

Peer Review File

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Reviewer A

- 1) First, the title needs to indicate that the current analysis was based on existing datasets and the development and validation of a prognosis prediction model.

Reply 1: Thanks for your advice. We have modified our text as advised (see Page 1, line 2-4).

- 2) Second, the abstract is not adequate. The background did not explain why the authors focused on Neutrophil and what the current knowledge gap is. The methods need to describe the datasets used, their clinical samples, how the predictors were identified, the generation of training and validation samples, and how the prediction accuracy was assessed. The results need to first summarize the characteristics of the sample, provide detailed figures and P values to support the findings, and the AUC values of the prognosis prediction model in both the training and validation samples. The conclusion needs more specific comments for the clinical implications of the findings.

Reply 2: Thanks for your advice. We have modified our text as advised (see Page 2-3, line 37-74)

- 3) Third, in the introduction of the main text, the authors need to have an overview of the known prognostic biomarkers and prognosis prediction models in LUSC, analyze their limitations, describe the potential strengths of neutrophils, and indicate the needs for identification of new biomarkers and the development of prognosis prediction models based on neutrophils.

Reply 3: Thanks for your advice. We have modified our text as advised (see Page 3, line 84-91, line 101-102; Page 4, line 114-116, line 119-121). The relevant literature has been supplemented (see Page 18-19, line 606-618; Page 19, line 627-629) and the serial number of the literature has been readjusted.

- 4) Fourth, in the methodology, it is necessary to have an overview of the research procedures and their corresponding questions to be answered. Please describe the clinical samples, clinical variables, prognosis outcomes, and follow up procedures of the datasets used. The authors need to describe how the training and validation samples were generated and the minimum AUC values for a good prediction model. As shown in the figure 3, the AUC values are all poor. The AUS values of the nomogram should also be reported.

Reply 4: Thanks for your advice. The data were obtained from the common accessible databases TCGA and GEO, with TCGA data as the training set and GEO data as the validation set. It was described in Page 4-5, line 132-155. And we added “Generally, if the AUC value of the ROC curve is above 0.6, the model is considered to meet the requirements.” in Page 8, line 252-253. We admit that the AUC value in the current results is not good enough, but the current AUC value almost meets the standard of 0.6, and the data has been verified by several

procedures, which is the true result of the data without procedural errors, and it may be due to the relatively balanced genes in the gene combination. Furthermore, In order to supplement the AUS (does it mean AUC?) values of the nomogram, we need to supplement the ROC curve of the nomogram. However, we found that the available data could not support the ROC curve, so the AUC value is difficult to obtain.

5) Finally, please consider to cite several related papers: 1. Du C, Cai J, Tang J, Chen Y, Díaz-Peña R, Tomita Y, Jassem J, Zhao J, Zheng D, Tu Z. Cell-free DNA methylation profile potential in the diagnosis of lung squamous cell carcinoma. *J Thorac Dis* 2024;16(1):553-563. doi: 10.21037/jtd-23-1827. 2. Zhao X, Yuan C, He X, Wang M, Zhang H, Cheng J, Wang H. Identification and in vitro validation of diagnostic and prognostic biomarkers for lung squamous cell carcinoma. *J Thorac Dis* 2022;14(4):1243-1255. doi: 10.21037/jtd-22-343. 3. Cao L, Zhong J, Liu Z, Jiang J, Zhu C, Liu F, Wang B. Increased LOXL2 expression is related to poor prognosis in lung squamous cell carcinoma. *J Thorac Dis* 2024;16(1):581-592. doi: 10.21037/jtd-23-1848.

