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Short Report

Impact of implementing respiratory point-of-care testing in a regional haemato-oncology unit

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SUMMARY

Respiratory point-of-care testing (POCT) for the detection of influenza A, influenza B and respiratory syncytial virus (RSV) was implemented in response to recent RSV outbreaks at a regional haemato-oncology unit in Glasgow. This descriptive study, undertaken pre- and post-POCT implementation, suggests that POCT reduces the time taken to receive results and increases diagnostic rates in outpatients. It is likely that the reduction in turnaround time afforded by POCT also leads to a faster time to antiviral treatment, prompt isolation and a reduction in the number of hospital-acquired infections.

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Introduction

Seasonal influenza and respiratory syncytial virus (RSV) are common causes of respiratory infection worldwide. Both influenza and RSV can cause serious complications in patients with underlying haematological conditions, leading to increased mortality in this patient population [1]. Outbreaks of influenza and RSV in such patients can cause devastating effects, leading to ward closures, increased healthcare costs and avoidable deaths.

In recent years, two outbreaks of RSV have occurred at Beatson West of Scotland Cancer Centre (BWoSCC), resulting in ward closures and significant disruption to a regional oncology unit [2]. Reviews of these outbreaks found that the time taken to receive respiratory virology results may have contributed to these outbreaks. The virology laboratory is situated 4 miles away from BWoSCC, and does not currently operate 24 h/day; therefore, centralized laboratory testing of respiratory specimens can be prolonged. In response to these outbreaks, point-of-care testing (POCT) for RSV and influenza were implemented on the haematology wards at BWoSCC.

Molecular POCT provides sensitive, rapid respiratory testing at the patient's bedside, with results available in <1 h [3]. Prompt diagnosis of influenza and RSV allows effective patient management and infection control procedures to be

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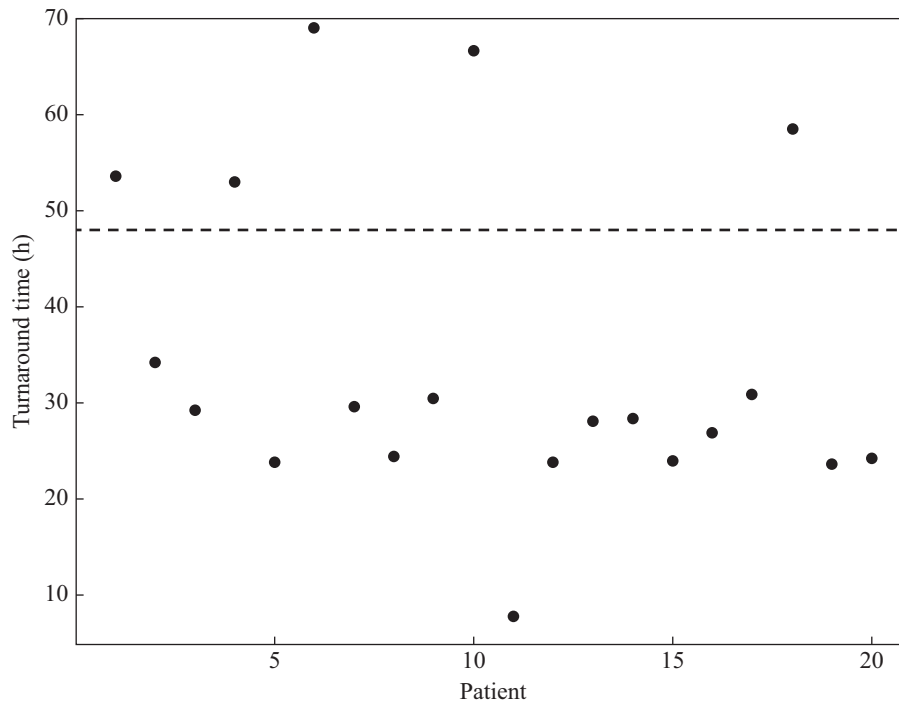


Figure 1. Turnaround time for positive samples tested by the standard laboratory test. Dashed line represents 48 h.

implemented, in turn reducing the risk of nosocomial transmission. Data for patients testing positive on POCT were compared with patients testing positive for influenza or RSV on the standard laboratory test prior to this intervention. This study investigated sample turnaround time (TAT), time to treatment, rates of hospital-acquired infection (HAI) and patient isolation, with the aim of evaluating the impact of POCT implementation at BWoSCC.

Methods

Setting

This study was set over three wards at BWoSCC, comprising two haemato-oncology wards and one bone marrow transplant (BMT) ward. One haemato-oncology ward consisted of 19 beds (five single rooms, one two-bedded room and three four-bedded rooms), and the other haemato-oncology ward was a 10-bedded ward with one two-bedded room, with the remainder being single rooms. The BMT ward had 10 single rooms.

Laboratory respiratory testing

Respiratory specimens received in the laboratory were tested for influenza A, influenza B, RSV, coronaviruses (229E, OC43, NL63), rhinovirus/enterovirus, human metapneumovirus, parainfluenza viruses (1–4), adenovirus and *Mycoplasma pneumoniae*. All samples were extracted using the MagNA Pure 96 System (Roche, Basel, Switzerland) and tested by in-house real-time polymerase chain reaction assays as described previously [2]. Samples were transferred from BWoSCC to the virology department at Glasgow Royal Infirmary using internal hospital transport, which delivers to the virology laboratory seven times per day on weekdays and four times per

day at weekends. At the time of the study, the virology laboratory was open from 8 am to 6 pm on weekdays and from 9 am to 2 pm at weekends.

Point-of-care respiratory testing

POCT was in place at BWoSCC over an 8-month period in 2017–2018. The Xpert Xpress Flu/RSV assay was used on the GeneXpert System (Cepheid, Sunnyvale, CA, USA). This test detects influenza A, influenza B and RSV. Gargle samples were validated internally as a suitable alternative to nasopharyngeal swabs for use with the Xpert Xpress Flu/RSV assay [4]; as such, gargle samples were the specimen of choice for POCT at BWoSCC. Nursing and medical staff in the haemato-oncology department were trained to perform POCT. Staff were initially trained by Cepheid, with new staff subsequently trained by a designated ward POCT trainer; all training concluded with a written and practical competency assessment. Training, competency, risk assessment and quality management of POCT were all overseen by the virology department.

Data collection and analysis

POCT was available to patients on three haematology wards from 9th October 2017 to 12th June 2018, and data from this period were compared with data from the same dates in the previous year. Laboratory data were extracted from the laboratory information management system, and POCT data were extracted directly from the GeneXpert System. POCT results without the correct patient identifiers were discounted from the analysis. Test results were only included for the first positive influenza and/or RSV result; subsequent positive and negative respiratory tests were not assessed. TAT was defined as the time taken from collection of the sample until the time the result was available for the laboratory test. Specific times

