

**RE: MS WJG 7121 The epidemiology of fatty liver: an update**

Dear Editor,

Please find enclosed the revised version of the above MS together with our replies to the Reviewers. We have followed the suggestions made by the Reviewers and we hope that our MS can now be accepted for publication.

Sincerely yours,

Giorgio Bedogni

## **Reviewer A**

This is an invited review on the topic of epidemiology of fatty liver. The authors write to the general public about the updates of recent studies of fatty liver. It is an important topic, and the authors did a good job to use a simple Q&A format to delineate the information to their intended audience. The reviewer would like to see some more work to improve the paper.

**Q1. The abstract should be rewritten to summarize the important updates about fatty liver the paper wants to delivery to the audience. It should have clear key points of the paper.**

A1. We thank the Reviewer for the suggestion. We now emphasize the three key points of the paper, namely: 1) the limitations of the AFL *vs.* NAFL dichotomization, 2) the role of FL as predictor of cardiometabolic disease, 3) the role of FL as predictor of mortality.

**Q2. The authors uses many abbreviation that might not be very well known to the general public (the intended audience of the paper). It would be better to give the full name at the first time and then use the abbreviation later. For example: AGA, EASL, HBV, HCV, and NHANES.**

A2. We thank the Reviewer for the suggestion. All acronyms are now spelled out on first use.

**Q3. When discussing about the population studies, it would be more informative to state the sample size (how many people were included) in the study. For example the Dionysos Nutrition and Liver Study.**

A3. The sample size of the Dionysos Nutrition and Liver Study and NHANES III are now specified.

## **Reviewer B**

Nonalcoholic fatty liver and NAFL disease are generally considered as a clinical condition associated with diabetes mellitus type 2 which may be pathological (or a compensatory physiological process at least in early stages. But as you and many others have noted, once we study this condition critically, we readily see a) lot of confusion associated with this condition from the nomenclature, diagnosis to pathogenesis (Ref.PMID:22105730. Biopsy is the gold standard but the so called gold standard suffers from sampling error and observer variability. The review is overall good and may be accepted for publication in WJG. Suggestions: The authors may include few more epidemiologically important aspects.

### **Q1. racial and regional difference**

A1. We thank the reviewer for the suggestion. We added this information under the paragraph "What is the prevalence of fatty liver"?

### **Q2. sexual/gender variation**

A2. We thank the reviewer for the suggestion. We added this information under the paragraph "What is the prevalence of fatty liver"?

**Q3. fatty liver in the lean and fatty liver in non-diabetic (which may be a separate disease mechanistically)**

A3. We thank the reviewer for the suggestion. We added this information under the paragraph “What is the relationship between fatty liver and the metabolic syndrome?”

**Q4. studies on validity of several indices-commercial and noncommercial based on biochemical/sonological- elastographic/imaging/genetic markers or other parameters**

A4. We thank the reviewer for the suggestion. However, we believe that this argument is worth an entire manuscript and that the excellent review of Festi et al. (2013) [8] can be consulted with profit from any interested reader.

**Q5. Fatty liver in the age extremes- children and old age**

A5. We added this information under the paragraph “What is the prevalence of fatty liver”?