ORIGINAL ARTICLE

Healthcare-Associated Influenza in Canadian Hospitals from 2006 to 2012

Geoffrey Taylor, MD;[1] Robyn Mitchell, MHSc;[2] Allison McGeer, MD;[3] Charles Frenette, MD;[4] Kathryn N. Suh, MD;[5] Alice Wong, MD;[6] Kevin Katz, MD;[7] Krista Wilkinson, MSc;[2] Barbara Amihod;[8] Denise Gravel, MSc;[2] Canadian Nosocomial Infection Surveillance Program[a]

OBJECTIVE. To determine trends, patient characteristics, and outcome of patients with healthcare-associated influenza in Canadian hospitals.

DESIGN. Prospective surveillance of laboratory-confirmed influenza among hospitalized adults was conducted from 2006 to 2012. Adults with positive test results at or after admission to the hospital were assessed. Influenza was considered to be healthcare associated if symptom onset was equal to or more than 96 hours after admission to a facility or if a patient was readmitted less than 96 hours after discharge or admitted less than 96 hours after transfer from another facility. Baseline characteristics of influenza patients were collected. Patients were reassessed at 30 days to determine the outcome.

SETTING. Acute care hospitals participating in the Canadian Nosocomial Infection Surveillance Program.

RESULTS. A total of 570 (17.3%) of 3,299 influenza cases were healthcare associated; 345 (60.5%) were acquired in a long-term care facility (LTCF), and 225 (39.5%) were acquired in an acute care facility (ACF). There was year-to-year variability in the rate and proportion of cases that were healthcare associated and variability in the proportion that were acquired in a LTCF versus an ACF. Patients with LTCF-associated cases were older, had a higher proportion of chronic heart disease, and were less likely to be immunocompromised compared with patients with ACF-associated cases; there was no significant difference in 30-day all-cause and influenza-specific mortality.

CONCLUSIONS. Healthcare-associated influenza is a major component of the burden of disease from influenza in hospitals, but the proportion of cases that are healthcare associated varies markedly from year to year, as does the proportion of healthcare-associated infections that are acquired in an ACF versus an LTCF.

Infect Control Hosp Epidemiol 2014;35(2):169-175

Transmission of influenza to patients in health care settings, including both acute and long-term care settings, is a recognized hazard.[1,2] A short incubation period (usually less than 72 hours); multiple sources of infection from other patients, visitors, or staff; and efficient transmission by respiratory droplets leads to frequent introduction of influenza into this population. Poor immunogenicity of influenza vaccine because of age and comorbidities leaves this group susceptible to infection.[3]

Most published reports describing the epidemiology of healthcare-associated influenza reflect the experience of outbreaks[4,5] or novel viruses, such as antiviral-resistant[6] or pandemic influenza.[7-10] There are few studies of endemic transmission of influenza in healthcare settings, and these reflect single-season[11] or single-institution experience.[12] Given the tendency for seasonal variation in influenza intensity, a better estimate of the impact of healthcare-associated influenza over the long term is needed.

We have conducted prospective surveillance for laboratory-confirmed influenza in adults in a network of Canadian hospitals since 2006.[13] To better understand the frequency, temporal trends, patient characteristics, and outcomes of healthcare-associated influenza, we compared community-associated influenza with healthcare-associated influenza in the hospitals in this network over a 6-year period. We also examined trends and patient characteristics and compared outcomes for patients who acquired influenza in long-term care facilities (LTCFs) with those for patients who acquired influenza in acute care facilities (ACFs).

Affiliations: 1. University of Alberta Hospital, Edmonton, Alberta, Canada; 2. Public Health Agency of Canada, Centre for Communicable Diseases and Infection Control, Ottawa, Ontario, Canada; 3. Mount Sinai Hospital, Toronto, Ontario, Canada; 4. McGill University Health Centre, Montreal, Quebec, Canada; 5. Ottawa Hospital, Ottawa, Ontario, Canada; 6. Royal University Hospital, Saskatoon, Saskatchewan, Canada; 7. North York General Hospital, Ontario, Canada; 8. Jewish General Hospital, Montreal, Quebec, Canada; a. Members of the Canadian Nosocomial Infection Surveillance Program are listed at the end of the text.

Received August 12, 2013; accepted October 20, 2013; electronically published January 8, 2013.

