Child and Youth Mortality Review Committee
Te Rōpū Arotake Auau Mate
o te Hunga Tamariki, Taiohi

Perinatal and Maternal Mortality Review Committee
He matenga ohorere, he wairua uiui, wairua mutungakore

Report for the Minister of Health from the Pandemic Influenza Mortality and Morbidity Review Group

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Chair's Introduction

Following the winter 2009 influenza pandemic, the Minister of Health formed the Pandemic Influenza Mortality and Morbidity Review Group to review the mortality and morbidity associated with the pandemic influenza A(H1N1) 2009 virus. This multidisciplinary group of experts reviewed all available information on the 49 deaths following pandemic influenza A(H1N1) 2009. The learnings from each of these cases were collated with a view to providing policy and clinical advice for future pandemic threats. Prior to a possible second wave in 2010, specific recommendations were made regarding risk factors for influenza complications, diagnostic testing, influenza immunization, and prescribing of antivirals. This report provides a summary of those recommendations.

Although there has been some speculation in the international media that the global response to the pandemic was an over reaction, this report clearly provides information suggesting that the New Zealand health services were stretched during the winter of 2009. The majority of the 49 deaths occurred in a younger age group than have typically died during past seasonal influenza epidemics. Intensive care services were stretched and there were considerably more admissions to hospital and more primary care consultations than during the preceding influenza seasons. It is clear that the pandemic presented the health services with a considerable logistical challenge.

It is with some relief to the working group that during the winter of 2010 to date there have been far fewer deaths from pandemic influenza A(H1N1) 2009 and considerably lower hospital admissions and primary care consultations. The lower incidence in 2010 may be explained by the overall high seroprevalence rate in the community along with an increased uptake of influenza vaccine.

Finally, I would like to thank the members of the working group and the Ministry of Health officials who assisted in the identification and review of the cases. Their expertise was welcome and invaluable, and their commitment and dedication to this task has meant that we were able to prepare this report in a timely fashion.

Professor Cindy Farquhar
Chairperson
Pandemic Influenza Mortality and Morbidity Review Group

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- the database coordinator of the Australian and New Zealand Intensive Care Society (ANZICS)
- Dr Lynn Sadler, epidemiologist for the Perinatal and Maternal Mortality Review Committee (PMMRC)
- the Australian and New Zealand Intensive Care Research Centre (ANZIC) Influenza Investigators (2009).

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Executive Summary and Recommendations

- On 26 April 2009, in the southern hemisphere autumn, a novel influenza A(H1N1) virus was declared a Public Health Emergency of international concern by the World Health Organization (WHO).
- On 29 April 2009, New Zealand made the influenza caused by the novel influenza A(H1N1) virus a notifiable disease.
- On 11 June 2009, the influenza A(H1N1) epidemic was declared a pandemic by the Director General of the WHO.
- The Minister of Health established the Pandemic Influenza Mortality and Morbidity Review Group (PIMMRG) in November 2009, as a joint sub-group of the Perinatal and Maternal Mortality Review Committee and the Child and Youth Mortality Review Committee. The group provided multi-disciplinary clinical review of deaths from pandemic influenza A(H1N1) 2009 and independent advice on clinical and prevention strategies to the Ministry prior to a possible second wave of pandemic influenza A(H1N1). This report provides a summary of that advice.
- In the winter months of 2009, a total of 49 New Zealand patients[1] died with pandemic influenza A(H1N1) 2009 virus infection. While the Ministry of Health identified 35 deaths from pandemic influenza A(H1N1) during the first wave, the processes arranged by the PIMMRG were able to collect information on an additional 14 deaths due to pandemic influenza A(H1N1). The PIMMRG process has provided a more in-depth review of pandemic deaths, and ensured that New Zealand has accurate pandemic influenza A(H1N1) mortality and morbidity statistics and that key prevention information was provided in a timely manner, to ensure preparedness for a second wave of pandemic influenza A(H1N1).
- The influenza (pandemic and seasonal) mortality rate was 1.38/100,000 population.
- During 2009, 119 patients were admitted to intensive care units and 1122 admitted to hospital with a primary diagnosis of pandemic influenza A(H1N1) 2009.
- Eighty-six percent of those who died during 2009 had co-morbidities and/or associated conditions; the most common of these were respiratory illnesses, morbid obesity and substance abuse.
- Surveillance estimated 116,335 patients attended their general practice with clinical influenza in 2009, which is 2.7% of the population.
- Pandemic influenza A(H1N1) 2009 peaked from July–September 2009 and, although this period was associated with fewer deaths than anticipated, hospitalisations and deaths attributable to influenza were higher than in the previous 15 years.

[1] This number includes one death of a New Zealand tourist in the Cook Islands, who has not been included in the New Zealand rate.

- The age distribution of deaths from influenza was younger than in previous years, and there were more deaths in 2009 (n=43) from influenza in those under the age of 65 years than for all of the years from 2000 to 2008 (n=14). (See Appendix 4.)
- The majority of these hospital admissions and health service attendances occurred during July 2009, creating a considerable challenge for health services.

Recommendations from the mortality and morbidity review for pandemic influenza A(H1N1) 2009

Recommendations for the Ministry of Health and District Health Boards

1. Pandemic influenza vaccination

While all individuals are encouraged to have an annual influenza vaccination, individuals at increased risk of complications* (see box) following pandemic influenza virus infection, are offered this preventative measure without charge.

Frontline health care workers should be offered vaccination.

Vaccination of family members and contacts of high-risk individuals should be encouraged.

District Health Boards (DHBs) should work with primary and secondary care providers to achieve high levels of coverage for patients at increased risk of complications* (see box) who are attending secondary care.

*** Individuals at increased risk of complications from pandemic influenza A(H1N1) 2009**

Children under 5 years of age, especially infants

Adults over 65 years of age

People who are morbidly obese (BMI ≥ 35 kg/m^2)

People with chronic respiratory disease, including asthma and chronic obstructive airways disease

People with cardiac disease

People with neurological conditions (that affect the ability to breathe and cough)

People with immunosuppressive conditions

People who have a history of substance abuse

Pregnant women and those in the postnatal period

2. Improving access to antivirals

Barriers to accessing antivirals (oseltamivir (*Tamiflu®*) and zanamivir (*Relenza®*)) should be reduced to support early treatment for any individuals presenting with symptoms of influenza. Strategies to ensure treatment of a greater proportion of individuals at increased risk of complications (see box under recommendation 1) should be considered.

Recommendations for district health boards and primary health organisations

3. Prevention of transmission of pandemic influenza A(H1N1) 2009

All care must be taken to protect staff and patients. The following strategies are suggested:

- using good hand and respiratory hygiene and using barrier protection
- actively promoting vaccination to health care workers and those at risk of complications from influenza
- encouraging staff to stay home at the onset of symptoms and consider taking antivirals
- discouraging anyone who may be infectious from entering hospitals unless they have clinical need.

Recommendations for health professionals

4. Assessing severity of influenza

The use of an early warning score system in primary care and in emergency departments is recommended to assist decision making about admission for people over 14 years old with pneumonia (an example is provided in Appendix 2). There is no validated early warning score for influenza and, therefore, it is common practice to refer to those used in community-acquired pneumonia. For children, a similar checklist is available (provided in Appendix 3).

5. Prescribing antivirals

Antivirals are most effective early in the illness (usually less than 48 hours after symptoms have started in adults and up to five days in children) without waiting for the laboratory test results for pandemic influenza A(H1N1) 2009 in primary and secondary care settings. The earlier antivirals are given during the course of the illness, the greater the benefit.

6. Testing for pandemic influenza A(H1N1) 2009

Any patient who attends a hospital with fever during times of increased influenza activity should be tested for influenza (unless there is an obvious non-influenza diagnosis). At times of increased influenza activity, wider indications for virological laboratory testing should be introduced, in discussion with the local laboratory. In particular, patients with severe underlying respiratory disease, morbid obesity, and who are immunosuppressed should have easy access to influenza diagnostic testing.

In all health care settings, isolation and treatment of individuals with symptoms should be initiated on clinical suspicion, without waiting for the influenza test results.

Routine, widespread use of influenza diagnostic testing is not feasible in primary care. Access should be available following consultation with the public health services and local laboratory services.

7. Specific advice for individuals with higher risk of complications

Individuals who are at increased risk of complications for pandemic influenza A(H1N1) 2009 are listed under recommendation 1.

Individuals at increased risk of complications, and their families, should be aware of the risk they face and encouraged to follow preventative and treatment advice. Public education (see recommendation 10 on public messages below) will help them to:

- recognise their increased risk
- be aware of the benefits of influenza immunisation
- seek medical advice during influenza outbreaks.

8. Specific advice for pregnant women

Pregnant women are at increased risk of severe outcomes from pandemic influenza A(H1N1), particularly if they have other risk factors such as obesity or asthma. They should be immunised against influenza and consult their midwife, general practitioner or specialist services as soon as symptoms of an influenza-like illness develop or if other family members are unwell.

The use of antivirals is considered safe in pregnancy.

If a woman has been immunised and presents with symptoms of influenza, then antivirals are recommended as the influenza vaccination is not 100% effective.

9. Specific advice for children

An annual influenza vaccination should be introduced into the National Immunisation Schedule for children under five years and infants, especially in areas of social and economic deprivation.

Influenza in childhood can present with a clinical picture that is hard to differentiate from many other common childhood febrile conditions, especially in children under two years of age.

The use of a checklist to help identify children who may be developing a significant complication is recommended. For example, infants with atypical bronchiolitis may need careful monitoring and early use of antivirals. (See Appendix 3 for a checklist.)

Care pathways need to be developed to ensure infants and children at increased risk of complications have high levels of vaccine coverage and receive timely health care tailored to their increased needs.

Early childhood centres and schools should encourage hand washing, respiratory hygiene and other preventative measures among children.

10. Recommendation for public messages

A set of simple messages for the public should be promoted, with the aims of:

- encouraging those with severe symptoms to seek medical help early
- encouraging those at higher risk of complications to self identify and seek annual influenza vaccination and early treatment when ill
- increasing awareness that influenza can be atypical, particularly among those with chronic health problems.

A full set of recommendations and public messages is provided in Section 5 of this report.

1 Background

On 26 April 2009, in the southern hemisphere autumn, a novel influenza A(H1N1) virus was declared a Public Health Emergency of international concern by the World Health Organization (WHO). Thereafter, on 29 April, New Zealand made the influenza caused by the novel influenza A(H1N1) 2009 virus a notifiable disease. On 11 June 2009, the influenza A(H1N1) epidemic was declared a pandemic by the Director General of the WHO. From June through to September 2009, there was a rise in cases in New Zealand with an accompanying increase in attendance at health care services, including admissions to hospitals and, in some cases, death.

In November 2009, the Minister of Health established a Pandemic Influenza Mortality and Morbidity Review Group (PIMMRG) as a joint sub-group of the Perinatal and Maternal Mortality Review Committee and the Child and Youth Mortality Review Committee. The Terms of Reference of the group were to review mortality and morbidity related to pandemic influenza A(H1N1) for New Zealanders of all ages for the purposes of:

a. gathering and reviewing accurate clinical information related to pandemic influenza A(H1N1) hospitalisations and deaths

b. disseminating guidance for health services based on clinical review with a view to improving systems and clinical outcomes for patients.

1.1 Definition of a pandemic death

The Minister of Health's Terms of Reference for the group defined a death associated with pandemic influenza A(H1N1) 2009 as "the death of a person with confirmed Influenza H1N1 infection determined from ante-mortem or post-mortem specimens, and who died from a clinically compatible illness or complications attributable to that infection". The Terms of Reference further specified that there "should be no period of complete recovery between illness and death, and no alternative cause of death agreed upon". In all cases of pandemic death included in this report, the committee agreed that the patient's death would not have occurred at that time if the patient had not become infected with pandemic influenza A(H1N1) 2009.

1.2 Terms of reference

The PIMMRG had 10 appointed members, who were selected with input from relevant members of the Ministry of Health. (A list of members is attached in Appendix 1.)

The group was able to gather clinical information from patients' clinical records and review any deaths that were possibly related to pandemic influenza at its discretion.

The group also reviewed morbidity related to pandemic influenza A(H1N1) at its discretion.

2 Methodology

2.1 Mortality review

The PIMMRG identified possible pandemic influenza A(H1N1) 2009 mortality cases using the following sources.

- The first cases identified (n = 42) were those of pandemic influenza A(H1N1) mortalities that were recorded by EpiSurv.[2]
- One additional case of pandemic influenza A(H1N1) that could not be subtyped was included on the grounds that it was thought likely to be pandemic influenza A(H1N1) 2009 as it occurred at the height of the pandemic.
- Other additional cases were identified by matching the dataset of all H1N1 notifications in EpiSurv with death notifications from Births, Deaths and Marriages in the six months from June to November 2009. If the individual was aged over 65 years and if the death occurred more than six weeks from the positive H1N1 test, then the death was not considered.
- One additional death was identified from the Child and Youth Mortality Review Committee (CYMRC) database.
- One additional case was identified from the National Minimum Dataset (NMDS).[3]

Once a case was identified, a full set of notes, including primary health care notes, was requested from the relevant District Health Board (DHB) and health professionals. Using a standardised template created by the PIMMRG, information from the case notes was collected. Each of the members of the group was sent the template and the notes for specific cases and asked to conduct an individual review of the case notes and to complete the template. At each meeting, the cases were presented and discussed and then the summary sheets were completed. The data were then summarised into a set of tables which are provided in this report.

