

H1N1 swine origin influenza infection in the United States and Europe in 2009 may be similar to H1N1 seasonal influenza infection in two Australian states in 2007 and 2008

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Background The population-based impact of infection with swine origin influenza A (H1N1) virus infection was not clear in the early days of the epidemic towards the end of May 2009. Australia had seven confirmed cases by 22 May 2009. We aimed to compare available data on swine origin influenza A (H1N1) virus infection overseas with seasonal influenza A (H1N1) virus infection in Australia to assist with forward planning.

Methods Data on infection with seasonal influenza A (H1N1) virus in patients recruited through sentinel general practices in Victoria and Western Australia in 2007 and 2008 were compared with early publications on infection with swine origin influenza A (H1N1) virus in the United States and Europe.

Results Influenza A (H1N1) virus infection was predominantly a disease of younger people, regardless of whether the virus was of swine or human origin. The median age of infection with swine origin virus was 20 years in the United States and 22 years in Spain, while the median age of infection with human origin virus was 18 years in Western Australia and 23 years in Victoria.

Conclusions The median age of infection with influenza A (H1N1) virus was around 20 ± 3 years, independent of the origin of the H1N1 virus but a higher proportion of swine origin influenza infections occurred in people aged 10–18 years. This is at least partially explained by biased sampling among surveillance patients, although it may also reflect a different infection pattern.

Keywords Seasonal H1N1 influenza, swine origin influenza.

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Introduction

Australia recorded its first case of swine origin influenza A (H1N1) virus infection on 7 May 2009 in a traveller returned from the United States (US) but by 27 May had recorded 61 confirmed cases. At the same time the World Health Organization (WHO) had documented almost 13 000 confirmed cases in 46 countries (<http://www.who.int/csr/disease/swineflu/en/index.html>). At that time spread within the community has been confined to a number of countries including Mexico, USA, Japan and Canada. However, it is anticipated community spread will occur in other countries as this virus appears to be at least as transmissible as seasonal influenza.¹ Towards the end of May it was not yet clear as to whether the rate of increase in cases in Mexico and the United States was

declining and, if so, whether this was a result of expected seasonal influences. Attention was moving to the southern hemisphere where influenza viruses circulate in the temperate southern climates between May and September.

In order to anticipate the type of preparations that might be needed in Australia in the event of circulation of H1N1 swine origin influenza virus in the autumn and winter months of 2009, we compared early available data on infection with H1N1 swine origin influenza with H1N1 seasonal influenza in the preceding two Australian influenza seasons. We used sentinel surveillance data for the primary comparisons, because most of the swine origin influenza infections have occurred in non-hospitalized patients and it is these patients who are captured by general practice sentinel surveillance. However, we also used data from diagnostic

testing to further explore the comparisons made from sentinel surveillance data.

Methods

We compared patients recruited through sentinel general practices in Victoria and Western Australia (WA) in 2007 and 2008 with the first published data on patients with H1N1 swine origin infection in the United States,² Spain³ and the United Kingdom.⁴

The sentinel surveillance systems in Victoria and WA have been described in detail elsewhere^{5–6} and consist of sentinel general practices throughout each state reporting each week on the proportion of patients seen with an influenza-like illness (ILI) defined as fever (documented or reported) with cough and fatigue/malaise.⁷ Combined nose/throat swabs are collected from all patients (with the exception of children under 5 years in WA who have nasal swabs only) and are tested for influenza viruses at the Victorian Infectious Diseases Reference Laboratory (VIDRL) in Victoria and at PathWest Laboratory Medicine WA (PathWest) in WA by in-house polymerase chain reaction (PCR) assays directed at matrix gene sequences of influenza A and B. Any sample positive for influenza virus A is sub-typed as influenza A (H1N1) or influenza A (H3N2) using specific PCR assays directed at haemagglutinin gene sequences. All samples in WA also undergo standard cell culture and positive culture samples are referred to the World Health Organization Collaborating Centre for Influenza Reference and Research in Melbourne, Australia, where the isolates are confirmed and antigenically typed and sub-typed.

