

7th April, 2015



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 17124-Mameli et al.doc).

Title: Explaining the increased mortality in type 1 diabetes

Author: Chiara Mameli, Sara Mazzantini, Moufida Ben Nasr, Paolo Fiorina, Andrea E Scaramuzza, Gian Vincenzo Zuccotti

Name of Journal: *World Journal of Diabetes*

ESPS Manuscript NO: 17124

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated

2. Revision has been made according to the suggestions of the reviewers:

1. Reviewer n° 01919991

The manuscript deals with an important issue: the increased excess mortality for patients with T1D with on-target Hb1Ac compared to age-matched population. It is well written on the whole, exception for some typos that need to be corrected. The manuscript provides a general and complete overview of the topic. However, a direct comparison with mortality data of T2D patients should be useful for a more comprehensive overview of the phenomenon

Thank you for your comment. The manuscript has been revised according to your suggestion.

2. Reviewer n° 00504962

In the present review, the authors described about the Type 1 diabetes and death rates. It is important topic in the field.

1.The authors described that patients with T1D and glycated hemoglobin (HbA1c) level of 6.9% or lower had a risk of death that was twice as high as the risk for matched controls. It would be better to add a description about hazard ratios for death according to HbA1c for a level of 7.0 to 7.8%, 7.9 to 8.7%, 8.8 to 9.6%, 9.7% or higher in the reference.

The hazard ratios for death according to HbA1c were added in Table 1.

2.The mortality rate is high in patients with T1D despite improvements in management of glucose levels and treatment of cardiovascular risk factors. It would be better to add a description about differences of death rates between T1D and T2D diabetes.

Thank you for your comment. The manuscript has been revised according to your suggestion.

3. It would be better to discuss how to improve outcomes of the mortality rate in patients with T1D in

greater detail.

Thank you for your comment. We discussed in greater detail how to improve outcomes in T1D. Please, see the revised manuscript.

3. Reviewer n° 00227496

The manuscript is well written regarding the cause of increased mortality in type1 diabetes. The authors well summarized the updated knowledge of epidemiology in the mortality of type 1 diabetes. This is important for adequate understanding the importance of cardiovascular risk and hypoglycemia and the underlying mechanisms in the increased mortality.

Thank you for this comment.

3. Reference list was update and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Diabetes*.

Sincerely yours,

Paolo Fiorina

A handwritten signature in black ink, appearing to read 'Paolo Fiorina', with a stylized, cursive script.

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