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ARTICLE

Epidemiology of influenza-associated hospitalization in adults, Toronto, 2007/8

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Abstract The purpose of this investigation was to identify when diagnostic testing and empirical antiviral therapy should be considered for adult patients requiring hospitalization during influenza seasons. During the 2007/8 influenza season, six acute care hospitals in the Greater Toronto Area participated in active surveillance for laboratory-confirmed influenza requiring hospitalization. Nasopharyngeal (NP) swabs were obtained from patients presenting with acute respiratory or cardiac illness, or with febrile illness without clear non-respiratory etiology. Predictors of influenza were analyzed by multivariable logistic regression analysis and likelihoods of influenza infection in various patient groups were calculated. Two hundred and eighty of 3,917 patients were found to have influenza. Thirty-five percent of patients with influenza presented with a triage temperature ≥38.0°C, 80% had respiratory symptoms in the emergency department, and 76% were ≥65 years old. Multivariable analysis revealed a triage temperature ≥38.0°C (odds ratio [OR] 3.1; 95% confidence interval [CI] 2.3–4.1), the presence of respiratory symptoms (OR 1.7; 95% CI 1.2–2.4), admission diagnosis of respiratory infection (OR 1.8; 95% CI 1.3–2.4), admission diagnosis of exacerbation of chronic obstructive pulmonary disease (COPD)/asthma or respiratory failure (OR 2.3; 95% CI 1.6–3.4), and admission in peak influenza weeks (OR 4.2; 95% CI 3.1–5.7) as independent predictors of influenza. The likelihood of influenza exceeded 15% in patients with respiratory infection or exacerbation of COPD/asthma if the triage temperature was ≥38.0°C or if they were admitted in the peak weeks during the influenza season. During influenza season, diagnostic testing and empiric antiviral therapy should be considered in patients requiring hospitalization if respiratory infection or exacerbation of COPD/asthma are suspected and if either the triage temperature is ≥38.0°C or admission is during the weeks of peak influenza activity.

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Introduction

The primary strategy for the protection of Canadians against influenza is immunization. In healthy adults, vaccination is about 80% effective against infection due to influenza when the vaccine is antigenically well matched to circulating virus [1]. In older adults, vaccination is substantially less effective; nonetheless, it has still been shown in randomized controlled trials to offer substantial protection [2, 3]. Annual influenza vaccine is provided free-of-charge to all residents of Ontario. Overall, 42% of Ontarians aged 12 years or older and 71% of residents over 64 years of age are vaccinated against influenza annually [4]. Despite these rates of annual immunization, influenza remains the most common infectious cause of death in Ontario, with an estimated 1,300 to 2,700 deaths annually in a population of approximately 11 million [5, 6].

In healthy adult outpatients, if treatment is started with a neuraminidase inhibitor within 48 h of symptom onset, the severity and duration of illness due to influenza can be reduced by 25–35% and the rate of complications by 40–65% [7, 8]. Several observations suggest that the benefits of treating influenza in immunocompromised patients, or those with severe illness requiring hospitalization, may be even greater [9, 10]. However, prior to the 2009 pandemic, influenza testing was rarely performed in severely ill adults in Ontario, and sensitive and specific tests whose results are available in a timely manner were not accessible in most hospitals. Although clinical algorithms with reasonable positive predictive values for influenza exist for healthy, young adults, no such algorithms exist for patients requiring hospitalization [11, 12].

The aims of this study were to describe the epidemiology of severe influenza in a highly vaccinated population, to identify predictors of influenza infection in adult patients requiring hospitalization in Toronto during the 2007/8 influenza season, and to determine when viral testing and empiric antiviral therapy should be considered in patients requiring hospitalization during influenza seasons.

