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Major Article

Reduction in total patient isolation days with a change in influenza testing methodology

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Background: Both hospital admissions and patient isolation increase during influenza season. Influenza testing methodologies that reduce turnaround time (TAT) could reduce time in isolation.
Methods: We assessed the impact of a new influenza test on TAT and isolation days. TAT and daily mean isolation days were compared at a single hospital over 2 influenza seasons. An automated real-time reverse-transcription polymerase chain reaction assay (rRT-PCR) with random access replaced a conventional rRT-PCR assay for the second influenza season. Automation and random access allowed continuous testing, rather than once daily testing 3-5 d/wk.
Results: Confirmed influenza cases (57 vs 68) and total patient days (66,308 vs. 66,366) were similar for the 2012-2013 and 2013-2014 influenza seasons. TAT fell from 35 to 3.6 hours. Daily mean isolation days (32.9 vs 27.7, $P < .01$) fell, as did days in contact precautions (25.0 vs 19.8, $P < .01$) and droplet precautions (6.0 vs 3.5, $P < .01$). Although daily mean droplet precaution days for confirmed influenza rose slightly (0.86 vs 1.1, $P = .16$), droplet precaution days for suspected influenza fell 85% (2.7 vs 0.41, $P < .001$).
Conclusions: Influenza testing technology that reduced TAT from days to hours resulted in a 42% reduction in droplet precaution days and reduced overall isolation days during influenza season.

Annual influenza epidemics affect >5% of the U.S. population annually.[1] As a result, there is a substantial increase in hospital admissions during peak periods of the influenza season because of both the direct and indirect impact of influenza on patients.[2,3] Patients assessed and admitted with suspected influenza require droplet and contact precautions and must be separated from other patients, ideally in a private room.[4]

Both the increase in hospital admissions and the increased need for isolation may adversely impact patient flow, particularly in hospitals where substantial numbers of patients continue to be cared for in multibed rooms, because patients may need to remain in the emergency department until a private room is available. Isolation may also be harmful to patients as a result of a reduction of visits by health care workers; however, this effect is controversial.[5,6]

In this context, influenza testing methodologies that reduce turnaround time (TAT) have the potential to reduce total days in isolation and therefore to improve patient flow and minimize the impact of isolation on patients; however, studies testing this hypothesis are not well described. These potential benefits are in addition to the epidemiologic and clinical benefits of obtaining more rapid results to support clinical diagnosis and management.

METHODS

To evaluate whether a novel influenza testing methodology could reduce TAT and daily mean time in droplet and contact precautions, we conducted a pretest-posttest study over 2 influenza seasons. The study was conducted at a 465-bed acute care academic hospital in Toronto, Canada. Data for all inpatients were included in the study.

During the 2012-2013 influenza season (November 6, 2012-April 5, 2013), testing of nasopharyngeal (NP) swabs for influenza A, pH1N1, and B was performed using a conventional real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) assay (RealStar Influenza S&T RT-PCR Kit 3.0; Altona Diagnostics, Hamburg, Germany). Testing was conducted in the molecular diagnostics area of our microbiology laboratory and was performed 3 times per week during influenza season, with testing frequency increased to 5 times

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per week during the peak of influenza season. Testing was not routinely performed on weekends except in exceptional cases and with the permission of the on-call microbiologist. During this influenza season, a total of 590 specimens were tested, of which 77% (n = 453) were NP swabs.

Prior to the 2013-2014 influenza season (November 18, 2013-May 25, 2014), our influenza testing methodology for NP swabs was changed to a fully automated rRT-PCR influenza diagnostic test (Xpert Flu Assay; Cepheid, Sunnyvale, CA). Similar to the conventional rRT-PCR, this assay detected influenza A, pH1N1, and influenza B. This influenza testing platform allowed random access, such that testing could commence immediately on receipt of specimens within the laboratory. The simplicity of the technology meant that all of our microbiology technologists (not just those with additional training or those working in the molecular laboratory) were able to perform influenza testing 7 d/wk throughout influenza season. This was implemented without any requirement for additional technologist time. All other (ie, non-NP swab) specimens where influenza testing was required continued to be tested using the conventional rRT-PCR 3 times per week. During this influenza season, a total of 663 specimens were tested, of which 86% (n = 571) were NP swabs.

In both seasons, the laboratory immediately phoned positive influenza results to infection control and to the ordering physician. During the first year of the study, the laboratory also communicated negative test results to infection control on the 3 days when batched testing was performed. When continuous real-time testing was adopted, infection control checked regularly and frequently for negative results, particularly for patients that met criteria for removing isolation precautions if the test was negative (see below). Wards also contacted infection control if they were aware of negative results that might affect isolation status.

In both seasons, all negative and influenza A nontyped specimens were forwarded to a reference laboratory, the Ontario Provincial Public Health Laboratory (OPPHL), for testing and strain confirmation. Although these results do not return within a clinically useful time frame, they did provide a means to determine the rate of false negative tests using our in-house testing methodologies over both influenza seasons and to estimate sensitivity and specificity (see below).

