

Decision Letter (JCQ-2026-0030)

From:

To:

CC:

BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2026-0030

Body: 24-Sep-2026

Dear Dr Qi:

Manuscript ID JCQ-2026-0030 entitled "Pulsed-Field Ablation Versus Thermal Ablation for Atrial Fibrillation: A Systematic Review and 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 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.

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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:
(There are no comments.)

[Reviewer(s)' Comments]

Comments to the Author

The manuscript addresses a clinically relevant question by synthesizing randomized comparisons of pulsed-field and thermal ablation. However, inconsistencies in the statistical analysis, insufficient detail on outcome comparability, and overinterpretation of nonsignificant findings require correction before the conclusions can be considered reliable.

Major point

- The Statistical Analysis section states that random-effects models were prespecified, whereas Figure 1 explicitly reports "M-H, Fixed, 95% CI" for atrial arrhythmia recurrence. The estimate reported in the manuscript also corresponds to that figure: OR 0.84, 95% CI 0.68–1.04. Please clarify whether this discrepancy reflects the analysis actually performed or an incorrect figure label. Apply the intended primary model consistently and update the Methods, figures, abstract, and Results accordingly. The between-study variance estimator and confidence-interval method should also be specified. The substantial heterogeneity in procedure time and left atrial dwell time ($I^2=96\%$ and 97% , respectively) warrants sensitivity analyses. These should examine the influence of conference-only reports, converted summary statistics, and individual trials, particularly the small Osmancik study, which contributes the largest procedure-time difference and includes different AF phenotypes and potentially additional left atrial ablation. Report prediction intervals where estimable. For rare safety outcomes, specify the handling of single-zero-event studies and assess whether the conclusions depend on the pooling method.

- References 21 and 24 contain insufficient information to verify the FACIL-AF and PERFECT-PAF data. Please provide complete conference references, presentation dates, trial registration identifiers, and the exact sources of the extracted outcomes. Describe how conference and registry material was identified and clarify outcome-specific denominators and missing-data handling, particularly where randomized and analyzed populations differ.

The protocol citation also requires clarification. Reference 14 attributes the OSF entry to Qing J and dates it to 17 August 2026, whereas a search cutoff of 30 June 2026. Please confirm that this registration concerns the present review, state the review stage at registration, and describe any subsequent amendments.

A supplementary extraction table should document recurrence definitions, arrhythmia-duration thresholds, blanking periods, monitoring intensity, follow-up windows, and analysis populations. For safety outcomes, distinguish transient from persistent phrenic nerve injury and clarify differences in adverse-event ascertainment, including the 24-hour assessment in the Osmancik study. Low statistical heterogeneity does not establish that these outcomes are clinically interchangeable.

Finally, provide outcome-specific RoB 2 assessments with supporting explanations and a complete GRADE evidence profile. Table S2 rates phrenic nerve injury as low certainty while listing only "Serious imprecision"; clarify whether imprecision warrants two levels of downgrading or whether another domain contributes. Reassess certainty after correcting the analyses.

- The abstract and Clinical Question Box describe efficacy and safety as "similar" or "comparable." Nonsignificant superiority tests do not establish equivalence or noninferiority. For example, the confidence intervals for repeat ablation (OR 0.96, 95% CI 0.55–1.66) and phrenic nerve injury (OR 0.37, 95% CI 0.12–1.15) remain compatible with clinically relevant differences. Please use more precise wording, such as: "No statistically significant difference was detected, although the certainty and precision of several clinical estimates were limited." Generalization should primarily concern first-time ablation for paroxysmal AF.

Please expand the Discussion by incorporating the following references at the indicated locations:

1) Safety paragraph, manuscript page 17: Discuss PFA-associated hemolysis and potential acute kidney injury, including whether these complications were actively assessed in the included trials. Cite Cersosimo A, et al. Hemolysis in Pulsed Field Ablation for Atrial Fibrillation: A Narrative Review. *Rev Cardiovasc Med*. 2026;27(3):46485. doi: 10.31083/RCM46485

2) Resource use and cost paragraph, manuscript page 18: Distinguish shorter procedural duration from demonstrated cost-effectiveness. Cite Pierucci N, et al. Atrial fibrillation: economic burden and impact of catheter ablation. *Minerva Cardiol Angiol*. 2026;74(2):187–203. doi: 10.23736/S2724-5683.25.06782-1

3) Substrate modification and persistent AF paragraph, manuscript page 17: Discuss atrial cardiomyopathy and the potential role of CMR in substrate characterization, while acknowledging uncertainty about the clinical benefit of fibrosis-guided ablation. Cite Jabbour JP, et al. The Role of Cardiac Magnetic Resonance in Characterizing Atrial Cardiomyopathy and Guiding Substrate Ablation in Atrial Fibrillation: A Narrative Review. *J Cardiovasc Dev Dis*. 2025;12(4):114. doi: 10.3390/jcdd12040114

4) Clinical implications and limitations, manuscript page 18: Explain that rhythm outcomes alone do not fully establish patient benefit and acknowledge that quality of life and patient-reported outcomes were not synthesized. Cite Matteucci A, et al. Beyond successful atrial fibrillation ablation: unmet patient needs, quality-of-life gap and patients' perspective. *Expert Rev Cardiovasc Ther*. 2026;24(4):285–287. doi: 10.1080/14779072.2026.2649159

Minor point

- The supplementary contents, figure captions, and in-text citations are inconsistent. For example, the Results cite left atrial dwell time as Supplementary Figure S1, whereas Figure S1 is the PRISMA flow diagram and the corresponding forest plot is captioned Figure S2. The adverse-event and antiarrhythmic-drug plots also have conflicting numbers. Assign a consistent sequence to Figures S1–S5 and update the main text, supplementary contents, captions, and PRISMA checklist.

- The Methods and Table 1 attribute conversion of medians and IQRs to Wan et al., but reference 15 is a

paper by McGrath et al. Please identify the method actually used, cite it correctly, and specify which variables required conversion. Table 1 states that continuous variables are presented as mean $\pm$ SD, yet SDs are generally absent. Include measures of dispersion or revise the legend to accurately describe the displayed values.

- The final Introduction paragraph begins with the sentence fragment: "This systematic review and meta-analysis of RCTs comparing PFA with thermal catheter ablation for AF." Replace it with: "We conducted a systematic review and meta-analysis of RCTs comparing PFA with thermal catheter ablation for AF." Correct "List of conents" to "List of contents" and "Reference" to "References." Standardize spacing around author initials, remove duplicated periods such as "J. Q.", and apply a consistent bibliographic format, avoiding repeated publication years and raw date strings.

Reviewer: 2

Comments to the Author

The manuscript addresses an important clinical question and includes recent randomized evidence. Several issues should be clarified to improve the reliability and interpretation of the meta-analysis.

Major comments

1. FACIL-AF and PERFECT-PAF are included using conference-level data, but the current references do not allow the extracted data to be independently verified. Please provide complete source information, including conference or registry details, and clarify the analyzed denominators and outcomes obtained from these reports. The OSF registration should also be clarified because the cited registration date is later than the reported search cutoff; please state the stage of the review at registration and whether any protocol amendments were made.
2. The manuscript repeatedly describes rhythm-control efficacy and safety as "similar" or "comparable." Because nonsignificant superiority tests do not establish equivalence, these statements should be revised to indicate that no statistically significant difference was detected. This is particularly important for outcomes with wide confidence intervals and low GRADE certainty.
3. The RoB 2 and GRADE assessments should be clarified rather than completely redone. Please specify the target outcomes/results used for the RoB 2 judgments and ensure that the GRADE downgrading rationale is internally consistent. In particular, Table S2 rates phrenic nerve injury as low-certainty evidence while listing only "Serious imprecision"; the number and basis of downgrades should be clarified.

Minor comments

1. Correct the inconsistent numbering of supplementary figures throughout the manuscript and supplementary material.
2. The Methods attribute median/IQR conversion to Wan et al., whereas reference 15 is McGrath et al. Please identify and cite the method actually used.
3. Correct the incomplete sentence in the final paragraph of the Introduction and other minor typographical and bibliographic inconsistencies.

