

## Author's Response to Reviewer's Comments:

**Reviewer's code:** 02874819

We appreciate thoughtful and thorough comments by the reviewers. We have revised our manuscript accordingly and feel it has improved and will be acceptable for publication. We would like to mention that the scope of our review article is to focus on all major CV outcome studies evaluating CV safety and efficacy of glucagon-like peptide-1 receptor agonists (GLP-1 RA) and sodium-glucose cotransporter-2 (SGLT-2) inhibitors. Following are the author's response to reviewer's comments.

1. **Originality of article:** We intend to submit the review article summarizing and comparing all major CV outcome studies of GLP-1 RA and SGLT2- inhibitors and provide the readers of the World Journal of Diabetes with the latest evidence. This is a "very hot" topic among clinicians managing diabetes and our review summarizes the most updated results of CV outcome trials. Since FDA now mandates that all new diabetes drugs have to demonstrate CV safety through large CV outcome trials, there is an abundance of data that needs constant updates. Two articles that reviewer cited (Ismail-Beigi F and Rahelić D et al), even though published in 2017, already requires updates. These articles only reviewed 2-3 CV outcome trials involving SGLT2-inhibitors and GLP-1 RA and in fact Rahelić D et al stated "Two ongoing randomized clinical trials involving other SGLT2 inhibitors, canagliflozin and dapagliflozin, will provide additional evidence of the beneficial effects of SGLT2 inhibitors in T2DM population." We have reviewed all major CV outcome trials of SGLT2-inhibitors and GLP-1 RA published to date including trials involving canagliflozin and dapagliflozin.
2. **Report about the glomerular filtrate to which SGLT2-inhibitors can be used:** Included in revised manuscript.
3. **Include renal outcome data of SGLT2-Inhibitors:** We have revised the manuscript to include information on renal outcomes of CANVAS trial. However, we would like to mention that due to abundance of data and heterogeneity in CV outcome trials results, we purposefully limited our review to just discussing results of CV endpoints. As clinicians and researchers, we share the reviewer's enthusiasm regarding exciting data on renal protective effects of SGLT-2 inhibitors.
4. **Future therapies:** This review discusses the CV outcome trials of FDA approved newer diabetes therapies (GLP-1 RA and SGLT2-inhibitors). We have included information on CV outcomes trials involving GLP-1 RA and SGLT2- inhibitor drugs that are not published yet (CV safety trials of dulaglutide and Ertugliflozin). Discussing experimental therapies is beyond the scope of this article. This review is focused on clinical CV outcome of newer FDA approved DM medications. However, if after careful review of revised manuscript, editors and reviewers feel that adding information on future experimental therapies will enhance the article, we will be happy to revise the manuscript further.
5. **Language quality:** Revised manuscript has been carefully reviewed and edited for language by native English speaking authors.

**Reviewer's code:** 02446694

**Reviewer's code:** 03764245

We would like to thank both the reviewers for taking time to peer review our review article.