Reply to Topeli et al. and to Akinosoglou et al.

From the Authors:

We would like to thank Topeli and colleagues and Akinosoglou and colleagues for their interest in our manuscript (1).

We carefully read the discussion by Topeli and colleagues on our data and their own results regarding quick sepsis-related organ dysfunction (qSOFA) and other scores for sepsis’ mortality prediction in Turkey. We congratulate the authors for their initiative, as we believe it is very important to have data from low- and middle-income countries (LMICs). These countries represent more than 80% of world population, and the data from these settings on sepsis epidemiology and mortality are scarce (2).

There are important similarities between the authors’ results and ours. They found that qSOFA score has the worst sensitivity to predict mortality in septic patients, which adds to previous LMICs’ studies showing that qSOFA has low sensitivity to predict sepsis mortality in this population (3, 4). However, there are also major differences comparing both results. Their study is a single-center retrospective cohort with a limited number of patients, as can be suggested by the large confidence intervals of the data. Additionally, they collected qSOFA variables from patients at 48 hours before ICU admission, whereas we collected qSOFA data considering only the worst values prior to the suspicion of infection or sepsis, which may have contributed to more accurate findings in our study. The time window is crucial in assessing the sensitivity of a screening tool, as it is expected that if the interval of data collection is increased, more patients that deteriorate and eventually die will have a qSOFA ≥2. It would also be important to evaluate in Topeli’s data whether the use of a single qSOFA variable would increase the sensitivity of the score, as we demonstrated in our study. This modified score could be suggested as an alternative to improve its accuracy in determining mortality in LMICs.

Akinosoglou and colleagues assessed the role of qSOFA according to site of infection in a cohort of 614 septic patients from their institution. They identified that qSOFA accuracy to predict survival is dependent on the focus of infection. Because mortality rates are variable with the site of sepsis, and qSOFA variables may also be affected by the disease itself, their data are very reasonable. It would be interesting to assess data from other series to confirm if qSOFA can have adequate performance in all sepsis sites, or if we should modify the score according to the probable site of infection.

Author disclosures are available with the text of this letter at www.atsjournals.org.

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2. Machado FR, Azevedo LCR. Sepsis: a threat that needs a global solution. Crit Care Med 2018;46:454–459.
3. Chen YX, Wang JY, Guo SB. Use of CRB-65 and quick sepsis-related organ failure assessment to predict site of care and mortality in pneumonia patients in the emergency department: a retrospective study. Crit Care 2016;20:167.
4. Boltia-Blanco N, Mbarak Z, Samaka J, Mlaganie T, Mamin A, Genton B, et al. Prognostic value of quickSOFA as a predictor of 28-day mortality among febrile adult patients presenting to emergency departments in Dar es Salaam, Tanzania. PLoS One 2018;13:e0197982.

Erratum: Pitolisant for Daytime Sleepiness in Patients with Obstructive Sleep Apnea Who Refuse Continuous Positive Airway Pressure Treatment. A Randomized Trial

There are errors in the article by Dauvilliers and colleagues (1), published in the May 1, 2020, issue of the Journal. In the list of HAROSA II Study Group collaborators that appears before the references, one of its members, Dr. Yüksel Peker, is incorrectly listed as Yeksel Peker. In addition, Dr. Peker’s current affiliation

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should have been included: Koç University School of Medicine, Istanbul, Turkey.

Finally, one of the authors of the article, Dr. Jan Hedner, is also mentioned in the collaborator section; this is incorrect; he should not have been included in that list.

Reference
1. Dauvilliers Y, Verbraecken J, Partinen M, Hedner J, Saarela R, Georgiev O, Tiholov R, Lecomte I, Tamisier R, Le Roy P, Scart-Gres C, Lecomte JM, Schwartz JC, Pepin J-L. HAROSA II Study Group collaborators. Pitolisant for daytime sleepiness in patients with obstructive sleep apnea who refuse continuous positive airway pressure treatment. A randomized trial. *Am J Respir Crit Care Med* 2020;201:1135–1145.

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Erratum: Validation of a Host Response Assay, SeptiCyte LAB, for Discriminating Sepsis from Systemic Inflammatory Response Syndrome in the ICU

The authors of the article by Miller and colleagues, published in the October 1, 2018, issue of the *Journal*, have alerted us to errors in Table 3. Because of a probable flaw in the original R script used to perform the calculations, incorrect values were inadvertently cited in the last row (“Forced”) of Table 3. The correct values for the last three cells in that row are 0.34, 0.84, and 0.53 (instead of 0.65, 0.91, and 0.69). There are additional small corrections (~0.01) to the values of the last three cells in the first row and in the antepenultimate cell in the middle row of the table; these corrections, in the second position to the right of the decimal point, are related to the way in which rounding was handled by the R script used for the original calculations. For the convenience of our readers, the corrected version of the table is included below, with the changes indicated in bold.

Finally, a value from Table 3 is mentioned at the bottom of the middle column on page 908; this should be corrected to read “negative predictive values were 0.84 or greater (Table 3),” not 0.89.

The authors do not believe that these changes affect the conclusions of the article; they would like to apologize for any confusion.

Reference
1. Miller RR III, Lopansri BK, Burke JP, Levy M, Opal S, Rothman RE, D'Alessio FR, Sidhaye VK, Aggarwal NR, Balk R, Greenberg JA, Yoder M, Patel G, Gilbert E, Afsar M, Parada JP, Martin GS, Esper AM, Kempfer JA, Narasimhan M, Tsegaye A, Hahn S, Mayo P, van der Poll T, Schultz MU, Scicluna BP, Klein Klouwenberg P, Rapisarda A, Seldon TA, McHugh LC, Yager TD, Cermelli S, Sampson D, Rothwell V, Newman R, Bhide S, Fox BA, Kirk JT, Nakaoka K, Davis RF, Brandon RA, Brandon RB. Validation of a host response assay, SeptiCyte LAB, for discriminating sepsis from systemic inflammatory response syndrome in the ICU. *Am J Respir Crit Care Med* 2018;198:903–913.

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**Table 3. Summary of Results from Binary Analysis of Complete Clinical Dataset**

| RPD | Description | Sepsis Prevalence | AUC | Sensitivity | Specificity | NPV | PPV |
|-----|-------------|------------------|-----|-------------|-------------|-----|-----|
| Unanimous, based on discharge evaluation (n = 290 of 447 [64.9%]) | All three panelists and site PI agree on SIRS (171 of 290 [59.0%]) or sepsis (119 of 290 [41.0%]) | 41.0% | 0.89 | 0.97 | 0.33 | 0.93 | 0.50 |
| Consensus (n = 410 of 447 [91.7%]) | Majority vote leads to exclusion of 37 indeterminates and classification of 230 of 410 (56.1%) as SIRS and 180 of 410 (43.9%) as sepsis | 43.9% | 0.85 | 0.94 | 0.34 | 0.89 | 0.53 |
| Forced (n = 447 of 447 [100.0%]) | All subjects classified as SIRS (245 of 447 [54.8%]) or sepsis (202 of 447 [45.2%]) | 45.2% | 0.82 | 0.92 | 0.34 | 0.84 | 0.53 |

**Definition of abbreviations:** AUC = area under the curve; NPV = negative predictive value; PI = principal investigator; PPV = positive predictive value; RPD = retrospective physician diagnosis; SIRS = systemic inflammatory response syndrome.

A SeptiCyte LAB cutoff value of 3.1 was used in the analysis. This value had been obtained previously from receiver operating curve analysis of an independent discovery dataset (4).

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