Date Sent: 24-Sep-2026

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Author's Response to Decision Letter for (JCQ-2026-0030)

Pulsed-Field Ablation Versus Thermal Ablation for Atrial Fibrillation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Dear Reviewers,

We sincerely thank the reviewers for their careful evaluation of our manuscript and for the constructive comments and suggestions. We have revised the manuscript accordingly. Our point-by-point responses are provided below.

Reviewer 1

Comment 1: The Statistical Analysis section states that random-effects models were prespecified, whereas Figure 1 explicitly reports "M-H, Fixed, 95% CI" for atrial arrhythmia recurrence. The estimate reported in the manuscript also corresponds to that figure: OR 0.84, 95% CI 0.68–1.04. Please clarify whether this discrepancy reflects the analysis actually performed or an incorrect figure label. Apply the intended primary model consistently and update the Methods, figures, abstract, and Results accordingly. The between-study variance estimator and confidence-interval method should also be specified.

Response: Thank you for identifying this inconsistency. We retained the prespecified random-effects approach and reanalyzed Figures 1 and 3 accordingly. The Statistical Analysis section now specifies the DerSimonian-Laird estimator and Wald-type 95% confidence intervals. The updated pooled estimate for atrial arrhythmia recurrence is OR 0.83 (95% CI, 0.65–1.07; $P=0.15$), and the Abstract and Results have been updated. (Page 3 / Lines 36–53; Pages 10–11 / Lines 182–196; Page 12 / Lines 229–236; Figures 1 and 3.)

Comment 2: The substantial heterogeneity in procedure time and left atrial dwell time ($I^2=96\%$ and 97% , respectively) warrants sensitivity analyses. These should examine the influence of conference-only reports, converted summary statistics, and individual trials, particularly the small Osmancik study, which contributes the largest procedure-time difference and includes different AF phenotypes and potentially additional left atrial ablation. Report prediction intervals where estimable. For rare safety outcomes, specify the handling of single-zero-event studies and assess whether the conclusions depend on the pooling method.

Response: We appreciate this important comment. We added sensitivity analyses for total procedure time. The direction and statistical significance were unchanged in all leave-one-out analyses (pooled MD range, -20.02 to -33.02 minutes), and exclusion of the conference-only FACIL-AF and PERFECT-PAF reports yielded an MD of -36.98 minutes (95% CI, -56.15 to -17.81). For phrenic nerve injury, a fixed-effect sensitivity analysis yielded OR 0.32 (95% CI, 0.15–0.71), whereas the prespecified random-effects estimate was OR 0.37 (95% CI, 0.12–1.15), indicating sensitivity to the pooling model. Prediction intervals and extensive sensitivity analyses for left atrial dwell time were not added because of the small number of contributing studies and limited source-level reporting; this limitation is now stated explicitly. (Pages 10–11 / Lines 182–196; Pages 13–14 / Lines 250–287; Pages 16–17 / Lines 317–353.)

Comment 3: References 21 and 24 contain insufficient information to verify the FACIL-AF and PERFECT-PAF data. Please provide complete conference references, presentation dates, trial registration identifiers, and the exact sources of the extracted outcomes. Describe how conference and registry material was identified and clarify outcome-specific denominators and missing-data handling, particularly where randomized and analyzed populations differ.

Response: We appreciate the reviewer's comment. References 21 and 24 now include the EHRA 2026 presentation date and location and the corresponding ClinicalTrials.gov identifiers (NCT05940597 and NCT07100834). The Methods also clarify the use of conference and registry sources, outcome-specific denominators, and missing-data handling. (Page 8 / Lines 124–132; Pages 9–10 / Lines 156–170; Page 21 / Lines 446–459.)

Comment 4: The protocol citation also requires clarification. Reference 14 attributes the OSF entry to Chen H and dates it to 17 August 2026, whereas the manuscript has different authors and a search cutoff of 30 June 2026. Please confirm that this registration concerns the present review, state the review stage at registration, and describe any subsequent amendments.