 0899-823X/2014/3502-0010$15.00. DOI: 10.1086/674858

METHODS

Surveillance Network

The Canadian Nosocomial Infection Surveillance Program (CNISP) is a network of 54 acute care hospitals from 10 provinces. CNISP is a partnership between the Public Health Agency of Canada (Agency), which provides funding and technical expertise, and the Canadian Hospital Epidemiology Committee (CHEC), a group of hospital-based physician infection prevention specialists. Surveillance for influenza in adults in participating hospitals is considered to be within the mandate of hospital infection prevention and control programs and therefore does not constitute human research. In most participating hospitals, this surveillance activity does not require institutional review board review.

Surveillance Period

From 2006 to 2008, CNISP conducted surveillance of laboratory-confirmed influenza among hospitalized inpatients 16 years of age and older during the traditional influenza season (November to June). Following the emergence of the pH1N1 influenza virus in 2009, the program was expanded to year-round surveillance,[13] which continued into the 2010–2011 season. During the 2011–2012 season, the surveillance period returned to the traditional influenza season (November to June).

Case Definition

During influenza season, clinical practice guidelines recommend testing an adult of any age who is hospitalized with fever and respiratory symptoms, including community acquired pneumonia.[14] A case patient with influenza was defined as any adult (greater than or equal to 16 years of age) with a positive influenza laboratory test result confirmed by rapid antigen test, reverse transcriptase polymerase chain reaction, or viral culture from a specimen collected during the surveillance period who was admitted to a participating hospital. Patients seen in outpatient clinics and emergency departments whose visits did not result in hospitalization were excluded. Source of acquisition was determined on the basis of the best available information. A healthcare-associated case was defined as symptom onset 96 hours or longer after admission or readmission with a positive test result less than 96 hours after discharge or a positive test result less than 96 hours after transfer from another facility. Healthcare-associated cases were subcategorized as acquired in an LTCF or an ACF. Cases of influenza associated with long-term care would only be included if the patient was transferred and admitted to an acute care CNISP hospital.

Case Finding

Cases were identified by concurrent or retrospective chart review by trained infection control practitioners. Detailed patient questionnaires were completed for each case and included patient laboratory information, patient demographic characteristics, risk factors, treatment, and outcomes. Records of patients who died within 30 days of their initial positive test result were reviewed by a CHEC physician to determine whether the death was directly related, indirectly related, or unrelated to influenza. Underlying medical conditions that were consistently collected for the 2006–2007, 2007–2008, and 2009–2010 to 2011–2012 seasons were chronic lung disease, chronic heart disease, immune suppression, diabetes mellitus, and kidney disease. Data for underlying medical conditions were not available for the 2008–2009 season.

Data Analysis

The data were stratified on the basis of site of acquisition (community- or healthcare-associated and ACF or LTCF). Univariate analysis was performed. Differences were assessed for categorical variables using the χ^2 test. Tests for normality were performed on continuous variables, and the Kruskall-Wallis test was performed to compare the median time from onset to treatment and age between groups. Multivariate logistic regression was performed to control for age for outcome variables when comparing healthcare-associated and community-associated cases. Odds ratios (ORs) were reported; 95% confidence intervals (CIs) and P values reflect a 2-tailed alpha level of .05. Missing data and responses that were unable to be assessed were removed from all calculations. Statistical analysis was performed using Stata, version 11 (StataCorp).

RESULTS

In the 6 surveillance seasons, there were 3,299 confirmed cases of influenza in 2,012,054 admissions; 570 (17.3%) were considered healthcare associated. Figure 1 demonstrates the pro-

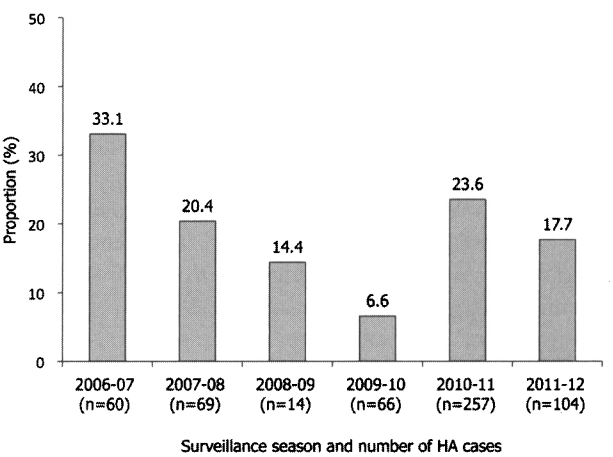

FIGURE 1. Proportion of hospitalized patients with laboratory-confirmed influenza cases that were healthcare associated (HA), by season, 2006–2012 (n = 570).