Some cases also fell under the Terms of Reference of the Perinatal and Maternal Mortality Review Committee (PMMRC) and the CYMRC. Information on these cases, which was held in the PMMRC and CYMRC databases, was collected using the PMMRC and CYMRC case review processes.[4]

[2] EpiSurv is New Zealand's national notifiable disease surveillance database. On behalf of the Ministry of Health, EpiSurv collates notifiable disease information on a real-time basis. For more information on EpiSurv, see http://www.surv.esr.cri.nz/EpiSurv/index.php.

[3] The National Minimum Dataset is a national collection of public and private hospital discharge information, including coded clinical data for inpatients and day patients. For more information see the website at: http://www.moh.govt.nz/moh.nsf/indexmh/dataandstatistics-collections-nmds.

[4] For more information on the PMMRC and CYMRC review processes, see their respective websites at: http://www.pmmrc.health.govt.nz/ and http://www.cymrc.health.govt.nz/.

2.2 Morbidity review

Two sources of data were used to consider hospitalisations following the pandemic influenza A(H1N1) 2009 infection.

2.2.1 **Admissions to New Zealand intensive care units** (ICUs) were reported by the intensive care admissions database of the ICU network for Australia and New Zealand.[5] This database was used to determine demographics, co-morbidities, length of illness, and final outcome (ANZIC Influenza Investigators 2009).

2.2.2 **The data from ESR's influenza annual reports for 2008 and 2009** were considered to establish a sense of the additional burden that pandemic influenza A(H1N1) 2009 placed on the New Zealand health services (ESR 2010a). Specifically, hospitalisations from pandemic influenza A(H1N1) and suspected influenza A virus infection in New Zealand from June–November 2009 were compared with the equivalent data for seasonal influenza during 2007 and 2008.

For both mortality and morbidity reviews, descriptive statistics were used to describe deaths and admissions to intensive care for patients with pandemic influenza A(H1N1) 2009. Continuous variables are presented as medians (with interquartile ranges) and categorical variables as percentages (with 95% confidence intervals, where appropriate). All rates are per 100,000 people, and directly age-standardised to the 2009 New Zealand population (Statistics New Zealand 2009). Confidence intervals were calculated by the Exact Method. Unknowns are excluded from the denominator for calculating percentages. For the calculation of body mass index (BMI) (kg/m^2) height was missing in eight adults but weight was available and therefore height was estimated based on gender and age norms for New Zealand.

2.3 Development of recommendations

Clinical and public health recommendations were developed taking into consideration the information provided by the mortality and morbidity review of the clinical notes, published literature and document searches.

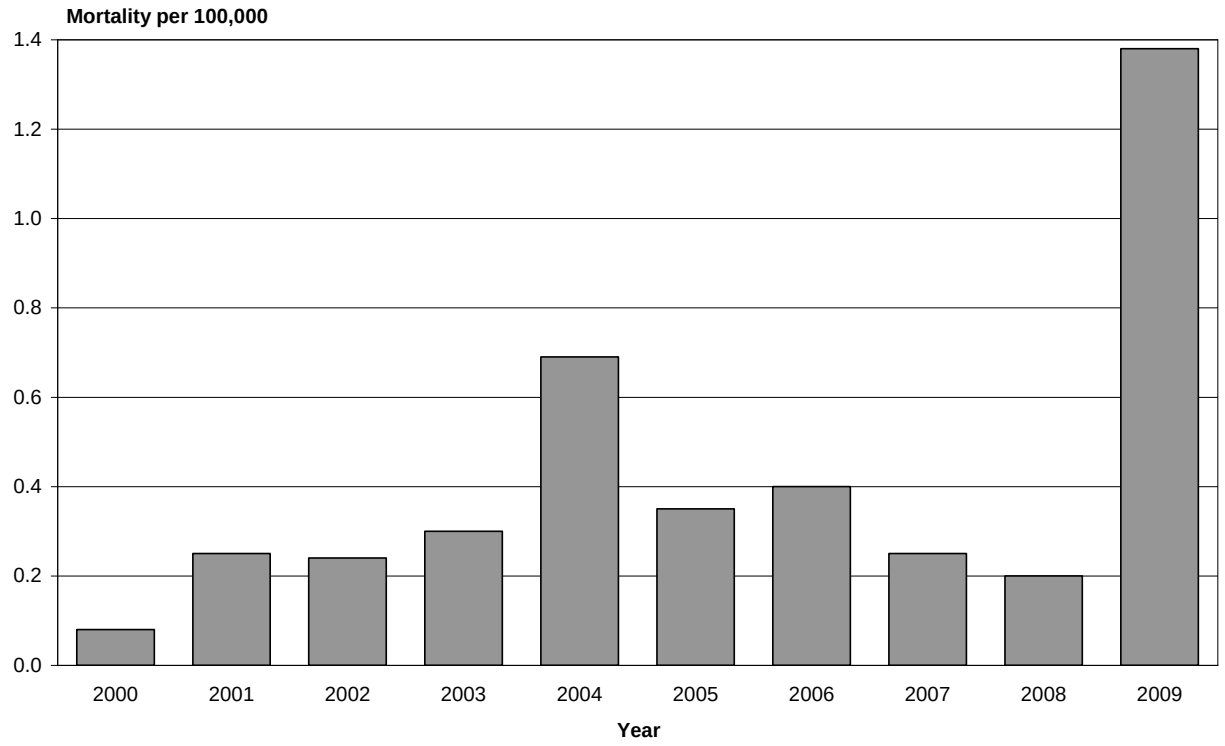
[5] For more information on the Australian and New Zealand Intensive Care Society see http://www.anzics.com.au/.

3 Findings

3.1 Deaths from pandemic influenza A(H1N1) 2009 in New Zealand from June to November 2009

From June–November 2009, a total of 49 deaths were considered to be associated with pandemic influenza A(H1N1) 2009.[6] Forty-eight patients had a positive pandemic influenza A(H1N1) 2009 laboratory diagnosis, either in life or at the time of post-mortem. One further patient was influenza A positive but unable to be subtyped for technical reasons but was included in the review because of the timing of the infection (mid July). There were a further 11 deaths that were coded as influenza deaths in 2009 (all occurred from July to December 2009) and who died within six weeks of a hospital admission. It is possible that some of these eleven were also deaths from pandemic influenza A(H1N1) 2009 but were not tested. This section of the report is only considering the 49 pandemic influenza A(H1N1) 2009 deaths.

Figure 1: Influenza mortality rates 2000–2009



Source: ESR (2010a). Note: 2007–2009 data is provisional.

[6] Forty-eight of the deaths occurred in New Zealand. There was one additional death of a New Zealand tourist who died in the Cook Islands and is not included in the mortality rate for New Zealand

In 2009 the influenza (pandemic and seasonal) mortality rate (excluding one death in the Cook Islands) was 1.38 per 100,000 (using a population of 4.33 million on 30 September 2009 as the denominator) (Statistics New Zealand 2009) (Appendix 4). As Figure 1 shows, this 2009 mortality rate was the highest rate reported in New Zealand since 2000 (ESR 2010a). The 2009 rate may be artefactually elevated compared with previous years because in 2009 all pandemic cases were laboratory confirmed.

3.1.1 Demography of deaths associated with pandemic influenza A(H1N1) 2009

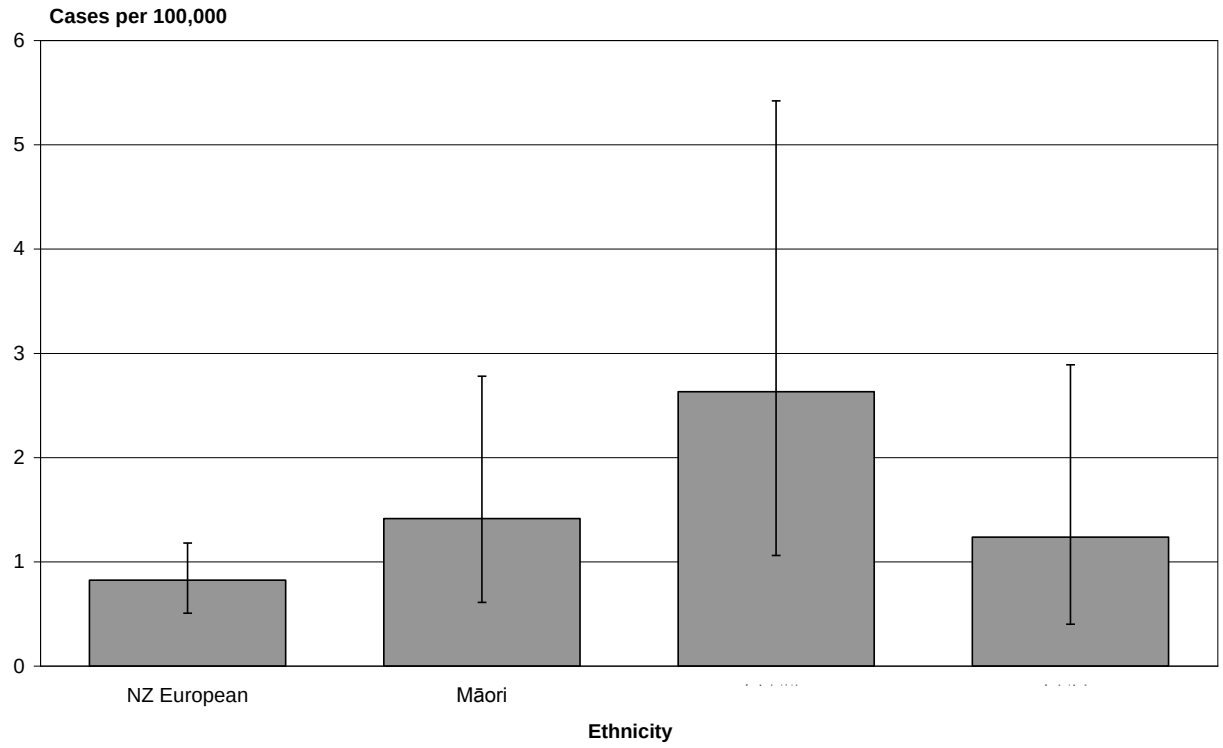
Of the total of 49 who died of pandemic influenza A(H1N1) 2009, 21 were investigated by the Coroner. Twenty-six deaths were female and 23 were male. Sixteen of the deaths occurred at home and 33 occurred in hospital. Of the 34 patients admitted to hospital, 21 were admitted to intensive care units and 17 required ventilation. One New Zealand European patient died shortly after arriving in the Cook Islands on vacation and it was agreed to review this death although it was not included in the mortality rate.

Table 1: Pandemic influenza A(H1N1) 2009 deaths by District Health Board of residence

District Health Board	Total deaths (N=49)		Population rate = cases/100,000
	n	%	
Waitemata	3	6	0.6
Auckland	5	10	1.1
Counties Manukau	9	18	1.9
Waikato	9	18	2.5
Tairawhiti	1	2	2.2
Hawke's Bay	1	2	0.6
Taranaki	1	2	0.9
MidCentral	1	2	0.6
Hutt Valley	1	2	0.7
Capital and Coast	6	12	2.1
Nelson Marlborough	1	2	0.7
Canterbury	5	10	1.0
South Canterbury	2	4	3.6
Otago	3	6	1.6
Southland	1	2	0.9

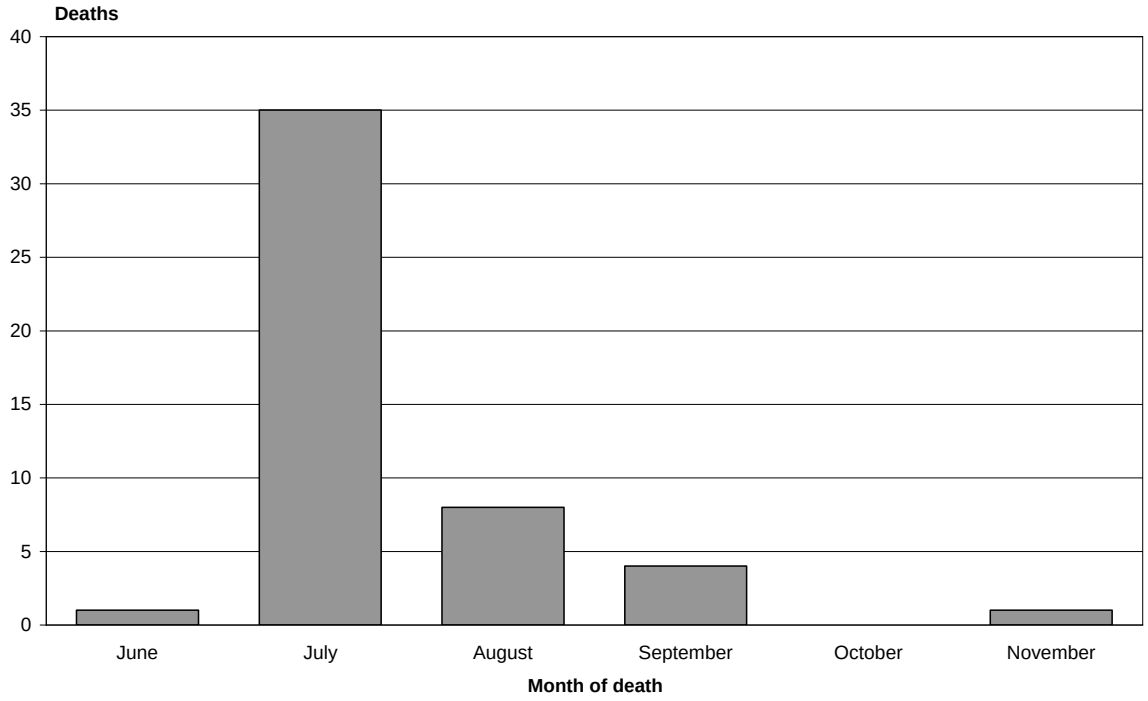
Table 1 shows the DHB of residence for each case. However, it is important to note that the DHB of residence is not necessarily the same as the DHB where treatment was provided. Furthermore, testing for influenza was not uniformly applied across DHBs so cases in some areas may not have been recognised.