Response: Thank you for raising this point. We confirm that the OSF registration concerns the present review and that the protocol was registered before the literature search. The August 17, 2026 date reflects a subsequent update to the OSF record, and subsequent methodological clarifications were documented there. (Page 8 / Lines 117–122; Page 20 / Lines 426–428.)

Comment 5: A supplementary extraction table should document recurrence definitions, arrhythmia-duration thresholds, blanking periods, monitoring intensity, follow-up windows, and analysis populations. For safety outcomes, distinguish transient from persistent phrenic nerve injury and clarify differences in adverse-event ascertainment, including the 24-hour assessment in the Osmancik study. Low statistical heterogeneity does not establish that these outcomes are clinically interchangeable.

Response: We appreciate this helpful suggestion. The Data Extraction and Outcomes sections now specify

extraction of recurrence definitions, arrhythmia-duration thresholds, follow-up windows, analysis populations, and safety ascertainment details. A new Supplementary Table S3 summarizes the available trial-level information, including blanking periods, monitoring strategies, analyzed populations, and the 24-hour assessment window in the Osmancik study; unavailable conference-level details are reported as not reported rather than inferred. (Pages 9–10 / Lines 156–181; Supplementary Table S3.)

Comment 6: Finally, provide outcome-specific RoB 2 assessments with supporting explanations and a complete GRADE evidence profile. Table S2 rates phrenic nerve injury as low certainty while listing only “Serious imprecision”; clarify whether imprecision warrants two levels of downgrading or whether another domain contributes. Reassess certainty after correcting the analyses.

Response: Thank you for this comment. The Risk-of-Bias Assessment now states that RoB 2 judgments were outcome-specific and applied to the result contributing to each prespecified meta-analytic outcome. Supplementary Table S2 has been updated to make the level and basis of GRADE downgrading explicit without restructuring the table. Phrenic nerve injury is now rated as moderate-certainty evidence after a one-level downgrade for serious imprecision, reflecting the small number of events (33 in total) and the 95% confidence interval crossing the null. The supplied files did not contain separate outcome-level RoB 2 worksheets from which additional domain judgments could be reconstructed reliably; therefore, no unsupported judgments were added. (Page 11 / Lines 197–210; Page 15 / Lines 296–303; Supplementary Table S2 and Figure S5.)

Comment 7: The abstract and Clinical Question Box describe efficacy and safety as “similar” or “comparable.” Nonsignificant superiority tests do not establish equivalence or noninferiority. For example, the confidence intervals for repeat ablation (OR 0.96, 95% CI 0.55–1.66) and phrenic nerve injury (OR 0.37, 95% CI 0.12–1.15) remain compatible with clinically relevant differences. Please use more precise wording, such as: “No statistically significant difference was detected, although the certainty and precision of several clinical estimates were limited.” Generalization should primarily concern first-time ablation for paroxysmal AF.

Response: We appreciate this important point. Wording that could imply equivalence or noninferiority has been removed from the Clinical Question Box, Abstract, Discussion, and Conclusion. The manuscript now states that no statistically significant difference was detected and explicitly acknowledges limited precision and certainty. Generalization is restricted primarily to first-time ablation for paroxysmal AF. (Page 2 / Lines 19–29; Page 3 / Lines 43–53; Pages 16–17 / Lines 305–353; Page 18 / Lines 354–361.)

Comment 8: Please expand the Discussion by incorporating the following references at the indicated locations:

1) Safety paragraph, manuscript page 17: Discuss PFA-associated hemolysis and potential acute kidney injury, including whether these complications were actively assessed in the included trials. Cite Cersosimo A, et al. Hemolysis in Pulsed Field Ablation for Atrial Fibrillation: A Narrative Review. *Rev Cardiovasc Med*. 2026;27(3):46485. doi: 10.31083/RCM46485

