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Improvement in turnaround time for rapid respiratory virus testing using Xpert® Flu/RSV: a retrospective cohort study during a high incidence influenza season

Eloise Williams [a,b,*,1], Amanda Dennison [a], Adam W Jenney [a,b,c], Denis W Spelman [a,b,c]

[a] Microbiology Unit, Alfred Health, 55 Commercial Rd, Melbourne, Victoria, Australia
[b] Department of Infectious Diseases, Alfred Health, 55 Commercial Rd, Melbourne, Victoria, Australia
[c] Department of Infectious Diseases, Monash University, Melbourne, Victoria, Australia

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ABSTRACT

Seasonal influenza like illness results in increased hospital presentations and unnecessary antibiotic use. Recent availability of rapid respiratory virus PCR testing allows rapid, accurate influenza diagnosis. A retrospective audit of turnaround time from sample collection to result availability after introduction of Xpert® Flu/RSV in a tertiary healthcare institution during a high incidence influenza season is described.

Seasonal influenza like illness (ILI) surges result in increased emergency department (ED) presentations and admissions (Casalino and Antoniol 2017), necessitate infection control precautions, and cause unnecessary antibiotic use.

The recent availability of rapid respiratory virus polymerase chain reaction (RVPCR) testing allows accurate, rapid influenza diagnosis. The Xpert® Flu/RSV (Cepheid, Sunnyvale, CA) is a random-access platform with high sensitivity (>95%) and specificity (≥99%) (Dugas et al. 2014; Salez et al. 2015; Wahrenbrock et al. 2016; Haglund et al. 2018) that can extract, amplify, and detect influenza A, influenza B, and RSV nucleic acid targets within 63 min.

We aimed to demonstrate improved turnaround time (TAT) from RVPCR sample collection to result availability in our tertiary healthcare institution in 2017 by using Xpert® Flu/RSV, extending hours of sample processing and modifying laboratory workflow. The 2017 influenza season in Australia saw the highest levels of activity since the 2009 pandemic year, with more than 2½ times the number of laboratory confirmed notifications of influenza compared to the previous year (Australian Government Department of Health 2017).

A retrospective audit was undertaken to assess TAT from sample collection to result availability for a number of different RVPCR laboratory protocols. Our tertiary healthcare institution comprises 3 campuses: the Alfred has 713 beds including a busy ED and a 45-bed intensive care unit; Sandringham has 70 beds including ED and maternity; Caulfield comprises 232 beds. Three different protocols for rapid RVPCR testing were each trialed for at least 30 days during winter 2017. Each used the Xpert® Flu/RSV platform processed continuously within the hours stipulated by trained microbiology staff; however, protocols differed regarding times of availability and target populations for rapid testing. These protocols were created to balance limited laboratory resources with clinical demand.

In protocol 1, rapid RVPCR was available 0800–2100 Monday to Friday and 0800–1700 Saturday and Sunday. All requests, both ED and non-ED, for RVPCR were analyzed using the Xpert ® Flu/RSV platform. In protocol 2, rapid RVPCR was available 0800–1700 Monday to Friday and not available on weekends. All RVPCR requests from the ED were analyzed using the Xpert ® Flu/RSV. RVPCR requests from outside the ED were analyzed using standard multiplexed tandem real-time PCR (MT-PCR) testing using the *Easy*-Plex Respiratory Pathogens B (16-well) platform (AusDiagnostics®, Mascot, NSW). In protocol 3, rapid RVPCR was available 0800–1700 Monday to Friday and 0800–1200 Saturday and Sunday. All RVPCR requests from the ED were analyzed using the Xpert® Flu/RSV platform. All RVPCR requests from outside the ED were processed using the AusDiagnostics® MT-PCR platform.

For all protocols, a positive rapid RVPCR result led to no further testing. Negative rapid RVPCR tests for patients in intensive care or with

* Corresponding author. Tel.: +6194572000; fax: +613-9457-3439.
E-mail address: eloise.williams@austin.org.au (E. Williams).
[1] Present address: Microbiology Unit, Austin Health, 145 Studley Rd., Heidelberg, Victoria, Australia

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Table 1
Primary and secondary outcomes.

