Higher proportion of older influenza A(H1N1)pdm09 cases in Victoria, 2011

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The influenza surveillance system in Victoria is comprised of several components, including a general practitioner sentinel surveillance system, surveillance for influenza-like illness (ILI) in consultations made by the Melbourne Medical Deputising Service, laboratory confirmed influenza notified to the Victorian Department of Health and strain typing performed by the World Health Organization Collaborating Centre for Reference and Research on Influenza.

As measured by ILI from both the MMDS and GPSS, the 2011 influenza season in Victoria was mild compared to previous seasons and was not dominated by any type or subtype of influenza. There were 13 laboratory confirmed influenza outbreaks in 2011, nearly all of which were in aged care facilities.

GPs continue to swab more patients, a trend started in 2009, with a significantly lower percent of these testing positive for influenza than previous years. The proportion of ILI and swabbed patients who were vaccinated was also significantly lower in 2011 than previously. Strain analysis undertaken by the WHO Collaborating Centre indicated a good antigenic match between the 2011 vaccine and circulating strains.

The Victorian influenza surveillance system continues to provide a reliable, consistent system for monitoring the epidemiology of ILI and laboratory confirmed influenza in Victoria.

Background

A sentinel general practice (GP) program for the surveillance of influenza-like illness (ILI) has been coordinated by the Victorian Infectious Diseases Reference Laboratory (VIDRL) in partnership with the Victorian Government Department of Health (DH) since 1993. Laboratory testing of a sample of ILI cases from the surveillance program commenced in 1998.1 The program operates between May and October each year and is approved for continuing professional development points by the Royal Australian College of General Practitioners and the Australian College of Rural and Remote Medicine. VIDRL also monitors diagnoses of ILI made by the locum medical practitioners through the Melbourne Medical Deputising Service (MMDS). The DH coordinates the surveillance of all laboratory confirmed influenza in Victoria, a prescribed Group B notifiable disease under the Victorian Public Health and Wellbeing Act 2008 and Public Health and Wellbeing Regulations 2009 for which notification is required within five days of diagnosis.

The objectives of the influenza surveillance system are to:

- monitor the epidemiology of laboratory confirmed influenza in Victoria;
- identify the onset, duration and relative severity of annual influenza seasons in Victoria;
- provide samples for the characterisation of circulating influenza strains in the community to assist in the evaluation of the current season; and formulation of the following season’s vaccine;
- provide potential for early recognition of new influenza viruses and new or emerging respiratory diseases; and
- estimate influenza vaccine effectiveness each year.

In this paper we summarise findings from the Victorian influenza surveillance system in 2011.

Methods

General practice sentinel surveillance

In 2011, 94 GPs (65 from 23 metropolitan practices and 29 from 13 rural practices) participated in the VIDRL GP Sentinel Surveillance (GPSS) program (Figures 1a and 1b). The GPSS program for 2011 operated from 2 May to 30 October (weeks 18–43) inclusive in which participating GPs reported total number of consultations per week and age, sex and vaccination status of any patients presenting with influenza like illness (ILI). GPs
submitted the data weekly by fax or online submission (http://www.victorianfluveillance.com.au). A case of ILI was defined as fever, cough and fatigue/malaise. ILI rates were calculated as the number of ILI patients per 1,000 consultations and compared to previously established activity thresholds for Victorian influenza seasons.3

RNA was extracted from clinical specimens and in-house validated real-time multiplex PCR assays were used to detect type A influenza viruses (matrix gene), type B influenza viruses (nucleoprotein gene) and type C influenza viruses (matrix gene). Influenza A virus-positive samples were sub-typed using individual real-time PCR assays incorporating primers and probes specific for the haemagglutinin gene of A(H1N1)pdm09,5 pre-pandemic A(H1N1) and A(H3N2) strains.

