



Influenza in New Zealand 2009

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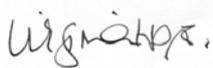
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Summary

During the 2009 winter season, 10 860 consultations for ILI were reported from a national sentinel network of 101 general practices. It is estimated that ILI resulting in a visit to a GP affected over 116 335 New Zealanders (2.7% of total population) during the season, compared with an estimated 50 550 in 2008 (1.0% of total population). The influenza activity peaked in July and the overall level of ILI in 2009 was the highest compared with the 1997-2008 period. The ILI consultation rates varied greatly between health districts with the highest rates being reported from the South Auckland and Wellington Health Districts. In 2009, the majority of the viruses were influenza A (99.9%) surpassing the influenza B viruses (0.1%). Among all typed and subtyped viruses, pandemic A(H1N1) 09 viruses (77.6%) and seasonal A(H1N1) (20.0%) viruses were two main co-predominant strains co-circulating during the season. All pandemic A(H1N1) 09 viruses tested showed they were sensitive against oseltamivir whereas all seasonal A(H1N1) viruses tested were resistant to oseltamivir. Significant antigenic shift for A(H1N1) and significant antigenic drift for A(H3N2) and B was observed among circulating influenza viruses, resulting in three vaccine components being updated for 2010.

Recommendations

1. That the sentinel influenza surveillance system be evaluated using standard surveillance system criteria and benchmarked against international best practice for an epidemic or pandemic. This should include the review of the following.
 - The performance characteristics of sentinel surveillance (sensitivity, specificity, representativeness and robustness) for a pandemic at a national and regional level during the containment phase for early detection as well as the management phase for monitoring.
 - Definition of ILI for sentinel surveillance.
 - Whether three swabs/week/GP is sufficient to provide information for predominant circulating strains at a national and regional level in a temporal fashion during an influenza epidemic or pandemic.
 - Electronic solutions for data collection and dissemination in order to ease workload on PHS, GPs, and virology laboratories, and improve timeliness of ILI and virology reporting.
 - Recording of swabs sent and received so isolation rates can be calculated with greater accuracy.
 - Need to obtain the demographic information for the total patient population from each sentinel GP in order to calculate accurate ILI rates among different age groups.
 - Explore other complimentary surveillance approaches for detecting early cases of ILI.
 - It has become increasingly important to establish and sustain a national antiviral monitoring program in New Zealand which would provide timely surveillance information to assist clinicians for choosing appropriate antiviral agents for their patients and assist public health officials for evidence-based decision on antiviral stockpiling and antiviral usage during a pandemic or epidemic.
2. That the sentinel influenza surveillance system be reviewed in terms of its potential for surveillance of other diseases and syndromes of public health importance.
3. That information be obtained from each virology laboratory on number of total swabs tested for influenza in order to understand specificity of the non-sentinel influenza surveillance system.

1. Introduction

Surveillance of influenza in New Zealand is based on sentinel general practice (GP) and laboratory-based reporting. This surveillance monitors the incidence and distribution of the disease and virus strains. Seasonal influenza is not a notifiable disease in New Zealand. However, non-seasonal influenza (capable of being transmitted between human beings) became a notifiable and quarantineable disease in New Zealand on 30 April 2009.

The purpose of influenza surveillance is:

- to understand incidence and distribution of influenza in the community
- to assist with early detection of influenza epidemics within the community and to guide the development and implementation of public health measures
- to identify the predominant circulating strains in the community and guide influenza vaccine composition for the subsequent year[1].

This report summarises results obtained from influenza surveillance in New Zealand for 2009, including some comparisons with previous years. It also includes information on hospitalisations for influenza (obtained from NMDS⁶), notifiable disease information for non-seasonal influenza (obtained from EpiSurv⁷) and influenza immunisation coverage data (obtained from Health Benefits Limited).

2. Methods

2.1. General Practice Sentinel Surveillance – Consultation and Isolate Data

The sentinel surveillance system, in its current form, commenced in 1991 as part of the WHO Global Programme for Influenza Surveillance. It is operated nationally by ESR and locally by influenza surveillance co-ordinators in the public health services (PHSs). Normally sentinel surveillance operates in the winter period, from May to September. However, due to pandemic influenza, the sentinel system was extended all year around to cover Spring-Summer-Autumn periods as well.

In 2009, national influenza sentinel surveillance was undertaken from May to December (week 18 to week 53 inclusive). Local surveillance co-ordinators recruited general practices within their region to participate on a voluntary basis. Where possible, the number of practices recruited was proportional to the size of the population in each health district covered by the PHS (approximately 1:50 000 population).

General practitioners (GPs) were required to record the number of consultations for influenza-like illness (ILI) each week and the age group (<1, 1-4, 5-19, 20-34, 35-49, 50-64, 65+) of each of these suspected cases on a standardised form.

⁶ National Minimum Dataset (Ministry of Health)

⁷ National web-based database operated by the Institute of Environmental Science and Research (ESR) and available for immediate analysis. This system also records hospitalised and fatal cases.

Influenza-like illness was defined by a standardised case definition, which was:

“Acute upper respiratory tract infection characterised by abrupt onset and two of the following: fever, chills, headache, and myalgia.”

Each participating GP also collects three respiratory samples (i.e., nasopharyngeal or throat swab) each week from the first ILI patient examined on Monday, Tuesday, and Wednesday. The GPs forward these samples to the WHO National Influenza Centre at ESR or to hospital virology laboratories in Auckland, Waikato, or Christchurch for virus characterization.

Information on the number of ILI consultations and swabs sent from each health district is forwarded to ESR by local co-ordinators each week (Monday to Sunday). ILI consultation data is received by the following Monday to Wednesday. Likewise virology laboratories report to ESR weekly with the total number of swabs received from each health district, the influenza viruses identified, together with updated details on type and strain. This data is collated, analysed and reported on a weekly, monthly and annual basis.

Consultation rates are calculated using the sum of the patient populations, reported by the participating practices, as the denominator. Because the age-specific patient population data were not provided by the participating practices, the denominator for the age-specific ILI rate calculation is based on the New Zealand census data with the assumption that age distribution of the GP patient population is the same as the New Zealand population. The national level of ILI activity is described using a set of threshold values.[2, 3] A weekly rate below 50 consultations per 100 000 patient population is described as baseline activity. A weekly consultation rate of 50-249 is considered indicative of normal seasonal influenza activity. Within the normal seasonal activity, 50 to 99 is low activity, 100-149 moderate, and 150 to 249 high. A rate of 250-399 indicates higher than expected influenza activity and ≥ 400 indicates an epidemic level of disease. GP practices are not uniformly spread throughout the population, this may affect the sensitivity in some health districts.

2.2. Laboratory-based Surveillance – Year-round Virology Data

In addition to influenza viruses identified from sentinel surveillance, year-round laboratory surveillance of influenza (and other viruses) is carried out by the four regional virus diagnostic laboratories at Auckland, Waikato, Wellington and Christchurch Hospitals, and by the WHO National Influenza Centre at ESR. Each week, all viral identifications, including influenza, largely from hospital inpatients and outpatients are reported to ESR. ESR in turn collates and reports virology surveillance data nationally.

Laboratory identification methods include molecular detection by polymerase chain reaction, isolation of the virus, or direct detection of viral antigen. Influenza viruses are typed and subtyped as influenza A, B, seasonal A, seasonal A (H1N1), seasonal A (H3N2), or pandemic A(H1N1) 09.

2.3. Non-seasonal influenza notifications

Non-seasonal influenza (capable of being transmitted between human beings) became a notifiable and quarantineable disease in New Zealand on 30 April 2009. In 2009, this meant notifying cases of pandemic A(H1N1) 09. Data derived from EpiSurv as of 12 February 2010 are presented in Section 4.

2.4. Hospitalisations

Hospitalisation data for influenza (ICD-10AM-VI code I (J09-J11) for 2009 which correlates to previous versions of ICD-10AM codes J10-J11) were extracted from the New Zealand Ministry of Health's National Minimum Dataset (NMDS) for the year 2009 (by discharge date). In this dataset, people who received less than one day of short hospital treatment in hospital's emergency departments were excluded from any time series analysis of influenza hospitalisations during 2000-2009. Influenza-related hospitalisations were conservatively taken to include only those where influenza was the principal diagnosis. Repeat admissions were included, as repeat infections with another influenza A subtype or B virus are possible.

2.5. Data Used for Calculating Rates

Denominator data used to determine the rates have been derived from 2009 mid-year population estimates published by Statistics New Zealand.

2.6. Immunisation Coverage

In 1997 influenza vaccination was made available free to those ≥ 65 years of age, and in 1999 free vaccination was extended to risk groups < 65 years.[4, 5] The data that medical practitioners provide to Health Benefits Limited to claim reimbursement were used to estimate coverage in 2009 among persons ≥ 65 years of age.

3. Results

3.1. Sentinel Practices

In 2009, 101 sentinel practices were recruited from all of the 24 health districts. All PHSs began reporting by the second week of May 2009. Some practices did not report every week. The average number of practices participating per week was 86, with an average patient population roll of 402 884, about 9.3% of the New Zealand total population.

3.2. Disease Burden

From May to December 2009, a total of 10 860 sentinel consultations for ILI were reported. The cumulative incidence rate of ILI consultation for 2009 during the influenza season was 2695.6 per 100 000 patient population. The average national weekly consultation rate in 2009 was 77.9 per 100 000 patient population. This rate is higher than the average weekly rates for 2008 (52.4 per 100 000 patient population) and 2007 (37.2 per 100 000 patient population).

Extrapolating ILI consultations obtained from the GP patient population to the New Zealand population, it is estimated that ILI resulting in a visit to a GP affected 116 335 New Zealanders during the influenza season (2.7% of total population). This is higher than the estimated 50 550 affected in 2008.

Figure 1 compares the weekly consultation rates for ILI in 2009 with 2008 and 2007. Influenza consultation activity remained at the baseline level from week 18 to 23, and then increased to a peak at week 29 (13-19 July) with a consultation rate 284.0 per 100 000 patient population. This corresponds with the first peak in 2008 (week 29) and two weeks earlier than the peak in 2007 (week 31) with rates of 93.3 per 100 000 patient population and 69.9 per 100 000 patient population respectively. Consultation activity then gradually declined, remaining at a moderate level until week 35, and dropping below the baseline in week 39.

Figure 1. Weekly consultation rates for influenza-like illness in New Zealand, 2007, 2008 and 2009

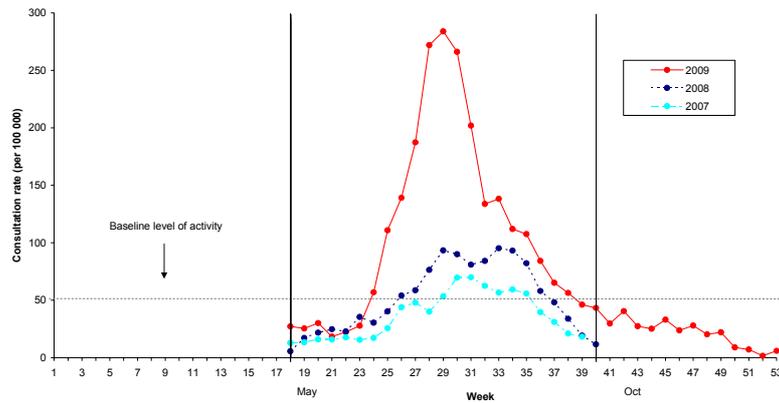


Figure 2. Total number of influenza viruses by surveillance type and week specimen taken, 2009