Materials and methods

Setting and maneuver

The Toronto Invasive Bacterial Diseases Network (TIBDN) is a collaborative network of microbiology laboratories, infection-control practitioners, and public health departments that performs population-based surveillance for infectious diseases in south-central Ontario. During the 2007/8 influenza season, six (two tertiary care and four community) acute care hospitals from the TIBDN participated in active surveillance for laboratory-confirmed influenza requiring hospitalization. All admissions to medical or medical/surgical intensive care units (ICUs) in all six hospitals and all admissions to medical services in four hospitals were eligible for surveillance. Prior to the influenza season, attending physicians in all departments agreed that, during the influenza season, nasopharyngeal (NP) swabs were clinically indicated in patients requiring hospital or ICU admission who presented with any acute respiratory or cardiac illness (independent of body temperature), or with any febrile illness without clear, non-respiratory etiology. During the influenza season, study staff screened all admissions daily and suggested orders for NP swabs in all patients with any acute cardiac or respiratory illness, or any febrile illness without a clear non-respiratory source who had not yet had them ordered. Demographic and medical information was collected from each patient by chart review; the admission diagnosis was as recorded in each chart. NP swabs were tested for the presence of influenza by direct fluorescent antigen (DFA) detection or enzyme immunoassay (EIA) on-site in 5 of 6 hospitals, and by polymerase chain reaction (PCR) and viral culture at the Ontario Public Health Laboratory for all specimens.

For the purposes of the study, the influenza season was defined as starting when the proportion of positive influenza tests among specimens submitted to the Ontario Public Health Laboratory for viral testing was greater than 5% for two consecutive weeks, and ending when the proportion of positive tests was below 5%; the peak season was defined as any week in which the proportion of submitted specimens yielding influenza was >15%. For logistical reasons, although the season was identified as starting on December 16th, 2007, the start of the surveillance was postponed to December 30th (the first day of week 1 of 2008).

Statistical analyses

Data were double entered and cleaned, then manually inspected for errors and outlying values, which were then confirmed or corrected with original records. The data were analyzed in SAS, version 9.1 for PC (SAS Institute, Cary, NC). Differences in group proportions were assessed by the χ^2 test or Fisher's exact test, and differences in medians were calculated with the Wilcoxon rank-sum test. Likelihoods were calculated as binomial proportions with 95% confidence intervals. A multivariable logistic regression analysis was performed to evaluate predictors of influenza. An estimated minimum number of 200 events was a priori determined to ensure an acceptable sample size for the given number of predictor variables in the model. All variables with a p-value <0.1 in univariable analysis were considered for inclusion in the multivariable model.

Supplementary analyses were performed stratified for influenza types and admission to ICU vs. medical ward to ensure that potential clinically important effects of these variables were not missed in the pooled analysis. Missing values were excluded throughout the analyses.

Ethics approval

The study was approved by the Research Ethics Boards of all participating hospitals.

Results

Influenza season

The influenza season in Toronto in 2007/8 was bi-modal, with a first "season" beginning on December 16th, 2007 (week 51) and ending February 3th, 2008 (week 6), and a second "season" beginning on February 24th, 2008 (week 9) and ending on May 3rd, 2008 (Fig. 1) [13]. Influenza activity was predominantly influenza A(H1N1) until week 7 of 2008. From week 8 to week 21, activity was mixed influenza A(H3N2) and influenza B. Overall in Canada, 39.1% of the samples tested were influenza A(H1N1), 13.1% were influenza A(H3N2), and 44.8% were influenza B [14]. The percentage of specimens yielding influenza was highest during weeks 8 to 21, when there was significant antigenic mismatch between both circulating influenza strains (A(H3N2) and B) and the antigens in the 2007 northern hemisphere influenza vaccine.