Sentinel general practitioners are asked to record the symptoms of patients from whom a nose/throat swab is taken. In addition, both laboratories, which are designated as National Influenza Centres by the WHO, perform routine diagnostic tests for influenza viruses, although the referral patterns are different in the two states. Data are summarized weekly and, in Victoria, recorded in a purpose-designed database (SL Digital). Data in WA are stored in spreadsheet format. Data were extracted from routine databases in both states and analysed in Excel (Microsoft) or STATA (STATA version 10; StataCorp, College Station, TX, USA). Differences in proportions were tested using Fisher's exact test.

Results

The influenza seasons of 2007 and 2008 were assessed as higher than normal seasonal activity in Australia, particularly in 2007 (Australian Influenza Report. Report No. 12, available at (<http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm>) (Grant K, Carville K, Fielding J. High proportion of influenza B characterises

the 2008 influenza season in Victoria. unpublished data).⁶ The number of surveillance samples from which influenza viruses were detected in 2007 and 2008 respectively was 223 and 116 in Victoria and 192 and 247 in WA. The type and subtype distribution of circulating influenza viruses in both states is shown by week in Figure 1. H1N1 contributed 124 (16%) of detected circulating viruses from sentinel patients across the 2 years.

We compared the reported data on the first 642 cases of swine origin influenza H1N1 infection in the United States² in 2009 with data on seasonal H1N1 infection in community surveillance samples in Victoria and WA in the 2007 and 2008 influenza seasons (Table 1). The median age for infection with swine origin influenza A (H1N1) virus was 20 years (range 0–81) in the United States, similar to the seasonal influenza A (H1N1) virus median age of 18 years (range 1–63) in WA and 23 years (range 3–75) in Victoria. The median age of infection for influenza B virus, 23 years (range 0–74) in Victoria and 19 years (0–87) in WA, was similar to the median age for H1N1 virus infection, but younger than the median age for influenza A (H3N2) infection [30 years (range 1–96) in Victoria and 31 years (range 2–88) in WA].

More detailed comparison of the age group distribution for H1N1 infections showed that, despite the similarity in the median age of infection, the proportion of positive samples peaked in the 19–50 year age group in the seasonal H1N1 cases, but in the 10–18 year group for the swine origin influenza A cases. The age distribution of the WA patients more closely resembled the US data than the Victorian patients (Table 1). There was a statistically significant difference in the proportion of patients aged 10–18 years in whom influenza A (H1N1) virus was detected in the United States compared with data from Victoria and WA combined (40% versus 24%, $P = 0.001$) but the comparison of the US and WA data was not significant for this age group (40% versus 32%, $P = 0.25$). This probably reflects differences in the age distribution of patients sampled in the two states, as the Victorian patients had a higher median age than the WA patients.

Fever and cough, recorded as part of the case definition for ILI in the Australian sentinel surveillance systems, occurred with similarly high frequencies in patients infected with seasonal influenza as in patients infected with swine origin influenza in the United States (Table 1). Fever was documented in 94% of the first 65 cases reported from the United Kingdom.⁴ In the Spanish case series of 98 patients, the most frequently reported symptoms were fever (96%) and cough (95%).³ Although based on very small numbers, a similar proportion of patients (~16%) were vaccinated in the United States and Victoria (Table 1), while the vaccination rate in WA (~7%) was more similar to that in Spain where 5/52 (10%) of cases were vaccinated.³

