

PANDEMIC H1N1 INFLUENZA SURVEILLANCE IN VICTORIA, AUSTRALIA, APRIL – SEPTEMBER, 2009

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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.

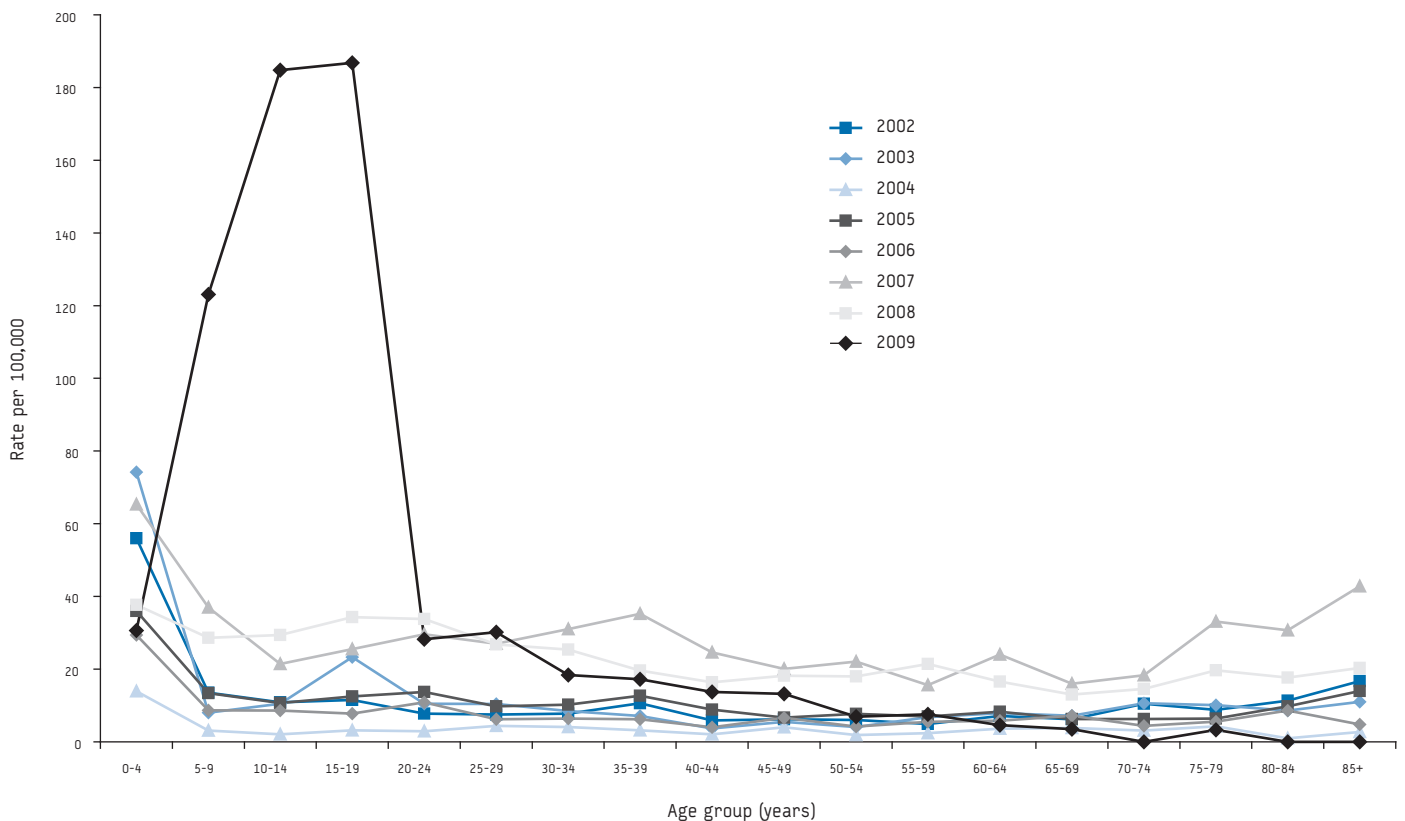
Results

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.

