

# **Influenza in New Zealand 2008**

Prepared as part of the Ministry of Health Contract  
(2008/09 Service Description: NCBID Virology)

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March 2009

Client Report  
FW0925

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## **ACKNOWLEDGEMENTS**

We would like to thank the general practitioners and their staff, the local surveillance coordinators, regional virology laboratories (Auckland, Waikato, Christchurch and Dunedin), and Medical Officers of Health involved in influenza surveillance for their time and cooperation. We would also like to acknowledge the WHO National Influenza Centre at ESR for the provision of laboratory data, Information Management group for the assistance in the running of the electronic flu database, and Dr Bruce Adlam for peer review. A special thanks to the WHO Collaborating Centre in Melbourne for providing further characterisations on the influenza viruses. A special thanks to Chris Lewis for providing influenza hospitalisation data and Dr Lance Jennings for providing influenza immunisation coverage data.

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## SUMMARY

During the 2008 winter season, 3 945 consultations for influenza-like illness (ILI) were reported from a national sentinel network of 85 general practices. It is estimated that ILI resulting in a visit to a general practitioner affected over 47 697 New Zealanders (1.2% of total population) during the season, compared with an estimated 32 771 in 2007. Compared with the 1997-2007 period, the influenza activity in 2008 is described as moderate with two peaks, one in the middle of July and another in the middle of August. The ILI consultation rates varied greatly among Health Districts with the highest rates being reported from Northland and Eastern Bay of Plenty Health Districts. In 2008, influenza A(H3N2) viruses predominated in June/July while influenza B predominated in August/September. Among all typed and subtyped viruses, influenza B/Victoria lineage viruses (44.6%) was the predominant strain with co-circulation of other strains---A(H3N2) (41.0%), B/Yamagata lineage (13.6%) and A(H1N1) (0.8%). In 2008, oseltamivir-resistant influenza A(H1N1) viruses were identified in New Zealand for the first time. Significant antigenic drift was observed among the A(H1N1) viruses, resulting in the update of the H1 vaccine component as A/Brisbane/59/2007 (H1N1) -like strain for 2009. This vaccine component is also protective against oseltamivir-resistant influenza A(H1N1) viruses.

## RECOMMENDATIONS

1. That the sentinel influenza surveillance system be enhanced using standard surveillance system criteria and benchmarked against international best practice. This should include the review of:
  - The case definition for ILI.
  - The methods of specimen collection from cases.
  - Extending the system beyond the period of May to September in order to monitor influenza activity beyond this period.
  - Greater use of electronic approaches to data collection and dissemination in order to ease workload on Public Health Services (PHSs) and GPs and improve timeliness of ILI reporting.
  - Greater use of electronic approaches to improve recording of swabs sent and received so virus detection rates can be calculated with greater accuracy.
  - Development of electronic information transfer systems such as Health-Link so influenza virology data can be captured accurately and efficiently.
  - Collection of the information on antiviral medication in the specimen request form in the surveillance program.
  - Obtaining the demographic information for the total patient population from each sentinel GP in order to calculate accurate ILI rates among different age groups.
  - Exploring other complimentary surveillance approaches for detecting early cases of ILI.
  - A national monitoring scheme for oseltamivir-resistant influenza viruses. This is now essential as it provides public health authorities and clinicians with the information to make informed decisions for the use of influenza antiviral medications in the setting of oseltamivir resistant influenza viruses.
2. That the sentinel influenza surveillance system be reviewed in terms of its potential during early, peak and late pandemic periods, also its feasibility for being classified as a laboratory notifiable disease.
3. That the sentinel influenza surveillance system be reviewed in terms of its potential for surveillance of other diseases and syndromes of public health importance.

## 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. Influenza is not a notifiable disease in New Zealand.

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 2008, including some comparisons with previous years. It also includes information on hospital admissions for influenza (obtained from NZHIS) and influenza immunisation coverage data (obtained from Health Benefits Limited).

## 2. METHODS

### 2.1. General Practice Sentinel Surveillance – Consultation and Isolate Data

The current sentinel surveillance system commenced in 1991 as part of the WHO Global Programme for Influenza Surveillance. It is operated nationally by the WHO National Influenza Centre at ESR and locally by influenza surveillance co-ordinators in the Public Health Services. Sentinel surveillance normally operates from May to September.

In 2008, national influenza sentinel surveillance was undertaken from May to September (week 18 to week 40 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 Public Health Service (approximately 1:50 000 population).

General practitioners (GPs) were required to record the number of consultations for influenza-like illness each week and the age group (current categories as per Figure 8) of each of these suspected cases on a standardised form.

Influenza-like illness (ILI) was defined by a standardised case definition:

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

Each practice was also asked to collect respiratory samples (nasopharyngeal or throat swab) from one patient (preferably the first) seen with an ILI on Monday, Tuesday and Wednesday of each week. The swabs were sent to a regional virus diagnostic laboratory and/or the WHO National Influenza Centre (NIC) at ESR for viral isolation and strain identification.

Information on the number of ILI consultations and swabs sent from each health district was forwarded to ESR by local co-ordinators each week (Monday to Sunday). ILI consultation

data was received by the following Monday to Wednesday. Likewise virology laboratories reported to ESR the total number of swabs received from each Health District, the influenza viruses identified, together with updated details on type and strain. This data was collated, analysed and reported on a weekly, monthly and annual basis.

Consultation rates were 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 was based on the New Zealand census data with the assumption that age distribution of the GP patient population was 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  $\geq 400$  indicates an epidemic level of disease.

## **2.2. Laboratory-based Surveillance – Year-round Isolate Data**

In addition to influenza viruses identified from sentinel surveillance, year-round laboratory surveillance of influenza (and other viruses) is carried out by the three regional virus diagnostic laboratories at Auckland, Waikato, 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.

The criteria for laboratory identification of influenza include the direct detection of viral antigen or isolation of the virus by culture or detection of viral nucleic acid. Virus isolation is the gold standard for influenza diagnosis, surveillance specificity and vaccine strain selection. All influenza isolates are typed and most influenza A viruses subtyped.

## **2.3. Hospitalisations**

Hospital admission data for influenza (ICD-10AM J10-J11) were extracted from the New Zealand Health Information Service's National Minimum Dataset (NMDS) for the year 2008 (by admission date). 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 is possible.

## **2.4. New Zealand Population**

Population data for each age group obtained from the Statistics New Zealand 2006 Census of Population and Dwellings were used.

## **2.5. Immunisation Coverage**

In 1997 influenza vaccination was made available free to those  $\geq 65$  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 2008 among persons  $\geq 65$  years of age.

### **3. RESULTS**

#### **3.1. Sentinel Practices**

In 2008, 85 sentinel practices were recruited from all of the 24 health districts. All PHSs began reporting by the beginning of May 2008. Some practices did not report every week. The average number of practices participating per week was 79, with an average patient population roll of 333 150, about 8.3% of the New Zealand total population.

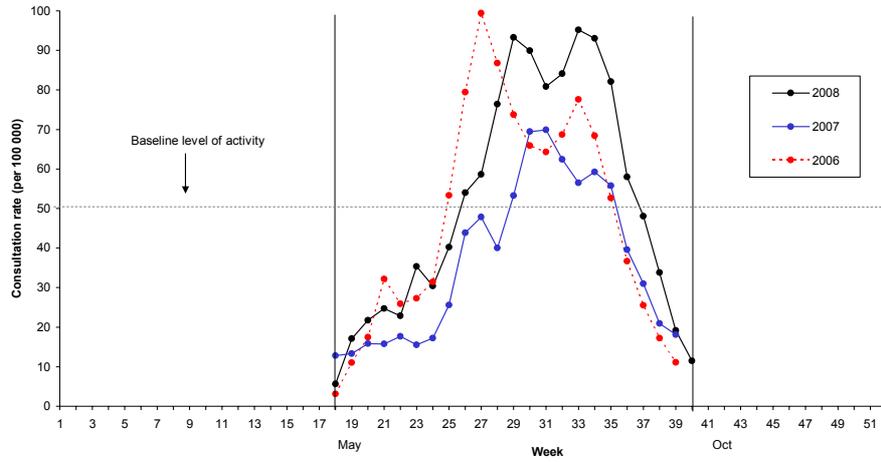
#### **3.2. Disease Burden**

From May to September 2008, a total of 3 945 sentinel consultations for influenza-like illness were reported. The cumulative incidence rate of ILI consultation for 2008 during the influenza season was 1184.2 per 100 000. This rate is higher than that of 2007 (775.0 per 100 000) and 2006 (994.8 per 100 000). The average national weekly consultation rate in 2008 was 52.4 per 100 000 patient population. This rate is higher than the average weekly rates for 2007 (37.2 per 100 000) and 2006 (48.6 per 100 000).

