Reviewer’s report

Title: A latent class approach for sepsis diagnosis supports use of procalcitonin in the emergency room

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Reviewer: Gordon P. Otto

Reviewer’s report:

Dear Members of the Editorial Office, Dear Authors,

Thanks for inviting me to review the article “A LATENT CLASS APPROACH FOR SEPSIS DIAGNOSIS SUPPORTS USE OF PROCALCITONIN IN THE EMERGENCY ROOM” from Fabián A. Jaimes and colleges.

In this manuscript the authors (i) used a novel approach for re-diagnosis of sepsis by latent class analysis (LCA) and (ii) identified new cut-off points of biomarkers with the special focus on PCT in an ER setting.

The topic of early and sufficient diagnosis of sepsis is of high interest for physicians and researchers. Especially, the weak and unspecific Gold Standard of sepsis diagnosis by clinical criteria leads to the search of new and re-validation of old-known biomarkers. Nevertheless, the paper has a few drawbacks.

Major issues:

1) My strongest personal issue is the mixture of both story lines. Firstly, the authors used LCA to overcome the lack of a gold standard and to identify patients with a “higher degree of sepsis or a more severe progression of disease”. This test based among others of PCT, CRP and DD levels. Afterwards, they defined in this “more severe ill” patient group new cut of values for PCT. As far as I understood the method, LCA included higher levels of PCT, CRP and DD to define the group of “more severe ill patients”. Therefore, after this “pre-testing” higher sensitivities and specificity are likely. Further, it is not clear how these new cut-offs are helpful for physicians since they have to use the new cut-offs in the overall not pre-tested patients cohort. Therefore, I would recommend to focusing on LCA as new diagnostic test for sepsis and to avoid a overstressing of the ROC-PCT results. Higher PCT results are useful in terms of confirmation of your LCA.

2) Without any personal association to the paper of Wacker C et al. in Lancet Infect Dis. I recommend to include and discuss the results of this meta analyses even though this paper did not focus on the ER setting.

3) I would recommend to characterize patients after re-classification by LCA in a overview using a Venn-diagram to compare the results to the clinical definition of sepsis.
Minor issues:

1) I would recommend not to state LCA as one of the two gold standards for sepsis diagnosis as done in the abstract.

2) Table 1. Please include p values. How do you explain the high rates of suspected infections in patients classified as non infected? The 28-day mortality rate should be presented more clearly (add %).

3) Table 2. can be excluded.

4) Table 4. Please include headlines in this table to clarify the meaning of cluster 1 and cluster 2. Please also include p values. I would recommend to include the levels of PCT, CRP and DD in this table.

Sincerely and with the best regards

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests