

Dear Madam/Sir Editor,

Please see our response to your comments. We appreciate your due diligence in review and look forward for speedy turnaround time. Thanks.

(Reviewer 1):

Q1: This is a potentially interesting article addressing the phenotypes of sepsis. However, there are major concerns with the reporting. 1. The study appeared confusing on the machine learning method. they did not describe how machine learning method was done. specifically, they need to describe which machine learning method did they use, neural network, unsupervised learning or others.

A1: Thank you. Supervised machine learning was used for creating sepsis computable phenotype. We have updated the manuscript throughout to reflect such.

Q2. the definition of sepsis 1 and 2: "Sepsis 1 and 2 was defined as blood culture and any culture drawn within 72 hours of ICU admission and SOFA score ≥ 2 on any ICU admission days 1-7 respectively. "; does not make sense. What did you intend to do by identifying two phenotypes of sepsis?

A2. The sepsis definition version 1 and 2 are based on yield of only blood culture or any culture and other parts of definition from Sepsis-3 definitions.

Q3. There are many studies (Crit Care. 2018 Dec 18;22(1):347. doi: 10.1186/s13054-018-2279-3. J Crit Care. 2018 Oct;47:70-79. doi: 10.1016/j.jcrc.2018.06.012. Am J Respir Crit Care Med. 2019 Feb 21. doi: 10.1164/rccm.201806-1197OC.) exploring the phenotypes of sepsis, but the present study did not use the appropriate method for doing so. cite these articles and describe how can the present study add to the literature.

A3. Thank you. These are excellent resources for different disease phenotype for sepsis. However, they are beyond the scope of our study. We only focused on sepsis-3 definitions to make its computerized identification.

Q4. "In the initial derivation cohort, the machine learning model achieved a sensitivity of 100% for sepsis"--from this sentence it appeared that the authors intended to use machine learning to predict/diagnose sepsis; however, the study cohort all had sepsis at enrollment. It is very unclear what is the target population in this study. The study population subheading needs to be expanded, eligibility criteria should be clearly specified.

A4. Thanks. We respectfully disagree. We didn't intend this manuscript to predict. It was validation of supervised machine learning method for automatic detection of sepsis via sepsis-3 definition. Also not all patients had sepsis in either cohort. We had some with sepsis as yes and some as sepsis as no diagnosis, thus the calculation of sensitivity and specificity. This is a critical care informatics project; the target population is any ICU admission. (Figure 1)

Q5. What is the rationale to use equal sample size for derivation and validation cohort?

A5. Thank you. Equal size of derivation and validation cohort to make sure we had enough purposeful sampling of true positives and true negative cases to not set ourselves for artificial accuracy. Any less number in validation cohort will raise eyebrows.