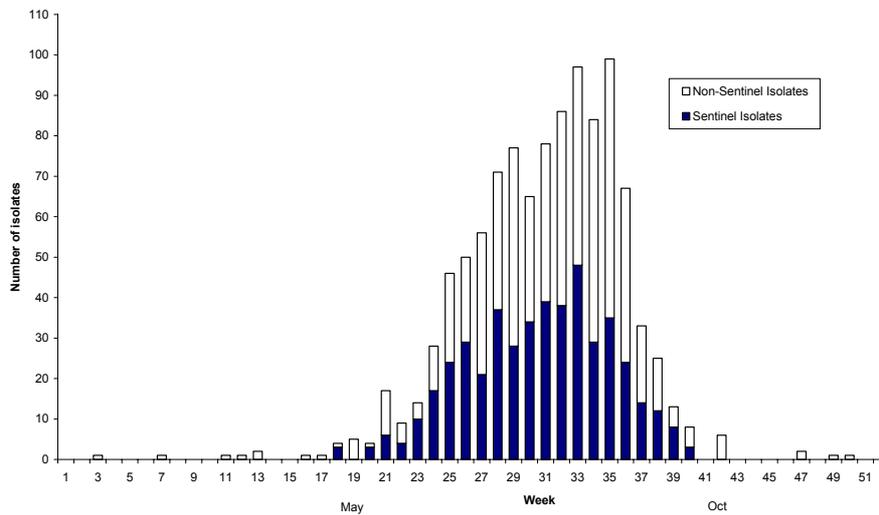
Extrapolating ILI consultations obtained from the GP patient population to the New Zealand population, it is estimated that ILI resulting in a visit to a general practitioner affected 47 697 New Zealanders during the influenza season (1.2% of total population). This is higher than the estimated 32 771 affected in 2007.

Figure 1 compares the weekly consultation rates for influenza-like illness in 2008 with 2007 and 2006. Influenza consultation rate remained at the baseline level from week 18 to 25. The consultation rates increased rapidly and remained at a high level for a broad period from week 27 (30 June-6 July) to week 36 (1-7 September) with two peaks. The first peak occurred at week 29 (14-20 July) with a consultation rate of 93.3 per 100 000 patient population. This is two weeks earlier than the peak in 2007 (week 31) and two weeks later than 2006 (week 27) with rates of 69.9 per 100 000 and 99.4 per 100 000 respectively. The second peak occurred at week 33 (11-17 August) with a consultation rate of 95.2 per 100 000 patient population. The consultation rate then declined below the baseline after week 37.

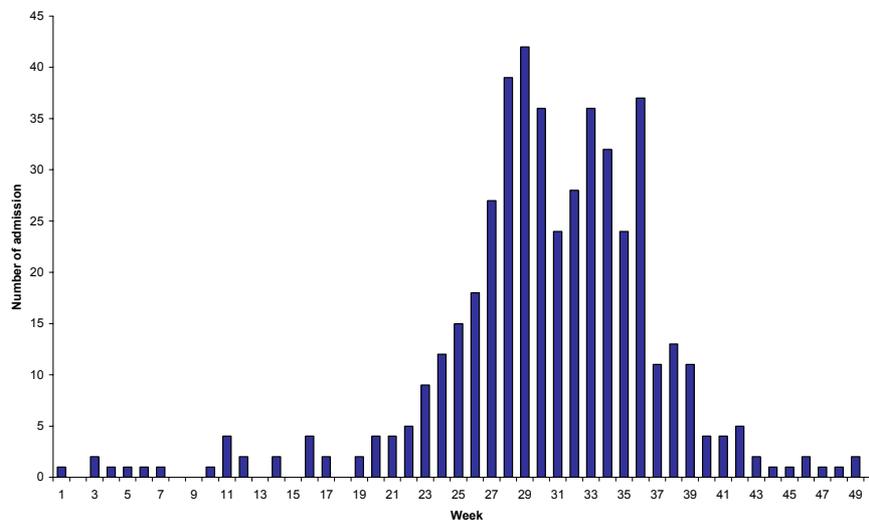
**Figure 1. Weekly consultation rates for influenza-like illness in New Zealand, 2006, 2007 and 2008**



**Figure 2. Total influenza viruses by surveillance type and week specimen taken, 2008**



**Figure 3. Influenza hospitalisation by week admitted, 2008**



A total of 1 054 influenza viruses were identified in 2008, higher than the 744 viruses in 2007 and 768 viruses in 2006. Of the 1 054 viruses, 466 came from sentinel practice surveillance during May to September. This is higher than the 239 sentinel viruses identified in 2007 and 315 viruses in 2006. There were 588 non-sentinel viruses identified in 2008, compared to 505 in 2007 and 453 in 2006.

Figure 2 shows influenza virus isolations each week throughout 2008. The biggest peak of sentinel viruses came from week 33 (48 viruses), this correlated with the biggest peak period in consultation rates (week 33). Sporadic influenza viruses were identified as early as January during the summer season, however the vast majority (1032, 97.9%) were from specimens taken during May to September. Non-sentinel viruses peaked in week 35 (64 viruses). Overall influenza viruses in 2008 were detected in the same time period as in 2007. Most sentinel and non-sentinel viruses (93.8%) came from the sentinel period (weeks 23 to 39).

In 2008, there were a total of 474 hospital admissions for influenza. This compares with 347 admissions in 2007 and 464 in 2006. Figure 3 shows these admissions by week, 87.8% (416) of which occurred during June to September. The highest number of admissions (151) occurred in July. Hospital admissions peaked in week 29, the same week as the first peak of the ILI consultation rate (week 29) and six weeks earlier than the peak of the non-sentinel influenza viruses (week 35).

### **3.3. Geographic Distribution**

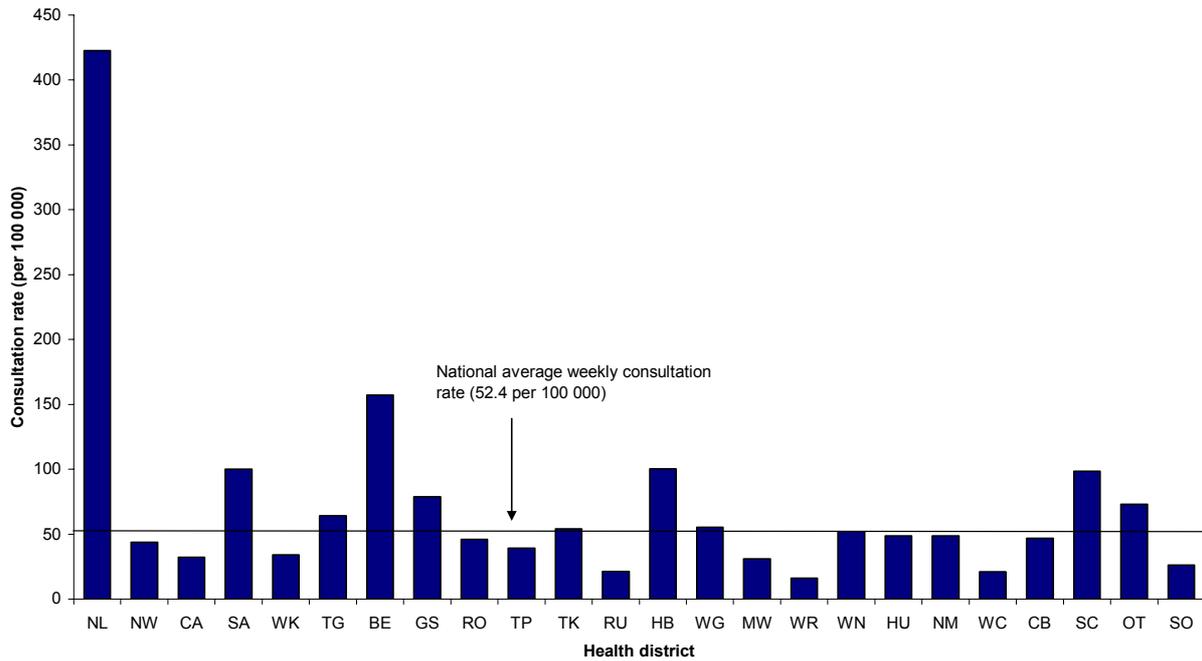
In addition to national activity, sentinel surveillance is able to provide an indication of the distribution of influenza-like illness and viral strains within New Zealand.

Figure 4 shows the sentinel average weekly consultation rates for each health district during May to September 2008. Consultation rates varied between health districts, with rates above the national average in 10 of the 24 health districts: Northland (422.5 per 100 000), Eastern Bay of Plenty (157.2 per 100 000), Hawke's Bay (100.5 per 100 000), South Auckland (100.1 per 100 000), South Canterbury (98.7 per 100 000), Gisborne (78.8 per 100 000), Otago (72.8 per 100 000), Tauranga (64.1 per 100 000), Wanganui (55.5 per 100 000), and Taranaki (54.0 per 100 000). Table 1 shows health districts codes and description.

