Influenza A testing and detection in patients admitted through emergency departments in Sydney during winter 2009: implications for rational testing

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ABSTRACT

Aim: To examine factors associated with testing and detection of influenza A in patients admitted to hospital for acute care during the winter 2009 pandemic influenza outbreak.

Design, setting and participants: Retrospective observational study of patients who were tested for influenza A after being admitted to hospital through emergency departments of the Sydney South West Area Health Service from 15 June to 30 August 2009.

Main outcome measures: The association of factors such as age, diagnosis at admission, hospital and week of admission with rates of testing and detection of influenza A.

Results: 17 681 patients were admitted through nine emergency departments; 1344 (7.6%) were tested for influenza A, of whom 356 (26.5%) tested positive for pandemic influenza. Testing rates were highest in 0–4-year-old children, in the peak period of the outbreak, and in patients presenting with a febrile or respiratory illness. Positive influenza test results were common across a range of diagnoses, but occurred most frequently in children aged 10–14 years (64.3%) and in patients with a diagnosis at admission of influenza-like illness (59.1%). Using multivariate logistic regression, patients with a diagnosis at admission of fever or a respiratory illness at admission were most likely to be tested (odds ratios [ORs], 15 [95% CI, 11–21] and 17 [95% CI, 15–19], respectively). These diagnoses were stronger predictors of influenza testing than the peak testing week (Week 4; OR, 7.0 [95% CI, 3.8–13]) or any age group. However, diagnosis at admission and age were significant but weak predictors of a positive test result, and the strongest predictor of a positive test result was the peak epidemic week (Week 3; OR, 120 [95% CI, 27–490]).

Conclusion: The strongest predictor of a clinician’s decision to test for influenza was the diagnosis at admission, but the strongest predictor of a positive test was the week of admission. A rational approach to influenza testing for patients who are admitted to hospital for acute care could include active tracking of influenza testing and detection rates, testing patients with a strong indication for antiviral treatment, and admitting only those who test negative to “clean” wards during the peak of an outbreak.

METHODS

The Sydney South West Area Health Service (SSWAHS) covers central and south-western Sydney, and incorporates nine public hospitals with emergency departments (EDs) that serve a total population of 1.4 million people. Patients admitted to hospital through any ED in the SSWAHS between 15 June and 30 August 2009 were enrolled in the study. Data were provided by NSW Health using the NSW Emergency Department Data Collection.

Two public hospital laboratories within the Sydney South West Pathology Service — at Liverpool Hospital and Royal Prince Alfred Hospital — performed all the influenza testing. Diagnostic testing for influenza A and pandemic influenza subtyping were similar in both laboratories. Following total nucleic acid extraction from nasopharyngeal swabs, influenza A and pandemic influenza were confirmed by polymerase chain reaction using assays which target the matrix protein (influenza A) and nucleocapsid protein gene segment (pandemic influenza) (Influenza 4, Influenza 6 and Respiratory pathogens 12 Easy-Plex assay kits [AusDiagnostics, Sydney, NSW]).

ED admissions were linked to laboratory data using each patient’s medical record number, sex and age. For patients with more than one ED admission, the admission corresponding with influenza testing was selected for linkage; for those who were not
tested, the first admission was selected. All patients for whom an influenza test had been requested but not performed were recorded as not tested. Patients who died in the ED from any cause were excluded.

The Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) admission diagnosis code for each patient was categorised to one of 13 diagnosis categories (Box 1). These included four main categories (respiratory conditions, fever, cardiac conditions and other conditions). Respiratory conditions were further divided into 10 diagnosis subcategories.

Rates of testing for influenza A and rates of detection of influenza A (per 100 patients admitted through EDs) were analysed by week of admission, hospital, age group, sex, admission destination (general ward or critical care unit), weekday of presentation, time of day of presentation, triage category, laboratory location (onsite or offsite) and admission diagnosis category. Statistical significance was assessed using the χ² test.

Multivariate logistic regression using STATA version 10 SE (StataCorp, College Station, Tex, USA) was performed to test whether the study factors were associated with testing for influenza A and, in patients who were tested, detection of influenza A. Variables that were significant in the univariate analysis were included in the multivariate logistic regression analyses. Non-significant associations (P>0.05) between these factors and the outcome were dropped until the simplest model of the association between significant study factors and these two outcomes was obtained. For both testing and detection of influenza A, the final model included only age group, week of admission and diagnosis category. Regression analyses were also adjusted for clustering by admitting hospital.

The study was approved by the SSWAHS Ethics Review Committee (RPAH Zone), and no formal funding was obtained to conduct the study.