Protocol	No. samples (*n*)	ED patients (%)	Positive results (%)	Median [IQR] TAT (h)	TAT ≤ 4 h (%)	*P* value	TAT ≤ 24 h (%)	*P* value
Protocol 1	481	41.8%	41.2%	3.6 [2.2–9.1]	53.8%	-	97.9%	-
Protocol 2	625	54.2%	41.6%	20.3 [8.5–31.2]	13.0%	<0.001	57.1%	<0.001
Protocol 3	559	62.8%	27.0%	15.3 [7.2–24.5]	17.7%	<0.001	74.4%	<0.001
August, 2016	395	39.7%	32.9%	28.7 [23.6–52.4]	0%	-	29.6%	<0.001

prior bone marrow or lung transplants underwent reflex MT-PCR testing.

Prior to 2017, we only used the MT-PCR assay, *Easy*-Plex Respiratory Pathogens B (16-well), for RVPCR testing. With this platform, samples were batched for testing Monday to Friday by specialized molecular microbiology staff, and each run took 6 h.

A retrospective audit was undertaken to measure the TAT from sample collection to result availability for each of the rapid RVPCR protocols and for a 1-month period in August 2016 using the MT-PCR assay to allow comparison between protocols. The secondary outcomes assessed were the proportion of RVPCR samples with a TAT ≤4 h and ≤24 h for each protocol.

There were 2948 RVPCR requests between 1 May and 31 October 2017 compared to 2015 in 2016. Of these, 880/2948 (29.9%) were positive for influenza A, influenza B, or RSV compared to 425/2015 (21.1%) in 2016 ($P < 0.001$). In the peak months of incidence, August and September 2017, 260/634 (41.0%) and 252/710 (35.5%) were positive, respectively.

The primary outcome of median TAT was 3.6 h [IQR 2.2–9.1] for protocol 1; 20.3 h [IQR 8.5–31.2] for protocol 2; 15.3 h [IQR 7.2–24.5 hours] for protocol 3; and 28.7 h [IQR 23.6–52.4] in August 2016. Secondary outcomes are shown in Table 1. Fig. 1 illustrates the TAT for the rapid RVPCR protocols.

Of the 122 samples that tested negative using the rapid RVPCR platform and were also tested using the MT-PCR platform, 3 were positive: 1 each for influenza A, influenza B, and RSV.

Despite a significant increase in RVPCR requests in 2017, the introduction of rapid RVPCR testing using Xpert® Flu/RSV significantly improved TAT compared to the standard MT-PCR protocol used in 2016. Protocol 1 (7-day availability of continuously processed rapid RVPCR for all patients) achieved the best TAT; however, it was the most resource-intensive. Cost-effectiveness was not able to be accurately assessed retrospectively using the microbiology laboratory information system in place for this study. However, we estimate that overall the hospital saved money due to an increase in safe discharges from the Emergency Department (thereby avoiding approximately AU$800 per person per day for unnecessary admissions) compared to the additional human resources required in the microbiology laboratory for protocol 1 (AU$566 for an additional staff member on weekends).

Xpert ® Flu/RSV RVPCR testing has shown reduced RVPCR analytical TAT while maintaining a sensitivity of >95% and specificity of ≥99%. (Dugas et al. 2014; Salez et al. 2015; Wahrenbrock et al. 2016; Haglund et al. 2018) To our knowledge, this is the largest study of rapid RVPCR TAT and is one of few that provides real-world data regarding clinically relevant TAT in 3 healthcare centers including 2 EDs and a tertiary-level care center. The results found in this study are similar to those of Soto et al.'s 2-center Spanish cohort study, where the TAT for rapid RVPCR testing for 691 adult hospitalized and ED patients after the introduction of Xpert® Flu/RSV testing was 4.3 h for ED patients and 5.8 h for hospitalized patients.(Soto et al. 2016) A cost-effectiveness analysis was performed in this study, with rapid RVPCR testing associated with a €103 reduction in cost per patient in the ED and €64 per hospitalized patient compared to a control group of 366 patients using an in-house real-time RVPCR (Soto et al. 2016). Hagland et al. have shown that a median TAT of 1.9 [IQR 1.6–2.5] h is achievable with Gene Xpert ® Flu/RSV testing when performed in a 24-h availability clinical chemistry laboratory (Haglund et al. 2018). However, to ensure quality control, we chose to continue rapid RVPCR testing within the microbiology laboratory by