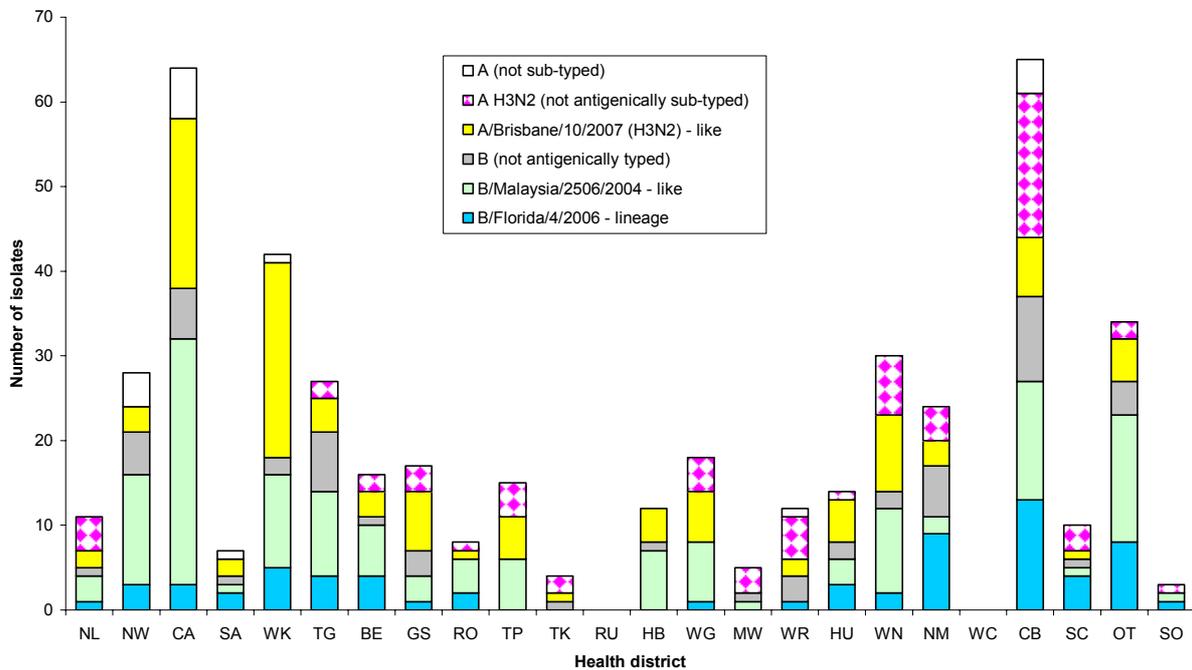
Figure 5 shows the distribution of sentinel influenza viruses based on the health district from which the specimen (swab) was taken. Most viruses came from the greater Auckland area, Canterbury, Waikato, Otago and Wellington regions. Influenza viruses were not identified in two health districts (Ruapehu--swabs sent but none detected and West Coast--no swabs received). The national virus detection rate for 2008, as illustrated in Figure 6, was 46.6% (466 viruses from 1001 swabs received) which is higher than the 2007 rate of 30.7% (778 swabs), and 2006 rate of 34.1% (924 swabs). The increase of the virus detection rate might be a result of the use of PCR detection which generally has a better sensitivity than viral isolation.

In interpreting 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 4. Sentinel average weekly consultation rate for influenza-like illness by health district, 2008**



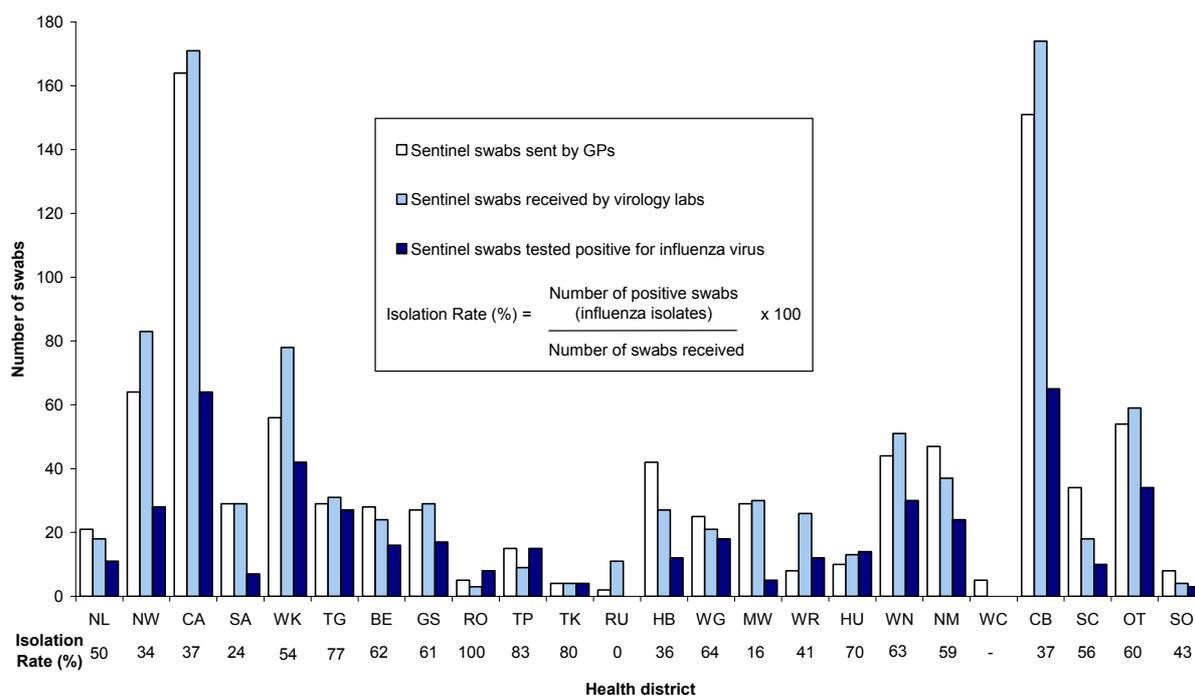
**Figure 5. Cumulative laboratory confirmed influenza viruses from sentinel surveillance by health district, May-September 2008**



**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 6. Sentinel swabs, sent, received and tested positive for influenza virus by health district, 2008**



### 3.4. Age Distribution

Figure 7 compares the morbidity rates in 2008 by age group. In 2008, the highest morbidity rates occurred in children aged under one year (120.1 per 100 000), followed by children aged 1-4 (28.8 per 100 000) and adults aged 65+ years (15.5 per 100 000).

**Figure 7. Morbidity rate by age group, 2008**

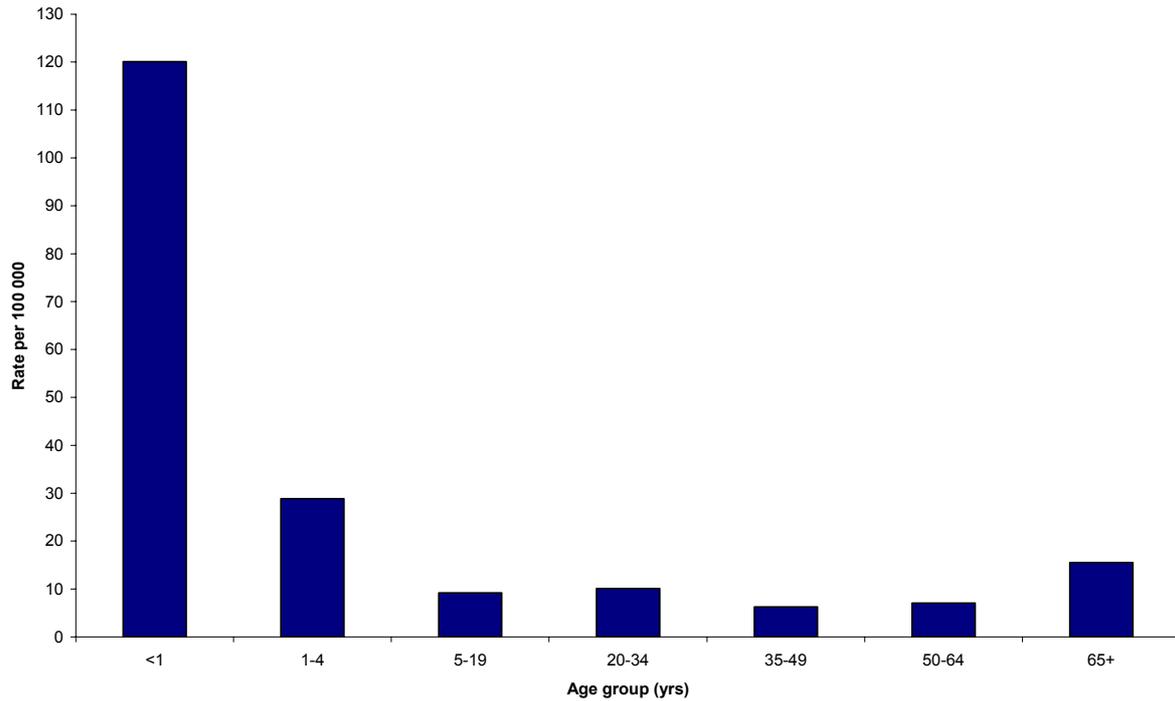
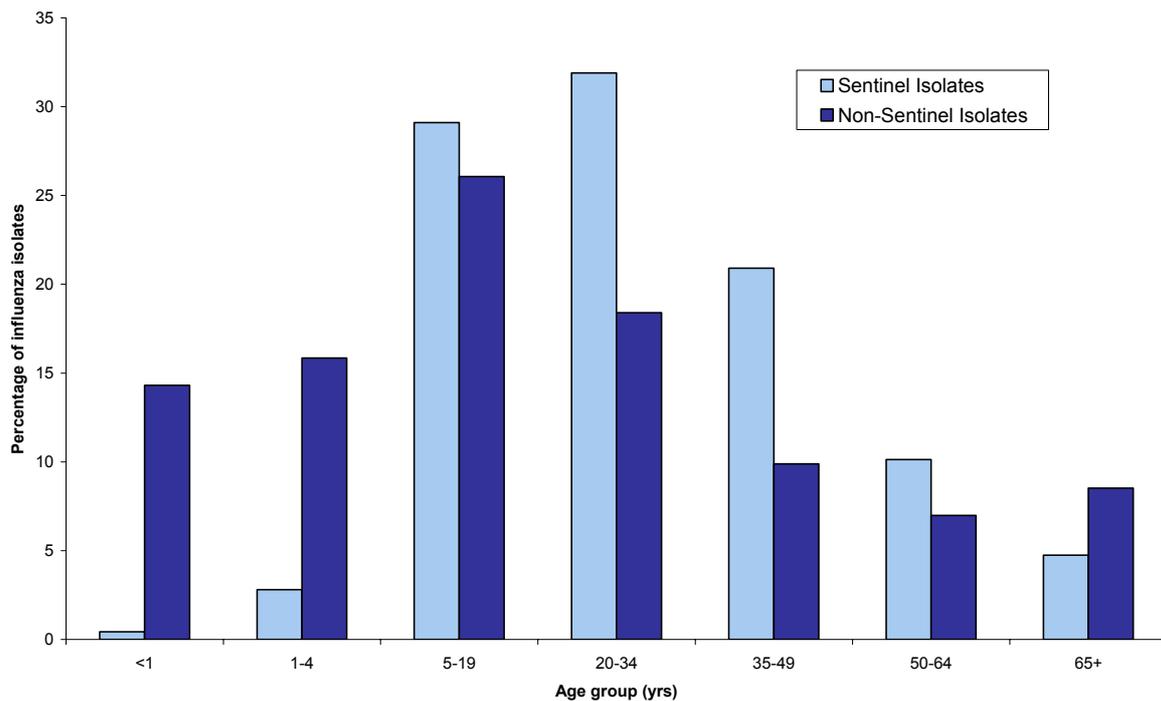


