Review of Deaths Occurring In Alberta During the 2009 Influenza Pandemic

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Executive Summary

In 2009, the World Health Organization (WHO) declared the first influenza pandemic in 41 years. The new strain was named influenza A(H1N1)pdm09. Alberta Health and Wellness (AHW) in collaboration with Alberta Health Services (AHS) and the Public Health Agency of Canada (PHAC), developed and deployed a case report form designed specifically for the collection and reporting of cases of severe respiratory illness (SRI), hospitalized laboratory confirmed and probable influenza cases, and related deaths. Directions were provided to AHS to report all hospitalized cases and deaths occurring among individuals known to have received a positive or probable laboratory result, regardless of the cause of the death.

A total of 72 deaths were reported to AHW during the pandemic. As part of a review conducted by the Health Quality Council of Alberta (HQCA) it was determined that inter-provincial differences in A(H1N1)pdm09 associated deaths were difficult to interpret. In response to questions raised through the review, AHW informed the HQCA that it would undertake a review of reported deaths to determine the role A(H1N1)pdm09 played in the death.

In addition to reviewing the details of each of the 72 cases, the Alberta Vital Statistics Death Registration Database was linked to the database containing all positive and probable A(H1N1)pdm09 laboratory results. This expanded the review to 123 potential cases. Each case was reviewed to assess the likelihood that influenza A(H1N1)pdm09 played a direct role, a contributory role, or was unrelated to the death. It was determined that 64 individuals died directly as a result of being infected with influenza A(H1N1)pdm09 for a crude mortality rate of 1.77 deaths per 100,000 population.

Examining both reported cases and Vital Statistics records showed that the mortality rate for 2009 was the third highest during the period 1983 to 2010. Also, the mean age of deaths attributed to influenza was significantly younger during 2009 by close to 30 years.

Having chronic obstructive pulmonary disease (COPD), chronic heart disease, chronic kidney disease, epilepsy, and immune suppression all increased the odds of death following infection with influenza A(H1N1)pdm09. Overall, the prevalence of chronic underlying health conditions among those dying was significantly greater than seen in the general population. Given the importance of chronic underlying health conditions, immunization of this subset of the population should remain a priority.

By linking multiple data sources it was possible to estimate the completeness of death reporting in Alberta. This review suggests that AHS was effective in identifying and reporting on all but three deaths that occurred within hospitals in the province. Of these three, two occurred in emergency departments and these individuals died prior to being admitted to hospital. These three deaths occurred in three separate hospitals located in three separate communities across Alberta.

The surveillance system put in place jointly by AHW and AHS was able to provide valuable and timely evidence on deaths and was virtually complete in its reporting.

Introduction

In April 2009, a new influenza virus strain was identified following reports of severe respiratory illness in Mexico and the identification of two cases of human swine influenza in California. On April 24, 2009, the World Health Organization (WHO) declared a Public Health Emergency of International Concern and later, on June 11, 2009 declared that there was a pandemic, the first such declaration in 41 years (WHO, 2009).[4]

The Public Health Agency of Canada (PHAC) National Microbiology Laboratory tested specimens from Mexico and registered the strain with GenBank, an open access database of genetic sequences for organisms, as A/Mexico/InDRE4487/2009(H1N1). Further analysis showed this strain to be virtually identical to A/California/07/2009 (H1N1). To ensure consistency in reports related to the pandemic, the nomenclature A(H1N1)pdm09 was adopted.

In April 2009, Alberta Health and Wellness (AHW) in collaboration with Alberta Health Services (AHS) and the Public Health Agency of Canada (PHAC), developed and deployed a case report form designed specifically for the collection and reporting of cases of severe respiratory illness (SRI) and hospitalized laboratory confirmed and probable influenza cases, and related deaths. Directions were provided to AHS to report all hospitalized cases and deaths occurring among individuals known to have received a positive or probable laboratory result, regardless of the cause of the death. The approach was designed to ensure that the fewest possible cases would be missed, and could include cases where their death was unrelated to being infected with A(H1N1)pdm09. Details on the Alberta experience with A(H1N1)pdm09 are published elsewhere.[1]

In 2010, the Minister of Alberta Health and Wellness asked the Health Quality Council of Alberta (HQCA) to conduct a comprehensive review of the Alberta response to A(H1N1)pdm09.[2] As part of this review, the HQCA noted that Alberta had a higher mortality rate for A(H1N1)pdm09 than other provinces.[2] The HQCA acknowledged that provincial differences in surveillance methods for identifying A(H1N1)pdm09 deaths made inter-provincial comparisons difficult to interpret. In response to questions raised through the review, AHW informed the HQCA that it would undertake a review of reported deaths to determine the role A(H1N1)pdm09 played in the death.

This review is an analysis of all deaths where the deceased had had a positive or probable laboratory result for A(H1N1)pdm09 and determines if influenza was directly related, was contributory, or unrelated to the deaths. Also, this review assessed how complete the reporting of deaths from whom there was a positive or probable laboratory test result for A(H1N1)pdm09.