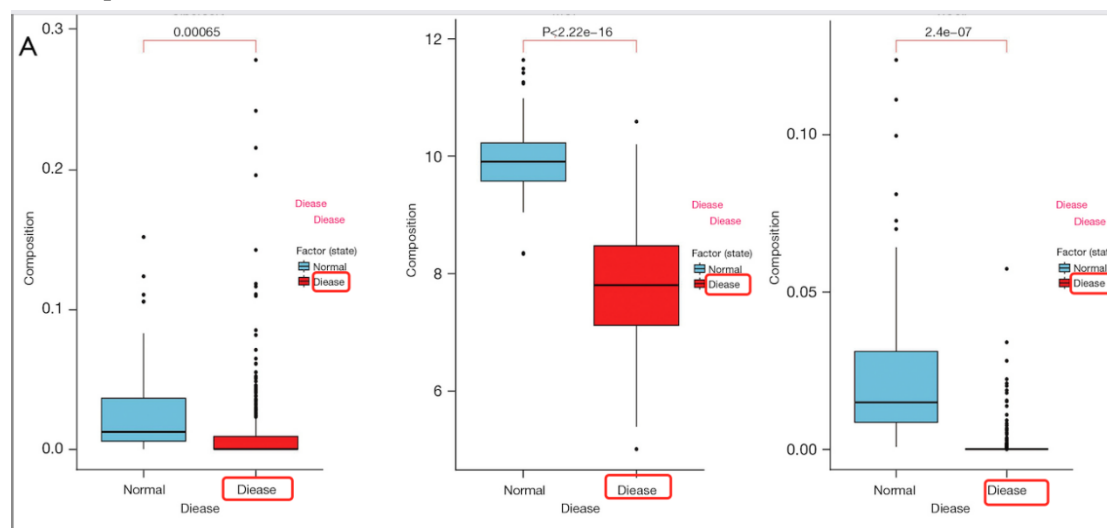
Reply 5: Thanks for your advice. We have added the relevant papers you suggested to the article (see Page 3, line 84-91; see Page 18, line 606-615).

Reviewer B

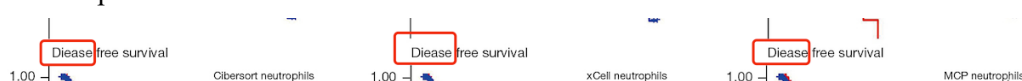
1. Figure 1

Please revise this typo.

1A: six places



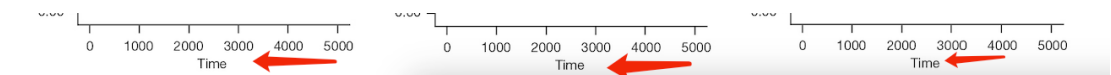
1B: three places



Reply: It has been modified as required (Figure 1-revised).

2. Figure 1B, 3C, S4D

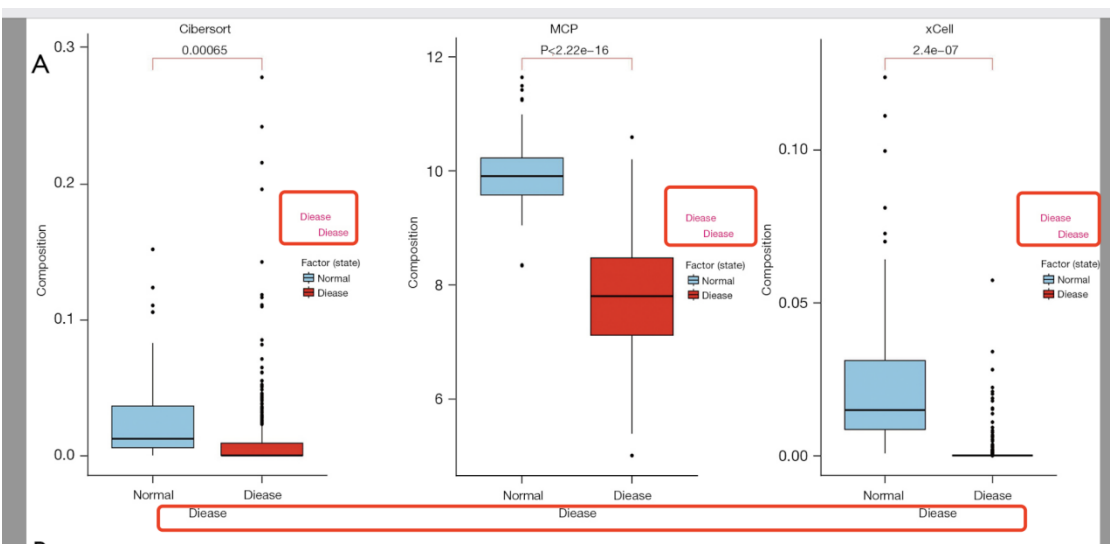
Please provide the unit for “Time”.