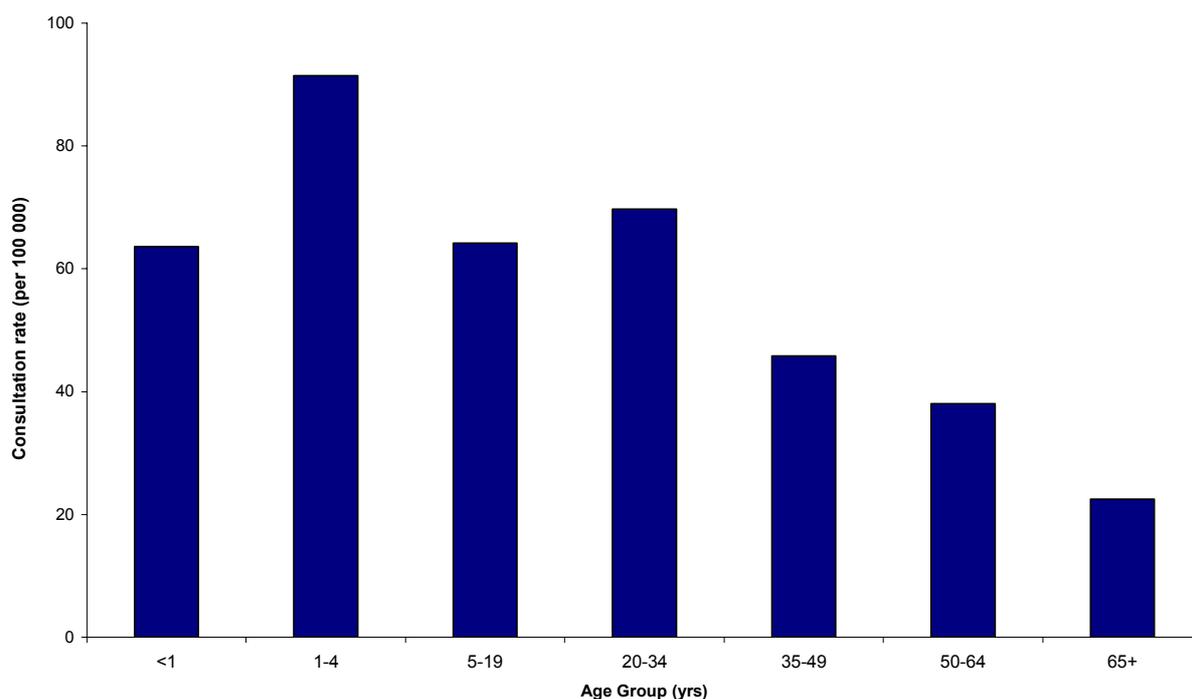
Figure 8 compares the percentage of influenza viruses between sentinel surveillance and non-sentinel for each age group. It is interesting to note that the age group under one year and 1-4 years and patients over 65 years were represented more in laboratory-based surveillance than in sentinel surveillance. This is consistent with the findings from the past 3-5 years.

**Figure 8. Percentage of sentinel and non-sentinel influenza viruses by age group, 2008**



In addition, rates of ILI by age group were calculated for the sentinel surveillance system. These rates are presented graphically in Figure 9. The highest consultation rate for influenza-like illness was in the children aged 1-4 years and those aged 20-34 years, with an average weekly consultation rate of 91.5 and 69.7 per 100 000 patient population respectively. Those in the 5-19 years had a rate 64.2 per 100 000 while infants aged <1 year had a rate of 63.6 per 100 000. Adults aged 35-49 years had a rate of 45.8 per 100 000, and adults aged 50-64 years had a slightly lower rate of 38.0 per 100 000. Elderly people (aged 65 years and over) had the lowest rate of 22.5 per 100 000.

**Figure 9. Sentinel consultation rate for influenza-like illness by age group, 2008**



#### **4. IMMUNISATION COVERAGE**

The uptake of influenza vaccine in New Zealand in 2008 among persons 65 years and over is 64%. Immunisation coverage for at risk individuals (children and adults) under the age of 65 years is estimated at 35%. The number of doses of influenza vaccine used during the 2008 season was 756 750 up 2 570 doses (or 1.5%) from 2007 (745 189).

Due to vaccine breakthrough and/or failure observed in 2004 (Influenza Annual Report, 2004), the need for surveying influenza vaccine breakthrough/failure was discussed and agreed by health professionals around the country. When GPs take swabs from three ILI patients each week, specimen request forms with necessary demographic information are required to be provided. One extra question is included to record whether the patient has been vaccinated against influenza in the same year as the onset of ILI.

A total of 26 vaccine breakthrough cases were recorded from the national influenza database (Table 2), comprising 2.5% of total viruses (26/1054). The clinical effectiveness of influenza

vaccines depends on the immunocompetence of the recipient, previous exposure to influenza and influenza vaccines, and the closeness of the match between the vaccine and circulating influenza strains. Of 26 vaccine breakthrough cases, 12 cases (46.2%) occurred in age groups >50 years. Of these, nine cases were in the 65+ years age group and three were in the 50-64 years age group. Immunological senescence may explain a higher proportion of vaccine breakthrough cases in the elderly population.

**Table 2. Influenza vaccine breakthrough cases by age group, 2008**

Age Group (yrs)	Influenza A(H3N2) by PCR	A/Brisbane/10/2007 (H3N2) - like	B	B/Florida/4/2006 - like	B/Malaysia/2506/2004-like	Total
<1	0	0	0	0	1	1
1-4	0	1	0	0	0	1
5-19	1	0	0	0	2	3
20-34	1	2	2	0	2	7
35-49	0	0	1	0	1	2
50-64	1	0	0	2	0	3
65+	3	3	2	0	1	9
<b>Total</b>	<b>6</b>	<b>6</b>	<b>5</b>	<b>2</b>	<b>7</b>	<b>26</b>

## 5. VIRUS STRAIN CHARACTERISATION

### 5.1. Viruses in 2008

Figure 10 shows influenza virus detections by type and subtype for each week throughout 2008, and the total percentage contribution of each. Table 3 shows influenza virus detections by type and subtype for 2008.

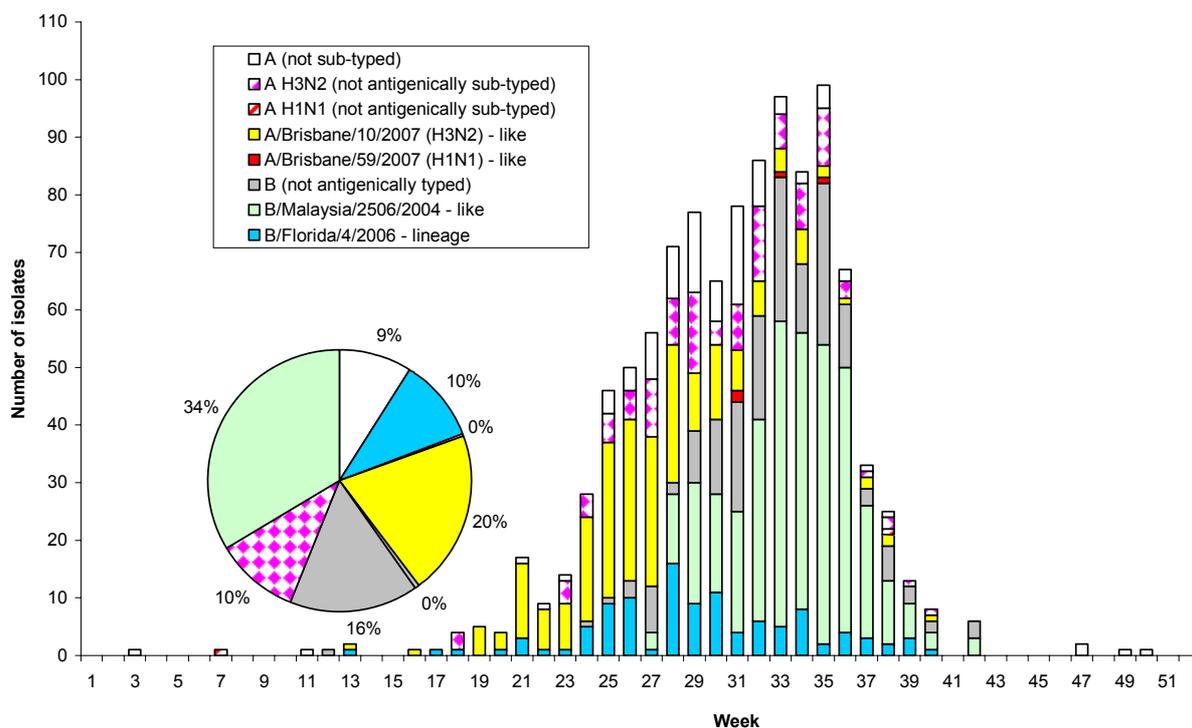
The majority of influenza viruses (630/1054 or 59.8% of all viruses) were characterised as influenza B and represented 58.3% (462/793) of the typed and subtyped viruses. Influenza A(H3N2) represented 41.0% (325/793) of the typed and subtyped viruses and 30.8% (325/1054) of the total viruses. Influenza A(H1N1) represented 0.8% (6/793) of the typed and subtyped viruses and 0.6% (6/1054) of the total viruses.