Methods

This review drew from multiple databases. First, all positive or probable laboratory results for influenza A(H1N1)pdm09 were extracted from the Alberta Provincial Laboratory for Public Health (Microbiology). These records were then linked, using deterministic methods (a linkage method based on personal health number, name, birth date, gender, and address), to the Alberta Vital Statistics death registration database using personal health number, surname, given name, sex, and date of birth as linking variables.

Next, these results were linked to the database containing data from the case report forms designed to record data collected on A(H1N1)pdm09-related hospitalized cases and deaths. In addition, the records were also linked to administrative health databases (i.e. physician claims, inpatient, emergency department) to determine the presence of chronic health conditions.

All linked records were then reviewed in more detail to determine if influenza was likely the: direct cause of death, contributory to the death, or was unrelated to the death. To make this determination, a medical officer of health, a medical microbiologist, a communicable disease nurse and an epidemiologist examined the record in detail and reached a consensus on the contribution of influenza to the death.

The criteria used were:

- the temporal relationship between laboratory proven influenza illness onset and death;
- the presence and nature of underlying medical conditions;
- the biological plausibility of influenza contributing to the death;
- and the absence of other more plausible causes of death.

Influenza directly related

In general, these cases were symptomatic and died within seven days of specimen collection. These individuals were previously healthy or had clear exacerbations of pre-existing respiratory or cardiac problems that worsened with influenza illness. Patients with severe medical problems that were clearly exacerbated by the influenza episode and had difficult and continuous stays in hospitals for up to 30 days before death were also included.

Influenza was contributory

These cases generally had a cause of death that was unrelated to influenza but could have been made worse by the influenza. For example, individuals with long documented history of coronary artery disease and a cause of death listed as myocardial infarction. Also included in this category were patients with serious underlying health conditions whose condition worsened after influenza, then recovered, but who died of their underlying condition within 30 days.

Death was unrelated to influenza

These cases did not have evidence of cardiac or respiratory illness exacerbation, did not have influenza, pneumonia nor other acute respiratory illness listed as a cause of death and had a plausible unrelated cause of death (such as suicide).

Logistic regression (a statistical method used to assess the contribution of a given factor to an outcome) models were created to estimate the odds of dying given a confirmed or probable A(H1N1)pdm09 laboratory test and the presence of underlying health conditions. Differences in ages between males and females were assessed using a t-test. Population estimates are based on the number of individuals registered with the Alberta Health Care Insurance Plan as of June 30 or each year.

Results

Between April 1, 2009 and September 30, 2010, there were 29,594 deaths registered with Alberta Vital Statistics. Of these, 124 were linked to either a confirmed or probable influenza A(H1N1)pdm09 laboratory test result. Details of the linkage results are found in Figure 1. Among the 124 linked cases, one individual was an out of province resident and this person's death was classified as being directly related to influenza A(H1N1)pdm09. Among the 123 Albertans, there were 117 laboratory confirmed cases and six probable cases. Among the probable cases, two were directly attributed to influenza A(H1N1)pdm09. Of the 117 deaths with laboratory confirmed A(H1N1)pdm09, 61 were determined to have A(H1N1)pdm09 as the direct cause of death. In total, there were 64 deaths were influenza A(H1N1) was the direct cause of death for a crude mortality rate of 1.77 per 100,000 population. Alberta Vital Statistics death registration data had 68 deaths coded with influenza as the underlying cause of death. It should be noted that not all deaths coded by Alberta Vital Statistics were laboratory confirmed.

