



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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to the Editor

Syndromic panels or the panels' syndrome? A perspective through the lens of respiratory tract infections: author's response

M.-C. Zanella^{1,2,3,*}, P. Meylan⁴, L. Kaiser^{1,2}

¹ Laboratory of Virology, Division of Laboratory Medicine and Division of Infectious Diseases, Geneva University Hospitals, Geneva, Switzerland

² University of Geneva Medical School, Geneva, Switzerland

³ Laboratory of Bacteriology, Division of Laboratory Medicine and Division of Infectious Diseases, Geneva University Hospitals, Geneva, Switzerland

⁴ University of Lausanne Faculty of Biology and Medicine, Lausanne, Switzerland

ARTICLE INFO

Article history:

Received 5 March 2020

Received in revised form

21 March 2020

Accepted 23 March 2020

Available online 28 March 2020

Editor: L. Leibovici

To the Editor

We thank Brendish et al. [1] for their interest in our commentary [2], and they rightly point out that it was not a systematic review. Our main intention was to provide food for thought and discussion regarding the use of panel assays in the light of some relevant publications. In particular, we aimed to discuss the limitations of their analytical aspects and clinical validation. We respectfully disagree with the statement that “*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*”. As microbiologists and clinicians, we rather suggest that we have the responsibility to promote diagnostic stewardship in order to integrate these new technologies into clinical management, while considering their strengths and limitations. We also highlight the value of a multiple-step approach to testing that does not necessarily preclude their use.

We agree with the implementation of rapid diagnostic assays for RVs given that several studies have shown a clinical impact with a more appropriate use of oseltamivir, reduced length of stay and fewer chest x-rays, as summarized in the meta-analysis of Vos et al.

[3], which included the ResPOC study [4]. However, it should be highlighted that there is not enough evidence so far for a reduction in antibiotic prescription and duration or hospital admission due to rapid molecular tests compared to conventional molecular ones [3]. The ResPOC study concluded that a point-of-care (POC) assay was associated with a more appropriate use of antiviral treatment, brief courses of antibiotics and shorter length of stay, but no difference was observed regarding the mean duration of antibiotic use [4]. In addition, only 45% of patients in the control group were tested, and the conclusions may have some limitations.

We agree that one of the important aspects of testing is that the results be obtained in a meaningful timeframe for clinicians. In particular, short turnaround times have an impact on clinical management when testing for influenza virus and respiratory syncytial virus (RSV). Among paediatric patients, the use of rapid tests demonstrated a decrease in emergency department length of stay, a reduction in further diagnostic tests, and an increase in the appropriate use of antibiotics and antivirals [5]. Similarly, a more appropriate use of oseltamivir, shorter time to isolation, and a reduction in length of stay were also shown among adults [6]. Nevertheless, considering the methodological limitations, we believe that the conclusions driven by the *post hoc* analysis of the ResPOC study regarding the impact of turnaround time on antibiotic use and length of stay should be interpreted with caution [7]. The impact of short turnaround times on patient clinical management has been well summarized in the commentary of Kuypers [8]. We have already implemented a POC test for influenza virus and RSV at our institution. However, we continue to perform conventional molecular testing for rhinovirus (RV) with in-house panels that encompass diverse viral targets according to clinical presentation and epidemiology. Regarding influenza virus infection specifically, we remind clinicians that antiviral treatment should be started as soon as possible for patients with a suspected or documented influenza infection and treatment and isolation measures should not be deferred while waiting for any assay result [9].

Clinicians should also be aware that clinical validation studies have assessed the performance of some respiratory panels with

* Corresponding author. Marie-Céline Zanella, Laboratory of Virology, Division of Laboratory Medicine and Division of Infectious Diseases, Geneva University Hospitals, 4 Rue Gabrielle Perret-Gentil, 1211, Geneva 14, Switzerland.