RESULTS
Between 15 June and 30 August 2009 inclusive, 17 787 unique patients were admitted through EDs in the SSWAHS. Of these patients, 106 died in the ED and were excluded. Of the remaining 17 681 patients, 1387 (7.8%) had an influenza test requested, but 43 of the requested tests were not performed. Of the 1344 patients who were tested for influenza (7.6% of the unique patients), 441 (32.8%) tested positive for influenza A and 356 (26.5%) tested positive for pandemic influenza. For those tested, the median time from admission to sample collection was 1 day. On univariate analysis, rates of testing and detection of influenza A were significantly associated
Rates of testing for influenza A and rates of detection of both influenza A and pandemic influenza varied by age group (Box 3). Although the proportion of patients tested was highest in the 0–4-years age group (299 of 1342; 22.3%), the rate of influenza A detection was highest in children aged 10–14 years (18 of 28; 64.3%). Older patients (≥60 years) were less likely to be infected with pandemic influenza than younger patients (Box 3).

Similarly, rates of testing and detection of influenza A varied by illness severity. Patients assigned to triage category 2 were more likely to have a test performed than patients assigned to triage category 5 (10.2% [355/3483] vs 2.5% [8/326]; P <0.001, χ² test). In contrast, patients assigned to lower triage categories were significantly more likely to test positive for influenza A compared with patients assigned to higher triage categories (P = 0.02, χ² test).

The proportion of patients who were tested for influenza A varied by diagnosis category (Box 4), with testing rates highest for patients with fever (28.1% tested) or a respiratory condition (27.3% tested). Among these patients, influenza A was most commonly detected in those diagnosed with influenza-like illness (59.1%), viral illness (50.0%) or a fever (48.4%). Within the other respiratory categories, 31.1% of those diagnosed with pneumonia and 30.2% with shortness of breath tested positive, while influenza A was relatively uncommon among patients with bronchiolitis (17.5%) (Box 4).

Multivariate regression analysis (Box 5) showed that diagnosis category had the strongest association with testing for influenza A. For patients with a febrile or a respiratory condition, the odds of being tested were 15 to 17 times higher compared with patients who did not have a febrile, respiratory or cardiac condition at admission. Controlling for age and diagnosis category, the odds of a patient being tested in the period 6 July to 12 July (Week 4) were sevenfold higher than for 15 June to 21 June (Week 1). Week of admission had by far the strongest association with testing for influenza A. For patients with a febrile or a respiratory condition, the odds of being tested were 15 to 17 times higher compared with patients who did not have a febrile, respiratory or cardiac condition at admission. Controlling for age and diagnosis category, the odds of a patient being tested in the period 6 July to 12 July (Week 4) were sevenfold higher than for 15 June to 21 June (Week 1). Week of admission had by far the strongest association with detection of influenza A. The odds of a positive influenza A result were 120 times higher in the period 29 June to 5 July (Week 3) compared with the period 17 August to 23 August (Week 10).

**DISCUSSION**

We examined the factors associated with testing for and detection of influenza A in patients admitted to hospital through EDs in
the SSWAHS during the winter 2009 pandemic influenza outbreak. Overall, 7.6% of admitted patients were tested, of whom 32.8% tested positive for influenza A. Testing peaked at 15.5% in Week 4 (6 July to 12 July), while the proportion of patients who tested positive for influenza A peaked at 56.2% in Week 3 (29 June to 5 July).

In a case series of patients admitted to hospital with confirmed influenza A during the 2009 southern hemisphere winter, classic features such as cough and fever were commonly reported, but the spectrum of illness was broad. Risk factors for severe disease, including pregnancy, airways disease, diabetes and high body mass, have been reported in an intensive care unit case series and an epidemiological summary of the first winter wave of the pandemic influenza outbreak. Our observational study design, in which two routine datasets were matched for a large sample of patients, enabled us to make broad conclusions about the approach of clinicians to testing for influenza and the features predictive of a positive test result. It only included patients who were admitted to hospital through EDs, hence the results may not be applicable to outpatients and to patients in non-acute-care settings such as general practice. In addition, clinical information, in the form of the SNOMED CT diagnosis codes, was provided at triage. Many of these codes only provide syndromic descriptions of the reason for admission, and the diagnosis codes entered by ED staff at the time of patient admission may not always accurately capture the final diagnosis. Nevertheless, the decision to test for influenza is usually made shortly after presentation, therefore, the diagnosis at admission is arguably a more accurate representation of the information available to the clinicians when they decide whether to test for influenza.

So, what factors guided clinicians in deciding whether to test for influenza in patients admitted to hospital for acute care? Controlling for age, week of admission, and illness severity, clinical presentations with a febrile or respiratory illness (especially patients presenting with an influenza-like illness) were the strongest predictors for influenza testing. The two other factors guiding testing were age and week of admission. The association with age was surprisingly weak; older patients (≥80 years) were least likely to be tested, with minor differences in testing rates among the other age groups. Week of admission had a moderate influence; and testing lagged behind the highest odds for a positive test by 1 week, suggesting that clinicians are influenced by recent positive test results.