https://doi.org/10.1086/674858 Published online by Cambridge University Press

portion of all patients with influenza who had healthcare-associated influenza by season, ranging from a high of 33.1% in 2006–2007 to a low of 6.6% in 2009–2010 (the pandemic H1N1 year). Of the 570 case patients, 60.5% (345 case patients) acquired influenza in a LTCF (9.9% of the patients with influenza). The remaining 39.5% (225 case patients) acquired influenza in an ACF (either the facility in which they were currently hospitalized or another ACF), which represented 6.8% of all influenza case patients. The healthcare-associated influenza rate was highest during 2007–2008 (7.2 cases per 10,000 admissions) and lowest during the 2009–2010 pandemic year (1.0 cases per 10,000 admissions). In the 2 seasons after the pandemic, the rate increased to 3.7 cases per 10,000 admissions (2010–2011) and 2.6 cases per 10,000 admissions (2011–2012).

Figure 2 demonstrates the proportion of healthcare-associated cases that were acquired in a LTCF versus an ACF by season. The proportion acquired in an ACF ranged from 93% in the 2008–2009 season to 32% in the 2010–2011 season. In the pandemic H1N1 year, 62% of healthcare-associated influenza cases were acquired in an ACF.

Table 1 compares characteristics and outcome for patients with influenza acquired in a LTCF with those for patients who acquired influenza in an ACF. Patients with LTC-acquired influenza had a higher median age than did patients with ACF-acquired cases (85 years vs 67 years). Compared with patients with ACF-acquired cases, a significantly higher proportion of patients who acquired influenza in a LTCF had a chronic heart condition, had received their annual influenza vaccination, and were treated with antiviral therapy for their infection. A significantly higher proportion of patients with ACF-acquired cases were immunosuppressed. Significantly fewer patients with LTC-acquired influenza were admitted to the ICU compared with patients with ACF-acquired cases (6.5% vs 11.5%; $P = .041$). At 30 days, the patient status was the same whether influenza had been acquired in a LTCF or an ACF, including the proportion who had been discharged. There was no significant difference in 30 day all-cause and influenza-specific mortality.

Table 2 compares the characteristics and outcomes for patients with healthcare-associated influenza with those for patients with community-associated influenza. Patients with healthcare-associated cases were older and had a higher frequency of some comorbid conditions than did patients with community-associated cases but did not have a higher frequency of any comorbidity. A greater proportion of patients with healthcare-associated cases received the influenza vaccine that season, although the vaccination rate for this population was still low (54.6%). Multivariate analysis indicated that patients with healthcare-associated cases had a lower ICU admission rate (age-adjusted OR, 0.52 [95% CI, 0.4–0.7]) but higher 30-day all-cause mortality (OR, 1.83 [95% CI, 1.3–2.5]). There was no significant difference in influenza-specific 30-day mortality.

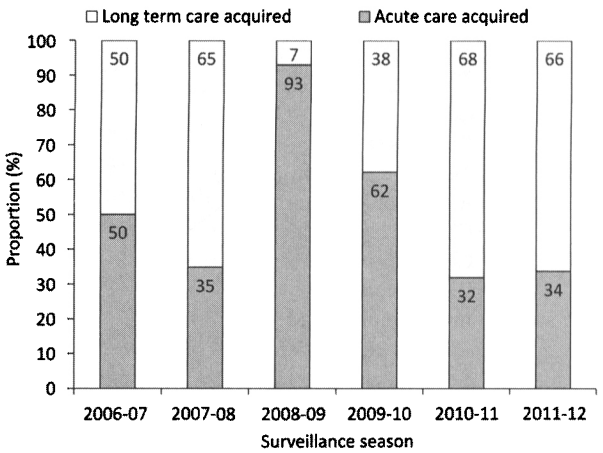

FIGURE 2. Proportion of laboratory-confirmed healthcare-associated influenza cases that were acquired in an acute care facility versus a long-term care facility, by season, 2006–2012 ($n = 570$).