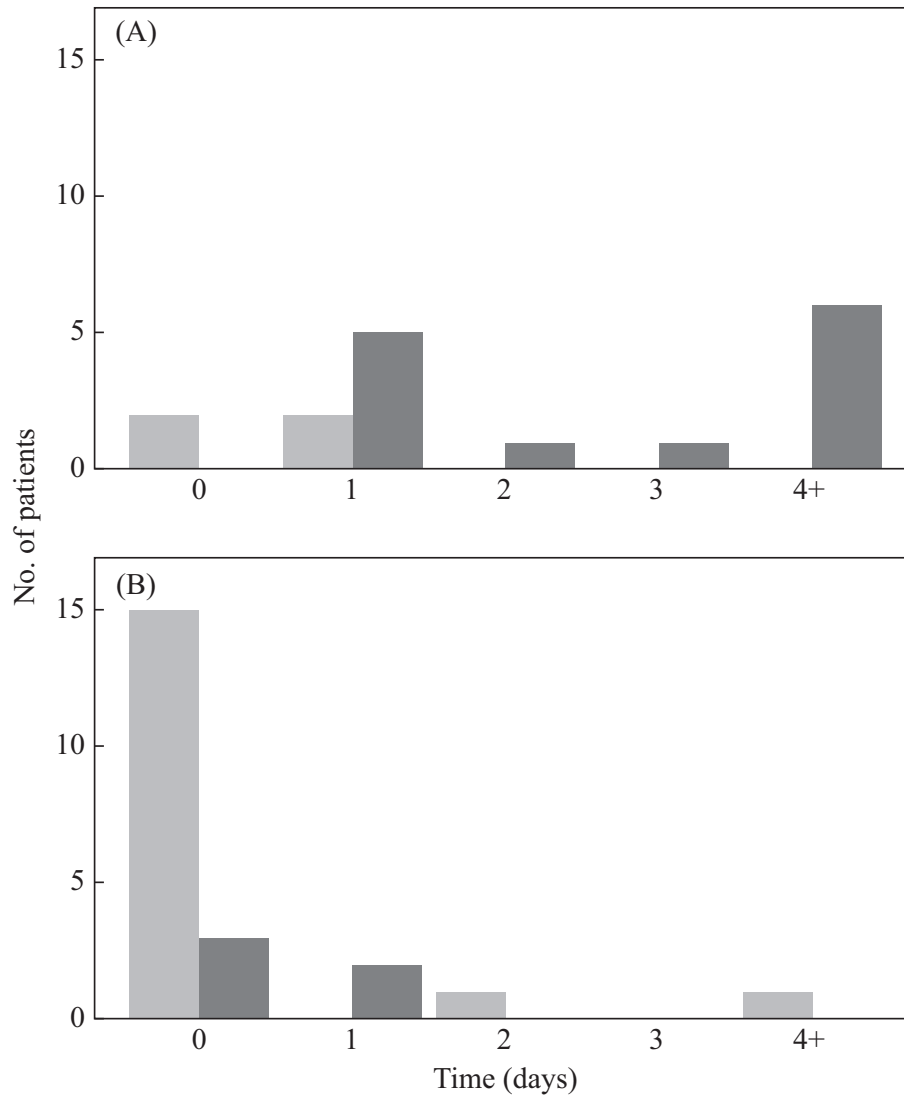


Figure 2. Time from sample collection to starting treatment in (A) laboratory tested patients and (B) point-of-care tested patients. Light grey bars, influenza; dark grey bars, respiratory syncytial virus.

for sample collection were not recorded for POCT patients; however, for this study, the time of collection was assumed to be very close to the time the test was performed, as local guidelines recommend collecting the sample immediately prior to POCT. Patient data were collected retrospectively from patients' electronic records. Prescription of neuraminidase inhibitors (NIs) for influenza and prescription of immunoglobulin and/or ribavirin for RSV infection were recorded. Patient placement (single or multi-bed room) was recorded at the time of sample collection for laboratory tested patients, or at the time of POCT in the POCT cohort. Patient placement was recorded again for the 48-h period following receipt of the positive influenza/RSV result. Patients were considered to have an HAI if they had been an inpatient for >48 h prior to sample collection.

Results

In total, 370 respiratory samples were tested by standard laboratory tests in 2016–2017; of these, 20 (5.4%) tested positive for influenza A, influenza B or RSV. Three patients tested

positive for influenza A, two for influenza B and 15 for RSV. Twelve of the 15 RSV-positive patients were part of an RSV outbreak that occurred at the end of 2016 at BWoSCC [2]. In 2017–2018, 259 samples from BWoSCC were tested via POCT; of these, 28 (10.8%) tested positive for influenza A, influenza B and/or RSV. In this group, nine patients tested positive for influenza A, eight for influenza B and 10 for RSV. One sample tested positive for both influenza A and RSV. Nine (32.1%) of the positive patients tested by POCT were outpatients at the time of testing, and six of them were subsequently admitted. None of the positive patients in the laboratory tested group were outpatients at the time of sample collection.

POCT takes approximately 32 min to complete; however, this does not include the time taken from collecting the sample until test loading, loading the machine or printing results. The authors do not have a calculated TAT for the POCT samples but it was assumed to be <1 h. Results for laboratory tested samples were available between 8 and 69 h from sample collection, with a median TAT of 29 h (Figure 1). All samples with TAT >48 h (N=5) were collected on a Friday or Saturday.