Results of surveillance

From December 30th, 2007, through May 24th, 2008, 6,236 eligible patients were admitted to participating hospitals/ICUs. Of these, 3,917 (62.8%) were tested for influenza infection and 280 (7.1% of those tested) were identified as infected with influenza (Fig. 2). DFA was positive for influenza in 3.1% (37/1,200) of tests submitted, EIA in 2.6% (44/1,708), viral culture in 4.5% (172/3,834), and PCR in 6.9% (245/3,567). Among patients with at least one test positive for influenza, DFA was positive in 53.6% (37/69), EIA in 29.7% (44/148), viral culture in 62.1% (172/277), and PCR in 98.4% (245/249). All specimens positive by EIA or DFA were also positive by culture and PCR, with the exception of 1 of 44 (2.3%) specimens positive by EIA that was negative by both culture and PCR (DFA was not performed). Similarly, of 174 specimens positive by culture, 171 were positive by PCR, one was negative, and two were PCR-indeterminate.

Specimens were more likely to be submitted in eligible patients if the triage temperature was ≥38.0°C (76% [523/688] vs. 62.7% [3,143/5,015] from patients with a triage temperature <38.0°C, $p<0.0001$), if the patient reported respiratory symptoms in the emergency department (67.8% [2,288/3,374] vs. 60.3% [1,420/2,354] of those without respiratory symptoms, $p<0.0001$), and if the admitting diagnosis was pneumonia, other respiratory infection, respiratory failure, exacerbation of asthma or chronic obstructive pulmonary disease (COPD) (75.6% [1,140/1,507] vs. 58.7% [2,777/4,729] in patients with other admission diagnoses, $p<0.0001$).

The temporal variation in the percentage of specimens yielding influenza in specimens from this study paralleled the yield in specimens submitted to the Ontario Public Health Laboratory: study hospitals: 2.9% positive tests in weeks 1–7 vs. 9.3% positive tests in weeks 8–21; Ontario surveillance: 7.7% positive tests in weeks 1–7 vs. 18.2% positive tests in weeks 8–21 ($p=0.23$). Patients with influenza admitted early during the influenza season (weeks 1–7, when A(H1N1) predominated) were significantly younger than those admitted later in the season (weeks 8–21) (median 68.0 years [IQR: 53.7–80.4 years] during weeks 1–7 vs. 81.8 years [IQR: 69.5–87.6 years] during weeks 8–21, $p=0.0005$). There were no other differences in patient characteristics between patients admitted during weeks 1–7 and those admitted during weeks 8–21 (data not shown).

Predictors of influenza infection

Table 1 shows the proportions of patients with influenza among those admitted to participating medical wards or ICUs according to the patient characteristics. Overall, 35.1% (94/268) of patients with influenza had a first temperature taken at triage in the emergency department ("triage temperature") that was ≥38.0°C, and 40.1% (68/167) had a maximum temperature ≥38.0°C during their first 24 h of admission. The majority (80.1%, 222/277) of patients with influenza reported respiratory symptoms in the emergency department, 75.7% (212/280) were 65 years or older, and 56.6% (164/280) were admitted with an initial diagnosis of respiratory infection, exacerbation of asthma or COPD, respiratory failure, or sepsis. Multivariable analysis revealed a triage temperature ≥38.0°C, the presence of respiratory symptoms in the emergency department, an admission diagnosis of respiratory infection (including "pneumonia" and "other respiratory infection"), an admission diagnosis of underlying lung disease (including "exacerbation of COPD", "exacerbation of asthma", and, in ICU patients, "respiratory failure"), and admission in weeks with >15% of surveillance specimens positive for influenza as independent predictors for an infection due to influenza A or B (Table 2). Admitting diagnosis of underlying lung disease turned out to be a predictor of

