Reviewer’s report

Title: Real-world evidence: How pragmatic are randomized controlled trials labeled as pragmatic?

Version: 1 Date: 04 Jan 2018

Reviewer: Russell Glasgow

Reviewer’s report:

This brief review and debate article on how pragmatic trials of medicines purporting to be pragmatic actually are is provocative and should be of considerable interest to readers. The ‘bottom line’ recommendation that authors should report the PRECIS-2 criteria when planning and submitting intervention studies is well argued. (I might suggest the authors also consider extending this recommendation to grant applications as well).

Below are more specific comments by section of the manuscript. I understand that some of these likely raise new issues as I was not one of the reviewers of the prior submission, and of course have a somewhat different perspective.

Abstract, title and introduction- it should be made very clear in all of these that this article is restricted to studies of medications. This is unfortunate from my perspective because I think this is a likely a very generalizable problem across most of health care (studies claiming to be pragmatic not really being so). The authors briefly address this in the discussion, but a) this selection should be justified in the introduction and b) some references demonstrating this issue in non-medication studies should be cited in the discussion (see below for some ideas- not definitive at all)

Pg. 4- the authors refer to comparisons of two or more medications: they should also make reference to Comparative Effectiveness Studies here; explain the similarities and differences of CER with pragmatic trials; and at least provide a reference to the large PCORI pragmatic trials and CER programs they support (PCORI is another possible source for considering the authors recommendations applied to grant proposals they receive for these projects). Finally, the new NIH Collaboratory for and resources on pragmatic trials should be cited: http://rethinkingclinicaltrials.org/

Pg. 5- The point about a pragmatic study needing the be conducted in multiple diverse settings is one that this reviewer agrees with, but to my knowledge is not part of the explicit PRECIS-2 criteria. I think it is fine, and maybe even important, that the authors keep this point but should be clear to identify what are their recommendations and what are directly taken from PRECIS-2.

Specifically, the PRECIS-2 directions on the website for "Setting" states: Setting - how different is the setting of the trial and the usual care setting?
Pg. 7- PRECIS and PRECIS-2 scores have been used quite a bit retrospectively for reviews, as the authors speculate, about but do not provide a reference. Again see below for a couple possible citations- also current ref #18- Johnson et al relevant to this point.

Discussion- there should be consideration that if PRECIS-2 scores are required by journals, that these ratings could be 'gamed' as mentioned in one of the references cited, these ratings are not entirely objective (this was one of the reasons for the PRECIS-2 revision). It is unlikely that editors or even reviewers would have the information or time to independently complete all the PRECIS-2 ratings themselves, so some solution- such as the study protocol being submitted to an independent review group should be recommended.

Possible additional references to consider citing:


Kelsey A. Luoma, MD,1 Ian M. Leavitt, MS,2 Joel C. Marrs, PharmD,3 Andrea L. Nederveld, MD,2 Judith G. Regensteiner, PhD,2,4 Andrea L. Dunn, PhD,5 Russell E. Glasgow, PhD,2 Amy G. Huebschmann, MD, MS2,4 How can clinical practices pragmatically increase physical activity for patients with type 2 diabetes? A systematic review. Transl Behav Med, 2017, June doi: 10.1007/s13142-017-0502-4


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