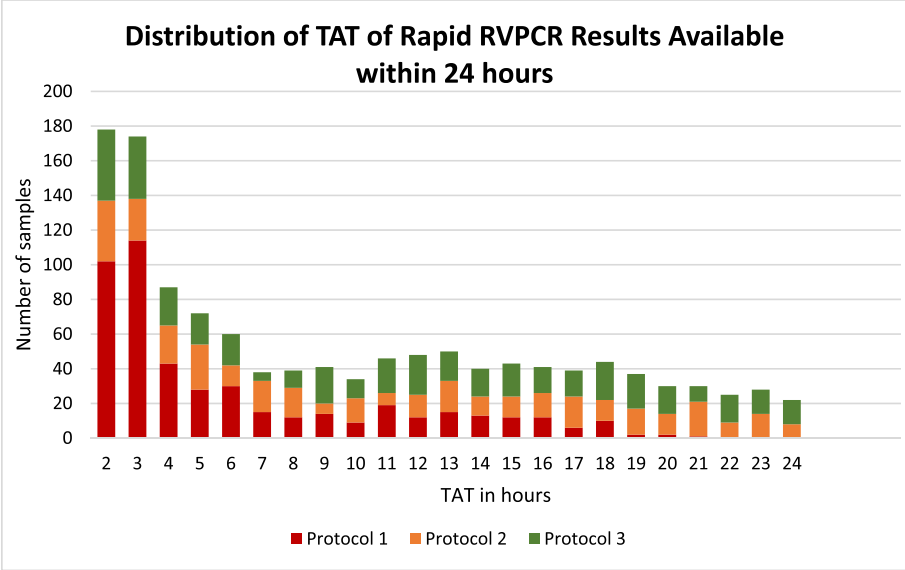

Fig. 1. Distribution of TAT of rapid RVPCR available within 24 h.

trained microbiology staff. Erroneous automated result interpretation has been reported with the Gene Xpert ® Flu/RSV; therefore, careful analysis of amplification curves and endpoints is required to avoid reporting false-negative results (Engelmann et al. 2017).

This study is limited by its retrospective design and absence of clinical impact data. However, clinical impacts of rapid RVPCR have been reported in a small number of studies that have demonstrated reduced antibacterial prescription (Linehan et al. 2018), hospital admission rates (Linehan et al. 2018), isolation days (Muller et al. 2016; Soto et al. 2016), and improved oseltamivir prescription (Linehan et al. 2018). An acute increase in demand for RVPCR testing during our study period in 2017 due to a high incidence influenza season in Australia (Australian Government Department of Health 2017) and limited laboratory resources necessitated adjustments to laboratory workflow. The high demand from ED patients resulted in prioritization of rapid RVPCR testing for this group in protocols 2 and 3, and employment of additional microbiology staff on weekends to improve this service in protocol 3.

On the basis of our results and the literature that supports the positive clinical impacts and cost-effectiveness of rapid RVPCR, we recommend that rapid RVPCR testing be performed continuously for all patients during all available hours of the microbiology laboratory. This study demonstrates that the use of rapid RVPCR testing provides timely results but requires planning and resource investment to enable sustainable service provision. Further studies investigating the clinical impacts and cost-effectiveness of improved TAT for rapid RVPCR testing are needed.

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Conflict of interest

The authors declare that there is no competing interest.

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