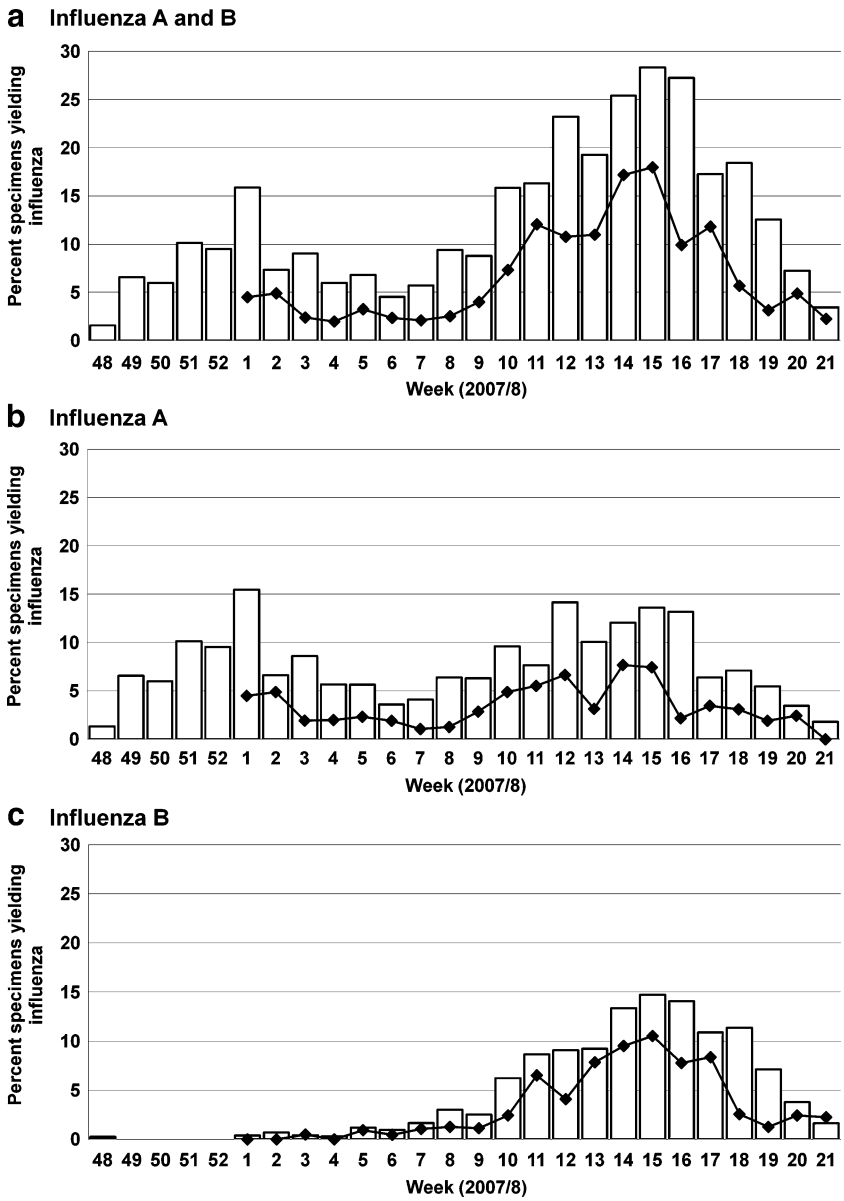

Fig. 1 Comparison of influenza activity by laboratory surveillance in Ontario expressed as the percentage of specimens submitted to reference virology laboratories yielding influenza (*bars*) and the percentage of screened patient admissions to medical wards and intensive care units (ICUs) of participating hospitals in Toronto positive for influenza (*lines*) during the 2007/8 influenza season

influenza infection in patients <65 years old (OR 5.4; 95% CI 2.7–11.0), but not in those ≥65 years of age (OR 1.5; 95% CI 0.9–2.5). No other differences in influenza predictors were identified between these two age groups (data not shown).

Predictors of influenza according to influenza type

Eighty-five of 136 (62.5%) influenza A strains were available for subtyping: 18 were influenza A(H1N1) and 67 were influenza A(H3N2). The results of univariable and multivariable analyses of influenza predictors performed for influenza A(H3N2) and influenza B are shown in Table 3. Influenza A(H1N1) was not included in the subanalysis due to the small number of case patients. In contrast to influenza A(H3N2), a diagnosis of influenza B was significantly more likely in patients with an admission diagnosis of pneumonia or other respiratory infection, exacerbation of asthma/COPD, or, in ICU patients, respiratory failure.