Figure 2: Pandemic influenza A(H1N1) 2009 deaths by prioritised ethnicity for 2009



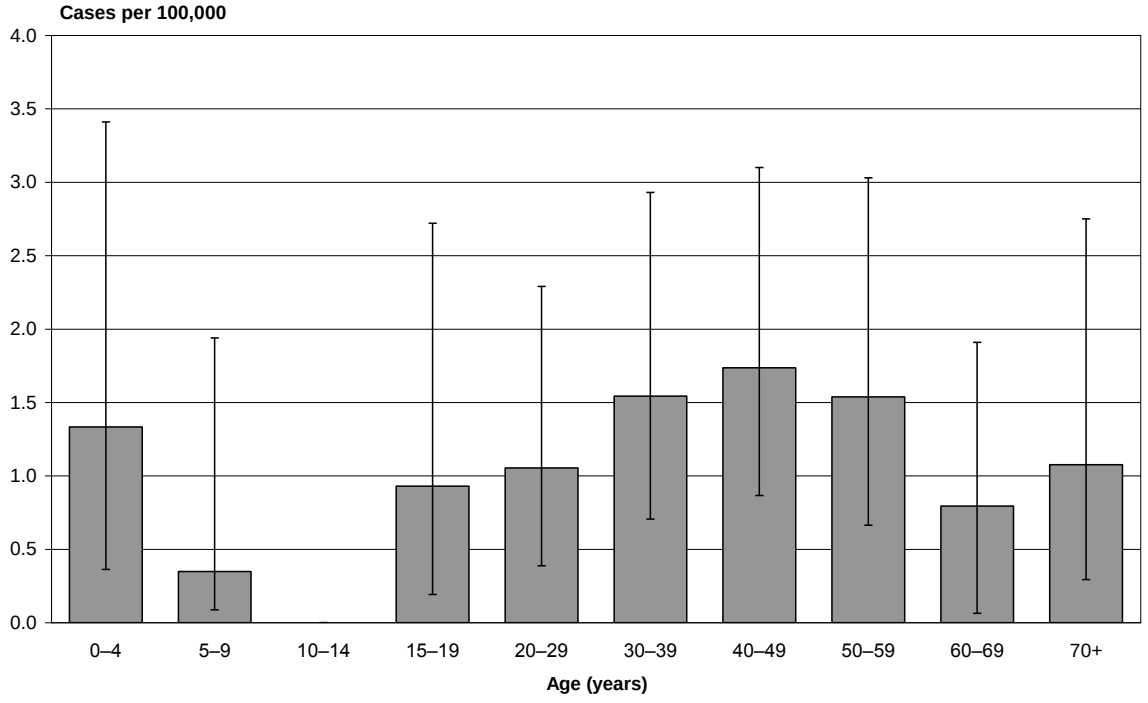
Although Pacific peoples had the highest number of pandemic deaths per 100,000 among the four main ethnic groups (Figure 2), because of the small number of cases involved there was no evidence of a statistically significant difference between any of the ethnic groups.

Figure 3: Distribution of pandemic influenza A(H1N1) 2009 deaths in New Zealand June–November 2009



The duration of the pandemic was short. Almost three-quarters of the total of 49 pandemic deaths occurred in July (Figure 3).

Figure 4: Age distribution for pandemic influenza A(H1N1) 2009 deaths in New Zealand in 2009



Of the four infants under five years old who died, three were under two years old. There were only five deaths in patients aged 65 years of more (Figure 4).

Figure 5: NZ Deprivation scores for patients who died of pandemic influenza A(H1N1) 2009

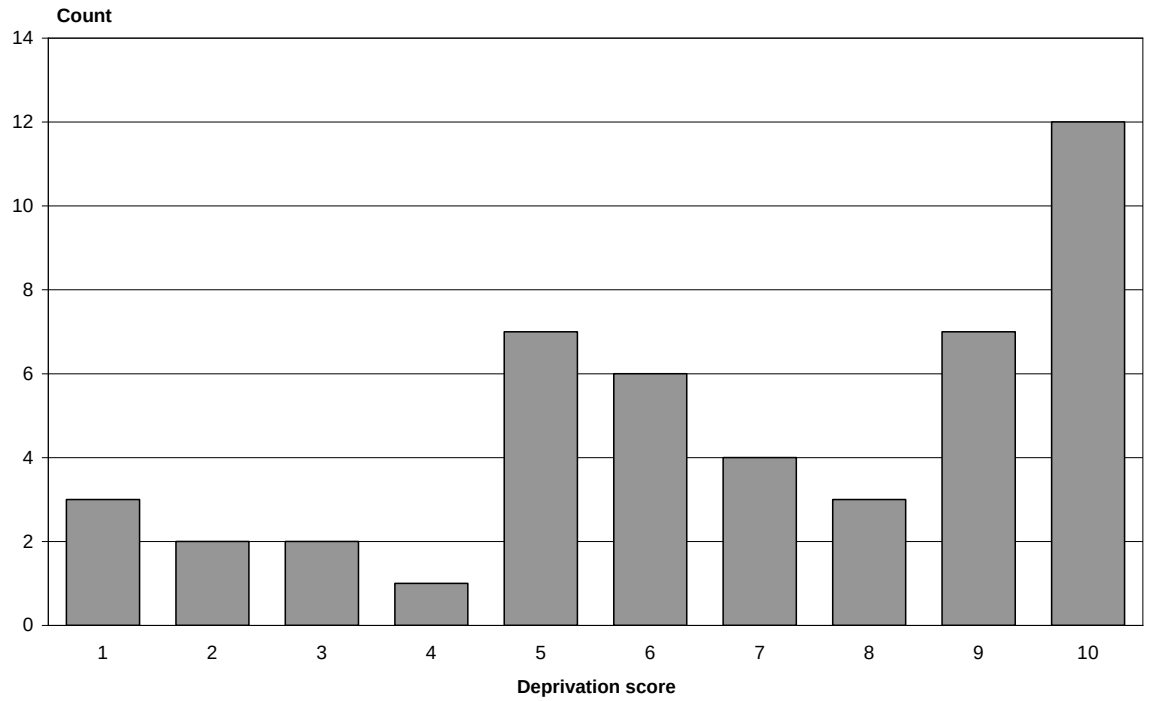


Figure 5 presents the distribution of socioeconomic deprivation scores (NZDep) among the 49 people who died, based on where they lived. When this distribution is compared with what might be expected among the general population, it is evident that 69% (34) had a deprivation score of 6 or more compared with the expected 50% of the population, and 39% (19) had a deprivation score of 9 or 10 compared with the expected 20% of the population.

Table 2: Co-morbidities and associated conditions of the individuals who died from pandemic influenza A (H1N1) 2009

Co-morbidities/associated conditions	Total deaths (N=49)		
	n	N	%
Immunocompromised	4	45	9
Malignancy	4	46	9
Cardiac disease	6	48	13
Haemoglobinopathy	1	46	2
Metabolic disease	2	46	4
Respiratory disease	22	45	49
Asthma	9	45	20
Other respiratory disease	13	45	29
Diabetes	6	45	13
Neurological disease (with respiratory impairment)	2	45	4
Morbid obesity: BMI ≥35	18	32	56
Obesity: BMI ≥30	23	32	74
Pregnant or postpartum (to 42 days)	4	49	8
Substance abuse	8	42	19
Alcohol abuse	5	40	13
Recreational drug use or methadone	3	41	7
No co-morbidity or associated condition noted	7	49	14

Note: More than one co-morbidity or associated condition could be recorded for any one patient. Data is missing for some variables. BMI is not calculated for children.

Table 2 presents the co-morbidities and associated conditions collected from the clinical records of the patients who died. It was not possible to collect complete information on past smoking status. Current smoking status was unknown in 10 patients. There were 11 known smokers and 28 patients who were not current smokers. Of those patients with BMI data available seventy-four percent of patients were obese (BMI ≥ 30 kg/m^2), and fifty-six percent were morbidly obese (BMI ≥ 35 kg/m^2). It should be recognised that BMI was not available in almost one quarter of adults and therefore these percentages may be an overrepresentation. The next most common condition was respiratory disease, including asthma and chronic obstructive pulmonary disease. There were three postpartum deaths following influenza in the third trimester of pregnancy (all infants survived), and one death following a miscarriage. Only 14% of patients who died did not have any co-morbidities or associated conditions.

Table 3: Description of the syndromes at the time of presentation of the patients who died of pandemic influenza A(H1N1) 2009

Influenza syndromes	Total deaths (n=49)	
	n	%
Classical influenza-like illnesses (ILI)* with no other symptoms	4	8
ILI plus other symptoms	16	33
Fever, no ILI, other symptoms	7	14
No fever or ILI, other symptoms only	18	37
Insufficient information to categorise	4	8

* Influenza-like illness (ILI) is defined as "(i) history of fever, chills, and sweating and/or clinically documented fever ≥38 °C, plus (ii) cough or sore throat" (Ministry of Health 2009).

Forty-one percent of the patients who died of pandemic influenza A(H1N1) 2009 presented with classical ILI, or with ILI with other symptoms. Thirty-seven percent of the patients presented with neither a fever nor influenza-like illness. Shortness of breath was present in 43% of the patients at presentation (n=21) and 10% (n=5) presented with confusion or drowsiness.

Table 4: Length of illness of the patients who died of pandemic influenza A (H1N1) 2009

	Median	Total range	Interquartile range (IQR)
Days from onset of symptoms to health care presentation (N=40)	3	0–21	2–6
Days from hospitalisation to death (N=33)*	10	1–94	2–24
Days from onset of illness to death (N=41)	13	1–95	7–28

* Does not include those patients who were not admitted to hospital

Table 4 shows available data on the length of illness among those who experienced a pandemic death. In eight patients there was no information on the number of days from the onset of symptoms to seeing a health care worker or to the time of death. There were 16 unexpected deaths at home or in the community. For the 33 patients who were hospitalised, some were admitted within a few days of becoming unwell and others had a more protracted illness with several visits to their general practitioner.

Table 5: Place of death and contact with the health care system among the patients who died of pandemic influenza A(H1N1) 2009

Place of death	Total deaths (N=49)	
	n	%
Community/home, unknown health care contact	5	10
Community/home, no health care contact	6	12
Community/home, consulted general practitioner or hospital admission	5	10
Hospital ≤ 7 days	14	29
Hospital > 7 days	19	39

Of the 16 patients who died at home or in the community (Table 5), four had seen their general practitioner after onset of symptoms, including one who had been discharged from hospital and the New Zealand tourist in the Cook Islands. Of the deaths in hospital, 21 occurred either in intensive care or shortly after discharge from intensive care. There were two patients who were admitted for other indications but contracted pandemic influenza A(H1N1) 2009 while in hospital.

3.1.2 First contact with a health professional

Of the 49 patients who died, 19 went to their general practitioner or accident and medical centre as their first point of contact, one was seen by maternity services, and 18 attended a hospital emergency department or outpatient services; for another five patients, the nature of their first contact is unknown. Six patients did not see any health professional during their illness.

3.1.3 Antiviral therapy

Of the 34 patients admitted to hospital, 24 had been prescribed antiviral therapy. The median length of time from the onset of illness to antivirals being prescribed was six days with an interquartile range of 4–8 days. Among the 16 patients who died unexpectedly at home, four had seen their general practitioner and one had been discharged from hospital but no antiviral therapy had been given. One patient self medicated without seeking medical assistance, six patients had not been seen by any health services and, of the remaining four, it was not known whether they had been seen by any health services.

3.1.4 Antibiotic therapy

Of the 49 patients who died, 10 received a single antibiotic, 24 received combined antibiotics, and 11 received no antibiotics; whether the remaining four received antibiotics is unknown. The median length of time from the onset of illness to antibiotics being prescribed was three days with an interquartile range of 1–6 days.

3.1.5 Influenza complications

Table 6: Influenza complications identified at the time of death of pandemic influenza A (H1N1) 2009

Complications	Total deaths (N=49)	
	n	%
Pneumonia (x-ray diagnosis)	27	55
Encephalitis/encephalopathy	3	6
Shock	6	12
Acute renal failure	15	29
Secondary bacterial infection	7	14
Rhabomyolysis	1	2

Note: More than one category could be allocated to any given patient.

As Table 6 shows, the most common complication identified clinically among the patients who died was pneumonia (55%).

3.1.6 Unexpected deaths at home from pandemic influenza A(H1N1) 2009

There were 16 unexpected deaths at home. Post-mortem results were available for 14 of these deaths, among which a primary respiratory cause of death such as pneumonia/pneumonitis was present in 11. The remaining cases were thromboembolism and myocarditis.

