Peer Review Report

Review Report on A 7-step guideline and checklist for qualitative synthesis and meta-analysis of observational studies in health sciences

Review, Public Health Rev

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Submitted on: 23 Jan 2023
Article DOI: 10.3389/phrs.2023.1605454

EVALUATION

Q 1 **Please summarize the main theme of the review.**

The majority of published literature in the field of evidence synthesis comprises observational studies. However, the inherent variability in observational study design, population, and analysis poses significant challenges to evidence synthesis, including threats of bias and selective reporting. In light of these challenges, this article presents a comprehensive and systematic guideline for the conduct of systematic reviews and meta-analyses of observational studies. The guideline is intended to provide reviewers with a comprehensive foundation for decision-making during the various stages of systematic review, including design, registration, conduct, and reporting. Additionally, the guideline provides guidance on the use of various statistical tools for addressing issues of heterogeneity, assessing potential sources of bias, and interpreting findings. Furthermore, the article also highlights the importance of considering the implications of the results for clinical and public health recommendations. By providing an in-depth and comprehensive guide for the conduct of systematic reviews and meta-analyses of observational studies, this guideline aims to encourage practitioners in the field of medicine and public health to integrate evidence from observational studies in their decision-making processes, thereby contributing to the advancement of evidence-based practice in these fields.

Q 2 **Please highlight the limitations and strengths.**

The limitations of this paper is that the authors have not validated. It would be useful to address this by pointing to 2-3 papers that the authors may have published using this approach to strengthen the presentation of their tool and guidelines.

Q 3 **Please provide your detailed review report to the authors, structured in major and minor comments.**

Minor comments

Authors have not mentioned some tools that are widely used in managing information for SRMAs (e.g. Rayyan, https://www.rayyan.ai/).

It would be nice to also suggest tools that visualize findings in a very graphical and communicative way (e.g. Microsoft Visio, Affinity Designer, Biorender, etc.) and point to one or two good references that have done so.

Major comments:

Lines 568-600: There are several tests and statistical methods that have been developed to detect and potentially correct for publication selection bias, some of which the authors mention, but some fail to mention. Some of these include:
-Egger's test (described by authors): This test uses linear regression to examine the association between the standard error and the effect size of the studies. It is used to detect publication bias in meta-analyses.

-Begg's test: Similar to Egger's test, this test uses linear regression to examine the association between the standard error and the effect size of the studies. It is also used to detect publication bias in meta-analyses. -Funnel plot: This is a graphical representation of the effect size and precision of the studies. It is used to visually detect publication bias by looking for asymmetry in the plot.
-Trim and fill method: This method uses the funnel plot to identify missing studies and estimates the effect size of the missing studies. It is used to adjust for publication bias by including the missing studies in the meta-analysis.
-Duval and Tweedie's trim and fill method: This method is an extension of the trim and fill method, which allows for the detection of small-study effects and the estimation of the number of missing studies.
-Fail-safe N: This method calculates the number of missing studies with null or opposite effects that would be required to change a significant result to a non-significant result.
-The comparison of effect size from the observational studies with that from randomized control trials (RCTs) if available, can also help detect the potential publication bias.
-The “file drawer problem”, which is a term used to describe the bias that occurs when studies with non-significant results are not published. This bias can be mitigated by the pre-registration of studies, which means that researchers have to submit their study design, hypotheses and methods before starting the study, making it more difficult to selectively report the results.

It is important for the authors to caution the reader that these methods are not always perfect and may not always detect or correct for all forms of publication bias, and they should be used in combination with other methods, such as sensitivity analysis.

Another remark for the authors is to strongly emphasize the relevance of their work to the science of public health. Authors should highlight the fact that taking decisions in public health should require the best possible evidence. Unfortunately, many of the decisions made today in our health care system are not supported by high-quality evidence derived from randomized, controlled trials or well-designed observational studies. But as rich, diverse sources of digital data become widely available for research and as analytical tools continue to grow in power and sophistication, the research and health care communities now have the opportunity to quickly and efficiently generate the scientific evidence needed to support improved decision making about health and health care. The pursuit of high-quality, data-driven evidence public health should be strongly emphasized.

