Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Influenza A/B and respiratory syncytial virus digital immunoassay evaluation in a paediatric emergency department

Dear Editor,

The influenza A and B viruses (FluA and FluB), and respiratory syncytial virus (RSV) are common respiratory pathogens which result in patients attending acute hospital portals. The transmissibility of these pathogens means that rapid diagnosis to allow institution of infection control procedures, and initiation of antiviral therapies if available, is key. In this study, we report an evaluation of a point-of-care (POC) lateral flow device (LFD) used in a paediatric emergency department in the United Kingdom.

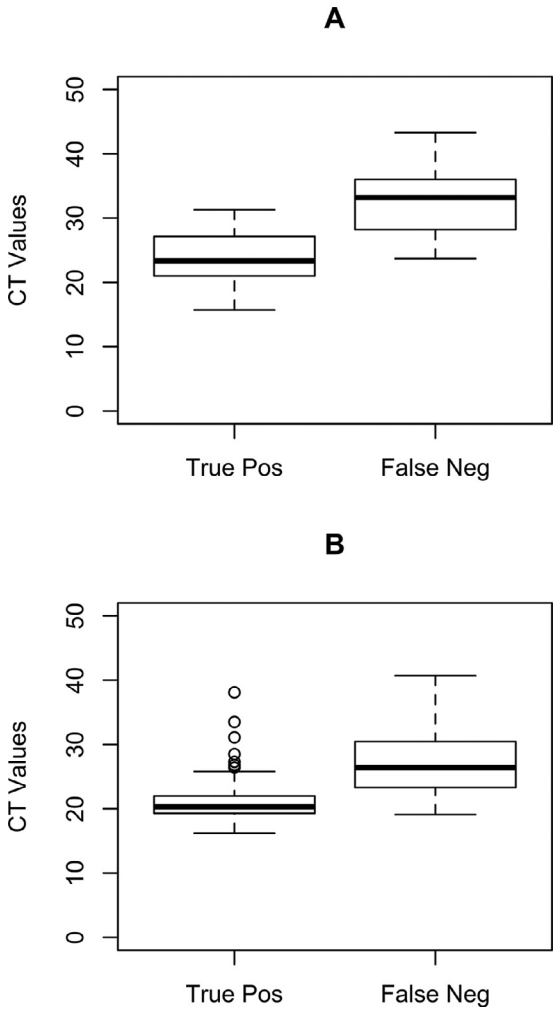

Fig. 1.. Comparison of C_t values for true positive and false negative lateral flow tests. A - Influenza A; B - RSV.

The National Health Service in England maintains a target of treating, admitting, or transferring >95% of emergency patients within 4 h of arrival[1]. During the 2019–2020 season, notable for the subsequent introduction and circulation of the SARS-CoV-2 virus to the population, influenza activity was relatively low compared to preceding years. Influenza had a medium impact on secondary care indicators[2], with hospital and intensive care/high dependency unit admissions similar to or lower than the preceding two seasons. POC testing for respiratory viruses has been explored as a means for rapid diagnosis and management, and has been shown to have a positive medico-economic impact on the management of patients in a paediatric emergency department setting [3]. Current tests, which have enhanced performance over previous devices, have been shown to be time efficient[4], and to have an acceptable level of sensitivity and specificity[4,5] for rapid diagnostic use.

During the 2019/2020 influenza and RSV seasons, Emergency department nursing staff were trained in the use of the BD Veritor™ Plus System analyser, and the corresponding Flu *A* + *B* and RSV lateral flow immunoassay kits. This system is a rapid chromatographic immunoassay using an analyser/reader that gives a direct qualitative result within 11 min.

Patients presenting with symptoms of viral respiratory tract infection had nasopharyngeal wash/aspirates taken and split into two aliquots. One was used for LFD testing, which was carried out within the emergency department. The second aliquot was sent for confirmatory testing using the laboratory based Hologic Panther Fusion® Flu A/B/RSV multiplex real-time PCR (RT-PCR) assay. LFD results were recorded in a logbook within the emergency department.

