Author's response to reviews

Title: Phase IV non-inferiority trials and additional claims of benefit

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Dear Editor,

We wish to submit a manuscript entitled, “Phase IV non-inferiority trials and additional claims of benefit.” We have earlier submitted this article to BMC Medicine but we were advised by the editors that our article is better suited to the scope and readership of BMC Medical Research Methodology.

The clinical value of phase IV non-inferiority trials cannot solely depend on efficacy endpoints, which were already established in pre-authorization trials. Notwithstanding the fact that all non-inferiority trials need to make additional benefit claims, the fact that phase IV trials should typically inform clinical decisions reinforces the moral obligation to design phase IV non-inferiority trials not only with effectiveness endpoints but with methodologically supported additional benefit claims as well. In our manuscript, we looked at 41 post-authorization non-inferiority trials and investigated whether 1.) these trials made additional benefit claims; and 2.) whether these additional benefit claims are scientifically supported by appropriate testing such as statistical tests. We found that only half of the post-authorization NI trials made additional benefit claims and that these benefit claims are seldom supported by appropriate tests. We conclude that there is more room for improvement in terms of proving additional benefit claims within the post-authorization phase.
Given the current drive to improve phase IV trials, including measures to improve the quantity and quality of postmarketing commitments, we are convinced that our manuscript is timely, relevant, and interesting, especially for the readers of BMC Medical Research Methodology.

Thank you.

Sincerely,

Rosemarie Bernabe, MA and
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For the co-authors:
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