

**Review comments and responses for the article “Epidemiological Link Between Obesity, Type 2 Diabetes Mellitus and Cancer – Manuscript No: 62606”**

*Reviewer #1:*

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** The reviewed manuscript, Epidemiological Link Between Obesity, Type 2 Diabetes Mellitus and Cancer, aimed to present a critical survey of current relevant to topic literature and synthesize with contemporary thinking to give a new perspective. The manuscript starts with reviewing epidemiological studies of obesity and diabetes to cancer and shows pathophysiological mechanisms such as IR/IGF-R and ER $\alpha$ /cytokine/ROS signalling pathways in the condition of hyperinsulinemia. The manuscript has recapitulated the role of adipose tissue influence on hypoxia and its consequences on oxidative stress, DNA damage, tumour angiogenesis, and inflammatory system. The Wnt/ $\beta$ -catenin, MAPK, PI3K, AMPK and mTOR signalling pathways were presented as therapeutic targets in patients with diabetes mellitus. The reviewed manuscript provides organized, analyzed balance views of critical points related to the topic. The manuscript needs the following revision. a. A clear explanation of terms at the beginning of each section b. Minor grammatical and spelling

**Answer:** Thanks for the encouraging comments after the expert review. We have now amended the manuscript to address the issues raised by the reviewer. We added an abbreviation list before introduction of the paper and provided explanations for each in the text. We have also corrected minor grammatical and spelling errors throughout in the revision as suggested

*Reviewer #2:*

**Scientific Quality:** Grade D (Fair)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Rejection

**Specific Comments to Authors:** This review by Cornelius J Fernandez et al summarized the recent progress in the epidemiological findings between obesity, type 2 diabetes mellitus and cancer, and the potential pathophysiological mechanisms linking obesity and diabetes to cancer, including IR/IGF-R signalling, ER $\alpha$ /cytokine/ROS, WAT remodelling, hypoxia and angiogenesis, oxidative stress and so on. However, this review summarized the association of obesity, diabetes and

cancer, instead of digestive system cancer, which did not meet the scope of the journal. Authors should focus on the digestive system related cancers.

*Answer:* Thanks for the review. Unfortunately, the reviewer misinterpreted that the article deals with digestive system cancer. We have done appropriate review of the epidemiological link between obesity, type 2 diabetes, and cancer in the paper.

#### **4 LANGUAGE QUALITY**

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing needs.

*Answer:* The manuscript originated from the United Kingdom and we have corrected the minor grammar and spelling errors in the revision appropriately.

#### **5 EDITORIAL OFFICE'S COMMENTS**

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

**(1) Science editor:** 1 Scientific quality: The manuscript describes a review of the epidemiological link between obesity, type 2 diabetes mellitus and cancer. The topic is within the scope of the WJM. (1) Classification: Grade D and Grade B; (2) Summary of the Peer-Review Report: The authors present a critical survey of current relevant to topic literature and synthesize with contemporary thinking to give a new perspective. However, the minor grammatical and spelling should be corrected. The questions raised by the reviewers should be answered; and (3) Format: There are 4 figures. (4) References: A total of 140 references are cited, including 49 references published in the last 3 years; (5) Self-cited references: There is 1 self-cited reference. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B and Grade B. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJM. 5 Issues raised: (1) The "Author Contributions" section is missing. Please provide the author contributions; (2) The

authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; and (3) Please obtain permission for the use of picture(s). If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable. 6 Recommendation: Conditional acceptance.

*Answer:* Thanks for the detailed advice for making the revision.

We have addressed all the reviewer suggestions appropriately and have now added the author contributions in the revision. We have also provided the power point images of each figure separately as suggested. All the figures were constructed by the authors to ensure originality and have no issues of copyright infringements.

**(2) Editorial office director:**

**(3) Company editor-in-chief:** I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Methodology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

*Answer:* Thanks for the suggestions. We have addressed all the issues raised by the reviewers and editorial office to ensure high quality of the paper in the submitted revision.

We are sure that this paper shall meet the high standard of the Journal and shall attract high enthusiasm among its global audience to achieve high citation rates to improve the impact factor of World J Methodology.

Thanks, and kind regards,

Joseph M Pappachan MD, FRCP