Melbourne medical deputising service
The MMDS is the largest medical locum service in Australia and has contributed to the Victorian influenza surveillance system since 2003. The MMDS provides a 24-hour medical service to patients in their own home or aged care facility in the Melbourne metropolitan area and Geelong. Weekly rates of influenza-related diagnoses by MMDS clinicians per 1,000 consultations were calculated from records returned from the MMDS clinical database using the search terms ‘influenza’ and ‘flu’. To avoid inclusion of those immunised prophylactically, records that contained the terms ‘Fluvax’, ‘at risk’ and ‘immunisation’ were excluded from the rate calculation.

Notified laboratory confirmed influenza
Records of all laboratory confirmed influenza cases with a 2011 notification date were extracted from the department’s Notifiable Infectious Diseases Surveillance database on 24 February 2012. For the purposes of analysis, ‘routinely notified cases’ were those identified by clinical presentation, and excluded those
identified from outbreak investigations and the GPSS.

Data from the three surveillance programs were analysed descriptively using Microsoft Excel software. The chi squared test was used to compare proportions in Stata version 10.0 statistical software, with p<0.05 considered statistically significant.

Strain typing
A selection of specimens and isolates collected in Victoria during 2011 were referred to the WHO Collaborating Centre for Reference and Research on Influenza (WHO Collaborating Centre). Tissue culture was attempted for all of the specimens/isolates received. Viruses that were successfully cultured were analysed by a haemagglutination inhibition assay to determine antigenic similarity to the current vaccine strains and a neuraminidase inhibition assay to determine susceptibility to the antiviral drugs oseltamivir and zanamivir. The haemagglutinin and neuraminidase genes of a selection of specimens and isolates were genetically analysed by Sanger sequencing or pyrosequencing.

Results
General practice sentinel surveillance
For the 26 week surveillance period, an average of 94 per cent (88/94) of GPs submitted tally sheets to ViDRL. GPs reported having conducted 194,469 consultations (135,593 metropolitan and 58,876 rural) and identified 945 ILI cases (769 metropolitan and 176 rural), corresponding to metropolitan and rural rates across the surveillance period of 5.7 and 3.0 ILI cases per 1,000 consultations respectively. Among the 945 ILI cases reported by GPs, 50 per cent were in females, 47 per cent in males and the remainder unknown. The median age was 28 years (range one to 88 years). Fourteen per cent of ILI cases were reported as vaccinated in 2011.

ILI rates during the 2011 season generally fell within the range of normal seasonal activity, and were low compared to previous years (Figure 2). The overall (metropolitan and rural) ILI rate rose above baseline levels of 2.5 ILI per 1,000 consultations in week 19 (week commencing 9 May), and declined to baseline levels by week 41 (week commencing 10 October). ILI activity peaked at 10.5 ILI per 1,000 consultations in week 32 (week commencing 8 August) in metropolitan practices and at 6.2 ILI per 1,000 consultations in week 35 (week commencing 29 August) in rural practices (Figure 3).

GPs swabbed a total of 670 (71 per cent) ILI patients in 2011, of which 185 (28 per cent) tested positive to influenza. Of these, 102 (55 per cent) were type A, 82 (44 per cent) were type B and one was type C. Of the 102 type A influenza viruses detected, 26 (25 per cent) were A(H1N1)pdm09, 62 (61 per cent) were A(H3N2) and the remaining 14 (14 per cent) were not further sub-typed (Table 1). Among the influenza positive patients, 164 (86 per cent) were reported as not vaccinated (Table 1). Twenty-five patients (four influenza positive and 21 influenza negative) had an unknown vaccination status. Overall, 14 per cent (92/645) of swabbed patients were vaccinated but significantly more influenza negative patients were
vaccinated (15 per cent) than influenza positive patients (nine per cent; p=0.01). There was no significant difference in the proportion of patients with a co-morbidity recommended for influenza vaccination between those that were positive for influenza (eight per cent) and those that were negative (12 per cent; p=0.10).