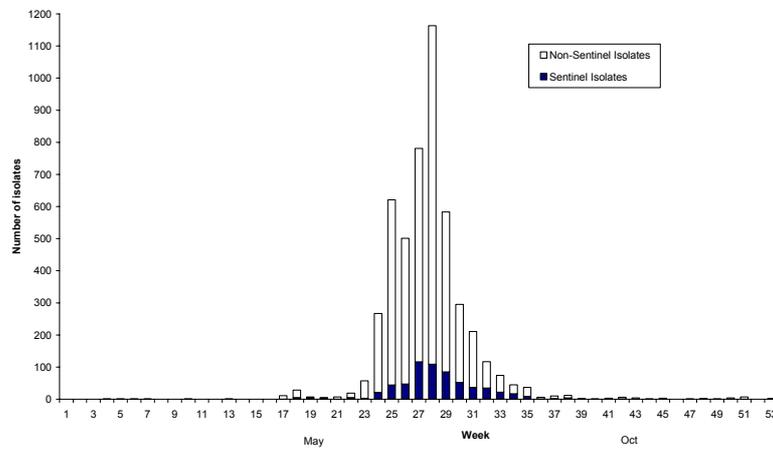
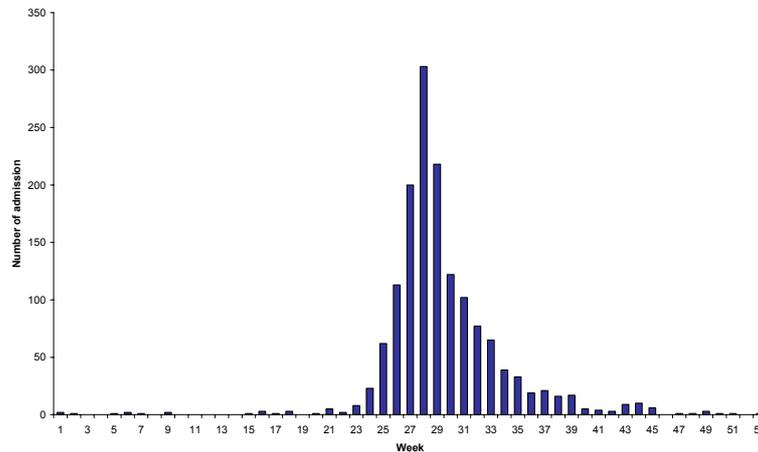


Figure 3. Influenza hospitalisation by week discharged, 2009



A total of 4900 influenza viruses were identified in 2009, higher than the 1054 and 744 viruses in 2008 and 2007 respectively. Of the 4900 viruses, 624 came from sentinel practice surveillance during May to December. This is higher compared to the 466 sentinel viruses identified in 2008 and 239 viruses in 2007. There were 4276 non-sentinel viruses identified in 2009 compared to 588 in 2008 and 505 in 2007.

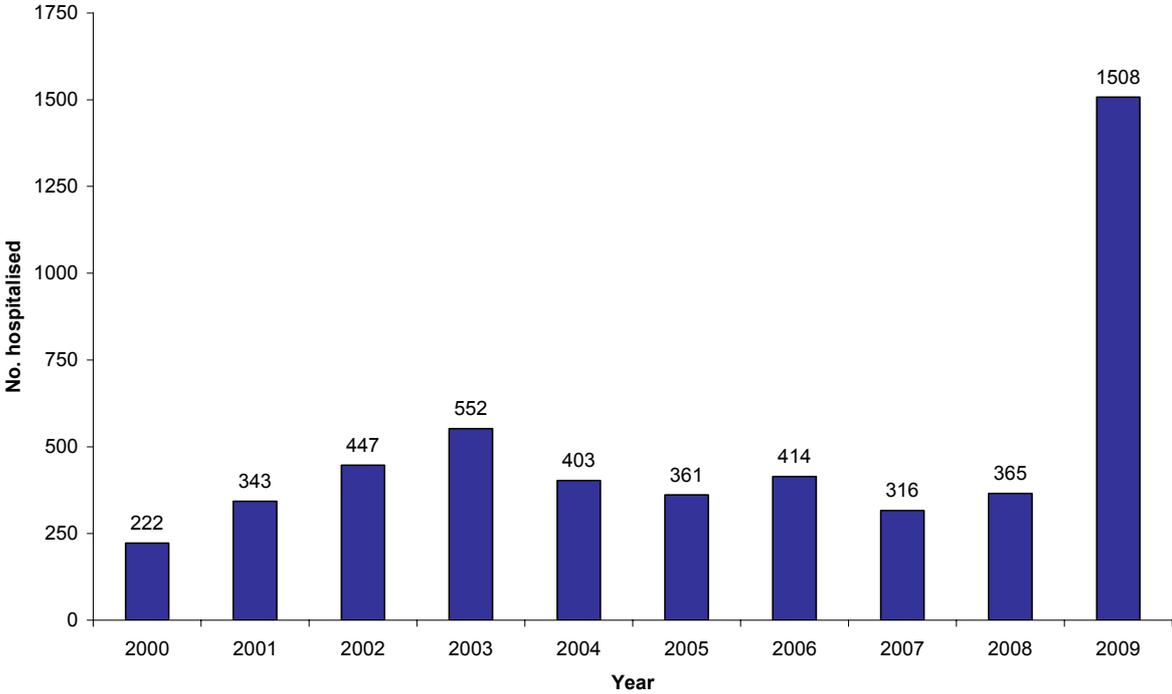
Figure 2 shows influenza viruses each week throughout 2009. The biggest peak of influenza virus detection occurred in week 28 (1163 viruses), a week earlier than the peak period in consultation rates (week 29). Sporadic influenza viruses were identified as early as January during the summer season, however the vast majority (4826, 98.5%) were from specimens taken during May to September. Sentinel viruses peaked in week 27 (116 viruses) while non-sentinel viruses peaked in week 28 (1054 viruses). Overall influenza viruses in 2009 were detected in the same time period as in 2008. Most sentinel and non-sentinel viruses (97.0%) came from the sentinel period (weeks 23 to 35).

In 2009, there were a total of 1508 hospitalisations for influenza and this was much higher than the 2008 and 2007 hospitalisations of 365 and 316 respectively. Figure 3 shows these hospitalisations by week, 95.6% (1441) of which occurred during June to September. The highest number of hospitalisations (857) occurred in July. Hospitalisations peaked in week 28 corresponding to the peak of the sentinel and non sentinel influenza virus detection, and a week earlier than the ILI consultation peak (week 29).

When influenza hospitalisation data in 2009 was compared to the data from 2000-2008, Figure 4 shows a substantial higher number of hospitalisations in 2009 than previous years.

The majority of influenza hospitalisations in 2009 were for pandemic A(H1N1) 09. See section 4 on non-seasonal influenza surveillance.

Figure 4. Influenza hospitalisations, 1990-2009



3.3. Geographic Distribution

In addition to provide influenza incidence at a national level, sentinel surveillance is able to provide an indication of the distribution of ILI and viral strains at a regional level.

Figure 5 shows the sentinel average weekly consultation rates for each health district during May to December 2009. ILI consultation rates varied between health districts, with rates above the national average at South Auckland (150.8 per 100 000 patient population), followed by Wellington (128.7), Hutt (108.8), Eastern Bay of Plenty (100.0), Northland (99.1), Gisborne (85.9), Otago (85.5), Tauranga (82.8), Hawke’s Bay (82.4), Rotorua (82.0), and South Canterbury (81.1). Table 1 shows health districts codes and description.

Figure 6 shows the distribution of sentinel influenza viruses based on the health district from which the specimen (swab) was taken. Most viruses came from Otago, Northland, Canterbury, Central Auckland, Wairarapa, South Canterbury, and Manawatu regions. Viruses were not identified in one health district (Ruapehu). The national influenza virus detection rate for 2009, illustrated in Figure 7 was 31.3% (624 viruses from 1993 swabs received), which is lower than the 2008 of 46.6% (1001 swabs) and slightly higher than the 2007 rate of 30.7% (778 swabs) respectively.

With regards to the geographical distribution of received influenza viruses, it is important to take into account that for some health districts there is a discrepancy in the reported number of swabs sent by sentinel GPs in that district, and the number of swabs recorded as received by virology labs.

Figure 5. Sentinel average weekly consultation rate for influenza-like illness by health district, 2009

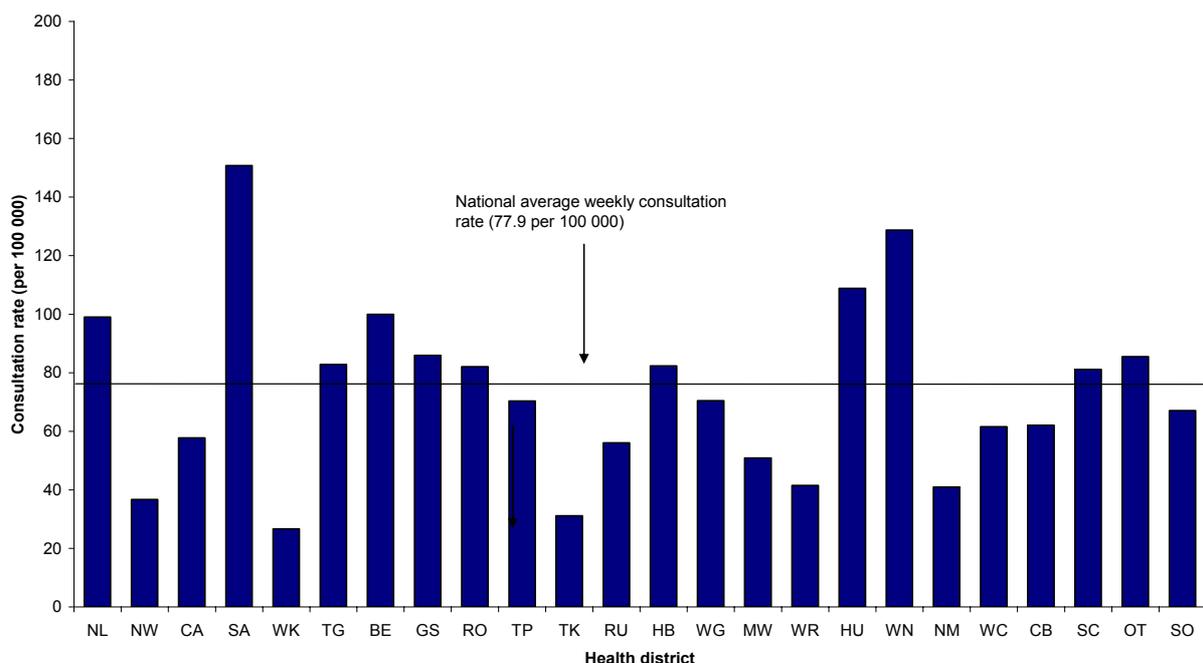


Figure 6. Cumulative laboratory confirmed influenza viruses from sentinel surveillance by health district, May-December 2009

