

From

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To

The Editor,

World Journal of Diabetes

Dear Editor,

Sub: regarding submission of revision of the invited review article “Diabetes mellitus and stroke: a clinical update” for publication in the World Journal of Diabetes.

Thank you very much for demanding revision of the above invited review article in the World Journal of Diabetes. We also extend our sincere thanks to the reviewers for the pain taken to peer review our paper and suggest modifications that improved the quality of our work. We have also modified the paper as per the editor’s comments. I am sure that the revised version of the paper would benefit the worldwide readers of the Journal.

This work is not published elsewhere and is not under consideration in other journals. There are no sources of funding for this work or any conflicts in interests among the authors. The authors have agreed to transfer the copyright of this article to World Journal of Diabetes.

The review comments, the editor’s comments and the responses are documented below. We have also included the signed copyright form, and also the competing interest statement forms, along with the audio clip of the core tip. As this work has originated from UK, an English speaking country with appropriate English language standards, a language certificate is not necessary.

Thanking you.

Sincerely yours,

Dr. Joseph M Pappachan,

25/02/2017

## Review comments and response to Reviewers

### Reviewer 1

It has been a very comprehensive and beautiful article. I had a few suggestions. Please specify them. - The EDIC study, long-term follow-up results of DCCT, should also be allocated (Association Between 7 Years of Intensive Treatment of Type 1 Diabetes and Long-term Mortality). Please add this in the relevant paragraph.

**Answer:** Thanks for the comment. We have addressed this issue in the highlighted revision in the relevant section.

- The statement on type 1 DM should also be included in the text (Type 1 Diabetes Mellitus and Cardiovascular Disease. A Scientific Statement From the American Heart Association and American Diabetes Association). Please add this in the relevant paragraph.

**Answer:** Thanks for the comment. We have addressed this issue in the highlighted revision in the relevant section.

- I do not think that the results of ACCORD and ADVANCE have not been discussed adequately. General CVD findings are mentioned and the results of direct stroke should be also mentioned in detail, and consequently the negative impact of tight glycemic control on CVD / mortality should be further highlighted. Tight glycemic control in risky patients increases mortality. It should also be noted that there are individualized glycemic targets. There should be an emphasis here especially on the ADA guideline. Unfortunately, this has not been brought into the forefront sufficiently in the article.

**Answer:** Thanks for the comment. We have addressed this issue in the highlighted revision in the relevant section. A thorough discussion is made in the revision.

- Please, also mention follow-up studies of UKPDS (10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes). And, of course, another important study, VADT and Steno-2, should be mentioned (Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes. Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study). It may be to profit by this metaanalysis (Intensive glucose control and macrovascular outcomes in type 2 diabetes. Diabetologia (2009) 52:2288–2298). Please specify them in the relevant paragraph.

**Answer:** Thanks for the comments. We have addressed all these points in the highlighted revision in the relevant section.

- It may also be discussed, which glycemic status influences the CV outcome, fasting? postprandial? (Effects of Prandial Versus Fasting Glycemia on Cardiovascular Outcomes in Type 2 Diabetes: The HEART2D trial). - The AHA / ASA Guideline

should be referred to when discussed to HT. There are important implications here, especially when making antihypertensive choices.

**Answer:** These points are addressed and changes are made accordingly in the highlighted revision in the relevant section.

## **Reviewer 2**

Dear author , Following minor corrections and revisions may be needed. 1.Under the heading of diabetes ,stroke ; epidemiology. see in line 3 correct spelling of 'summarizes' and also correct this word in other areas.

**Answer:** Thanks for the comment. We have corrected this in the highlighted revision in the relevant section.

2.Please correct the spelling of 'Endarterectomy' in the heading of 'Carotid Endarterectomy'

**Answer:** We have made this correction in the highlighted revision in the relevant section.

3.under the heading of 'Diabetes and stroke: recent developments' correct spelling of 'optimize' in the last line of paragraph

**Answer:** Correction is made in the revision.

4.In the heading of obesity it will be better to describe physical exercise along with heart healthy diet.

**Answer:** Necessary change is made in the revision.

5.In the table no 5 it is appealing to mention USPSTF guide lines for use of aspirin in antiplatelet therapy and for screening of lipids.

**Answer:** Thanks for the comment. We have addressed this issue in the highlighted revision in the relevant section.

6. Reference no 119,120,121 are too old and may be omitted

**Answer:** We have changed the old references except the ISIS-2 study that is still relevant to the paper.