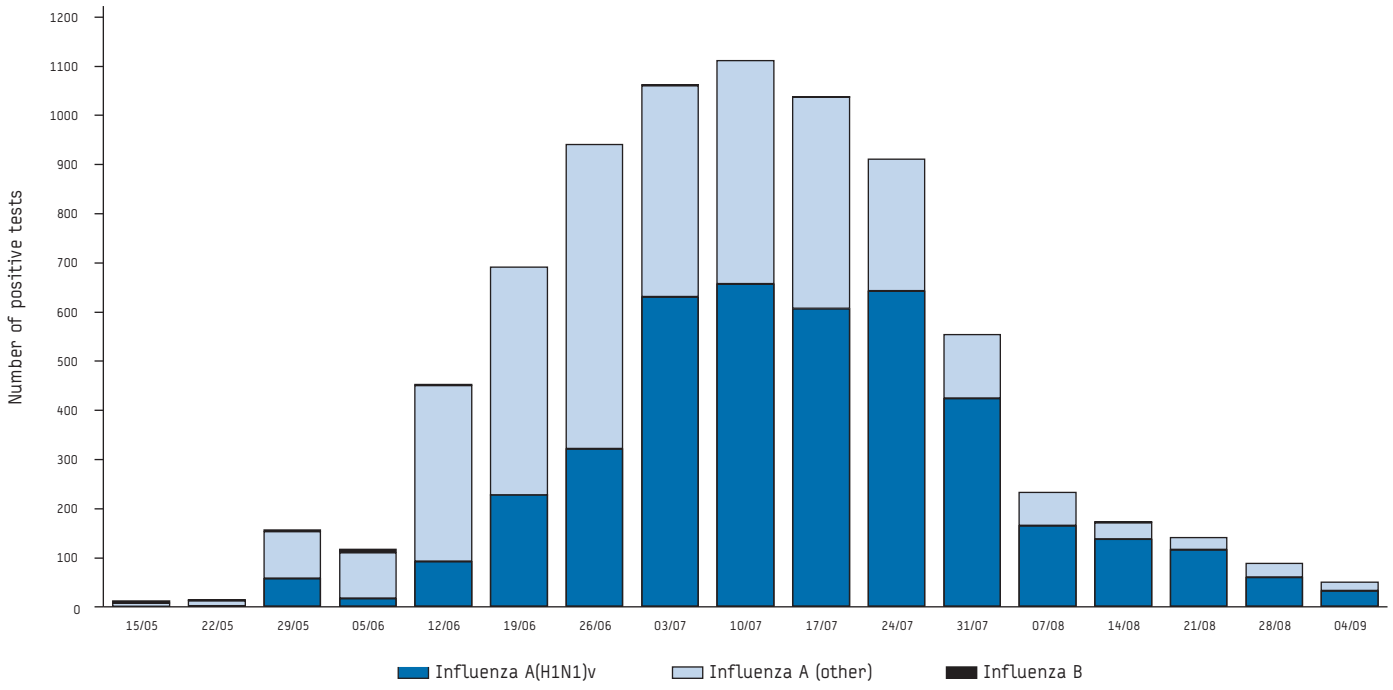
Laboratory notifications and hospital admissions

There was a substantial increase in the number of laboratory tests performed for influenza A during June and July 2009, with a rapid increase in the proportion of positive results. The pandemic influenza A(H1N1)v virus rapidly replaced other circulating strains of influenza A and B (Figure 1).

As of 31 August 2009, 5,106 laboratory-confirmed cases of pandemic H1N1 influenza were identified in NSW. The median age of cases was 23 years, and 50.2% were male. Of confirmed cases, 1,214 (17.2 per 100,000) were admitted to hospital. Hospitalised cases tended to be older than other confirmed cases, with a median age of 31 years. Compared to the past five years' influenza seasons there was a shift towards more adults being admitted to hospital with influenza in 2009, particularly in the 50-69 year age group

Figure 1

Number of positive laboratory tests for influenza for weeks ending 15 May to 4 September 2009, New South Wales, Australia



Source: NSW Department of Health

(data not shown). The median length of stay for those admitted to hospital was four days for adults, three days for children, and four days overall. Children (aged under 16 years) made up 32% of all confirmed cases admitted to hospital. Children aged 0-4 years old represented the largest proportion of hospital admissions (21.7%; Table).

The epidemic initially took hold in the metropolitan areas of NSW, particularly in the west and south-western suburbs of Sydney. As community transmission became more established the epidemic spread out in a patchy fashion to regional and rural NSW communities. A broad peak in hospital admissions associated with confirmed pandemic H1N1 influenza occurred during July, but this was partly attributable to regional variation in epidemic progression. The highest rate of hospital admissions related to H1N1 influenza was seen in the south-west region of Sydney (25 per 100,000 population), while the lowest rate was seen in the northern Sydney and Central Coast region (8 per 100,000). The outbreak lasted approximately 10 weeks (Figure 2).

Intensive care unit admissions

Of those hospitalised, 225 (18.5%) confirmed cases were admitted to intensive care units (ICUs). The median age of cases admitted to intensive care was 43 years. Of ICU admissions, 197 (87.6%) were adults aged 16 and older, and 28 (12.4%) were children. Of children, nine (32%) were aged 6 months or less. The

Table

Age distribution and rates of laboratory-confirmed cases of pandemic H1N1 influenza, emergency department presentations, hospital admission, intensive care unit admission and death per 100,000 population with comparison to the general population of New South Wales, Australia, to 31 August 2009

	Confirmed cases of pandemic H1N1 influenza (8 May to 16 June 2009)			Emergency department presentations with influenza-like illness (17 June to 31 August 2009)#				Hospital admission in association with confirmed pandemic H1N1 influenza infection (8 May to 31 August 2009)				Intensive care unit admission in association with confirmed pandemic H1N1 influenza infection (1 June to 31 August 2009)				Death due to pandemic H1N1 influenza infection (8 May to 31 August 2009)			
	n	%	RR^	n	%	Rate^^	RR^	n	%	Rate^^	RR^	n	%	Rate^^	RR^	n	%	Rate^^	RR^
Age group																			
0-4	26	6.6	1	779	10.3	167.5	1.6	263	21.7	56.6	3.3	17	7.6	3.7	1.1	0	0.0	0.0	0.0
5-9	40	10.2	1.6	598	7.9	137.2	1.3	69	5.7	15.8	0.9	7	3.1	1.6	0.5	1	2.1	0.2	0.3
10-14	44	11.2	1.7	555	7.3	121.7	1.1	44	3.6	9.6	0.6	2	0.9	0.4	0.1	0	0.0	0.0	0.0
15-19	36	9.2	1.4	867	11.4	184.1	1.7	64	5.3	13.6	0.8	8	3.6	1.7	0.5	0	0.0	0.0	0.0
20-24	57	14.5	2.1	1015	13.4	207.9	1.9	78	6.4	16.0	0.9	10	4.4	2.0	0.6	1	2.1	0.2	0.3
25-29	51	13	1.9	870	11.5	177.3	1.6	75	6.2	15.3	0.9	15	6.7	3.1	1.0	2	4.2	0.4	0.6
30-34	33	8.4	1.2	601	7.9	123.7	1.2	72	5.9	14.8	0.9	15	6.7	3.1	1.0	0	0.0	0.0	0.0
35-39	29	7.4	1.0	541	7.1	105.7	1.0	68	5.6	13.3	0.8	23	10.2	4.5	1.4	1	2.1	0.2	0.3
40-44	21	5.3	0.8	414	5.5	84.0	0.8	68	5.6	13.8	0.8	22	9.8	4.5	1.4	5	10.4	1.0	1.5
45-49	23	5.9	0.8	381	5.0	76.4	0.7	65	5.4	13.0	0.8	13	5.8	2.6	0.8	3	6.3	0.6	0.9
50-54	17	4.3	0.7	329	4.3	70.2	0.7	103	8.5	22.0	1.3	29	12.9	6.2	1.9	3	6.3	0.6	0.9
55-59	4	1	0.2	212	2.8	50.5	0.5	87	7.1	20.7	1.2	20	8.9	4.8	1.5	13	27.1	3.1	4.5
60-64	7	1.8	0.3	146	1.9	38.2	0.4	41	3.4	10.7	0.6	14	6.2	3.7	1.1	5	10.4	1.3	1.9
65 and over	4	1	0.1	272	3.6	27.7	0.3	115	9.5	11.7	0.7	30	13.4	3.0	1.0	14	29.2	1.4	2.1
Total (95% Conf Interval)	393	100	1.0	7580	100	107.5 (105.1-109.9)	1.0	1214	100.0	17.2 (16.2-18.2)	1.0	225	100	3.2 (2.8-3.6)	1.0	48	100.0	0.7 (0.5-0.9)	1.0
Sex																			
Male	201	51.1	1.0	3587	47.3	102.7	1.0	601	49.5	17.2	1.0	105	46.7	3.0	0.9	32	66.7	0.9	1.3
Female	188	47.8	0.9	3993	52.7	112.2	1.0	606	50.0	17.0	1.0	120	53.3	3.4	1.1	16	33.3	0.4	0.7
Risk factors																			
Aboriginal**	--			246	3.6	160.3	1.6	96	7.9	62.6	3.6	14	6.9	9.1	3.1	5	10.4	3.3	4.7
Pregnancy*	--			--				--				16	28.5	22.2	5.8	1	50.0	1.4	10.2
Obesity† (≥30kg/m²)	--			--				--				73	44.0	4.1	1.7	7	14.9	0.4	0.6
Morbid obesity† (≥40kg/m²)	--			--				--				24	14.5	11.4	4.7	4	8.5	1.9	2.7
No identified risk factors	--			--				--				23	10.2			5	10.4		

Source: NSW Department of Health and ANZIC Research Centre, Melbourne.
* Pregnancy includes pregnancy and the immediate post-partum period (the 28 days post-delivery). The risk in pregnant women was compared to the population of child-bearing age women (women aged 15-44 years).
**Aboriginal includes Aboriginal and Torres Strait Islander people
† In adults only, compared to the adult population
^ Relative risk calculated by comparison with the general NSW population. Source: ABS population estimates (HOIST), Centre for Epidemiology and Research, NSW Department of Health
^^ Rate per 100,000 population per period to which the column relates
# Does not include presentations to NSW public hospital influenza clinics located outside emergency departments

age distribution of those admitted to hospital differed substantially from those admitted to intensive care (Table). The median length of stay in intensive care was eight days for adults, four days for children, and seven days overall.

NSW public hospitals have 310 ventilated ICU beds for adults (5.5 per 100,000 adult population). At the peak, adult cases admitted to intensive care with confirmed H1N1 influenza occupied 15% of adult intensive care capacity, and cases admitted to intensive care units with confirmed influenza A (unsubtyped) or suspected influenza-related illness occupied an additional 15% of ICU capacity, together accounting for around 30% of adult intensive care unit capacity in NSW public hospitals. The demand for intensive care unit beds was sustained for a number of weeks after the overall level of influenza in NSW had started to decrease (Figure 3). Half of the patients admitted to intensive care required admission within one day of presentation to hospital. Of the 205 patients admitted to intensive care for whom risk factor information was available, 23 (10%) had no identifiable risk factor for severe illness.

Of patients admitted to intensive care, 159 (70.6%) required assistance with ventilation, 125 (55.6%) required invasive mechanical ventilation, and 27 (12%) required extracorporeal membrane oxygenation (ECMO). The majority (97%) of patients requiring ECMO were adults. The length of stay in intensive care for those who required invasive mechanical ventilation was 12 days, while those who required ECMO spent a median of 30 days in intensive care. Of patients admitted to intensive care, 26 (11.6%) required inter-ICU transfer due to the severity of their illness. Those at increased risk of admission to intensive care or death included pregnant women, Aboriginal and Torres Strait Islander people, and morbidly obese adults (Table).

Influenza clinics

NSW public hospitals set up influenza clinics to provide rapid assessment and management of patients presenting with influenza-like illness who did not require emergency medical attention. At the peak of the epidemic, NSW influenza clinics were assessing 300 patients per day. Of these patients, around 24% were provided with free anti-influenza medication, and 19% were referred to an emergency department for further assessment.

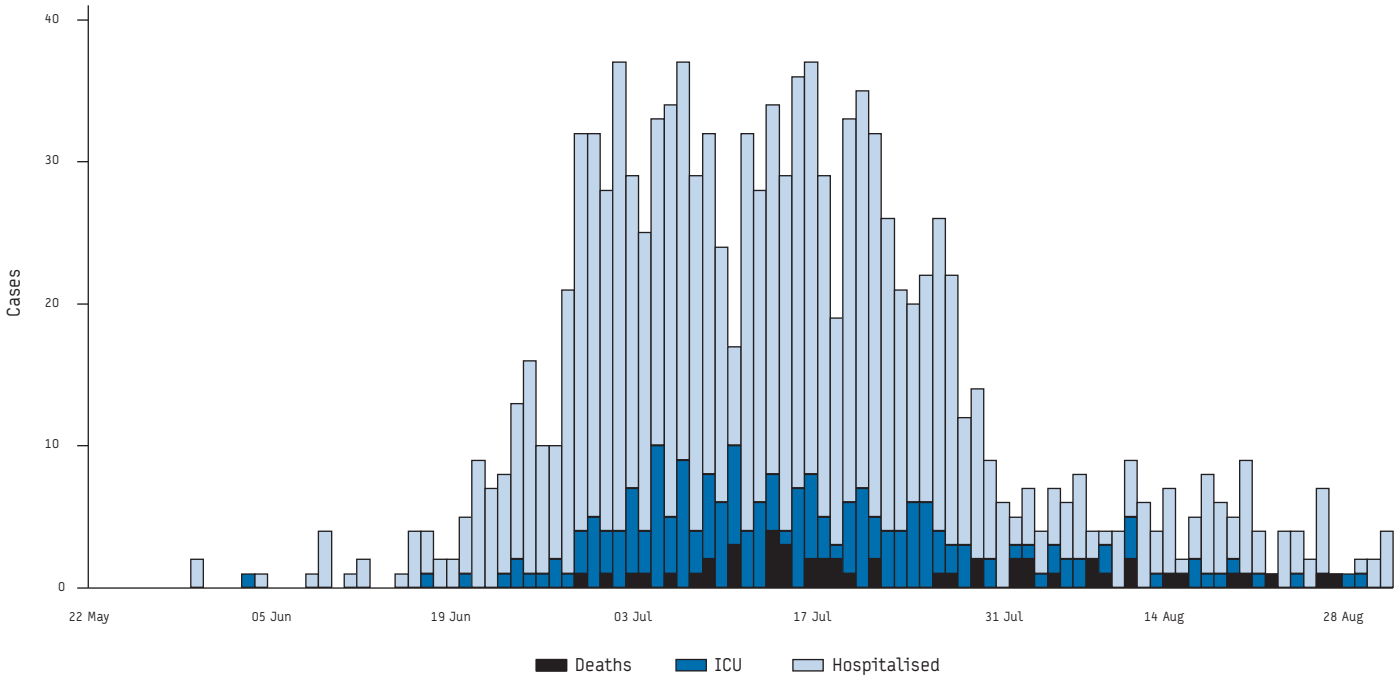
Emergency department presentations

From 22 May to 3 September 2009, there were 528,654 presentations to the 52 NSW hospitals participating in the ED surveillance system. This was 31,415 (6.3%) more than in the same period in 2008. The number of presentations in school-aged children 5-16 years old increased the most (10% higher than in the same period in 2008), followed by 17-34 year-olds (8%), 0-4 year-olds (7%), 35-64 year-olds (7%) and those aged 65 years or more (1%). Over the same 15-week period, 128,865 patients presenting to these EDs were admitted to hospital; 2,570 (2.0%) more than in 2008.