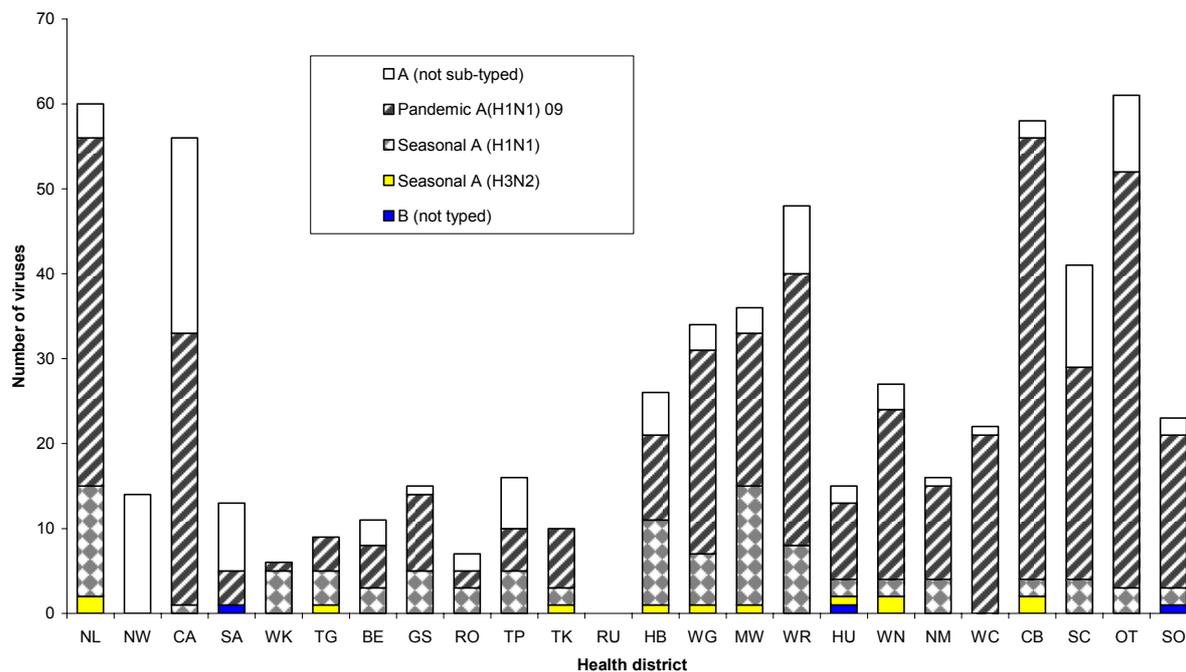
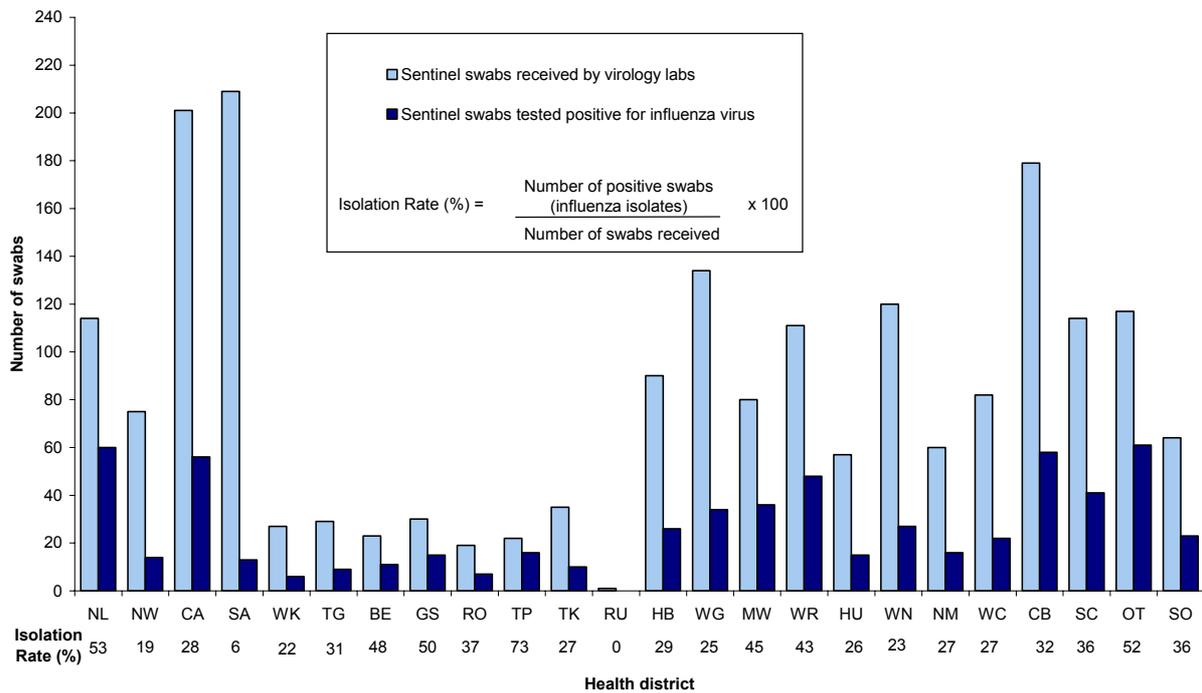


Table 1. Health District Codes and Description

Code	Description	Code	Description
NL	Northland	HB	Hawke's Bay
NW	North West Auckland	WG	Wanganui
CA	Central Auckland	MW	Manawatu
SA	South Auckland	WR	Wairarapa
WK	Waikato	WN	Wellington
TG	Tauranga	HU	Hutt
BE	Eastern Bay of Plenty	NM	Nelson Marlborough
GS	Gisborne	WC	West Coast
RO	Rotorua	CB	Canterbury
TP	Taupo	SC	South Canterbury
TK	Taranaki	OT	Otago
RU	Ruapehu	SO	Southland

Figure 7. Sentinel swabs received and tested positive for influenza virus by health district, 2009



3.4. Age Distribution

Figure 8 compares the hospitalisation rates in 2009 by age group. In 2009, the highest hospitalisation rates occurred in children aged under one year (274.3 per 100 000), followed by children aged 1-4 (84.1 per 100 000) and adults aged 20-34 years (33.6 per 100 000).

Figure 8. Influenza hospitalisation rate by age group, 2009

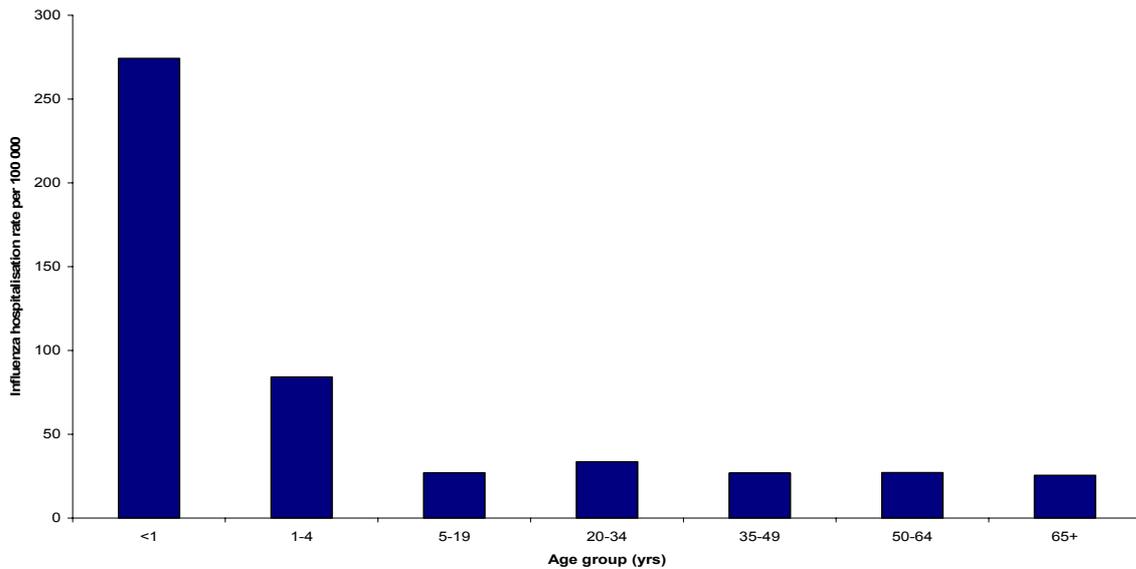
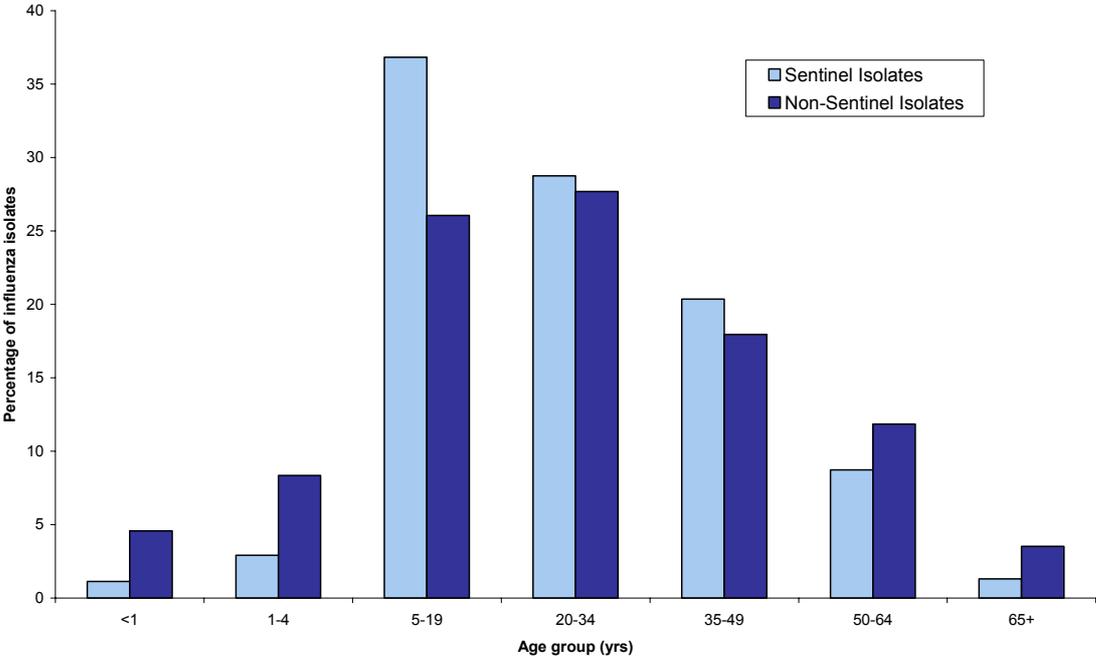


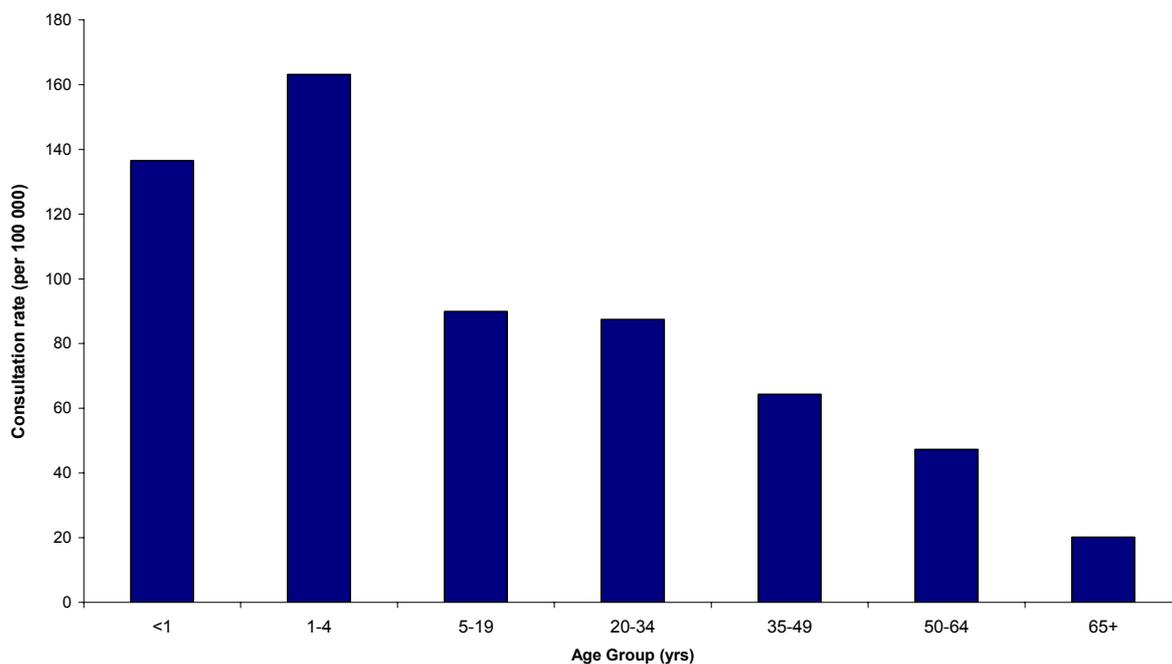
Figure 9 compares the percentage of influenza viruses between sentinel surveillance and non-sentinel for each age group. It is interesting to note that the age group under one year and 1-4 years and patients over 65 years were represented more in non-sentinel surveillance than in sentinel surveillance. This is consistent with the findings from the past 10 years. In 2009, the 50-64 years age group were also represented more in non-sentinel surveillance and this is different from the finding in previous years.

Figure 9. Percentage of sentinel and non-sentinel influenza viruses by age group, 2009



In addition, average weekly ILI consultation rates by age group were calculated for the sentinel surveillance system. These rates are presented graphically in Figure 10.