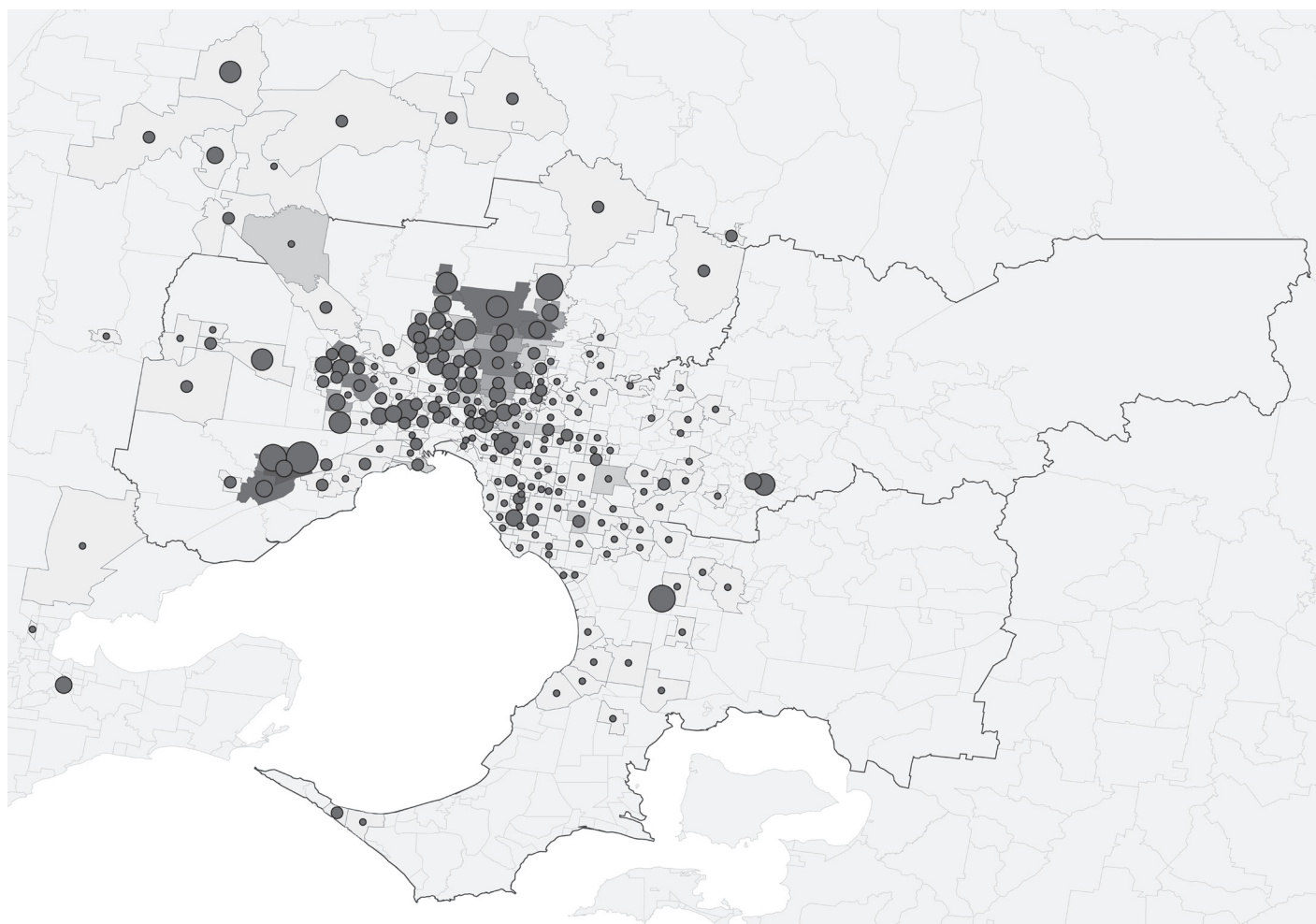
Data on contacts of confirmed cases were available for 908 (93%) of the 977 cases of pandemic H1N1 influenza. Details were available for 5,807 contacts with only 70 (7%) who could not be contacted. The number of total contacts per case ranged from 0 to 129 (median=4), and the number of household contacts 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].