Likelihood of influenza in different patient groups

Table 4 depicts the likelihoods of influenza in various patient groups. The likelihood of influenza exceeded 30% in patients admitted during peak influenza weeks who had a fever at triage and who had either a diagnosis of respiratory tract infection, exacerbation of COPD or asthma, or complained of any respiratory symptoms in the emergency department. It exceeded 15% in patients with respiratory

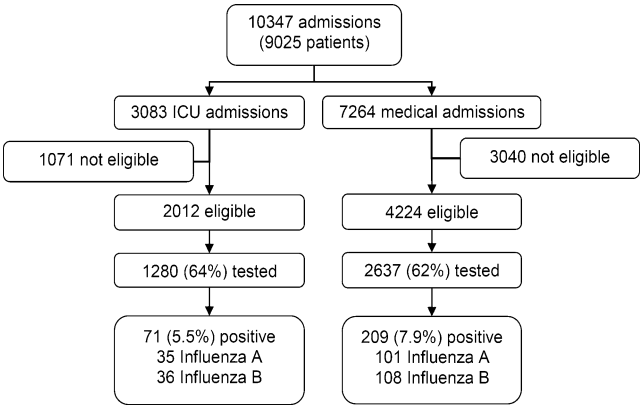

Fig. 2 Flow chart of study subjects admitted to the medical wards and ICUs of six acute care hospitals in Toronto during the 2007/8 influenza season

infections or exacerbations of COPD/asthma if the triage temperature was ≥38.0°C at any time during the season or during peak weeks (i.e., weeks with >15% of surveillance specimens positive) with any triage temperature.

However, in weeks with <15% specimens positive (off-peak weeks) or if the admitting diagnosis was something other than a respiratory infection or an exacerbation of COPD/asthma, the likelihood of influenza dropped below 10%, even in febrile patients with respiratory symptoms. Similarly, afebrile patients with respiratory infections or obstructive pulmonary disorders had a low likelihood of influenza infection if admission was during off-peak weeks. The likelihood of influenza was below 2% in afebrile patients with respiratory symptoms during off-peak weeks when the admitting diagnosis was something other than respiratory infections or exacerbation of chronic lung disease.

Discussion

In prospective surveillance for laboratory-confirmed influenza infection in patients admitted to six participating hospitals in Toronto during the 2007/8 influenza season, a

Table 1 Characteristics of patients screened for influenza who were admitted to medical wards and intensive care units (ICUs) in participating hospitals, Toronto, 2007/8 influenza season

Characteristics	No. of influenza-positive/total (%)	
	Medical admissions (n=2,637)	ICU admissions (n=1,280)
Gender		
Male	96/1,208 (7.9%)	34/687 (4.9%)
Female	113/1,416 (7.9%)	37/591 (6.2%)
Age group		
14–44 years	18/192 (9.4%)	3/93 (3.2%)
45–64 years	28/448 (6.3%)	19/356 (5.3%)
65–84 years	78/1,219 (6.4%)	36/664 (5.4%)
≥85 years	85/776 (10.9%)	13/167 (7.8%)
Temperature (°C) at triage		
<37.0	67/1,547 (4.3%)	34/788 (4.3%)
37.0–37.9	58/556 (10.4%)	15/252 (6.0%)
38.0–38.5	42/209 (20.1%)	12/74 (16.2%)
>38.5	32/175 (18.3%)	8/65 (12.3%)
Respiratory symptoms in ED		
No	46/999 (4.6%)	9/421 (2.1%)
Yes	160/1,531 (10.5%)	62/757 (8.2%)
Admission diagnosis		
Respiratory infection[a]	79/592 (13.3%)	22/184 (12.0%)
Exacerbation of asthma/COPD	30/241 (12.4%)	8/53 (15.1%)
Respiratory failure NOS	-	9/70 (12.9%)
Sepsis NYD	13/127 (10.2%)	3/74 (4.1%)
Diabetes	3/24 (12.5%)	0/16 (0.0%)
Febrile neutropenia	5/41 (12.2%)	-
Arrhythmia	7/129 (5.4%)	4/124 (3.2%)
Other respiratory diagnosis	8/142 (5.6%)	3/47 (6.3%)
Other cardiac diagnosis	13/571 (2.3%)	14/544 (2.6%)
Other diagnosis	51/770 (6.6%)	8/167 (4.8%)