Figure 10. Sentinel average weekly consultation rate for influenza-like illness by age group, 2009



The highest consultation rate for ILI was in the children aged 1-4 years and those <1 year with an average weekly consultation rate of 163.1 per 100 000 patient population and 136.5 per 100 000 patient population respectively. This was followed by 5-19 years (89.9), adults 20-34 years (87.4), 35-49 years (64.3) and 50-64 years (47.2). Elderly people (aged 65 years and over) had had the lowest rate of 20.1 per 100 000 patient population.

4. Non-seasonal influenza surveillance

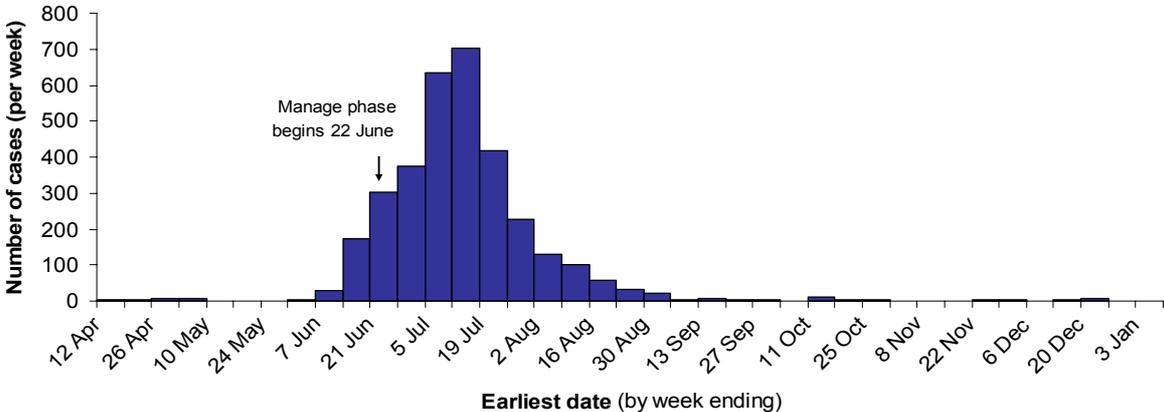
Pandemic A(H1N1) 09 was made a notifiable disease on 30 April 2009. Data are entered into EpiSurv.

On 25 April 2009, New Zealand was the first country in the southern hemisphere to report importation of pandemic A(H1N1) 09 infection, following the return of an airline flight containing a group of high school students who had travelled in Mexico. A concerted containment effort (e.g. screening arriving airline passengers for ILI, case isolation, quarantine of contacts, and treatment with oseltamivir) by the government, public health officials, border officials, hospitals, primary-care workers and laboratories appeared to delay establishment of community transmission for several weeks. New Zealand entered its management phase on 22 June after sentinel and non-sentinel surveillance data indicated that 2009 pandemic A(H1N1) 09 had established sustained community transmission.

As of 31 December 2009, a total of 3668 cases were reported in EpiSurv: confirmed 3211, probable 69, under investigation 17, and suspect 371. Data analysed for the rest of the section is for confirmed and probable cases only (3280). Note that the suspect status category was dropped in June 2009 following confirmation of community transmission of pandemic A(H1N1) 09 virus within New Zealand.

The epidemic curve is shown in Figure 11. This epidemic curve was constructed using the earliest date recorded in EpiSurv (onset, hospitalised or report date) and is displayed as cases per week since 6 April 2009. For the purposes of this epidemic curve confirmed and probable cases were combined.

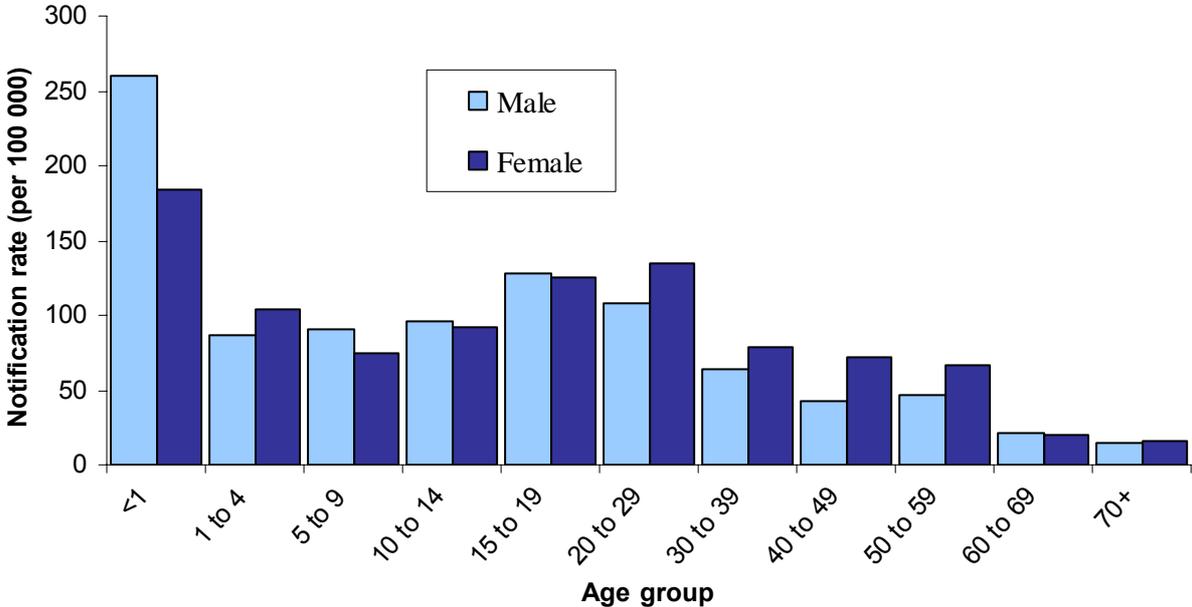
Figure 11. Total cases of pandemic A(H1N1) 09 (confirmed and probable)



Confirmed cases n=3211, probable cases n=69

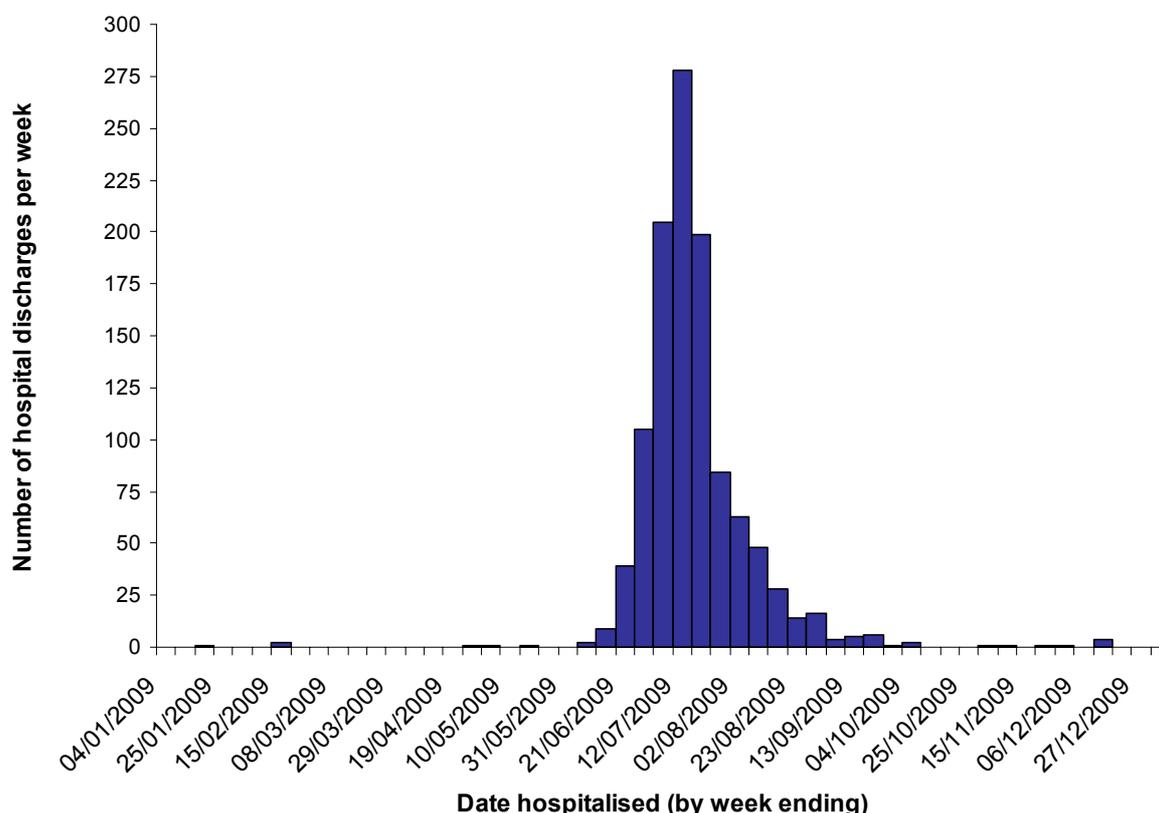
The age distribution of cases by gender is shown in Figure 12. The highest reported notification rate was in the under one year old age group followed by persons aged 15-29 years old.

Figure 12. Cumulative rate of pandemic A(H1N1) 09 cases by age and sex



There were 1122 hospital discharges where the primary diagnosis of influenza was known to be due to pandemic A(H1N1) 09 virus.⁸ This is a subset of the 1508 hospitalisations for all influenza. The median age was 26.7 years and ranged from 19 days to 91 years. A total of 278 hospitalisations were reported in week 28 (July 6-12) which corresponds to the peak in notifications.

Figure 13. Hospitalisations of confirmed pandemic A(H1N1) 09

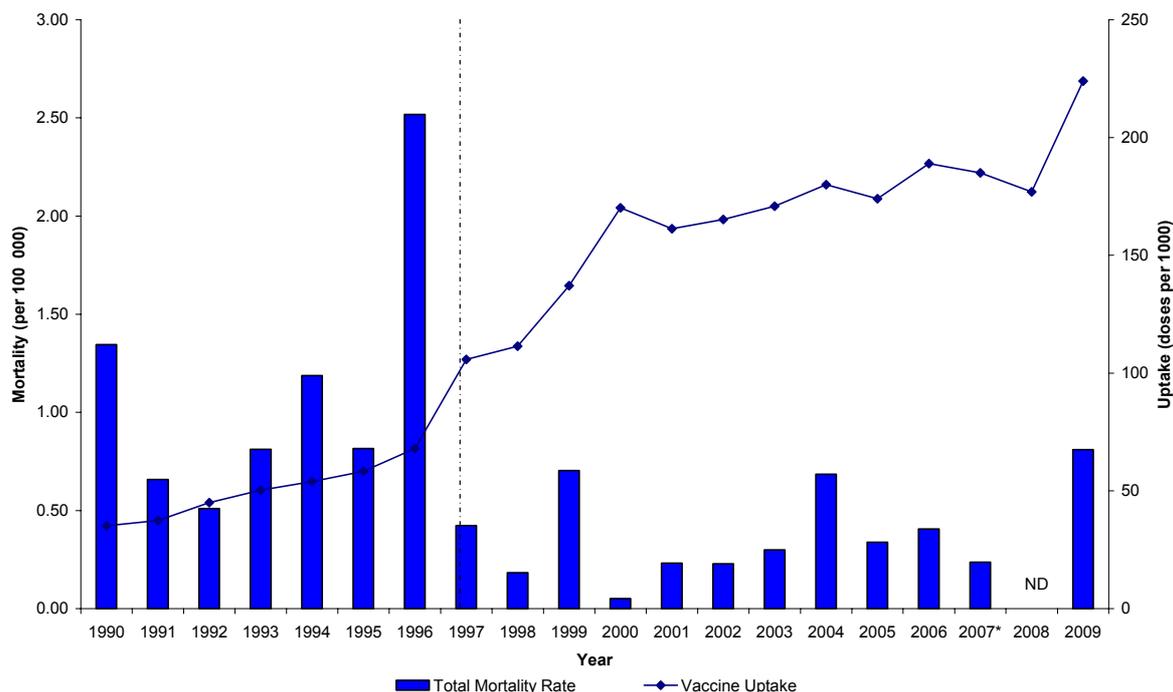


At the time of this report, **thirty-five deaths** have been reported in New Zealand as a pandemic A(H1N1) 09 - associated death⁹. The median age was 40 years and ranged from 19 days to 79 years. This gave rise to the mortality rate of 0.81 per 100 000 for 2009. **When the 2009 influenza mortality rate was compared to that of 1990-2007** (Figure 14), it is noted that the **2009 mortality rate was the fifth highest rate recorded during 1990-2007**. The first (2.52 per 100 000) and second (1.34 per 100 000) highest mortality rates were recorded in 1996 and 1990 respectively.