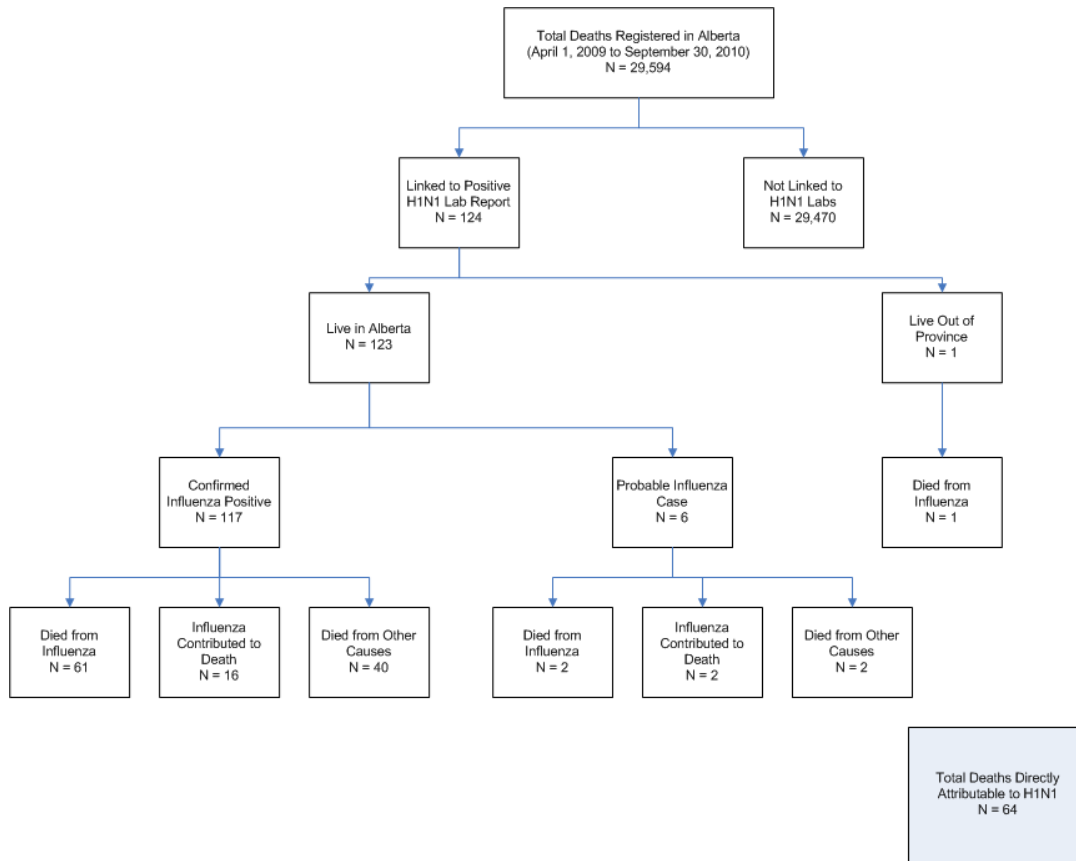**Figure 1:** Classification of Deaths Related to A(H1N1)pdm09 in Alberta

Figure 2 provides a graphical representation of time between the collection of the nasopharyngeal swab and date the individual was hospitalized and/or died. For individuals where influenza was considered directly related, the time periods between these events was shorter than for individuals categorized as having influenza being contributory or unrelated. The greater the time period between these events, the less likely influenza could have played a role in the death.

Figure 2: Date of nasopharyngeal collection, hospital admission, and death for individuals with laboratory confirmed or probable influenza A(H1N1)pdm09 in Alberta
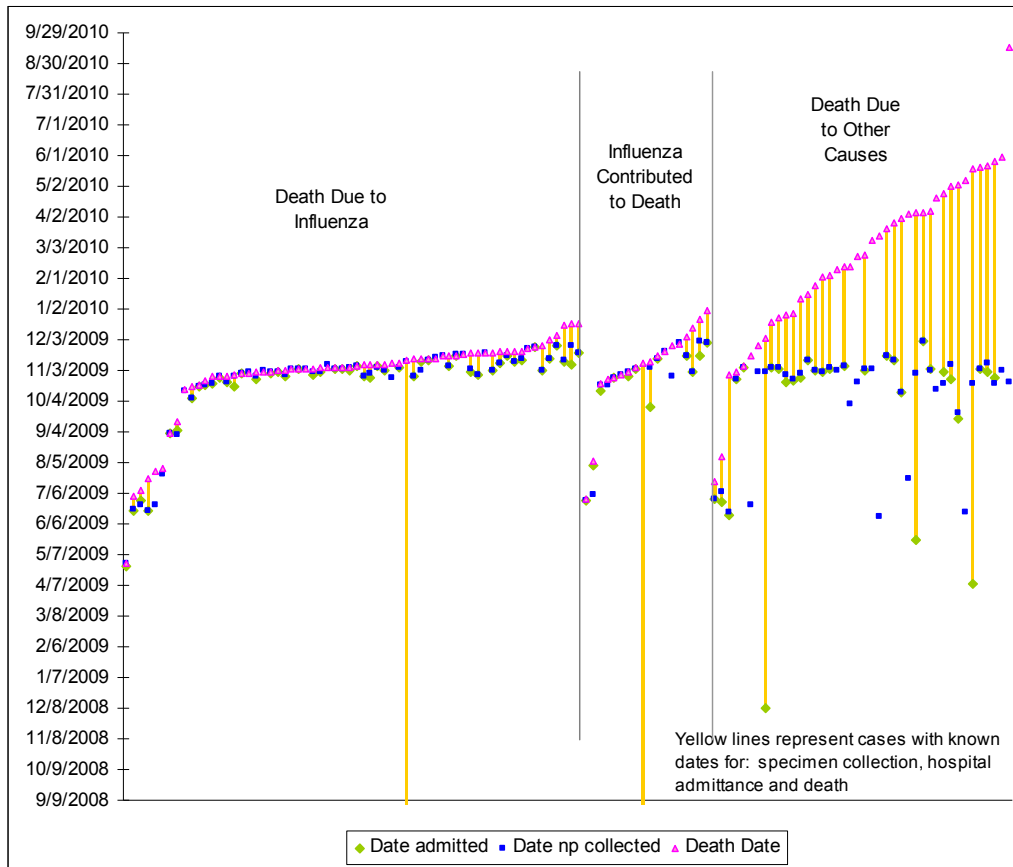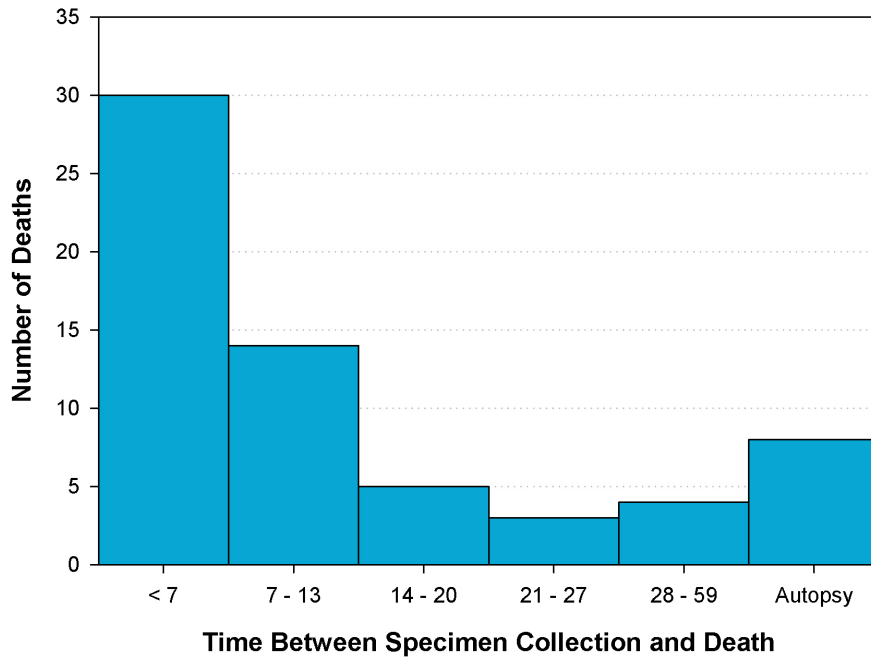

