Decision Letter (JCQ-2025-0041)

From: [redacted]
To:
CC:
BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2025-0041

Body: 1-Dec-2025

Dear Dr Cao,

Manuscript ID JCQ-2025-0041 entitled "Benefit of Islet Transplantation in Type 1 Diabetes: A Systematic Review and Meta-Analysis" which you submitted to the Journal of Clinical Question, has been reviewed. The comments of the reviewer(s) are included at the bottom of this letter.

The reviewer(s) have recommended publication, but also suggest some revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript.

To submit your revised manuscript, follow the below steps.
1. Access to https://mc.manuscriptcentral.com/jcq and log into the site.
2. Click "Author" at the top left of the screen at "Home" page.
3. Click "Manuscripts with Decisions" on Author Dashboard page.
4. Click "create a revision" on the manuscript you are going to revise.
5. The system creates your revision manuscript form. Provide your comments about the revised points at the response field, fill in on each field step by step as same as you did for the original submission, and submit your revised manuscript.
IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.
Your manuscript number has been appended to denote a revision.

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Please also highlight the changes to your manuscript within the document by using the track changes mode in MS Word or by using bold or colored text.

Once the revised manuscript is prepared, you can upload it and submit it through your Author Center.

When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) in the space provided. You can use this space to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s).

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to the Journal of Clinical Question, your revised manuscript should be uploaded as soon as possible. If it is not possible for you to submit your revision in a reasonable amount of time, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to the Journal of Clinical Question and I look forward to receiving your revision.

Sincerely,
Richard S. Isaacs
Editor in Chief
Journal of Clinical Question

[Editor's Comments]
Associate Editor
Comments to the Author:
1. Check grammar and flow for minor errors.
2. Ensure all abbreviations are defined on first use in both abstract and main text.
3. Add ORCID IDs for authors if available

[Reviewer(s)' Comments]
Reviewer: 1

Comments to the Author
In the manuscript entitled “Benefit of Islet Transplantation in Type 1 Diabetes: A Systematic Review and Meta-Analysis,” Xiao-Qin and colleagues report the results of a meta-analysis focusing on insulin independence rates and 5-year mortality following islet transplantation. Although the findings themselves are not unexpected, the topic addressed by the authors is important for the continued advancement of clinical islet transplantation.
However, there are two critical issues that must be addressed prior to publication.
1. Omission of key literature:
The authors failed to include one of the most important and comprehensive studies in this field: “Pancreatic islet transplantation in type 1 diabetes: 20-year experience from a single-centre cohort in Canada” (Lancet Diabetes Endocrinol 2022;10:519–532). This study provides essential long-term outcome data and should be incorporated into the meta-analysis.
2. Inclusion of an inappropriate study:
Conversely, the inclusion of the CITR 2025 allograft report is inappropriate. This report is based on registry data and is highly likely to overlap with other published studies already included in the analysis, thereby introducing potential duplication. The authors should exclude this report from the meta-analysis.
Minor Points
1. The authors should specify which missing or unclear data were obtained through direct correspondence with the original study authors.
2. The definition of graft dysfunction should be clearly described.
3. The meta-analysis does not address outcomes related to glycemic stability or hypoglycemic episodes. This limitation should be explicitly acknowledged.
4. In Table 1, Anazawa et al. (2025) should be correctly identified as a prospective study.
5. In Table 1, Chetboun et al. (2023) and Tan et al. (2008) are listed but not included in the reference list.
6. The authors should clearly state that only intraportal islet transplantation cases were included in the analysis.
7. The statement that no language restrictions were applied is questionable and should be clarified or justified.

Reviewer: 2

Comments to the Author
This systematic review and meta-analysis addresses an important clinical question and provides a comprehensive synthesis of contemporary evidence on islet transplantation outcomes in adults with type 1 diabetes. The manuscript is generally well written, methodologically sound, and offers clinically relevant insights into insulin independence, graft durability, and safety.
Minor revisions:
In the Introduction, please correct minor grammatical issues (e.g., "the globally, the number of individuals" → "globally, the number of individuals") to improve readability.
Clarify the rationale for excluding simultaneous islet–kidney (SIK) transplantation from the quantitative analyses, as it is mentioned in the eligibility criteria but not included in pooled results.
In the Methods section, specify how insulin independence was defined across studies and whether definitions were harmonized for meta-analysis.
Consider adding a brief comment in the Discussion on how advances such as FDA-approved allogeneic islet products (e.g., Donislecel) may influence the generalizability of the findings.
Ensure consistency in terminology and abbreviations throughout the manuscript (e.g., ITA, IAK, SIK) and correct minor typographical errors in tables and figure captions.

