February 5, 2016

Dear Ze-Mao Gong,

Science Editor of *World Journal of Gastroenterology*

We thank the editor and reviewers for the opportunity to submit our revised manuscript (Word format file name: 23812_Edited after revision) entitled: NON-ALCOHOLIC FATTY LIVER DISEASE IS NOT ASSOCIATED WITH A LOWER HEALTH PERCEPTION.

The manuscript has been corrected in accordance with the reviewer's every comments. All the corrections in the manuscript are in **underlined bold**.

Attached is a point-by point reply to the reviewers.

Reviewer 1. (Reviewer's code: 01136482)

COMMENTS: Introduction section: the last data on epidemiology of NAFLD, were reported in a recent review of Masarone et al. (Rev Recent Clin Trials. 2014). In line with the title of the paper, recently literature report that NAFLD patients have scarce readiness to lifestyle changes (the only treatment recognized). Defining stages of change and motivation, offers the opportunity to improve clinical care of NAFLD people. Please report this concept in the text. - Discussion section: NAFLD has the potential for major economic impact on healthcare costs, in particular related to morbidity and mortality. Please the Author report in the text suggestions for health policy approach to improve the perception of the disease.

Response: We would like to thank the reviewer for the important comments. In the introduction section, the concept of stages of change and motivation were added (Page 5). In the discussion section, the important topic of suggested health policy approaches to improve NAFLD perception was addressed (Page 14).

Reviewer 2. (Reviewer's code: 00058353)

COMMENTS: I think that the paper is ready to be published. It is a very useful investigation in a prevalent condition. The authors should emphasize their own commentaries about, the miss-utilization of health services among the NAFLD diagnosed subjects. This finding combined with the equivalent health perception might point towards lack of awareness and understanding

that NAFLD is in fact a progressive disease that requires a closer medical surveillance. The misperception of NAFLD as a non-significant disease may also be attributed to the way the health practitioners perceive NAFLD, perhaps not as a disease in itself with potentially severe outcomes, and as a consequence the information they provide to patients and their disease management. Several studies have demonstrated that hepatogastroenterologists [42], primary care practitioners [43] and hospital non-hepatologists specialists [44] do consider NAFLD as a disease and major health problem and follow NAFLD patients, but it is still unclear how firm is the message provided to the patients. Specially the last comment about the maybe poor translate to the patient about the awareness to the severe outcome of this condition. It would be of a great interest to run a survey in health care providers (gastrohepatologist, diabetologist and general practitioners) to evaluate the knolewdge of NAFLD, and how the message is transmitted to their patients. NAFLD is mayor risk factor for Hepatocarcinoma and justify an US screening and should be included in a surveillance program

Response: We thank the reviewer for the support.

Reviewer 3. (Reviewer's code: 00053433)

COMMENTS: This is a cross sectional study aimed at evaluating the self-rated general health perception in a cohort of 213 subjects form a health survey in Israel. The article is generally well-written and has scientific value, given the high prevalence of NAFLD and the potential implications of its findings in formulating health care policies. Authors are requested to address the following issues. 1. Please clarify which variables were included into the

"full model of multivariate analysis". 2. From the results presented, one could infer that a poor self-rated general health perception in NAFLD patients with early disease is "mediated" by overweight/obesity. However, it would be interesting to briefly discuss the possible impact of multicollinearity between BMI and NAFLD on underestimating the association between NAFLD and poor health perception.

Response: We thank the reviewer for the important comments.

1. The variables that were included into the "full model of multivariate analysis" are listed in the statistical methods section: "The potential confounders included in the multivariate model were: gender, age, body mass index (BMI) and behavioral factors: current smoking and duration of performance of leisure time physical activity in the past year". For better clarity we added a short description of the model also to the results section (Page 11).
2. We agree that multicollinearity exists between NAFLD and obesity. We aimed to learn if NAFLD as a distinct entity is associated with a lower health perception and for that reason controlled for BMI. To do that, we not only controlled for BMI in multivariate analysis, but we also stratified on it and in both cases it attenuated the association between the presence of NAFLD and self-reported health perception. Moreover, this lack of difference was demonstrated in the prospective evaluation of the deterioration of health perception with time, which could not be predicted by NAFLD and the fact that patients with a recent diagnosis of NAFLD (on the follow-up survey) had similar health perception as those with "long standing" NAFLD, both groups were overweight. Therefore, we believe that the multicollinearity cannot explain the lack of association between NAFLD and poor health perception. We

referred to this important issue in the discussion section on page 11.

We hope that the revised manuscript will be accepted for publication in the *World Journal of Gastroenterology*.

Sincerely yours,

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