Deaths due directly to influenza

There were 64 deaths directly determined to be the result of being infected with influenza A(H1N1)pdm09. The mean (standard deviation) and median ages were 46.5 (SD = 19.25) and 48 years, respectively. There was no difference in the mean age between males and females, (t(62) = 0.06, p>0.05). The youngest death was an infant and the oldest was 90 years of age. Both the mean and median ages of death were lower than previous influenza seasons by close to 30 years.

Forty-seven per cent of deaths occurred within seven days of a specimen being collected for laboratory testing (see Figure 3). Only six per cent of deaths occurred more than a month after the onset of symptoms.

Figure 3: Number of days from specimen collection date to date of death

Of the 64 deaths classified as directly related to influenza, 42 (66.7 per cent) had influenza coded as the underlying cause of death and four (6.4 per cent) were coded as pneumonia with Alberta Vital Statistics. The remaining deaths were coded as heart disease (9.5 per cent), infectious disease (4.8 per cent), cancer (3.8 per cent), or endocrine system (1.6 per cent).

Figure 4 shows the age-specific mortality rate, per 100,000 population, among laboratory positive influenza A(H1N1)pdm09 cases (confirmed and probable) where the death was directly related to influenza, where influenza was contributory, or where influenza was unrelated. Mortality directly related to influenza was higher among those aged 20–49 years of age when compared with the other two categories. Mortality where influenza was directly or indirectly responsible for death showed a J-shaped curve with higher rates among those under five years of age and then increasing mortality with those over age 20.

Figure 4: Age-Specific Mortality per 100,000 Population Among Individuals Testing Positive for A(H1N1)pdm09 in Alberta
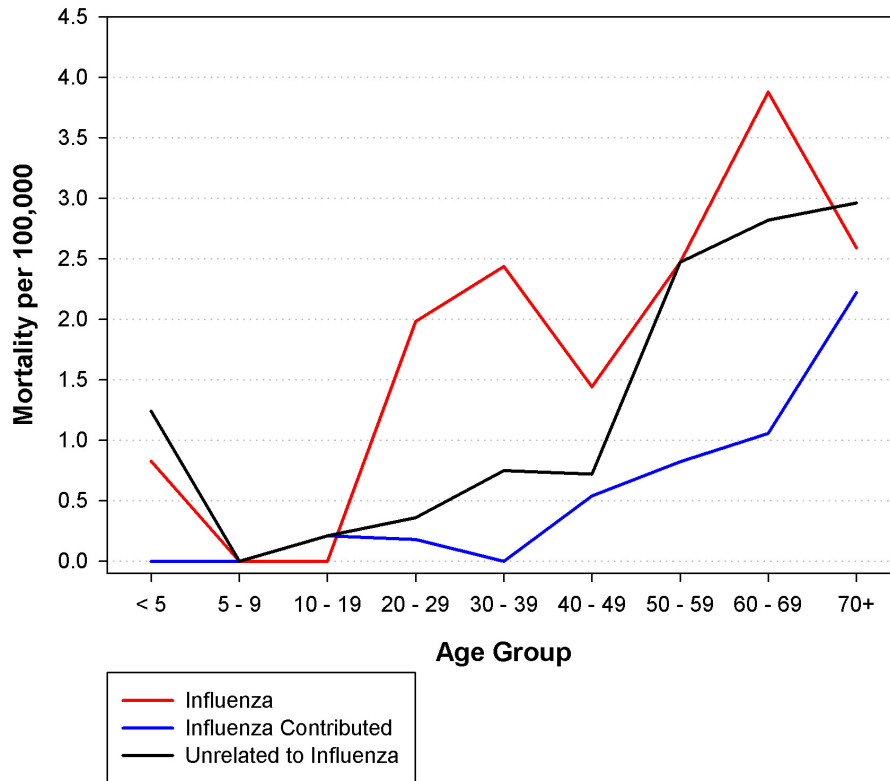

