**Letter to the Editor**

**Title**

Reply to:Concerns regarding the validity of the conclusion in a recently published paper on Roche Liat implementation

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Lisby and Schneider comment on our findings that the Cobas Liat influenza A/B and respiratory syncytial virus (RSV) assay (Liat) had a sensitivity for Influenza A or B of 85.4% [1]. They point out that this value is lower than the sensitivity of 97.9%-100.0% found in previous verification studies. We agree with this point, and referenced this higher sensitivity estimate in our paper whilst offering an explanation for why our estimate differed [2].

It is important to distinguish between the analytical performance of a test when used under ideal conditions in a verification study as opposed to that following real-world implementation. Many studies have already demonstrated a very high analystical sensitivity of the Liat and we did not seek to repeat this work. In contrast, the purpose of our study, was to evaluate and report the performance of Liat in clinical practice after implementation into an Emergency Department (ED). The lower sensitivity we observed is likely a combination of errors in sample collection, and transcription errors as the instrument was initially not interface into the laboratory LIMS.The testing of samples and recording of results was a new experience for the regular nursing staff alongside their normal, and highly intense clinical activities, and outside a formal research setting.

An important corollary of our findings is that the analytical sensitivity of an instrument such as the Liat is not the only factor to consider when deploying such point of care tests. We have reported our experience in the first year of use [3]. Subsequently, we have improved training, audit and monitoring of the use of the Liat including Liat interfacing directly into our hospital computer systems and continue to improve the reliablility of the diagnostic process as a whole.

Lisby and Schneider also refer to the fact that negative Liat patients were retested more frequently than positive Liat patients creating a selection bias. The repeat testing of our negative results was to identify other pathogens in a wider screen while further identifying any missed influenza cases. We discussed some implications of this in our paper but are thankful to Lisby and Schneider for pointing out the effect that this would have upon the estimate of Liat sensitivity.

If we assume that there are no systematic differences between the positive Liat patients that were and were not included (and the same for negative Liat patients) then we can estimate the magnitude of this effect. We know that 308/1027 of Liat tests were positive for Influenza A or B. In the modified analysis 87 Liat positive patients were included: 76 true positive and 11 false negative. If we weight these values by 308/87 (3.54) then this predicts that 269/308 positive Liats would have been true positives. Applying the same method to the negative Liats we predict 703/719 Liats would have been true negatives. This provides the following estimates of performance:

Sensitivty 269/285 (94.4%, 95% CI 91.0-96.8). Specificty 703/742 (94.7, 95% CI 92.9-96.2). Positive predictive value 269/308 (87.3, 95% CI 83.5-90.4). Negative predictive value 703/719 (97.8, 95% CI 96.5-98.6).

From this analysis, including a higher proportion of Liat negative patients may have underestimated sensitivity, but also *overestimated* specificity. As such the effect on positive and negative predictive values would have been minimal i.e. the negative and positive predictive values here are necessarily identical to those in our initial analysis. In our paper we then adjusted these values in an attempt to compensate for the known prevalence in the tested population as determined by the Liat [2].

Lisby and Schneider comment on the fact that the 15 false negative Liats were all detected at high Cycle threshold values by rPCR and so may actually represent false positive rPCR results. As there was no evidence of assay and systems contamination during this study by examination of random internal controls and the CT valves for these rPCR positives were <39 it its likely they represented true low levels of target rather than false positive results. Our own interpretation of the significance of the high Ct values is discussed in our paper [2].

Overall our conclusion was that Liat performed well in a real ED department and the impact on infection prevention and control outcomes in our accompanying paper was impressive [3]. We continue to use Liat during the current 2018/19 influenza season and improve the performance of this point of care pathway as a whole in our ED departments.

**References:**

1. [Lisby JG](https://www.ncbi.nlm.nih.gov/pubmed/?term=Lisby%20JG%5BAuthor%5D&cauthor=true&cauthor_uid=30802525), [Schneider UV](https://www.ncbi.nlm.nih.gov/pubmed/?term=Schneider%20UV%5BAuthor%5D&cauthor=true&cauthor_uid=30802525). Concerns regarding the validity of the conclusion in a recently published paper on Roche Liat implementation. [*J Hosp Infect.*](https://www.ncbi.nlm.nih.gov/pubmed/?term=Concerns+regarding+the+validity+of+the+conclusion+in+a+recently+published+paper+on+Roche+Liat+implementation)2019 [in press] pii: S0195-6701(19)30094-5. doi: 10.1016/j.jhin.2019.02.011
2. Youngs J, Iqbal Y, Glass S, Riley P, Pope C, Planche T, et al. Implementation of the cobas Liat influenza point-of-care-test into an emergency department during a high-incidence season: a retrospective evaluation following real-world implementation. *J Hosp Infect* 2019;101(3):285-288
3. Youngs J, Marshall B, Farragher M, Whitney L, Glass S, Pope C, et al. Implementation of influenza point-of-care testing and patient cohorting during a high-incidence season: a retrospective analysis of impact on infection prevention and control and clinical outcomes. *J Hosp Infect* 2019;101(3):276-284