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Caution in underrepresentation of older adults in clinical trials on COVID-19 vaccines

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ABSTRACT

We read with great interest the article “Underrepresentation of older adults in clinical trials on COVID-19 vaccines: A systematic review” written by Nicola Veronese et al. in 2021 (Veronese et al., 2021). This important work demonstrated that medications and vaccines commonly used in older adults have not been adequately evaluated. Concerning this systematic review, we shall like to mention some certain points deserved to be attended by the authors.

First, this study only searched PubMed and Clinicaltrials.gov. Based on the findings of this study "older adults are underrepresented in COVID-19 vaccine clinical trials", we recommend that the researchers should increase the other databases (Embase, Web of Science, BIOSIS Previews) and other clinical trial registration platform (https://www.chictr.org.cn, WHO ICTRP) in order to find all available published and unpublished work to address this research issue. We also suggest that authors search for similar articles and track references. In addition, during the COVID-19 epidemic, most of the evidence of vaccines came from China, Germany, India, indicating that a considerable number of studies were published in non-English, which may lead to important biases in the retrieved studies. Given this study was a global level, authors should at least discuss the potential bias in the limitation section.

Our second concern is that the search terms used by the authors are not comprehensive. In Supplementary Table 1 (Search strategy used in this systematic review), we found that the authors used “randomized controlled trial[Filter]” to identify randomized controlled trials (RCTs), which may miss a considerable number of eligible studies. We suggest that the authors use “Clinical Trials, Phase II as Topic”[Mesh] OR "Clinical Trials, Phase III as Topic”[Mesh] OR 'Clinical Trials, Phase IV as Topic”[Mesh] OR "Controlled Clinical Trials as Topic”[Mesh] OR 'Randomized Controlled Trials as Topic”[Mesh] OR "Intention to Treat Analysis”[Mesh] OR "Pragmatic Clinical Trials as Topic”[Mesh] OR 'Single-Blind Method’[Mesh] OR "Double-Blind Method’[Mesh] OR random”[Title/Abstract] OR blind”[Title/Abstract] OR doubleblind”[Title/Abstract] OR tripleblind”[Title/Abstract] to search RCTs.

Third, the authors did not assess the risk of bias of included studies. Based on the Cochrane Collaboration, reporting risk of bias can help the readers to know about the justifications on which judgments are made and provides greater transparency and credibility of findings as risk of bias often threatens the validity of each of each individual studies (Higgins and Thomas, 2021).

Fourth, study protocols help to increase the transparency of the review methods and avoid bias in outcome reporting (Stewart et al., 2012). However, the authors did not report information about registration, which may result in the post hoc modification of methods.

Fifth, we noticed that statistical analysis is included in the “outcome section”. We suggest the authors add a section titled “statistical analysis”, and report more details about the statistical analysis.

Sixth, the inclusion criteria of this systematic review “double-blind design”, which was too strict. We recommend using ROB 2.0 to assess the quality of the study rather than restricting the blind method only. (Siddaway et al., 2019) Double blindness does not guarantee high quality of the study.

Overall, we would like to congratulate the authors for writing an informative article with novelty. However, the results of this systematic review should be interpreted with caution due to the limitations mentioned above.

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Declaration of Competing Interest

The authors report no declarations of interest.

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