Figure 11 shows the general pattern of influenza virus isolations. This indicates the early onset of ILI activity and then a rapid rise to peak in week 35. The majority of influenza A viruses occurred in June and July. Influenza B predominated in August and September, the second half of the season. Influenza B/Victoria lineage viruses (most representative strain--B/Malaysia/2506/2004-like) were the predominant lineage viruses representing 44.6% (354/793) of typed and subtyped viruses. Influenza B/Yamagata lineage viruses (most representative strain—B/Florida/4/2006-like) represented 13.6% (108/793) of typed and subtyped viruses. In addition, there were six influenza A(H1N1) viruses identified in 2008. Of which, four were A/Brisbane/59/2007 (H1N1)-like strains and they were all resistant to oseltamivir. A total of 325 influenza A(H3N2) viruses were identified. Of which, 215 were A/Brisbane/10/2007 (H3N2)-like strains.

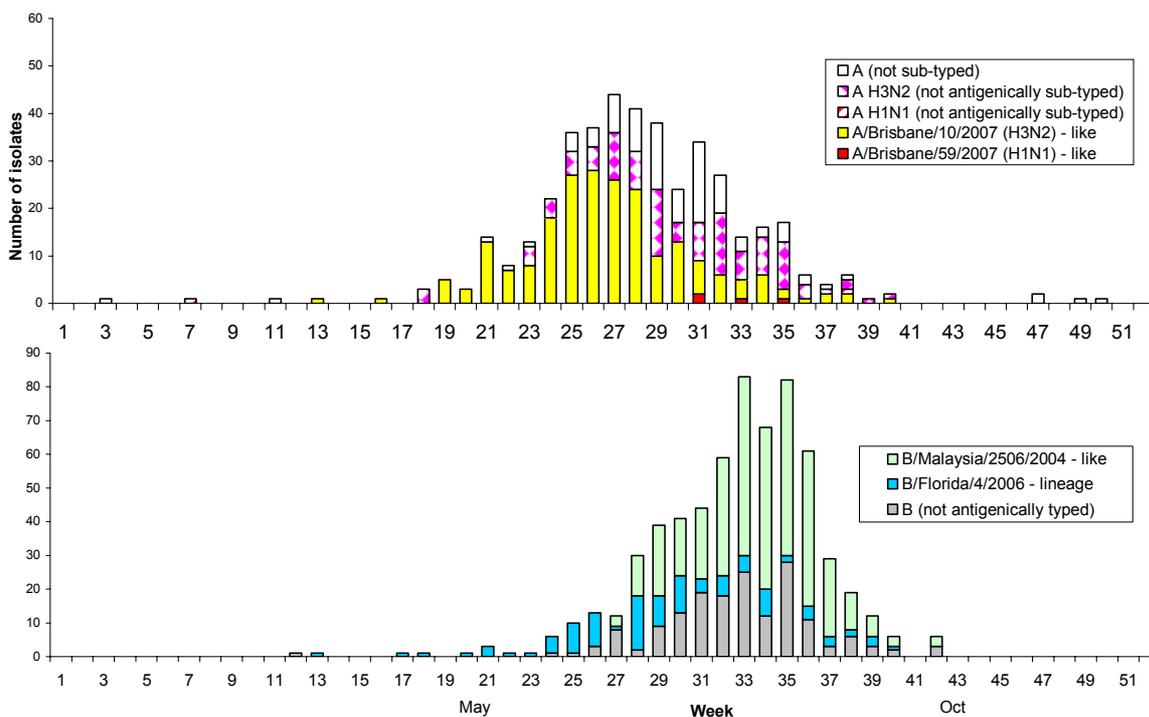
**Table 3. Influenza viruses by type and subtype, 2008**

<b>Virus</b>	<b>All viruses n=1054 (%)</b>	<b>Typed/Subtyped n= 793 (%)</b>
<b>Influenza A</b>		
Influenza A (not sub-typed)	93 (8.8)	
<b>Influenza A(H3N2)</b>		
Influenza A subtype H3N2 by PCR	110 (10.4)	110 (13.9)
A/Brisbane/10/2007 (H3N2) - like	215 (20.4)	215 (27.1)
<b>Subtotal A(H3N2)</b>	<b>325 (30.8)</b>	<b>325 (41.0)</b>
<b>Influenza A(H1N1)</b>		
Influenza A subtype H1N1 by PCR	2 (0.2)	2 (0.3)
A/Brisbane/59/2007 (H1N1) - like	4 (0.4)	4 (0.5)
<b>Subtotal A(H1N1)</b>	<b>6 (0.6)</b>	<b>6 (0.8)</b>
<b>Influenza B</b>		
B/Florida/4/2006 - like	108 (10.2)	108 (13.6)
B/Malaysia/2506/2004 - like	354 (33.6)	354 (44.6)
B (not antigenically typed)	168 (15.9)	
<b>Subtotal B</b>	<b>630 (59.8)</b>	<b>462 (58.3)</b>
<b>Total</b>	<b>1054 (100)</b>	<b>793 (100)</b>

**Figure 10. Total influenza viruses by type and week specimen taken, 2008**



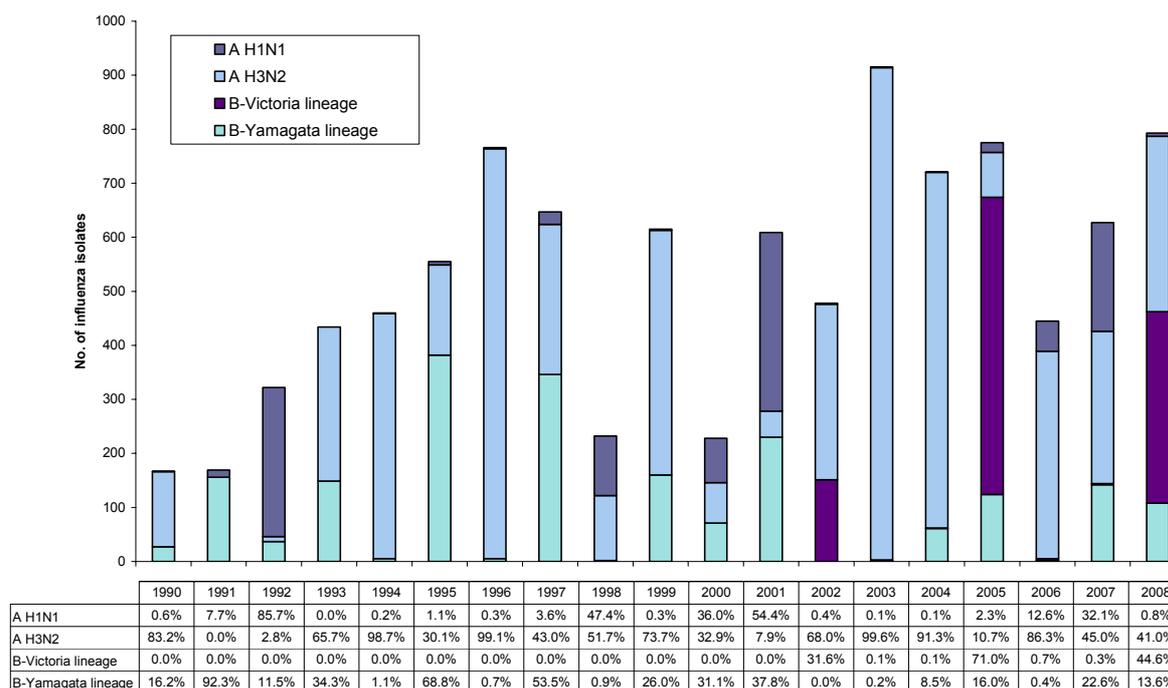
**Figure 11. Total influenza viruses by type and week specimen taken, 2008**



## 5.2. Changes in viruses 1990-2008

Figure 12 shows the number and percentage of typed and subtyped (not total) influenza viruses from 1990 to 2008. The noticeable changes in terms of predominant patterns are described below:

Figure 12. Influenza viruses by type, 1990-2008



## 5.3. Influenza A(H1N1)

During the period from 1990 to 2008, influenza A(H1N1) viruses predominated for three seasons in 1992 (85.7%), 2000 (36.0%) and 2001 (54.4%). Influenza A(H1N1) viruses circulated in significant proportion in 2007 (32.1%). In 2008, only six A(H1N1) viruses (0.8%) were detected, of which, only four were available for antiviral susceptibility testing at the WHO National Influenza Centre (NIC) at ESR. The results of the fluorometric neuraminidase inhibition assay indicated that the four viruses had highly reduced sensitivity to oseltamivir with IC<sub>50</sub> values in the range of 500-1700 nM, typical of the recently global emerging oseltamivir-resistant A(H1N1) viruses. Genetic analysis of the neuraminidase gene confirmed that the four viruses had the H274Y mutation (histidine-to-tyrosine at codon 274 in N2 nomenclature), conferring resistance to oseltamivir. These four viruses were isolated from patients aged 2-month-old male infant (1), 15-year-old female (1) and 49-year-old female (2). None of the patients or their close contacts had received Tamiflu prior to sample collection. NIC has reported the findings to the WHO.