3.2 Number of intensive care admissions from pandemic influenza A(H1N1) 2009 in New Zealand from June to November 2009

In New Zealand, 119 patients with confirmed pandemic influenza A(H1N1) or probable pandemic influenza were admitted to intensive care units (including three patients who could not be subtyped) (ANZIC Influenza Investigators 2009). Eighty-two patients (69%) of those admitted to intensive care required mechanical ventilation and, of those, eight (10%) required extracorporeal membrane oxygenation (ECMO) and four subsequently died. Twenty-two (18%) of the patients admitted to ICU died.

Table 7: Intensive care admissions for pandemic influenza A (H1N1) 2009

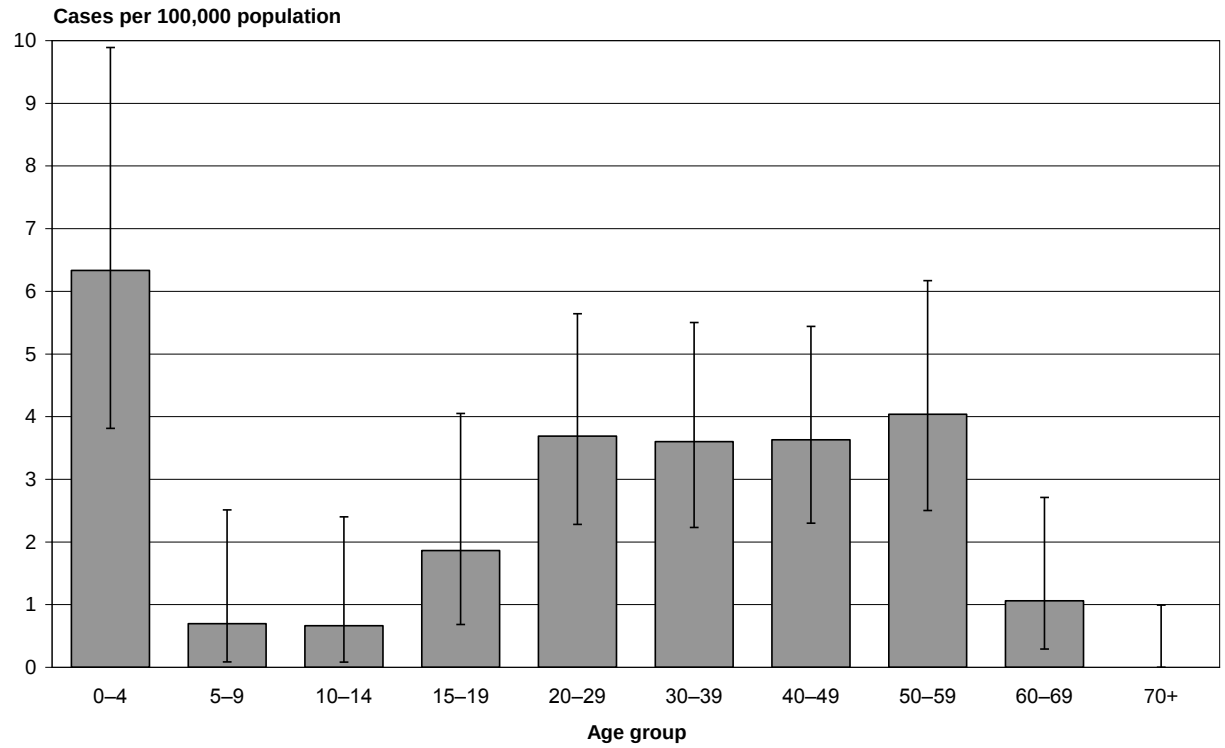
	Primary ICU admission	Transfers in / re-admissions	DHB population	Primary admissions per 100,000	p value (vs rest of New Zealand)*
Northland	4		155,800	2.6	ns
Waitemata	14	1	528,500	2.6	ns
Auckland	15	15	444,100	3.4	ns
Counties Manukau	23	1	481,700	4.8	0.005
Waikato	12	2	360,000	3.3	ns
Lakes	1		101,800	1.0	ns
Bay of Plenty	2		207,700	1.0	ns
Tairawhiti	4		46,200	8.7	0.015
Taranaki	0		108,300	0.0	ns
Hawke's Bay	6		153,900	3.9	ns
Whanganui	0		63,200	0.0	ns
MidCentral	1		166,000	0.6	ns
Wairarapa	0		39,900	0.0	ns
Hutt Valley	4		142,700	2.8	ns
Capital and Coast	11		288,100	3.8	ns
Nelson Marlborough	2		136,800	1.5	ns
West Coast	0		32,600	0.0	ns
Canterbury	14	2	502,000	2.8	ns
South Canterbury	1		556,00	1.8	ns
Otago	2		188,700	1.1	ns
Southland	3	1	111,700	2.7	ns
Total	**119**	**22**	**4,315,300**	**2.8**	

Source: ANZIC Influenza Investigators 2010

* The analysis is compared with the New Zealand rate.

As Table 7 shows, the only DHBs with significantly higher ICU admission rates than the national rate were Counties Manukau and Tairawhiti.

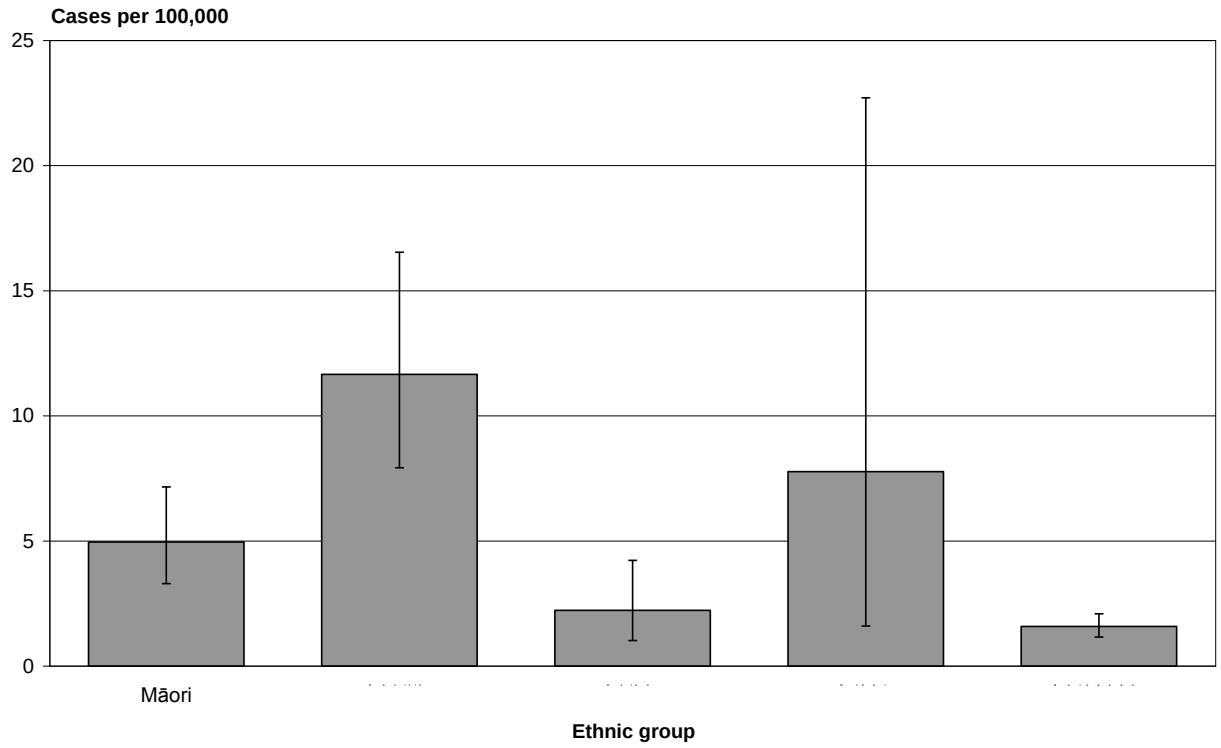
Figure 6: Intensive care admissions for pandemic influenza A(H1N1) 2009 by age



Note: Confidence intervals calculated by the Exact Method.

Children under the age of five years were more likely to be admitted to an ICU for pandemic influenza A(H1N1) 2009 than children aged 5–14 years old or those aged older than 60 years (Figure 6). Of the 19 children aged 0–4 years who were admitted, 17 were aged under two years.

Figure 7: Intensive care admissions for pandemic influenza A(H1N1) 2009 by prioritised ethnicity



3.2.1 Co-morbidities among those admitted to intensive care units

Body mass index was available for 67 of the 92 (73%) adults (18 years or older) admitted to ICU. Among these patients, the median BMI was 33 kg/m^2 with an interquartile range of 27–44 kg/m^2. In this group, 66% were obese (BMI ≥ 30 kg/m^2) and 45% were morbidly obese (BMI ≥ 35 kg/m^2), compared with 26% and 9% respectively in the general New Zealand population (Ministry of Health 2008).

Table 8: Co-morbidities/associated conditions of patients with pandemic influenza A(H1N1) 2009 admitted to ICU†

Co-morbidity/associated conditions	n/N	%
Obese (adults only) (BMI ≥ 30 kg/m^2)	42/67	66
Morbidly obese (adults only) (BMI ≥ 35 kg/m^2)	30/67	45
Diabetes (all types)	20/119	17
Chronic lung disease (CORD, restrictive lung disease, bronchiectasis, all actively treated before admission)	35/119	29
Chronic heart failure (on treatment or confirmed by echo cardiogram or moderate or severe valve disease on echo cardiogram)	6/119	5
Pregnancy or postpartum	10†/119	8
Other significant co-morbidity (not including any of the above)*	21/119	18
Overall (one or more of the above)	66/119	55
No co-morbidities	53/119	45

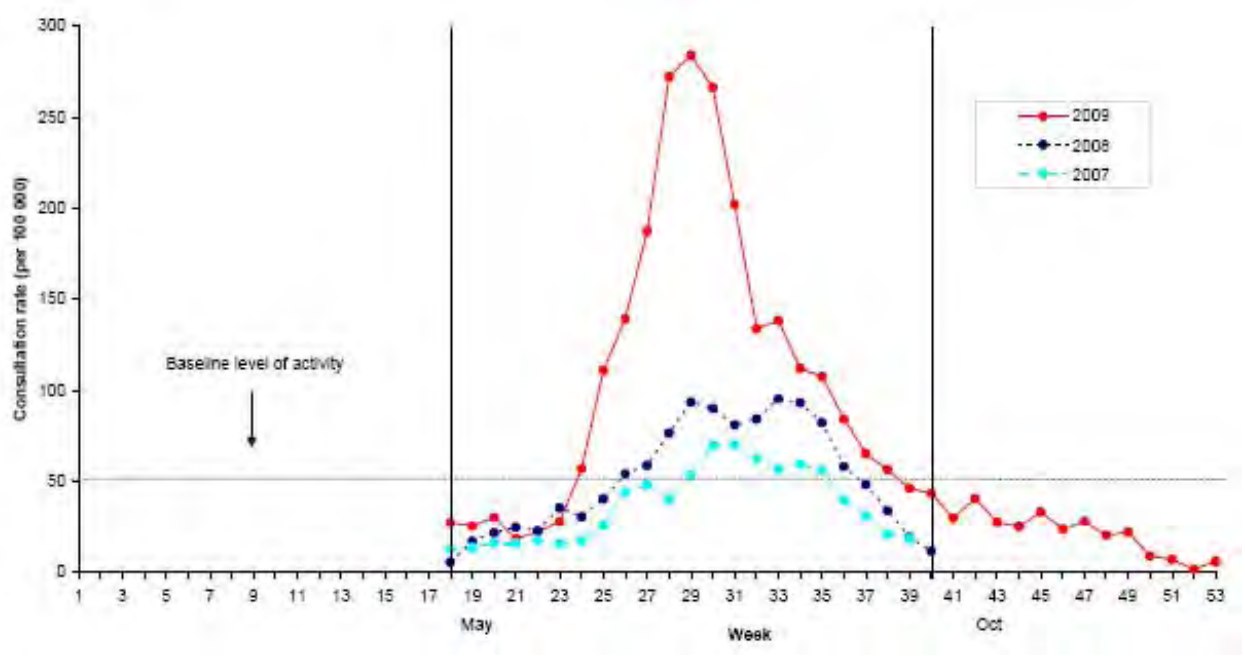
† Includes three cases with influenza A unable to be subtyped.

* Defined in the APACHE III scoring system for adult ICU patients as AIDS, hepatic failure, lymphoma, leukaemia or myeloma, cirrhosis, Class 3 or 4 respiratory or cardiac symptoms, disease- or treatment-induced immunosuppression. For children other significant co-morbidity was defined as prematurity, immunodeficiency, cystic fibrosis, congenital heart disease, neuromuscular disorder or chronic neurological impairment.

3.3 Number of consultations and hospitalisations for pandemic influenza A(H1N1) 2009 / suspected influenza A in New Zealand from June to November 2009 compared with seasonal influenza in 2008

The data in this section of the report have been extracted from the ESR report (2010a). During the winter months (May to September 2009), using extrapolations from the national sentinel network of 101 general practices, it has been estimated that 116,335 New Zealanders (2.7%) had an influenza-like illness resulting in a visit to a general practice (ESR 2010a, p i).