For the 49 EDs with good diagnosis completeness in 2008-2009, there were 90,305 presentations assigned a respiratory or 'unspecified infection' ED diagnosis over the same period. This was 19,519 (28%) more than in 2008. Within the respiratory category, 14,635 presentations were assigned a diagnosis of pneumonia or

Figure 2

Patients with confirmed pandemic H1N1 influenza who were admitted to hospital or intensive care unit or who died, by date of hospital admission, intensive care unit admission or death, 22 May to 31 August 2009, New South Wales, Australia



Source: NSW Department of Health and ANZIC Research Centre, Melbourne
Note: Patients who were admitted to an intensive care unit are represented twice, and patients who were admitted to intensive care and died are represented three times.

influenza-like illness combined, 6,987 (110%) more than 2008. There were 8,997 presentations in the influenza-like illness category alone, 7,921 (736%) more than in 2008.

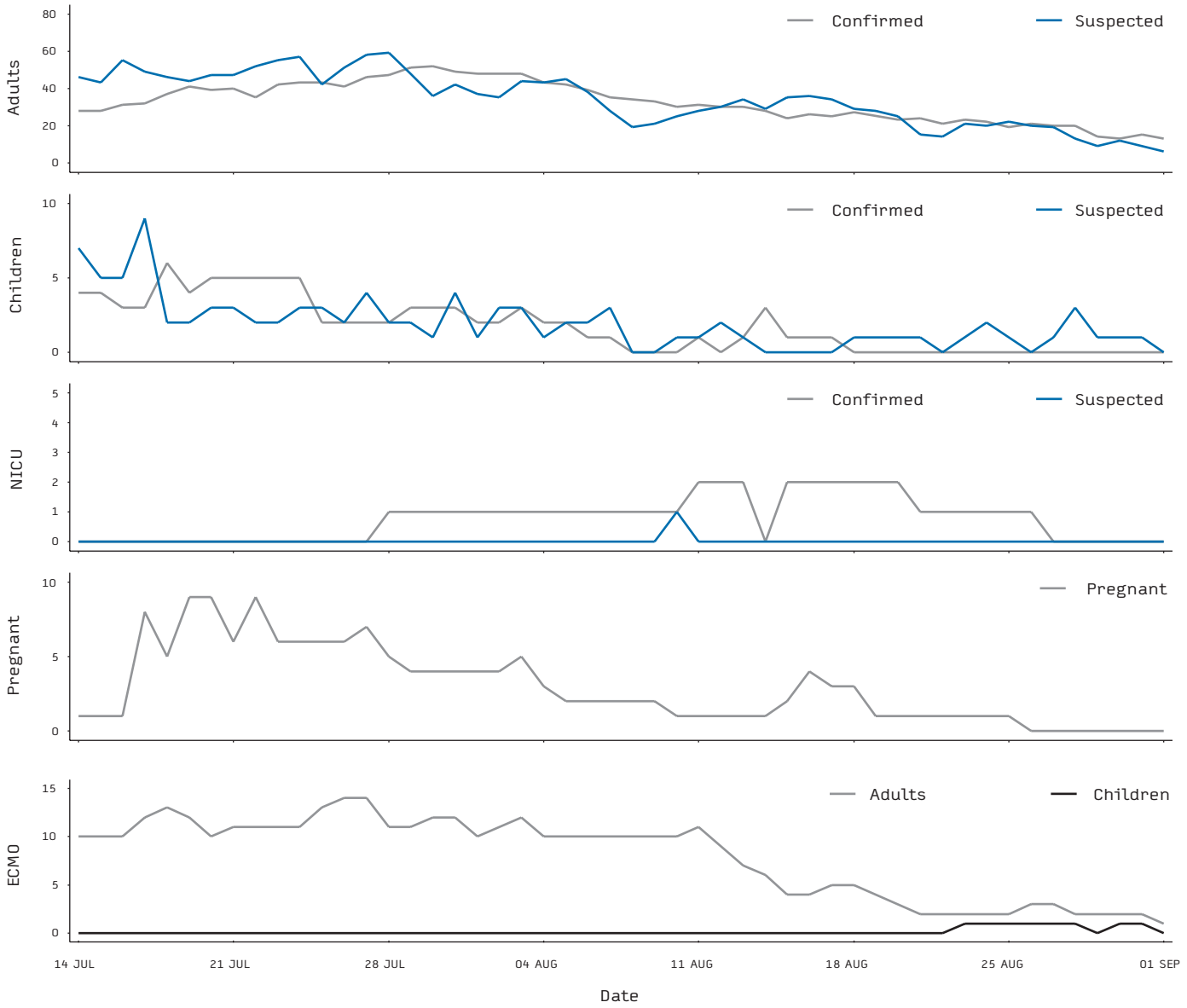
During the four weeks of greatest influenza-related activity from 1 July 2009, the proportion of patients with influenza-like illness admitted to hospital was 6.7%. This compares with 5.6% for the same period in the previous five years. The weekly peak in overall presentations to the 52 EDs occurred in the week ending 4 July 2009, with 40,597 presentations, 7,448 (22.5%) above the same week in 2008. Again, presentations in school-aged children 5-16 years old increased the most (58% higher), followed by 0-4 year-olds (26%), 17-34 year-olds (24%), 35-64 year-olds (16%) and those aged 65 years or more (5%). In the same week, there were 8,608 respiratory and unspecified infection presentations to 49 EDs, almost double (94% above) the same week in 2008, while 1,486 presentations were assigned a diagnosis of influenza-like illness or pneumonia combined (a 256% increase) and 977 presentations were assigned a diagnosis of influenza-like illness alone (2,405% increase; Figure 4).

Ambulance service activity

There was a clearly defined rise in ambulance activity above seasonally expected levels over a one-month period starting in the last week of June (data not shown). As for EDs, the peak in overall excess ambulance activity occurred in the week ending 4 July

Figure 3

Daily aggregate counts of patients with suspected or confirmed influenza admitted to intensive care units, 14 July to 31 August 2009, New South Wales, Australia

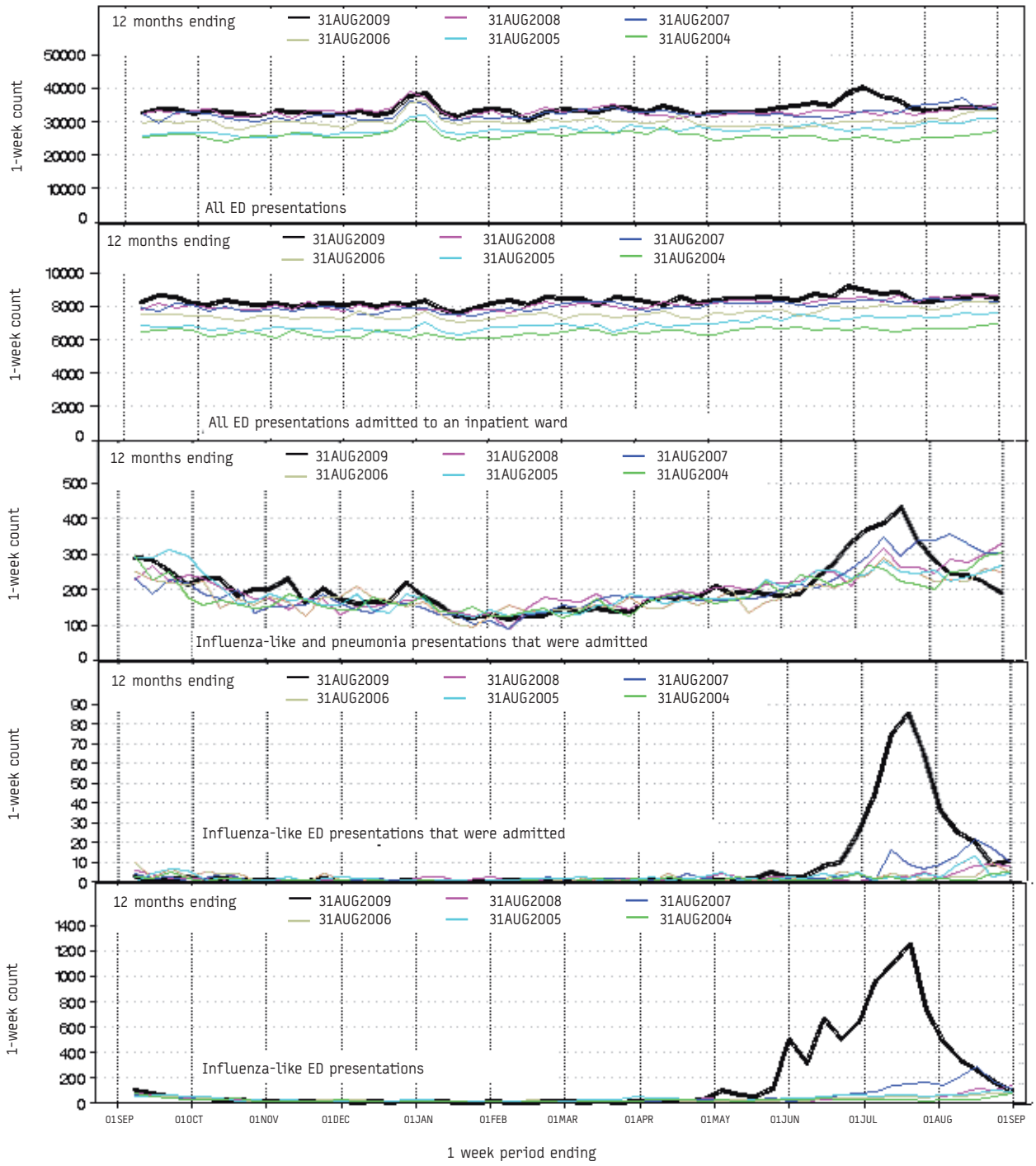


Source: NSW Department of Health

2009. In that week there were 7,480 calls, 853 (13%) more than in the same week in 2008. In the same week, there were 1,295 calls for breathing problems, 466 (56%) more than in the same week in 2008. Other problem categories that clearly increased

FIGURE 4

Weekly Emergency Department presentations and resulting inpatient admissions in the 12 months from 8 September 2008 to 31 August 2009, compared with the same period in each of the seasons from 2003-4 to 2007-8*, by category, New South Wales, Australia



Source: NSW Department of Health
* Some people presenting to New South Wales (NSW) emergency departments (ED) were referred to an influenza clinic without being recorded in the regular ED information system. Influenza-like and pneumonia presentations based on ED diagnosis. Includes 52 hospitals for all presentations and admissions, and 43 hospitals for influenza and pneumonia categories due to limited diagnosis completeness for some hospitals over the 6 years.

over the same period were 'headache', 'person ill', 'unconscious/fainting', 'fitting/convulsions' (particularly 0-4 year-olds), and 'chest pain'.

Deaths

By 31 August 2009, 48 people aged between 9 and 85 years had died in NSW of complications associated with pandemic H1N1 influenza (47 adults and 1 child). The median age of those who died was 58 years. Of those who died, 88.5% had a chronic underlying condition, while five (10%) had no risk factor identified. Chronic lung disease (33%), chronic cardiovascular disease (23%) and asthma (17%) were the most common underlying conditions in those who died. Five deaths were in Aboriginal or Torres Strait Islander people (Table).

The impact of the epidemic was comparable to previous seasonal influenza epidemics in terms of deaths due to influenza and pneumonia (Figure 5). Similarly, the impact on all cause mortality was comparable to normal seasonal effects (data not shown).

The impact of the epidemic was lower than in recent influenza seasons, with the weekly proportion of deaths recording influenza or pneumonia on the death certificate remaining markedly lower than the seasonal threshold of excess activity (Figure 5). Similarly, weekly counts of all-cause mortality remained well below several seasonal peaks of recent years (data not shown).

Discussion

Summary

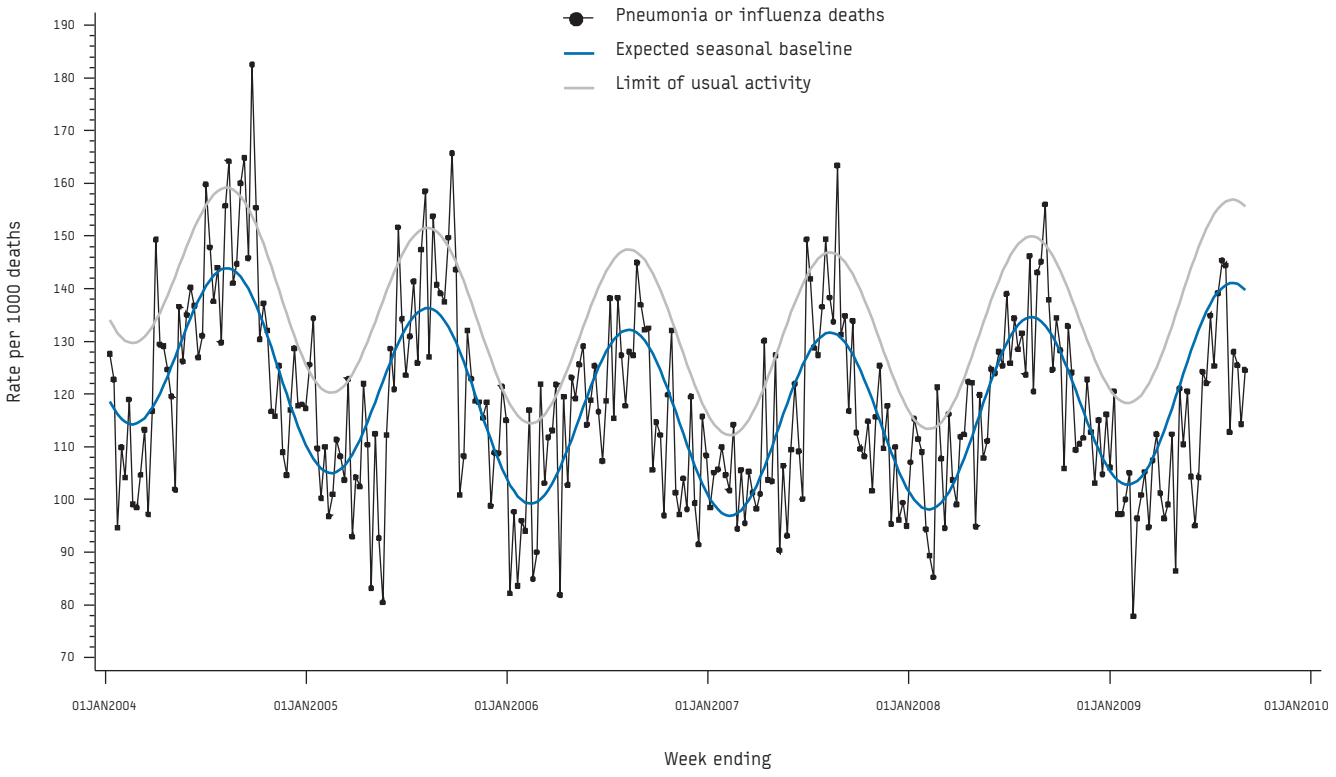
The onset of community transmission of pandemic H1N1 influenza at the beginning of winter resulted in a well-defined influenza epidemic in New South Wales. The epidemic lasted 10 weeks. The most notable features of this epidemic were the rapid establishment of community transmission, geographic variability in incidence of hospitalisation, brief and moderately severe capacity problems in emergency departments, more severe and sustained capacity problems in intensive care units, an increased risk of severe illness in those aged between 35 and 60 years, no evidence of greater overall or influenza or pneumonia-related mortality compared to previous influenza seasons, and abrupt cessation of community transmission. The increased demand for intensive care during the epidemic led to postponement of elective surgery in many public hospitals.