The number of days from sample collection until prescription of treatment was recorded. In the laboratory tested group, all five influenza-positive patients were treated with NIs, and three patients received ribavirin for RSV. Thirty-eight percent of these patients were treated on the day of sample collection (Figure 2). In the POCT cohort, 16 patients received NIs and three patients received ribavirin. Seventy-nine percent of patients were treated on the day of sample collection.

To investigate the potential effect of POCT on patient isolation, patient placement was recorded at the time of sample collection up until 48 h after a positive result was available for both cohorts. Five patients in the POCT cohort were located in single rooms and 15 patients were in multi-bed rooms at the time of sample collection. Thirteen of the 14 (93%) patients in multi-bed rooms at the time of sample collection were moved to single rooms after a POCT-positive result was received. All of these patients were moved within 17 h of the result, with a mean time of 7 h (range 0.5–17 h) from receipt of result until appropriate isolation. The patient that was not isolated did not have respiratory symptoms. In the laboratory tested group, 12 patients were already in single rooms when respiratory samples were collected; however, eight patients were in multi-bed rooms. One patient was discharged on the same day as the result was received, and none of the remaining seven patients were moved to single rooms within 48 h of receiving a positive result; however, these seven patients were part of a known RSV outbreak and had been cohorted.

Twenty-one percent ($N=4/19$) of the POCT patients who were tested whilst an inpatient were considered to have an HAI, compared with 90% ($N=18/20$) of laboratory tested patients. However, it should be noted that 12 of these 18 patients were part of the known RSV outbreak; when these patients are excluded, the rate of HAI in the laboratory tested group is 75% ($N=6/8$).

Discussion

Rapid diagnosis of influenza and RSV is essential in vulnerable groups such as haematology patients. Prompt diagnosis allows appropriate infection control procedures to be implemented without delay, potentially reducing the likelihood of outbreaks occurring in this high-risk patient group. Results for samples tested at the off-site virology laboratory were available, on average, 29 h after sample collection, whereas, in contrast, POCT can be performed within 1 h. The reduction in TAT described in this study is likely to have had a considerable impact on patient isolation, with 93% of POCT patients moved from multi-bed to single rooms within 24 h of a positive result, with movement, on average, 7 h after testing. This was sooner than even the earliest laboratory test result was available. However, data in the laboratory tested group were not available for direct comparison, as all patients in multi-bed rooms were part of an ongoing RSV outbreak and had been cohorted in bays due to a lack of available single rooms. It is interesting to note that even with the decreased TAT, it still took an average of 7 h to isolate patients in the POCT group. Such delays are likely to be due to a lack of available single rooms, as these wards often run at near-maximal bed occupancy, and freeing up bed space is a logistically complex procedure. Therefore, further reducing the test TAT is unlikely to have a significant effect on the time taken to appropriately isolate infected

patients, as there are other post-test aspects that will continue to influence patient movement. Delays in receiving laboratory results may increase the risk of outbreaks of respiratory viruses; hence, the improvements in TAT, and subsequent isolation, seen in the POCT cohort should lead to a reduction in nosocomial transmissions. These results also highlight the difference in TAT for samples tested over the weekend, with all laboratory tested samples with a TAT >48 h being collected on a Friday or Saturday. This emphasizes the importance of having testing available 24/7, allowing a consistent approach to testing and downstream management, regardless of the day or time of sample collection.