Abbreviations: ED: emergency department; COPD: chronic obstructive pulmonary disease; NOS: not otherwise specified; NYD: not yet diagnosed

[a] Respiratory infection includes: pneumonia, acute bronchitis, croup, and other lower respiratory tract infection

Table 2 Predictors of influenza in adult patients admitted to medical wards and ICUs, Toronto, 2007/8 influenza season

Predictor	Univariable analysis		Multivariable analysis	
	Odds ratio (95% CI)	*p*-value	Odds ratio (95% CI)	*p*-value
Age ≥65 years	1.2 (0.9–1.6)	0.1889		
Female gender	1.1 (0.9–1.4)	0.4470		
Residence in long-term care facility	1.3 (0.9–1.8)	0.1524		
Triage temperature ≥38.0°C	3.8 (2.9–4.9)	<0.0001	3.1 (2.3–4.1)	<0.0001
Respiratory symptoms in ED	2.7 (2.0–3.7)	<0.0001	1.7 (1.2–2.4)	0.0030
Admission diagnosis				
Pneumonia/other respiratory infection	2.5 (1.9–3.2)	<0.0001	1.8 (1.3–2.4)	0.0006
COPD/asthma/respiratory failure NOS	2.1 (1.5–3.0)	<0.0001	2.3 (1.6–3.4)	<0.0001
ICU admission	0.7 (0.5–0.9)	0.0057		
Week with >15% specimens positive	4.1 (3.1–5.5)	<0.0001	4.2 (3.1–5.7)	<0.0001

Abbreviations: ED: emergency department; COPD: chronic obstructive pulmonary disease; NOS: not otherwise specified

triage temperature ≥38.0°C, the presence of respiratory symptoms, admission diagnosis of respiratory infection, or exacerbation of COPD or asthma, and admission during peak influenza weeks were independent predictors for influenza. The likelihood of influenza exceeded 15% in patients with suspected respiratory infection or exacerbation of COPD/asthma if they were admitted in peak weeks during the influenza season, and exceeded 20% for patients who were febrile at triage and had a respiratory diagnosis or respiratory symptoms in the emergency department. These findings may assist clinicians in decisions regarding influenza testing of patients being hospitalized, and may better guide decisions regarding empiric antiviral therapy in adult acute care.

Our data suggest that these findings hold true for both influenza A and B, for both younger and older adults, and in patients being admitted to both medical services and ICUs. While they are limited to a single geographic area during a single influenza season, they are similar to those from previous studies in other years in both North America and Europe. Walsh et al., in a single hospital over three influenza seasons from 2001–2004, identified that 154 of 1471 (10.5%) older adults admitted with a cardiopulmonary diagnosis during the influenza season had influenza, and that fever was more than twice as common in patients with influenza as patients without [15]. van den Dool et al., during the peaks of two influenza seasons, identified that 8.5% of patients (23 of 271) admitted to internal medicine,

Table 3 Predictors of influenza according to different types of influenza in adult patients admitted to medical wards and ICUs, Toronto, 2007/8 influenza season