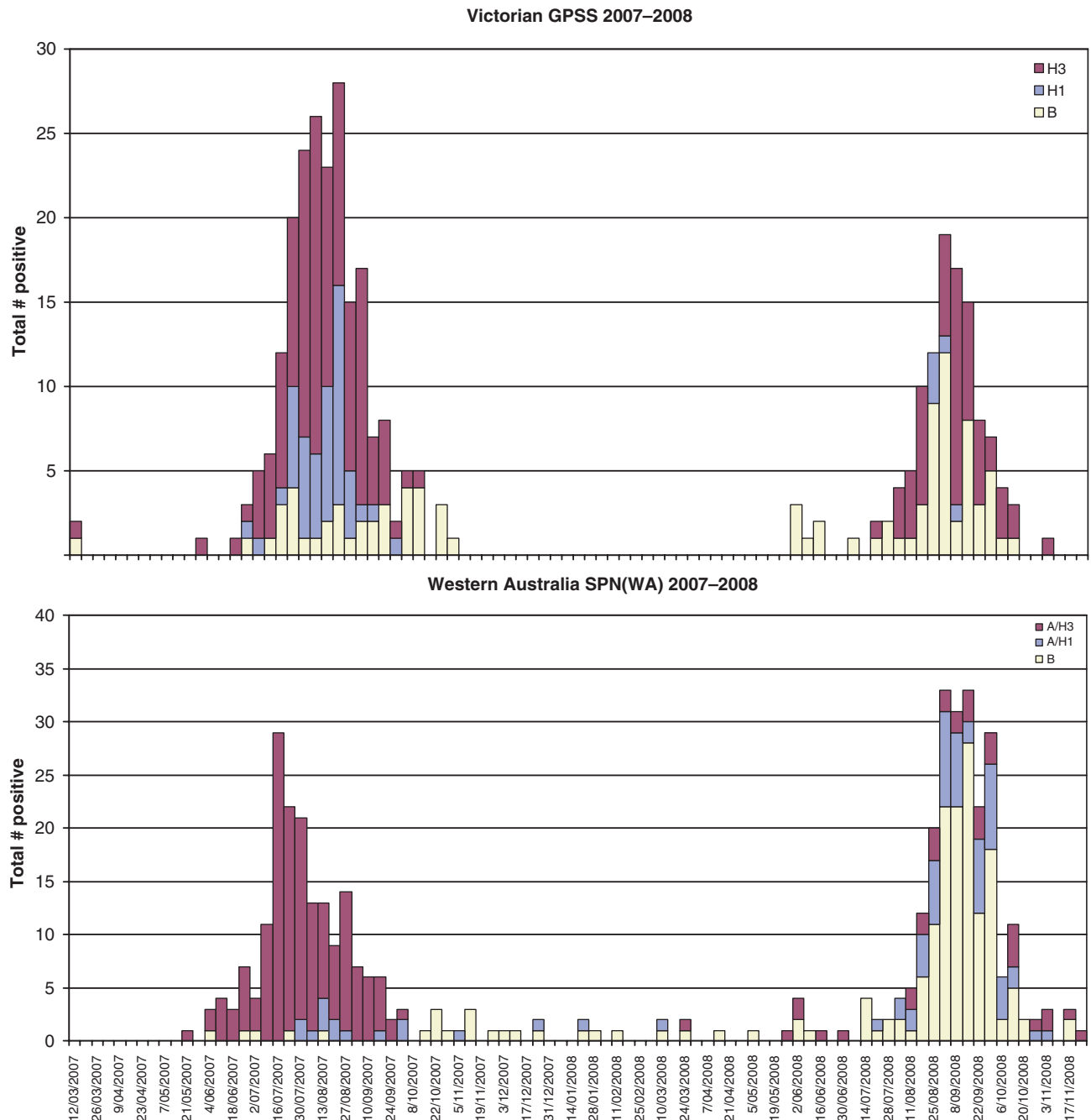


Figure 1. Weekly influenza detections by type and subtype in Victorian and Western Australian sentinel surveillance patients, 2007 and 2008.