Figure 8: Weekly consultation rates at sentinel general practices for influenza-like illness in New Zealand 2007–2009

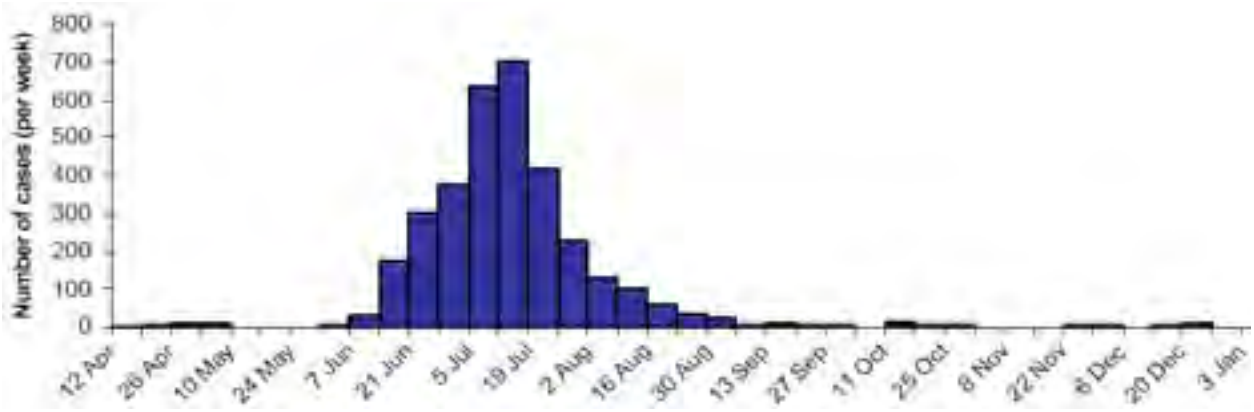


Source: ESR (2010a), p 4

Figure 8 shows trends in the consultation rate at sentinel general practices in the winter months over three years from 2007 to 2009. For the winter months of 2009, the average national consultation rate at sentinel general practices was 77.9 per 100,000 patient population, which is higher that the average weekly rate over the same period for 2008 (52.4 per 100,000 patient population) and 2007 (37.2 per 100,000 patient population) (ESR 2010a, p 2).

The overall level of influenza-like illness in 2009 was higher than the level for any of the previous 11 years (1997–2008) (ESR 2010a, p 5). The influenza-like illness consultation rates varied greatly between health districts; Counties Manukau and Capital and Coast DHBs had the highest rates (ESR 2010a, p 6). Among all typed and subtyped viruses, 78% of the viruses were pandemic influenza A(H1N1) 2009 and 20% were seasonal A(H1N1) viruses (ESR 2010a, p 14). All pandemic influenza A(H1N1) 2009 viruses tested were sensitive to oseltamivir whereas all seasonal A(H1N1) viruses were resistant to oseltamivir (ESR 2010a, p 20).

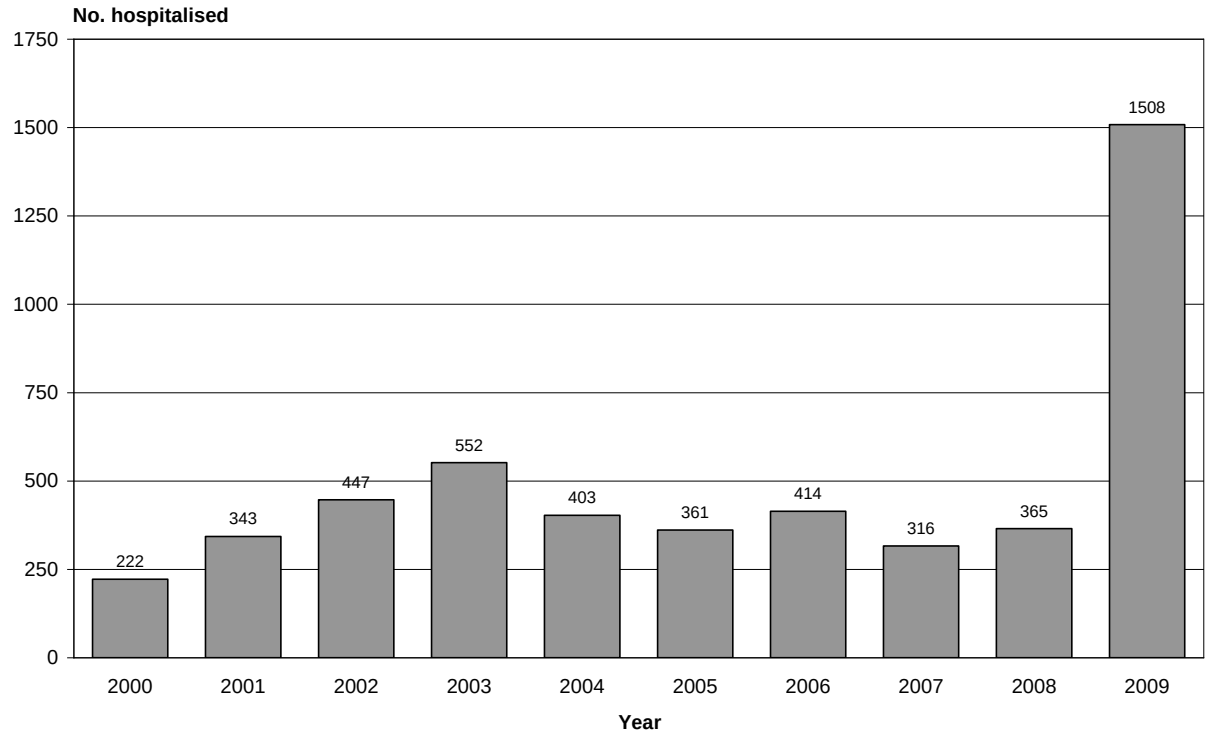
Figure 9: Total number of cases of pandemic influenza A(H1N1) 2009 (confirmed and probable)



Source: ESR (2010a), p 11

Figure 9 presents the total number of cases of pandemic influenza A(H1N1) 2009 reported in EpiSurv from 12 April 2009 to 3 January 2010.

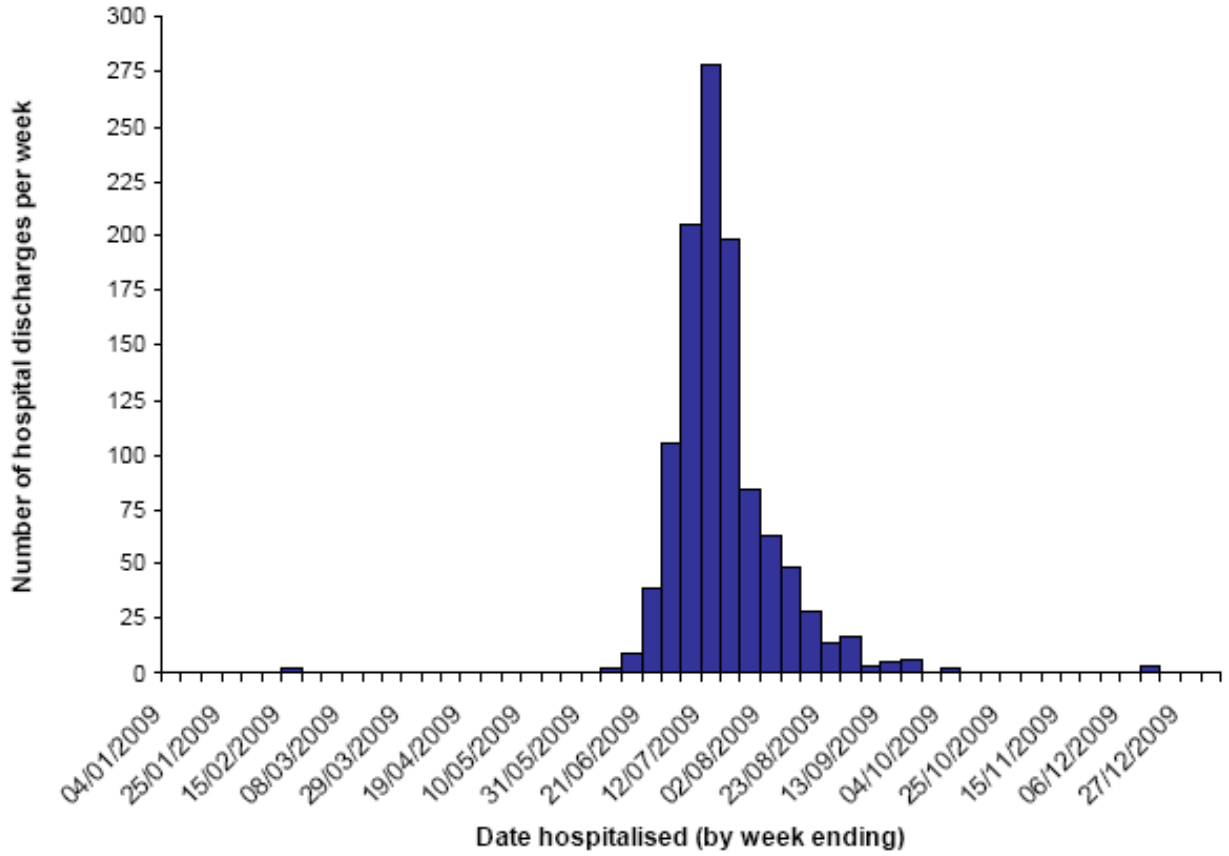
Figure 10: Influenza hospitalisations 2000–2009



Source: ESR (2010a), p 5

In 2009 there were 1508 hospitalisations for influenza, which represents a four-fold increase on the 365 hospitalisations for influenza in 2008. The highest number of hospitalisations occurred in July. Among the 1508 patients hospitalised, 1122 (74%) had a primary diagnosis of pandemic influenza A(H1N1) 2009. The median age was 26.7 years and the range was from 19 days to 91 years.

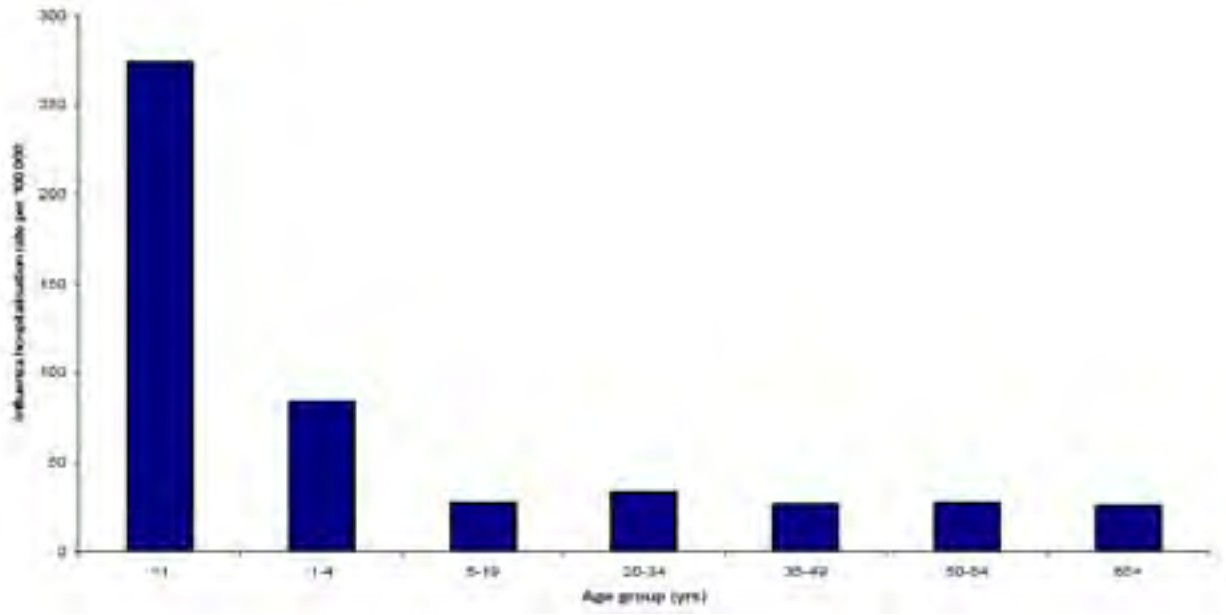
Figure 11: Hospitalisations for confirmed pandemic influenza A (H1N1) 2009



Source: ESR (2010a), p 12

Figure 11 shows the distribution of hospitalisations for confirmed pandemic influenza A (H1N1) on a weekly basis over 2009. A total of 278 hospitalisations were reported in the peak week of notifications, 6–12 July 2009.