([http://www.who.int/csr/disease/influenza/NICsummaryreport\\_NZ\\_2008.pdf](http://www.who.int/csr/disease/influenza/NICsummaryreport_NZ_2008.pdf)).

#### **5.4. Influenza A(H3N2)**

Influenza A(H3N2) viruses have often been associated with more severe disease and with excess pneumonia and influenza mortality. Influenza A(H3N2) subtype has been the most frequent predominant strain in New Zealand over the past 19 years. In the period 1990-2008, influenza A(H3N2) viruses predominated for 11 seasons; 1990 (83.2%), 1993 (65.7%), 1994 (98.7%), 1996 (99.1%), 1998 (51.7%), 1999 (73.7%), 2002 (68.0%), 2003 (99.6%), 2004 (91.3%), 2006 (86.3%) and 2007 (45.0%). The highest number of ILI related deaths (94) in New Zealand was recorded in 1996 during an A(H3N2) epidemic. The highest number of hospitalisations (591) was recorded in 2003 during an A(H3N2) predominant season. In 2008, Influenza A(H3N2) viruses circulated in significant proportion (41.0% of typed and subtyped viruses) and they predominated during the first part of the winter season from week 21 (19-25 May) to week 28 (7-13 July).

#### **5.5. Influenza B**

During the period from 1990 to 2008, influenza B viruses predominated for five years; 1991 (92.3%), 1995 (68.8%), 1997 (53.5%), 2005 (87.0%) and 2008 (58.3%). Two antigenically distinct lineages of influenza B have co-circulated in many countries since the late 1980's. The B/Yamagata/16/88 lineage (most recently representative strain-B/Florida/4/2006) circulated worldwide whereas the B/Victoria/2/87 lineage viruses only circulated 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, the B/Victoria/2/87 lineage viruses remained geographically restricted to Asia until 2001. During 1990-2001, B/Yamagata lineage viruses circulated exclusively in New Zealand. For the first time in 2002, the B/Victoria lineage viruses spread to New Zealand and completely replaced B/Yamagata lineage viruses. Since 2003, the two lineage viruses have been co-circulating in New Zealand with the B/Victoria lineage predominating every three years in 2005 and 2008. The influenza B was associated with high disease burden in young children and the B/Victoria lineage viruses tended to be associated with more explosive school outbreaks than the B/Yamagata lineage viruses in New Zealand. In 2008, influenza B viruses were the predominant viruses with more B/Victoria viruses (44.6% of typed/subtyped viruses) than B/Yamagata viruses (13.6% of typed/subtyped viruses). The influenza B activity was particularly high during the second part of the winter season in August and September. Influenza B/Yamagata lineage viruses consisted of a higher proportion than influenza B/Victoria lineage viruses during the period from week 13 (24-30 March) to week 24 (7-13 June). This was soon reverted to B/Victoria virus predominance for the remaining of the late winter season.

### **6. VACCINE FORMULATION - SOUTHERN HEMISPHERE TRENDS**

A combination of antigenic and genetic analyses is used to identify emergent antigenic variants of potential future epidemic importance and for consideration of their inclusion in vaccines. World Health Organisation (WHO) makes twice-yearly recommendations, one for northern hemisphere and another for southern hemisphere, to guide national/regional authorities on the formulation of influenza vaccines. However, the reference strains recommended by WHO may or may not be suitable for vaccine production. Thus, it is

necessary for country/regional authorities to approve the specific vaccine strains to be used in their countries.

Since 1969 an Australian Influenza Vaccine Committee (AIVC), with representatives from New Zealand, Australia and South Africa, has met annually in October to approve or update the WHO recommended formulation for influenza vaccines intended for the following winter (March to September of the following year) for these countries. New Zealand uses the influenza vaccine strains recommended by AIVC for the use in the subsequent year. During discussions at the AIVC meeting in October 2008, the following trends were noted:

### **6.1. Influenza A(H1N1)**

Influenza A(H1N1) subtype viruses, which re-emerged in 1977, closely resemble strains that circulated until 1956. Because of this, they initially had little impact in the older population. With further antigenic drift in the subtype, there has been some evidence of increasing impact in the elderly. Two antigenically distinct lines of influenza A(H1N1) have circulated in recent years and these are A/New Caledonia/20/99 and A/Bayern/7/95. In the past few years, however, viruses of the A/New Caledonia/20/99 lineage viruses have completely replaced A/Bayern/7/99-like strains.

The WHO Collaborating Centre (WHOCC) for Influenza in Melbourne has analysed 120 A(H1) isolates from nine countries since January 2008. Most of recent viruses, including those oseltamivir-resistant A(H1) viruses, were antigenically similar to A/Brisbane/59/2007-like strains. Few viruses were antigenically similar to A/Solomon Islands/3/2006 strains. In addition, sequence analysis of the A(H1) haemagglutinin and neuraminidase genes indicated that viruses fell into 2 major clades: Clade 2B—most of New Zealand, Australia and South Africa viruses and Clade 2C—most of South East Asian viruses. Almost all oseltamivir resistant A(H1N1) viruses from New Zealand fell into Clade 2B (Figures 1 and 2 in Appendix). Vaccines containing A/Brisbane/59/2007 antigen stimulated similar HA antibody titres to recent A(H1N1) influenza viruses as well as to the vaccine virus.

Based on the southern hemisphere and global data, the WHO Consultative Group and Australia Influenza Vaccine Committee recommended vaccines containing an A/Brisbane/59/2007 (H1N1)-like strain as the H1 component for 2009.

### **6.2. 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 in Melbourne has analysed 436 A(H3) viruses from 11 countries since January 2008. Most recent viruses were antigenically similar to A/Brisbane/10/2007-like strains. Sequence analysis of the A(H3) haemagglutinin gene indicated that most of viruses from New Zealand, Australia, Thailand and Singapore fell into the K173Q group (Figure 3 in Appendix). Vaccines containing A/Brisbane/10/2007 antigen stimulated similar HA antibody titres to recent influenza A(H3N2) viruses as well as to the vaccine virus. As a result, an A/Brisbane/10/2008 (H3N2)-like strain was recommended by WHO and the Australia

Influenza Vaccine Committee to be the H3 component of the influenza vaccine for southern hemisphere for 2009.

### 6.3. Influenza B

As mentioned above, two antigenically distinct lineages of influenza B have been circulating in New Zealand during recent years. B/Yamagata/16/88 lineage (most recently representative strain--B/Florida/4/2006) had circulated exclusively in New Zealand from 1990 to 2001. B/Victoria/2/87 lineage (most recently representative strain--B/Malaysia/2504/2004) spread to New Zealand in 2002 and has been co-circulating with B/Yamagata lineage since 2003.

In 2008, varying proportions of the two lineage viruses were seen in many countries. B/Yamagata lineage viruses predominated in New Zealand and Australia in early winter season (June/July), whereas B/Victoria lineage viruses predominated in late winter season (August/September) in these two countries. The WHOCC in Melbourne has analysed 529 influenza B viruses from 13 countries since January 2008. Most of B viruses analysed at WHOCC were B/Yamagata lineage viruses. They were antigenically similar to B/Florida/4/2006-like viruses. Sequence analysis of the B haemagglutinin gene for B/Yamagata viruses indicated that most of viruses fell into the third group with a signature mutation of S150I (Figure 4 in Appendix). The B/Victoria lineage viruses showed little genetic drift from the current reference vaccine virus B/Malaysia/2506/2004 except for recent New Zealand and Australia viruses which formed a distinct subclade with 4 amino acid changes (N75K, V146I, N165K, S172P) (Figure 4 in Appendix). Vaccines containing B/Florida/4/2006 antigen stimulated similar HA antibody titres to recent B/Yamagata viruses as well as to the vaccine virus. As a result, a B/Florida/4/2006-like strain was recommended by WHO and the Australia Influenza Vaccine Committee to be the B component of the influenza vaccine for southern hemisphere for 2009.

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 2009 is:

- **A(H1N1)** an A/Brisbane/59/2007 (H1N1) - like strain
- **A(H3N2)** an A/Brisbane/10/2007 (H3N2) - like strain
- **B** a B/Florida/4/2006 - like strain

## DISCUSSION

Influenza activity in 2008 is described as moderate when sentinel consultation data were compared from 1997 to 2008 in terms of the cumulative incidence rates, average weekly consultation rates and peak consultation rates.

It is estimated that influenza-like illness resulting in a visit to a general practitioner affected over 47 697 New Zealanders in 2008 or about 1.2% of total 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 general practitioner when they have an influenza-like illness.

When the overall pattern for sentinel consultation rates, viral identifications and influenza hospitalisations are compared for 2008 (Figures 1-3), they follow a similar pattern—a broad high activity from week 27 (30 June – 6 July) to week 36 (1-7 September) and then declining to the baseline level in late September. The robustness of the sentinel influenza surveillance has been validated externally by another system, GPSURV [6]. The sentinel surveillance usually operates from May through September. However, in 2000, influenza activity peaked in October through laboratory-based (non-sentinel) surveillance. Due to the variability of influenza activity from year to year, it is necessary for sentinel surveillance to be flexible enough to operate beyond the current May to September period.