In addition to an improvement in patient isolation, there was also a trend towards commencing antivirals more swiftly, with 79% of patients in the POCT group treated on the day of sample collection, compared with 38% of patients in the laboratory tested group. Although this is encouraging, it may be confounded by the two different respiratory seasons considered in this study, skewing the interpretation. The 2017–2018 season was a more severe influenza season than 2016–2017 [5]; as such, there was a considerably higher proportion of influenza-positive patients in the POCT cohort. Guidelines for treating influenza recommend treating with NIs prior to receiving a laboratory confirmed diagnosis [6]; however, treatment of RSV in adults is less well defined [7]. The prompt prescription of antivirals in the POCT group may have been due to empirical prescribing in patients suspected to be infected with influenza, rather than a direct result of the diagnosis provided by POCT. These data also suggest a decrease in HAI after implementation of POCT, with HAI decreasing from >75% to 21% in this study; however, the numbers in this study are small and a direct comparison of the 2 years is difficult due to the RSV outbreak present in the 2016–2017 data. In addition, POCT was used in an outpatient setting in which laboratory testing is not appropriate due to the long TAT. The ability to test for influenza and RSV in this setting allows informed decisions to be made regarding admission and appropriate patient placement, again reducing the risk of nosocomial transmission.

The POCT utilized in this study only detects influenza and RSV, both of which can be associated with devastating nosocomial outbreaks. Other viruses, such as parainfluenza viruses and rhinoviruses, can cause significant mortality in haematology patients [1], and, although not considered a substantial cause of ward outbreaks, are still important diagnoses for the clinical management of individual patients. Therefore, careful consideration must be given to replacing extended respiratory testing in the laboratory with POCT which only detects a limited number of pathogens. Utilizing POCT for rapid diagnosis of nosocomial pathogens, in addition to further testing in symptomatic patients who are negative via POCT, may be considered; however, such testing algorithms are likely to have significant cost implications.

Previous studies have also demonstrated a correlation between POCT and improved infection control and antiviral stewardship [8]; however, limited data are available in haematology patients. Due to the small size of the dataset presented herein, statistical analysis was not deemed appropriate. Therefore, further investigation with a larger cohort, including patients testing negative for influenza and RSV, is warranted to provide stronger evidence for the role of POCT in this patient population. This study was performed prior to the severe acute respiratory syndrome coronavirus-2 (SARS-

CoV-2) pandemic, which has undoubtedly altered respiratory testing protocols in all hospital settings. However, the data presented herein may be extrapolated to SARS-CoV-2 POCT, which is now widely available. Such testing is likely to reduce TAT compared with standard laboratory testing, and allow faster isolation, or de-escalation of isolation, in a patient group in which SARS-CoV-2 infection can cause severe disease [9].

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Conflict of interest statement

None declared.

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None.

References

- [1] Popescu CM, Ursache AL, Feketea G, Bocsan C, Jimbu L, Mesaros O, et al. Are community acquired respiratory viral infections an underestimated burden in hematology patients? *Microorganisms* 2019;7:353–9.
- [2] Inkster T, Ferguson K, Edwardson A, Gunson R, Soutar R. Consecutive yearly outbreaks of respiratory syncytial virus in a haematology ward and efficacy of infection control measures. *J Hosp Infect* 2017;96:353–9.
- [3] Public Health England. Point of care tests for influenza and other respiratory viruses: winter 2019 to 2020. London: PHE; 2019.
- [4] Bennett S, MacLean A, Gunson R. Verification of Cepheid Xpert Xpress Flu/RSV assay for use with gargle samples, sputa and endotracheal secretions. *J Hosp Infect* 2019;101:114–5.
- [5] Public Health England. Surveillance of influenza and other respiratory viruses in the UK: winter 2017 to 2018. London: PHE; 2018.
- [6] Public Health England. PHE guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza. London: PHE; 2019.
- [7] Khawaja F, Chemaly RF. Respiratory syncytial virus in hematopoietic cell transplant recipients and patients with hematologic malignancies. *Haematologica* 2019;104:1322–31.
- [8] Petrozzino JJ, Smith C, Atkinson MJ. Rapid diagnostic testing for seasonal influenza: an evidence-based review and comparison with unaided clinical diagnosis. *J Emerg Med* 2010;39:476–90.e1.
- [9] Cook G, Ashcroft AJ, Pratt G, Popat R, Ramasamy K, Kaiser M, et al. Real-world assessment of the clinical impact of symptomatic infection with severe acute respiratory syndrome coronavirus (COVID-19 disease) in patients with multiple myeloma receiving systemic anti-cancer therapy. *Br J Haematol* 2020;190:e83–6.