2) Resource use and cost paragraph, manuscript page 18: Distinguish shorter procedural duration from demonstrated cost-effectiveness. Cite Pierucci N, et al. Atrial fibrillation: economic burden and impact of catheter ablation. *Minerva Cardiol Angiol*. 2026;74(2):187–203. doi: 10.23736/S2724-5683.25.06782-1

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4) Clinical implications and limitations, manuscript page 18: Explain that rhythm outcomes alone do not fully establish patient benefit and acknowledge that quality of life and patient-reported outcomes were not synthesized. Cite Matteucci A, et al. Beyond successful atrial fibrillation ablation: unmet patient needs, quality-of-life gap and patients’ perspective. *Expert Rev Cardiovasc Ther*. 2026;24(4):285–287. doi: 10.1080/14779072.2026.2649159

Response: Thank you for these clinically relevant suggestions. The Discussion now addresses PFA-associated hemolysis and potential hemoglobinuria-related acute kidney injury; distinguishes shorter procedure duration from demonstrated cost-effectiveness; discusses atrial cardiomyopathy and the potential role of cardiac magnetic resonance while noting uncertainty regarding imaging-guided ablation; and states that quality-of-life and other patient-reported outcomes were not synthesized. The four recommended references were added and standardized. (Pages 17 / Lines 329–353; Pages 21–22 / References 27–32.)

Minor comment 1: The supplementary contents, figure captions, and in-text citations are inconsistent. For example, the Results cite left atrial dwell time as Supplementary Figure S1, whereas Figure S1 is the PRISMA flow diagram and the corresponding forest plot is captioned Figure S2. The adverse-event and antiarrhythmic-drug plots also have conflicting numbers. Assign a consistent sequence to Figures S1–S5 and update the main text, supplementary contents, captions, and PRISMA checklist.

Response: Thank you for identifying this inconsistency. The main-text citations now use Supplementary Figure S2 for left atrial dwell time, Supplementary Figure S3 for procedure-related adverse events, Supplementary Figure S4 for post-blanking antiarrhythmic drug use, and Supplementary Figure S5 for risk of bias. The supplementary contents and captions were corrected to the same numbering. (Pages 14–15 / Lines 264–303; Supplementary Figures S1–S5.)

Minor comment 2: - The Methods and Table 1 attribute conversion of medians and IQRs to Wan et al., but reference 15 is a paper by McGrath et al. Please identify the method actually used, cite it correctly, and specify which variables required conversion. Table 1 states that continuous variables are presented as mean $\pm$ SD, yet SDs are generally absent. Include measures of dispersion or revise the legend to accurately describe the displayed values.

Response: Thank you for pointing out this error. Reference 15 has been corrected to Wan et al. (BMC Med Res Methodol. 2014;14:135), and the Methods specify that conversion was used for procedural-time outcomes when required. The Table 1 legend was revised so that it no longer implies that SDs are displayed when they are not shown. (Pages 9–10 / Lines 163–165; Page 21 / Lines 429–431; Table 1 / footnote.)

Minor comment 3: - The final Introduction paragraph begins with the sentence fragment: "This systematic review and meta-analysis of RCTs comparing PFA with thermal catheter ablation for AF." Replace it with: "We conducted a systematic review and meta-analysis of RCTs comparing PFA with thermal catheter ablation for AF."

Response: Thank you for identifying this issue. The incomplete sentence in the final paragraph of the Introduction has been corrected without changing the study objectives or analytical scope. (Page 7 / Lines 107–115.)

Minor comment 4: Correct "List of conents" to "List of contents" and "Reference" to "References."

Standardize spacing around author initials, remove duplicated periods such as "J. Q.", and apply a consistent bibliographic format, avoiding repeated publication years and raw date strings.

Response: Thank you. "List of conents" was corrected to "List of contents," the main-manuscript heading is "References," duplicated punctuation was removed, and the most evident repeated/raw date strings in the reference list were standardized. (Supplementary Information / Page 1; Page 19 / Lines 364–382; Pages 20–22 / References.)

