Reviewer’s report

Title: WHAT'S THE UPTAKE? Pragmatic RCTs may be used to estimate uptake, and thereby population impact of interventions, but better reporting of trial recruitment processes is needed.

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Reviewer: Lisa Susan Wieland

Reviewer's report:

This is an ingenious approach to estimating the effectiveness of interventions, and an interesting read. However, some limitations and further explanations might be considered.

In general, there could be additional attention given to the ways in which trials are different from practice, and in which they may affect practice. For example, isn't it possible that the willingness to participate in trials which are designed to estimate the efficacy of an intervention, might be different from uptake of interventions when their efficacy has been established? I would expect that rates of participation in a trial of an intervention for which there is uncertainty about efficacy may not be similar to rates of participation in an intervention where the intervention has been shown to be efficacious. Furthermore, interventions that have been shown to be efficacious or effective may be promoted or even mandated in ways which would affect participation in practice. You have shown that the uptake in previous practice of delayed prescribing is similar to the uptake rate you estimated. However, estimates of participation from trials may only be starting points, and not so relevant to the actual population impact later on, as the results of trials are (one hopes) used to influence practice.

Related to this, there is a lack of clarity in the paper about efficacy trials versus effectiveness trials. For example, were the interventions to reduce antibiotics compared to usual care in the SRs? Are these efficacy trials or effectiveness trials? This wasn't clear to me and would be helpful in understanding the context of recruitment. Might the nature of the trials influence rates of participation? Perhaps include a discussion of how estimating uptake from trials does or does not depend on the trials being oriented towards either efficacy or effectiveness.

Note that effectiveness is highly context-dependent, and may not be easily translated across different settings. Could the same be said of uptake? How would you address this?

Finally, note that rates of participation in the trial on the part of clinicians and/or patients do not necessarily extend to rates of compliance with the intervention when in practice, and thus may not reflect the actual effects of the intervention. I guess this is obvious, but it may be worth addressing in the discussion.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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