⁸ This includes 1029 hospitalisations coded in NMDS as J09 (used for pandemic influenza) at the time of discharge, plus 93 hospitalisations coded in NMDS as J10-11 (other influenza) at the time of discharge but known to be lab-confirmed pandemic influenza (EpiSurv data). J09 coding for pandemic influenza was not introduced until July 2009.

⁹ A **pandemic A(H1N1) 09 – associated death** is defined, as: A person with confirmed pandemic A(H1N1) 09 infection determined from ante-mortem or post-mortem specimens, and who died from a clinically compatible illness or complications attributable to that infection. There should be no period of complete recovery between illness and death, and no alternative agreed upon cause of death.

Figure 14. Influenza mortality rates and vaccine uptake, 1990-2009



(Note: In 1997, the Ministry of Health made influenza vaccination available free to persons aged 65 years and older. In 1999, this policy was extended to at risk groups <65 years old. 2007 mortality data is provisional. ND means no data.)

5. Immunisation Coverage

The uptake of seasonal influenza vaccine in New Zealand in 2009 among persons 65 years and over was 65.5%. The number of doses of influenza vaccine used during the 2009 season was 224 doses per 1000 population substantially higher than the 177 doses per 1000 population in 2008 with overall uptake rate of 64% (among persons 65 years and over).

6. Virus Strain Characterisation

6.1. Circulating viral strains in 2009

Figure 15 shows influenza virus identifications by type and subtype for each week throughout 2009, and the total percentage contribution of each. Table 2 shows influenza virus identifications by type and subtype for 2009.

The majority of influenza viruses (4894/4900 or 99.9% of all viruses) were characterised as influenza A. A very small number of influenza B viruses (6) were detected. Influenza B strain represented 0.1% (6/4900) of all viruses.

Overall, pandemic A(H1N1) 09 virus was the predominant strain among all influenza viruses. The pandemic A(H1N1) 09 strain represented 57.2% (2803/4900) of all viruses and 77.6% (2803/3614) of all typed and subtyped viruses.

Seasonal influenza A(H1N1) was the predominant strain among all seasonal influenza viruses. It represented 14.8% (724/4900) of all viruses and 20.0% (724/3614) of all typed and subtyped viruses.

Seasonal influenza A(H3N2) strain represented 1.7% (81/4900) of all viruses and 2.2% (81/3614) of all typed and subtyped viruses.

Figure 16 shows the general pattern of influenza virus identifications. This indicates the early onset of ILI activity and then a rapid rise to peak in week 28. The majority of influenza A viruses occurred in the middle of the season. Pandemic A(H1N1) 09 virus and seasonal influenza A(H1N1) and A(H3N2) viruses co-circulated for the all of the influenza season (from week 18 to 38). Pandemic A(H1N1) 09 virus predominated. Only six influenza B viruses (0.1%, 6/4900) were identified in 2009.

Table 2. Influenza virus identifications by type and subtype, 2009

Viruses	All viruses		Typed-Sub-typed	
	No.	%	No.	%
Influenza A				
Influenza A (not sub-typed) by PCR	1286	26.2		
Pandemic A(H1N1) 09				
Pandemic A(H1N1) 09 by PCR	2403	49.0	2403	66.5
A/California/7/2009 (H1N1) - like	400	8.2	400	11.1
Subtotal pandemic A(H1N1) 09	2803	57.2	2803	77.6
Seasonal Influenza A(H1N1)				
Seasonal Influenza A (H1N1) by PCR	564	11.5	564	15.6
A/Brisbane/59/2007 (H1N1) - like	160	3.3	160	4.4
Subtotal seasonal A(H1N1)	724	14.8	724	20.0
Influenza A(H3N2)				
Influenza A sub-type H3N2 by PCR	78	1.6	78	2.2
A/Brisbane/10/2007 (H3N2) - like	3	0.1	3	0.1
Subtotal seasonal A(H3N2)	81	1.7	81	2.2
Influenza B				
Influenza B by PCR	6	0.1	6	0.2
Subtotal B	6	0.1	6	0.2
Total	4900	100	3614	100

Figure 15. Total influenza viruses by type and week specimen taken, 2009

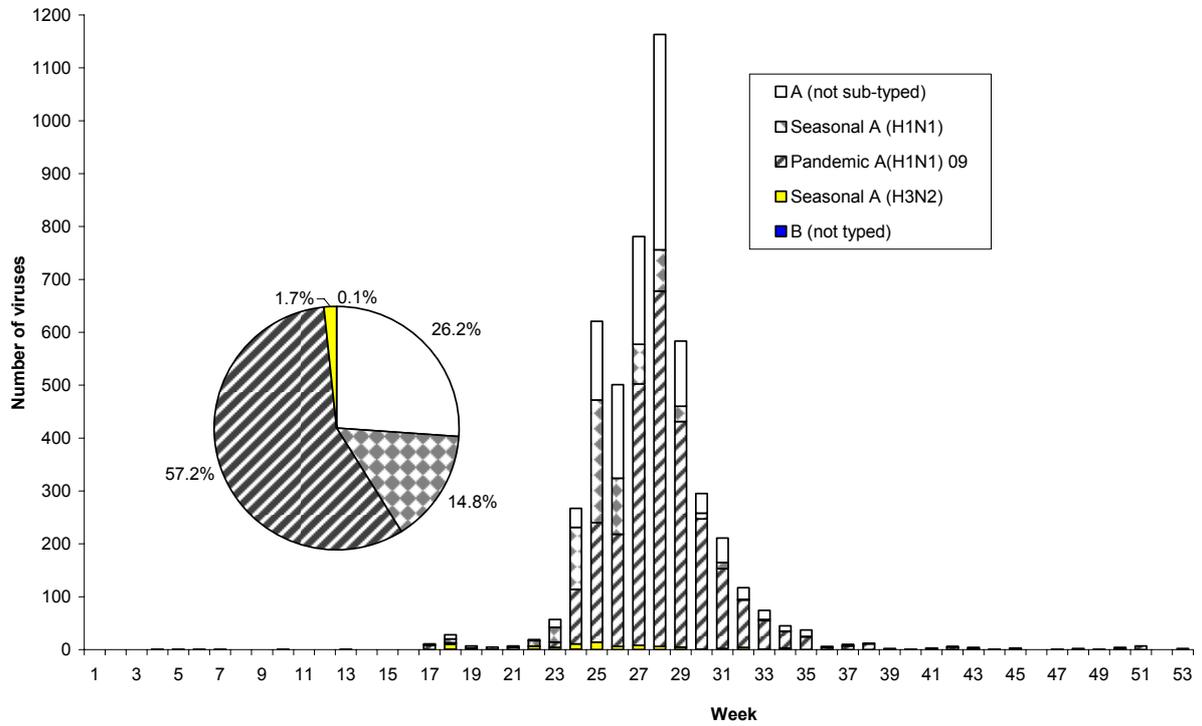


Figure 16. Total influenza virus viruses by type and week specimen taken, 2009

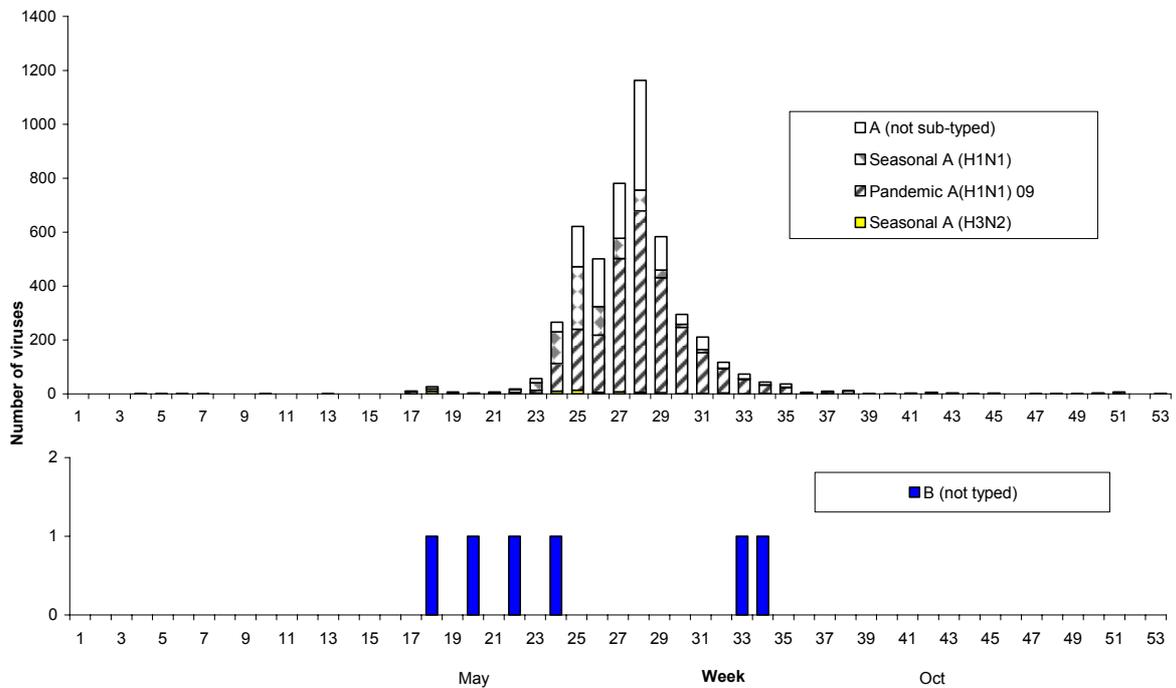
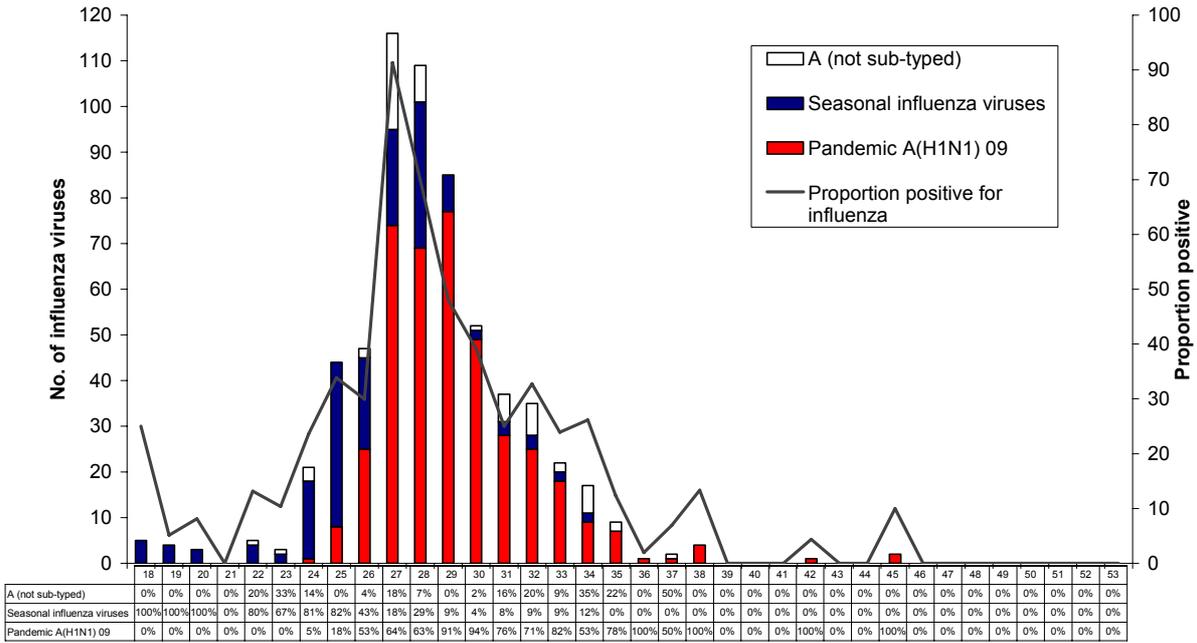