The median age of influenza A(H1N1) pdm09 cases detected from the GPSS was 32 years (range: 1–55 years), compared to 27 years for A(H3N2) (range: 1–72 years) and 14 years for type B influenza (range: 1–74 years). The one influenza C case was aged 51 years. Forty-three percent of GPSS influenza positive patients were in the 20–49 year age group (Figure 4). Fifty-six percent of influenza type B cases were younger than 20 years while 67 per cent of A(H1n1) pdm09 cases were in the 20–49 years age group. There was no statistically significant difference in the proportion of ILI patients that were swabbed across age groups (p=0.23) (Figure 5). The proportion of patients that were vaccinated increased with age, particularly those aged 65 years and older, while the proportion positive for influenza was highest in the 20–49 years age group.

Notified laboratory confirmed influenza

There were 3,007 routinely notified cases of influenza made to the department in 2011. Of these, 2,184 (73 per cent) were type A, 787 (26 per cent) were type B, 34 (1 per cent) were type A and B co-infections, and two were type C influenza (Table 1). The number of cases, particularly influenza A, increased from week to week.
28 (week commencing 18 July) in a pattern that was generally consistent with GPss and MMDs iLi rates (Figure 3). Notified cases of both type A and type B influenza peaked in week 39 (week commencing 19 September), two weeks and four weeks after the peaks in the MMDs and the GPss iLi rates respectively.

Of the 2,184 type A cases, 213 (10 per cent) were A(H1n1)pdm09, 15 (<1 per cent) were A(H3n2), and 2,080 (95 per cent) were untyped. The median age of routinely notified influenza A(H1n1)pdm09 cases was 33 years (range: 0–88 years), 44 years for A(H3n2) (range: 3–90 years) and 20 years for type b cases (range: 0–90 years) (Table 1). Fifty-five per cent of notified influenza A(H1n1) pdm09 cases were in the 20–49 years age group (55 per cent) (Figure 4). Females comprised 53 per cent of the routinely notified cases in 2011.

Seven cases were reported to have died as a result of their influenza infection in 2011. These cases were aged 24 to 85 years with a median of 63 years. With the exception of one case, all were due to type A infection, of which three were further subtyped: two as A(H1N1)pdm09 and one as A(H3N2). One death was due to type B.

### Strain typing

Of the 771 specimens and four isolates received at the WHO Collaborating Centre, 388 (50 per cent) yielded an influenza positive isolate following cell culture. Of these, 243 (63 per cent) were type A and 145 (37 per cent) were type B. Of the influenza A viruses, 89 were A/H1N1pdm09 (A/California/7/09) strains and 154 were A/H3N2 viruses. Eighty-eight (98 per cent) of the A(H1N1) viruses were antigenically similar to the 2011 vaccine strain A/California/7/2009, while 135 (88 per cent) of the A(H3N2) strain viruses were similar to the 2011 vaccine strain A/Perth/16/2009.

All influenza type B strains except one were of the B/Victoria/2/87 lineage, with 130 (90 per cent) being similar to the 2011 vaccine strain B/Brisbane/60/2008. One type B virus was from the B/Yamagata/16/88 lineage. All of the Victorian influenza positive isolates were tested for susceptibility to the neuraminidase inhibitors oseltamivir and zanamivir. One of the 89 A(H1N1)pdm09 viruses tested (one per cent) was found to be oseltamivir resistant due to a H275Y mutation in the neuraminidase gene. It is unknown if this patient was being treated with oseltamivir prior to specimen collection. None of the A(H3N2) or B viruses were resistant to oseltamivir or zanamivir.