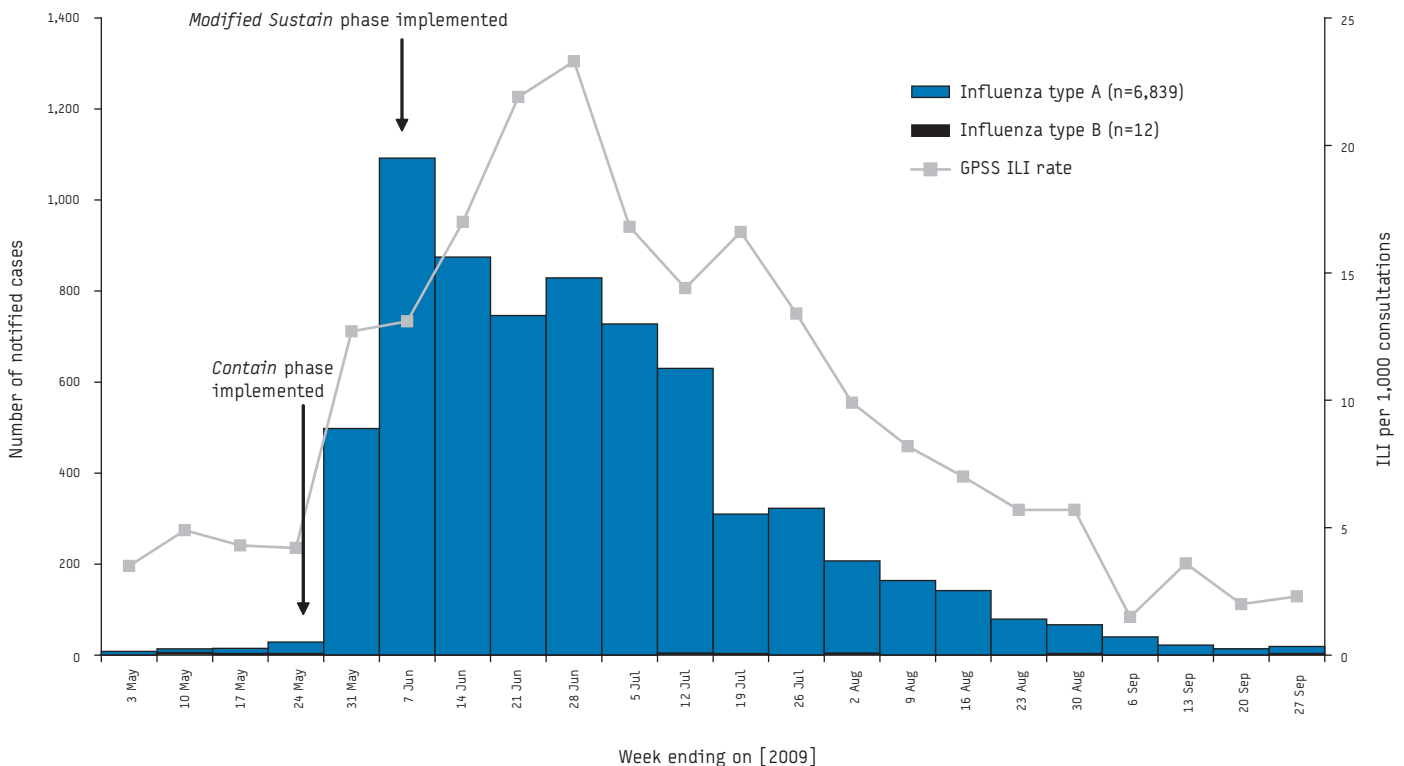
A total of 6,895 cases of laboratory-confirmed influenza, of which 3,058 were confirmed influenza A(H1N1)v, were notified from 1 January until 27 September. This was more than four times the previous highest annual total of 1,591 cases in 2007. The peak