To evaluate whether the change in influenza testing methodology for NP swabs resulted in meaningful benefits in terms of the burden of isolation, we compared TAT, total mean inpatient isolation days, isolation days by indication (ie, contact, droplet contact, airborne isolation), and isolation days for suspected or confirmed influenza between the 2012-2013 and 2013-2014 influenza seasons. TAT was defined as the time from receipt of the specimen in the laboratory to the time a result was finalized. Data on isolation days were obtained from infection control. Infection control provides the hospital with a daily census (weekday only) of patients in isolation and the type and indication for isolation. These data were entered, for both influenza seasons, into an Excel database (Microsoft, Redmond, WA).

Using the results obtained from the OPPHL, we determined the incidence of false negative results during both influenza seasons, using the OPPHL results as our reference method. Results were considered concordant if our in-house test and the OPPHL result were either both negative (and all negative in-house tests were confirmed in this fashion) or both positive (only results that were influenza A nontypeable on the in-house test were confirmed at OPPHL).

Sensitivity and specificity were estimated, once again using the OPPHL testing as the reference method, to determine true positive and true negative tests results. As previously stated, only a subset of positive tests were confirmed at OPPHL, whereas all negative test results were confirmed. However, because previous measurements for both in-house test methodologies yielded specificities of 100% (ie, no false positive results), we believe this approach should yield valid estimates of both sensitivity and specificity.

Infection control practices for patients with suspected or confirmed influenza did not change over the 2-year study period. During influenza season, all patients with suspected influenza are placed into droplet and contact precautions in a private room until they are afebrile for 24 hours, clinically improving, and 5 days have elapsed from the onset of symptoms (if treated with an effective antiviral) or 7 days have elapsed (if untreated). For patients with febrile respiratory illness not caused by influenza, isolation is discontinued when the patient is afebrile for 24 hours.

Statistical analysis was conducted in SAS 9.4 (SAS Institute, Cary, NC). Continuous variables were compared using the *t* test when normally distributed, and the Wilcoxon rank-sum test was used when distributions were not normal.

RESULTS

The total number of admitted patients with laboratory-confirmed influenza was 57 in 2012-2013 and 68 in 2013-2014 (Fig 1). Total patient days for the hospital over the 2 influenza seasons were almost identical (66,308 vs 66,366), suggesting that the incidence of influenza was slightly higher during 2013-2014.

Adoption of the fully automated rRT-PCR assay with 7 d/wk testing resulted in a 31.4-hour reduction in TAT from 35 hours in 2012-2013 to 3.6 hours in 2013-2014. During the complete influenza season after implementation of the new test, mean daily isolation days for all indications fell 16% from 32.9 to 27.7 days ($P < .001$).

When type of isolation was considered, we found a 22% reduction in contact isolation days, from 25.0 to 19.8 days ($P < .001$), that we believe was partially related to a large methicillin-resistant *Staphylococcus aureus* outbreak during the 2012-2013 influenza season, a 42% reduction in mean daily droplet-contact isolation, from 6.0 to 3.5 ($P < .001$), and an 11% increase in mean daily airborne isolation, from 2.6 to 2.9 days ($P = .20$) (Table 1 and Fig. 2). These results suggest that 32% of the reduction in total isolation seen between 2012-2013 and 2013-2014 was caused by the reduction in droplet-contact precautions.

We then evaluated the specific indications for droplet-contact precautions over the 2 influenza seasons studied. Although there was no statistically significant change in droplet and contact precautions unrelated to suspected or confirmed influenza (2.4 vs 2.0, $P = .17$), there was an 85% reduction in daily mean isolation days for suspected influenza, from 2.7 to 0.41 ($P < .001$). At the same time,

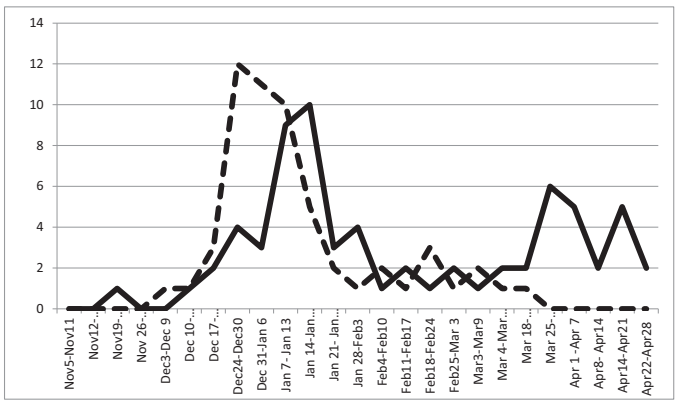

Fig 1. Inpatients with laboratory-confirmed influenza, 2012-2013 (dashed) and 2013-2014 (solid) influenza seasons.