Date Sent: 1-Dec-2025

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Author's Response to Decision Letter for (JCQ-2025-0041)

Benefit of Islet Transplantation in Type 1 Diabetes: A Systematic Review and Meta-Analysis

Dear Editor and Reviewers,
We sincerely thank the Associate Editor and the reviewers for their careful evaluation of our manuscript entitled "Benefit of Islet Transplantation in Type 1 Diabetes: A Systematic Review and Meta-Analysis." We appreciate their constructive comments, which have substantially improved the quality, clarity, and rigor of our work. Below, we provide a detailed point-by-point response to all comments. All changes have been incorporated into the revised manuscript unless otherwise stated.

Editor's Comments
1. Check grammar and flow for minor errors.
Response: We have carefully revised the entire manuscript to improve grammar, sentence structure, and overall flow. Minor grammatical errors and awkward phrasing have been corrected throughout the Abstract, Introduction, Methods, Results, and Discussion sections.

2. Ensure all abbreviations are defined on first use in both abstract and main text.
Response: All abbreviations are now defined at first mention in both the Abstract and the main text. We also reviewed the manuscript to ensure consistent use of abbreviations throughout (e.g., ITA, IAK, SIK).

3. Add ORCID IDs for authors if available
Response: ORCID IDs have been added for all authors for whom they are available.

Reviewer: 1
In the manuscript entitled "Benefit of Islet Transplantation in Type 1 Diabetes: A Systematic Review and Meta-Analysis," Xiao-Qin and colleagues report the results of a meta-analysis focusing on insulin independence rates and 5-year mortality following islet transplantation. Although the findings themselves are not unexpected, the topic addressed by the authors is important for the continued advancement of clinical islet transplantation.
However, there are two critical issues that must be addressed prior to publication.
1. Omission of key literature
The authors failed to include one of the most important and comprehensive studies in this field: "Pancreatic islet transplantation in type 1 diabetes: 20-year experience from a single-centre cohort in Canada" (Lancet Diabetes Endocrinol 2022;10:519–532). This study provides essential long-term outcome data and should be incorporated into the meta-analysis.
Response: We thank the reviewer for highlighting this important and comprehensive study. To maximize patient inclusion while avoiding duplicate enrollment, we prioritized data from the Collaborative Islet Transplant Registry (CITR). All included studies were carefully cross-checked against participating islet transplant centers within the CITR. As the cohort described in the cited Lancet Diabetes & Endocrinology study is incorporated within the CITR dataset, it was not listed as a separate reference to prevent duplication. However, given the relevance of the subgroup analysis on donor HLA-DQ8 status, we have incorporated this important finding into the Discussion section as follows: "Notably, one study reported an association between donor HLA-DQ8 positivity and superior graft outcomes."

2. Inclusion of an inappropriate study:
Conversely, the inclusion of the CITR 2025 allograft report is inappropriate. This report is based on registry data and is highly likely to overlap with other published studies already included in the analysis, thereby introducing potential duplication. The authors should exclude this report from the meta-analysis.
Response: We appreciate the reviewer's comment. Given the relatively small number of patients reported in islet transplantation studies, we sought to include all available registry-level data to comprehensively evaluate outcomes. The CITR 2025 allograft report was therefore included to enhance statistical power. To minimize potential overlap with individual cohort studies, we carefully reviewed the list of contributing islet transplant centers within the CITR and excluded overlapping cohorts from individual study tables. This approach was undertaken to balance completeness with avoidance of duplication.

Minor Points
1. The authors should specify which missing or unclear data were obtained through direct correspondence with the original study authors.
Response: Thank you for this comment. We have clarified in the Methods section that no missing or unclear data were obtained through direct correspondence with the original study authors; all data were extracted exclusively from the published reports.

