Author's response to reviews

**Title:** The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method

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**Author's response to reviews:** see over
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Your reference:
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Subject:
Manuscript of IntHout, Ioannidis, Borm.
New title: The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method

Dear Editor,

Thank you very much for your favorable response on our manuscript.

We have revised the manuscript according to the suggestions of the reviewers. We hope you will consider our paper now suitable for publication in BMC Medical Research Methods.

On the following pages we included the manuscript details and an itemized, point-to-point response to the comments of the reviewers. We have incorporated these comments into the revised version of the manuscript.
We attached a clean and a marked version of our revised manuscript. Changes in the marked version are highlighted in red as tracked changes.

In addition to the step-by-step method described in the paper, we have added an excel sheet as supplementary material. This is mentioned in the full text as: “An Excel sheet is available as supplementary web material.” This Excel file aims to make the HKSJ method even more accessible. We do hope that you agree.

We are looking forward to hear from you. Please do not hesitate to contact us in case of questions.

Yours faithfully,

On behalf of all co-authors,

Joanna IntHout, MSc
Manuscript & author details

In total the paper contains four tables and one figure, plus two figures and an Excel sheet as additional web material. Number of words in body text of manuscript: 4435. The manuscript has been submitted solely to your journal and it is not published, in press, or submitted elsewhere. We prepared the complete text, and it is suitable for anonymous review. We don’t have any conflict of interest. We have seen, read, and understood your guidelines on copyright. The names of all the co-authors have been included in the manuscript and these co-authors all had an active part in the final manuscript.

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Competing interests
The authors declare that they have no competing interests.

Authors' contributions
GB conceived the idea. JIH contributed substantially to the study design, developed the software and performed the statistical analyses. JIH, GB and JPAI drafted the manuscript, and read and approved the final manuscript.

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We would like to thank The Cochrane Library, London, UK for supplying the statistical data of intervention studies added in 2012 to the Cochrane Database of Systematic Reviews. In addition we would like to thank the reviewers Guido Knapp and Julio Sánchez-Meca for their helpful comments that improved this manuscript.
Reviewers’ Reports

Reviewer’s Report  - Julio Sánchez-Meca
“The authors have satisfactorily addressed all my suggestions. So, I have not more comments about this paper.”

Author’s response:
Thank you.

Reviewer’s Report  - Guido Knapp
Version: 1 Date: 3 December 2013

Major Compulsory Revisions

Comment 1:
“Maybe you can add at the end of the section on "Methods-Simulations" that meta-analysis is done on the log scale for dichotomous outcomes and the results are then backtransformed to the original scale. The error rates are then determined for OR = 1 or RR = 1. More details are given in the appendix.”

Author’s response 1:
Thank you for your suggestion. We added the following text: “In these cases, meta-analysis was done on the logarithmic scale, and the error rates were determined for OR = 1 or RR = 1. More details can be found in Appendices 1 and 2.”
Our simulation aimed at the evaluation of error rates; therefore we did not back-transform the simulation results.

Comment 2:
“I would prefer to see Figure 1 and 2 in one figure like the two figures in the supplementary material. Then it is easier to compare the two methods.”

Author’s response 2:
Thank you for your suggestion. We have replaced Figures 1 and 2 by one figure as suggested.
Comment 3:
“The simulation for risk ratio is more difficult than for odds ratio. How do you guarantee that \( p_a \) and \( p_b \) are in the interval \((0,1)\) when simulating the risk ratio? Given small or large values of \( p_0 \), it must occur that \( p_a \) and \( p_b \) are outside the unit interval.”

Author’s response 3:
Thank you for your comment. Indeed with this simulation the risks can go outside the \([0,1]\) interval. Therefore in the (original) simulations there was a threshold on the values of \( p_a \) and \( p_b \). This was not yet explicitly mentioned in the appendix. We have added the following sentence to Appendix 2C:

“Event rates below 0.01 or above 0.99 were replaced by 0.01 or 0.99, respectively.”

Minor Essential Revisions

Comment 1:
“In Appendix 1, \( \tau^2 \) is the heterogeneity parameter, I think, not \( \tau \)."

Author’s response 1:
Thank you. We corrected the typo.

Comment 2:
In Appendix 1, check the variance formula \( \text{var}_{\text{HKSJ}} \); there are two weird parentheses around \( y_i \)

Author’s response 3:
We do apologize, but in our (word) version we do not see any strange parentheses around \( y_i \). In order to prevent similar confusion in the future, we have changed the HKSJ variance formula into a more common notation:

\[
\text{var}_{\text{HKSJ}} = \frac{\sum w_i (y_i - \bar{y}_R)^2}{(k-1) \sum w_i^2}
\]
Comment 3:
"There is a figure with heading: Method=1, scenario=3: one large trial, which does not fit to the other figures."

Author’s response 3:
Thank you for your comment. The figure was deleted.