DISCUSSION

This 6-year multi-institutional prospective surveillance represents the largest study to date examining the epidemiology of healthcare-associated influenza and the only study yet published examining multiple influenza seasons. These data allow us to provide an assessment of the burden of healthcare-associated influenza in major urban Canadian hospitals (the hospitals represented by the CNISP network) using a conservative definition of onset of symptoms more than 96 hours after admission or less than 96 hours since last discharge from the hospital. Furthermore, because influenza testing methods in some facilities were less sensitive, particularly in the early years of the study, we feel that our data on the burden of healthcare-associated influenza represents a minimum estimate. This burden is substantial: 17.3% of all patients hospitalized with influenza acquired their infection in a healthcare facility. The proportion of cases that were healthcare associated and the 6.8% of cases that were acquired in ACFs appear to be higher than estimates in the 2 previously published studies of nosocomial influenza: 4.3% in an Australian study conducted during 2 influenza seasons and involving 8–15 hospitals and 2.0% in 75 UK hospitals in the pandemic 2009–2010 year.[11,12] However, comparisons between studies should be made with caution given that all use passive surveillance and that different surveillance periods and definitions were used. An advantage of our multiyear surveillance, covering both seasonal and pandemic years, is that we are able to evaluate year-to-year variability in the occurrence of healthcare-associated influenza, a phenomenon known to be important in community settings. As shown by our data, there is substantial year-to-year variability in the proportion of patients hospitalized with influenza that is healthcare associated, from a low of 6.6% during the 2009 pandemic to a

TABLE 1. Patient Characteristics, Treatment, and Outcomes of Laboratory-Confirmed Influenza Acquired in Acute Care Facilities (ACFs) and Long-Term Care Facilities (LTCFs), 2006–2012 (n = 570)

Variable	LTCF	ACF	P
Cases	345 (60.5)	225 (39.5)	
Female sex	171 (49.6)	125 (53.8)	.3
Age, years, median (range)	85 (20–101)	67 (17–95)	<.001
Any chronic comorbidity	289/344 (84.0)	184/212 (86.8)	.4
Chronic heart disease	115/315 (36.5)	48/200 (24.0)	.003
Chronic lung disease	78/315 (24.8)	41/200 (20.5)	.3
Diabetes	69/315 (21.9)	35/200 (17.5)	.2
Immunosuppressed	32/315 (10.2)	44/200 (22.0)	<.001
Chronic kidney disease	33/315 (10.5)	30/200 (15.0)	.1
Received annual vaccine	84/121 (69.4)	28/84 (33.3)	<.001
Received antivirals	287/342 (83.9)	169/223 (75.8)	.02
Days from symptom onset to treatment, median (IQR)	2 (0–8)	2 (1–12)	
ICU admission	22/339 (6.5)	24/209 (11.5)	.04
Thirty-day outcome			
Discharged	196 (56.8)	140 (62.2)	.2
Remained hospitalized	112 (32.5)	56 (24.9)	.05
Died	37 (10.7)	29 (12.9)	.4
Death attributable to influenza[a]	26 (7.5)	20 (8.9)	.6

NOTE. Data are no. (%) of cases, unless otherwise indicated. ICU, intensive care unit; IQR, interquartile range.

[a] Attributable influenza deaths were defined as those in which influenza was the primary or contributing cause of death.

high of 33.1% in 2006–2007. Following the historic low rate during the pandemic, the healthcare-associated proportion returned to prepandemic levels. Although this may in part be explained by the lower attack rate of A(H1N1) compared with A(H3N2) and influenza B in older adults,[15,16] it suggests that preventative measures instituted during the pandemic were more effective or more consistently applied than during the prepandemic or postpandemic periods. Similarly, there is marked year-to-year variability in the proportion of healthcare-associated influenza cases that are ACF acquired, ranging from 7% to 68%. There is no ready explanation for this extreme variability of site of acquisition of healthcare-associated infection.