rate of ILI measured by the GPSS in 2009 was relatively 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

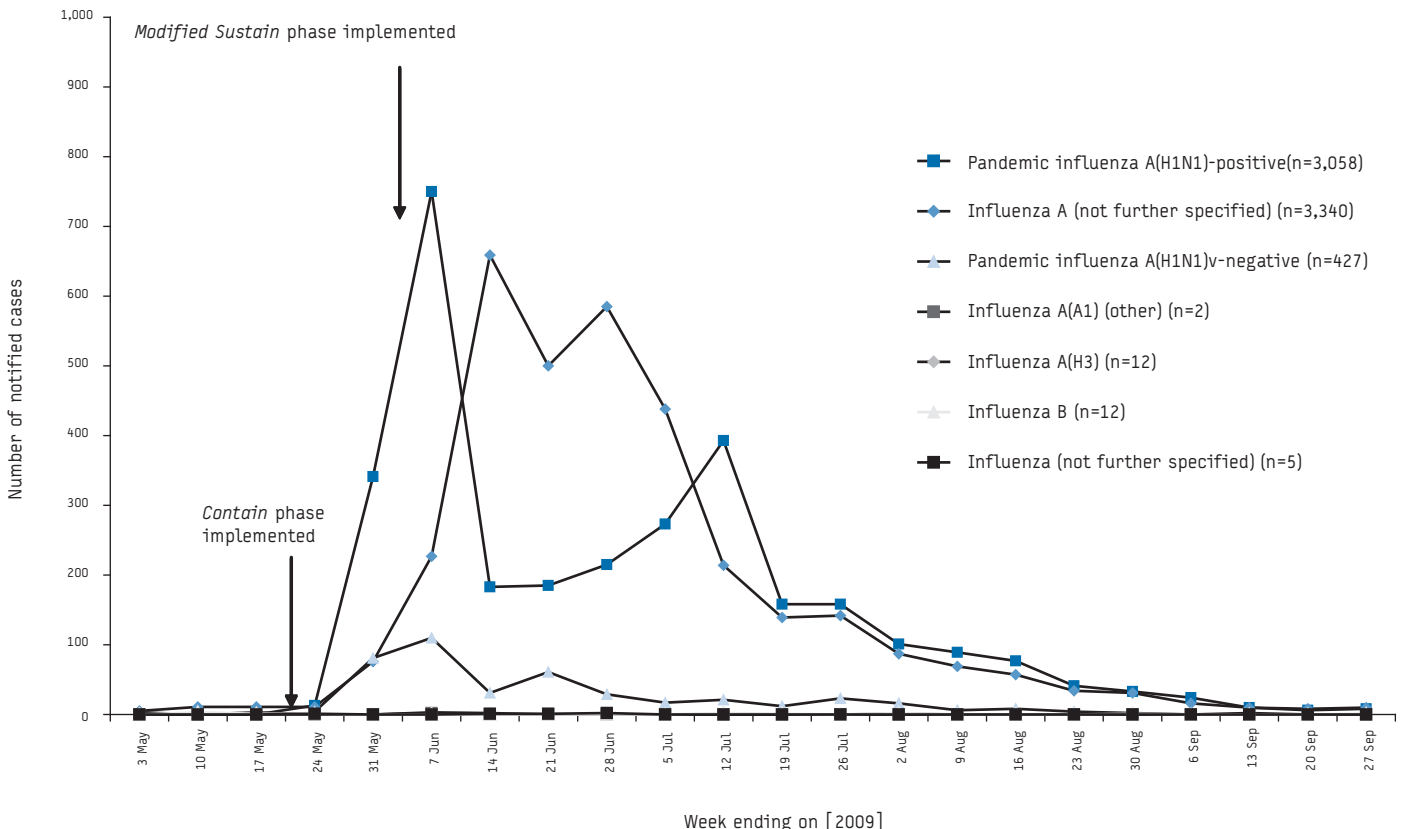
similar period investigators in New Zealand also reported sequential replacement of seasonal influenza strains throughout the pandemic [14].