Reply: It has been modified as required (Figure 1-revised, Figure 3-revised, Figure S4-revised).

3. Figure 1

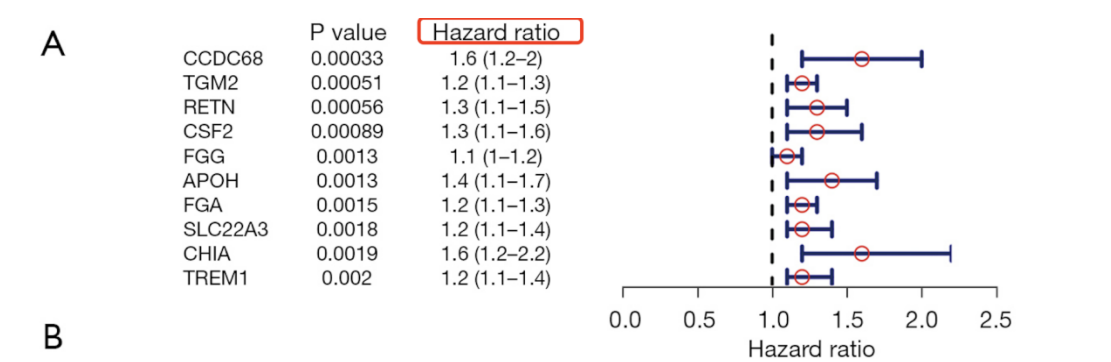
The “Diease” in Red boxes (nine places) is confusing. Please check and confirm whether they should be deleted.



Reply: It has been deleted as requested (Figure 1-revised).

4. Figure 3A, 4A, 4B

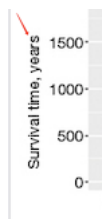
Please add “95% CI” after “Hazard ratio”.



Reply: “95% CI” has been added as required (Figure 3-revised, Figure 4-revised).

5. Figure 3C (2 places)

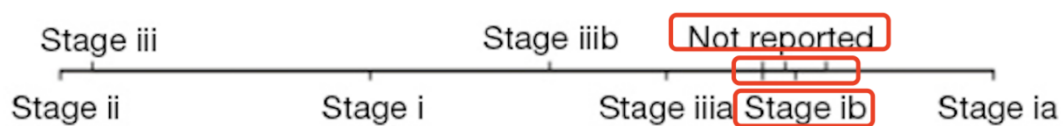
The unit “years” looks shocking, since the data are from 0-1500. Please check and revise.



Reply: Thank you for pointing out this mistake and it has been modified to “days” (Figure 3-revised).

6. Figure 4C

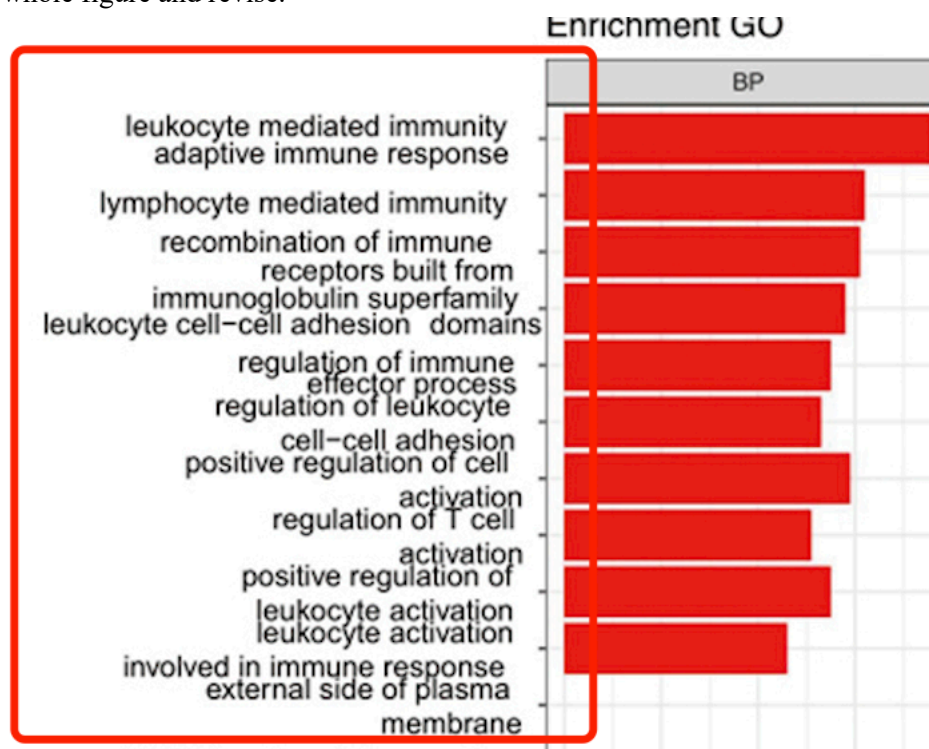
One bar corresponds to one content. Which bar is for “Not reported” and for “Stage ib”? Please indicate clearly and delete the unnecessary bars.



