31044 – Answering reviewers

We would like to thank the 3 reviewers for their very positive comments and suggestions which will undoubtedly improve the manuscript. The amendments are marked in red in the manuscript (all new sections as required in the manuscript as per provided guidelines are also marked in red).

Thanking you

Professor Sudarshan Ramachandran

Reviewed by 00674619

The comments: The manuscript by Dr. Geoffrey Hackett investigates the effects of commonly used treatments such as statin, phosphodiesterase 5 inhibitors (PDE5I) and testosterone (TRT) on the association between age and mortality in men with type 2 diabetes. The results of this manuscript confirmed that statin, TRT and PDE5I reduce mortality in studied cohort and have described how they influenced the relationship between age and mortality. The main idea of this study is interesting and gives us new data for the future regarding the use of these drugs for type 2 diabetic patients. This work is descriptive, but contains interesting data, is well organized and appears timely. My opinion is that, this paper is very good regarding the drug options for patients with diabetes. The manuscript is state-of-the-art and the presented results are of potential interest for a wide readership, therefore I recommend publication in 'World Journal of Diabetes'.

No issues to address

Reviewed by 02842871

I accepted the opinion that the principal reason for PDE5I prescribing was ED, but treatment with PDE5I can also improve endothelial dysfunction (might be major reason for cardiac and cerebral vessel accident and death) and this can be good for general health and might be the exact reason for the conclusion in this MS (PDE5I,

alone and in combination with the other 2 agents significantly altered the association between age and mortality.). Therefore, it is better to supplement some discussion.

A sentence *"These results are compatible with studies showing that in T2DM patients, treatment with vardenafil results in improved endothelial parameters including flow-mediated dilation, interleukin-6 and testosterone levels [29] and ...."* has been added to the discussion (marked in red - page 13) with the relevant reference (No 29 – page 19).

Reviewed by 03445718

Comments to the Authors This is a very interesting retrospective study investigating whether the mortality rate follows the pattern described by Gompertz and estimating how testosterone status and treatments (statins, testosterone replacement therapy and phosphodiesterase 5 inhibitors) alter the mortality rate. A substantial and extremely meticulous work has been done and the findings are consistent. Specific comments: Introduction: -P4L18: "Phosphodiesterase 5 inhibitors" there is no need to capitalize the "P" Please replace with "phosphodiesterase5 inhibitors - P8L2: "P=0.0.028" Please correct according your data. Discussion: -P9L21: Reference is missing. Please add it. -P10L20: "We showed than mortality rates in men with T2DM" Please replace "than" with "that"

P4L18: "Phosphodiesterase 5 inhibitors" there is no need to capitalize the "P" – corrected

P9L21: Reference is missing – reference has been added (as it had been previously quoted no additional reference was required).

We showed than mortality rates in men with T2DM" Please replace "than" with "that"

corrected.