Table 1 displays the prevalence of selected underlying health conditions for those dying from influenza and the Alberta prevalence, where available. With the exception of being a current smoker, the prevalence of each condition/factor was higher among those dying from influenza A(H1N1)pdm09.

Overall, 84.4 per cent of deaths directly related to influenza A(H1N1)pdm09 had one or more chronic underlying health condition. Among those with laboratory-confirmed or probable influenza A(H1N1)pdm09, the presence of one or more chronic underlying health conditions increased the odds of death nearly eight-fold (Odds Ratio = 7.9, 95 per cent confidence interval 4.2 to 15.6).

Table 1: Prevalence of selected health conditions among individuals dying from influenza and the general Alberta population, 2009

Health Condition / Risk Factor	Per Cent (N = 64)	Alberta Prevalence (per 100)
Asthma	35.9	9.0
COPD	28.1	3.5
Chronic Heart Disease	20.3	4.0
Chronic Liver Disease	3.1	n/a
Chronic Kidney Disease	14.1	n/a
Diabetes	25.0	5.0
Epilepsy	18.8	1.3
Hypertension	37.5	14.1
Immune Suppressed	9.4	n/a
Current Smoker	18.8	22.5
Obese	25.0	19.5
Aboriginal	12.5	3.6

Immunization clinics opened to the public on October 26, 2009, and were suspended on October 31, 2009 due to a country-wide shortage of vaccine. Clinics reopened in a staged approach on November 4, 2009. Full details are published elsewhere.[1]

Twelve (18.8 per cent) of the deaths occurred prior to the pandemic vaccine being available. Ten deaths had their first specimen collected between October 27–31 indicating they were likely infected before to the immunization program started. Nine additional deaths had their specimen collection between November 1–3. This equates to 50 per cent of the deaths having an onset either before vaccine was available or as the immunization program was beginning. The remaining cases all had specimen collection dates between November 4–28, 2009.

Review of cases reported to Alberta Health and Wellness

Of the 72 deaths reported to Alberta Health and Wellness, it was determined that influenza was directly responsible for 56 (77.8 per cent) of the deaths, was a contributing factor to 12 (16.7 per cent), and was not a factor in four (5.6 per cent).

Table 2 shows the proportion of reported deaths with selected chronic health conditions. A logistic regression analysis was performed to determine the odds of death among laboratory confirmed cases given these conditions. Individuals with chronic obstructive pulmonary disease (COPD), chronic heart disease, chronic kidney disease, epilepsy and immune suppressed all had a statistically significantly increased likelihood of dying than influenza positive cases without these chronic conditions. In addition, individuals of Aboriginal descent were nearly twice as likely to die than non-Aboriginal Albertans.

Table 2: Proportion of deaths with a selected health condition/risk factor

Health Condition / Risk Factor	Per Cent (N = 68)	Odds Ratio	95 % Confidence Interval
Asthma	36.8	1.19	0.72, 1.96
COPD	30.9	1.90*	1.03, 3.48
Chronic Heart Disease	23.5	2.97*	1.62, 5.45
Chronic Liver Disease	2.9	0.54	0.19, 1.53
Chronic Kidney Disease	19.1	3.05*	1.61, 5.78
Diabetes	22.1	0.87	0.47, 1.61
Epilepsy	17.7	4.22*	2.22, 8.05
Hypertension	42.7	0.82	0.43, 1.55
Immune Suppressed	13.2	2.45*	1.15, 5.23
Aboriginal Descent	13.2	1.96*	1.04, 3.71

* $p < 0.05$

Review of confirmed and contributory Cases

There were 82 deaths that had a confirmed or probable laboratory test where influenza was either directly related to the death or contributed to the death. Logistic regression was used to estimate the odds of a person dying given they had a confirmed or probable influenza laboratory test.

Underlying chronic health conditions were examined for all laboratory confirmed and probable cases. Individuals with COPD, chronic kidney disease, epilepsy or immune suppression had statistically significantly increased odds of dying post-infection. Being of Aboriginal descent did not lead to statistically significantly increased odds of dying suggesting that the presence of underlying chronic health conditions in this population contributed to a higher overall mortality rate.