We also examined the median age of patients with influenza who were tested for routine diagnostic purposes, that is, not part of sentinel surveillance. These patients were more diverse with patients tested routinely likely to be younger in WA (Table 2). In Victoria, but not in WA, many samples were referred from major adult teaching hospitals. The median age of the patients referred from hospitals with influenza was 37 years (range 0–96) compared with 28 years (range 0–96) for the Victorian commu-

nity surveillance patients. However, we saw in Victoria a similar pattern of younger median ages of patients with influenza A (H1N1) virus (29 years) and influenza B virus infections (34 years), compared with the median age for patients with influenza A (H3N2) infection of 37 years.

The median age of WA patients positive for influenza following routine testing was lower than that of the sentinel general practice patients (20 years versus 25 years), reflecting the inclusion of more paediatric patients in the routine samples

Patient details	Patients infected with swine origin influenza A(H1N1) virus, United States 2009 ²	Patients from general practice sentinel surveillance infected with seasonal influenza A(H1N1) virus, 2007 and 2008	
		Victoria	Western Australia
Number	642	52	72
Male sex (%)	302/592 (51)	31/52 (60)	28/72 (39)
Median age (years)	20	23	18
Range (years)	3 months to 81 years	3–75 years	1–63 years
Age group – no./total no. (%)			
0–23 months	14/532 (3)	0/52 (0)	1/72 (1)
2–4 years	27/532 (5)	2/52 (4)	5/72 (7)
5–9 years	65/532 (12)	3/52 (6)	8/72 (11)
10–18 years	212/532 (40)	7/52 (13)	23/72 (32)
19–50 years	187/532 (35)	35/52 (67)	32/72 (44)
>50 years	27/532 (5)	6/52 (12)	3/72 (4)
Fever	371/394 (94)	51/52 (98)	47/47 (100)
Cough	365/397 (92)	48/52 (92)	45/47 (96)
Vaccinated during current season	3/19 (16)	9/52 (17)	4/54 (7)

Table 1. Comparison of patients infected with swine origin influenza A(H1N1) virus, United States, 2009 with patients from general practice sentinel surveillance infected with seasonal influenza A(H1N1) virus, Victoria and Western Australia, 2007 and 2008

Patient source	All tested	Influenza virus detected	Influenza A (H1N1)	Influenza A (H3N2)	Influenza B
Victorian surveillance					
Number	881	339	52	169	102
Median age, years (range)	33 (0–96)	28 (0–96)	23 (3–75)	30 (1–96)	23 (0–74)
Victorian diagnostic					
Number	9536	822	124	413	193
Median age, years (range)	41 (0–102)	35 (0–97)	29 (0–83)	37 (0–97)	34 (0–96)
WA surveillance					
Number	1365	439	72	199	168
Median age, years (range)	29 (0–91)	25 (0–87)	18 (1–63)	31 (2–88)	19 (0–87)
WA diagnostic					
Number	7623	795	130	452	211
Median age, years (range)	Not available	20 (0–95)	13 (0–78)	22 (0–95)	20 (0–85)

Table 2. Age of testing for, and infection with, influenza viruses in general practice sentinel surveillance and diagnostic patients, Victoria and Western Australia, 2007 and 2008

from WA. Again, the median age for patients with influenza A (H1N1) virus infection was lower than for patients with influenza A (H3N2) virus infection (13 years versus 22 years). The median age for influenza B infection was 20 years.

Discussion

We have shown that, in the influenza seasons of 2007 and 2008, the median age of seasonal influenza A (H1N1) virus infection for community surveillance patients was 23 years

in Victoria and 18 years in WA, very similar to the median age of patients with H1N1 swine origin influenza virus infection in the United States of 20 years² and Spain of 22 years.³ The age distribution of indigenous cases in the UK was reported as being predominantly in the 10–19 year age group.⁴ This suggests that the reported younger age of patients with H1N1 swine origin influenza compared with the usual seasonal influenza may simply reflect H1N1 virus infection, rather than any other biological differences. This distinction is important in predicting the likely impact of

H1N1 swine origin influenza compared with the current seasonal H1N1 viruses.

