Reviewer’s report

Title: The implications of biomarker evidence for systematic reviews

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Reviewer: Pentti Nieminen

Reviewer’s report:

This article explores the proportion of biomarker based RCTs in systematic reviews and meta-analyses. The study focuses on an interesting issue and uses bibliometric data from Medline. I have some observations that should receive the attention of the authors.

Major compulsory revisions:

1. Figures 1-5 are very helpful and interesting. For example, Figure 3 shows that the number of published non-biomarker clinical trials per year has been quite stable almost two decades, but the number of research synthesis (systematic reviews and meta-analysis) has grown during those years. If we compare this to studies with biomarkers (Figure 2), we can see that there the number of clinical trials with biomarkers has grown during the years. The ratio does not grow so much because both the numerator and the denominator increase. This might explains why the ratio of non-biomarker-SR/biomarker RCT is higher than the ratio of biomarker studies. This reflects the fact that more and more meta-analyses have been published at the same time when more RCT studies with biomarkers have been conducted but the number of non-biomarker RCTs has not grown. I would not say that this is bias against inclusion of biomarker-based studies.

2. The search strategy used in this study seems to identify primarily genetic biomarkers.

3. Discussion, first paragraph, possible explanations: Unfortunately, biomedical research articles often include poor reporting of statistical methods. Incomplete reporting of statistical analysis limit or prevent the use of these studies in the systematic reviews.

Minor essential revisions:

1. Background, last paragraph, item 1: Help your reader and rephrase.

2. Page 5, second paragraph: Define abbreviation RCT/CCT.

3. Page 6: Define abbreviations SR/MT and SR/MA.

4. Figures 1-3: I would like to see lines connecting the symbols as in the figures 4 and 5.

Level of interest: An article of limited interest
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.