REPLY

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Although the Tromp et al[1] used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) to assess the confidence of the estimates, the GRADE results were not considered in the ranking process. We suggest that they use the GRADE contextualized framework to rank the treatments,[5] which could avoid the limitations of SUCRA. If Tromp et al do this, they might get different but more reliable rankings.

To conclude, when ranking the effectiveness and/or harm of treatments in an NMA, we suggest that researchers should not rely only on the SUCRA scores of treatments but also consider the certainty of evidence to avoid making misleading conclusions.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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REPLY: A Systematic Review and Network Meta-Analysis of Pharmacological Treatment of HFrEF

We appreciate the excellent comments from Mr Du and colleagues on our recently published paper.[1] The authors rightfully point out that ranking treatments based on the surface under the cumulative ranking (SUCRA) score[2] might lead to unreliable results. Therefore, the confidence of the evidence—captured by the Grading of Recommendations Assessment, Development and Evaluation (GRADE)—should also be considered.

In our published paper, treatment combinations presented in the forest plots were ranked according to their strength of association and number of medications. The SUCRA *P* values were provided in the supplemental material. We considered most articles to be of high quality according to the GRADE criteria because most studies were single- or double-blind phase III randomized controlled trials. The 4 studies with the highest risk of bias were not double-blinded, which might have introduced bias.[3-6] However, when excluding these 16 studies, our results do not meaningfully change (**Figure 1**). The most significant difference is seen in digoxin studies. The limited differences between these results and our published study are mainly because most of the included studies were considered high or very high quality. Therefore, stratifying our results according to the GRADE criteria would not affect our findings. However, we agree with the authors that the value of different treatment combinations in network meta-analyses should not be judged solely based on the SUCRA *P* values or strength of association. Other factors should be considered, including the quality and quantity of the available evidence.

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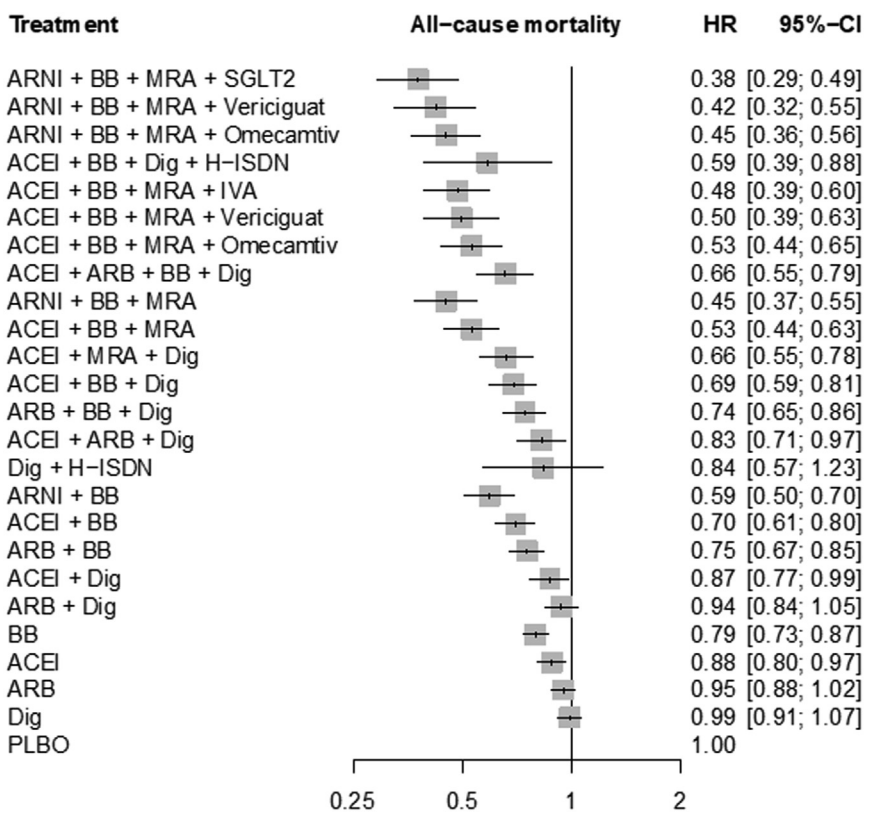
FIGURE 1 Relative Risk Reduction for All-Cause Mortality of Different Pharmacologic Treatment Combinations for Heart Failure Derived From Studies With High Quality



ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; ARNI = angiotensin receptor-neprilysin inhibitors; BB = beta blockers; Dig = digoxin; H-ISDN = hydralazine-isosorbide dinitrate; IVA = ivabradine; MRA = mineralocorticoid receptor antagonists; PLBO = placebo; SGLT2 = sodium glucose cotransporter-2.

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