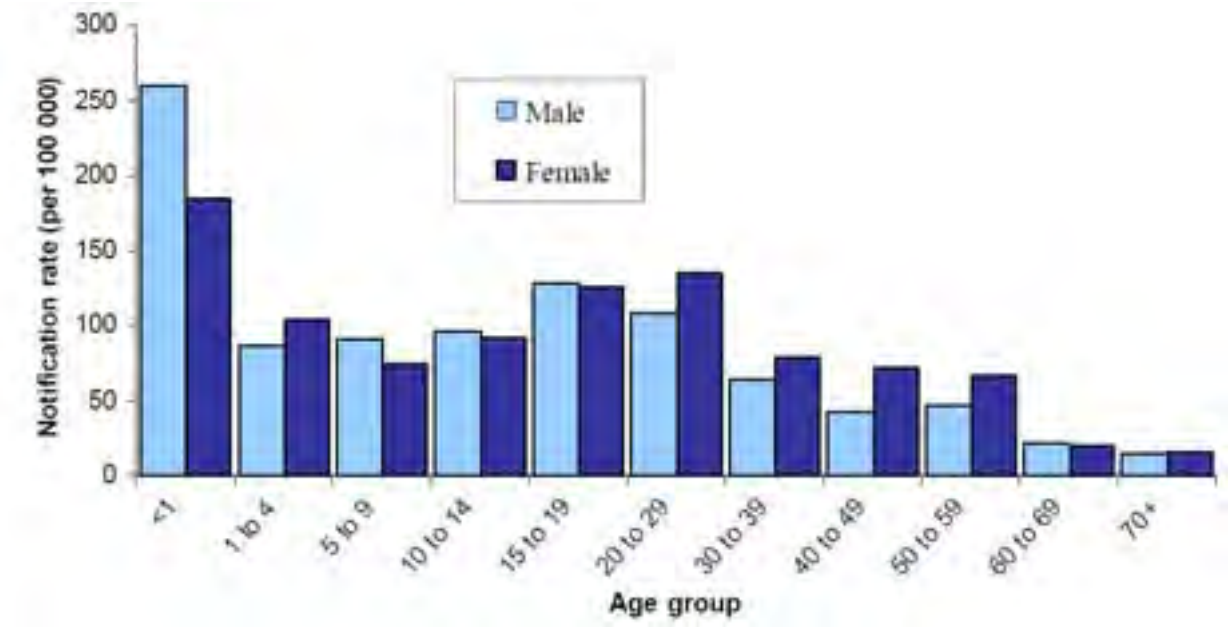
Figure 12: Influenza hospital admission rate by age group 2009



Source: ESR (2010a), p 8

Figure 12 compares the hospitalisation rates in 2009 by age group. The highest rates reported were for children under one.

Figure 13: Cumulative rate of pandemic influenza A(H1N1) 2009 notifications by age and sex



Source: ESR (2010a), p 11

Figure 13 reports on the age distribution of notifications of pandemic influenza A(H1N1) 2009 by age and sex. The highest reported notification was for those aged under one year, followed by people aged 15 to 29 years.

4 Discussion

There were 49 New Zealand patients (including one New Zealand tourist in the Cook Islands) who died in the winter months of 2009 with pandemic influenza A(H1N1) 2009 virus infection. A total of 1122 patients were admitted to hospital with a primary diagnosis of pandemic influenza A(H1N1) 2009, including 118 patients admitted to intensive care units. An estimated 116,335 patients attended their general practice (2.7% of the population). Another group of patients is likely to have attended either an influenza centre or emergency department. Pandemic influenza A(H1N1) 2009 peaked between July and September 2009 and, although this period was associated with fewer deaths than some projections, hospitalisations and deaths from influenza were higher than in the previous 15 years. The majority of these admissions and attendances occurred during July 2009, creating a considerable logistical challenge for laboratories and primary and secondary health services.

The absolute number of deaths was small and statistical analysis is, therefore, limited. However, the morbidity data support the findings suggested in the mortality data. There were common themes among the patients who were admitted to intensive care, or who died. Pacific peoples were over-represented among hospitalised cases, although the seroprevalence study results show that the high rate of infection among Pacific peoples relates almost wholly to the younger age group (Jain et al 2009). Other groups that were over-represented in hospitalisations and intensive care admissions were infants and the socioeconomically deprived. Obesity was a frequent co-morbidity, although this condition is linked with ethnicity and socioeconomic deprivation and it is not clear which of these factors is critical. Not surprisingly, people with pre-existing respiratory illnesses were often affected more severely. Those with chronic respiratory disorders and those who were obese appear to have been particularly vulnerable to severe illness. Sixteen patients died at home or in the community; in most cases they had not seen a health professional and were socially isolated. Pregnant women and women recently postpartum were also among the data for deaths, hospitalisations and intensive care admissions. The majority of patients who died (86%) and of patients admitted to ICU (55%) had co-morbidities or associated conditions. These findings are consistent with other international reports where the proportion of influenza cases with no co-morbidities or associated conditions ranges from 2% to 51% (Dominguez-Cherit et al 2009; Jain et al 2009; Kumar et al 2009). In one report from China, however, only 8% of patients had any co-morbidities prior to becoming unwell with influenza (Cao et al 2009).

The burden of mortality and morbidity from pandemic influenza A(H1N1) 2009 has largely fallen on a younger age group in New Zealand, which is markedly different from the age distribution for influenza deaths in previous years (see Appendix 4). For example, there were more deaths in 2009 from pandemic influenza A(H1N1) in those under the age of 65 (n=43 deaths) than for all the years from 2000 to 2008 (n=14) (data provided by the ESR; note that the 2007, 2008 and 2009 data is provisional). The findings highlight the susceptibility of the younger age group to this virus and suggest that the older age groups were protected by earlier exposure to influenza A. Prior to 2009, the last year when a large number of influenza deaths was reported in New Zealand was in 1996 when there were 94 deaths from influenza, but 93 of these deaths occurred in those aged 65 years or older (ESR 2010a). These findings are consistent with reports of mortality from pandemic influenza A(H1N1) 2009 in the United States and France (Lemaitre and Carrat 2010).

The clinical presentation of disease among patients who subsequently died was varied. Many of these patients did not receive antiviral therapy or presented late and, therefore, started it late in the course of their illness. Only 41% of the patients who died presented with the classical symptoms of influenza-like illness (ILI) and 37% had no fever or ILI. Shortness of breath was present in 43%. It was also concerning that 16 patients died at home or in the community, only a few of whom had sought the assistance of the health services. There is a need for further work on public health messages so that they convey the range of influenza presentations.

Although it was not the focus of this report to consider seroprevalence to the pandemic influenza A(H1N1) 2009, it is noted that by early 2010 an estimated 29.5% of the population had immunity to pandemic influenza A(H1N1) 2009 and an estimated 45% of those who tested seropositive did not experience symptoms (ESR 2010b).

In primary care there have been two main approaches to treating influenza, and pandemic influenza A(H1N1) 2009 in particular. First, the pandemic influenza A(H1N1) 2009 was sensitive to antiviral treatment (ESR 2010a) and early antiviral treatment has been shown to shorten the illness although not necessarily reduce mortality (Burch et al 2009; Jefferson et al 2010a). The second approach was to treat with antibiotics as secondary bacterial infection is common. In general, both health care workers and patients alike are more familiar with prescribing antibiotics than antivirals. This general familiarity may explain, in part, why the use of antibiotics was more common than the use of antivirals. The other explanation is that access to antivirals was restricted in primary care whereas access to antibiotics was not.

The review group has identified more deaths from pandemic influenza A(H1N1) 2009 than were initially identified by the EpiSurv database. We were able to draw on a broader range of data by matching the dataset of the pandemic influenza A(H1N1) notifications with death notifications from Births, Deaths and Marriages. In addition, the databases of the PMMRC and the CYMRC provided information on one additional case, the INFINITE database of the ANZICS provided additional clinical data, and one case was identified from the National Minimum Dataset (NMDS). The strength of this approach has been to establish with a high degree of certainty that all cases of deaths and admissions associated with pandemic influenza A(H1N1) 2009 in New Zealand have been identified. In regard to the admissions to intensive care, it is possible that some cases have not been notified although the data collection methods are considered reliable. It is also possible that some patients with pandemic influenza A(H1N1)2009 did not have specimens collected and, therefore, were not identified.

The influenza (pandemic and seasonal) mortality rate for 2009 (excluding one death of a New Zealand tourist in the Cook Islands) was 1.38 per 100,000 population for 2009. This 2009 mortality rate was the highest rate in New Zealand reported since 2000. In 2009 the uptake of the seasonal influenza vaccine among people aged 65 years and over was 65.5%. Unfortunately, the seasonal influenza vaccine in 2009 did not offer immunity against pandemic influenza A(H1N1) 2009 and the development time for a pandemic-specific vaccine meant that it was not available until after pandemic influenza in 2009 was on the wane in New Zealand. At the time of writing there were no international reports of pandemic influenza A(H1N1) 2009 mortality with which to compare the New Zealand rate. Any such data will be added to the report if they become available prior to publication.

5 Recommendations from the Mortality and Morbidity Review for Pandemic Influenza A(H1N1) 2009

Recommendations for the Ministry of Health and District Health Boards

1. Pandemic influenza vaccination

While all individuals are encouraged to have an annual influenza vaccination, individuals at increased risk of complications* (see box) following pandemic influenza virus infection are offered this preventative measure without charge.

Note:

- The vaccine cannot be given to infants under six months of age.
- Individuals under nine years require two doses if they have not previously had an influenza vaccine.
- Adults who are at greatest risk of seasonal influenza (such as those 65 years or older) should also be offered the trivalent seasonal vaccine as viruses other than H1N1 are likely to be circulating.

Frontline health care workers should be offered vaccination.

Vaccination of family members and contacts of high-risk individuals should be encouraged.

DHBs should work with primary and secondary care providers to achieve high levels of coverage for patients at increased risk of complications* (see box) who are attending secondary care.

*** Individuals at increased risk of complications from pandemic influenza A(H1N1) 2009**

Children under 5 years of age, especially infants

Adults over 65 years of age

People who are morbidly obese (BMI ≥ 35 kg/m^2)

People with chronic respiratory disease, including asthma and chronic obstructive airways disease

People with cardiac disease

People with neurological conditions (that affect the ability to breathe and cough)

People with immunosuppressive conditions

People who have a history of substance abuse

Pregnant women and those in the postnatal period

Justification for the recommendation

(a) From the mortality and morbidity review

Among the patients who died of pandemic influenza, 86% had co-morbidities. The most common co-morbidities were respiratory illnesses (asthma and chronic obstructive pulmonary disease) (49%), morbid obesity (BMI ≥ 35 kg/m^2) (56%), substance abuse (19%) and cardiac disease (13%).

Family members of some patients died also had had an influenza-like illness.

Children are a major reservoir of respiratory viruses in the community as they have high levels of infection and are very likely to introduce infection into family settings (ESR 2010a; Miller et al 2010).

Children aged two years and under (especially children under one) are disproportionately represented in cases admitted to intensive care and hospital.

Many adults with co-morbidities and associated conditions did not present with classical influenza-like illness and therefore may have been less likely to be diagnosed and treated.

(b) Other evidence

Vaccine studies of healthy volunteers have shown immunogenicity with the newly developed pandemic influenza A(H1N1) 2009 vaccine (Plennevaux et al 2010; Vajo et al 2010; Xiao-Feng 2010).

Immediate vaccination will confer increasing immunogenicity in the exposed patient within 10 days with some evidence of protective immunity from day 3 (Zuckerman et al 1993).

Studies have confirmed that children under the age of five are at increased risk, although children with underlying medical conditions account for most deaths in this age group (Zuckerman et al 1993).

Likely outcome of recommendation

This strategy would reduce morbidity and the transmission of influenza among those most at risk of complications, and among their families, and protect frontline health workers who come into contact with patients with influenza.

2. Improving access to antivirals

Barriers to accessing antivirals (oseltamivir (*Tamiflu®*) and zanamivir (*Relenza®*)) should be reduced to support early treatment for any individuals presenting with symptoms of influenza. Strategies to ensure treatment of a greater proportion of individuals at increased risk of complications (see box under recommendation 1) should be considered.

The following are options for making antivirals more widely available and facilitating their timely administration.

- Provide antivirals free to general practices so that GPs can dispense them directly free of charge.
- Make antivirals available to pharmacies free of charge so that pharmacists can dispense them after following a simple checklist of symptoms as well as giving a leaflet to patients to seek medical care if their symptoms worsen. (Patients who have more than mild symptoms should be advised to see their doctor.)
- Make antivirals accessible through Healthline. On calling Healthline, the patient would answer questions from a simple checklist regarding severity of symptoms and then arrangements would be made with the relevant DHB and/or pharmacy staff to deliver antivirals.
- Provide patients in high-risk categories with antiviral medications at home which they could commence following a telephone consultation.

Justification for the recommendation

(a) From the mortality and morbidity review

Among the patients who died of pandemic influenza, the median time from the start of the symptoms to receiving antivirals was six days. In some cases patients had been in contact with health services during this time but had not commenced antivirals. The majority of the patients who died had not received antivirals in the first 48 hours of symptoms.

(b) Other evidence

- Systematic reviews of antivirals in seasonal influenza suggest that taking antivirals within 48 hours of the start of symptoms shortens the illness by 0.5 to 1.5 days (Burch et al 2009; Jefferson et al 2010a). The use of antivirals also shortens the viral shedding period (Aoki et al 2003; American Academy of Pediatrics Committee on Infectious Diseases 2007). One systematic review suggested this treatment is more effective in patients with co-morbidities, including children (Burch et al 2009). Emerging pandemic evidence suggests that early initiation of oseltamivir within 24 hours is associated with a reduced risk of death (Farias et al 2010).
- Pandemic influenza A(H1N1) 2009 has been shown to be sensitive to antivirals in the laboratory (ESR 2010a).
- The average incubation period for pandemic influenza A(H1N1) is two days, although it can be up to seven days (time between being exposed to influenza and presentation of symptoms) (HPIH and SD PIP 2009).
- Anecdotal evidence from general practitioners in some areas suggests that there are barriers to prescribing antivirals, including the cost of the prescription for patients and the process of getting approval for free antivirals.
- Many health care providers did not seem to be familiar with the use of antiviral medications to ensure timely, appropriate use.