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

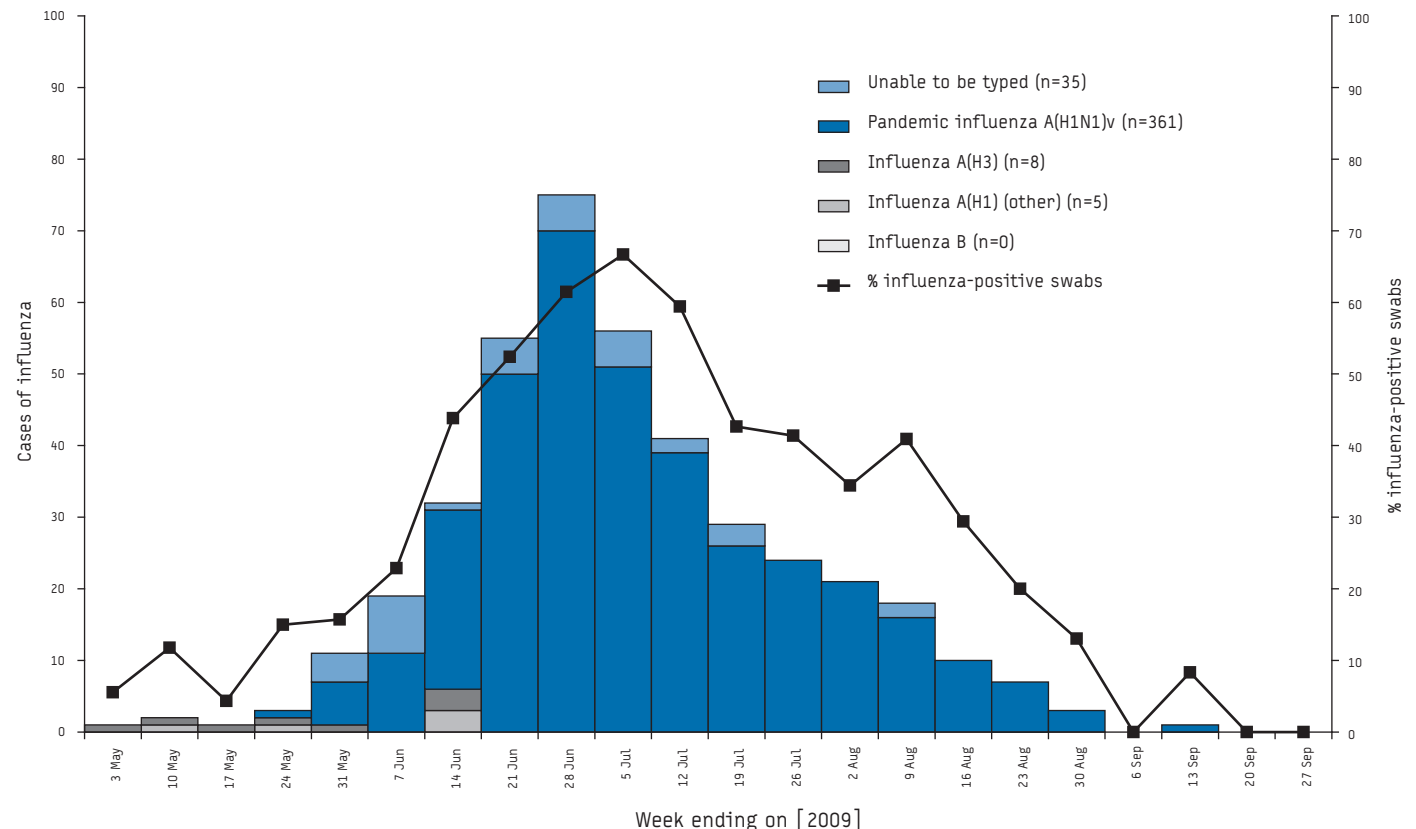
patients in the US had dropped from 20 years to 13 years by the time approximately 10,000 cases had been notified (Lyn Finelli, US Centers for Disease Control and Prevention, personal communication), which we suggest also reflects amplification of the pandemic in school-aged children and intense follow-up 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



