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.

Diagnostic performance of antigen testing for severe acute respiratory syndrome coronavirus 2

To the Editor:

We read the brief report by Villaverde et al[1] in which the authors posit a low diagnostic performance of antigen testing for severe acute respiratory syndrome coronavirus 2 in children. We agree that reverse transcriptase polymerase chain reaction (RT-PCR) testing is the diagnostic gold standard and that it would be desirable to perform timely RT-PCR testing in every suspect case, which unfortunately is not realistic. After a detailed consideration of their article, we want to offer the following remarks.

When validating a diagnostic tool a proper definition of the gold standard is required.[2] The authors claimed that testing targeted E and RdRp genes,[1] but no description of the RT-PCR kit or kits that were used were presented, nor were the definitions of "positive RT-PCR test" specified in terms of the required number of replicated genes and the cycle threshold cut-off values. Because in a pandemic setting even a low viral load in a symptomatic patient should prompt a coronavirus disease 2019 (COVID-19) diagnosis,[3] the quantitative aspect of this issue seems to be minor in contrast to the reproducibility issues.

In addition, the study is stated to be retrospective,[1] so it is unclear why (and how many) patients were asked consent for paired sampling, and when the sample size was estimated. If patients truly were enrolled retrospectively, selection criteria and whether paired sampling was standard of care in the participating centers should be clarified. Simply put, a diagnostic test validation study should not have a retrospective design.[2]

Lastly, we want to remark that 98 out of every 100 negative-testing patients in the study were not infected by severe acute respiratory syndrome coronavirus 2,[1] which should be reassuring for clinicians in their everyday emergency department practice.

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https://doi.org/10.1016/j.jpeds.2021.02.052

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Reply

To the Editor:

We welcome the opportunity to explain our findings further. First, we want to clarify that we included 6 expert microbiologists from the centers involved in the study. All co-authors played a fundamental role in the design and methodology of the study, as well as in the interpretation of the results. We want to especially highlight the input of microbiologists concerning these critical issues in our research.

Reverse transcriptase polymerase chain reaction (RT-PCR) positivity criteria are determined by the identification of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) E and RdRp genes.[1] However, there is currently no clear consensus on which cycle threshold marks the positivity of the RT-PCR test.[2] The pandemic situation entails a shortage of microbiological diagnostic resources, which has not allowed Spanish microbiology laboratories to use a single RT-PCR technique. Furthermore, RNA extraction equipment also varies between laboratories. For all of these reasons, it would not be accurate to set a singular criterion for the required number of replicated genes and the cut-off values of cycle threshold. Regarding the reproducibility between laboratories, although the use of different techniques is a potential source of variability, all RT-PCR techniques used in the laboratories involved in this study are validated and accredited by the European Union.[3] All subjects included were symptomatic (inclusion criteria) and have been reported qualitatively, therefore, in our opinion, the results are comparable.

At the time of the design of our study, we calculated the sample size choosing a prevalence of SARS-CoV-2 infection of 5% and an expected sensitivity of the antigen test of 90%. We collected data from the paired samples taken at participating hospitals after verbal consent and followed the Panbio Coronavirus Disease 2019 Ag Rapid Test Device (Abbott Rapid Diagnostic Jena GmbH) manufacturer's instructions and the implementation protocols of the sites.[4,5] As we describe in our report, patients with inclusion criteria were children age 0-16 years with symptoms compatible with SARS-CoV-2 infection within 5 days of attendance at an emergency department of 1 of 7 centers involved.

We agree that the validation of a diagnostic technique should be carried out with prospectively collected data. As mentioned in our discussion, this pilot study has allowed the working group (EPICO-AEP) to initiate a prospective validation study on the diagnostic accuracy of the Panbio

SARS-CoV-2 antigen rapid test. We think that although the study has several limitations, already described, the information gained should be considered by clinicians and policymakers.

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https://doi.org/10.1016/j.jpeds.2021.02.051

Supported by a specific Research Grant of the Spanish Society of Pediatrics (Asociación Española de Pediatría). This study was funded by project PI20/00095, from the Instituto de Salud Carlos III (Ministry of Economy, Industry and Competitiveness) and cofounded by the European Regional Development Funds. S.V. is funded by the Spanish Ministry of Science and Innovation—Instituto de Salud Carlos III and Fondos FEDER since January 1, 2021 (Contrato Río Hortega CM20/00173). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The authors declare no conflicts of interest.

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Corrected QT in diabetic ketoacidosis

To the Editor:

I read with interest the retrospective observational study by Perez et al in which the authors had demonstrated a significant association between corrected QT (QTc) intervals and the severity of diabetic ketoacidosis (DKA).[1] Although their point on appropriate cardiac monitoring in moderate or severe DKA is well taken, several observations are noteworthy.

In their study, a greater heart rate was noted with increasing DKA severity, which is not unexpected, given the well-established correlation between degree of hypovolemia and severity of DKA. Importantly, the QTc interval calculated using the Bazett formula invariably relates to the heart rate. Although clinically useful at normal heart rates, this formula is known to overestimate the duration of cardiac repolarisation at extremely high heart rates.[2,3] This has to be taken into consideration while interpreting the QTc intervals in this study, where the heart rates of patients were all in the tachycardic range, especially because the largest magnitude of difference between the QTc intervals of the 3 groups is only 15 milliseconds.

There appeared to be baseline differences in the serum potassium and magnesium levels between the 3 groups of DKA severity. The authors did acknowledge the effects that serum electrolytes (potassium, calcium, and magnesium) may have on QTc intervals and considered these in the