- It has been recommended that women who have suspected or confirmed pandemic influenza A(H1N1 2009) and are pregnant or have delivered an infant within the previous two weeks should receive antiviral treatment and close monitoring (CDC 2009a). Starting antiviral treatment more than 48 hours after the onset of symptoms is associated with a greater risk of ICU admission and death (RR 4.3; 95% CI 1.4–13.7) (Louie et al 2010). No additional risks for adverse events in pregnant women receiving oseltamivir have been reported (CDC 2009a).The WHO recommends the use of antivirals as soon as possible in high-risk populations, children and those with immunosuppression (WHO 2010).

Likely outcome of recommendation

This strategy would increase access to antivirals and reduce patients' movement in the community, and may reduce severe morbidities, hospital admissions and mortality.

Recommendations for District Health Boards and Primary Health Organisations

3. Prevention of transmission of pandemic influenza A(H1N1) 2009

All care must be taken to protect staff and patients. The following strategies are suggested:

- using good hand and respiratory hygiene and use of barrier protection
- actively promoting vaccination to health care workers and those at risk of complications from influenza
- encouraging staff to stay home at the onset of symptoms and consider taking antivirals
- discouraging anyone who may be infectious from entering hospitals unless they have a clinical need.

Health services for health care workers should focus on providing rapid assessment and care within primary or secondary care, and ensuring access to antivirals at the first onset of symptoms.

In all health care settings, isolation and treatment of individuals with symptoms should be initiated on clinical suspicion, without waiting for the influenza test results.

To protect people who are at increased risk of complications from infection associated with health care, special care needs to be taken to diagnose and isolate cases admitted to health care facilities, including hospitals and long-term care facilities. Vulnerable patients should be vaccinated and each facility's general hygiene measures and practice should minimise transmission from unrecognised cases.

Justification for the recommendation

(a) From the mortality and morbidity review

Some patients who died from pandemic influenza A(H1N1) 2009 were probably infected within health care settings as patients admitted for other reasons became unwell and died several days after their admission. One health care worker also became unwell and died from pandemic influenza. The source of the infection in these cases (staff, visitors or other patients) was unclear to the review group.

Seroprevalence data have shown similar rates of seroprevalence among health care workers (27.5% for nurses, 29.9% for doctors) compared with an overall seroprevalence rate of 26.7% (ESR 2010b).

(b) Other evidence

The average incubation period for pandemic influenza A(H1N1) 2009 is two days although it can be up to seven days (time between being exposed to influenza and presentation of symptoms) (HPIH and SD PIP 2009).

The use of personal protective equipment and correct hand hygiene has been shown to reduce the spread of influenza, including pandemic influenza A(H1N1) (HPIH and SD PIP 2009; Jefferson et al 2010b).

Likely outcome from recommendation

This strategy would reduce transmission of pandemic influenza A(H1N1) 2009 in hospitals and in other health care services, which in turn would reduce the number of influenza-related deaths and staff absences.

Recommendations for health professionals

4. Assessing severity of influenza

The use of an early warning score system in primary care and in emergency departments is recommended to assist decision making about admission for people over 14 years old with pneumonia (an example is provided in Appendix 2). There is no validated early warning score for influenza and, therefore, it is common practice to refer to those used in community-acquired pneumonia. For children, a similar checklist is available (provided in Appendix 3).

Justification for the recommendation

(a) From the mortality and morbidity review

The majority of patients who died had a CRB65 score of two or more at presentation but were not always admitted or treated urgently.

In some cases, the severity of the patient's symptoms was not recognised by the patient, the family members or their medical attendants.

(b) Other evidence

The use of CRB65 scores can predict mortality in patients with community-acquired pneumonia with a score of 2 or more having a sensitivity of 80% (Lim et al 2003; Capelastegui et al 2006).

Likely outcome from recommendation

This strategy would enable more accurate identification of patients who may benefit from inpatient care.

5. Prescribing antivirals

Antivirals are most effective early in the illness (usually less than 48 hours after symptoms have started in adults and up to five days for children) without waiting for the laboratory test results for pandemic influenza A(H1N1) 2009 in primary and secondary care settings. The earlier antivirals are given during the course of the illness, the greater the benefit.

This advice also applies to children under two years old and to pregnant women.

Individuals who are at high risk of complications from pandemic influenza (see box in recommendation 1) could be offered treatment with antivirals if other family members have symptoms of influenza.

Justification for the recommendation

(a) From the mortality and morbidity review

There was evidence that the majority of patients who died of pandemic influenza A(H1N1) 2009 started antivirals later than 48 hours after onset of symptoms in spite of seeing a health care provider prior to that during their illness. The median time from onset of symptoms to commencing antivirals was six days.

Among the patients who died of pandemic influenza A(H1N1) 2009, 86% had co-morbidities. The most common co-morbidities were respiratory (asthma, chronic obstructive pulmonary disease) (49%), morbid obesity (BMI ≥ 35 kg/m^2) (55%), substance abuse (19%) and cardiac disease (13%).

(b) Other evidence

- Systematic reviews suggest that taking antivirals within 48 hours of the onset of symptoms of seasonal influenza shortens the illness by 0.5 to 1.5 days (Burch et al 2009; Jefferson et al 2010a). Other studies suggest the use of antivirals also shortens the viral shedding period (American Academy of Pediatrics Committee on Infectious Diseases 2007). In addition, the earlier antivirals are given during the course of the illness, the greater the benefit (Aoki et al 2003).
- Anecdotal evidence from general practitioners in some areas suggests that there are barriers to prescribing antivirals, including the cost of the prescription for patients and the process of getting approval for free antivirals.

- Evidence for post exposure treatment of individuals at higher risk of complications is limited but the likelihood of adverse events from antiviral treatment is low (ESR 2010b; WHO 2010). The most common adverse event is increased risk of nausea with oseltamivir.

Likely outcome from recommendation

This strategy would:

- enable timely prescribing of antivirals, particularly for patients with co-morbidities who are at risk of complications
- reduce infectivity to other family members
- enable an earlier return to daily activities
- possibly reduce hospital and ICU admissions and deaths.

6. Testing for pandemic influenza A(H1N1) 2009

Any patient who attends a hospital with fever during times of increased influenza activity (unless there is an obvious non-influenza diagnosis) should be tested for influenza (as well as other clinically indicated laboratory diagnostic tests). At times of increased influenza activity, wider indications for virological laboratory testing should be introduced, in discussion with the local laboratory. In particular, patients with severe underlying respiratory disease, morbid obesity, and who are immunosuppressed should have easy access to influenza diagnostic testing.

In all health care settings, isolation and treatment of individuals with symptoms should be initiated on clinical suspicion, without waiting for the influenza test results.

Routine, widespread use of influenza diagnostic testing is not feasible in primary care. Access should be available following consultation with the public health services and local laboratory services.

Justification for the recommendation

(a) From the mortality and morbidity review

Limited testing for pandemic influenza A(H1N1) 2009, particularly in some patients who died of influenza-like illnesses, has made it difficult to undertake a retrospective review of the impact of the pandemic in New Zealand.

The majority of patients identified as dying of influenza infection did not have classical ILI.

Nosocomial infections were reported in three patients who died. This number may have been reduced if testing had occurred and appropriate measures had been undertaken subsequently.

(b) Other evidence

The Center for Disease Control and Prevention (CDC) recommends initiating treatment before laboratory confirmation of influenza (CDC 2009b).

The CDC further recommends that definitive testing for pandemic influenza A(H1N1) 2009, using real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) or viral culture, is a priority for patients with influenza-like illness requiring hospitalisation (CDC 2009b).

Likely outcome from recommendation

This strategy would enable earlier identification of infections in patients and would reduce hospital, in-service transmission of influenza to patients and staff.

7. Specific advice for individuals with higher risk of complications

Individuals who are at increased risk of complications for pandemic influenza A(H1N1) 2009 are listed under recommendation 1.

Individuals at increased risk of complications, and their families, should be aware of their risks and encouraged to follow preventative and treatment advice. Public education (see recommendation 10 on public messages below) will help them to:

- recognise their increased risk
- be aware of the benefits of influenza immunisation
- seek medical advice during influenza outbreaks.

All health care services should be organised to identify individuals at increased risk of complications or who are very unwell so that preventative care and timely access to treatment is offered.

- Health providers should develop systems to recall high-risk individuals for preventative care.
- Primary care should focus efforts on obtaining high levels of influenza vaccine coverage.
- Secondary care may have a role in supporting primary care by identifying individuals at increased risk of complications and supporting influenza vaccination.
- Where families contain individuals at increased risk, ensure they are well briefed on basic preventative interventions such as hand washing, respiratory hygiene, social isolation and avoiding risky situations.
- Efforts to prevent nosocomial infection should focus on preventing spread to those at increased risk of complications.
- Telephone help lines and telephone triage systems should be used to assess risk of complications and give tailored advice to callers.
- Primary and secondary care need to use care pathways that recognise risk factors and tailor treatment accordingly.

Justification for the recommendation

(a) From the mortality and morbidity review

Among the 49 patients who died, one third died at home and some did not seek any medical attention.

In some cases the severity of the patient's symptoms was not recognised by the patient, their family members or medical attendants.

Eighty-six percent of the patients who died were in the high-risk group for complications and may have benefited from earlier treatment if their risk status had been identified by either the patient or the family.

Some patients at higher risk of complications did not seem to be aware of their increased risk and did not seek health care as early as they might have.

(b) Other evidence

Other studies of pandemic influenza A(H1N1)2009 confirm the groups of individuals at higher risk of complications identified above (Cao et al 2009; Dominguez-Cherit et al 2009; Jain et al 2009; Kumar et al 2009; Verrall et al 2010).

Likely outcome of the recommendation

This strategy would allow patients at greater risk of complications to receive optimal preventative care and early antiviral therapy.

8. Specific advice for pregnant women

Pregnant women are at increased risk of severe outcomes from pandemic influenza A(H1N1), particularly if they have other risk factors such as obesity or asthma. They should be immunised against influenza and consult their midwife, general practitioner or specialist services as soon as symptoms of an influenza-like illness develop or if other family members are unwell.

The use of antivirals is considered safe in pregnancy.

If a woman has been immunised and presents with symptoms of influenza, then antivirals are recommended as the influenza vaccination is not 100% effective.

Justification for the recommendation

(a) From the mortality and morbidity review

Nine percent of ICU admissions with pandemic influenza A(H1N1) 2009 in Australia and New Zealand, and four deaths (10%) from the illness in New Zealand, were of pregnant women (ANZIC Influenza Investigators 2009; ANZIC Influenza Investigators and AMOSS 2010). Three of the four maternal deaths had significant co-morbidities such as morbid obesity or respiratory conditions.

(b) Other evidence

No additional risks for adverse events in pregnant women receiving oseltamivir have been reported (Louie et al 2010).

Likely outcome from recommendation

This strategy would increase the:

- uptake of seasonal influenza vaccines during pregnancy
- use of antivirals during pregnancy in those women with symptoms of influenza and if other family members have an influenza-like illness.

9. Specific advice for children

An annual influenza vaccination should be introduced into the National Immunisation Schedule for children under five years and infants, especially in areas of social and economic deprivation.

Influenza in childhood can present with a clinical picture that is hard to differentiate from many other common childhood febrile conditions, especially in children under two years of age.

The use of a checklist to help identify children who may be developing a significant complication is recommended. For example, infants with atypical bronchiolitis may need careful monitoring and early use of antivirals. (See the Appendix 3.)

Care pathways need to be developed to ensure infants and children at increased risk of complications have high levels of vaccine coverage and receive timely health care tailored to their increased needs.

Early childhood centres and schools should encourage hand washing, respiratory hygiene and other preventative measures among children.

Justification for the recommendation

(a) From the mortality and morbidity review

Among the 49 people who died, 11 were children and young people, six of whom had co-morbidities.

Children aged two years and under (especially children under one) are disproportionately represented in cases admitted to intensive care and hospital. Of the 119 children admitted to intensive care, 19 were children under four years (6.3/100,000 cases) and three of these died (16%).

(b) Other evidence

Children are major spreaders of infectious disease in the community as they have high levels of infection and are efficient transmitters (Jain and Goldman 2009).

Likely outcome from recommendation

This strategy would:

- enable more accurate identification of children who are at higher risk of complications and those suffering complications
- reduce hospital admissions and morbidity among infants and children
- reduce the burden of disease for the whole community.

10. Recommendation for public messages

A set of simple messages for the public should be promoted with the aims of:

- encouraging those with severe symptoms to seek medical help early
- encouraging those at higher risk of complications to self identify and seek annual vaccination and early treatment when ill
- increasing awareness that influenza can be atypical, particularly among those with chronic health problems.

Some suggestions for public messages are presented in the boxes on the following pages.

Justification for the recommendation

(a) From the mortality and morbidity review

Among the 49 patients who died, 86% were at high risk of complications and may have benefited from earlier treatment if their risk status had been identified by either the patient or the family.

Thirty-three percent of the patients died unexpectedly at home or in the community and some patients did not seek any medical assistance.

In some cases, the severity of the patient's symptoms was not recognised by the patient, the family members or their medical attendants.

Some patients at higher risk of complications did not seem to be aware of their increased risk and did not seek health care as early as they might have.

For the patients who died, antivirals were started after the symptoms had been present for several days (median 6 days), which is usually considered to be ineffective.

(b) Other evidence

Two systematic reviews have reported that antivirals are more effective in reducing symptom duration by 0.5 to 1.5 days when given within 48 hours of onset of symptoms, but it is noted that these reviews are for seasonal influenza only (Burch et al 2009; Jefferson et al 2010a). Evidence relating to pandemic influenza (A(H1N1)) 2009 suggests that the virus is sensitive to antivirals (ESR 2010a).

