

Reply letter to comment on “Impact of insulin use on outcomes of diabetic breast cancer patients: a systematic review and meta-analysis”

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Dear Author,

At the outset, we thank Wang et al¹ for their interest in our article and their subsequent comments. However, we would like to clarify that not all the flaws pointed out by Wang et al¹ are true.

Foremost, we agree with the authors that a systematic review should be able to include all available studies in literature and ideally should search for all possible databases. However, this has to be balanced against the constraints of time and resources as well. PubMed and CENTRAL have been recommended to search for studies for systematic reviews; and other databases like Embase, CINAHL, Web of Science can also be used to extend the search². However, more important are the keywords used and the absence of filters which can make or break search results. In our study, while we used only PubMed, Embase and CENTRAL, our search strategy was broad and without any filters to include maximum search results. We firmly believe searching these databases was sufficient and no studies were missed. The two studies pointed out by Wang et al¹ as being “missed” in our review are incorrect. The study of Redaniel et al³ has only compared the risk of breast cancer between insulin users and non-users. While at the outset, they planned to compare risk of mortality between breast cancer patients based on the type of diabetic drug, the authors mention in their article that: “There were not enough women with breast cancer to assess associations of treatments for diabetes with mortality outcomes”. The second study pointed by Wang et al¹ as being missed is that of Baglia et al⁴. On the contrary, this study has already been included in our review with reference number 16.

Secondly, the random-effects model has been used for several years for conducting meta-analysis when there is significant heterogeneity amongst the included studies and this model was followed in our review as well. However, we would like to thank the authors for bringing to our notice the IVhet model which reportedly performs better than the random effects model⁵. It was wonderful on the part of the authors to re-test our results based on this model as it provides the readers with a comprehensive analysis. While most of our results were similar to the IVhet model, the outcome for all-cause mortality was non-significant (HR = 1.30, 95% CI 1.00 to 1.69). It is important to note that the lower end of the 95% CI is 1 and the over HR is 1.3, which suggests a tendency of increased mortality with insulin use.

Lastly, as per the authors our results should be interpreted with caution due to several limitations of the included studies. This has already been pointed out in our article wherein the limitations of included studies are described in detail in the discussion. In the conclusion section, we ourselves have mentioned that: “Results should be interpreted with caution due to the several limitations of the review.”

We once again thank the authors for their comments but reiterate the correctness of our study as well.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

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