Progression and impact

The first case of pandemic influenza in New South Wales was detected in a traveller returning from overseas on 21 May. Case-based detection and containment efforts were overwhelmed in some urban areas of Sydney by the second week of June. Week one of the epidemic in New South Wales commenced on June 15, while emergency department activity peaked in early to mid-July - weeks 3 and 4 of the epidemic. The peak in influenza-like ED presentations and hospital admissions for influenza and pneumonia was around four weeks earlier than usual influenza

FIGURE 5

Weekly rate of deaths attributed to influenza or pneumonia per 1,000 deaths during 2004-2009, to 4 September 2009, by week of death, New South Wales, Australia



Source: NSW Registry of Births, Deaths and Marriages and Health Outcomes and Information Statistical Toolkit (HOIST), NSW Department of Health
Note: includes deaths registered as at 29 September 2009

seasons. There was a rapid return to normal seasonal activity levels by the beginning of September.

Overall presentations to EDs during the epidemic period were around 6% higher than in the same period in 2008. Intensive care units were more severely affected. The peak number of suspected and confirmed cases occupying adult intensive care beds peaked at around 15% of capacity in late July, placing considerable strain on ICU resources and requiring additional investments in high-end ventilators and ECMO machines. The epidemic created substantially increased demand for medical retrieval as well as difficulties transporting those with critical illness who required ECMO. Half of the patients admitted to intensive care required admission within one day of presentation to hospital, while 12% required inter-ICU transfer due to the severity of their illness.

Geographic spread

Emergency department surveillance and notifications of laboratory-confirmed patients admitted to hospital provided a guide to the geographic spread of the epidemic. Hospital admission rates varied at least three-fold over health service administrative regions, and up to 50-fold between smaller local government areas. This is likely to reflect real variation rather than variation in intensity of testing, given the general concordance of emergency department, hospital admission and ICU admission surveillance data and the unified administrative arrangements for all public hospitals in NSW, which receive almost all acute admissions. Heterogeneous spread of activity did assist health services to cope by allowing transfers of critically ill patients from highly affected areas to those areas that remained relatively unaffected.

Persons affected

Rates of hospital admission were highest in children less than five years old, and lowest in 10-14-year-olds. The average length of stay of children was three days, and only 12% were admitted to intensive care. This is generally consistent with the majority of children having relatively uncomplicated hospital stays. Only one child with a compromised respiratory system was identified to have died from H1N1-related illness.

Almost one quarter of adults aged 20-59 years admitted to hospital were admitted to intensive care and they accounted for approximately two thirds of intensive care admissions overall. Age-specific rates of admission to hospital and intensive care peaked in the 50-54 year age group. Death rates peaked in 55-59-year-olds. The main identifiable risk factors for death were chronic respiratory disease, pregnancy, Aboriginal or Torres Strait Islander status and morbid obesity. Pregnant women experienced the greatest relative increase in risk of severe illness or death. Over 10% of patients with confirmed H1N1-related illness admitted to intensive care required ECMO due to severe respiratory failure, while 10% of adult patients admitted to intensive care were healthy individuals with no identifiable risk factors.

Compared with other age groups, adults aged 60 years and over had lower rates of hospital admission, average rates of admission to intensive care (approximately half that of 50-54-year-olds), and above average rates of death associated with pandemic H1N1 influenza.

Overall there were only a small number of H1N1-related deaths in confirmed cases. This was supported by indirect information derived from death certificate surveillance, which indicated that influenza-related excess mortality was relatively low compared with seasonal activity in most recent years. Since most seasonal deaths from influenza and pneumonia occur in the elderly, [5] this finding is consistent with the relatively low level of H1N1 activity seen in the elderly through other surveillance systems. This data suggests that older population groups were largely protected, while some younger people, especially middle-aged adults and pregnant women were severely affected.

Limitations

The relatively mild clinical profile of most cases of influenza and the change in testing policy at the start of the 'protect' phase means that most cases of influenza in the community are not represented in our data. However, as influenza is a notifiable disease in NSW, and all pandemic H1N1 influenza notifications were entered into one database, the reporting of confirmed cases is likely to be almost 100% complete.

Ascertainment of all hospitalised cases is likely to be less than complete despite intensive testing of patients admitted to hospitals and intensive care units. Firstly, it is important to note that the sensitivity of the PCR test for pandemic influenza A(H1N1)v may be less than 100%, and is dependent on timely and high quality specimen collection, which may not have been possible for all patients [11]. We know that counts of cases of clinically suspected influenza-related illness in intensive care units tracked at the same levels as cases of confirmed H1N1-related illness, therefore the impact of influenza A(H1N1)v on intensive care capacity may be under-estimated. Secondly, the level of case ascertainment for hospitalised patients could not be cross-checked with the NSW public hospital inpatient records at the time of writing, as these records usually take some months to be coded and reported. Finally, data collection was censored as of 29 September 2009, which means that information relating to the period to 31 August may be incomplete. Further investigation of the level of H1N1 case ascertainment, in particular ascertainment in intensive care units is warranted.

While it is possible that public health messages which encouraged patients to seek medical help at emergency departments during the containment phase were partly responsible for the increased level of emergency department presentations for influenza-like illness seen at this time, during the 'protect' phase patients with influenza-like illness who were at risk of severe disease were encouraged to present early to their local general practitioner rather than the emergency department. Some patients may have attended emergency departments regardless; however the proportion requiring admission to hospital during July was higher than in previous influenza seasons. This indicates that increased community anxiety was probably not a major factor driving the increased number of presentations to emergency departments during the peak of the epidemic.

Information on the population seroconversion rate and clinical attack rate is not yet available. Seroprevalence data could provide direct support for our inferences from hospital admission data that transmission in optimal winter conditions has been patchy, and will be important to explain the varying rate of illness observed in different age groups.

Conclusion

NSW experienced a well-defined epidemic of influenza A(H1N1)v during the winter of 2009. This epidemic had a substantial impact on public health, emergency department and intensive care services, but influenza-related mortality and

overall mortality was lower than during several recent influenza seasons. Particular features of the epidemic included the severity of respiratory failure in some adult patients who required admission to intensive care, and the increased risk of severe illness in pregnant women.

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Writing committee

Cretikos MA[1,2], Muscatello DJ[1,3], Patterson J[1], Conaty S[4], Churches T[1], Fizzell J[1], Chant KG[1], McAnulty JM[1], Thackway S[1]

1. NSW Department of Health, Sydney, New South Wales, Australia
2. School of Public Health, The University of Sydney, Sydney, New South Wales, Australia
3. School of Public Health and Community Medicine, University of New South Wales, Australia
4. Sydney South West Area Health Service, New South Wales, Australia

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Pandemic H1N1 influenza surveillance in Victoria, Australia, April – September, 2009

J E Fielding (james.fielding@mh.org.au)[1], N Higgins[1], J E Gregory[1], K A Grant[2], M G Catton[2], I Bergeri[3], R A Lester[1], H A Kelly[2]

1. Victorian Department of Health, Melbourne, Australia
2. Victorian Infectious Diseases Reference Laboratory, Melbourne, Australia
3. Burnet Institute, Melbourne, Australia

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Victoria was the first Australian state to report widespread transmission of pandemic H1N1 2009 influenza. Notifiable laboratory-confirmed influenza and a general practitioner sentinel surveillance system measuring influenza-like illness (ILI), including laboratory confirmation of influenza as the cause of ILI, were used to assess the pandemic. The pandemic influenza A(H1N1)v virus quickly became the dominant circulating strain and notification rates were highest in children and young adults. Despite a high number of notified cases, comparison of ILI rates suggested the season peaked in late June, was similar in magnitude to 2003 and 2007 and less severe than 1997. The majority of clinical presentations were mild, but one quarter of hospitalised cases required admission to intensive care. Given the low proportion of imported cases in the Victorian pandemic, the rapid increase in cases with no travel history and the low median age of cases notified during the phases of intense surveillance, we suggest there may have been silent importations of pandemic virus into Victoria before the first case was recognised. The usefulness of a general practitioner sentinel surveillance system to provide a comparable assessment of influenza and ILI activity over time was clearly demonstrated, and the need for similar hospital and mortality surveillance systems for influenza in Victoria was highlighted.

Introduction

Following its identification and emergence in North America in March and April 2009, pandemic H1N1 2009 influenza was reported to have spread to an additional 27 countries by 12 May [1]. Four of these were countries in the southern hemisphere, including Australia where the first case was notified in the state of Queensland on 9 May [2]. Australia's second case was confirmed in the state of Victoria on 20 May. After that date, the number of reported cases in the state escalated rapidly. By 3 June cases from Victoria accounted for 86% of the national total [3], although Victoria only accounts for approximately one quarter of Australia's 22 million inhabitants. By early June at least nine other countries in the southern hemisphere had reported cases, although only Chile was comparable in numbers to Victoria [4].

Victoria was also the first state or territory in Australia to observe an apparent peak in its pandemic H1N1 influenza outbreak [5], and the key indicators of influenza activity had returned to baseline levels by the end of September. Here we present the surveillance findings for the entire influenza season, dominated by pandemic H1N1 influenza. The response to the pandemic in Victoria was implemented according to phases outlined in the Australian Health Management Plan for Pandemic Influenza (AHMPPI) [6]. The Victorian experience may provide an indication of what to expect during the first northern hemisphere winter in which pandemic H1N1 influenza is likely to be the dominant circulating strain.

Methods

Several surveillance methods for influenza and influenza-like illness (ILI) are used in Victoria, but here we report on the findings from the two principal systems. Laboratory-confirmed influenza is a notifiable disease in Victoria and it is a legal requirement that cases, including information on demography, symptoms and outcome, are notified in writing by the responsible laboratory and medical practitioner within five days of diagnosis to the Victorian Government Department of Health (the department) [7].

During the *Delay* and *Contain* phases of the Victorian response to the 2009 H1N1 influenza pandemic, testing of all suspected cases was authorised by the department [8]. A suspected case of pandemic H1N1 influenza was defined as: a person with fever and recent onset of at least one of following symptoms: rhinorrhoea, nasal congestion, sore throat or cough, AND either close contact with a confirmed case in the seven days prior to onset or travel in the seven days prior to onset to a country with evidence of local transmission. A confirmed case of pandemic H1N1 influenza was defined as a person with fever and recent onset of at least one of the following: rhinorrhoea, nasal congestion, sore throat or cough, AND confirmation of infection by real-time polymerase chain reaction (PCR), using an in-house assay specific for pandemic influenza at the Victorian Infectious Diseases Reference Laboratory (VIDRL). A confirmed case of influenza of unspecified subtype was defined according to the case definition promulgated by the Communicable Diseases Network Australia, with laboratory confirmation of infection from an appropriate respiratory specimen by viral culture, PCR, antigen detection, or an at least fourfold rise or single peak in the antibody titre to influenza virus [9].

All confirmed cases of pandemic H1N1 influenza notified during the Delay and Contain phases were followed up by departmental officers for clinical characteristics and exposure data, although data on vaccination status were not collected. Attempts were made to identify all close contacts of confirmed cases – defined

as within one metre of the confirmed case (while infectious) for more than 15 minutes, or in the same room as a confirmed case for more than four hours. Appropriate anti-viral prophylaxis and/or quarantine advice was then provided, which included closure of schools or classrooms in which there were confirmed cases. However, there were no large-scale scheduled school closures as part of the Victorian government's response to the pandemic.

Transition to the *Modified Sustain* phase was announced on 3 June. During this and the Protect phase, which commenced on 23 June, testing was recommended only for those with moderate or severe disease and those in particular risk groups. These included infants, healthcare workers, those in nursing homes and children in special development schools [8]. We assumed all cases notified to the department until 4 June inclusive were tested during the *Delay* or *Contain* phases.

Data were entered into the Notifiable Infectious Diseases Surveillance (NIDS) database at the department. Records of all laboratory-confirmed influenza cases with a 2009 notification date were extracted from the NIDS database on 2 October 2009 and analysed using Microsoft Excel software. Mapping was undertaken with ArcGIS software.

VIDRL operates the General Practitioner Sentinel Surveillance (GPSS) on behalf of the department. In 2009 the GPSS comprised 80 general practitioners (GPs) in metropolitan and rural areas across Victoria. Surveillance is conducted from May to October inclusive each year. Participating GPs report the total number of consultations per week, and the age, sex and vaccination status of any patients presenting with ILI. The ILI case definition was fever, cough, and fatigue or malaise [10]. ILI rates were calculated as the number of ILI patients per 1,000 consultations. Testing for influenza A viruses involved extraction of RNA from clinical specimens using a Corbett extraction robot, followed by reverse transcription using random hexamers. cDNA was amplified using an ABI-7500 Fast Real-Time PCR System incorporating primers and probes (sequences available on request) targeting the matrix gene of type A influenza viruses, including the pandemic influenza A(H1N1)v virus. Samples that tested positive in this assay were confirmed as positive or negative for influenza A(H1N1)v in a second real-time PCR assay incorporating primers and probe specific for the haemagglutinin (HA) gene of that virus. Influenza B viruses were identified by a separate PCR assay.

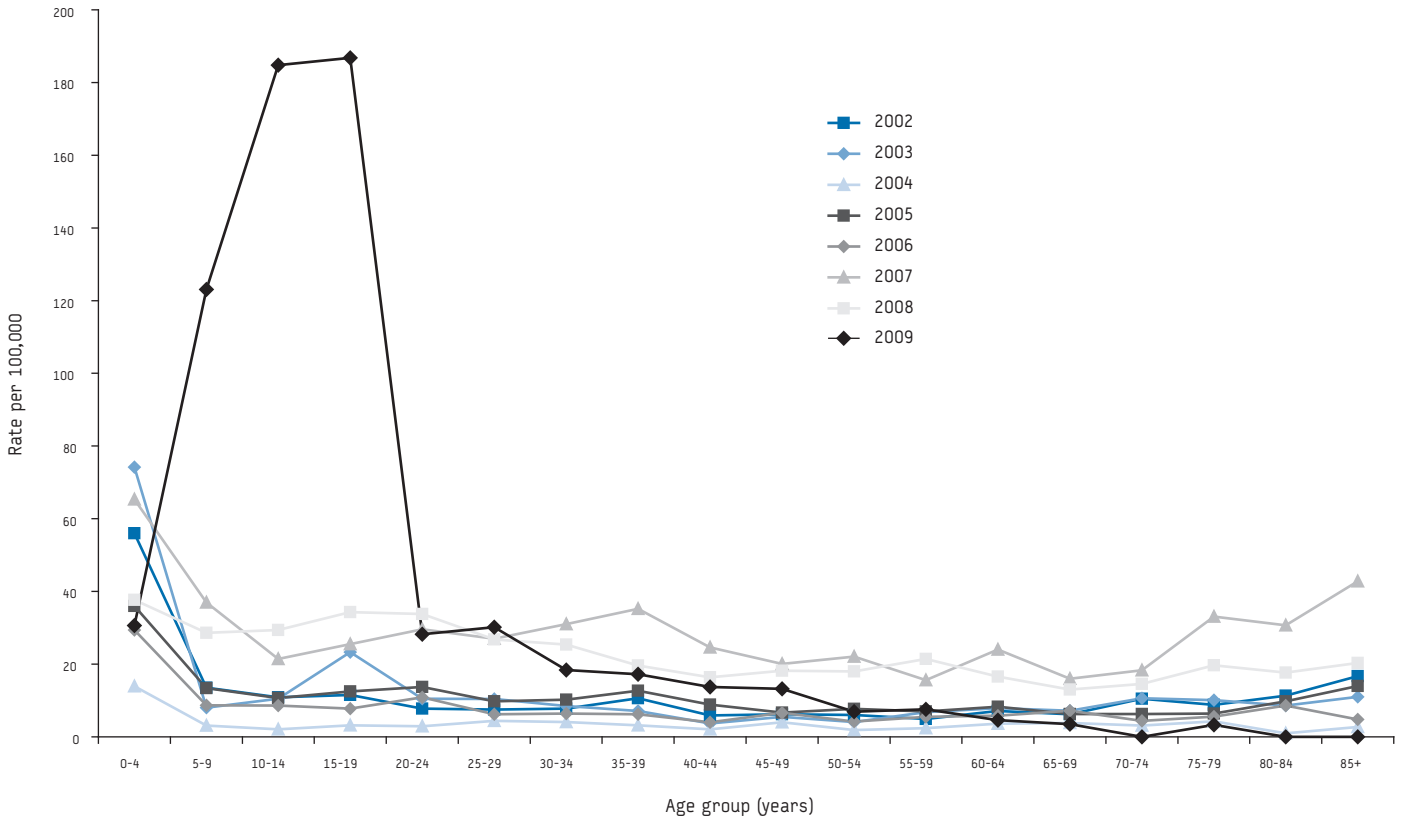
Results

Surveillance during the Delay and Contain phases

The first confirmed Victorian case of pandemic H1N1 influenza was reported on 20 May 2009 in a child who had returned from travel with family to the United States (US). Two siblings of this case, as well as a traveller from Mexico and a returned traveller from the US were notified in the following two days. A sixth case, notified on 21 May, had no travel history and was epidemiologically linked through a school to one of the siblings. The first case identified from the GPSS was notified on 22 May, as was another locally acquired case whose onset was found to be on 16 May, the earliest onset date of any of the notified cases. The number of notifications rose sharply towards the end of May, peaking at 250 cases on 2

Figure 1

Notification rates of laboratory-confirmed influenza by year and age group, Victoria, 1 January 2002 to 4 June 2009



June. Transition to the *Modified Sustain* phase was announced on 3 June, and by the end of 4 June, a total of 977 confirmed cases of pandemic influenza had been notified to the department. Only eight cases notified during this period had a reported history of travel to an affected area.