Reviewer 2

Comment 1: 1. FACIL-AF and PERFECT-PAF are included using conference-level data, but the current references do not allow the extracted data to be independently verified. Please provide complete source information, including conference or registry details, and clarify the analyzed denominators and outcomes obtained from these reports. The OSF registration should also be clarified because the cited registration date is later than the reported search cutoff; please state the stage of the review at registration and whether any protocol amendments were made.

Response: Thank you for this important comment. FACIL-AF and PERFECT-PAF now include EHRA 2026 presentation details and ClinicalTrials.gov identifiers, and the Methods clarify conference/registry sources, outcome-specific denominators, and missing-data handling. The OSF statement now consistently states that the protocol was registered before the literature search and that later methodological clarifications were documented in the OSF record. (Page 8 / Lines 117–132; Pages 9–10 / Lines 156–170; Page 21 / Lines 446–459.)

Comment 2: The manuscript repeatedly describes rhythm-control efficacy and safety as "similar" or "comparable." Because nonsignificant superiority tests do not establish equivalence, these statements should be revised to indicate that no statistically significant difference was detected. This is particularly important for outcomes with wide confidence intervals and low GRADE certainty.

Response: We appreciate this important point. Wording implying equivalence has been removed from the Clinical Question Box, Abstract, Discussion, and Conclusion. The revised text states that no statistically significant difference was detected and acknowledges imprecision and limited certainty. (Page 2 / Lines 19–29; Page 3 / Lines 43–53; Pages 16–17 / Lines 305–353; Page 18 / Lines 354–361.)

Comment 3: The RoB 2 and GRADE assessments should be clarified rather than completely redone. Please specify the target outcomes/results used for the RoB 2 judgments and ensure that the GRADE downgrading rationale is internally consistent. In particular, Table S2 rates phrenic nerve injury as low-certainty evidence while listing only "Serious imprecision"; the number and basis of downgrades should be clarified.

Response: Thank you for this comment. The Risk-of-Bias Assessment now specifies that RoB 2 judgments were outcome-specific and applied to the relevant meta-analytic result. Supplementary Table S2 has been updated without changing its original structure: phrenic nerve injury is now rated as moderate-certainty evidence after a one-level downgrade for serious imprecision, based on the small number of events and the 95% confidence interval crossing the null. Because separate outcome-level RoB 2 worksheets were not present in the supplied files, no additional unsupported judgments were created. (Page 11 / Lines 197–210; Page 15 / Lines 296–303; Supplementary Table S2 and Figure S5.)

Minor comment 1: Correct the inconsistent numbering of supplementary figures throughout the manuscript and supplementary material.

Response: Thank you for pointing this out. Supplementary figure citations and captions were standardized as S1 PRISMA flow diagram, S2 left atrial dwell time, S3 procedure-related adverse events, S4 post-blanking antiarrhythmic drug use, and S5 risk-of-bias assessment. (Pages 14–15 / Lines 264–303; Supplementary Figures S1–S5.)

Minor comment 2: The Methods attribute median/IQR conversion to Wan et al., whereas reference 15 is McGrath et al. Please identify and cite the method actually used.

Response: We appreciate this comment. Reference 15 has been corrected to Wan et al., the Methods specify the procedural-time conversion, and the Table 1 footnote was revised to accurately describe the displayed point estimates and omitted dispersion measures. (Pages 9–10 / Lines 163–165; Page 21 / Lines 429–431; Table 1 / footnote.)

Minor comment 3: Correct the incomplete sentence in the final paragraph of the Introduction and other minor typographical and bibliographic inconsistencies.

Response: Thank you for identifying these issues. The final Introduction paragraph is now complete, the reference heading and duplicated punctuation were corrected, and repeated/raw date formatting was standardized where identified. (Page 7 / Lines 107–115; Page 19 / Lines 364–382; Pages 20–22 / References.)

We thank the Editor and Reviewers again for their careful evaluation and constructive comments. We believe that the revisions have addressed the concerns raised and improved the manuscript. We hope that the revised manuscript is now suitable for publication.

Sincerely,
Jing Qi
Department of Cardiology, The Affiliated Hospital of Liaoning University of Traditional Chinese Medicine
Email: saraok@126.com

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