Dear Editor

Thank you very much for the helpful comments. Please find enclosed a detailed response to the reviewers' comments and a revised version of our manuscript. Please note all changes to the original manuscript have been highlighted.

Yours sincerely,

Xing Wang, Bin Wu on behalf of co-authors

Response to comments of reviewers

Reviewer #1: The manuscript by Wang et al describes a retrospective study of the population characteristics of patients hospitalized for liver cirrhosis at a single hospital in south China over the period of 2001-2020. The entire cohort was over 33,000, which is an impressive number. Overall, the changes in the population and the underlying etiology of LC did not show dramatic changes, which is perhaps not surprising for a slowly developing chronic condition. However, some significant trends were noted. Overall, the manuscript is a reasonable effort, but questions arise regarding the choices made for the analyses presented. These are listed below.

1. Why is no information given about the hospital/medical center? How many beds? Was it unchanged over the 20 years? Which raises a question about Fig. 1: why are there so many more patients in 2011-2020 relative to 2001-2010? What changed?

Thank you for the question and we apologize for your confusion. Our hospital the research was performed is a tertiary medical and liver center with over 2,600 inpatient beds, and the number of beds has changed over the study period. During 2001-2010 period, our hospital had approximately 1300 beds in total. During 2011-2020 period, with the completion of expansion project and opening of new branch hospital, the total bed number nearly doubled. The rapid increased bed number may partly explain the 3-fold increased number of included patients in 2011-2020 relative to 2001-2010. Moreover, the decreasing in-hospital stay period over years, reflecting improved efficiency of hospitalization, may also contribute to the increased patient number. We added a brief description of our hospital in the section "MATERIALS AND METHODS".

2. Fig. 2 shows a continuous line, when in fact it should be discontinuous. There are 8 overlapping three year intervals covering 2001-2010, and another 8 covering 2011-2020. Why not plot the each year separately? These decisions need to be justified.

Thank you for the comments and suggestion. The average ages in each period of time is discontinuous, but the line is a simulation to illustrate the increasing trend in average age of study population. The method we used was 3-year moving average analysis, which has been widely used in biomedical researches to depict long-term trends by smoothing out data fluctuations through mean of the data (Enomoto H, et al. *J Gastroenterol* 2020; 55: 353-362; Alsirafy SA, et al. *BMC*

Palliat Care 2022;21:123). We believe this method is appropriate to show the trend in average age, and we revised the figure, the labels in horizontal axis and the legend for this figure to better explain the values in the line. However, plotting with each year separately is also reasonable and we added a figure below illustrating the trend in the mean age of the study population by separated years for review. The new figure showed a similar increasing trend in mean age but more fluctuant (lower coefficient R^2=0.520) compared to our original Figure 2.

Figure. Trend in the mean age of the study population in 2001-2020 by separated years
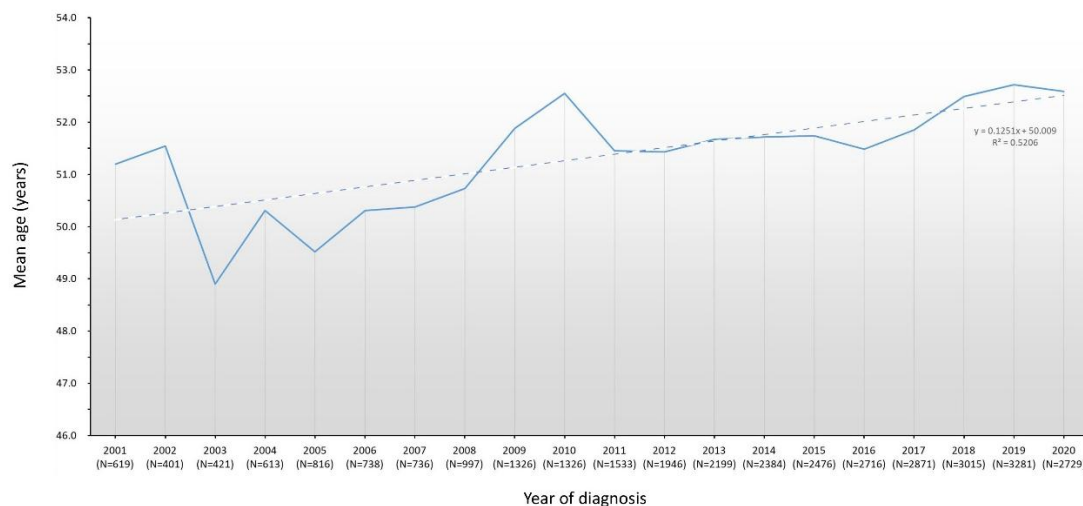
3. Fig. 3 is not needed.

Thank you for the comments. We have removed the "Figure 3. Transition in the proportion of male and female patients in 2001-2020" from our manuscript.

4. Table 2: What is the rationale for breaking into 5 year cohorts? Again, needs justification.

5-year block is a widely used time-block to depict trend over long time period, especially for comparing proportions and prevalence rates (Wong MCS, et al. *Nat Rev Gastroenterol Hepatol* 2019; 16: 57-73; Li M, et al. *Biomed Environ Sci* 2020; 33: 1-10). Moreover, the 5-year block method is consistent with our previous work (Wang X, et al. *World J Gastroenterol* 2014; 20: 13546-13555), and makes the results comparable and persistent over the 20 years period. Furthermore, except the 5-year comparison, we also performed comparisons of proportions of separated years from 2001-2020 in Figure 4 and computed P for trend, as shown in Table 2.

5. Good discussion of strengths and limitations.

Thank you very much!

Reviewer #2: This is a well written article and I enjoyed reading it.

1. Please change NAFLD and ALD with the new proposed terminology (Rinella ME, et al. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol 2023)

Thanks a lot for your compliments and helpful comments. We have replaced NAFLD in our manuscript with the new nomenclature as metabolic dysfunction-associated steatotic liver disease (MASLD) according to updated statement on new fatty liver disease nomenclature. Despite the consensus introduced a new nomenclature as metabolic and alcohol associated liver disease (MetALD), the term was selected to define patients who consumed greater amounts of alcohol on the basis of MASLD. Therefore, traditional definition of ALD is not changed, and we did not change the nomenclature of ALD in our manuscript.