

Cover Letter

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "A new analysis of real-time fatality rate in the initial stage of COVID-19 (entropy2406618)". Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval.

The main corrections in the paper and the responds to the reviewers' comments are as following:

Reviewer #1:

1. Response to comment:

(The English should be thoroughly revised since some sentences are difficult to be understood and some others are incompletes or with errors)

Response: We check the manuscript carefully for typos and grammatical errors and make corresponding revisions.

a. In Abstract, we make a lot of revisions. "In this paper, a test method of variance analysis using permutation test is proposed to test the null hypothesis that the real-time fatality rate of multiple groups is equal during epidemics. A large-scale simulation study have been carried out in

this paper, the result shows that the proposed test method can accurately identify the differences between different groups and has satisfactory performance. The proposed method is applied to compare the...” switches to “In this paper, a permutation test method of variance analysis is proposed to test the null hypothesis that the real-time fatality rates of multiple groups are equal during the epidemic period. In virtue of a large-scale simulation studies, the proposed test method can accurately identify the differences between different groups and display satisfactory performance. Applying the proposed method to the real data set of the COVID-19 epidemic in mainland China”

b. In P.1 first of first para, “A epidemic” switches to “The epidemic”.

c. In P.1, Line 9 of first para, “spread” switches to “spreads”; “the outbreak” switches to “the initial outbreak”,

d. In P.2, Line 2 of first para, “as” switches to “up to”.

e. In P. 2, Line 10 of second para, “has proved” switches to “has been proved”. Some long sentences are decomposed for several short sentences. See the revised revision.

f. In P.3, Line 7 of first para, “on the other hand” switches to “However”.

g. In P.3, Line 8 of first para, “In order to solve the above problem, it is necessary to carry out relevant statistical test and compare the severity of diseases between multiple groups according to a simple data structure.” Is placed in the third para.

h. In P.3, Line 4 of the third para, “it can also test” switches to “it can also be tested”.

i. In P.3, the last sentence of the third para, there is a big change. The revised sentence is “We recall that Zhao et al. [14] tested the clinical symptoms of patients using Remdesivir and other therapeutic drugs through survival analysis of Log-rank, and found that the survival rate of patients using Remdesivir was significantly improved within 8 weeks. In essence, the potential use of multi-group trials is to compare the changes of the real-time fatality rate with Remdesivir and standard treatment. In "Empirical analysis" section, we will compare the differences of real-time fatality rate among different regions. The results suggest the effectiveness of interventions and medical resource assistance implemented by government departments during public health emergencies are useful and critical.”

j. In P.3, the fourth para, there are some revised sentence. See the revised revision for the para “In Section 2, the test statistic is putted forward to study the asymptotic distribution. In Section 3, the relevant knowledge of the permutation test is introduced. In Section 4, simulation experiments are carried out to evaluate the effectiveness of the proposed test method in different scenarios. In Section 5, the proposed test procedure is applied to the comparison of disease severity among three independent clusters during the outbreak. Here three independent

clusters are: mainland China (excluding Hubei Province), Hubei Province (excluding Wuhan) and Wuhan. In Section 6, we summary the provides the results.”

k. In P.4, Line 3 of the third para, “there are” switches to “then we have”

l. In P.5, Line 21, there is a revised formula.

The following sentences is the revision:

“With the evolving of time, the severity of the epidemic will change, the above-mentioned real-time fatality rate can be used to compare the changes on the severity of the epidemic among different groups, the following hypothesis

$$H_0: p_1(t)=p_2(t)=\dots=p_k(t), \quad H_1: p_i(t), \quad 1 \leq i \leq k, \\ \text{not all equal}$$

is proposed by considering death and recovery as two competing risks. It is easy to see that the above hypothesis is equal to

H_0 :

$$\frac{p_{1,D}(t)}{p_{1,R}(t)}=\frac{p_{2,D}(t)}{p_{2,R}(t)}=\dots=\frac{p_{k,D}(t)}{p_{k,R}(t)}, \quad H_1: \frac{p_{i,D}(t)}{p_{i,R}(t)}, \quad 1 \leq i \leq k, \\ \text{not all equal},$$

m. In P.7, Line 1 of the ninth para, “formula (11)” switches to “Here F”.

n. In P. 11, there some revised sentences. See the revision.

o. We also make some modification in Conclusion. See the revision.

We remove the last sentence.

2. Response to comment

(The paper adds no relevant results on the subject considered or any interesting application or improvement concerning in the methods employed for the analysis)

Response: The paper discusses the difference in the severity of the disease among three independent clusters in virtue of permutation test. As we know that there is no paper dealt with the problem. In addition, it is interesting project for studying the severity of the early disease of COVID-19, which may be related to the effectiveness of interventions and the improvement of medical resources. So We add three references which are published in 2023.

3. Response to comment

(As a side comment, it is not well written also in the section describing the methodology employed. The formula shown should be thoroughly revised)

Response: We check the manuscript carefully and give some exactly modification. See the section on Permutation test in the revised manuscript.

Reviewer #2:

Response to comment

(Authors should read thoroughly and correct all typographical errors in t

he manuscript.

Authors should place the tables in the manuscript properly. I suspect this is due to the latex command used by authors. It was difficult to understand the tables as some parts are cut off.)

Response:

We check the manuscript carefully for typos and grammatical errors and make corresponding revisions.

We tried our best to place the tables in the manuscript properly. Due to latex command, the tables maybe change a litter. But this does not affect the reading.

Reviewer #3:

(Dear authors, please explain why you have excluded some major cities?

This should be addressed and its possible influences on the results should be discussed.)

Response:

The manuscript mainly discusses the Permutation test, one non-parametric test, and studies the severity of the early disease of COVID-19, which may be related to the effectiveness of interventions and the improvement of medical resources. The paper underlines the method. In particular, the method can be applied to the case of k samples. In essence, this allows researchers to study more clinical questions in concrete real-life situations. This is our future work.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. These changes are not listed but the readers can see those once they read the original manuscript and revised version.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestion.

Best Regards

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