### Discussion

The 2011 influenza season in Victoria, as measured by ILI from both the MMDs and GPSS, was mild compared to previous seasons. The season overall was not dominated by any type or subtype of influenza, although type A cases tended to be more common earlier in the season and type B in the latter part. There were no detections of pre-pandemic H1N1 influenza strains, confirming
that influenza A(H1N1)pdm09 is now the seasonal influenza A(H1N1) strain. There were 13 laboratory confirmed influenza outbreaks in 2011, nearly all of which were in aged care facilities, and although this represents a considerable increase on the six reported in 2010 it may be indicative of the re-emergence of influenza A(H3N2) which is generally associated with older age groups.7

In 2011 the proportion of GPSS ILI cases that were swabbed was 71 per cent, similar to 2010 (70 per cent)6 and 2009 (68 per cent) but significantly higher than from 2003 to 2008 in which 35–50 per cent of ILI patients were swabbed (p<0.001).8 This suggests higher awareness and/or concern regarding influenza and an increase in the ease of testing since the 2009 pandemic. However, only 28 per cent of tests were positive for influenza, which was low compared to the previous years 2006 to 2010 in which the median proportion positive was 35 per cent (range: 28–45 per cent) (p<0.001).

The proportion of total ILI cases that were vaccinated was 14 per cent in 2011, significantly lower than the average of the years 2006–2010 (18 per cent, p<0.001).6,9–11 Similarly, 14 per cent of swabbed ILI cases in 2011 were vaccinated, significantly lower than the average of the previous five years 2006–2010 (19 per cent, p<0.001). This suggests that while patients are being tested more, fewer are being vaccinated.

As indicated by the median ages and age distributions for both GPSS laboratory confirmed influenza and routine notifications, type B influenza cases were generally younger than type A(H3N2) cases, consistent with the typically observed age distributions for these influenza types.7 The median age of A(H1N1) pdm09 has risen from 20 years in 2009, 26 (GPSS) and 21 (routine notifications) in 2010 to 32 (GPSS) and 33 (routine notifications) in 2011. This increase in age was also observed in the United Kingdom Severe Influenza Surveillance System where the median age of A(H1N1) pdm09 increased from 20 years in 2009 to 35 years in 2010.12 Such a shift in the median age of cases is not unexpected following the emergence of a pandemic influenza strain in which higher attack rates in younger age groups that have no prior immunity are observed during the initial outbreak, followed by a shift to older age groups as immunity increases in the young.13,14

The trivalent influenza vaccine for the 2011 southern hemisphere season contained California/7/2009 (H1N1)-like virus, A/Perth/16/2009 (H3N2)-like virus and B/Brisbane/60/2008-like virus. Strain analysis undertaken by the WHO Collaborating Centre indicated a good antigenic match between the 2011 vaccine and circulating strains, with 88 per cent of the A(H1N1) viruses matching the vaccine strain A/California/7/2009, 88 per cent of the A(H3N2) viruses matching the vaccine strain A/Perth/16/2009 and 90 per cent of type B viruses similar to the B/Brisbane/60/2008 strain in the vaccine. We have previously shown that type- and subtype-stratified adjusted vaccine effectiveness estimates (A(H1N1)pdm09: 78 per cent; A(H3N2): 58 per cent; B: 53 per cent) were broadly consistent with a good match between vaccine and circulating strains.15

In previous years the ILI rate as measured by the MMDS has generally peaked prior to that of the GPSS, followed several weeks later by a peak in routine notifications. However in 2011 GPSS ILI rates peaked two weeks prior to that of the MMDS. The reasons for this are unclear, but may be an artefact of a season with low or mild ILI activity in which a peak is less well defined and exacerbated by the non-specific ILI case definition. Routine notifications, given the time taken for testing and the notification to be made to the department peaked the latest. The age distribution of laboratory confirmed influenza was consistent with previous years, with a majority of those from the GPSS comprised of working age adults, while there was a higher proportion of elderly among the cases routinely notified to the department, likely to be a reflection of hospitalised influenza patients.

The Victorian influenza surveillance system continues to provide a reliable, consistent system for monitoring the epidemiology of ILI and laboratory confirmed influenza in Victoria. Victorian influenza surveillance system reports are available at https://www.victorianflusurveillance.com.au/

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