Authors should expand in the part of leave-one-analysis. There are several ways to perform a leave-one-out analysis, which is a statistical method used to assess the robustness of a model or analysis by iteratively leaving out each data point and re-running the analysis. There are a few ways to perform a leave-one-out analysis in different platforms the authors should consider (but I leave this up to them):
-Using a for loop: This method involves using a for loop to iterate over the data points, leaving out one data point at a time and re-running the analysis for each iteration.
-Using the caret package in R: This package includes a built-in function called "trainControl" that allows you to specify the method of resampling, such as leave-one-out analysis.
-Using the leave-one-out function in Python: This function allows you to perform leave-one-out analysis in Python. It can be used to iterate over the data points and leave out one data point at a time and re-run the analysis.
-Using the leaveOneOut() method in Scikit-learn: This method is part of the cross-validation module in Scikit-learn and can be used to perform leave-one-out analysis.
-Using the boot package in R: This package has a function called "boot" that allows you to perform leave-one-out analysis.
-Using the leaveOneOut() method in Matlab: This method is part of the cross-validation module in Matlab and can be used to perform leave-one-out analysis.
It is important to caution the reader in any case that leave-one-out analysis can be computationally expensive, especially for large datasets, so it is a good idea to use a subset of the data for this analysis.

Thea uthors have pointed out the appraoch of meta-regression. Meta-regression approaches are used in public health meta-analyses and reviews to examine the sources of variability and heterogeneity in the results of multiple studies. Authors (based on their judgment) should extend their elaboration on established meta-

regression approaches in healthcare meta-analyses and reviews. In addition to random-effects meta-regression, (i.e an approach which assumes that the true effect size varies between studies and estimates the between-study variance as well as the overall effect size) and fixed-effects meta-regression (i.e. an approach that assumes that the true effect size is the same across studies and estimates the overall effect size) there is:
- Bayesian meta-regression: This approach uses Bayesian statistics to estimate the effect size and the between-study variance. It allows for the incorporation of prior information and can be useful when there is limited data available.
-Meta-regression with restricted maximum likelihood: This approach estimates the between-study variance and the overall effect size using restricted maximum likelihood.
-Meta-regression with multivariate meta-analysis: This approach allows for the examination of multiple outcomes or multiple subgroups within the same meta-analysis.
-Meta-regression with network meta-analysis: This approach allows for the comparison of multiple treatments in a single meta-analysis, taking into account both direct and indirect evidence.
-Meta-regression with machine learning: This approach uses machine learning techniques to identify important predictors of treatment effects and can be used to make predictions about future studies.
It is important to mention to the reader that the choice of meta-regression approach will depend on the specifics of the analysis, such as the type of data, the number of studies, and the research question.

PLEASE COMMENT

Q 4 **Does the reference list cover the relevant literature adequately and in an unbiased manner?**

Yes, but there is room for improvement

Q 5 **Does this manuscript refer only to published data? (unpublished data is not allowed for Reviews)**

Yes.

Q 6 **Does the manuscript cover the issue in an objective and analytical manner**

Yes.

Q 7 **Was a review on the issue published in the past 12 months?**

No.

Q 8 **Does the review have international or global implications?**

The topic is much needed, as during the past years we know that when choices were made about health and health care without adequate evidence to inform them, those choices were ineffective at best and at worst caused actual harm. But when patients and clinicians have ready access to high-quality evidence, they are better equipped to make decisions that maximize benefits while minimizing risks, ultimately leading to improved health not just at the level of the individual but across entire communities. All of us — patients, consumers, families, clinicians, and society as a whole — will benefit from a learning health system that takes full advantage of methods that help us make informed choices.

Q 9 Is the title appropriate, concise, attractive?

Yes

Q 10 Are the keywords appropriate?

Yes

Q 11 Is the English language of sufficient quality?

Yes

Q 12 Is the quality of the figures and tables satisfactory?

Yes.

QUALITY ASSESSMENT

Q 13 Quality of generalization and summary

Q 14 Significance to the field

Q 15 Interest to a general audience

Q 16 Quality of the writing

REVISION LEVEL

Q 17 Please take a decision based on your comments:

Minor revisions.