Consultation rates varied greatly among health districts. The use of a common case definition and a reminder to clinicians of the importance to apply this case definition for the purposes of surveillance should help minimise regional differences. 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. Northland recorded more than 8-fold higher consultation rate (422.5 per 100 000 patient population) than the national average rate (Figure 4). This might result from the small number of practices with small denominators. Eastern Bay of Plenty recorded 3-fold higher consultation rate (157.2 per 100 000 patient population) than the national average rate.

One of the strengths of the sentinel surveillance system in New Zealand is the combination of disease surveillance (influenza-like illness) 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. Consequently, an important part of the sentinel system is for GPs to take nasopharyngeal and/or throat swabs for viral identification. However, the influenza detection rate varied among different health districts (Figure 6). Some health districts had an influenza virus detection rate lower than the national average of 46.6%. Many factors could contribute to low detection rates. For example, some health districts had only a small number of swabs or no swabs taken at all which could influence the reported rates in those health districts. In addition, sampling technique can also influence the detection rate. Sampling of the respiratory tract for clinical viral detection 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 [7]. 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 detection 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 three hospital 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. Advances in information transfer using systems such as Health-Link would greatly streamline this process.

In 2008, the highest influenza hospitalisation rates occurred in children aged <1 and 1-4 years (Figure 7). When influenza hospitalisation rates among different age groups were compared for the two periods (1997-2006 vs. 1990-1996), it was noted that children aged <1, 1-4, and 5-19 years had a statistically significant increase in average hospitalisation rates [8]. High rates of hospitalisations among young children have also been reported in the United States. New measures to prevent influenza-related hospitalisations among young children in New Zealand are needed.

When comparing age data for positive influenza viruses 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.

When community ILI consultation rates among different age groups were compared (Figure 9), the highest ILI consultation rate was in children aged 1-4 years and young adults aged 20-34 years. We advise caution in interpreting 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 practice 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.

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. Previously, viruses carrying this mutation are presumed to exhibit attenuated pathogenicity [9], compromised transmission [10], and reduced lethality [11]. However, current widespread circulation of oseltamivir-resistant influenza A(H1N1) viruses associated with typical influenza illnesses and viral pneumonia suggest that these viruses retain significant transmissibility and pathogenicity [12, 13]. Preliminary data indicate that oseltamivir-resistant influenza A (H1N1) viruses do not cause different or more severe symptoms compared to

oseltamivir sensitive influenza A (H1N1) viruses [14, 15]. For the first time since 2008, these oseltamivir-resistant influenza A(H1N1) viruses have spread to New Zealand (Figures 1 and 2 in Appendix). These oseltamivir-resistant influenza A (H1N1) viruses pose challenges for the selection of antiviral medications for treatment and chemoprophylaxis of influenza. CDC has issued interim recommendations [16]. It has become increasingly important to establish and sustain a national antiviral monitoring program in New Zealand which would provide timely local surveillance information to assist clinicians for choosing appropriate antiviral agents for their patients. It also provides compelling reasons for clinicians to test patients for influenza virus infection in order to select appropriate antiviral medications. So far, these oseltamivir-resistant influenza A (H1N1) viruses are antigenically similar to the influenza A/Brisbane/59/2007 (H1N1)-like strain represented in the New Zealand vaccine for 2009, and vaccination should continue to be considered the primary prevention strategy regardless of oseltamivir sensitivity.

Annual influenza immunisation is the primary method for reducing the impact of influenza in New Zealand. In 1997, the Ministry of Health made influenza vaccination freely available to persons aged 65 years and older and in 1999, this policy was extended to risk groups less than 65 years [17]. Introduction of routine influenza vaccination among the New Zealand elderly was associated with a significant decrease of influenza mortality [8]. A statistical association can't be taken as proof of cause and we cannot make claim that the policy changes resulting in greater uptake of the influenza vaccine is directly responsible for the decrease in mortality. However, the observed inverse relationship gives some justifications for us to speculate that this might be so. Further studies on the vaccine effectiveness are needed to understand the extent of beneficial effect of vaccination in New Zealand. The effectiveness of influenza vaccination in reducing influenza related mortality in the elderly is currently under debate [18-20]. Influenza vaccination has been reported to be highly effective at reducing influenza-related mortality in elderly people [21-23], although Simonsen et al reported no improvement of influenza related mortality in the US elderly despite increasing influenza vaccination coverage [19]. Despite the current scientific debate, people aged 65 years and older should continue to get influenza vaccination every year since the burden of influenza in this group is high and even modest protection for severe outcomes is certainly better than none at all. To ensure influenza vaccine coverage reaches a target of 75%, a new promotion group, the National Influenza Immunisation Strategy Group (NIISG) was established in 2000 with the goal of improving coverage through public and healthcare provider education. The "Influenza Kit" and "Education Manual" were specifically developed for this purpose. Other education resources include pamphlets, radio and television advertising, healthcare professional education sessions and developing close links with the National Influenza Pandemic Planning Committee. 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.

Optimal vaccine efficacy is dependent upon achieving a close antigenic match between the vaccine and circulating strains. Achieving this close match is possible through the WHO Global Influenza Surveillance Network (GISN). New Zealand has been an active participant of GISN since 1954. As a result, some influenza viruses such as A/Wellington/1/2004 have been selected as vaccine strains in the past. The head of the WHO National Influenza Centre participates and contributes in influenza vaccine recommendations for the Southern Hemisphere as a member of the Australia Influenza Vaccine Committee.

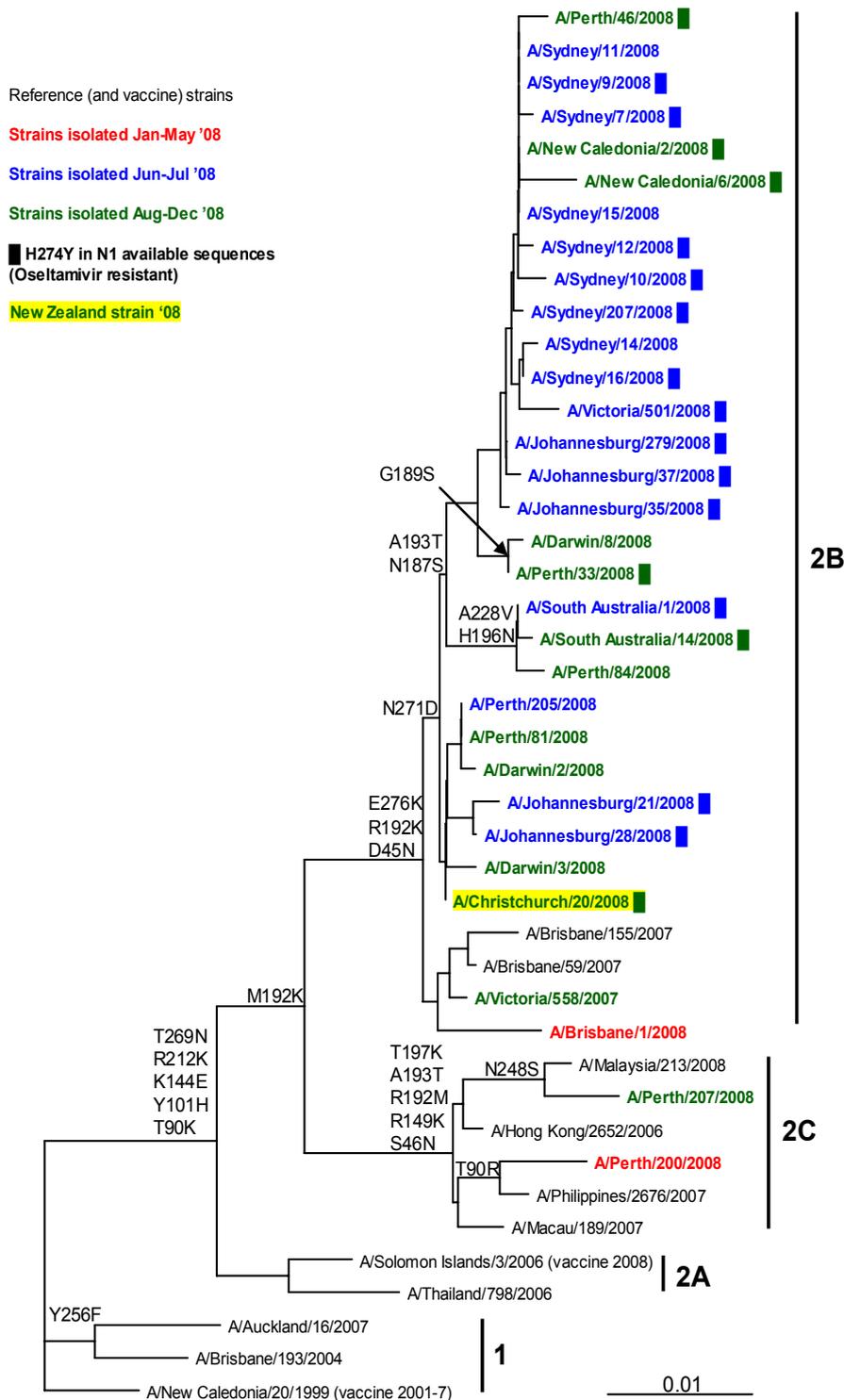
Overall, the sentinel surveillance system is very useful in measuring disease burden in the community. However, there are some limitations to the sentinel surveillance data. For example, sentinel data cannot be extrapolated precisely to the rest of the population since not all people suffering from influenza 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.