The age range of the 977 notified cases notified prior to the introduction of the *Modified Sustain* phase was five months to 79 years with a median age of 15 years. School-aged children (5-17 years inclusive) comprised 67% of all cases, with the highest notification rates in the 10-14 and 15-19 years age groups. High notification rates in older children and younger adults and low rates among people aged 65 years and above contrasted with all other years since 2002, the first full year in which laboratory-confirmed influenza was a notifiable infectious disease (Figure 1). Males comprised a slight majority (55%) of cases. Twenty-one cases (2.1%) were hospitalised and there were no reported deaths in this period.

Almost all confirmed cases (99.5%) of pandemic H1N1 influenza were residents of metropolitan Melbourne or suburbs bordering the metropolitan area. Cases were generally reported over a wide area of the city, although there were higher rates, indicated by darker red shading and larger dots in Figure 2, and apparent foci in suburbs on the northern and western peripheries of the city.

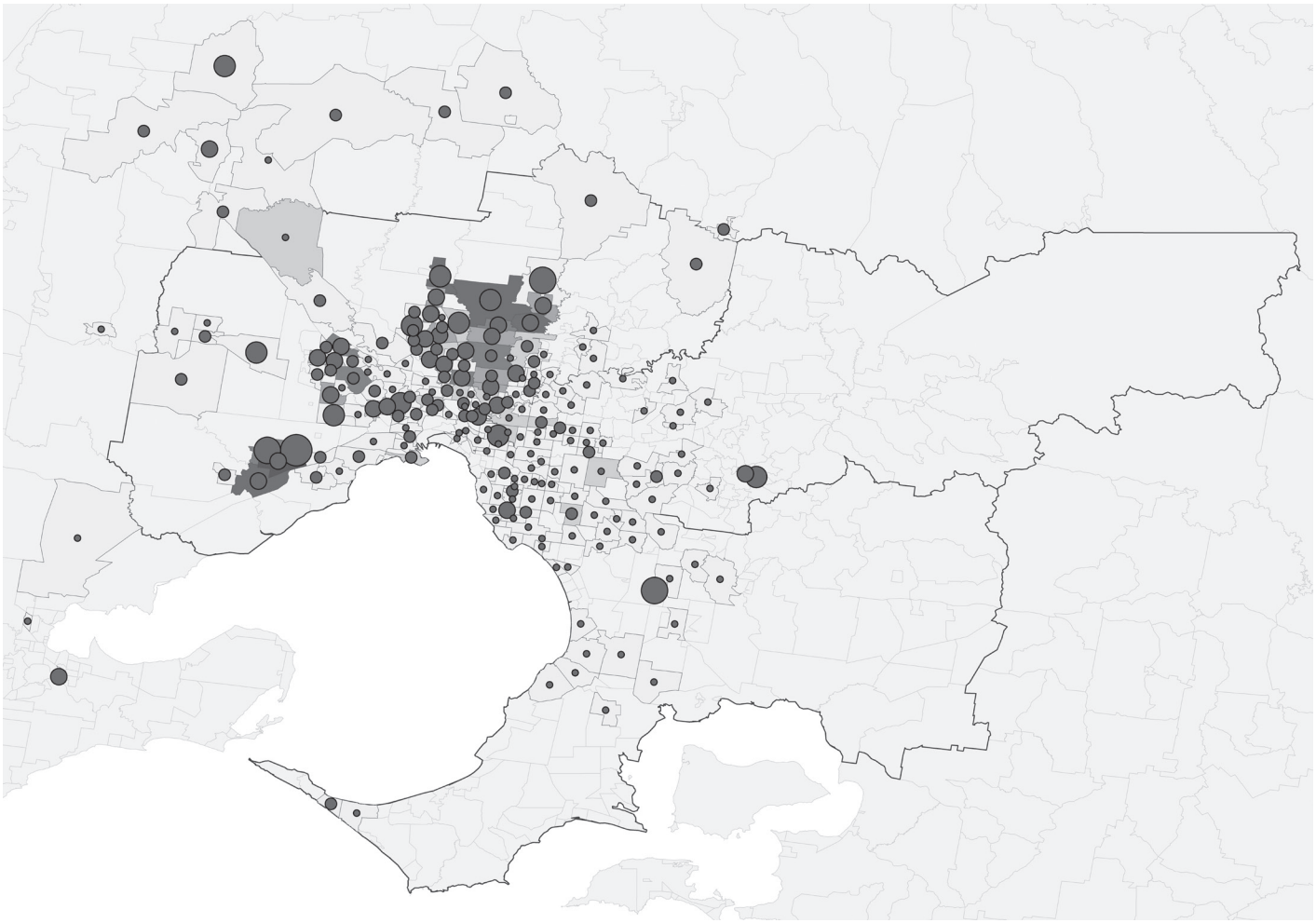
Data on contacts of confirmed cases were available for 908 (93%) of the 977 cases of pandemic H1N1 influenza. Details were available for 5,807 contacts with only 70 (7%) who could not be contacted. The number of total contacts per case ranged from 0 to 129 (median=4), and the number of household contacts per case ranged from 0 to 40 (median=3) including one case who was a student at a boarding school. There were at least 88 schools with one or more confirmed cases. Seven schools had more than ten confirmed cases and one school had 70 cases. There were 74 households with more than one confirmed case.

Almost half of the first 977 pandemic H1N1 influenza cases had a nose or throat swab collected within one day of symptom onset and, by three days since symptom onset, the proportion from whom a swab had been collected increased to 83% (median=2 days; range: 0-12 days). Approximately three quarters of the cases had been notified within three days of specimen collection (median=2 days; range: 0-8 days).

Surveillance during the Modified Sustain *and* Protect *phases*

Figure 2

Relative notification rate of pandemic H1N1 influenza by suburb, Melbourne, 20 May to 4 June 2009



The number of notified laboratory-confirmed influenza cases dropped, once the *Modified Sustain* phase was declared and emphasis was placed on detection of more severe cases (Figure 3). The season's peak as measured by the ILI rate occurred in late June and was accompanied by a secondary peak in the number of notified laboratory-confirmed influenza cases. Both the number of notified cases and the ILI rate fell steadily to baseline levels over the following three months.

As observed from surveillance during the *Delay* and *Contain* phases, the age distribution of laboratory-confirmed influenza cases identified from GP sentinel surveillance for the entire season was similarly skewed towards younger age groups with 70% of cases aged under 30 years. Those aged 20-24 years comprised the modal age group.

A majority of laboratory-confirmed cases of influenza notified to the department during the *Contain* phase were the pandemic influenza A(H1N1)v strain. Most testing was referred to VIDRL, but there was an increase in notified cases of unspecified influenza A cases in June as private pathology laboratories resumed routine testing (Figure 4). The number of influenza A-positive but influenza A(H1N1)v-negative cases followed a similar trend to that of unspecified type A influenza cases. Only 12 cases of type B influenza were notified between 27 April and 27 September 2009. Where subtyping was possible, influenza detections from the GPSS showed that strain replacement was almost complete by mid-June (Figure 5). By the peak of the pandemic in late June, the pandemic strain comprised at least 95% of all weekly notifications from the GPSS [11]. The proportion of all notifications positive for influenza from the GPSS was 39% [12], not substantially different to the proportion of 37% positives for the years 2003 to 2007 [13].

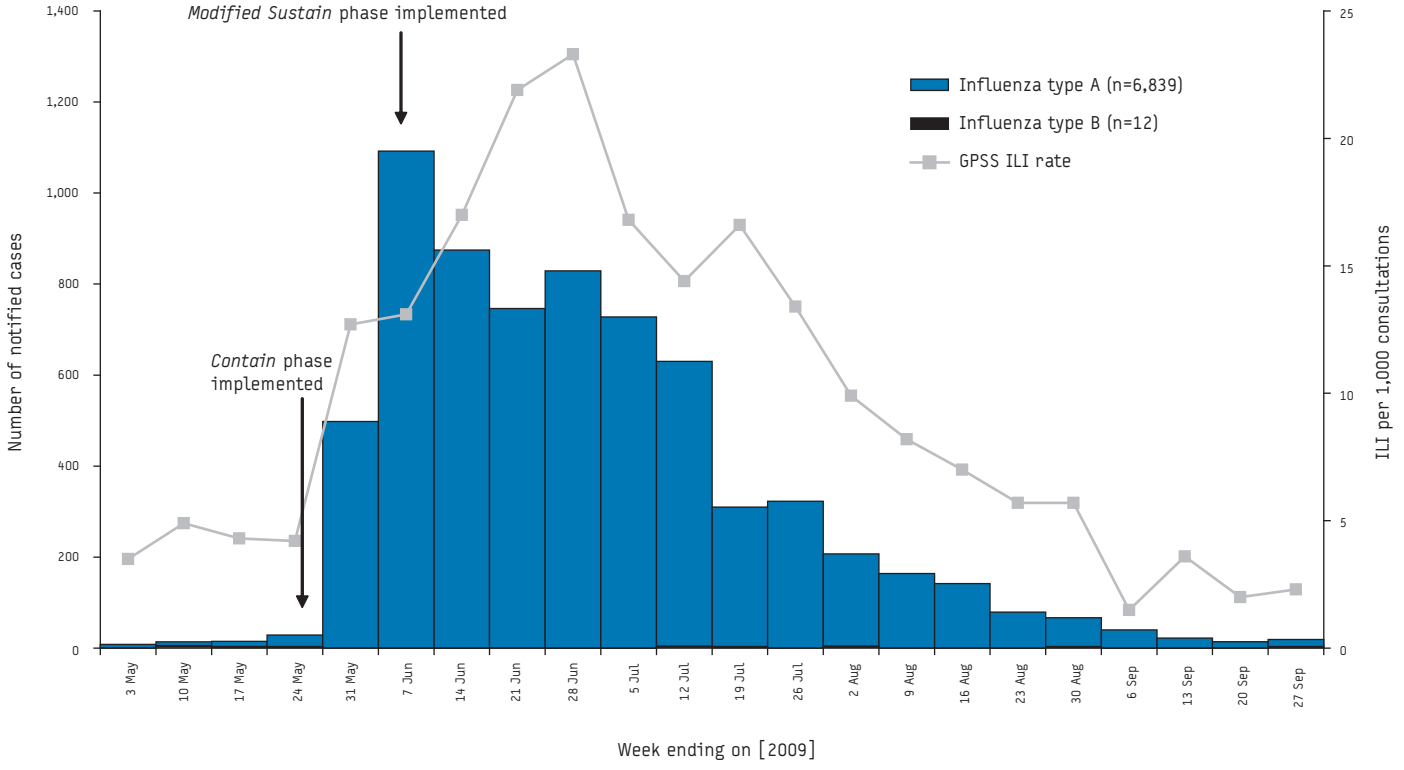
A total of 6,895 cases of laboratory-confirmed influenza, of which 3,058 were confirmed influenza A(H1N1)v, were notified from 1 January until 27 September. This was more than four times the previous highest annual total of 1,591 cases in 2007. The peak rate of ILI measured by the GPSS in 2009 was relatively high but comparable to the seasons of 2003 and 2007 (Figure 6), and lower than that for 1997 [12]. The relative length of the 2009 season as measured by both surveillance systems was comparable to other years but started two to three months earlier than recent seasons.

Hospitalisations and deaths

Hospitalisations reported by the Victorian Health Emergency Coordination Centre totalled 513, of which the department received enhanced hospitalisation data for 415 cases. Of the 415 hospitalised cases, 108 (26%) required admission to an intensive care unit (ICU). A further 224 cases were reported to be ward-based, and for the remaining 83, information on illness severity was not available (Table). There were 24 deaths reported among confirmed cases. A wide age distribution was observed in hospitalised patients, but more severe outcomes were generally associated with older patients. Among the 24 reported deaths, three were in children aged between two and seven years. A majority of ward-based cases and deaths were male, although this trend was

Figure 3

Notified cases of laboratory-confirmed influenza by type and GPSS ILI rate by week, Victoria, 27 April to 27 September 2009



GPSS: General Practitioner Sentinel Surveillance; ILI: influenza-like illness.

reversed among ICU cases. Data on indigenous background were not provided for 381 (92%) of the 415 hospitalised cases.

Between 2005 and 2007, 40-55% of notified cases of laboratory-confirmed type A influenza were reported as being hospitalised. In 2008, a season in which type B influenza was predominant, 13% of type A influenza cases were reported as hospitalised. The annual number of deaths among notified cases of influenza has ranged from 1-14 (median=3) cases between 2002 and 2008 inclusive.

Respiratory disease outbreaks

During the surveillance period the department was notified of 24 respiratory outbreaks in nursing homes. Ten were of unknown aetiology, four were due to respiratory syncytial virus, three to picornavirus and one due to parainfluenza virus. Six outbreaks were caused by type A influenza, of which five were negative for pandemic H1N1 influenza. The only reported outbreak of pandemic H1N1 influenza in a nursing home affected three staff members, two of which were laboratory-confirmed, but no residents.

Discussion

The 2009 influenza season in Victoria was characterised by a relatively early onset. Although a record number of laboratory-confirmed cases were notified, the magnitude of the season as measured by ILI activity was comparable to 2003 and 2007. Data from the GPSS indicated that influenza A(H1N1)v was the dominant strain throughout the season, with sequential replacement of seasonal influenza strains by the pandemic virus [11]. Over a similar period investigators in New Zealand also reported sequential replacement of seasonal influenza strains throughout the pandemic [14].