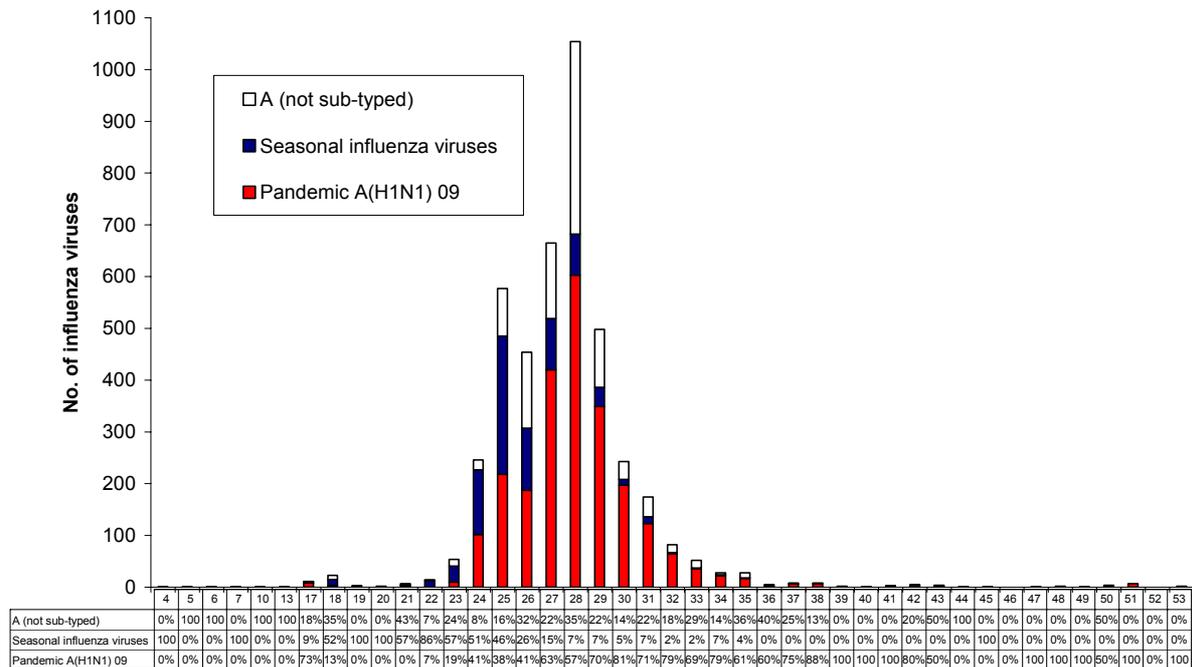
Figure 17 shows the temporal distribution of influenza viruses for sentinel surveillance from weeks 18-53. The pandemic A(H1N1) 09 virus has rapidly overtaken existing seasonal influenza viruses. In a period of three weeks, the pandemic A(H1N1) 09 virus has jumped from 5% in week 24 (8-14 June) to 64% in week 27 (29 June – 5 July) and 63% in week 28 (6-12 July) among all influenza viruses identified, becoming the predominant strain in New Zealand.

Figure 17. Total influenza viruses from sentinel surveillance by type and week reported, 2009



The temporal distribution is shown in Figure 18 for influenza viruses reported by type and subtype for each week from non-sentinel surveillance from weeks 7-53. Again, the pandemic A(H1N1) 09 virus has rapidly outnumbered existing seasonal influenza viruses. In a period of four weeks, the pandemic A(H1N1) 09 virus has increased from 7% in week 24 (8-14 June) to 63% in week 27 (29 June-5 July) and 57% in week 28 (6-12 July) of all influenza viruses identified, becoming the predominant strain in New Zealand.

Figure 18. Total influenza viruses from non-sentinel surveillance by type and week reported, 2009

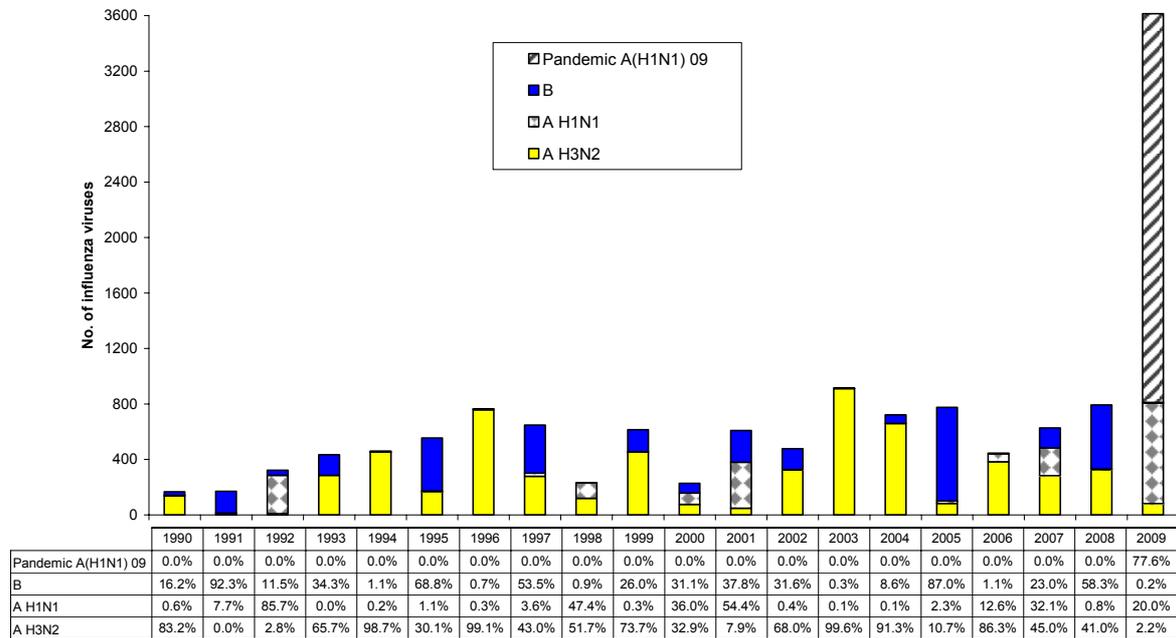


6.2. Predominant strain during 1990-2009

Figure 19 shows the number and percentage of typed and subtyped (not total) influenza viruses from 1990 to 2009. There are noticeable changes in terms of predominant patterns.

- Pandemic A(H1N1) 09 strain has become the predominant strain in 2009.
- Seasonal influenza A(H1N1) strain predominated in three seasons (1992, 2000 and 2001) with associated relatively low hospitalisations (193 in 1992, 228 in 2000 and 379 in 2001).
- Seasonal influenza A(H3N2) strain predominated for 11 seasons (1990, 1993, 1994, 1996, 1998, 1999, 2002, 2003, 2004, 2006, and 2007). A/Fujian/411/02 (H3N2)-like strain predominated in 2003 with the highest recorded hospitalizations during 1990-2008. A A/Wuhan/359/95 (H3N2)-like strain predominated in 1996 with associated 94 deaths (93 out of 94 deaths occurred for people aged 65+).
- Influenza B strains predominated for five seasons (1991, 1995, 1997, 2005 and 2008). B/HongKong/330/2001-like strain (B-Victoria lineage) predominated in 2005 and the disease burden was high in children aged 5-19 years with associated deaths in three children.

Figure 19. Influenza viruses by type, 1990-2009



6.3. Pandemic A(H1N1) 09

Representative pandemic A(H1N1) 09 isolates (400) were antigenically subtyped. Some of these isolates were also sent to WHO Collaborating Centres, WHOCC-Melbourne and WHOCC-CDC-Atlanta. Results from these centres all indicated that New Zealand isolates were homogeneous and no drift was observed. New Zealand isolates were antigenically closely related to the pandemic A(H1N1) 09 vaccine candidate strain A/California/7/2009 (H1N1).

Genetic analysis of the hemagglutinin (HA) gene of representative pandemic A(H1N1) 09 virus showed that the New Zealand isolates were homogeneous and stable (Appendix-Figure 1). Genetic analysis of the neuraminidase (NA) gene of representative pandemic A(H1N1) 09 virus showed that the New Zealand isolates were also homogeneous and stable (Appendix-Figure 2). No H275Y mutations were detected, suggesting they were sensitive to oseltamivir.

6.4. Seasonal influenza A(H1N1)

Representative seasonal influenza A(H1N1) isolates (160) were antigenically subtyped. Some of these isolates were also sent to WHOCC-Melbourne and WHOCC-CDC-Atlanta. Results from these centres all indicated that New Zealand isolates were antigenically closely related to the reference strain A/Brisbane/59/2007 (H1N1).

Genetic analysis of the neuraminidase (NA) gene of representative seasonal influenza A(H1N1) strains. Appendix-Figure 3 showed that all New Zealand isolates tested had H275Y mutations, suggesting they were resistant to oseltamivir.

6.5. Influenza A(H3N2)

Three representative seasonal influenza A(H3N2) isolates were antigenically subtyped. These isolates were also sent to WHOCC-Melbourne. Two early isolates were low reactors against the reference strain A/Brisbane/10/2007 (H3N2), indicating these two isolates were antigenically drifted away from A/Brisbane/10/2007 (H3N2)-like strain. One late isolate was antigenically closely related to A/Perth/16/2009-like strain.

6.6. Influenza B

There were only six influenza B viruses identified in 2009 and no viral isolate was obtained for antigenic typing.

6.7. Oseltamivir resistance monitoring

Since January 2008, a global emergence and rapid spread of oseltamivir-resistant seasonal influenza A(H1N1) viruses has been observed. During the 2009 winter season in New Zealand, a total of 28 seasonal A(H1N1) viruses have been tested for the H275Y mutation (histidine-to-tyrosine mutation at the codon of 275 in N1 numbering) which is known to confer resistance to oseltamivir. All 28 viruses had the H275Y mutation. In addition, a total of 25 seasonal A(H1N1) viruses were tested using a phenotypic assay called fluorometric neuraminidase inhibition assay. The results of the fluorometric neuraminidase inhibition assay indicated that these viruses had highly reduced sensitivity to oseltamivir with IC50 values in the range of 305-7912 nM, typical of the recently global emerging oseltamivir-resistant A(H1N1) viruses. (Table 4).

Six pandemic A(H1N1) 09 viruses were sequenced to see whether they possess the H275Y mutation. Among these viruses, three were from samples collected in April 2009 and another three viruses were from samples collected in late June 2009. All six viruses did not possess the H275Y mutation. This indicates that these viruses are sensitive to oseltamivir. In addition, a total of 521 pandemic A(H1N1) 09 viruses were tested using the phenotypic assay and all 521 viruses were sensitive to oseltamivir with IC50 values in the range of 0.2 to 1.4 nM (Table 3).

Table 3. Oseltamivir resistance, 2006-2009

Influenza type/subtype	Seasonal A(H1N1)				Pandemic A(H1N1) 09
	2006	2007	2008	2009	
Year	2006	2007	2008	2009	2009
Number of viruses	17	138	4	25	521
Mean IC50*	1.84	0.83	728	1399	
Std. dev.	0.71	0.63	136	1990	0.392
Min IC50	0.25	0.01	547	305	
Max IC50	3.099	4.219	870	7912	0.231

*IC50: Concentration of oseltamivir (nM) at which there is 50% inhibition of neuraminidase activity.

7. Vaccine strain recommendations for Southern Hemisphere

In October 2009, the Australian Influenza Vaccine Committee (AIVC), with a New Zealand representative, met to decide on the composition of the influenza vaccine for the 2009 winter season for New Zealand, Australia and South Africa. During these discussions, the following trends were noted.