Apart from the Acute Flaccid Paralysis programme, the GP sentinel surveillance system for influenza is possibly the only other ongoing syndromic surveillance system in New Zealand. Most other surveillance systems are passive, based on collecting data on diagnosed disease. Active syndromic surveillance systems are being increasingly to detect emerging and re-emerging pathogens.[24, 25] Enhanced influenza surveillance is also a key strategy for improving New Zealand’s preparedness for pandemic influenza [26]. The GP sentinel surveillance system for influenza would readily adapt to monitor the early stages and progress of pandemic influenza. Alternatively it may be time to consider the benefits of improved timeliness and efficiency of reporting influenza through classifying influenza as a laboratory notifiable disease. However, objectives for detection of the first pandemic case(s) would not be met by a GP sentinel system due to lack of sensitivity. Hospital-based active sentinel surveillance for severe acute respiratory infections could be a way to improve the sensitivity for detection of the early pandemic cases and other emerging respiratory diseases. Enhancement in light of preparations for pandemic influenza could include age, gender, and ethnicity information. In addition, whether or not the patient has been using antivirals or received influenza immunisations could also provide useful information on antiviral resistance and vaccine efficacy. There is therefore a good case for reviewing New Zealand’s existing influenza surveillance system in light of these potential enhancements.

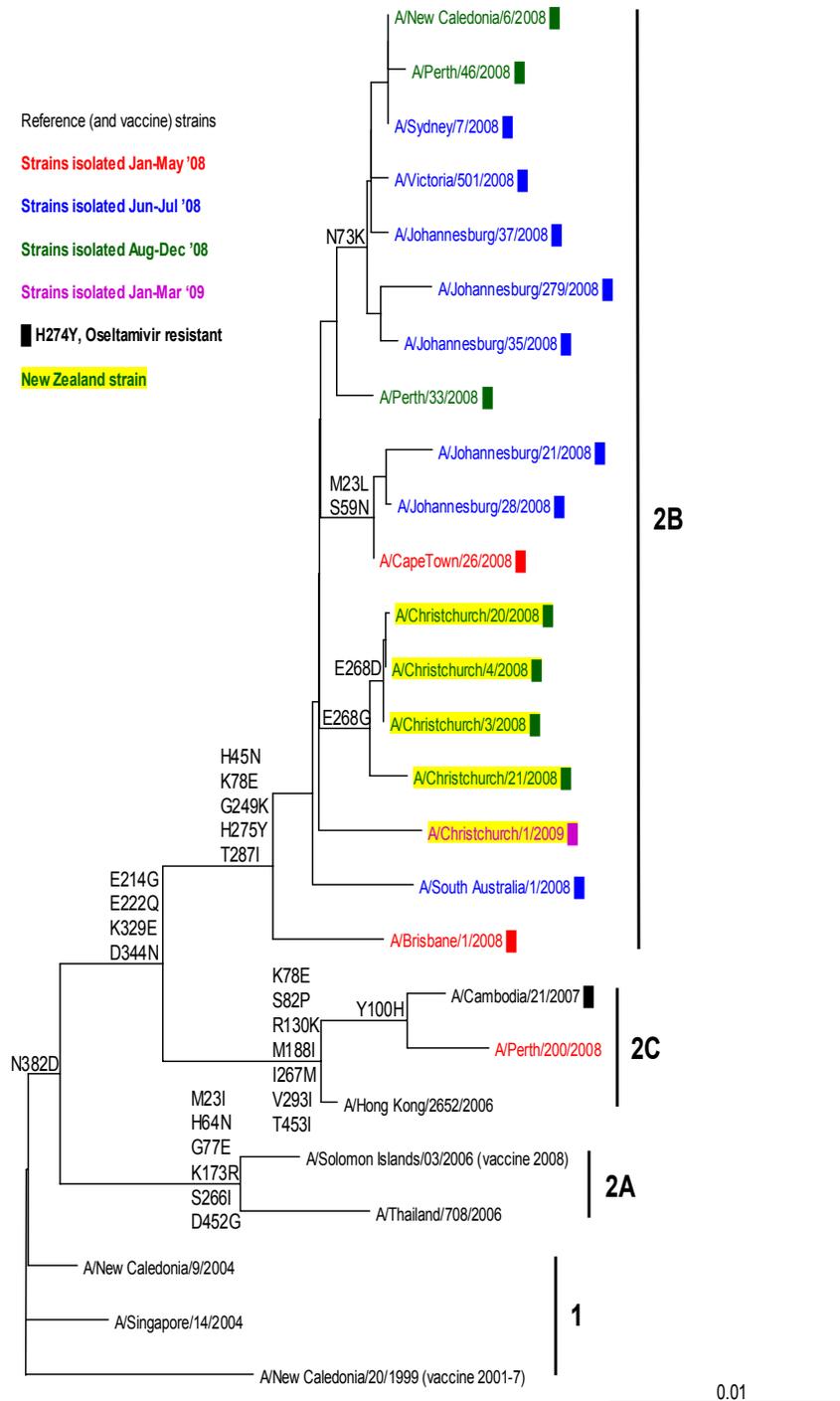
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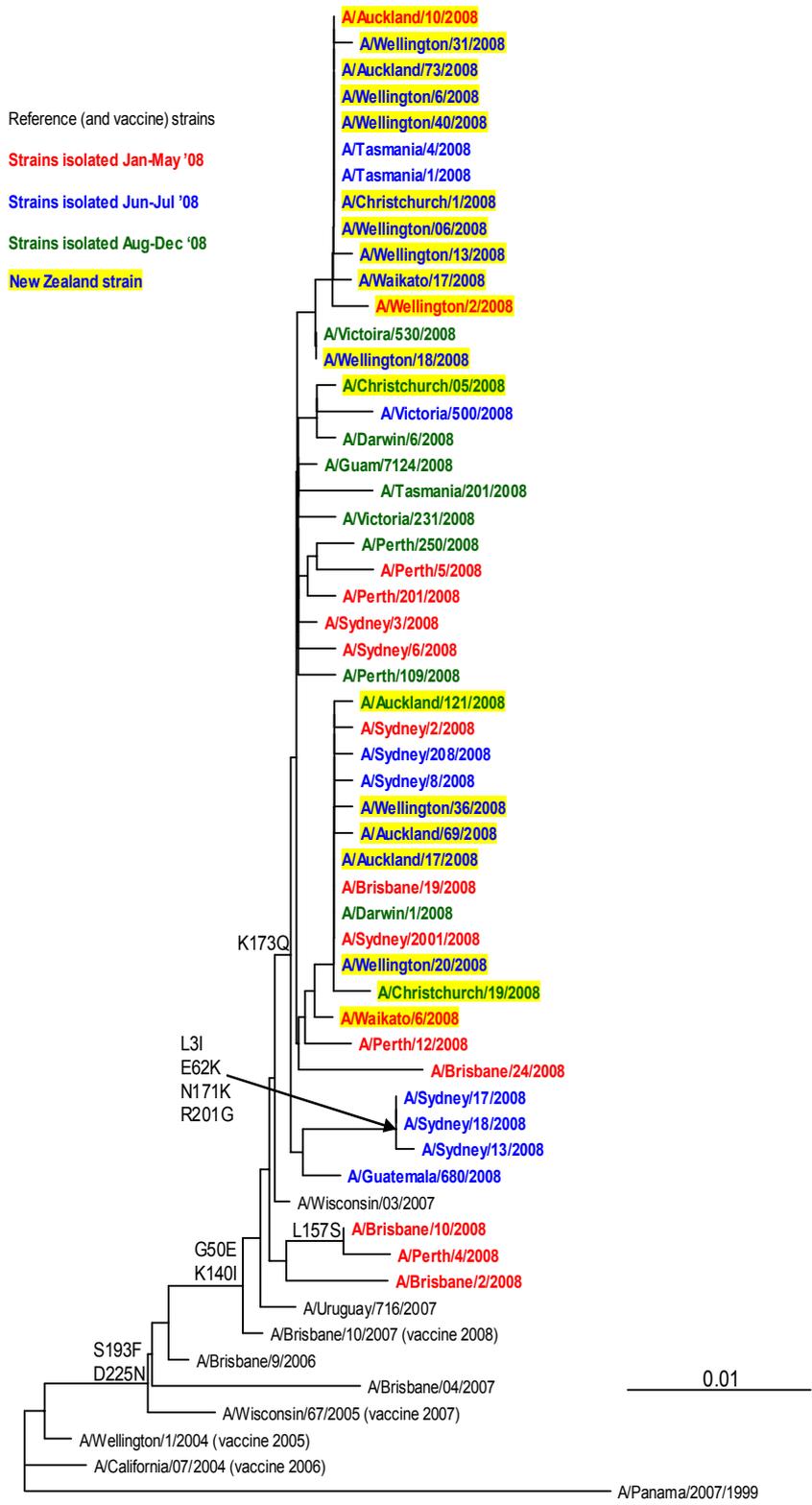
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**Appendix--Figure 1.** Phylogenetic relationships among influenza A (H1) HA1 genes for 2008. Scale is represented as substitutions per site. Clades are indicated to the left in bold.



**Appendix–Figure 2.** Phylogenetic relationships among influenza A (H1) NA genes for 2008 to early 2009. Scale is represented as substitutions per site. Clades are indicated to the left in bold.



**Appendix--Figure 3.** Phylogenetic relationships among influenza A (H3) HA1 genes for 2008. Scale is represented as substitutions per site.