There is anecdotal evidence that patients found some public messages from the first wave to be confusing.

Likely outcome from recommendation

This strategy would:

- encourage patients who have symptoms suggestive of a more serious illness to seek medical help earlier
- increase uptake of antivirals earlier in the illness
- assist individuals at increased risk of complications to seek and receive health care tailored to their risk status.

Messages for the public about influenza

The following individuals should be **immunised**:

- children under five years of age, including infants
- adults over 65 years of age
- people who are morbidly obese (BMI ≥ 35 kg/m^2)
- people with chronic respiratory disease, including asthma and chronic obstructive airways disease
- people with cardiac disease
- people with neurological conditions (that affect the ability to breathe and cough)
- people with immunosuppressive conditions
- people who have a history of substance abuse
- women who are pregnant or have been pregnant recently.

The **common symptoms of influenza** are:

- fever
- cough, sore throat, runny nose
- headache
- muscle pains
- lethargy

Influenza can be a serious illness although for most people it is mild and they recover without treatment.

During influenza outbreaks patients are advised to seek urgent medical advice (from their GP or Healthline) if they have any one of the following symptoms or if their condition deteriorates:

- severe chills or shaking
- difficulty breathing
- blue or purple discolouration of the lips
- marked pallor, especially in infants
- extreme lethargy
- confusion
- vomiting and unable to keep fluids down
- signs of dehydration such as fainting, or not passing urine.

Awareness of symptoms of influenza in those who are at higher risk of complications

The public need to be aware of symptoms of influenza (see public message above regarding common symptoms of influenza) in order to seek medical attention. This awareness is especially important among those individuals who can be considered to be at "high risk" for developing complications from influenza.

"High risk" includes those who are:

- children under five years of age, including infants
- adults > 65 years old
- people who are morbidly obese (BMI ≥ 35 kg/m^2)
- people with respiratory disease, including asthma and chronic obstructive airways disease
- people with cardiac disease
- people with neurological conditions that affect the ability to breathe and cough
- people with immunosuppressive conditions
- people involved with substance abuse
- women who are pregnant or have been pregnant recently.

If individuals are in one of the above high-risk groups and other family members are symptomatic, then the high-risk individual should be considered for antivirals either as a preventative measure or as soon as symptoms occur.

General advice

For most people, if you have mild influenza symptoms, then it is recommended that you stay at home and avoid public places to prevent spreading the virus in the community. If, however, you know you are at increased risk of complications, you should seek early advice about options for treatment.

Any person who develops any of the following symptoms should seek urgent medical attention:

- severe chills and/or shaking
- difficulty breathing
- blue or purple discolouration of the lips
- marked pallor, especially in children
- extreme fatigue
- confusion
- vomiting and inability to maintain fluids
- signs of dehydration, such as fainting or not passing urine.

Take-home advice for patients leaving health services

Please return if any of the above symptoms occur or your symptoms worsen.

I don't want to get influenza or pass it on

Individuals in the higher-risk groups who are caring for family members (eg, parents with infants) are at increased risk of becoming unwell themselves and should have an annual vaccination as a preventative measure, or receive a delayed prescription for antivirals and be given advice to start medication only once symptoms occur.

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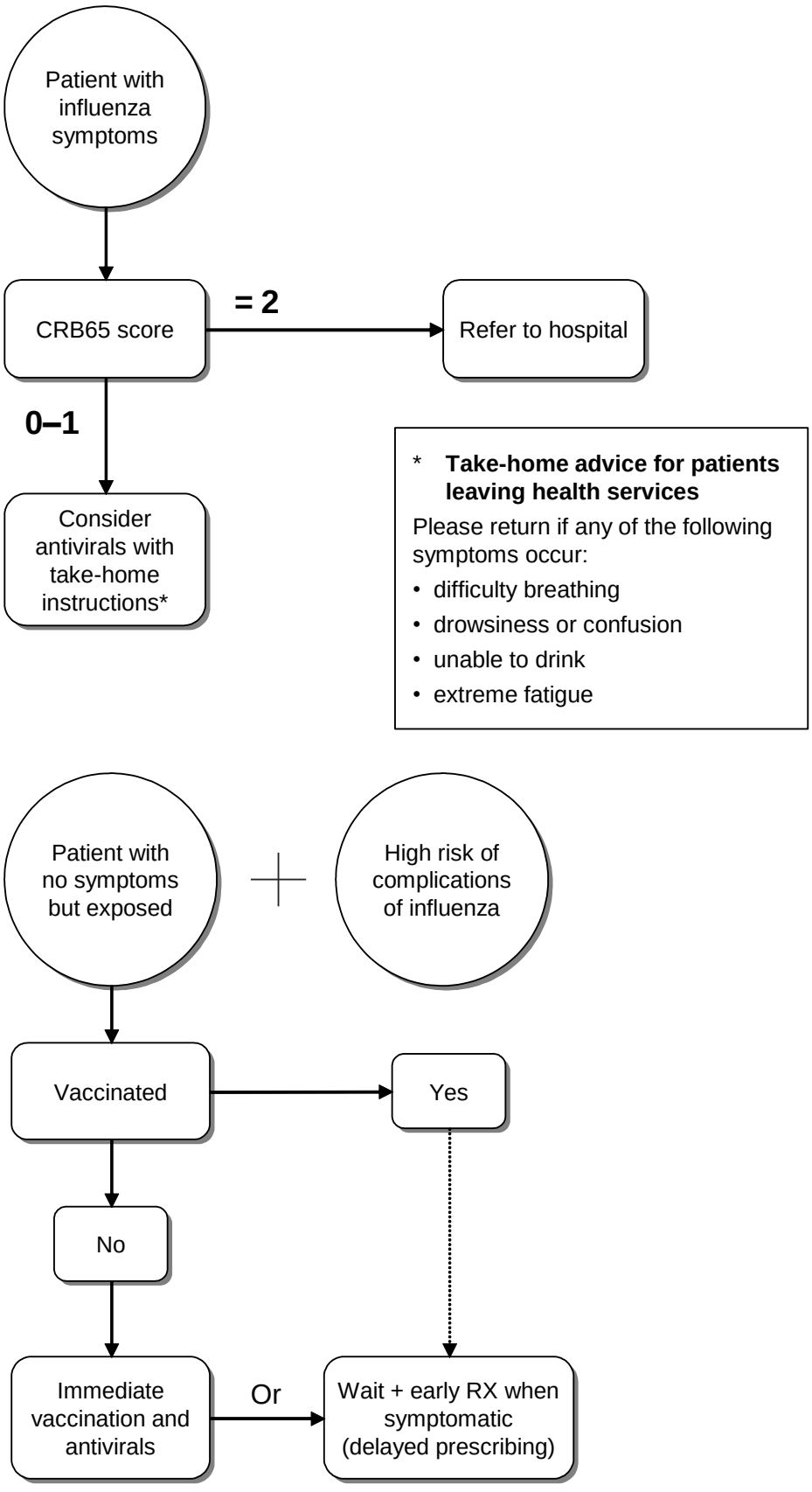
Appendix 1: Pandemic Influenza Mortality and Morbidity Review Group Members

Name	Occupation	Conflict of interest declaration
Professor Cynthia Farquhar (Chair)	Professor of Obstetrics and Gynaecology, University of Auckland	PMMRC Chair Past member of QIC Past Chair of the NZ Guidelines Group Co-director of the New Zealand Cochrane Branch Employed by the University of Auckland
Dr Nicholas Baker (Deputy Chair)	Community Paediatrician, Nelson Marlborough DHB	Community Paediatrician, NMDHB CYMRC Chair Senior Clinical Lecturer, Community Child Health, Wellington School of Medicine Board Member, NZ Telepaediatric Trust Member PSNZ Chair, CYAERG, NMDHB Chair IMM Steering Group NMDHB FRACP Past President PSNZ Past Member QIC Member of Steering Group, NZ Child and Youth Epidemiology Service Wife is a graphic artist who does some health-related work
Dr Colin McArthur	Intensivist, Auckland City Hospital, and Chairman of the New Zealand ICU Influenza Advisory Group	Chairman of the New Zealand ICU influenza advisory group Technical advisor to the WHO Western Pacific Regional Office
Dr Lance Jennings	Virologist, Canterbury Health Laboratories	Assoc Prof, Pathology Department, University of Otago, Christchurch Member PITAG Member NISG Member CDHB Pandemic and Canterbury Primary Pandemic Groups Chair APACI (sponsored by GSK, Novartis, Roche, Solvay, Sanofi Pasteur) WHO short-term consultant – Global Research Agenda (Geneva and WPRO) Chair/member several industry PI/vaccine advisory groups (GSK, Wyeth, Novartis, Baxter, MedImmune, CSL, Kimberly Clark)

Name	Occupation	Conflict of interest declaration
Dr Tim Blackmore	Infectious Disease Physician / Pathologist, Capital & Coast DHB	Adjunct Professor, Victoria University of Wellington Member of PITAG Member of Immunisation Technical Forum FRACP, FRCPA, PhD Member virology laboratory network Has received travel support for hepatitis, HIV and mycology conference attendance from Pfizer, GSK and Roche: none related to influenza
Dr Ramon Pink	Public Health Physician, Canterbury DHB	None declared
Dr Api Talemaitoga	Chief Advisor Pacific Health, Ministry of Health	General practitioner, Christchurch FRNZCGP Member, Pasifika Medical Association
Dr Mark O'Carroll	Respiratory Physician, Auckland City Hospital	None declared
Dr Sally Talbot	Primary Care Physician, Wellington (RNZCGP nominee)	GP in suburban partnership RNZCGP nominee member of Pandemic Health Care Working Group (PPHCWG) from October 2009 and ongoing Previous experience: ▪ SARS research and advisor – with Pat Tuohy 2003/04 ▪ 2005/07 worked on emerging infectious diseases and pandemic planning with Gillian Bohm and Ailsa Jacobson Other: ▪ David Talbot (brother) is the GM business development and marketing at ESR, Kenepuru Wellington
Dr Fran McGrath (ex-officio member)	Public Health Physician, Deputy Director of Public Health, Ministry of Health	None declared

Appendix 2: Suggested Clinical Pathway for Primary Care



Appendix 3: Assessing Severity of Influenza

Criteria for individuals aged 14 years and over

CRB65 scores*

- Confusion
- Respiratory rate ≥ 30
- Systolic BP ≤ 90 or diastolic BP ≤ 60
- Age ≥ 65

The use of CRB65 scores can predict mortality in patients with community acquired pneumonia with a score of 2 or more having a sensitivity of 80% (Burch et al 2009; Miller et al 2009).

Criteria for children under 14 years old

Criteria label	**Clinical triage criteria** (likely to justify admission to hospital) The presence of any of the following suggests a complication of flu:
A	**Severe respiratory distress** Chest wall indrawing, sternal recession, grunting, or noisy breathing when calm.
B	**Sustained increase in respiratory rate** measured over at least 30 seconds on more than one occasion ≥ 50 breaths per minute if under 1 year, or ≥ 40 breaths per minute if ≥ 1 year.
C	**Oxygen saturation ≤ 92% on pulse oximetry, breathing air *or* on oxygen** Absence of cyanosis is a poor discriminator for severe illness. Pallor may be a sign of hypoxia.
D	**Respiratory exhaustion or apnoeic episode** Apnoea defined as a ≥ 20 second pause in breathing.
E	**Evidence of severe clinical dehydration or clinical shock** Sternal capillary refill time > 2 seconds, reduced skin turgor, sunken eyes or fontanelle.
F	**Altered conscious level** Strikingly agitated or irritable, seizures, or floppy infant.
G	**Causing other clinical concern to their own GP or clinical team, or underlying condition** eg, a rapidly progressive or an unusually prolonged illness.

Source: UK Department of Health (2009)

For infants under six months of age

Assessment of infants under six months is difficult and a low threshold for seeking expert support should be maintained. When this support is not available the Baby Check Tool at http://nicutools.org/default.htm can be helpful.

See also: http://www.moh.govt.nz/moh.nsf/indexmh/influenza-a-h1n1-healthsector#downloads.

Appendix 4: Deaths due to Influenza (2000–2009)

Year	0–4	5–9	10–14	15–19	20–29	30–39	40–49	50–59	60–69	70–79	80+	Total
2000	0	0	0	0	0	0	0	0	0	0	1	2
2001	0	0	0	0	0	0	0	0	1	1	7	9
2002	0	0	0	0	0	0	1	0	0	3	5	9
2003	1	0	0	0	0	0	0	1	2	2	6	12
2004	0	0	0	0	0	0	0	0	1	4	23	28
2005	1	0	1	1	0	0	1	1	1	0	8	14
2006	0	0	0	0	1	0	0	0	1	2	13	17
2007*	0	0	0	0	0	0	0	1	0	2	7	10
2008*	1	0	1	0	0	0	0	0	1	0	6	9
2009*	5(1)	1	0	5(2)	8(2)	10(1)	11	8	4(1)	3(1)	5(3)	60(11)**

Source: ESR for 2002-2008 data. NMDS and PIMMRG for 2009 data.

(ICD-10 codes J10–11 except for 2010 when J9 was used for H1N1.[7])

* Provisional data only.

** Number in brackets for 2009 were eleven deaths from seasonal influenza and not H1N1 2009.

[7] For more information on ICD-10 codes see: http://www.who.int/classifications/icd/en/.