Table 3: Proportion of deaths with a selected health condition/risk factor

Health Condition / Risk Factor	Per Cent (N = 82)	Odds Ratio	95 % Confidence Interval
Asthma	35.4	1.13	0.68, 1.91
Chronic Obstructive Pulmonary Disease (COPD)	31.7	1.86*	1.00, 3.45
Chronic Heart Disease	25.6	2.04*	1.07, 3.88
Chronic Liver Disease	2.4	0.26	0.05, 1.22
Chronic Kidney Disease	20.7	3.79*	1.91, 7.49
Diabetes	24.4	0.87	0.45, 1.66
Epilepsy	17.1	4.88*	2.57, 9.30
Hypertension	43.9	0.87	0.45, 1.66
Immune Suppressed	12.2	2.88*	1.31, 6.32
Aboriginal Descent	12.2	1.48	0.71, 3.10

* $p < 0.05$

Table 4 shows the ICD-10 chapter for the underlying cause of death recorded for the 82 deaths where influenza was either assessed to be directly related or contributory. Nearly two thirds where classified as respiratory. Of the 53 coded as respiratory, 37 were coded as A(H1N1)pdm09 and seven as influenza with no strain specified.

Table 4: Distribution of underlying cause of death, by ICD-10 Chapter

ICD-10 Chapter	Number of Deaths (%)
1. Certain infectious and parasitic disease	5 (6.2)
2. Neoplasms	5 (6.3)
6. Diseases of the nervous system	3 (3.7)
9. Diseases of the circulatory system	12 (14.8)
10. Diseases of the respiratory system	53 (65.4)
Other	4 (4.8)
Total	**82**

Review of Alberta Vital Statistics records

Alberta Vital Statistics death registration records were also reviewed. Alberta Vital Statistics registers all deaths occurring within Alberta and records the underlying cause of death. Coding is done by Statistics Canada using the 10th revision of the *International Classification of Diseases* (ICD-10). Laboratory confirmation is not required to assign underlying causes of death.

Figures 5 and 6 respectively show the number of deaths and mortality rates, by year, where influenza was coded as the underlying cause of death. Mortality rates per 100,000 population were computed for the period 1983–2010. The highest mortality rate and total deaths occurred in 1999 followed by 1998–2009. The mortality rate per 100,000 population in 1999 was nearly double that of 2009. The 1998– 1999 influenza season had the highest mortality rate during the 28 years examined. In 2009, there were 68 deaths registered with influenza listed as the underlying cause of death. Of these, 44 were explicitly coded as pandemic influenza.

Figure 5: Number of deaths with influenza recorded as the underlying cause of death, Alberta 1983 to 2010
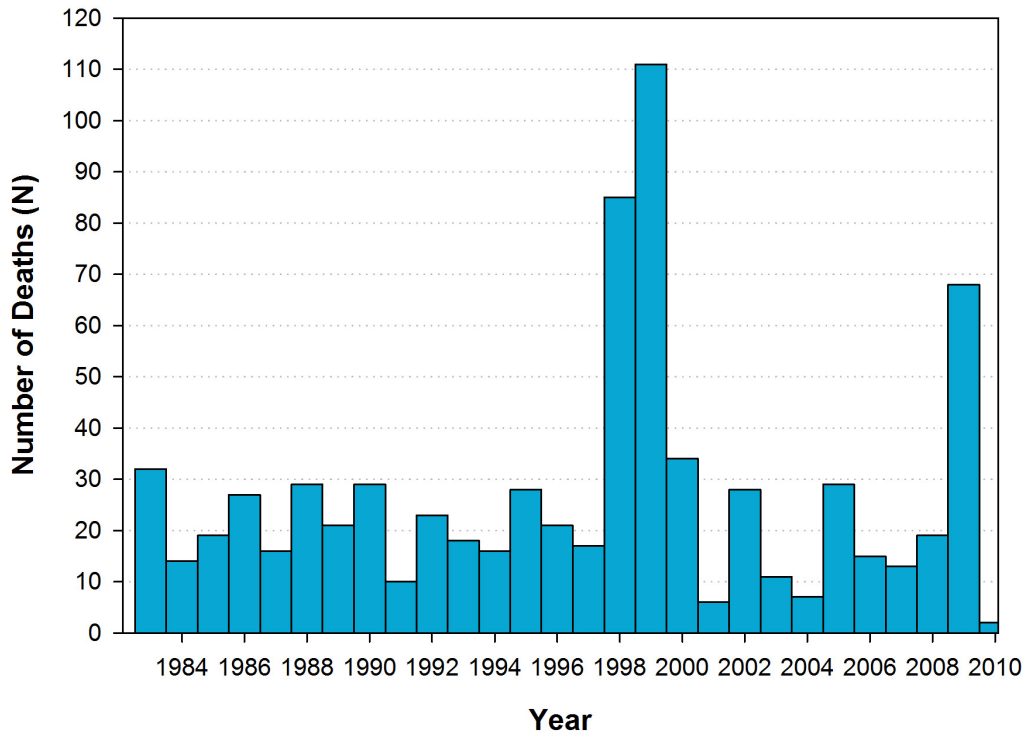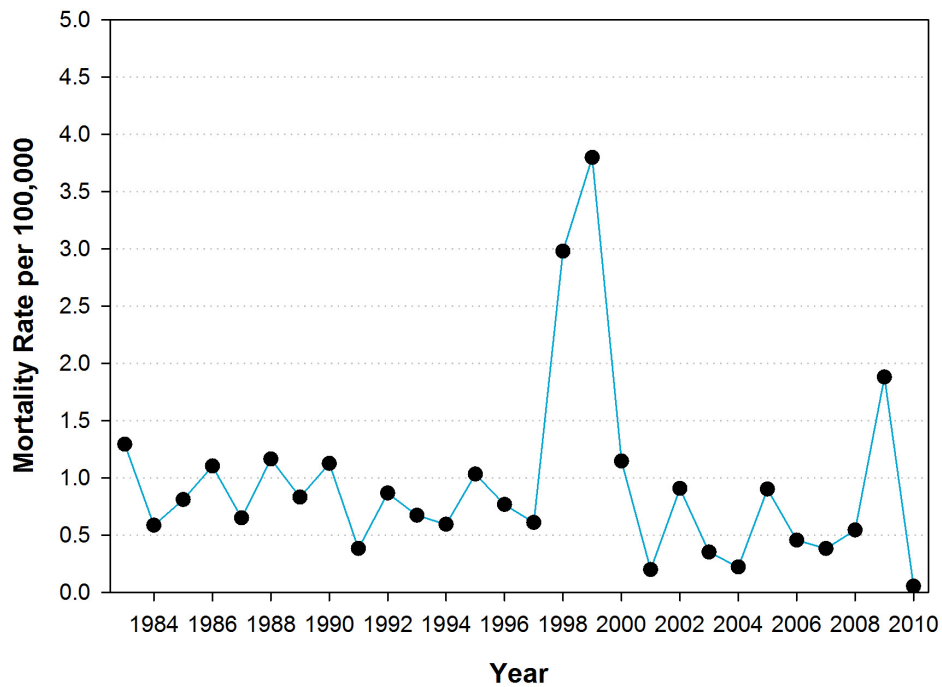