However, as the median age difference may be due to differences in the age groups sampled in the different locations, or because we are comparing surveillance samples in Australia with active case finding overseas, we compared the median age of surveillance patients with the median age of patients tested routinely. Surveillance data were used for the primary comparative analysis because we believed patients tested through sentinel surveillance were most like patients sampled for H1N1 swine origin influenza, that is, patients in the community with mild illnesses who may not have been tested in other years. We do know, however, that the age distribution of patients recruited through sentinel surveillance is biased by the willingness of general practitioners to take a combined nose/throat swab. Almost three-quarters of sentinel patients were aged 20–60 years in Victoria, with younger aged patients under-represented in patients from whom a swab was taken (Grant K, Carville K, Fielding J. High proportion of influenza B characterises the 2008 influenza season in Victoria. unpublished data).

Younger aged patients were better represented in WA in 2008 when the Western Australian Influenza Vaccine Effectiveness (WAIVE) study was implemented to assess influenza vaccine effectiveness in children aged 6–59 months (H. Kelly *et al.* Assessing the protective effect of influenza vaccine against laboratory confirmed influenza in healthy children aged 6–59 months presenting to general practice, the emergency department or admitted to hospital: the first year of the WAIVE study. Unpublished data). Indeed, the median age of all influenza-positive surveillance patients in WA in 2007 was 32 years, similar to the corresponding median age of 28 years in Victoria in 2007 and 2008, but dropped to 18 years in WA in 2008 when the WAIVE study commenced. In both years, and in both states, the H1N1 cases had a lower median age than the H3N2 cases (data not shown). Although it is probable that patients sampled for influenza in the Victorian sentinel surveillance scheme in 2007 and 2008, and in the WA scheme in 2007, included fewer children than the patients tested for H1N1 swine origin influenza overseas; median ages of patients were nonetheless similar. Moreover the median age of the first 30 cases hospitalized in California with H1N1 swine origin influenza, reported as 27.5 years (range 0–89),⁸ was again similar to the median age (29 years, range 0–83) of 124 patients referred from hospitals in Victoria and testing positive for H1N1 seasonal influenza.

We have also consistently shown that influenza A H1N1 is found in a younger population than influenza A H3N2, which may partly explain the observation that H3N2 infections are generally associated with more severe outcomes.⁹

Investigators in both the United States² and Spain³ speculated that the median age of H1N1 swine origin influenza

virus infection reflected the age of those most likely to travel and that many infections could be traced to recent travel, at least in the Spanish patients. However, our data suggest that the lower median age of H1N1 influenza viruses may be an inherent characteristic of human infections that is not limited to H1N1 swine origin influenza virus infection. In fact the biggest difference in the age distribution was noted in the 10–18 year old age group in Victoria, an age group perhaps less likely to travel than older people.

It has been postulated that the observed younger age of infection may signal a virus with pandemic potential.¹⁰ We have shown, at least outside Mexico, this may not be a specific feature of H1N1 swine origin influenza infection. Furthermore, the frequency of fever and cough was similar for seasonal H1N1 in Victoria and WA and for H1N1 swine origin influenza virus. We did not collect data on the more serious manifestations of seasonal H1N1 influenza infection, and clinical data from Mexico suggest that H1N1 swine origin influenza virus has a potentially more serious outcome, and higher secondary attack rates than seasonal influenza.¹

In conclusion, there is substantial evidence that the younger age distribution of H1N1 swine origin influenza virus compared with seasonal influenza, which is due to a variable mixture of influenza A (H1N1), influenza A (H3N2) and influenza B viruses, may be partially explained by the inherent characteristics of all influenza A (H1N1) viruses. The reported younger median age of infection should not necessarily be interpreted as an indicator of the pandemic potential of this virus.

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