Author's response to reviews

Title: Even more suicide attempts in clinical trials with paroxetine randomised against placebo.

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Author’s response to reviews:

Dear Editor,

Authors’ comments
Article:
Even more suicide attempts in clinical trials with paroxetine randomised against placebo

General:
We feel that we have entered into a rather peculiar situation after reading the reports of the two reviewers. One reviewer, who also has reviewed the predecessor of the present paper, is very positive, mainly asking for some clarifications. The second reviewer dislikes the way we present our Bayesian analysis and is hence very negative. However, our statistical analysis is just the one that was used in the previous paper and was the end product of a dialogue with the reviewer Anthony O'Hagan. For one, we feel it would be confusing for the readers to change the statistical approach in this follow up paper. Secondly, the p-value approach suggested by the second reviewer is extremely hard to communicate, especially in this short commentary article.

We notice that the second reviewer states that our article provides "... publicity for this interesting admission ...." A major reason for submitting our contribution in the present manner is that this "admission" by GSK has not been properly published. It has only been pasted on a website, unsearchable by librarian means and hardly commented scientifically nor in public media.

Specific comments:
Reviewer I:
Minor Essential Revisions:
1. References 4 and 5 can be opened. (Notice to remove the inverted commas.)
2. They are accessible.
3. Yes, done. (Given in the list of references.)
4. We now write:" We let thetap and thetad be the mean number, or intensity, per year of a suicide attempt for a random patient in the 19 studies in the placebo and treatment group, respectively. We performed simulations by making 80 000 random draws of thetap and thetad, from their independent posterior distributions. We computed the logarithms of the ratios thetad/ thetap, and constructed posterior probability density plots by applying a standard density estimation technique to these 80 000 numbers." 
5. We have added:" Hence, we can be at least 98 % sure that paroxetine increases suicide attempts."

Reviewer II:
Major Compulsory Revision
The reviewer states that "any Bayesian analysis must be accompanied by an indication of the parameter values supported by the likelihood, ......" This is just what we do in our concluding remark: "We conclude that irrespective of the various prior assumptions, we now see clearer that the data strongly suggest that the use of antidepressant drugs is connected with an increased intensity of suicide attempts per year, not only among young people, but also among adults."

Furthermore, we agree that the comparison of our findings with the p-value from GSK is of less importance. Hence, we have for instance removed the sentence in the Results section: "This is much stronger evidence than the p value equal to 0,058 reported by GSK."
The Bayesian emphasis is also reduced by removing in the conclusion on page 1: "...and we look forward to Bayesian statistics being regularly used during clinical trial evaluations."

Since we were asked by BMC Medicine to write a full article after first having written a letter, we uphold the choice of a full article. We hope, based on the information provided by us, that BMC Medicine can accept the revised version of our manuscript.

If you are still in doubt on the statistical issue, with reference to the link between the second reviewer and the GSK, we suggest that you ask Anthony O'Hagan for a short comment, which we believe he will accept.