Figure 6: Crude mortality rate per 100,000 population where influenza was recorded as the underlying cause of death, Alberta 1983 to 2010

The mean ages of those dying with influenza listed as the underlying cause of death are displayed in Figure 7. The mean age of death was significantly younger in 2009 when compared to the average over the other years. The mean age of influenza deaths in Alberta between 1983 and 2010, excluding 2009, was 83.1 years. In 2009, the mean age was nearly 30 years younger at 53.8 years.

Figure 7: Mean age of deaths with influenza coded as the underlying cause of death, Alberta 1983 to 2010
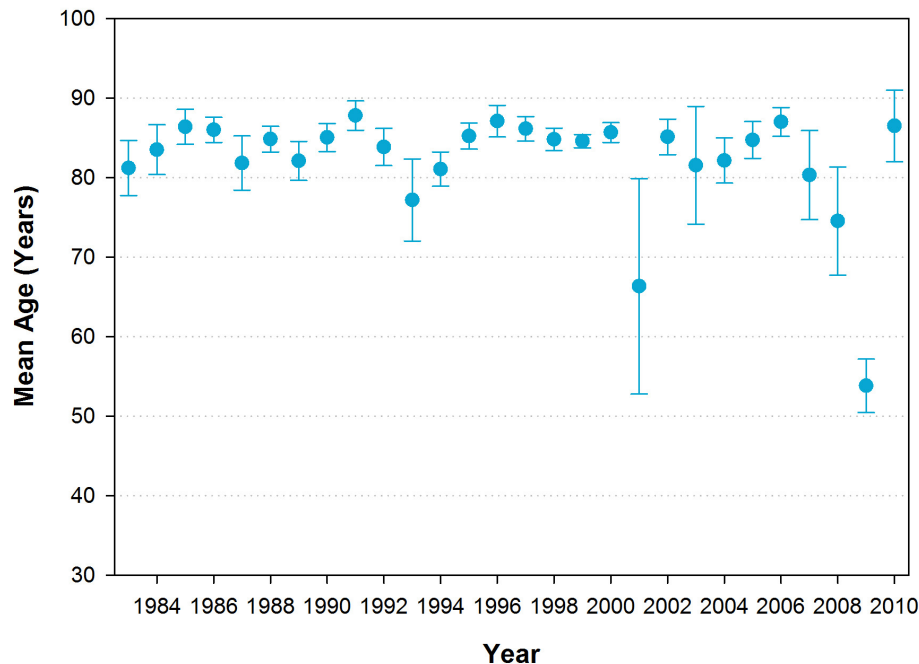
Completeness of reporting

Alberta Health Services (AHS) was provided direction on reporting of both hospitalized cases and deaths among individuals who had a laboratory test indicating the person was confirmed as being A(H1N1)pdm09 positive. By linking death registration records with laboratory results it is possible to estimate the completeness of reporting from AHS to Alberta Health and Wellness (AHW).

