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References

[1] Bok K, Green KY. Norovirus gastroenteritis in immunocompromised patients. N Engl J Med 2016;367:2126–32.
[2] Schorn R, Hohne M, Meerbach A, Bossart W, Wuthrich RP, Schreier E, et al. Chronic norovirus infection after kidney transplantation: molecular evidence for immune-driven viral evolution. Clin Infect Dis 2010;51:307–14.
[3] Ludwig A, Adams O, Laws HJ, Schroten H, Tenenbaum T. Quantitative detection of norovirus excretion in pediatric patients with cancer and prolonged gastroenteritis and shedding of norovirus. J Med Virol 2008;80:1461–7.
[4] Roddie C, Paul JPV, Benjamin R, Gallimore CI, Xerry J, Gray JJ, et al. Allogeneic hematopoietic stem cell transplantation and norovirus gastroenteritis: a previously unrecognized cause of morbidity. Clin Infect Dis 2009;49:1061–8.
[5] Garvey MI, Bradley CW, Jumaa P. Environmental decontamination following occupancy of a burns patient with multiple carbapenemase-producing organisms. J Hosp Infect 2016;93:136–40.
[6] Cepheid Xpert norovirus manufacturers guidance. Cepheid; 2015. Available at: http://mail.csvlab.com.br/Norovorus-Bula-Cepheid.pdf [last accessed February 2019].
[7] Mitchell BG, Dancer SJ, Anderson M, Dehn E. Risk of organism acquisition from prior room occupants: a systematic review and meta-analysis. J Hosp Infect 2015;91:211–7.

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

Sir,

We have read the publication by Youngs *et al.* with great interest [1]. As molecular-based point-of-care infectious disease diagnostics are currently being implemented widely, data regarding the usability of these tests at the point-of-care setting are highly warranted. We are however, concerned about the validity of the main conclusion of the study, claiming a low sensitivity (85.4%) of the Roche Liat Influenza A/B and RSV assay for influenza A/B compared to Fast Track Diagnostics respiratory pathogens 21 multiplex assay.

First, this finding is in conflict with previously published studies, which report an excellent sensitivity by Liat Influenza A/B testing (97.9%–100.0%) [2–6], and the authors do not offer any explanation for this finding besides an 'increased risk of errors such as testing the wrong sample because of transcription errors or poor use of the equipment by non-laboratory staff'. Although this concern should be addressed as part of quality control of any routine point-of-care implementation, the authors did not address this issue, e.g. by re-testing all Liat point-of-care tested samples by Liat in a laboratory setting.

Second, the study protocol called for a differentiated re-testing of Liat-positive and Liat-negative samples; only 29.9% of Liat-positive samples were re-tested by either Fast Track respiratory pathogens 21 multiplex or Cepheid Xpert Xpress Flu/RSV assays, whereas 83.9% of Liat-negative samples were re-tested by Fast Track respiratory pathogens 21 multiplex assay. This lack of an established gold standard compromises calculations of sensitivity and specificity and complicates comparison with other reported studies. It also creates a selection bias that increases the chance of discordant results for Liat-negative samples because a much higher proportion of negatives are re-tested and therefore included in the analysis.

Third, and most importantly, no discrepancy testing was performed. Since all 15 false-negative Liat results were detected with high Ct values in the Fast Track respiratory pathogens 21 multiplex assay, the results could also be regarded as false positive by Fast Track respiratory pathogens 21 multiplex assay. As variations between different NAT tests at the lower end of the detection ranges are well known, calculating sensitivities and specificities in the absence of a discrepancy test makes little or no sense. Especially considering the findings of all other published studies of the Liat Influenza A/B and RSV assay, which found excellent sensitivity, robust discrepancy testing is critical and the assumption in the publication by Youngs *et al.* that the routine laboratory reference is correct is problematic [1].

Thus, we feel that the main conclusion in the publication by Youngs *et al.*, claiming a low sensitivity for influenza by the Liat Influenza A/B and RSV assay compared to Fast Track Diagnostics Respiratory Pathogens 21 multiplex assay, is unsubstantiated [1].

Conflict of interest statement
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References

[1] 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;101:285—8. http://dx.doi.org/10.1016/j.jhin.2018.12.008.
[2] Gibson J, Schechter-Perkins EM, Mitchell P, Mace S, Tian Y, Williams K, et al. Multi-center evaluation of the cobas(R) Liat(R) Influenza A/B & RSV assay for rapid point of care diagnosis. J Clin Virol 2017;95:5—9.
[3] Schmidt RLJ, Simon A, Popow-Kraupp T, Laggner A, Haslacher H, Fritzer-Szekeres M, et al. A novel PCR-based point-of-care method facilitates rapid, efficient, and sensitive diagnosis of influenza virus infection. Clin Microbiol Infect 2018. http://dx.doi.org/10.1016/j.cmi.2018.12.017.
[4] Banerjee D, Kanwar N, Hassan F, Essmyer C, Selvarangan R. Comparison of six sample-to-answer Influenza A/B and Respiratory Syncytial Virus Nucleic Acid Amplification Assays using respiratory specimens from children. J Clin Microbiol 2018;56(11).
[5] Ling L, Kaplan SE, Lopez JC, Stiles J, Lu X, Tang YW. Parallel validation of three molecular devices for simultaneous detection and identification of influenza A and B and respiratory syncytial viruses. J Clin Microbiol 2018;56(3).
[6] Pedersen CJ, Rogan DT, Yang S, Quinn JV. Using a novel rapid viral test to improve triage of emergency department patients with acute respiratory illness during flu season. J Clin Virol 2018;108:72—6.

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

Sir,

Lisby and Schneider comment on our finding that the Cobas Liat influenza A/B and respiratory syncytial virus assay (Liat; Roche, Basel, Switzerland) had 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 analytical sensitivity of 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 due to combination of errors in sample collection, and transcription errors as the instrument was not initially interfaced into the laboratory information management system (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 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 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 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 grateful 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), we can estimate the magnitude of this effect. We know that 308/1027 Liat tests were positive for influenza A or B. In the modified analysis, 87 Liat-positive patients were included: 76 true