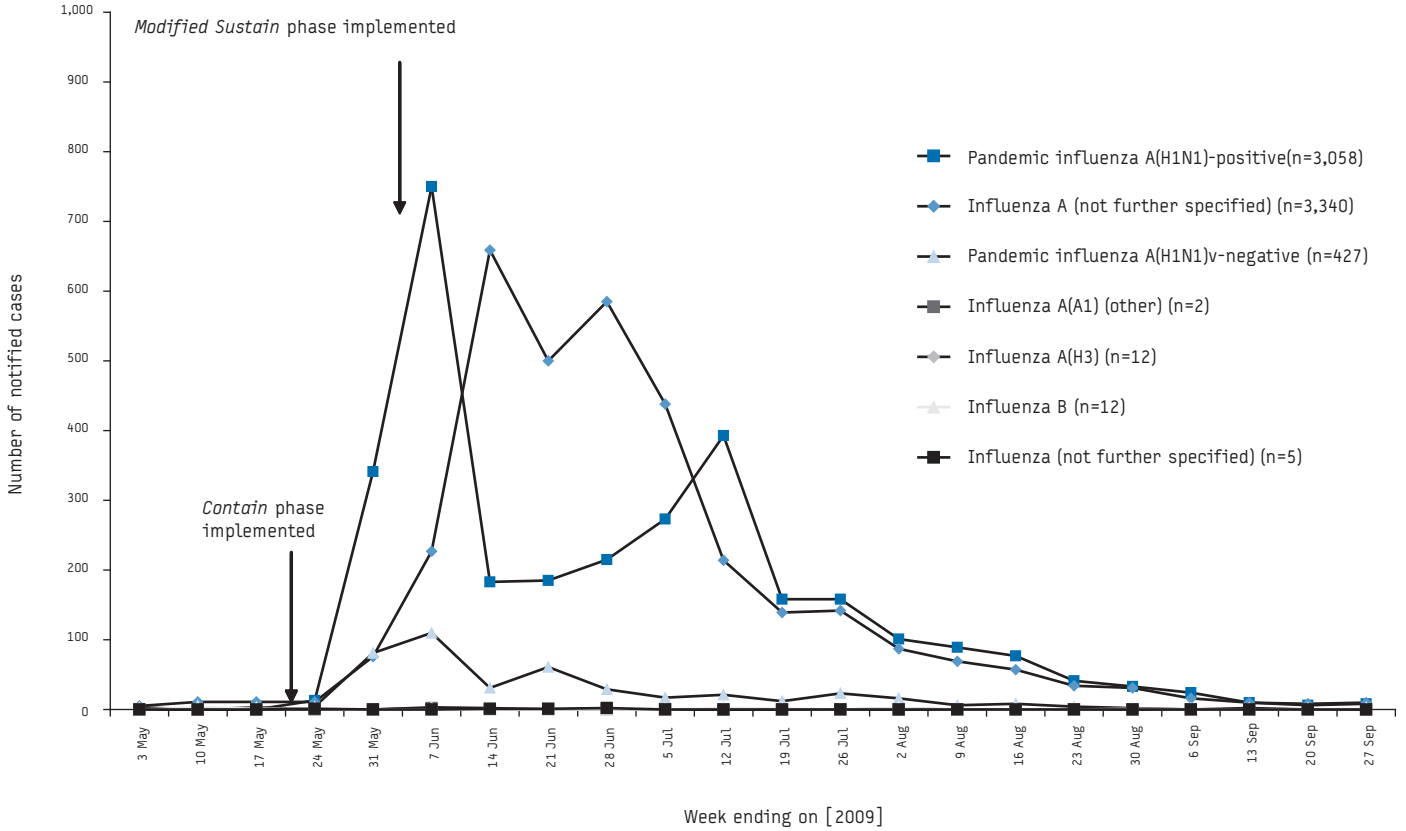
There were a number of epidemiological features to distinguish the pandemic from previous influenza seasons, particularly the high notification rates in young adults and a generally mild manifestation of infection, as indicated by a low proportion of hospitalised cases. However, approximately one quarter of hospitalised cases were severe enough to warrant admission to an ICU, a phenomenon we have previously described as 'the pandemic paradox' [15]. Compared to previous influenza seasons, pregnant women were at increased risk of hospitalisation and ICU admission.

The geographic distribution of confirmed cases notified during the period in which any person with symptoms and contact with a confirmed case was eligible for testing indicated infection foci on the northern and western peripheries of the Melbourne metropolitan area. This probably represents a snapshot of disease activity during the limited period for which intense community level surveillance was undertaken, given that notified cases and higher ILI rates were reported in other areas across the state over subsequent weeks.

Three observations suggest that pandemic H1N1 influenza may have been established in Victoria before it was detected by surveillance. Firstly, in contrast to reports from other countries, where the proportion of early imported cases has ranged from 44-78% [16-18], only 5% of the first 100 Victorian cases with

Figure 4

Notified cases of laboratory-confirmed influenza by type/subtype/strain and week, Victoria, 27 April to 27 September 2009



pandemic influenza infection were reported as acquired overseas. Travel history and exposure were collected for all 977 cases reported here, so that no cases with a travel history or exposure to travellers would have been missed.

Secondly, there was a rapid rise in the number of notifications of locally acquired cases with no apparent links to the cases acquired overseas. This rapid rise could not be a consequence of exposure to five documented imported cases, given that all cases were isolated and their close contacts quarantined. The use of a case definition in the Delay phase, which required travel history to an affected country, would have excluded the identification of any locally acquired cases that arose from previous silent importations. This restricted case definition was used on the assumption that cases would be imported, or linked to an importation.

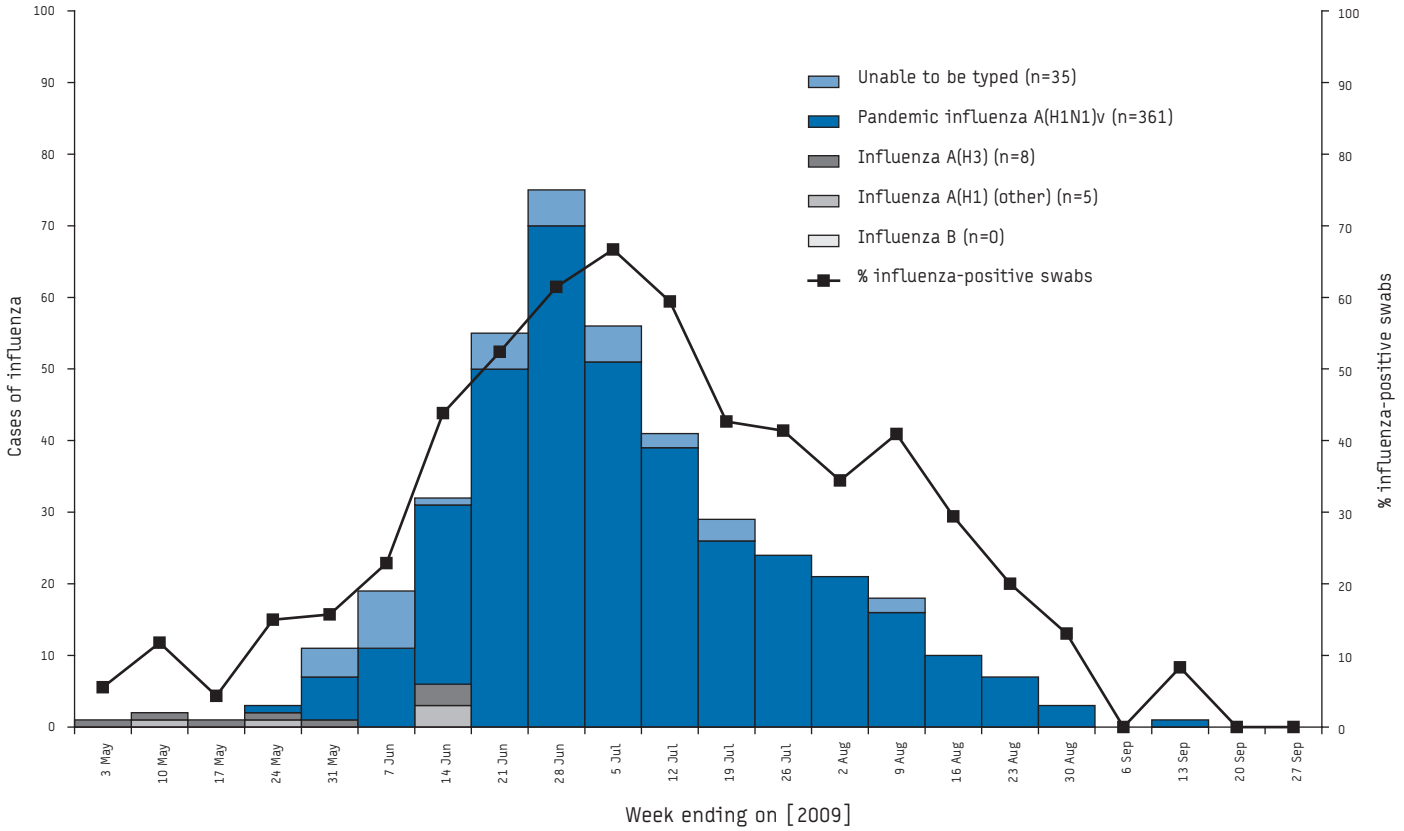
Thirdly, the lower median age of cases identified from the initial intense surveillance in Victoria compared to pandemic surveillance elsewhere suggests that an amplification of the pandemic in school-aged children was being detected during this period. The median age of 15 years – which ranged between 13.5 and 15 years for the 10 strata of 100 consecutively notified cases during the *Delay* and *Contain* phases (data not shown) – was in contrast to the median age of cases during the early stages of the pandemic in the US (20 years) [19] and Spain (22 years) [16] as well as the state of Western Australia (22 years) [20] and Victorian cases from the GPSS (21 years) [11]. However, the median age of pandemic patients in the US had dropped from 20 years to 13 years by the time approximately 10,000 cases had been notified (Lyn Finelli, US Centers for Disease Control and Prevention, personal communication), which we suggest also reflects amplification of the pandemic in school-aged children and intense follow-up and testing of cases in this age group. Clearly the early stages of the pandemic in Victoria were very different to the reported early stages in other countries.

During the *Delay* and *Contain* phases, the rapid escalation of notified cases in Victoria placed enormous strain on the institutions managing the diagnosis and investigation of the response, as these phases called for active follow-up of all cases and contacts. This level of surveillance was being maintained until the notification rate reached approximately 184 cases per million population, compared to the US, which started to focus on testing only the more severe cases when the notification rate was approximately 26 cases per million (Lyn Finelli, personal communication).

In order to manage the surveillance and other elements of the response in a sustainable way, Victoria independently moved to the *Modified Sustain* phase, although the declaration of the pandemic phases had previously been nationally consistent. This was necessary given the considerably lower levels of pandemic influenza activity in all other Australian jurisdictions at the time and highlights the need for flexibility in national plans.

Figure 5

General Practice Sentinel Surveillance influenza cases by type/subtype and proportion of positive nose/throat swabs, Victoria, 27 April to 27 September 2009

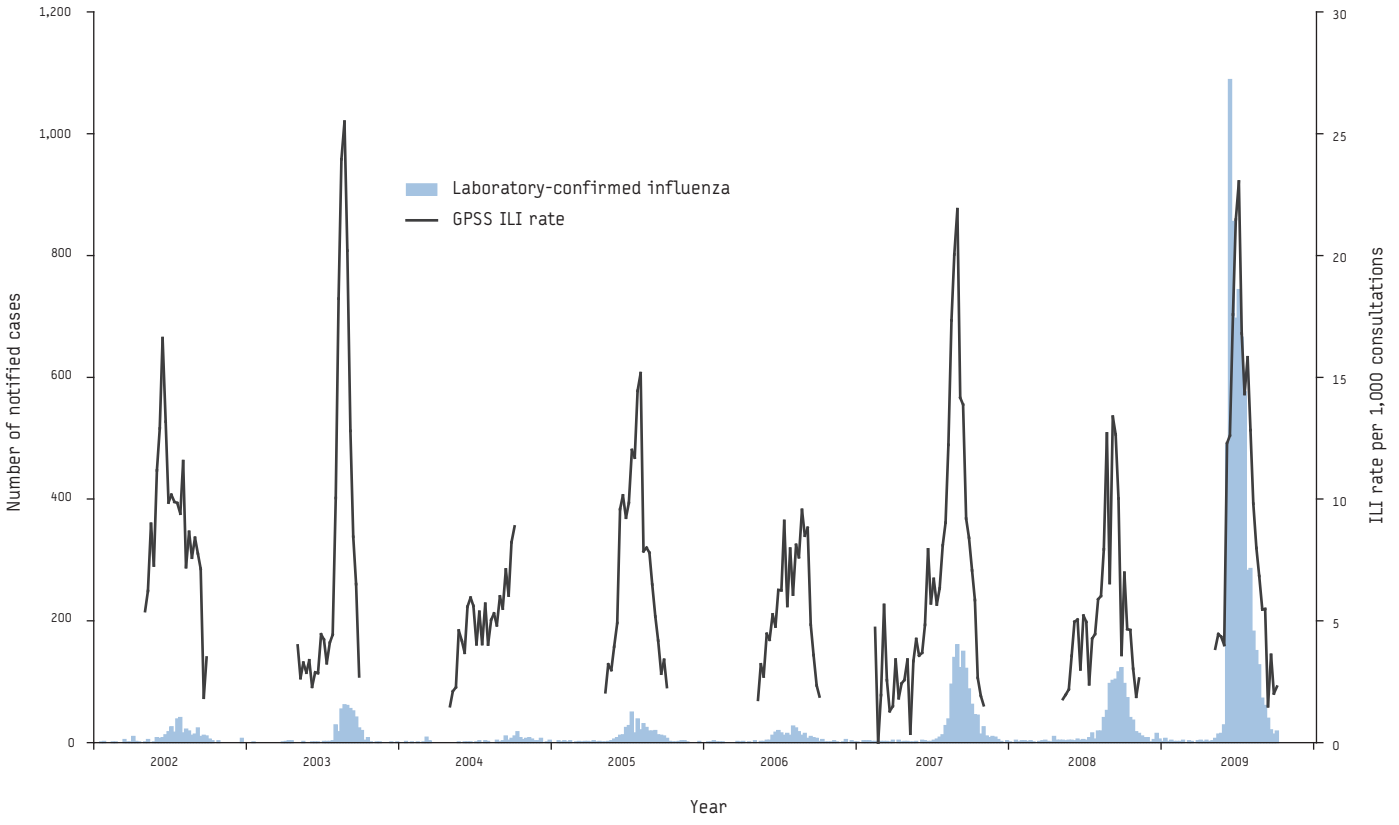


Compulsory notification of laboratory-confirmed influenza is a critical influenza surveillance tool and provides not only epidemiological data about confirmed diagnoses, but the opportunity to understand the emergence of novel influenza strains. However, interpretation of notification data must be undertaken with caution, as these data are sensitive to testing practices that vary from season to season. ILI data suggested a season characterised as higher than normal seasonal activity, while notification data suggested unprecedented levels of disease in the community. This discrepancy is undoubtedly explained by increased testing for influenza in 2009 compared with previous seasons. When we attempt to correct for this by comparing the proportion of laboratory tests positive for influenza at VIDRL over a number of consecutive seasons, the proportion of positive tests in 2009 was similar to the proportions positive in 2004, 2006 and 2008, years characterised by normal seasonal activity [15]. The ILI rate measured by the GPSS was a consistent measure of respiratory illness activity across the entire season, a consistency that could not be provided by notification data because of the necessary change in surveillance practice for laboratory-confirmed influenza during the pandemic.

Our inability to compare notified cases of laboratory-confirmed influenza over time also created a difficulty in comparing the profiles of severe presentations and mortality to previous influenza seasons. It is accepted that notified cases underestimate the number of deaths that can be attributed to seasonal influenza [21]

Figure 6

Notified cases of laboratory-confirmed influenza and GPSS ILI rate by week, Victoria, 1 January 2002 to 27 September 2009



GPSS: General Practitioner Sentinel Surveillance; ILI: influenza-like illness.

