Decision Letter (JCQ-2025-0010)

From: [redacted]
To:
CC:
BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2025-0010

Body: 04-May-2025

Dear Professor Elsharkawy:

Manuscript ID JCQ-2025-0010 entitled "Efficacy of Antihypertensive Therapy in Primary IgA Nephropathy in Adults: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials" 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 minor 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,
Professor Richard Isaacs
Editor in Chief, Journal of Clinical Question
jcqeic@gleampub.com

[Editor's Comments]
Associate Editor
Comments to the Author:
(There are no comments.)

[Reviewer(s)' Comments]

Reviewer: 1

Comments to the Author
This NMA covers a good topic. The improvement is needed in the English language of manuscript.

Reviewer: 2

Comments to the Author
This manuscript presents a methodologically sound and clinically relevant systematic review and network meta-analysis (NMA) assessing the comparative efficacy of antihypertensive agents in adults with primary IgA nephropathy (IgAN). It addresses an important therapeutic gap by evaluating both conventional RAAS inhibitors and emerging endothelin receptor antagonists (ERAs). The study adheres well to PRISMA and GRADE guidelines, and the overall structure is clear and comprehensive.

Comment 1: Heterogeneity and Inconsistency
There is evidence of moderate-to-high heterogeneity in some outcomes, such as proteinuria reduction and serum creatinine (Scr). While Cochran's Q and I^2 statistics are reported, the manuscript would benefit from additional visual representation (e.g., forest plots or inconsistency networks).
Suggestion: Include graphical illustrations of heterogeneity and results from node-splitting analyses in either the main text or supplementary materials to aid readers in interpreting consistency across comparisons.

Comment 2: Interpretation of SUCRA Rankings vs. Statistical Significance
Although Sparsentan achieved the highest SUCRA ranking for proteinuria reduction, the differences were not statistically significant compared to other RAAS agents. This important nuance is briefly acknowledged but should be more explicitly emphasized.
Suggestion: Clearly distinguish between ranking-based findings and statistically significant results in both the abstract and main results sections to avoid overinterpretation.

Comment 3: Limited Safety Analysis
The safety analysis is underdeveloped, as NMA could not be performed due to limited available data. Although this limitation is noted, it warrants stronger emphasis given its clinical importance.
Suggestion: Discuss this limitation more prominently and consider recommending that future RCTs include standardized and detailed safety outcome reporting.

Comment 4: Interpretation of eGFR Results
While Sparsentan showed the greatest improvement in eGFR, the wide confidence interval (−30.7 to 55.8) indicates high imprecision. The current discussion may overstate the finding.
Suggestion: Add a brief clarification about the imprecision and interpret the eGFR findings with appropriate caution, especially in light of the non-significant comparisons.

Date Sent: 04-May-2025

Journal of Clinical Question

Author's Response to Decision Letter for (JCQ-2025-0010)

Efficacy of Antihypertensive Therapy in Primary IgA Nephropathy in Adults: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials

Dear Reviewers,
We sincerely thank the reviewers for their thoughtful and constructive feedback on our manuscript. We have carefully addressed each comment and implemented the suggested revisions to improve the quality, clarity, and rigor of our work. Below, we provide a detailed, point-by-point response to all reviewer comments.

Reviewer: 1
Comment: This NMA covers a good topic. The improvement is needed in the English language of the manuscript.
Response: We appreciate the reviewer's positive assessment. Regarding the language comment, a native English speaker with expertise in academic writing has carefully revised the entire manuscript for clarity and fluency. We believe these changes have significantly improved the manuscript's readability and precision.

Reviewer: 2
Comment 1:There is evidence of moderate-to-high heterogeneity in some outcomes, such as proteinuria reduction and serum creatinine (Scr). While Cochran's Q and I^2 statistics are reported, the manuscript would benefit from additional visual representation (e.g., forest plots or inconsistency networks).
Suggestion: Include graphical illustrations of heterogeneity and results from node-splitting analyses in either the main text or supplementary materials to aid readers in interpreting consistency across comparisons.
Response: Thank you for this valuable suggestion. To improve the visualization and interpretation of heterogeneity and network consistency, we have added heat plots for the outcomes of proteinuria reduction and serum creatinine, now included in the supplementary materials as Supplementary Figures S10 and S11. These plots highlight the contribution of each comparison to overall inconsistency, with the Enalapril vs. Losartan comparison showing a relatively higher inconsistency in both outcomes. Relevant references to these figures have been added to the Results and Discussion sections to enhance transparency and support a more nuanced understanding of the network findings.

Comment 2: Although Sparsentan achieved the highest SUCRA ranking for proteinuria reduction, the differences were not statistically significant compared to other RAAS agents. This important nuance is briefly acknowledged but should be more explicitly emphasized. Suggestion: Clearly distinguish between ranking-based findings and statistically significant results in both the abstract and main results sections to avoid overinterpretation.
Response: We fully agree with the reviewer's important observation. Specifically, we now emphasize that although Sparsentan demonstrated the highest SUCRA ranking for proteinuria reduction, the differences compared to other RAAS agents were not statistically significant. This clarification is crucial to prevent overinterpretation and reflects the probabilistic nature of ranking metrics. The absence of statistical significance may be attributed to limited sample sizes, overlapping confidence intervals, and variations in study design and patient characteristics across included trials. We believe these revisions contribute to a more accurate and balanced interpretation of the findings. Page 16,17, line 276-278.

Comment 3: The safety analysis is underdeveloped, as NMA could not be performed due to limited available data. Although this limitation is noted, it warrants stronger emphasis given its clinical importance. Suggestion: Discuss this limitation more prominently and consider recommending that future RCTs include standardized and detailed safety outcome reporting.
Response: We appreciate this important point. We have expanded the Discussion section to underscore the limitation of insufficient data for a formal safety NMA. Furthermore, we now explicitly recommend that future RCTs provide standardized, detailed safety outcome reporting to facilitate more robust comparisons. (page 18, line 316-319)

Comment 4: While Sparsentan showed the greatest improvement in eGFR, the wide confidence interval (−30.7 to 55.8) indicates high imprecision. The current discussion may overstate the finding. Suggestion: Add a brief clarification about the imprecision and interpret the eGFR findings with appropriate caution, especially in light of the non-significant comparisons.
Response: Thank you for highlighting this. We have revised the corresponding sentence in the Discussion section to acknowledge the wide confidence interval and lack of statistical significance. The eGFR finding is now interpreted with appropriate caution, and we have emphasized the need for more precise estimates from future studies. (page 18, line 309-312)

We hope that the revisions and clarifications provided in this response adequately address the reviewers'

concerns. We appreciate the opportunity to revise our manuscript and are grateful for the reviewers' valuable insights, which have contributed meaningfully to strengthening this study. We look forward to your further consideration.

Sincerely,
Magdy Elsharkawy
Department of Nephrology, Ain-Shams University
1 Elsarayat St., Abbaseya, Cairo, Egypt, 11517
Email: magdi35@hotmail.com
Phone: (+20) 26831231

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