

**Reply to reviewer No. 57695:**

**Question1:**

Please, address the issue of generalizability (external validity) of your findings and its applicability to the rest of the Chinese population and other populations of the world.

**Answer1:**

It is a preliminary study which is the first to investigate the relationship between AFU level and NAFLD. But the limitation (not stated in the manuscript) is that it is single-center experience. It is hard to confirm the generation of our findings. So now we are planning to conduct a multi-center large cohort study (hangzhou, shanghai, wuhan and guangzhou etc.) to investigate the applicability of our findings to the rest of the Chinese population. If possible, we hope to make a international cooperation to see whether our findings apply to the other races or not. We are confident that AFU is a promising marker to predict NAFLD. So we are making efforts to find a new algorithm (including AFU) to predict NAFLD better.

**Question2:**

Also, I am concerned that the 2 groups (NAFLD vs. non-NAFLD) are not matched regarding age, sex and BMI. I am sure this has a major impact on your results and would like you to explain this thoroughly.

**Answer2:**

As seen in Table3 in the manuscript, after adjusting for the 19 variables listed in Table 1 using a multivariate stepwise logistic analysis (including Age, Sex and BMI), AFU remains significantly associated with the risk factors for NAFLD ( $P < 0.001$ ).

The 2 groups (NAFLD vs. non-NAFLD) in this study are not matched regarding age, sex and BMI. And several previous studies have also shown that age, sex and BMI are risk factors for NAFLD, including Chinese population[1, 2], Korean population[3], Arabic population[4] etc. People with NAFLD are often older, male and fatter. So we it is hard to completely eliminate the effects of the three factors (age, sex and BMI).

**Other comments:** the manuscript has been revised accordng to the “other comments”

**Reply to reviewer No. 2939706:** the manuscript has been revised by Non-Native Speakers of English.

**Reply to editor:**

Question:

Please provide the decomposable figure of Figures, whose parts are movable and can be edited.

Answer:

Please allow me to apologize that the Figrures were made by software and presented

as a whole, so it is hard to make these parts movable. Sorry for bringing troubles.

### All of the revisions made to the revised manuscript

1	ESPS Manuscript NO	ESPS Manuscript NO: 21432
2	Zhenya Lu et al. Risks of non-alcoholic fatty liver disease	Lu ZY et al. Risks of non-alcoholic fatty liver disease
3	Zhenya Lu, Chao Cen, Zhou Shao, Xinhua Chen, Chengfu Xu, Youming Li	Zhen-Ya Lu, Chao Cen, Zhou Shao, Xin-Hua Chen, Cheng-Fu Xu, You-Ming Li
4	Zhenya Lu, Department of Internal Medicine, The First Affiliated Hospital, School of Medicine, Zhejiang University, 79 QingChun Road, Hangzhou, Zhejiang 310009, P.R. China	Zhen-Ya Lu, Department of Internal Medicine, The First Affiliated Hospital, School of Medicine, Zhejiang University, 79 QingChun Road, Hangzhou, Zhejiang 310009, P.R. China
5	Author contributions: Zhenya Lu and Chao Cen contributed equally to this work; Zhenya Lu, Chao Cen and Xinhua Chen designed the research; Zhenya Lu collected the data and Chao Cen, Zhou Shao, Xinhua Chen, Chengfu Xu analyzed the data; Chao Cen and Chengfu Xu wrote the paper; all authors have read and approved the final version to be published.	Author contributions: Lu ZY and Cen C contributed equally to this work; Lu ZY, Cen C and Chen XH designed the research; Lu ZY collected the data and Cen C, Shao Z, Chen XH, Xu CF analyzed the data; Cen C and Xu CF wrote the paper; all authors have read and approved the final version to be published.
6	Biostatistics statement:	Biostatistics statement: The statistical methods of this study were reviewed by Prof. You-Ming Li from department of gastroenterology, the first affiliated hospital, school of medicine, Zhejiang University.
7	Correspondence to: Youming Li, MD	Correspondence to: You-Ming Li, MD
8	Key words: $\alpha$ -L-fucosidase, non-alcoholic fatty liver disease, metabolic syndrome, biomarker, cross-sectional study	Key words: $\alpha$ -L-fucosidase; Non-alcoholic fatty liver disease; Metabolic syndrome; Biomarker; Cross-sectional study

9	1. INTRODCITION	INTRODCITION
10	20–30%	20%–30%
11	Diabetic medicine : a journal of the British Diabetic Association 2005; 22(9)	Diabet Med 2005; 22
12	Abbreviation: BMI, Body mass index;	Abbreviation: NAFLD, non-alcoholic fatty liver disease; BMI, Body mass index;
13	Table1、 Table3	All Abbreviation are listed and explained.

1. Xu, C., et al., *Prevalence and risk factors for the development of nonalcoholic fatty liver disease in a nonobese Chinese population: the Zhejiang Zhenhai Study*. Am J Gastroenterol, 2013. **108**(8): p. 1299-304.
2. Xu, P., et al., *Association between serum alpha-fetoprotein levels and fatty liver disease: a cross-sectional study*. World Journal of Gastroenterology, 2014. **20**(33): p. 11865-11870.
3. Ryoo, J.H., et al., *The clinical availability of non alcoholic fatty liver disease as an early predictor of the metabolic syndrome in Korean men: 5-Year's prospective cohort study*. Atherosclerosis, 2013. **227**(2): p. 398-403.
4. Zelber-Sagi, S., et al., *Non-alcoholic fatty liver disease independently predicts prediabetes during a 7-year prospective follow-up*. Liver International, 2013. **33**(9): p. 1406-1412.