

## ROUND 1

Reviewer #1:

Comments 1. Table 1 is not found.

Response: We are really sorry that we forgot to upload Table 1. In the revised manuscript, we have uploaded the Table 1.

2. Please give NAFLD burden before COCLDs.

Response: Thank you for your comments. In introduction section, we have illustrated the NAFLD burden as such” It is estimated that 25% of the global population suffers from NAFLD, and the prevalence of nonalcoholic steatohepatitis (NASH) is predicted to increase by as much as 56% in the following decade<sup>1</sup>. NAFLD encompasses a range of liver damage, from simple steatosis to NASH, fibrosis, cirrhosis, and even hepatocellular carcinoma<sup>2</sup>. A study reported that among all metabolic diseases, NAFLD has become the fifth leading cause of death among young adults, and by 2050, its projected to increase in death rate is 158.4%<sup>3</sup>. However, another study revealed that whereas the age-standardized prevalence rate (ASPR) of NAFLD increased, the age-standardized death rate (ASDR) and age-standardized disability-adjusted life year (DALY) rate (ASDAR) decreased from 1990 to 2019”

3. Please put Figure number in each figure.

Response: Thank you for your suggestion. We have uploaded editable PPT files of Figures which included Figure number in each Figure.

4. In the expected Figure 2, the name marks of each color line are incomplete. Please arrange those lines sequence according to the degree of SDI.

Response: Thank you for your suggestion. We have revised the Figure 2 legend according to the degree of SDI.

Reviewer #2:

This is a very good and comprehensive study on the burden of NAFLD worldwide over an extended period of time (1990-2019). This paper has the potential to become a milestone in the literature on the topic. Therefore, I feel that the Authors should make a major effort to improve readability of the paper. Indeed, the text is very hard to follow, and also Tables (although provided as supplementary material) are very difficult to

read.

Response: Thank you for your insightful feedback on our paper. We greatly appreciate your positive assessment of our study's comprehensiveness and potential significance in the field. Your recognition of its potential as a milestone is truly encouraging.

We also acknowledge your concern about the readability of the paper. We understand the importance of presenting our research in a clear and accessible manner. We have taken your feedback seriously and made a concerted effort to enhance the overall readability of the manuscript. We have improved the structure and flow of the text to make it easier to follow.

If you have any specific suggestions or recommendations on how we can achieve better readability, we would be more than grateful to receive them. Your expertise and guidance are invaluable to us as we strive to improve our paper. Once again, thank you for your thoughtful review and constructive feedback.

## Round 2

### Reviewer #1:

This review collects global data of cirrhosis or other chronic liver diseases (COCLD) from patients with NAFLD. They found that the age standardized COCLD prevalence rates increased during the past three decades. Whereas the age-standardized death rate and age-standardized DALY rate decreased.

### Comment

1. When global prevalence of COCLD of NAFLD and its outcome were concerned, it will be clearer to list global prevalence of NAFLD in each region.

Our Response: Thank you for your comments. In introduction section, we have illustrated the NAFLD burden as such “Recent estimates suggest that approximately 25% of the world's population is affected by NAFLD, with projections indicating a potential 56% surge in the prevalence of nonalcoholic steatohepatitis (NASH) within the coming decade. NAFLD encompasses a spectrum of liver damage, ranging from simple steatosis to NASH, fibrosis, cirrhosis, and even hepatocellular carcinoma. It is noteworthy that NAFLD now stands as the fifth leading cause of mortality among young adults within the category of metabolic diseases. Alarming forecasts predict a staggering 158.4% increase in its death rate by the year 2050%. Conversely, another separate study demonstrated divergent trends, finding that the age-standardized prevalence rate (ASPR) of NAFLD increased while the age-standardized death rate (ASDR) and age-standardized disability-adjusted life year (DALY) rate (ASDAR) decreased from 1990 to 2019” (Line 198-209, Page 5). In the present study, we focus on the burden of COCLD of NAFLD, and the prevalence of NAFLD can be found in previous article (Wang D, Xu Y, Zhu Z, Li Y, Li X, Li Y, Shen H, Wu W, Liu Y, Han C. Changes in the global, regional, and national burdens of NAFLD from 1990 to 2019: A systematic analysis of the global burden of disease study 2019. *Front Nutr.* 2022 Dec 21;9:1047129. doi: 10.3389/fnut.2022.1047129).

2. In the conclusion of abstract, the first sentence 'COCLDs due to NAFLD have emerged as a large and growing public health burden worldwide' may be deleted or move to background.

Our Response: Thank you for your constructive suggestion, we have followed the suggestion of the reviewer and deleted the sentence in the revised manuscript (Line 158, Page 4)

3. In the characteristic line of Table 1, counts are not directly understandable and not specific. Please directly name the item counted. For example: Death cases among COCLD, Total COCLD No., DALY No. among COCLD. Please add abbreviation (COCLD) to the Table title. Please change ASR to ASDR or ASDAR to where it is appropriated. Similar changes may be applying to supplementary Tables.

Our Response: Thank you for your constructive suggestion, we have followed the suggestion of the reviewer and rename "count" to "Death cases among COCLDs due to NAFLD", "Prevalence cases among COCLDs due to NAFLD" and "DALYs cases among COCLDs due to NAFLD" respectively (Table1). We have also changed the "ASR" to "ASDR", "ASPR" or "ASDAR" in all tables and figures across the whole article and "cirrhosis and other chronic liver diseases" was replaced by the abbreviation of COCLD in Table title.

4. The supplementary Table included both sexes and mentioned in all the supplementary Tables except supplementary Table 2. Why sex should be mentioned? There is no sex column in these Tables.

Our Response: Thank you for your constructive suggestion, we have deleted both sexes in all tables in supplementary.

5. In the second paragraph of discussion, the last sentence mentioned 'although the diagnostic criteria of MAFLD were more accurate than those of NAFLD. To my understanding these two classifications have different definitions. There is no which is more accurate than other's issue.

Our Response: Thank you for your constructive suggestion, we followed the suggestion of the reviewer and deleted "although the diagnostic criteria of MAFLD were more accurate than those of NAFLD" in the discussion sections (Line 654-655, Page 12).

6. In the last paragraph of discussion, the reviewer suggest weight loss is the most effective strategy of therapy. The reviewers neglect the contribution of exercise without weight loss in reduction of liver steatosis. Furthermore, there is no reference in this paragraph.

Our Response: Thank you for your suggestion, we followed the suggestion of the reviewer and modified it to "Consequently, interventions targeting weight loss could be efficacious and cost-effective strategies to avert the progression of NAFLD to COCLDs. In addition, exercise interventions without significant weight loss have also had a beneficial effect on alleviating NAFLD. Thus, it is imperative to emphasize the critical role of weight management and exercise within public health programs [46]" (Line 801-806, Page 15). One reference have added in the revised discussion section (Line

1027-1029, Page 15).

Reference:

- 46 Babu A F, et al. Positive Effects of Exercise Intervention without Weight Loss and Dietary Changes in NAFLD-Related Clinical Parameters: A Systematic Review and Meta-Analysis. *Nutrients* **9**, 3135, doi:10.3390/nu13093135(2021).

Reviewer #2:

Many thanks for considering my comments. readability has improved. Again congratulations on this study.

Our Response: Thank you for your feedback on our paper. We greatly appreciate your positive assessment of our study's. Your recognition of the overall readability of the manuscript is truly encouraging. Once again, thank you for your thoughtful review and constructive feedback