7.1. Influenza A(H1N1)

The epidemiological data from the New Zealand 2009 influenza season and worldwide indicate that the pandemic A(H1N1) 09 virus became the predominant circulating strain. The antigenic data from New Zealand isolates indicate that the current circulating pandemic A(H1N1) 09 viruses are homogeneous, closely matching the vaccine candidate strain A/California/7/2009 (H1N1). Sequence analysis of the pandemic A(H1N1) 09 virus also indicated that they were genetically homogeneous. The limited serological study for New Zealanders conducted in WHOCC-Melbourne and in the National Influenza Centre at ESR indicated that the pandemic A(H1N1) 09 virus does not cross-react with seasonal A(H1N1) viruses. The epidemiological, virological and serological data clearly suggests a need to have the pandemic A(H1N1) 09 strain to be included in the seasonal influenza vaccines.

On the other hand, seasonal influenza A(H1N1) viruses were associated with outbreaks during the early winter season in New Zealand and the numbers of viruses diminished significantly by August. The majority of recent viruses were antigenically and genetically similar to the vaccine virus A/Brisbane/59/2007.

Based on the southern hemisphere and global data, the WHO Consultative Group and AIVC recommended vaccines containing a pandemic influenza A/California/7/2009 (H1N1)-like strain as the H1 component for 2010.

7.2. Influenza A(H3N2)

Influenza A(H3N2) has been frequently associated with severe disease and excess mortality in high-risk groups. This subtype has also shown the greatest tendency for antigenic drift as illustrated by the frequency of vaccine formulation changes recommended by the WHO and the AIVC.

The WHOCC-Melbourne Melbourne has analysed 690 A(H3N2) isolates from 16 countries since January 2009. Most recent isolates had antigenically drifted away from A/Brisbane/10/2007 (H3N2)-like strain and were antigenically closely related to A/Perth/16/2009-like strain. Current vaccines containing the A/Brisbane/10/2007 (H3N2) antigen stimulated HA antibodies against recent influenza A(H3N2) isolates that were somewhat lower in titre and frequency than to the vaccine virus. As a result, an A/Perth/16/2009-like strain was recommended by WHO and the AIVC to be the H3 component of the influenza vaccine for southern hemisphere for 2010.

7.3. Influenza B

Two distinct lines of influenza B have co-circulated in many countries during recent years. This dates from the late 1980's when the B/Panama/45/90 variant of influenza B was first observed. This strain and its further variants-B/Yamagata/16/88 lineage (most recently representative strain-B/Shanghai/361/2002) spread worldwide whereas strains of the previous B/Victoria/2/87 lineage viruses continued to circulate in Asia and subsequently underwent

independent evolution as an antigenically distinct lineage (most recent representative strain-B/Malaysia/2504/2004). For reasons not wholly understood, these remained geographically restricted to Asia until 2001. In 2002 the B/Victoria-lineage strains became the predominant viruses worldwide. In 2009, varying proportions of the two lineage viruses were seen in many countries with B/Yamagata lineage strains predominating in New Zealand and Australia but with small numbers.

Both recent B/Victoria-like strains (B/Brisbane/60/2008 is the current reference strain) and B/Yamagata-like strains (B/Florida/4/2006 is the current reference strain) continued to be isolated worldwide in 2009. Varying proportions of the two lineages were seen in many countries with mainly B/Victoria-like lineage strains circulating in southern hemisphere countries. The majority of isolates were antigenically closely related to B/Brisbane/60/2008-like strain. Current vaccines containing B/Brisbane/60/2008 antigen stimulated HA antibodies that were similar in titre to recently isolated B/Brisbane/60/2008-like viruses. Based on the southern hemisphere and global data, the WHO Consultative Group and AIVC recommended vaccines containing a B/Brisbane/60/2008-like strain to be the B component of the influenza vaccine for southern hemisphere for 2010.

In summary, the AIVC agreed to adopt the recommendations made by the WHO consultation group as per the box below.

The recommended influenza vaccine formulation for New Zealand in 2010 is:

- **A(H1N1) an A/California/7/2009 (H1N1) - like strain***
- **A(H3N2) an A/Perth/16/2009 (H3N2) - like strain**
- **B a B/Brisbane/60/2008 - like strain**

***Note: A/California/7/2009 is a pandemic A(H1N1) 09 strain**

8. Discussion

Based on sentinel consultation data using a set of threshold values, the peak of influenza activity in 2009 is described as high. When the peak of weekly consultation rates for ILI from 1997 to 2009 are compared, 2009 has the highest while 2000 had the lowest level of influenza activity.

It is estimated that ILI resulting in a visit to a GP affected over 116 335 New Zealanders in 2009 or about 2.7% of the population. The number of cases reported through the sentinel network is likely to be a considerable underestimate of the true number, as many people do not consult a GP when they have an ILI. In particular, public health advice during the management phase of the pandemic is not to go to a GP unless the individual is getting more seriously ill or is in a higher risk group for more serious illness.

The sentinel GP surveillance, one of the syndrome surveillance systems in New Zealand, has operated continuously in New Zealand since its establishment in 1991[3]. It is a relatively stable system to monitor year-to-year disease trends in the community. It is one of the best means for monitoring the burden of disease in the community during an epidemic. Active syndromic surveillance systems are being increasingly utilised to detect emerging and re-emerging pathogens.[12, 13] Enhanced influenza surveillance is also a key strategy for improving New Zealand's preparedness for pandemic influenza.[14]. The usefulness of the GP sentinel surveillance during a pandemic has been tested in 2009. The GP sentinel surveillance system has been adapted to monitor the early and late stages of a pandemic. The sensitivity of sentinel surveillance during the containment phase of the pandemic is encouraging but requires further evaluation. When enhanced public health surveillance targeting returning travellers from affected areas indicated some evidence of transmission within the community in weeks 23-24, the ILI consultation rate of sentinel surveillance surpassed the baseline to 56.1 per 100 000 patient population and the pandemic A(H1N1) 09 virus was also detected from sentinel surveillance during week 24 (8-14 June). The performance characteristics of sentinel surveillance (sensitivity, specificity, representativeness and robustness) for a mild pandemic at a national and regional level during the containment phase for early detection as well as the management phase for monitoring should be evaluated against other influenza surveillance systems.

Consultation rates varied greatly among health districts. The use of a common case definition for the purposes of surveillance should minimise regional differences in the criteria for diagnosis of influenza. However, in health districts where only a single practice or a small number of practices participate, consultation rates are more likely to be subject to variations in individual diagnostic practices. The health district reporting the highest rate was South Auckland (150.8 per 100 000 patient population).

Figure 9 compares ILI consultation rate in the community among different age groups. Caution is required in interpretation of this data. Because no demographic information on the total patient population is provided from each practice, it was assumed that the total patient population of all sentinel practices collectively had the same age distribution as the New Zealand population. However, individual practices may have differing age distribution of their patient population when compared to census data. Therefore it would be useful to have the demographic information on the total patient population from sentinel GPs in order to obtain the accurate ILI consultation rates among different age groups.

One of the strengths of the sentinel surveillance system in New Zealand is the combination of disease surveillance (ILI) and strain surveillance (virological identification). A definitive diagnosis of influenza requires laboratory confirmation, since clinical diagnosis on the basis of clinical symptoms is not highly specific. In fact, sentinel surveillance is the only syndromic surveillance system that obtains appropriate respiratory swabs for verification of clinical diagnosis. Consequently, an important part of the sentinel system is for GPs to take nasopharyngeal and/or throat swabs from patients presenting with an ILI. In the current protocol, three swabs are required from each GP for the first patient seen on Monday, Tuesday and Wednesday of each week. An evaluation should be conducted to see whether three swabs/week/GP is sufficient enough to provide information for predominant circulating strains at a national and regional level in a temporal fashion during influenza epidemic and pandemic.

A global emergence and rapid spread of oseltamivir-resistant influenza A(H1N1) viruses carrying a neuraminidase gene with an H274Y (Histidine to Tyrosine mutation at the codon of 274 by N2 numbering) amino acid substitution has been observed since January 2008. These oseltamivir-resistant seasonal influenza A(H1N1) viruses have spread to New Zealand since 2008 and all seasonal influenza A(H1N1) viruses (25) tested in 2009 showed that they were resistant to oseltamivir. On the other hand, all pandemic A(H1N1) 09 viruses (521) tested showed that they were sensitive to oseltamivir. The oseltamivir resistance viruses pose challenges for the selection of antiviral medications for treatment and chemoprophylaxis of influenza. They also pose potential risks for generating a new variant of pandemic A(H1N1) 09 virus carrying oseltamivir resistant gene via co-infection and reassortment. It has become increasingly important to establish and sustain a national antiviral monitoring program in New Zealand which would provide timely surveillance information to assist clinicians for choosing appropriate antiviral agents for their patients and assist public health officials for evidence-based decision on antiviral stockpiling and antiviral usage during a pandemic or epidemic. It also provides compelling reasons for clinicians to test patients for influenza virus infection in order to select appropriate antiviral medications.

Although the sampling criteria of non-sentinel surveillance were not consistent, this surveillance is also essential during a pandemic. When comparing age data for positive influenza virus isolates from sentinel and non-sentinel surveillance (Figure 8), the non-sentinel system tends to detect more influenza viruses in the under 5's and over 65 years olds than that of the sentinel system. This may reflect the fact that influenza presented more severely in the very young and the elderly populations, resulting in hospitalisations or it may reflect a greater reluctance among sentinel GP's to take swabs from very young children and elderly patients. Overall, these data indicate that sentinel and non-sentinel surveillance complement each other, providing a better description of influenza disease burden for the different age groups. In addition, in order to understand specificity of non-sentinel surveillance, it is essential to collect information on total swabs being tested for influenza.

For sentinel surveillance from May to December 2009, four virology laboratories tested 1993 respiratory specimens for influenza viruses and 624 (31.3%) specimens were positive for influenza viruses. However, the influenza isolation rate varied among different health districts (Figure 6). Some health districts had an influenza virus isolation rate lower than the national average of 31.3%. Many factors could contribute to low isolation rates, including sampling techniques. Sampling of the respiratory tract for clinical viral isolation should maximise the harvest of virally infected columnar epithelial cells. Ideally, nasopharyngeal washes or aspirates would be the best specimens since they contain a higher cellular content

than nasopharyngeal swabs.[14] By comparison, throat swabs or throat washings are of limited use in the diagnosis of influenza since the majority of cells captured by this technique are squamous epithelia. However, a combined nose (i.e. nasopharyngeal) and throat swab can be a useful specimen for influenza virus isolation and it is selected for influenza surveillance because of its convenience. Nasopharyngeal swabs should be cotton-, rayon- or dacron-tipped, plastic-coated swabs. The swab should be inserted deeply into the nasopharynx, rotated vigorously to collect columnar epithelia cells, removed, replaced into viral transport medium (VTM), chilled and couriered to the virology laboratory without delay.

Since 2001, the four virology laboratories have been using the ESR-designed electronic influenza virus input form for data entry. This process requires the retrieval of the necessary demographic data from the hospital information system and re-keying this information onto ESR virus input form. This is time-consuming system and inevitably creates data error. Timely reporting for virology weekly report has been one of the biggest challenges during the pandemic response. Advances in information transfer using systems such as Health-Link would greatly streamline this process.

Overall, the sentinel surveillance system is very useful in measuring disease burden in the community. However, the result of sentinel surveillance has some limitations. For example, sentinel data cannot be extrapolated precisely to the rest of the population since not all people suffering from influenza in the community attend their GP. Also, the sentinel general practices are not truly representative. Practices are not randomly selected and consist of GPs who participate through goodwill, usually due to an interest in influenza surveillance. In addition, ILI consultation rates use the number of patients in the practice as the denominator. These data are provided at the beginning of the season and do not take into account the number of patients entering or leaving the practice during that time. GPs may also see “casual” patients who are not part of the practice population. Despite these problems, the system is useful in meeting the purposes of influenza surveillance, as described in the introduction. Importantly it is the only influenza surveillance system that obtains appropriate naso-pharyngeal swabs for verification of clinical diagnoses.