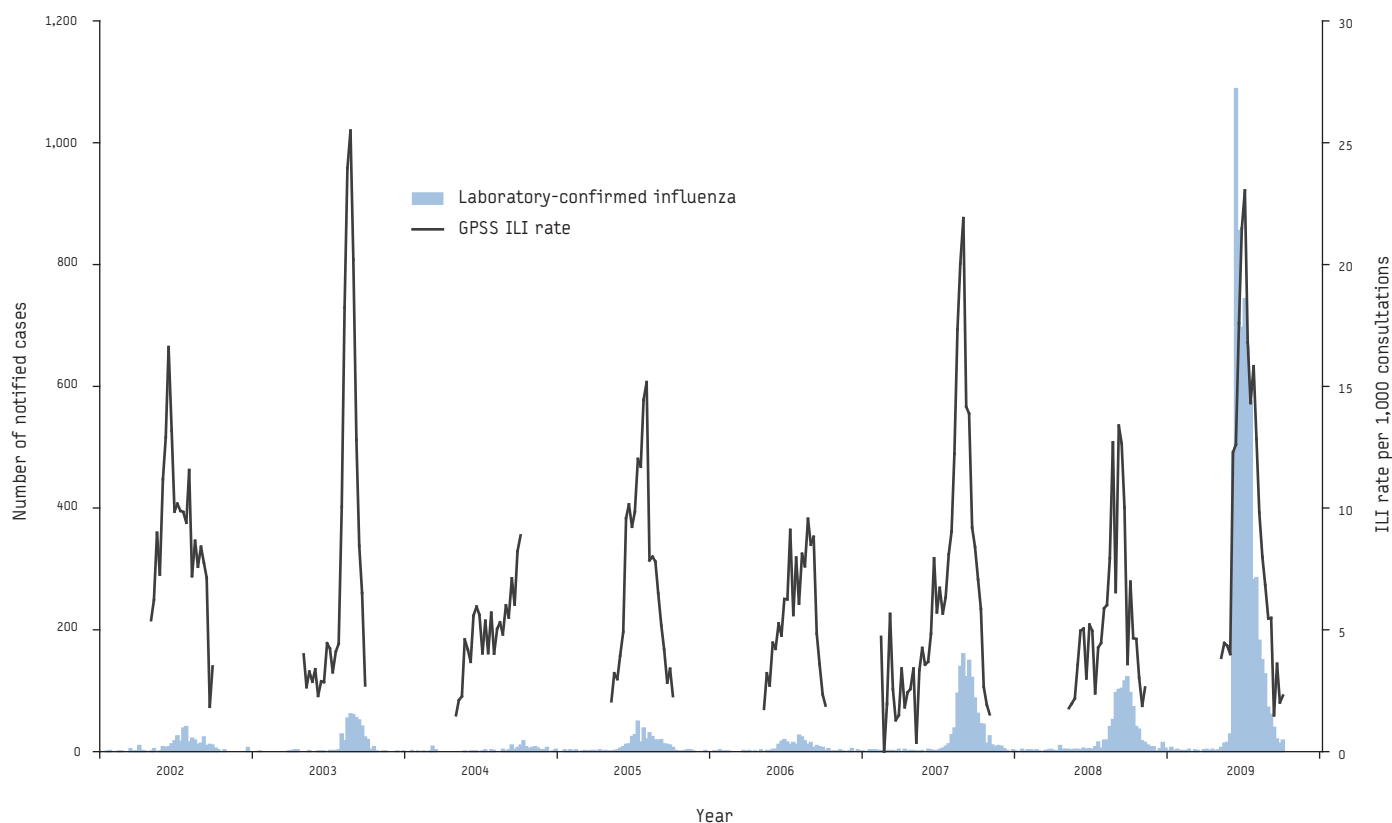
Compulsory notification of laboratory-confirmed influenza is a critical influenza surveillance tool and provides not only epidemiological data about confirmed diagnoses, but the opportunity to understand the emergence of novel influenza strains. However, interpretation of notification data must be undertaken 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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