The BD Veritor™ system is quoted as having a positive percent agreement (PPA) and negative percent agreement (NPA) versus PCR respectively for FluA (83.6%, 97.5%), and FluB (81.3%, 98.2%)[6], and as having a sensitivity and specificity vs viral culture for RSV of 91.8% and 93.3% respectively[7]. Previous evaluations of the system when evaluated in a laboratory setting have taken place for RSV[5,8], and influenza *A* + *B*[4,9]. The Hologic Panther Fusion® System has a stated sensitivity and specificity respectively versus viral culture/DFA for Flu A (99.2%, 97.9%), Flu B (97.9%, 99.7%), and RSV (98.7%, 95.1%)[10].

A retrospective anonymised performance evaluation of BD Veritor LFD relative to RT-PCR was carried out. PPA and NPA of the LFD against the RT-PCR assay were assessed. A secondary analysis of Cycle Threshold (C_T) values was then performed to determine whether false negatives were due to low levels of virus present in the samples. Welch's *t*-test was calculated for this data, and boxplots produced using R-Studio Desktop (RStudio PBC).

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Table 1.
Assay evaluation results for FluA, FluB, and RSV.

FluA (*n* = 442)		
	TP	24
	FN	10
	TN	376
	FP	32
	PPA	71% (95% CI 53%–85%)
	NPA	92% (95% CI 89%–95%)
FluB (*n* = 441)		
	TP	0
	FN	5
	TN	432
	FP	4
	PPA	0% (95% CI 0%–60%)
	NPA	99% (95% CI 97%–100%)
RSV (*n* = 441)		
	TP	217
	FN	71
	TN	144
	FP	9
	PPA	75% (95% CI 70%–80%)
	NPA	94% (95% CI 89%–97%)

TP = True Positives; FN = False Negatives; TN = True Negatives; FP = False Positives; PPA = Positive Percent Agreement; NPA = Negative Percent Agreement.

As this evaluation used de-identified data taken from routinely collected tests already in use within the hospital trust, specific ethical approval was not required.

In total, between October 2019 and January 2020, 442 patients were tested using the Flu *A* + *B* LFD (Of which only 441 Flu B results were recorded), and 441 using the RSV LFD. Results are shown in Table 1.

Analysis of C_T -value data showed a significant difference between true positive and false negative lateral flow assay samples for both FluA and RSV (Fig. 1). For FluA, $t = -4.20$ (95% CI −13.49 – −4.33, $p = 0.001$). For the RSV samples, $t = -9.77$ (95% CI −8.33 – −5.51, $p < 0.001$). C_T values for FluB false negative values were relatively high (mean 34, range 29.4–40.7), which may be the reason these cases were not detected by the LFD.

Our data from a practical real-world setting showed that the RSV LFD had a lower PPA compared to RT-PCR than the sensitivity stated by the manufacturer. As the quoted performance is in comparison to viral culture, it is possible that the LFD appears less sensitive when compared to PCR due to the detection of non-viable viral genetic material. However, our influenza A data also shows a lower PPA compared to PCR than that stated in the product literature, suggesting that other effects are likely to be influencing the performance of these assays in a real-world setting.

In addition, analysis of C_T value data suggests that where the BD Veritor system does not identify positive cases, this is in samples giving a higher C_T value, and thus lower viral loads, which may pose a lower risk of cross-infection, or represent immunisation with the live attenuated influenza vaccine. These results are similar to those described previously[5,8,9].

Unfortunately, there were too few influenza B cases during this season to accurately evaluate the FluB assay, although the available data is presented in Table 1.

While the performance of these point-of-care devices may be lower in practice than previous studies have suggested, a positive percent agreement of over 70%, combined with a high negative percent agreement suggests they do add utility. The rapid results allow prompt triage and decision making for positive cases in a busy emergency setting. However, negative results still require follow up with confirmatory testing, such as RT-PCR.

Declarations of Competing Interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2021.08.014.

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