Table

Notified cases of pandemic H1N1 influenza by hospitalisation and outcome status, age, sex, length of stay and pregnancy, Victoria, Australia 27 April to 27 September 2009

	Ward-based	ICU	Deaths
Total cases	224	108	24
Median age [years (range)]	23 (1 month–87 years)	38 (21 days–86 years)	50 (2–85 years)
Males	54%	45%	58%
Length of stay [median (range)]	3 (1–79 days)	10 (1–63 days)	
Pregnant cases [number (% of female cases)]	14 (14%)	9 (15%)	1 (10%)

and increased testing associated with the pandemic undoubtedly accounted for increased recognition of influenza as a contributing cause of death in 2009. It is therefore impossible to determine whether the fact that the annual number of influenza deaths in 2009 was the highest in the eight years of notifiable influenza surveillance is attributable to the disease or to a surveillance artefact. This emphasises the need for establishment of an influenza mortality surveillance system in Victoria, such as the system in New South Wales. Monitoring of seasonal deaths due to pneumonia and influenza in New South Wales suggested that there were no excess deaths during 2009 - and may even suggest a decrease in seasonal deaths [22]. This observation would be consistent with the relative absence of older people amongst those infected with pandemic H1N1 influenza. Whilst a system for critical care surveillance was quickly established in Victoria during the pandemic in 2009 [23], its integration with existing influenza surveillance systems was limited and options for better linkage of these datasets and more sustainable hospital-based surveillance should be explored.

We have previously suggested that the existing influenza surveillance schemes in Victoria might not be adequate in a pandemic [24]. The pandemic of 2009 has confirmed this suggestion, highlighting both the usefulness of existing surveillance schemes and the need for an expansion of the timely surveillance of indicators of morbidity and mortality.

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Early transmission characteristics of influenza A(H1N1)v in Australia: Victorian state, 16 May – 3 June 2009

E S McBryde (Emma.McBryde@mh.org.au)[1,2,3], I Bergeri[4], C van Gemert[4,5], J Rotty[3], E J Headley[3], K Simpson[3], R A Lester[3], M Hellard[4], J E Fielding[3]

1. Victorian Infectious Diseases Service, Royal Melbourne Hospital, Melbourne, Victoria, Australia
2. Department of Medicine, University of Melbourne, Melbourne, Victoria, Australia
3. Victorian Department of Health, Melbourne, Victoria, Australia
4. Burnet Institute, Melbourne, Victoria, Australia
5. National Centre for Epidemiology and Public Health, ANU College of Medicine and Health Sciences, Australian National University, Australia

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Australia was one of the first countries of the southern hemisphere to experience influenza A(H1N1)v with community transmission apparent in Victoria, Australia, by 22 May 2009. With few identified imported cases, the epidemic spread through schools and communities leading to 897 confirmed cases by 3 June 2009. The estimated reproduction ratio up to 31 May 2009 was 2.4 (95% credible interval (CI): 2.1-2.6). Methods designed to account for undetected transmission reduce this estimate to 1.6 (95% CI: 1.5-1.8). Time varying reproduction ratio estimates show a steady decline in observed transmission over the first 14 days of the epidemic. This could be accounted for by ascertainment bias or a true impact of interventions including antiviral prophylaxis, treatment and school closure. Most cases (78%) in the first 19 days in Victoria were under the age of 20 years-old. Estimates suggest that the average youth primary case infected at least two other youths in the early growth phase, which was sufficient to drive the epidemic.

Introduction

Pandemic H1N1 influenza was first identified in Mexico in mid-March 2009, and by the end of April, cases had been reported throughout North America [1]. On 25 April 2009, the World Health Organization (WHO) declared the situation to be a public health emergency of international concern [2] and raised the level of influenza pandemic alert to level 3 and then level 4 within one week of the declaration [3]. The virus spread rapidly around the globe and by 12 May cases were reported in 30 countries including Australia's first imported case in the state of Queensland. Victoria, a state of Australia with a population of 5.4 million, subsequently reported rapid community spread.

The first confirmed case of pandemic H1N1 influenza in Victoria was on 20 May in a traveller who had returned to Victoria from the United States of America on 19 May (symptom onset 17 May). In the following two days, this case's two siblings and a Mexican on holiday in Australia were also notified in Victoria. After further case ascertainment, the first onset date of pandemic H1N1 influenza for a Victorian was found to be 16 May. This case was locally acquired. At that time, Victoria was in the *Delay* phase of the pandemic (as classified by the Australian government [4]) during which time the testing algorithm for influenza A(H1N1)v was dependent on a travel history to an affected country. The identification of locally acquired cases resulted in the pandemic phase being upgraded to *Contain*, and from 22 May, anyone with influenza-like symptoms was encouraged to seek testing from their doctor. By 3 June 2009, 897 cases had been notified in the state of Victoria, many from school outbreaks. Modified Sustain phase then commenced and testing was recommended for high risk people only [5]. During the *Contain* phase all notified cases were followed up for information about illness, exposure and contacts in order to decide on the necessity of quarantine (including school closures) and antiviral treatment of cases and prophylaxis for contacts of cases.

Important public health priorities in a new pandemic are to identify the transmission characteristics of the new infection, to determine its severity and to assess the impact of mitigation strategies [6]. Early reports indicated that there were regional differences in the transmission characteristics of influenza A(H1N1)v, with the suggestion that the transmission varied depending on the season. For this reason, particular attention has been paid to the countries of the southern hemisphere to determine the transmissibility during winter.

A key summary measure of the transmissibility of an emerging contagious disease is the reproduction ratio (R) which is the expected number of secondary cases generated per primary case. This number is highly predictive of the likely impact of interventions on the spread of an emerging infectious disease [6] as well as the ultimate community attack rate [7]. The reproduction ratio for influenza A(H1N1)v has been estimated in several countries with differing results, including Mexico with R estimates of 1.4–1.6 [8] Japan with 2.0–2.6 [9], the Netherlands with 0.5 [10], Thailand with 1.78-2.07 [11], New Zealand with 1.80-2.15 [12] and Peru with 1.2-1.7 [13]. The differences in transmission rates

could be due to ascertainment biases from under-reporting early in the epidemics, real differences due to season or social mixing patterns or to the mitigation strategies used, or else reflect the sub-populations in which influenza was introduced. Mitigation strategies varied from country to country, with respect to the use of school closure, cancellation of mass gatherings, other social distancing measures [14], home quarantine and antiviral prophylaxis.

In this paper we assessed the transmissibility of influenza A(H1N1)v using the onset times of cases in Victoria, Australia. Victorian onset times have not been available in the public domain to date. We estimated the generation interval using linked cases. The reproduction ratio is examined, with summary, time-varying and age-specific estimates. A method that leads to a more robust estimate of *R* in this setting is presented, reducing ascertainment bias by imputing undetected transmission. Additionally, we considered the sensitivity of estimates to differences in generation interval.

Methods

Exponential growth rate

During the exponential growth phase of an epidemic, the relationship between past daily incidence $I(t-\tau)$ and current daily incidence $I(t)$ of symptom onset can be expressed as $I(t)=I(t-\tau)e^{r\tau}$, where r is the exponential growth rate, and τ is the time difference. The exponential growth rate was estimated from the daily incidence curve, using Poisson regression.

Estimation of the generation interval

Of the initial 897 cases in the Victorian influenza A(H1N1) pandemic 2009, 750 had data on contacts and 37 had an identified primary contact, with source case and contact case onset dates known. The generation interval was defined as the time between the onset of symptoms in case A to the onset of symptoms in case B, given that case A infected case B. The generation interval was parameterised to a *Gamma (alpha, beta)* distribution, using the *gammfit* function in Matlab™.

Estimation of the reproduction ratio

Method A

We estimated the reproduction ratio (R) using the exponential growth rate (r) and the gamma distribution fitted to the generation interval. It has been shown previously [15] that R can be estimated from r, using the relationship

$$R = \frac{1}{M(-r)}$$

where M is the moment generating function of the generation interval. For the gamma distribution this leads to

We estimated R using the onset date of the influenza

$$R = (1 + \beta r)^{\alpha}$$

A(H1N1)v cases in Victoria from 16 May 2009 (earliest known onset date) until the end of the exponential growth phase. Estimates of R are sensitive to the choice of end-date of this phase, so three different time intervals were examined 16-27 May, 16-29 May and 16-31 May 2009.

Method B

To estimate R in a time-varying manner, we adapted the generation interval-informed method of White *et al.* [16], using the formula

Eq(1)

$$L(R_z, \mathbf{p}) = \prod_{t=T_{z-1}+1}^{T_z} \frac{e^{-\mu_t} \mu_t^{A_t}}{A_t!},$$

where

$$\mu_t = \sum_{j=1}^{\min(t,k)} R_z^{I(t-j>T_z)} R_{z-1}^{I(t-j<T_z)} N_{t-j} p_j$$

and P_j is the probability function for the generation interval on day j. R_z is the estimated R over time period, z, bounded by $T_{z-1}+1$ to T_z. I is the indicator function, and is equal to one if the statement in parentheses is true and zero otherwise. N_t is the total number of cases on day t, and A_t is the number of autochthonous cases. Estimates were made using Bayesian inference, with uninformative conjugate gamma (10^{-3}, 10^{3}) prior distribution for R and a Poisson likelihood function from equation 1.

Sensitivity to generation interval

Sensitivity analysis of generation interval on estimates of the reproduction ratio was conducted. Using method B, we repeated the estimated of R using generation intervals of 1.5, 2, 2.5, 3 and 3.5 days.

Age specific transmission

Method C

The next generation matrix is an estimate of the type-specific reproduction ratios. We divided the population into youth (under 20 years-old) and adult (20 years-old or older). The epidemic curve was then divided into discrete generations from 16 to 27 May, based on onset date. We examined the sensitivity to generation time by investigating generation time of two days for six generations and three days for four generations.

The expected number of cases of youths (Y) and adults (A), respectively, in generation T is given by

where a is the youth → youth, b is the youth → adult, c is the adult → youth, and d is the adult → adult type-specific reproduction ratio.

The parameters, a, b, c and d were estimated assuming a Poisson relationship between E(A) and E(Y) and their respective observed values.

$$E(Y_T) = a\ Y_{T-1} + b\ A_{T-1}$$
$$E(A_T) = c\ Y_{T-1} + d\ A_{T-1},$$

Sensitivity to ascertainment bias from unobserved transmission

Method D

For this analysis, unobserved transmissions were imputed, and R was estimated from this augmented dataset, rather than the observed data. We assumed that incident cases were incompletely observed during the *Delay* phase of the pandemic, which lasted from the time of the WHO alert, 24 April [17], until 22 May 2009. We assumed the observed data from 22 May until 30 May were accurate. The incidence data were partitioned into generations of three days, with the observed data starting on 22 May.

Let the vector ***G*** represent the augmented dataset, being the incidence by generation. ***G*** consists of observed incidence for the final three generations (22-24, 25-27 and 28-30 May) and imputed incidence for all generations preceding 22 May. The imputed cases are generated from the relationship

Eq(2)

$$G_A(n+1) \sim Poisson(R(G_A(n)+\varepsilon(n)))$$

where $G_A(n)$ is the number of autochthonous cases in the nth generation and $\varepsilon(n)$ is a small, generation-dependent number to account for importations. Exponential growth was assumed for $\varepsilon(n)$, reflecting a global incidence of influenza A(H1N1)v (that is $\varepsilon(n+1) = R\ \varepsilon(n)$). For the fully observed generations, it was assumed that importations were fully observed as Poisson realisations of $\varepsilon(n)$.

The likelihood of R is given by

$$L(R) = \prod_{n=1}^{\max(n)} Poisson(G_A(n), R(G_A(n-1)+\varepsilon(n-1))).$$

Using Bayesian tools of Metropolis-Hastings updates, R was estimated concurrently with the number of generations that preceded the *Contain* phase. The number of preceding generations was estimated by beginning with the first generation of the *Contain* phase and working backwards, using Gibbs updates. When $G_A(n+1)$ was two or more, $G_A(n)$ was estimated with the sampling distribution determined by Eq(2), that is

$$\Pr(G_A(n) = X \mid G_A(n+1)) = \frac{\Pr(G_A(n+1) \mid G_A(n) = X)\Pr(G_A = X)}{\sum_{i=1}^{\infty} (G_A(n+1) \mid G_A(n) = i)\Pr(G_A = i)}$$

where $\Pr(G_A(n+1) \mid GT(n) = X)$ is given by Eq(2). In practice, this formula was implemented by putting an upper limit on the value of X, so that X could only take the values {0, max(40, $2G_A(n+1)$}.

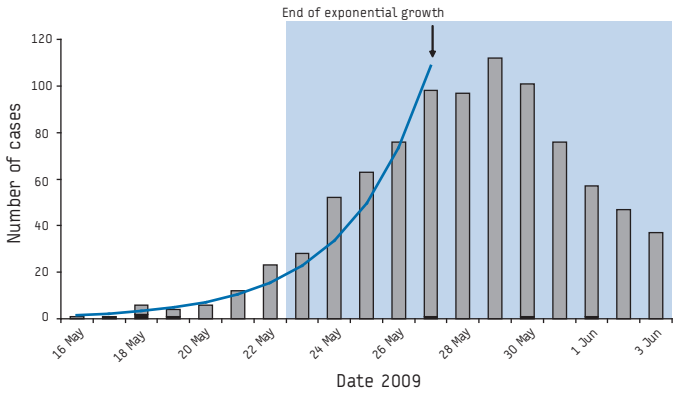
Uniform discrete priors were used for the $\Pr(G_A=X)$, simplifying the sampling distribution of G_A to

$$\Pr(G_A(n) = X \mid G_A(n+1)) = \frac{\Pr(G_A(n+1) \mid G_A(n) = X)\Pr(G_A = X)}{\sum_{i=1}^{\max(40,2n)} \Pr(G_A(n+1) \mid G_A(n) = i)}.$$

If $G_A(n)$ was <2, the algorithm was terminated. The process was iterated until convergence was achieved for both R and the number of preceding generations. No adjustment was made for the change in model complexity as each successive generation was added.

Figure 1

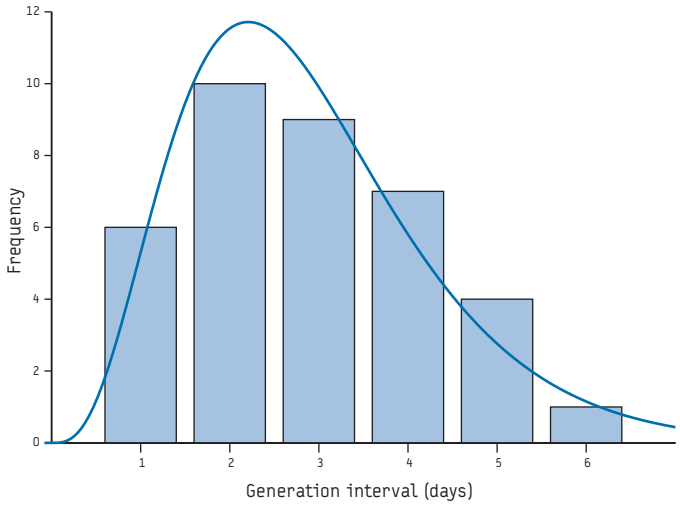
Epidemic curve by date of symptom onset of laboratory-confirmed cases of influenza A(H1N1)v, 16 May – 3 June 2009 Victoria, Australia (n= 897)



Light blue background: *Contain* phase; arrow : the end of the exponential growth phase, from which estimates were made; black bars: imported cases; gray bars: autochthonous cases; dark blue line: fitted exponential growth curve.