2. The definition of graft dysfunction should be clearly described.
Response: Thank you for this comment. We have added the following definition to the Methods section: "Graft dysfunction was defined as a decline in islet graft performance characterized by detectable C-peptide levels (>0.3 ng/mL) with deterioration in glycemic control and/or a renewed requirement for exogenous insulin."
3. The meta-analysis does not address outcomes related to glycemic stability or hypoglycemic episodes. This limitation should be explicitly acknowledged.
Response: We have explicitly acknowledged this limitation in the Discussion section, noting that outcomes related to glycemic stability and hypoglycemic episodes were not consistently reported across included studies and therefore could not be meta-analyzed.
4. In Table 1, Anazawa et al. (2025) should be correctly identified as a prospective study.
Response: Thank you for pointing this out. Anazawa et al. (2025) is now correctly identified as a prospective study in Table 1.

5. In Table 1, Chetboun et al. (2023) and Tan et al. (2008) are listed but not included in the reference list.
Response: Thank you for this comment. As addressed in Major Comments 1 and 2, these cohorts are incorporated within the CITR dataset and were therefore not listed as separate references to avoid duplication.

6. The authors should clearly state that only intraportal islet transplantation cases were included in the analysis.
Response: Thank you for this comment. We have clarified in the Methods section that only intraportal islet transplantation cases were included, as specified in the inclusion criteria.

7. The statement that no language restrictions were applied is questionable and should be clarified or justified.
Response: Thank you for this comment. We have clarified that only studies published in the English language were included in this meta-analysis; no non-English articles were reviewed or analyzed.

Reviewer: 2
This systematic review and meta-analysis addresses an important clinical question and provides a comprehensive synthesis of contemporary evidence on islet transplantation outcomes in adults with type 1 diabetes. The manuscript is generally well written, methodologically sound, and offers clinically relevant insights into insulin independence, graft durability, and safety.
Minor revisions:
In the Introduction, please correct minor grammatical issues (e.g., "the globally, the number of individuals" → "globally, the number of individuals") to improve readability.
Response: Thank you for your comment on this point. The identified grammatical issue, along with similar minor errors in the Introduction, has been corrected to improve readability.

Clarify the rationale for excluding simultaneous islet–kidney (SIK) transplantation from the quantitative analyses, as it is mentioned in the eligibility criteria but not included in pooled results.
Response: Thank you for your comment on this point. Only one included study focused on SIK transplantation; therefore, its data were analyzed together with the IAK group and not pooled separately.

In the Methods section, specify how insulin independence was defined across studies and whether definitions were harmonized for meta-analysis.
Response: Thank you for your comment on this point. As suggested by Reviewer 1, we have added a dedicated section in the Methods defining insulin independence, graft dysfunction, and graft failure, and clarified that these definitions were applied as reported in the included studies.

Consider adding a brief comment in the Discussion on how advances such as FDA-approved allogeneic islet products (e.g., Donislecel) may influence the generalizability of the findings.
Response: Thank you for your comment on this point. We have added a brief discussion addressing how recent advances in islet transplantation, including U.S. Food and Drug Administration approval of standardized allogeneic islet products such as donislecel, may influence the generalizability of the findings. These products offer improved consistency in islet manufacturing, quality control, and regulatory oversight compared with earlier center-specific isolation protocols represented in the included studies. Consequently, outcomes associated with contemporary allogeneic islet products may differ from those reported herein, and future studies will be needed to determine whether these advances translate into improved long-term graft durability and broader clinical applicability.

Ensure consistency in terminology and abbreviations throughout the manuscript (e.g., ITA, IAK, SIK) and correct minor typographical errors in tables and figure captions.
Response: Thank you for your comment on this point. Terminology and abbreviations have been standardized throughout the manuscript, and minor typographical errors in tables and figure captions have been corrected.

Once again, we sincerely thank the Editor and Reviewers for their insightful and constructive feedback. We believe that the revisions have substantially strengthened the manuscript and clarified its clinical relevance. We hope that the revised version meets the journal's standards and look forward to your further consideration.

Sincerely,
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Email: caojingzhu1020@163.com

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