Of those dying who also had a positive laboratory result, there were 20 cases that required further review to determine if they should have been reported by AHS. These 20 cases were linked to hospital inpatient data to determine if they had been in hospital during or after the April 1, 2009. None of the 20 cases had been hospitalized meaning it would not have been possible for AHS to become aware of these deaths so that a detailed case report form could be completed.

Ten of the deaths occurred more than 90 days after a positive laboratory result, one case was confirmed during autopsy and this death was reported by the Chief Medical Examiner's

office, five deaths occurred within seven days, and four were between two weeks and two months. It was determined that five of these 20 deaths were directly attributed to influenza, four had influenza as a contributory factor, and 11 were unrelated to A(H1N1)pdm09.

Among the five deaths described above, three occurred in hospital. Of these, two individuals died in emergency departments, and one died from pneumonia after being admitted to hospital. Each of these three events occurred in different hospitals located in three different AHS health service zones.

Conclusions

During the 2009 influenza pandemic, 72 deaths were reported to Alberta Health and Wellness (AHW) as part of its surveillance activities. Expanding the search to include any death registered with Alberta Vital Statistics that had been a laboratory confirmed or probable case generated a list of 123 potential cases. Upon examination of each case, it was determined that 64 individuals died directly as a result of being infected with influenza A(H1N1)pdm09 for a crude mortality rate of 1.77 per 100,000 population. Without information on the completeness of reporting or similar reviews by other provinces and territories, it is not possible to fully assess Alberta's mortality rate against other provinces and territories.

The reported mortality rate for Alberta was the fifth highest in Canada after Newfoundland and Labrador and the three northern territories.[2] There are a number of possible reasons for this, but assigning precise contributions to each is not possible. The reasons could include: more complete reporting in Alberta; differences in the use of case definitions by provinces and territories; or greater exposure to more susceptible populations. For example, low socioeconomic status, Aboriginal status, crowding, or earlier entry of influenza into Alberta resulting in an opportunity for more people to be affected before a vaccine was released may have all contributed. Alberta was the first provinces to identify cases.[1]

The Alberta influenza A(H1N1)pdm09 vaccine coverage was 37 per cent which was lower than the national average of 41 per cent.[2] While a lower vaccine coverage rate is an important consideration, the Alberta coverage was the same as British Columbia and Manitoba and higher than Ontario. Therefore it does not seem likely that there is a single reason for the higher mortality rates.

Achieving optimum levels of vaccine coverage requires the individuals to consent to being immunized. An AHW survey of Albertans conducted before the influenza season found that 44 per cent of the adult population indicated that they had intended to be immunized.[2] With 37 per cent of the population immunized, this suggests that the immunization program reached the majority of those indicating an intention to immunize. Also, it is possible that some individuals changed there mind about immunization with some opting to be immunized while others opted not to get immunized. During the implementation of the immunization program, individuals with chronic underlying health conditions were encouraged to get immunized. By the end of the program, 32 per cent of individuals with a chronic underlying health condition received the influenza A(H1N1)pdm09 vaccine.[1]

Examining both reported cases and Vital Statistics records showed that the mortality rate for 2009 was the third highest during the period 1983 to 2010. Also, the mean age of deaths attributed to influenza was significantly younger during 2009 by close to 30 years. This suggests there is some cross protective immunity among older populations.

While First Nations populations had a higher mortality rate, it appears that the presence of chronic underlying health conditions played a significant role in explaining the difference in rates. In other words, the higher mortality among First Nations can, in part, be attributed to the higher prevalence of underlying chronic health conditions in this population.

Having COPD, chronic heart disease, chronic kidney disease, epilepsy, and being immune suppressed all increased the odds of death following infection with influenza A(H1N1)pdm09. Overall, the prevalence of chronic underlying health conditions among those dying was significantly greater than seen in the general population. This finding is consistent with other studies[3,5] and highlights the importance of chronic health conditions as risk factors for adverse outcomes following influenza infection. Given the importance of chronic underlying health conditions, immunization of this subset of the population should remain a priority.

By linking multiple data sources it was possible to estimate the completeness of death reporting in Alberta. This review suggests that Alberta Health Services (AHS) was effective in identifying and reporting on deaths that occurred within hospitals in the province. Based on this review, AHS was able to find and report on all but three deaths that occurred in hospital. There was no clustering of these three events by location.

This conclusion highlights the value of linking multiple data sources both as a means of understanding the epidemiology of influenza A(H1N1)pdm09 and as an evaluation of the overall surveillance system put in place. The surveillance system put in place jointly by AHW and AHS was able to provide valuable and timely evidence on deaths and was virtually complete in its reporting.

Acknowledgements

This report was peer reviewed by Dr. Jeff Kwong, Scientist, Institute for Clinical Evaluative Sciences, and Assistant Professor, Dalla Lana School of Public Health, University of Toronto.

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