Figure 2

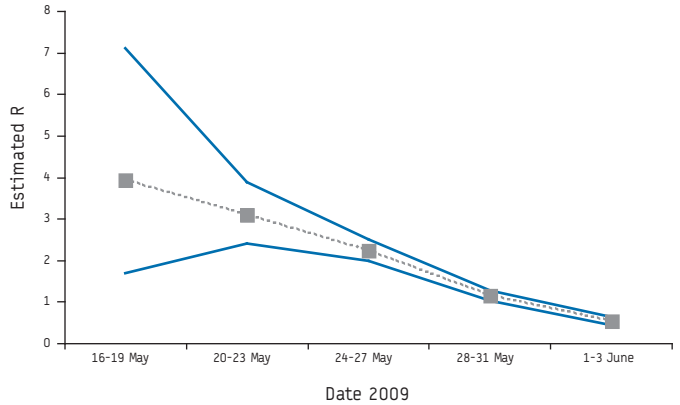
Histogram of the frequency of the known linked cases by generation interval, influenza A(H1N1)v, 16 May – 3 June 2009 Victoria, Australia



The dark blue curve is the fitted gamma distribution.

Figure 3

Time-varying reproduction ratio *R*(t), influenza A(H1N1)v, 16 May - 3 June 2009, Victoria, Australia



Dark blue lines represent the 95% credible interval, under the assumptions of the model.

Final size

We can estimate the expected number of people who developed infection by the end of the epidemic using the relationship between R and final size, given by the numeric solution to the transcendental equation

$$\log(s_\infty) = R_0(s_\infty - 1)$$

where s_∞ is the proportion of the population who remain susceptible, hence $1\text{-}s_\infty$ is the proportion infected by the end of the epidemic, referred to as the final size of the epidemic [7]. This assumes that the population is fully susceptible initially, that there are no effective mitigation measures and that homogenous mixing of the population takes place.

Results

Exponential growth rate

In the state of Victoria, Australia, following the first known imported cases, the number of incident cases of notified laboratory-confirmed influenza A(H1N1)v was growing exponentially. There were eight imported cases and 889 autochthonous cases during the period from 16 May to 3 June 2009. Figure 1 shows the temporal distribution of confirmed influenza A(H1N1)v cases in Victoria. Exponential growth of the epidemic lasted approximately 12 days (16 to 27 May inclusive). The epidemic growth rate during this period is estimated to have been 0.40 (95% CI: 0.39-0.41) per day, giving a doubling time for the epidemic of 1.7 days.

Generation interval

The generation interval had a mean of 2.9 days and standard deviation of 1.4 days. The optimal gamma distribution fit was the Gamma (4.2, 0.68) distribution. Figure 2 shows the frequency of generation intervals with fitted gamma curve.

Estimates of reproduction ratio

Method A

Using Method A, the reproduction ratio is estimated to be 2.4 for the period 16-31 May 2009.

However, this method is sensitive to the assumed length of the period in which the epidemic was growing exponentially. The table gives the estimates for exponential growth rate and the corresponding estimates of *R* assuming three different dates for the end of exponential growth: 27 May, 29 May and 31 May.

Method B

Using Method B, the estimated reproduction rate from the first case (16 May) to the end of the exponential growth phase (27 May) is 2.4 (95% CI: 2.1-2.6). To assess the sensitivity of results to the observed generation interval of 2.9 days, we examined the estimates assuming generation intervals from 1.5 to 3.5 days. The estimated reproduction ratio for the first 12 days of the epidemic was very sensitive to the generation interval. When the generation interval was 1.5, 2, 2.5, 3 and 3.5 days, *R* was estimated to be 1.6 (95% CI: 1.4-1.7), 1.8 (95% CI: 1.6-1.9), 2.1 (95% CI: 1.9-2.4), 2.5 (95% CI: 2.3-2.7) and 2.8 (95% CI: 2.6-3.1), respectively. These results all assume the reproduction ratio remained constant throughout the period.

Relaxing this assumption produces a time-varying reproduction ratio. Figure 2 shows the time-varying reproduction ratio from 16 May until 3 June. The estimated R begins at 3.9 and falls to less than one by the beginning of June.

Method C

During the *Contain* phase, the overall median age of incident cases was 15 years. The daily median during this period ranged from 13-17 years and there was no trend in age distribution over time.

As shown in the table, the estimated youth to youth transmission was higher than transmission between adults only and between

Table

Reproduction ratio estimates of influenza A(H1N1)v, 16 May - 3 June 2009, Victoria, Australia

Estimation of reproduction ratio			
Conditions of estimation	R (95% Credible interval)	r (95% Credible interval)	
Method A Epidemic growth rate 16-27 May 2009	2.8 (2.70-2.8)	0.40 (0.39-0.41)	
Method A Epidemic growth rate 16-29 May 2009	2.6 (2.5-2.6)	0.37 (0.36-0.37)	
Method A Epidemic growth rate 16-31 May 2009	2.4 (2.3-2.4)	0.33 (0.32-0.33)	
Method D Undetected transmission prior to 22 May 2009	1.6 (1.5-1.8)		
Estimate of age-specific reproduction ratios			
Description of parameter		Generation interval two days	Generation interval three days
Estimated number of secondary cases of youths following each primary youth	Youth to youth	1.8	2.7
Estimated number of secondary cases of youths following each primary adult	Adult to youth	0.5	0.5
Estimated number of secondary cases of adults following each primary youth	Youth to adult	0.5	0.7
Estimated number of secondary cases of adults following each primary adults	Adult to adult	0.2	0.4

youths and adults. The dominant eigenvalue of the next generation matrix, given by

$$\mathbf{M} = \begin{pmatrix} a & b \\ c & d \end{pmatrix}$$

gives us an estimated R [7] of 2.8, assuming a generation time of three days, and 1.9 assuming a generation time of two days, in keeping with estimates using Methods A and B.

Method D

Allowing for undetected community transmission prior to the start of the *Contain* phase on 22 May 2009, the estimate for R over the exponential growth phase (until 30 May) was 1.6 (95% CI: 1.5-1.8), compared with 2.4 (for the same end date of the epidemic) if detection was assumed to be complete. This corresponds to an estimated final proportion of the population infected (final size) of 64% if we correct for undetected transmission, and of 88% using the uncorrected measure. The estimated number of generations that preceded 22 May, incompletely observed, was 9 (95% CI: 6-13), suggesting that transmission may have been occurring in Victoria from late April, under Method D assumptions. The estimated number of unobserved cases is 170 (95% CI: 120-230), 60% of which occurred between 16 and 21 May 2009.

Discussion and conclusions

The epidemic in Victoria had a relatively high estimated transmission rate compared with other countries. The reproduction ratio was estimated to be 2.4 for the epidemic during the second half of May 2009, although it may have started above 3. After accounting for unobserved transmission early in the epidemic (ascertainment bias), this value may be as low as 1.6. Time-varying analysis suggests the reproduction ratio fell during the *Contain* phase.

Age-specific analysis of transmission showed that transmission amongst youth (under the age of 20 years) was sufficient to sustain transmission in its own right, whereas transmission between youth and adults was initially minimal. This is consistent with the view that the early transmission of influenza A(H1N1)v in Victoria in the second half of May 2009 was driven by school age children and occurred in the absence of multiple importations.

These estimated reproduction rates are higher than those in Mexico [8] and Europe [10], but similar to those estimated in Japan [9], Thailand [11] and New Zealand [12]. Japan, which also had a school-fuelled outbreak, had similar age-specific transmission with a sustained transmission in the under 20 year-olds [9].

Even using the more conservative estimate in this study of R=1.6, transmission was relatively high compared, for example, with seasonal influenza in Australia, which from 1972-1997 had a mean of 1.3 (95% CI: 1.2-1.4) [18]. While the increase in transmission measured in the Victorian influenza season 2009 may seem slight, the reproduction ratio has large nonlinear effects on attack rate and efficacy of public health measures. The final proportion of the population predicted to be infected during an epidemic, assuming that no effective mitigation takes place, is 64% for R=1.6 and 42% for R=1.3, if homogenous mixing is assumed. It is probable that the true proportion of people infected with influenza A(H1N1)v in Victoria this year will be smaller than the estimation based on the initial reproduction ratio. This is to be expected, if the effective reproduction ratio declines over time, if a large proportion of the population have prior immunity [19], or if the population mixing patterns lead to substantial groups of the population not being exposed to influenza cases. Serosurveillance studies are awaited to determine the influence of these three factors on the epidemic.

The reproduction ratio also has implications for the potential impact of mitigation strategies that have been considered, such as antiviral treatment and prophylaxis, school closure [20] and vaccination [21]. The falling reproduction ratio observed in Victoria may reflect the impact of mitigation strategies carried out during this time, such as reactive school closure, quarantine, antiviral treatment and prophylaxis, which was offered to all contacts of confirmed cases during *Contain* phase. Voluntary social distancing may also have played a role.

This study is strengthened by the use of case data, particularly symptom onset dates, that were collected from 20 until 31 May 2009, allowing inferences to be made about transmission. Despite this, there are possible inconsistencies of case ascertainment, given that the information is based on surveillance data in a rapidly evolving epidemic. Undetected cases prior to the *Contain* phase could have lead to overestimates in the transmission rates. This study used a method that allowed for hidden transmission in an effort to get more robust estimates of reproduction ratios. However, the assumptions of complete observation from 22-30 May could be false and would lead to an underestimate of the reproduction ratio if the proportion of clinical cases tested decreased over this period. From 3 June, testing was not conducted on cases that were not considered high risk. Given the delay from symptom onset to testing it appears that data based on onset dates are not reliable after 29 May. Active case finding in schools could have led to overestimates of transmission. A lesson from the southern hemisphere experience is that the difficulties in the early analysis of transmissibility could be overcome by consistent measures to ascertain the case incidence which, for the northern hemisphere, could be in place prior to the expected influenza surge in the winter season 2009-10.

Despite the limitations of this study, our results support the value of public health interventions that target the school age population. Governments considering mitigation strategies that involve major social disruption, such as school closure, need to weigh the relative costs and benefits of such action. Results from modelling suggest that school closure is effective if done early and universally, and if it leads to reduced contact [20]. Pre-emptive school closure is predicted to be more effective than reactive school closure. However, the effects of any school closure are estimated to be greater in settings where school transmission is high [22], such as Victoria, where school age children account for the majority of early transmission.

The likely impact of interventions and the cost-benefit profile critically depends on both the severity of disease and its transmissibility. In general, if an infectious disease is highly transmissible, outbreaks are much harder to contain, and interventions have a reduced impact on the final proportion of people infected. The relatively high reproduction ratio may be the reason why the pandemic influenza progressed in Victoria, and other Australian states and territories, despite public health interventions.

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The 2009 pandemic H1N1 influenza and indigenous populations of the Americas and the Pacific

G La Ruche (g.laruche@invs.sante.fr)[1], A Tarantola[1], P Barboza[1], L Vaillant[1], J Gueguen[1], M Gastellu-Etchegorry[1], for the epidemic intelligence team at InVS[1,2]

1. French Institute for Public Health Surveillance (Institut de Veille Sanitaire, InVS), St Maurice, France
2. The members of the epidemic intelligence team at InVS are listed at the end of the article

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There are few structured data available to assess the risks associated with pandemic influenza A(H1N1)v infection according to ethnic groups. In countries of the Americas and the Pacific where these data are available, the attack rates are higher in indigenous populations, who also appear to be at approximately three to six-fold higher risk of developing severe disease and of dying. These observations may be associated with documented risk factors for severe disease and death associated with pandemic H1N1 influenza infection (especially the generally higher prevalence of diabetes, obesity, asthma, chronic obstructive pulmonary disease and pregnancy in indigenous populations). More speculative factors include those associated with the risk of infection (e.g. family size, crowding and poverty), differences in access to health services and, perhaps, genetic factors. Whatever the causes, this increased vulnerability of indigenous populations justify specific immediate actions in the control of the current pandemic including primary prevention (intensified hygiene promotion, chemoprophylaxis and vaccination) and secondary prevention (improved access to services and early treatment following symptoms onset) of severe pandemic H1N1 influenza infection.

Introduction

Five months into its progression, the pandemic H1N1 influenza has affected countries on all continents. In Mexico, where the pandemic is likely to have started, the outbreak affected the central states first and then extended to other parts of the country. In the northern hemisphere (United States, Canada, Japan and the United Kingdom), imported cases were followed by sustained community transmission and epidemics in some countries. Importation in the southern hemisphere of cases from the northern hemisphere coincided with the beginning of the austral winter and influenza season, with a much more intense epidemic in several of these countries.

To date, hundreds of thousands of confirmed cases have been reported throughout the world, including over 4,735 confirmed and notified deaths [1]. The actual number of clinical cases is probably in the millions. Much progress has been made in documenting the pandemic and the causative virus. Some major risk factors for severe disease and death have been described. The role of pregnancy, asthma, chronic obstructive pulmonary disease and metabolic conditions (diabetes mellitus - a recognized risk factor for severe disease associated with seasonal flu - and obesity which has not been considered as a risk factor in previous pandemics or for seasonal influenza) in the occurrence of severe pandemic H1N1 influenza infection has been documented [2,3].

Initial data from several countries showed increased rates of hospitalisation and deaths associated with the current pandemic in indigenous populations [4-10]. We sought to estimate relative risks of hospitalisation and death associated with pandemic H1N1 influenza in indigenous populations of the Americas and the Pacific and discuss explanatory hypotheses.

Method

We use the term "indigenous populations" to refer to the ethnic groups related to the first recorded settlers in the various territories examined. In some countries such as Canada, Australia and New Zealand, the term "indigenous populations" has pertained to several, sometimes major, ethnic groups. Belonging to an indigenous population has been, in most data sources, self-declared.

Constant monitoring of international and national sources on public health alerts worldwide is ongoing at the Institut de Veille Sanitaire (InVS) [11]. Data on severe pandemic H1N1 influenza cases (hospitalised) and deaths by ethnicity were collected from countries or territories which published them on their official websites (institutes of public health and ministries of health). Data were also communicated by public health institutes in French territories of the Pacific during collaborative missions by InVS epidemiologists. The most recent population data, as available from official sources (governments, census organisations or indigenous populations health bureaus), were used as denominators to compute rates. Recent data on the prevalence for risk factors and relative risks in indigenous populations were obtained from official websites and scientific literature. Our search centred on diabetes, obesity (defined by the World Health Organization as a body mass index equal or more than 30 kg/m^2) and pregnancy. When available, the birth rate in indigenous populations was used to estimate the relative proportion of pregnant women.

In Canada, the ethnic distribution of cases was only available as percentages. The number of cases by ethnic group was obtained by multiplying this percentage by the total number of cases. The same was done for deaths.

Rates of pandemic H1N1 influenza hospitalised cases and deaths per 100,000 inhabitants were computed in indigenous populations and in the rest of the population using official case figures and population denominator data. Relative risks between indigenous and non-indigenous groups for severe disease and death associated with pandemic H1N1 influenza were estimated using rate ratios. Prevalences for various risk factors were compared between these groups using risk ratios.

Results

Pandemic H1N1 influenza data

The most structured and easily accessible nationwide data were available from Canada, Australia and New Zealand. Pandemic H1N1 influenza data collected from official sources and data which we calculated from available sources are shown in Table 1.

In the Americas

In Canada [12] and the United States (US) [13], indigenous populations represent less than 5% of the general population. They account, however, for a much bigger proportion of hospitalised cases of pandemic H1N1 influenza: 17.6% in Canada [4] and 17.5% in Arizona, US [5] (Table 1). These indigenous populations, especially Amerindians and Inuit, also seem at higher risk of death due to pandemic H1N1 influenza as compared to non-indigenous populations.