E-mail address: marie-celine.zanella@hcuge.ch (M.-C. Zanella).

suboptimal approaches and reported cumulative performance results or positive and negative percentage agreement as surrogates of sensitivity and specificity [10]. Notably, certain panels encompass bacterial targets that have been validated with fewer than ten positive samples, and performance has sometimes been reported to be lower than that for viral targets [10]. Thus, clinicians should be particularly attentive when interpreting cumulative performance results or percentage agreement values, which may represent an important and underappreciated limitation.

Overall, we consider that respiratory panels can be integrated into clinical management, but we encourage the use of smaller, more targeted panels for pathogens that actually impact on clinical management as part of a multiple-step approach for testing. Indeed, systematic first-line testing for a broad range of pathogens that are neither clinically nor epidemiologically suspected, and with no demonstrated impact on clinical endpoints and cost-effectiveness, is contrary to appropriate diagnostic stewardship and evidence-based decisions for diagnostic and therapeutic strategies. Importantly, new technologies should serve the clinician's needs and not be driven by marketing strategies. Furthermore, in the era of the SARS-CoV-2 epidemic, targeted testing is needed more than ever.

Finally, we agree with Kuypers [8] that the decision to implement a rapid molecular assay for respiratory pathogens requires consideration of clinical and economic factors unique to each healthcare facility. Well-designed multicentre studies are needed using methods and standards that allow others to use the results in evidence-based laboratory practice guidelines, as well as to increase evidence regarding their impact in clinical management and cost-effectiveness.

Author contributions

MCZ and LK contributed to the conceptualization of the letter. MCZ contributed to the writing of the original draft, reviewing and editing of the letter. LK contributed to the supervision, reviewing and editing of the letter. PM contributed to the reviewing and editing.

Transparency declaration

The authors have no conflicts of interest to declare. No funding was received for this letter.

References

- [1] Brendish NJ, Poole S, Clark TW. Re: syndromic panels or 'panel syndrome'? A perspective through the lens of respiratory-tract infections' by Zanella et al. *Clin Microbiol Infect* 2020;S1198–743X:30087–92. <https://doi.org/10.1016/j.cmi.2020.02.008>.
- [2] Zanella MC, Meylan P, Kaiser L. Syndromic panels or 'panel syndrome'? A perspective through the lens of respiratory tract infections. *Clin Microbiol Infect* 2020;26:665–8. <https://doi.org/10.1016/j.cmi.2019.12.018>.
- [3] Vos LM, Bruning AHL, Reitsma JB, Schuurman R, Riezebos-Brilman A, Hoepelman AIM, et al. Rapid molecular tests for influenza, respiratory syncytial virus, and other respiratory viruses: a systematic review of diagnostic accuracy and clinical impact studies. *Clin Infect Dis* 2019;69:1243–53. <https://doi.org/10.1093/cid/ciz056>.
- [4] 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.
- [5] Rogan DT, Kochar MS, Yang S, Quinn JV. Impact of rapid molecular respiratory virus testing on real-time decision making in a pediatric emergency department. *J Mol Diagn* 2017;19:460–7.
- [6] Garvey MI, Wilkinson M, Bradley CW, Biggs M, Reddy-Kolanu V, Osman H, et al. Impact of a PCR point of care test for influenza A/B on an acute medical unit in a large UK teaching hospital: results of an observational, pre and post intervention study. *Antimicrob Resist Infect Control* 2019;8:120.
- [7] 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.
- [8] Kuypers J. Impact of rapid molecular detection of respiratory viruses on clinical outcomes and patient management. *J Clin Microbiol* 2019;57:e01890–918.
- [9] Uyeki TM, Bernstein HH, Bradley JS, Englund JA, File TM, Fry AM, et al. Clinical practice guidelines by the infectious diseases society of America: 2018 update on diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. *Clin Infect Dis* 2019;68:895–902.
- [10] Bouzid D, Zanella MC, Kerneis S, Visseaux B, May L, Schrenzel J, et al. Rapid diagnostic tests for infectious diseases in the emergency department. *Clin Microbiol Infect* 2020. <https://doi.org/10.1016/j.cmi.2020.02.024>. [Epub ahead of print].