Predictor	Influenza A(H3N2)		Influenza B	
	Odds ratio (95% CI)		Odds ratio (95% CI)	
	Univariable analysis	Multivariable analysis	Univariable analysis	Multivariable analysis
Age ≥65 years	1.3 (0.7–2.3)		1.5 (1.0–2.3)	1.4 (0.9–2.1)
Female gender	0.9 (0.6–1.5)		1.1 (0.8–1.6)	
Residence in long-term care facility	1.1 (0.5–2.2)		1.3 (0.8–2.1)	
Triage temperature ≥38.0°C	5.5 (3.4–9.0)	4.8 (2.8–8.0)	3.6 (2.5–5.1)	3.0 (2.1–4.5)
Respiratory symptoms in ED	2.4 (1.4–4.3)	1.8 (1.0–3.4)	3.0 (2.0–4.6)	1.8 (1.1–3.0)
Admission diagnosis				
Pneumonia/other respiratory infection	2.5 (1.5–4.1)	1.2 (0.7–2.1)	2.6 (1.8–3.7)	1.7 (1.1–2.6)
COPD/asthma/respiratory failure NOS	1.6 (0.8–3.2)		2.2 (1.4–3.5)	2.2 (1.3–3.8)
ICU admission	0.5 (0.3–0.8)		0.7 (0.5–1.0)	
Week with >15% specimens positive	6.0 (3.2–11.5)	6.5 (3.3–12.7)	7.5 (4.6–12.2)	7.0 (4.3–11.4)

Abbreviations: ED: emergency department; COPD: chronic obstructive pulmonary disease; NOS: not otherwise specified

Table 4 Likelihood of influenza in different groups of screened patients admitted to medical wards and ICUs in Toronto, 2007/8 influenza season

Admitting diagnosis/clinical characteristics	Triage temperature	Timing during season	Likelihood of influenza (95% CI)
COPD/asthma exacerbation[a]	≥38°C	Peak weeks	0.35 (0.14–0.56)
	≥38°C	Any time	0.32 (0.17–0.46)
	Any	Peak weeks	0.17 (0.12–0.23)
	Any	Any	0.13 (0.10–0.16)
	<38°C	Early or late weeks	0.05 (0.02–0.09)
Respiratory infection[b]	≥38°C	Peak weeks	0.30 (0.22–0.38)
	≥38°C	Any time	0.20 (0.15–0.25)
	Any	Peak weeks	0.20 (0.16–0.24)
	Any	Any	0.13 (0.11–0.16)
	<38°C	Early or late weeks	0.04 (0.01–0.06)
Respiratory symptoms reported in ED	≥38°C	Peak weeks	0.31 (0.25–0.38)
	≥38°C	Any time	0.21 (0.17–0.26)
	Any	Peak weeks	0.15 (0.13–0.17)
	Any	Any	0.10 (0.09–0.11)
Diagnosis other than respiratory infection or COPD exacerbation, but with respiratory symptoms in ED	≥38°C	Early or late weeks	0.06 (0.00–0.12)
	<38°C	Early or late weeks	0.01 (0.00–0.12)

Abbreviations: ED: emergency department; COPD: chronic obstructive pulmonary disease

[a] COPD/asthma exacerbation includes "exacerbation of COPD (chronic obstructive pulmonary disease)", "exacerbation of asthma", and "respiratory failure NOS (not otherwise specified)"

[b] Respiratory infection includes "pneumonia" and "other respiratory infection"

geriatrics, respirology, or infectious diseases wards with any diagnosis had influenza [16].

These studies, and that of Babcock et al., also found that clinical signs and symptoms are of limited value in diagnosing influenza [17]. Walsh et al. found that, during a one-year epidemic period, the complex of cough, temperature of 38°C or higher, and illness duration of 7 days or less in older adults with a cardiopulmonary admitting diagnosis yielded a sensitivity of 78% and a specificity of 73%, a positive predictive value of 40%, and a negative predictive value of 91% [15]. However, other authors have, in general, not been able to identify symptoms complexes with positive or negative predictive values much above 50%. As Call et al. noted in their 2005 meta-analysis: "Unfortunately, no specific symptom or combination of symptoms is diagnostic of this common infection" [18].