As the impact of influenza can be reduced by annual immunisation, this information is particularly important in raising awareness of the disease amongst health professionals and the public, and planning vaccine formulation and delivery. Influenza vaccines are recommended for persons at risk of developing complications following infection because of their age or because of some underlying chronic condition, and are available free each year. [15]. In 1997, New Zealand introduced free influenza vaccination to all New Zealanders aged 65 years and older, and set a target of 75% coverage for the year 2000. In 1999 free vaccination was extended to include those under 65 years with certain chronic medical condition.[15, 16] National Influenza Immunisation Strategy Group (NIISG) was established in 2000 with the purpose of improving coverage through public and healthcare provider education. The “Influenza Kit” and “Education Manual” were specifically developed for increasing health professional enthusiasm and support for immunisation. Other education resources include pamphlets, radio and television advertising, healthcare professional education sessions and developing close links with the National Influenza Pandemic Planning Committee. Media evaluation and research has been initiated into attitudes to influenza immunisation in primary health providers and those 65 years and older.[17] A national approach to promotion, coupled with local initiatives, has been a key to lifting coverage to 65% amongst those at greatest risk, people 65 year and older. Quality coverage data are

essential for the continuing development of this programme, while continuing surveillance ensures the provision of effective vaccines to reduce the burden of influenza in New Zealand.

9. References

1. *Report of the WHO/GEIG Informal Consultation on the Standardization and Improvement of Influenza Surveillance, Monaco.* 1991.
2. Dedman DJ, et al., *Influenza surveillance in England and Wales: October 1996 to June 1997.* CDR Rev 1997. **13**: p. R212-219.
3. Jennings L, et al., *Influenza surveillance and immunisation in New Zealand, 1990-1999.* NZPHR, 2001. **8**: p. 9-12.
4. Ministry of Health, *Influenza vaccine. [Circular letter] to health professionals.* 1996.
5. Jennings LC and Baker S. Government policy change in 1997 was essential for the implementation of an influenza vaccination strategy for New Zealand, ed. Osterhaus ADME, et al, and editors. 2001: Elsevier.
6. Huang, Q.S., Lopez, L.D., McCallum, L., Adlam B., *Influenza surveillance and immunisation in New Zealand, 1997-2006.* Influenza and Other Respiratory Viruses, 2008. **2**(4): p. 139-145.
7. Rana A, et al., *Surveillance for unexplained deaths and critical illnesses due to possibly infectious causes, United States, 1995–1998.* EID, 2002. **8**: p. 145-153.
8. *Outbreaks of avian influenza A (H5N1) in Asia and interim recommendations for evaluation and reporting of suspected cases—United States, 2004.* MMWR, 2004. **53**: p. 97-100.
9. WHO. *Influenza Pandemic Preparedness Plan: The role of WHO and guidelines for national and regional planning. WHO/CDS/CSR/EDC/99.1.* in Geneva: WHO, April 1999.
10. Wilson, N., et al., *Interpreting Google flu trends data for pandemic H1N1 influenza: the New Zealand experience.* Euro Surveill, 2009. **14**(44).
11. Baker, M.G., et al., *Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009.* Euro Surveill, 2009. **14**(34).
12. Hall, R.J., et al., *Pandemic influenza A(H1N1)v viruses currently circulating in New Zealand are sensitive to oseltamivir.* Euro Surveill, 2009. **14**(30): p. 19282.
13. *Surveillance for the 2009 pandemic influenza A (H1N1) virus and seasonal influenza viruses - New Zealand, 2009.* MMWR Morb Mortal Wkly Rep, 2009. **58**(33): p. 918-21.
14. Monte AS and Kioumeh F, *The Tecumseh study of respiratory illness. IX Occurrence of influenza in the community.* AMJE, 1975. **102**: p. 553-563.
15. Centers for Disease Control, *Update: influenza-associated deaths reported among children aged <18 years - United States, 2003-4 influenza season.* MMWR, 2003. **52**: p. 1286-1288.
16. Zambon M, *Textbook of Influenza.* Laboratory Diagnosis of Influenza, ed. W.R. Nicholson KG, Hay AJ, eds. 1998: London: Blackwell Science Ltd.
17. Weir R, Brunton C, and Jennings LC, *Attitudes to influenza immunisation amongst General practitioners, Practice nurses and those 65 years and older,* in *New Zealand Immunisation Conference.* 2002: Christchurch.

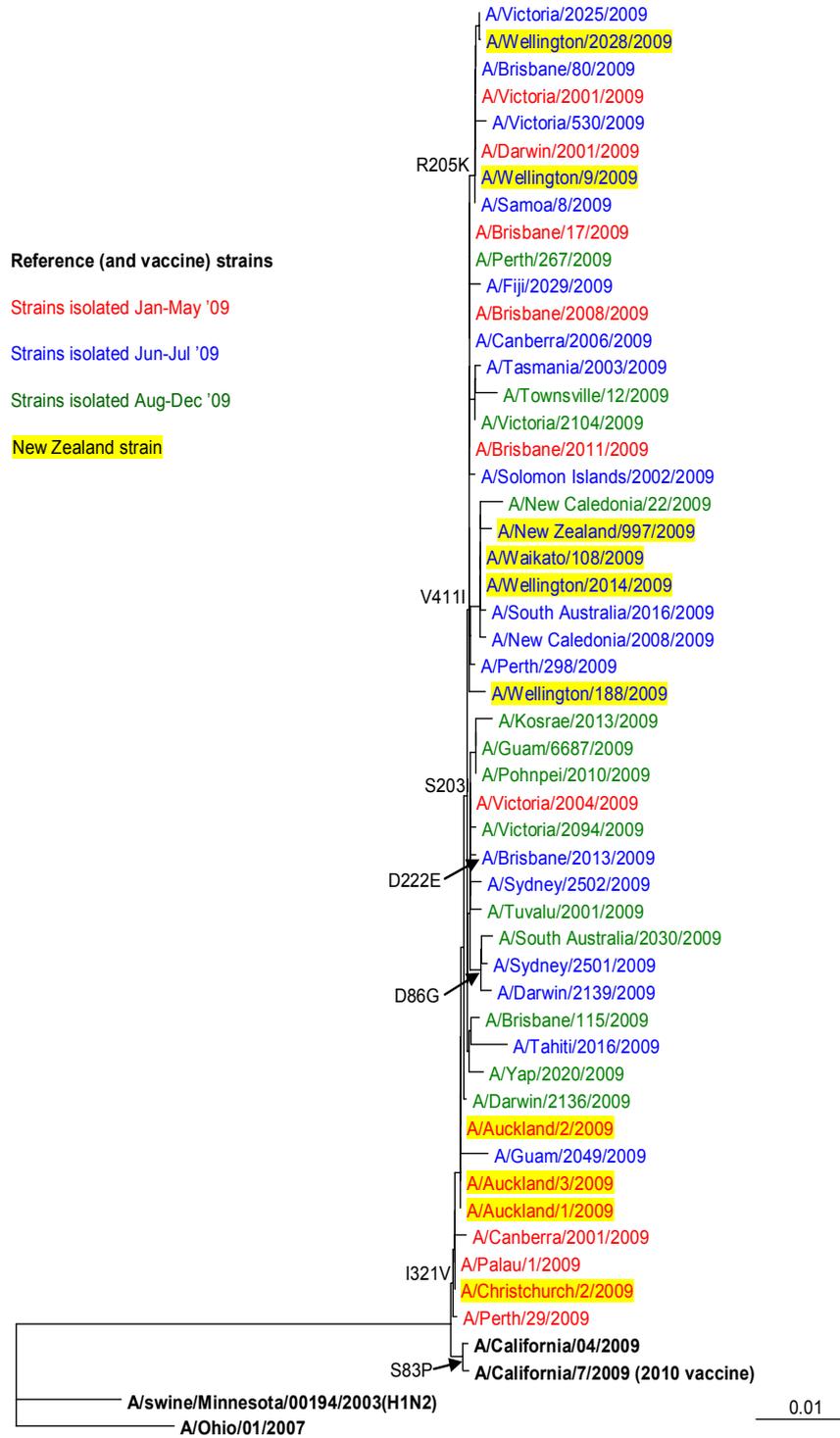


Figure 1. Phylogenetic relationships among pandemic A/H1N1 2009 influenza HA genes from 2009. Scale is represented as substitutions per site. Amino acid mutations are numbered according to A/California/4/2009. No viruses contained a D222G mutation.



Figure 2. Phylogenetic relationships among pandemic A/H1N1 2009 influenza NA genes from 2009. Scale is represented as substitutions per site. Amino acid mutations are numbered according to A/California/04/2009. No strains represented here contain the H275Y mutation.

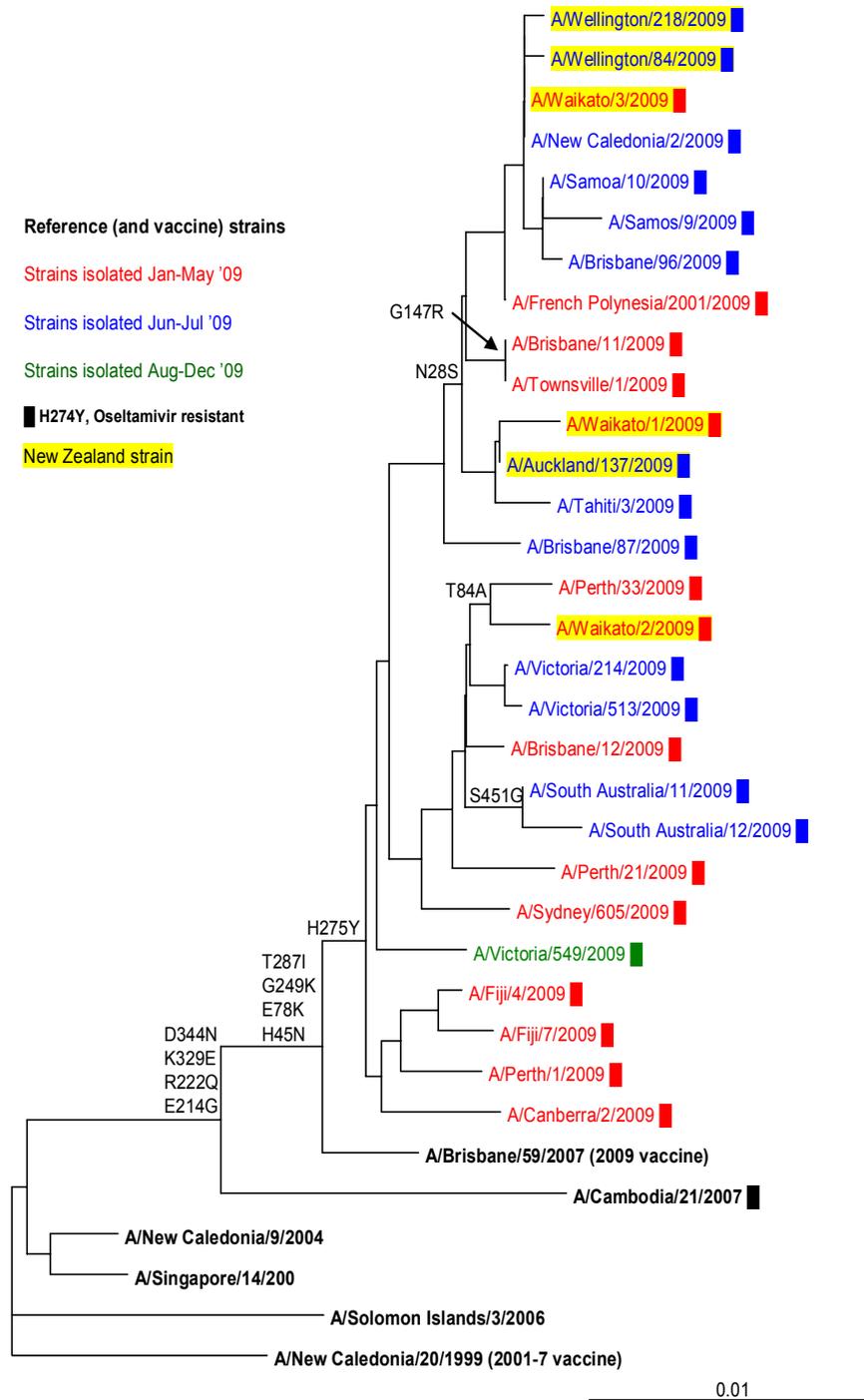


Figure 3. Phylogenetic relationships among seasonal influenza A/H1N1 NA genes from 2009. Scale is represented as substitutions per site. Virus clades are indicated to the left in bold. Amino acid mutations are numbered according to H1 numbering.