Reply: It has been modified as required (Figure 4-revised).

7. Figure S3

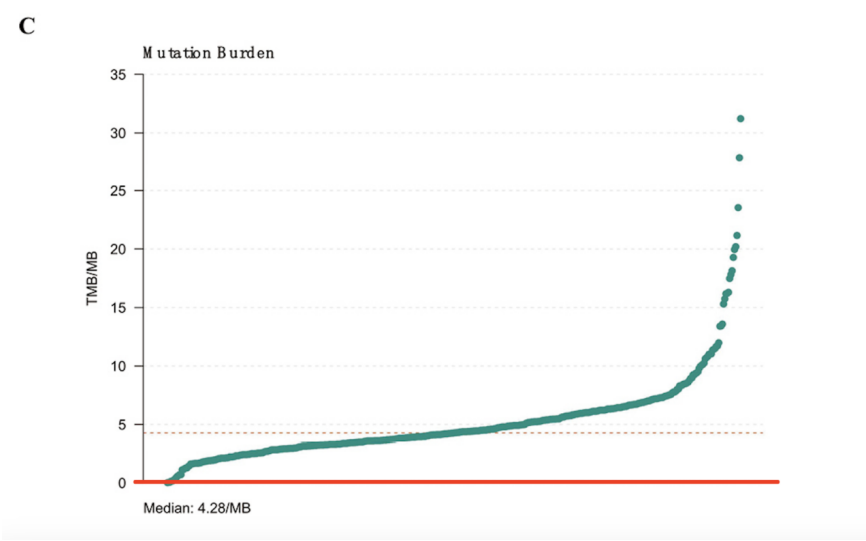
One bar corresponds to one content. The current version is confusing. Please capitalize the first letter for the information to avoid any misunderstanding. Please check the whole figure and revise.



Reply: It has been modified as required (Figure S3-revised).

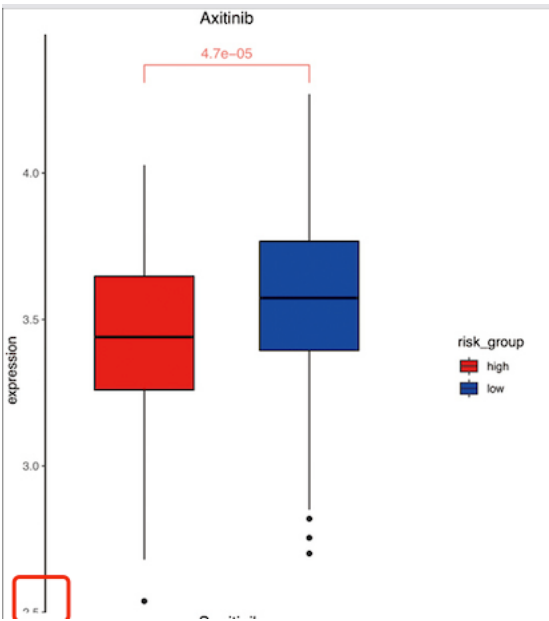
8. Figure S4C

Should Figure S4C have x-axis? Please provide.



Reply: We added a note on the X-axis in “Figure S4-revised”.

9. Fig S5 is incomplete as the pointed word is covered. Please revise.



Reply: Figure S5 has been modified (Figure S5-revised).