The goal of this study, however, was not to identify symptom complexes that could diagnose influenza, but, rather, to identify populations of patients in whom the probability of influenza was high enough that either diagnostic testing or empiric antiviral therapy were warranted. An increasing number of studies suggest that specific antiviral therapy is effective in reducing the morbidity and mortality associated with influenza [7, 8], and current guidelines for both seasonal and pandemic influenza recommend the treatment of patients requiring hospitalization for influenza [19, 20]. In outpatients, early therapy with specific antivirals is more effective than later therapy [21], and there is good evidence for bacterial infection requiring hospitalization that early, effective antibacterial therapy improves outcomes [22–24]. Our data may be particularly important for clinicians considering empiric antiviral therapy, where understanding the pre-test probability of acute infection is needed for rational use.

As in other studies of influenza in adults, our data suggest that reverse transcriptase polymerase chain reaction (RT-PCR) is significantly more sensitive than viral culture or DFA for influenza diagnosis, and these tests are, in turn, more sensitive than commercial rapid influenza tests. In adult patients requiring hospital admission, RT-PCR is the only diagnostic test with adequate performance characteristics for the diagnosis of influenza [19].

There are a number of limitations to our study. Only 63% of eligible patients were tested for influenza, suggesting that the proportion of persons actually infected might be significantly higher than our estimate. The fact that patients in whom clinicians accepted recommended orders were

more likely to be febrile, have respiratory symptoms, or have a high-risk diagnosis suggests that clinicians were selecting out patients more likely to have influenza for testing. As in Babcock et al.'s study [17], it is possible that patients whose clinicians did not order specimens did not have influenza. However, other unknown biases may have existed. Data collection by chart review limited the number of risk factors that might have been considered, and meant that we could not consider any differences that might have been found between vaccinated and unvaccinated persons. In addition, we assessed only respiratory symptoms overall rather than individual specific respiratory symptoms (e.g., cough, shortness of breath). Although our results are similar to those of studies in other seasons and geographic areas, there may still be significant year-to-year and area-to-area variation. In support of this, risk factors for infection with influenza A(H3N2) and influenza B appear to be somewhat different in our analysis. In addition, as expected, patients admitted with influenza during weeks with predominant A (H1N1) activity were younger than others [25]. Although there were too few A(H1N1) infections diagnosed to compare risk factors for A(H1N1) compared to A(H3N2) and B infections, such predictors may be different, in part, because patients infected with influenza A(H1N1) are expected to be younger than patients infected with influenza A(H3N2) or B [25]. Finally, patients who are admitted to hospital with influenza infection likely do not constitute a homogenous group. The proportion of patients who need specific antiviral therapy to control influenza infection versus the proportion who are suffering from a complication of influenza but are able to control viral replication themselves remains unknown. Further study to define the causes of hospitalization due to influenza and the potential of antiviral therapy are clearly needed.

The identification of patients shedding influenza virus is also important for infection prevention. If additional precautions for patients admitted with influenza are an important element of the control of transmission of influenza in acute care hospitals, then our data suggest that additional precautions should be implemented for all patients with respiratory infections and COPD or asthma exacerbations during the influenza season, until the results of influenza testing rule out influenza. The cost and impact on patient care of such an approach highlights the need for a better understanding of when patients with influenza are infectious and of the epidemiology of healthcare-associated influenza transmission.

In conclusion, we believe that, in febrile patients with suspected respiratory infection or exacerbation of COPD or asthma, influenza testing and empiric antiviral therapy may be warranted during influenza seasons. During weeks in which >15% of surveillance specimens are expected to be positive for influenza, testing and empirical treatment might be indicated in any patient with respiratory symptoms. This approach may not contribute to the development of resistance, as the treatment of patients who do not have influenza does not create selective pressure for drug resistance, because current antivirals are influenza-specific.

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