Computed rate ratios for hospitalisation between indigenous and non-indigenous populations varied from 4.1 (Arizona) to 5.4 (Canada) (Table 1). Computed rate ratios for death varied from 3.5 (Canada) to 4.3 (Arizona). The risk of severe disease and death, however, may be unevenly distributed among ethnic groups in a given country. For example, Inuit are estimated to have a seven-fold higher rate of hospital admissions and deaths associated with pandemic H1N1 influenza as compared to First Nations people (rates for hospitalisation and death being 158.5 versus 22.5 per 100,000 and 4.0 versus 0.7 per 100,000, respectively) [4]. According to Canadian sources, Inuit cases tend to be younger, are less often admitted to intensive care units and have fewer underlying diseases than First Nations people [4].

There were no specific data on pandemic H1N1 influenza hospitalised cases and deaths by ethnicity in Brazil. The majority of influenza viruses isolated from patients with severe upper respiratory infections for epidemiological weeks 29-33* inclusive were pandemic H1N1 influenza [6]. Other data show that during July and August 2009, the incidence of severe acute respiratory illness in Amerindians was 4.5 times higher than in the rest of the population of Brazil (Table 1) [6,7,14,15].

In the Pacific

Computed rate ratios for hospitalisation in indigenous versus non indigenous populations varied from 3.0 (New Zealand) [9] to 7.7 (Australia) [8]. Computed rate ratios for death varied from 5.1 (Australia [8]) to 5.3 (New Caledonia [10]; JP Grangeon, personal communication, 27 September 2009) (Table 1). No medical data are routinely collected by ethnicity in all French territories. There are however indirect indications of greater vulnerability to pandemic H1N1 influenza in indigenous populations in the three French territories of the Pacific, where attack rates of influenza-like illness (ILI) were particularly high.

The percentage of Polynesians in French Polynesia (population: 270,000) is estimated at approximately 83% [16]. During the austral winter epidemic of 2009, the ILI attack rate was estimated by French Polynesia health authorities at approximately 13%, with some variation between the archipelagos (up to 20% in Moorea Island and Austral Islands).

In Wallis (pop. 9,200) and Futuna (pop. 4,200), where most (95%) inhabitants are of Polynesian origin [17], the attack rate for ILI was estimated by local public health authorities at 28% in Wallis and 38% in Futuna.

In New Caledonia (pop. 249,000), the percentage of indigenous Oceanians is estimated at approximately 57% (including Melanesians 44.1%, Wallisians 9.0%, Tahitians 2.6% and ni-Vanuatu 1.1%) [18]. Public health authorities in New Caledonia have estimated the attack rate for ILI during the austral winter wave of pandemic H1N1 influenza at about 18%. According to these authorities, higher attack rates were observed among Oceanian populations. In Nouméa, New Caledonia, among children hospitalised with pandemic H1N1 influenza between 27 July and 13 September 2009 with available data on ethnicity (n=62), 74% were of Melanesian origin, 10% of Wallisian origin and 8% of European origin (A Facchin, personal communication, 19 September 2009). According to local practitioners, the percentage of children of Oceanian origin seemed high as compared to foreseeable bed occupancy (JP Grangeon, personal communication, 27 September 2009).

Health status of indigenous populations

Almost all indigenous populations considered in this paper have greater prevalence of diabetes, obesity and chronic respiratory diseases such as asthma and chronic obstructive pulmonary disease [19-29] (Table 2).

Available data also show that fertility rates are higher in indigenous populations than in the rest of the population. In Canada, the 1996-2001 birth rate in Inuit women was 3.4, while the rates in First Nations people, Métis and all women in Canada were 2.9, 2.2 and 1.5, respectively [30]. In Australia, the average number of live births in indigenous women and all Australian women in 2003 was estimated to be 2.2 and 1.8, respectively [31]. In New Zealand, birth rates were also higher in Māori (2.59) and Pacific peoples (2.94) as compared to population of European descent (1.74) [32]. Indicators of fertility, however, seemed comparable between Native Americans and the rest of the population in Arizona. Tobacco use tends to be higher in indigenous populations in most, but not all, countries [20,26,27,33]. Furthermore, although tobacco seems linked with both risk of infection and severity of illness due to seasonal influenza [34], such an association has not been systematically found [35] and an independent link between tobacco use and severe pandemic H1N1 influenza infection and death has not been established to our knowledge. It is therefore not considered in our analysis.

Discussion

Indigenous populations were hard hit by the 1918-19 influenza pandemic: between 1 October 1918 and 30 June 1919, a total of 78,177 influenza cases and 6,632 deaths were reported in indigenous people of North America (computed case-fatality rate (CFR) of 8.5% versus 2.5% in the general population) [36]. The highest CFR was reported in Utah indigenous peoples (15.9%).

Table 1

Pandemic H1N1 influenza-confirmed cases, deaths and rates per 100,000 inhabitants, by ethnic group, Americas and the Pacific Region, 2009

Country or area Pandemic H1N1 influenza data sources	Population in million inhabitants (% of total population)	Data until	Hospitalisation					Deaths				
			Number (%) [1]		Rates (per 100,000)			Number (%) [1]		Rates (per 100,000)		
			Indigenous	Non-indigenous	Indigenous (a)	Non-indigenous (b)	Rate ratios (a/b)	Indigenous	Non-indigenous	Indigenous (c)	Non-indigenous (d)	Rate ratios (c/d)
Americas												
Canada [4]	31.60											
First Nations, Inuit and Métis	1.15 (3.64%)	26/09/2009	260 (17.60)	1,219 (82.40)	22.61	4	5.7	9 (11.50)	69 (88.50)	0.78	0.23	3.4
Arizona (United States) [5]	6.50											
American Indians	0.32 (4.90%)	16/09/2009	52 (17.51)	245 (82.49)	16.3	4	4.1	4 (18.18)	18 (81.82)	1.3	0.3	4.3
Brazil [2] [6,7]	191.80											
Amerindians	0.46 (0.24%)	15/07 – 15/08/09	328 (1.06)	30,526 (98.93)	71	16	4.4	NA	NA	NA	NA	NA
Pacific												
Australia [8]	20.70											
Aborigines and Torres Straits Islanders	0.52 (2.50%)	09/10/2009	796 (16.43)	4,048 (83.57)	153	20	7.7	21 (11.48)	162 (88.52)	4.1	0.8	5.1
New Zealand [9]	4.33											
Māori	0.63 (14.60%)	23/09/2009	NA	NA	43.0	14.1	3.0	NA	NA	NA	NA	NA
Pacific peoples	0.64 (14.70%)		NA	NA	94.2		6.7	NA	NA	NA	NA	NA
New Caledonia [10]	0.25											
Indigenous Oceanians [3]	0.14 (56.80%)	07/09/2009	NA	NA	NA	NA	NA	7	1	4.93	0.93	5.3

1 Percentage of total cases for the country or area.
2 Acute severe respiratory illness in Amerindians and others used as proxy for pandemic H1N1 influenza.
3 Includes Melanesians, Polynesians, Wallisians and ni-Vanuatu.
NA: not available.

Table 2

Estimated risk ratios of main risk factors for severe pandemic H1N1 influenza cases in Indigenous populations as compared to non-Indigenous populations in some countries in the Americas and the Pacific Region

Country or area	Risk ratio for DM	Risk ratio for obesity (BMI of at least 30)	Risk ratio for asthma	Risk ratio for COPD or emphysema
Americas				
Canada				
First Nations	7.1 [1]	2.4 [2]	2.4 [1]	2.5 [1]
United States				
American Indians and Alaska Natives	1.7 [3]	1.5 [4]	2.1 [4]	2.0 [4]
Brazil				

Amerindians	NA	NA	NA	NA
Pacific				
Australia				
Aborigines and Torres Straits Islanders	5.6 [5]	1.9 [6]	2.7 [7]	5.0 [7]
New Zealand				
Māori	1.8 [8]	1.9 [8]	1.3 [8]	2.0 [8]
Pacific peoples	3.2 [8]	2.8 [8]	0.8 [8]	0.9 [8]
New Caledonia				
Melanesians	1.0 [9]	2.7 [10]	NA	NA
Polynesians	1.8 [9]	3.0 [10]	NA	NA

[1] Age-adjusted hospital separation rates (2000): First Nations compared to general population in West Canada (British Columbia, Alberta, Saskatchewan and Manitoba) [19].
[2] Prevalence among First Nations living on-reserve (2002-03) compared to total general Canadian population living off-reserve (2003), 18 years or older [20].
[3] Prevalence among American Indians and Alaska Natives who receive care from the Indian Health Service compared to general population, 20 years or older, 2002 [21].
[4] Age-adjusted prevalence among American Indians and Alaska Natives adults (18 years or older), 2004-2006 [22] compared to prevalence among general American adult (18 years or older) population in 2005 for obesity [23] and emphysema [24], in 2004-2006 for asthma [25].
[5] Hospitalisations of Indigenous persons compared to other Australians for a principal diagnosis of diabetes for the two-year period July 2002 to June 2004 for Queensland, Western Australia, South Australia and the Northern Territory [26].
[6] Age-adjusted prevalence among Indigenous Australians compared to other Australians, 18 years or older (2004-2005) [26].
[7] Age-adjusted ambulatory care sensitive hospital admissions rate (2002-04), Indigenous compared to non-Indigenous [26].
[8] Age-adjusted prevalence among Māori vs. non-Māori and Pacific peoples vs. non-Pacific peoples, 15 years or older (45 years or older for COPD), 2006-2007 [27].
[9] Age-adjusted prevalence among Melanesians and Polynesians compared to Europeans, aged 30-59 years, 1992-1994 [28].
[10] Prevalence in non-diabetic adults among Melanesians and Polynesians compared to Europeans, aged 30-59 years, 1992-1994 [29].
DM: diabetes mellitus (predominantly, but not exclusively, of type 2). BMI: body mass index. COPD: chronic obstructive pulmonary disease (defined by emphysema or chronic bronchitis). NA: not available.

Similarly in New Zealand, the mortality rate in Māori was seven times greater than in Europeans [37]. At present, indigenous populations in Canada and the US [19,38] are also more severely affected by seasonal influenza than the rest of the population.

Although information available to date does not permit to identify all determinants and causative mechanisms, these data show that indigenous populations seem to be at higher risk of severe pandemic H1N1 influenza infection in several countries of the Americas and the Pacific. The occurrence of more severe forms of the infection could be explained by the following hypotheses: much higher prevalence of identified risk factors for severe disease and death, differences in approaches to health, difficulties in accessing health care and increased genetic susceptibility. The impact of a close-knit community lifestyle on viral transmission dynamics is a plausible risk factor for infection, as well. High attack rates during a short period (around three weeks), especially in Wallis and Futuna and in some islands of French Polynesia deserve notice. In these cases, the small size of these islands may have played a role.

This study and data comparisons have several limitations. The first is that the analysis bore on data collected from multiple sources. Some rates were computed by the authors using approximate population numbers, in other cases the situation was well-documented but only for a limited part of a territory (such as Arizona instead of the entire US). Despite the fact that several countries have a sizeable indigenous population, only few have made surveillance data by ethnicity available on the web. This may be due, to a large extent, to the fact that many countries do not collect statistical data by ethnicity.

Furthermore, data pertain to small numbers of cases and must therefore be viewed with great caution, especially when using them for comparison between ethnic groups. There may also be underreporting of pandemic H1N1 influenza cases because of low testing rates during intense epidemic. Underreporting, however, is probably lower for hospitalised cases, especially in intensive care units [39], and deaths which are the focus of this analysis.

Differences in accessing health care may lead to various reporting biases. Special programmes and attention directed toward indigenous minorities may lead to differences in clinical management such as more systematic hospitalisation. Usually, however, difficulty in access to health care has the opposite effect resulting in an underestimation of severe forms.

There are no published data by both ethnicity and age group. The fact that there are more cases among indigenous populations in the countries examined could be partly explained by higher birth rates in indigenous compared to non-indigenous populations. Although the pandemic influenza A(H1N1)v virus targets younger age groups, severe cases, however, are found mainly among adults [2]. As older populations seem somewhat protected [40,41], a younger population age structure may overestimate the populations' intrinsic susceptibility to this virus, but probably not to severe or lethal forms, which are the object of this article.

Data on incidences by socio-economic groups were also lacking. It is known, however, that First Nations people in Canada, Australian Aborigines and Māori and Pacific peoples in New Zealand, to name a few examples, are overrepresented among the poor.

The absence of fine distinction between ethnic groups in a given country could lead to over- or underestimation for certain ethnic subgroups if well-identified vulnerabilities are documented in larger indigenous populations and extrapolated to all. Data are lacking, for instance, to determine with accuracy the exact risk in Aboriginal Australians and Torres Straits Islanders, respectively. Pacific populations of various origin probably do not share the same level of risk. Finally, self-declaration of "indigenous" ethnic status (e.g. Māori) by persons of mixed ancestry could lead to classification bias and underestimate risks in persons fully descended from these ethnic groups.

Conclusions

Means of prevention and case management for acute and chronic illness have progressed greatly since the influenza pandemic of 1918. Health inequities, however, remain rife between indigenous populations of the Americas and the Pacific and the rest of the populations in the countries considered. The role of access to care and economic status deserves further study. In countries which have data by ethnic group, baseline prevalence is higher for diabetes mellitus, obesity, asthma, chronic obstructive pulmonary disease, and greater numbers of pregnancies at an early age in indigenous populations. These factors are known to be closely associated with cases of severe illness and death due to pandemic H1N1 influenza infection. The available data does not allow for fine distinctions and it is not possible to precisely quantify risks by individual ethnic group within the indigenous populations of most countries. In a short-term perspective, the precise risk quantification, however, does not have any practical implications for the response to the pandemic and there is no public health need to distinguish these groups further at this stage. All indigenous populations described here should be considered at greater risk than the rest of the population, for a host of reasons. This observation does not preclude a potentially higher incidence of severe forms in other, non-indigenous population subgroups. It also does not mean that diabetes, obesity, asthma and chronic obstructive pulmonary disease should not be controlled in all populations.

Further research is needed to describe the impact of the 2009 H1N1 influenza pandemic in indigenous populations and document the determinants of severe forms. In the meantime and when feasible, Indigenous populations should be the focus of special, targeted and culturally acceptable interventions against the 2009 H1N1 influenza pandemic, such as implemented in Australia [42] and US [43]. These need to include primary prevention (intensified hygiene promotion, chemoprophylaxis and vaccination) and secondary prevention (improved access to services and early treatment following symptoms onset) of severe pandemic H1N1 influenza infection.

These conclusions are relevant to European countries for at least two reasons. Firstly, indigenous populations live in territories linked administratively to the European Union. France is the EU country with the largest number of citizens of indigenous origin, in the Americas (around 4,500 Amerindians in French Guyana [44]) and in the Pacific (224,000 Polynesians in Polynesia [16]; 142,000 Melanesians and Polynesians in New Caledonia [18]; 13,000 Wallisians in Wallis and Futuna [17]). There is also a sizeable indigenous (Inuit) population of EU citizens in Greenland (estimated at around 50,000 inhabitants) [45]. Secondly, further research on risk factors in indigenous populations worldwide may help in identifying and understanding mechanisms and risk factors for severe diseases. These could be relevant to other population subgroups, such as those living in poverty or crowded settings, in cities of Europe and elsewhere.

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The epidemic intelligence team includes (in alphabetical order):

F Aït el-Belghiti, P Barboza, C Baudon, L Cherie-Challine, S Cohuet, M-A Degail, D Dejour-Salamanca, M Gastellu-Etchegorry, V Gauthier, J Gueguen, G La Ruche, A Rachas, A Tarantola, L Vaillant.

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