By simultaneously assessing both community-associated and healthcare-associated influenza over an extended period, we are able to compare influenza in these distinct settings. Again, baseline characteristics of age and presence of comorbidities were different. Adjusting for age, healthcare-associated cases had a higher ICU admission rate and higher 30-day all-cause mortality, but there was no difference in death attributable to influenza. Not surprisingly, we found significant differences in patient characteristics between influenza acquired in LTCFs and ACFs, particularly that patients with LTCF-acquired cases were much older. Despite these baseline differences, the 30-day outcomes of the influenza-associated hospitalization, including influenza-associated mortality, were very similar. It is possible that the higher median age and higher proportion of chronic heart disease in the LTCF group was balanced by a much higher proportion of immunosuppression in the ACF group and, surprisingly, a lower proportion of patients who received antiviral treatment in that group (83.9% vs 75.8%).[17]

Our study is subject to several limitations. These findings are observational surveillance data collected by chart review; they reflect the experience of large, urban Canadian hospitals and so are likely not entirely representative of all hospitalized adults in Canada. It is likely that not all patients hospitalized with influenza were captured, because testing indications were not standardized across hospitals or seasons. Although clinical practice guidelines for testing of inpatients with suspected influenza have not changed since our surveillance began, wider use of more sensitive molecular testing methods and increased clinical suspicion of influenza in hospitalized adults may have led to increased identification of influenza over time.

In summary, over a 6-year period, 17.3% of adult patients with test results positive for influenza while hospitalized at a network of major Canadian hospitals were found to have acquired their infection in a healthcare facility (60.5% in LTCFs, and 39.5% in ACFs). There was marked year-to-year variability in the frequency of healthcare-associated influenza, with the lowest proportion (6.6%) being seen in the 2009 pandemic year. The all-cause 30-day healthcare-associated influenza mortality was 11.6%, and 30-day influenza-specific mortality was 8.1%.

Given the documented high frequency, morbidity, and mortality associated with healthcare-acquired influenza, hospitals and hospital infection prevention and control

TABLE 2. Patient Characteristics, Treatment, and Outcomes of Laboratory-Confirmed Influenza, by Source of Acquisition, 2006–2012 (n = 3,299)

Variable	Community associated	Healthcare associated	Age-adjusted OR	P
Univariate analysis				
Cases	2,729 (82.7)	570 (17.3)	...	
Female sex	1,451 (53.2)	292 (51.2)	...	.4
Age, years, median (range)	59 (16–104)	81 (17–101)	...	<.001
Any chronic comorbidity	2,215/2,627 (84.3)	473/556 (85.1)	...	.7
Chronic heart disease	609/2,520 (24.2)	163/515 (31.7)	...	<.001
Chronic lung disease	896/2,520 (35.6)	119/515 (23.1)	...	<.001
Diabetes	505/2,520 (20.0)	104/515 (2.2)	...	.9
Immunosuppressed	462/2,520 (18.3)	76/515 (14.6)	...	.05
Chronic kidney disease	200/2,520 (7.9)	63/515 (12.2)	...	.002
Received annual vaccine	402/1,109 (36.3)	112/205 (54.6)	...	<.001
Received antivirals	1,908/2,644 (71.6)	456/565 (80.7)	...	<.001
Days from symptom onset to treatment, median (IQR)	3 (0–22)	2 (0–12)	...	<.001
ICU admission	504/2,700 (18.7)	46/548 (8.4)	...	<.001
Thirty-day outcome				
Discharged	2,394 (87.9)	336 (59.0)	...	<.001
Remained hospitalized	167 (6.1)	168 (29.5)	...	<.001
Died	162 (5.9)	66 (11.6)	...	<.001
Death attributable to influenza[a]	108 (4.0)	46 (8.1)	...	<.001
Multivariate analysis				
ICU admission	504/2,700 (18.7)	46/548 (8.4)	0.52 (0.4–0.7)	<.001
30-day outcome				
Discharged	2,394 (87.9)	336 (59.0)	0.23 (0.2–0.3)	<.001
Remained hospitalized	167 (6.1)	168 (29.5)	5.70 (4.6–7.4)	<.001
Died	162 (5.9)	66 (11.6)	1.83 (1.3–2.5)	<.001
Death attributable to influenza[a]	108 (4.0)	46 (8.1)	1.23 (0.6–2.4)	.5

NOTE. CI, confidence interval; ICU, intensive care unit; IQR, interquartile range; OR, odds ratio.
[a] Attributable influenza deaths were defined as those in which influenza was the primary or contributing cause of death.

