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## Letter to the Editor

## Re: 'Syndromic panels or "panel syndrome"? A perspective through the lens of respiratory-tract infections' by Zanella et al

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## To the Editor

We read with interest the article by Zanella et al. [1]. The authors suggest that the increasing use of rapid, automated, syndromic molecular panels for respiratory viruses (RVs) should be abandoned in favour of more limited PCR testing for RVs (e.g. testing for influenza alone or influenza and RSV combined) due to the high cost and uncertain clinical impact of detecting non-influenza viruses.

In their article they repeatedly call for an evidence-based approach for RV diagnostic testing and cite a lack of evidence for the clinical impact and cost-effectiveness of syndromic RV panels as the justification for this position [1]. They do not, however, attempt a systematic review of the literature but instead present data from selected papers and so have neglected to review and discuss important elements of the current evidence base.

We feel that the issue central to this debate is that for acutely unwell patients in hospital, neither testing by syndromic panel nor limited RV testing are useful if the results are not delivered to clinical and infection control teams in a meaningful time frame. Several studies—including randomized controlled trials (RCTs)—have shown that laboratory PCR results for RVs do not lead to

changes in clinical management when results are only available 24 h later (a standard turnaround time for RV testing in most hospital laboratories) compared to not testing at all [2,3]. In this sense no current laboratory-based PCR testing for RVs, either by syndromic panel or by limited testing, can in fact be called evidence-based or cost-effective. In comparison, there is a growing body of evidence from observational studies and RCTs for the clinical impact and cost-effectiveness of molecular point-of-care testing (mPOCT) for RVs, by both syndromic panels and by limited RV testing. These studies demonstrate consistent benefits compared to laboratory testing [4–6] in hospitalized patients. The ResPOC RCT, by Brendish et al., demonstrates that syndromic testing for RVs at the point of care with results available in 1–2 h, compared to 'syndromic' laboratory PCR with result available at around 24 h, was associated with several improvements in clinical management, including more patients treated with only a brief course of antibiotics, a reduction in length of hospital stay, directed influenza antivirals, and better use of isolation facilities [6]. These benefits were dependent on a very short turnaround time (TAT) for results and were best when the TAT was <1.6 h, which is not achievable in most centralized laboratories [7]. Health economic analysis from the ResPOC trials also suggests that syndromic mPOCT is in fact cost-saving compared to centralized laboratory testing, or at worst is cost-neutral [8].

The only way to definitively assess any added value of a syndromic RV mPOCT compared to limited RV mPOCT would be to evaluate their impact in a head-to-head RCT, which to date has not been done. The ResPOC trial does however give us some important insights into the potential advantages of syndromic testing above limited RV testing at the point of care. In the study, patients who had positive results for RVs by mPOCT had their antibiotics stopped earlier than those who were negative. In these patients rhino/enterovirus was the most frequently detected virus type and not influenza (many patients had an exacerbation of airways disease). In addition, over a third of the patients who had their antibiotics stopped early had either hMPV, parainfluenza, coronavirus or adenovirus detected, and so testing for only influenza, or influenza and RSV, would not have resulted in most of the early antibiotic discontinuations seen in this trial [9]. The reduction in length of

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stay seen in the ResPOC trial was similarly due to early discharge in a proportion of patients, and these also occurred predominantly in patients testing positive for viruses. As with the antibiotic changes, these were associated with a wide range of RVs and not just influenza, and so would not have occurred with limited RV testing.

Finally, there are also clear additional advantages to those already discussed by testing for the broad range of pathogens detected by syndromic RV panels compared to limited RV testing, including enabling enhanced infection control measures for non-influenza viruses, which may also be associated with nosocomial transmission and a high risk of mortality in typically elderly, comorbid, and frail patients present in medical wards [10].

In conclusion, we feel that ultimately the purpose of diagnostic testing is to elucidate the cause of a patient's infection as rapidly and comprehensively as possible so as to inform their management and to protect others. Syndromic testing performed at the point of care enables this to happen accurately and in real time and has been associated with improvement in clinical management in RCTs.

#### Author contributions

NJB conceived this letter and outlined the first draft. TWC led the writing of the manuscript. SP contributed to the manuscript. All authors contributed to, and agreed, the final version of the manuscript. No writing or editorial assistance was used in this article.

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#### References

- [1] Zanella MC, Meylan P, Kaiser L. Syndromic panels or "panel syndrome"? A perspective through the lens of respiratory-tract infections. *Clin Microbiol Infect* 2020;S1198–743X:30675–85.
- [2] Saarela E, Tapiainen T, Kauppila J, Pokka T, Uhari M, Kauma H, et al. Impact of multiplex respiratory virus testing on antimicrobial consumption in adults in acute care: a randomized clinical trial. *Clin Microbiol Infect* 2019;S1198–743X:30498–507.
- [3] Chu HY, Englund JA, Huang D, Scott E, Chan JD, Jain R, et al. Impact of rapid influenza PCR testing on hospitalization and antiviral use: a retrospective cohort study. *J Med Virol* 2015;87:2021–6.
- [4] Trabattoni E, Le V, Pilmis B, Ponfilly PG de, Caisso C, Couzigou C, et al. Implementation of Aleré i Influenza A & B point of care test for the diagnosis of influenza in an emergency department. *Am J Emerg Med* 2018;36:916–21.
- [5] 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;101:276–84.
- [6] Brendish NJ, Malachira AK, Armstrong L, Houghton R, Aitken S, Nyimbili E, et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. *Lancet Respir Med* 2017;5:401–11.
- [7] Brendish NJ, Rose M, Lord J, Clark TW. The impact on health care resource utilisation and cost of routine molecular point-of-care testing for respiratory viruses in adults hospitalised with acute respiratory illness: further analysis form a pragmatic randomised, controlled trial (RESPOC). 2019. Poster presented at ECCMID.
- [8] Brendish NJ, Malachira AK, Beard KR, Ewings S, Clark TW. Impact of turnaround time on outcome with point-of-care testing for respiratory viruses: a post hoc analysis from a randomised controlled trial. *Eur Respir J* 2018;9:52.
- [9] Brendish NJ, Mills S, Ewings S, Clark TW. Impact of point-of-care testing for respiratory viruses on antibiotic use in adults with exacerbation of airways disease. *J Infect* 2019;79:357–62.
- [10] Boivin G, De Serres G, Hamelin ME, Côté S, Argouin M, Maranda-Aubut R, et al. An outbreak of severe respiratory tract infection due to human metapneumovirus in a long-term care facility. *Clin Infect Dis* 2007;44:1152–8.