So, what factors were most predictive of a positive influenza test result? Week of admission had the strongest association with influenza A detection, outweighing age and diagnosis category. The strong seasonality of influenza is well described, but the strength of this association is surprising. Although testing intensity was highest in children under 10 years of age, the highest rates of influenza detection were in 10–14-year-old children. This concurs with epidemiological data suggesting a higher incidence of pandemic influenza infection in school-aged children. Similarly, the lower rates of testing and detection in older patients, especially those 80 years and older, suggests a low incidence of disease in older patients, possibly due to pre-existing immunity. After controlling for age and week of admission, the association between diagnosis at admission and a positive test result was weak. A diagnosis of fever or a respiratory condition (excluding the category “other respiratory condition”) increased the odds of a positive test result. However, only an influenza-like illness diagnosis stood out in both univariate and logistic regression analyses, with a 59% rate of influenza A detection and sevenfold higher odds of a positive influenza test result compared with cardiac conditions. Rates of testing of patients with non-respiratory and non-febrile conditions were low (2.2%–3.1%), but detection rates for these patients were comparable to respiratory diagnosis categories. This result

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Tested for influenza A (95% CI)*</th>
<th>Influenza A detected (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>2.6 (0.9–7.4)</td>
<td>3.7 (2.0–6.8)</td>
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<tr>
<td>5–14</td>
<td>2.7 (1.0–7.2)</td>
<td>6.0 (2.4–14)</td>
</tr>
<tr>
<td>15–24</td>
<td>1.6 (0.8–3.3)</td>
<td>2.9 (1.6–5.4)</td>
</tr>
<tr>
<td>25–39</td>
<td>2.5 (1.7–3.7)</td>
<td>2.9 (2.0–4.0)</td>
</tr>
<tr>
<td>40–59</td>
<td>2.5 (1.9–3.4)</td>
<td>3.3 (2.3–4.6)</td>
</tr>
<tr>
<td>60–79</td>
<td>1.8 (1.5–2.2)</td>
<td>1.4 (1.0–1.8)</td>
</tr>
<tr>
<td>≥ 80</td>
<td>1.0†</td>
<td>1.0†</td>
</tr>
</tbody>
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* Adjusted for clustering by admitting hospital. † Reference category.
highlights the varying presentations of influenza. In addition, it confirms the insensitivity of any particular influenza case definition, because the broadest definition (anyone with fever or a respiratory condition) identified 81.9% (361,441) of influenza cases in our study. Thus, to prevent hospital transmission, especially in patients at risk of severe influenza-related illness (such as those in haematology and oncology wards), strict infection-control procedures are required for all patients. Testing individuals who present to EDs during an influenza outbreak is only useful if a positive result will guide the use or discontinuation of an intervention. For maximum utility, a rapid test turnaround time is essential. Testing should be selective, as testing all potential cases in peak periods (about 3681 patients were admitted with a febrile or respiratory condition during our study period) could overwhelm the capacity of laboratories to perform tests in a timely manner.

So, what should be the rational approach to influenza testing for patients who are admitted to hospital for acute care? First, we suggest that there could be a role for intermittent laboratory testing to complement existing that there could be a role for intermittent laboratory testing to complement existing sources of surveillance information. Documenting the upswing, peak and tail of the outbreak with active tracking of testing and detection rates could be a cost-effective method to guide clinical management of influenza, particularly the use of anti-influenza therapy.

Second, during an influenza outbreak it is prudent to test patients with a strong indication for antiviral treatment, such as immunocompromised patients and those who require intensive care. Anti-influenza treatment should be initiated in all these patients, with cessation of antiviral therapy possible following a negative influenza test result.

Finally, we suggest that the main role of testing is to provide guidance for cohorting hospitalised patients during an influenza outbreak, and thereby prevent hospital transmission. Testing should be used to ensure that certain wards, designated as “clean”, remain free of influenza by restricting patient movement to these wards to only those who test negative to influenza or have received 72 hours of antiviral therapy.

In our study, the strongest predictor of a clinician’s decision to test for influenza was the diagnosis at admission, but the strongest predictor of a positive test was the week of admission. Hence, diagnosis at admission provides poor guidance for rational testing. A testing strategy that includes testing on the basis of outbreak progression should be considered.

ACKNOWLEDGEMENTS
We thank the Public Health Real-time Emergency Department Surveillance System team at NSW Health, and the ED and laboratory staff of SSWAHS.

COMPETING INTERESTS
None identified.

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