programs should focus attention on this problem, including promotion of testing to detect cases and surveillance to assess trends. Strategies are needed to improve uptake of annual vaccination among admitted patients and the staff who care for them. Additional research is needed to address many remaining questions in this area. Why is there such significant variation in the annual rate and proportion of patients with healthcare-associated influenza and variation in the site of acquisition? What is the relative importance of different sources of influenza in hospitals (eg, other patients, staff, or visitors)? If healthcare providers are an important source, can strategies such as mandatory influenza vaccination of providers reduce transmission risk?[18,19]

MEMBERS OF THE CANADIAN NOSOCOMIAL INFECTION SURVEILLANCE PROGRAM

David Boyd, National Microbiology Laboratory, Public Health Agency of Canada; Natalie Bridger, Eastern Health-Health Sciences Centre, St. John's, Newfoundland; Elizabeth Bryce, Vancouver Coastal Health Authority, Vancouver, British Columbia; John Conly, Foothills Medical Centre, Calgary, Alberta; André Dascal, Sir Mortimer B. Davis–Jewish General Hospital, Montreal, Quebec; Janice de Heer, Interior Health Authority, Kelowna, British Columbia; John Embil, Health Sciences Centre, Winnipeg, Manitoba; Joanne Embree, Health Sciences Centre, Winnipeg, Manitoba; Gerald Evans, Kingston General Hospital, Kingston, Ontario; Sarah Forgie, Stollery Children's Hospital, Edmonton, Alberta; Charles Frenette, McGill University Health Centre, Montreal, Quebec; David Haldane, Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia; Gregory German, Queen Elizabeth Hospital, Charlottetown, Prince Edward Island; George Golding, National Microbiology Laboratory, Public Health Agency of Canada; Denise Gravel, Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada; Deanna Hembroff, University Hospital of Northern British Columbia, Prince George, British Columbia; Elizabeth Henderson, Alberta Health Services, Calgary, Alberta; Michael John, London Health Sciences Centre, London, Ontario; Lynn Johnston, Queen Elizabeth II Health Sciences Centre, Halifax,

Nova Scotia; Kevin Katz, North York General Hospital, Toronto, Ontario; Pamela Kibsey, Victoria General Hospital, Victoria, British Columbia; Magdalena Kuhn, South East Regional Health Authority, Moncton, New Brunswick; Joanne Langley, IWK Health Centre, Halifax, Nova Scotia; Camille Lemieux, University Health Network, Toronto, Ontario; Nicole Le Saux, Children's Hospital of Eastern Ontario, Ottawa, Ontario; Mark Loeb, Hamilton Health Sciences Corporation, Hamilton, Ontario; Susan Richardson, Hospital for Sick Children, Toronto, Ontario; Allison McGeer, Mount Sinai Hospital, Toronto, Ontario; Dominik Mertz, Hamilton Health Sciences Corporation, Hamilton, Ontario; Mark Miller, Sir Mortimer B. Davis-Jewish General Hospital, Montreal, Quebec; Robyn Mitchell, Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada; Dorothy Moore, Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec; Aboubakar Mounchili, Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada; Michael Mulvey, National Microbiology Laboratory, Public Health Agency of Canada; Suzanne Pelletier, Health Sciences North, Sudbury, Ontario; Linda Pelude, Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada; Caroline Quach, Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec; Virginia Roth, The Ottawa Hospital, Ottawa, Ontario; Andrew Simor, Sunnybrook Health Sciences Centre, Toronto, Ontario; Stephanie Smith, University of Alberta Hospital, Edmonton, Alberta; Kathryn Suh, The Ottawa Hospital, Ottawa, Ontario; Geoffrey Taylor, University of Alberta Hospital, Edmonton, Alberta; Eva Thomas, Children's and Women's Health Center, Vancouver, British Columbia; Nathalie Turgeon, Centre Hospitalier de Universitaire de Québec–Hôtel-Dieu, Quebec, Quebec; Mary Vearncombe, Sunnybrook Health Sciences Centre, Toronto, Ontario; Joseph Vayalumkal, Alberta Children's Hospital, Calgary, Alberta; Karl Weiss, Maisonneuve-Rosemont Hospital, Montreal, Quebec; Alice Wong, Royal University Hospital, Saskatoon, Saskatchewan.

ACKNOWLEDGMENTS

We thank the infection control practitioners, laboratory personnel, physicians, and medical microbiologists from all of the Canadian Nosocomial Infection Surveillance Program hospitals for their invaluable assistance in data collection and laboratory testing.

Financial support. This work was supported by the Public Health Agency of Canada.

