Response to reviewer's comments:

Thank you for reviewing our article for publication.

Reviewer 1

Comments on Relative Impact of Different Immunosuppressants on the Incidence of Post-Transplant Diabetes Mellitus across Solid Organ Transplant Recipients: Systematic Review and Meta-Analysis

1) Introduction section The sentence "However, it is still associated with several complications including Post-Transplant Diabetes Mellitus (PTDM) in the post-transplant period" is confused, but understandable.
   The sentence has been altered.
2) Authors state that "PTDM is associated with increased cardiovascular risk, infection and graft failure". Please, add proper references.
   References introduced:
   1)Matas AJ, Gillingham KJ, Humar A, Ibrahim HN, Payne WD, Gruessner RWG, et al. Posttransplant diabetes mellitus and acute rejection: impact on kidney transplant outcome. Transplantation. 2008;85(3):338–43.
   2)Siraj ES, Abacan C, Chinnappa P, Wojtowicz J, Braun W. Risk factors and outcomes associated with posttransplant diabetes mellitus in kidney transplant recipients. Transplant Proc. 2010;42(5):1685–9

3) Not all PTDM cases can be explained by the immunosuppressive regimen. Maybe the main risk factor is steroid dose or the number of high steroid pulses and not the baseline immunossuppresive regimen itself. Please, add an explanatory comment.
   Sentence added in introduction - In some instances, hyperglycemia develops in response to steroid doses and pulsed steroids required during episodes of acute rejection rather than baseline immunosuppression and care must be taken in making the diagnosis.

4) Is it important that the name NODAT was replaced by PTDM? Why? Both terms could describe the new appearance of diabetes after a solid organ implantation.
   This was written to highlight that various terms have been used in the past and that PTDM is the term that needs to be used currently.

5) Do authors recommend per protocol oral glucose tolerance tests to early diagnose PTDM? ADA 2021 criteria for diabetes states "A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assa (https://care.diabetesjournals.org/content/44/Supplement_1/S15). So, it could be that some of the PTDM diagnoses are misleading.
   This is possible

6) Authors state “The pathophysiology is incompletely understood, both impaired insulin resistance and insulin secretion (destruction of pancreatic B-cells) have been implicated”. The sentence is confused.
This sentence has been altered

7) If PTDM is associated to traditional risk factors, why is it necessary to search for more risk factors like the immunosuppressive treatment? Otherwise, do immunosuppressive add real risk over the traditional risk factors?
Traditional risk factors do not account for all the PTDM cases hence various studies have looked into immunosuppressives as the cause.

8) The authors state: “PTDM has a significant impact on post-transplant outcomes. Various studies have reported decreased graft survival and an increase in cardiovascular, renal and infection complications”. Please add proper references.
References added

9) Objective paragraph: Please replace cyclophosphamide by cyclosporine.
Changed

10) A secondary objective could be to study the incremental risk of diabetes due to the immunosuppressive drugs over the classical baseline risk factors.
This was not mentioned as we did not calculate this in our network analysis

11) Methods section Why the difference between the systematic literature review in February 2017 and he actual manuscript in June 2021? Is there new and significant new data in the meantime? For example, Lawendy et al found more relevant articles in a recent review in liver transplant recipients (https://doi.org/10.1111/ctr.14340).
The complex analysis took time from the time of the search – thus the delay between search and publication. There were few studies in this duration as mentioned but we felt repeating the full analysis would not dramatically change the current outcomes we report and would lead to further delays.

12) Sttistical analysis: Why the third time period is 5 or more years and not more than 3 years of follow-up? Why to exclude the 3-5 period after the transplantation?
We felt analysis at various time points would be informative and chose these periods rather than yearly. We felt 3 or more years may be too short and 5 or > 5 years may give extra information.

13) The following sentence is confused: “In this analysis, we only pooled data from cohort and randomized studies where pre-existing DM was known or studies where patients with pre-existing DM were excluded”.
The sentence has been changed.

14) Results section Population characteristics: Please add mean follow-up time of the solid organ recipients.

Unfortunately this info is not available

15) Table 1: OK Figure 1: What is intending to represent with the red and black lines? It is not evident neither in the legend nor in the figure.

The red data points denotes the studies which did not report the percentage of diabetes pre-existing before transplant. The black data points denotes the studies, which report the percentage of pre-transplant diabetes in the patients. The three graphs show the results stratified by main immunosupressive agent. We will include this in legend.

16) The sentence: "Meta-analysis using the random-effects model was used to calculate the incidence of PTDM" this sentence belongs to Methods instead of the Results section.

This sentence has been removed

17) Please explain or clarify what is intending to compare with the red and black lines in the three graphs and between them as well.

The red data points denotes the studies which did not report the percentage of diabetes pre-existing before transplant. The black data points denotes the studies, which report the percentage of pre-transplant diabetes in the patients. The three graphs show the results stratified by main immunosupressive agent. We will include this in legend.

18) PTDM incidence numbers: Please, put the main result outside the 95% CI parenthesis. So, replace "(12.3%, 95% CI 10.6% - 14.3%, I2 = 95.4 %)" by "12.3% (95%...)" and the same in all analogous figures. Maybe, it would be easier to read if all these numbers could be contained in a single Table.

This has been done

19) NMA paragraph: Please, replace "oddz" by "odds".

Changed

20) Subgroup analysis by organ transplanted. Please, replace "PTDM was 18.9" by "PTDM was 18.9%"

Changed

21) Discussion section The variability in PTDM diagnosis also could be explained by different approaches to look for this complication. In authors' opinion and based in their own results. Which immunosuppressive drug choose for a patient waitlisted to receive a second solid organ transplantation that is older than 50 years, has high BMI and a family history of diabetes mellitus? Please, comment if some of the observed

results could be related to different steroid tapering between all the articles reviewed in the meta- analysis and not to the main immunosuppressant drug used. Or if sirolimus receiving patients could have suffered more acute rejection episodes requiring high dose steroids in pulses as it was observed in the Elite-Symphony trial (DOI: 10.1056/NEJMoa067411). .

We have commented on this in limitations

(1) Science editor:

1 Scientific quality: The manuscript describes a Meta-Analysis of the Relative impact of different immunosuppressants on the incidence of post-transplant diabetes mellitus across solid organ transplant recipients. The topic is within the scope of the WJT. (1) Classification: Grade B;

(2) Summary of the Peer-Review Report: This study is overall in good quality. The questions raised by the reviewers should be answered;

Reviewer's questions have been answered as above

(3) Format: There are 2 tables and 3 figures;

(4) References: A total of 27 references are cited, including 2 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 (i.e. those that are most closely related to the topic of the manuscript) and remove all 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

We only have 1 self-cited reference= <10%

(6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

Nil concerns from us

2 Language evaluation: Classification: Grade B.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate. No academic misconduct was found in the Bing search.

4 Supplementary comments: This is an unsolicited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJT.

5 Issues raised:

(1)The title is too long, and it should be no more than 18 words;

This has been altered to 18 words

(2) The "Author Contributions" section is missing. Please provide the author contributions;

This has been added

(3) 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;

This has been provided

(4) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

This has been done

(5) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text; and

This has been done

(6) Please provide all authors' ORCIDs, and fill them into the "All Author List" on the online submission system.

This has been done

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Transplantation, 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. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

Title has been shortened