Insulin Detemir vs Neutral Protamine Hagedorn in Pregnancy: a reply

We thank Dr Singh and colleagues for their insightful comments regarding “Detemir vs Neutral Protamine Hagedorn insulin for diabetes mellitus in pregnancy: a comparative effectiveness, randomized controlled trial.”

First, the authors commented on differences in the study groups’ baseline characteristics. Although we appreciate their comment, testing for baseline differences between the groups in randomized controlled trials (RCTs) is inappropriate, as pointed out by several papers and the Consolidated Standards of Reporting Trials statement.1,2 An RCT ensures that allocation of patients to treatments is left purely to chance. Although random assignment prevents selection bias, it does not guarantee that the groups are equivalent at baseline. However, any differences are the result of chance rather than bias.2

Second, the authors commented on glycemic control. Although we do have glucose levels, that is not the focus of this manuscript. There are many glucose recordings for each patient with each visit, and we think that reporting a median fasting or postprandial glucose in each group could be biased from number of visits, number of glucose recordings the patient brought to each visit, etc. As the authors stated, we agree that the neonatal and maternal outcomes will reflect glucose control during pregnancy.

Third, the authors commented on the use of lunchtime insulin with Neutral Protamine Hagedorn. As stated in the article, there was no difference in the use rate of short-acting insulin between the groups.

Fourth, the authors commented on the classification of gestational diabetes mellitus diagnosed before 20 weeks in pregnancy as an overt type 2 diabetes mellitus. This classification is based on the American Diabetes Association criteria, as stated and cited in the manuscript.

Lastly, the authors have asked to provide P values and adjustments for confounders. We designed this study as a Bayesian RCT to provide probabilities of benefit and harm from either intervention. It is not possible to calculate these quantities from frequentist statistics. Furthermore, P values and confidence intervals are often misinterpreted and incorrectly dichotomized into “significant” and “nonsignificant” results.3 To avoid these pitfalls, we chose a Bayesian design and analysis that is less prone to these issues while providing probabilities that can be directly used for decision-making. Regarding the small sample size, as stated in the manuscript, a confirmatory RCT with a larger sample size may be needed to ascertain if uncommon events occur with similar frequency in the 2 groups. We encourage the authors to conduct a similar trial at their institute.

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