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article. All authors submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

Address correspondence to Geoffrey Taylor, MD, 2D3 05 WMC, University of Alberta, Edmonton, Alberta T6G 2B7, Canada (geoff.taylor@ualberta.ca).

REFERENCES

1. Salgado CD, Farr BM, Hall KK, Hayden FG. Influenza in the acute hospital setting. *Lancet Infect Dis* 2002;2:145–155.
2. Bradley SF. Prevention of influenza in long-term-care facilities. Long-Term Care Committee of the Society for Healthcare Epidemiology of America. *Infect Control Hosp Epidemiol* 1999; 20(9):629–637.
3. Coles FB, Balzano GJ, Morse DL. An outbreak of influenza A (H3N2) in a well immunized nursing home population. *J Am Geriatr Soc* 1992;40(6):589–592.
4. Voirin N, Barret B, Metzger MH, Vanhems P. Hospital-acquired influenza: a synthesis using the Outbreak Reports and Intervention Studies of Nosocomial Infection (ORION) statement. *J Hosp Infect* 2009;71(1):1–14.
5. Morens DM, Rash VM. Lessons from a nursing home outbreak of influenza A. *Infect Control Hosp Epidemiol* 1995;16(5):275–280.
6. Cohen NJ, Morita JY, Plate DK, et al. Control of an outbreak due to an adamantine-resistant strain of influenza A (H3N2) in a chronic care facility. *Infection* 2008;36(5):458–462.
7. Alexander DC, Winter AL, Eshaghi A, et al. Transmission of influenza A pandemic (H1N1) 2009 virus in a long-term care facility in Ontario, Canada. *Infect Control Hosp Epidemiol* 2010; 31(12):1300–1302.
8. Enstone JE, Myles PR, Openshaw PJM, et al. Nosocomial pandemic (H1N1) 2009, United Kingdom, 2009–2010. *Emerg Infect Dis* 2011;17:592–598.
9. Khandaker G, Rashid H, Zurynski Y, et al Nosocomial vs community-acquired pandemic influenza A (H1N1) 2009: a nested case-control study. *J Hosp Infect* 2012;82(2):94–100.
10. Veenith T, Sanfilippo F, Ercole A, et al Nosocomial H1N1 infection during 2010–2011 pandemic: a retrospective cohort study from a tertiary referral hospital. *J Hosp Infect* 2012;81(3): 202–205.
11. Macesic N, Kotsimbos TC, Kelly P, Cheng AC. Hospital-acquired influenza in an Australian sentinel surveillance system. *MJA* 2013;198:370–372.
12. Vanhems P, Voirin N, Roche S, et al. Risk of influenza-like illness in an acute health care setting during community influenza epidemics in 2004–2005, 2005–2006, and 2006–2007. *Arch Intern Med* 2011;171(2):151–157.
13. Wilkinson K, Mitchell R, Taylor G, et al. Laboratory-confirmed pandemic H1N1 influenza in hospitalized adults: findings from the Canadian Nosocomial Infections Surveillance Program, 2009–2010. *Infect Control Hosp Epidemiol* 2012;33(10):1043–1046.
14. Harper SA, Bradley JS, Englund JA, et al. Seasonal influenza in adults and children-diagnosis, treatment, chemoprophylaxis and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. *Clin Infect Dis* 2009;48:1003–1032.
15. Skowronski DM, Hottes TS, McElhaney JE, et al. Immunoepidemiologic correlates of pandemic H1N1 surveillance observations: higher antibody and lower cell-mediated immune responses with advanced age. *J Infect Dis* 2011;203:158–167.
16. Hall WN, Goodman RA, Noble GR, Kendal AP, Steece RS. An outbreak of influenza B in an elderly population. *J Infect Dis* 1981;144(4):297–302.
17. Aoki F, Hayden F. The beneficial effects of neuraminidase in-

hibitor drug therapy on severe patient outcomes during the 2009–2010 influenza A virus subtype H1N1pandemic. *J Infect Dis* 2013;207:547–549.
18. Bryce E, Embree J, Evans G, et al. AMMI Canada position paper: mandatory influenza immunization of health care workers. *Can J Infect Dis Med Microbiol* 2012;23:e93–e95.
19. Gardam M, Lemieux C. Mandatory influenza vaccination? first we need a better vaccine. *CMAJ* 2013;185:639–640.