Methods Symposium: Advanced Methods and Innovative Technologies for Evidence Synthesis

Session One: Complexity in Systematic Reviews

February 16, 2021

Questions and Answers

1. Dr. Samet, are you aware of ROBIS-E tool that is currently being developed?

Answer: I can answer for Dr. Samet... he is very aware of all these tools, thanks!

2. To what extent have systematic reviews played a role in the evaluation of research grant programs?

Answer: Today, it is expected that decisions about health are informed by evidence (evidence-based medicine, evidence-based healthcare, and evidence-based public health). 'Evidence-based research' is also needed to ensure that trials and other types of research are scientific, ethically justified, and not wasteful. The National Institute of Health Research, a major public funder of clinical trials in the United Kingdom, explicitly requires justification for new research both in terms of time and relevance, and emphasizes that it "will only fund primary research where the proposed research is informed by a review of the existing evidence". However, few ethics review boards or funding agencies require explicit consideration of existing research.

3. Could the effect of complex interventions within the system vary due to factors related to health inequity?

Answer: Yes, absolutely. There is mounting evidence that well intended interventions can increase inequalities and that analysis by e.g., socioeconomic status can explain (some) variance in intervention effect.

4. Could high heterogeneity of a meta-analysis sometimes be evidence of components that have not been addressed or taken into account? Complexity?

Answer: Yes, it's possible. The challenge is that there are often many more ways that studies might differ from one another than there are studies - so we have a very difficult challenge in understanding or explaining the causes of heterogeneity.

5. Are there implications for specifying outcomes and outcomes sets considering that rigorous researchers should be correcting p-values for multiple comparisons (even though many don't)?

Answer: The multiple comparisons issue is more an issue of analysis than one of outcome choice. That being said, core outcome sets involve two separate stages/steps: the "what" (i.e., outcome domains) and then the "how" (i.e., how each outcome domain should be measured and such). Indirectly, part of the analysis problem you raise is intended to be prevented by specifying in the core outcome set how each outcome should be measured.

6. When we are looking at outcomes how do we deal with differences in outcome definition? For example, one might look at the incidence of a disease (e.g. preeclampsia or low birth weight)

when these outcomes are defined differently in primary studies. Should core outcome set define the outcomes as well?

Answer: As best we can, we should pre-specify in our review protocols the outcome definitions we are interested in. You're absolutely right that the studies we include may not use the same definitions we use. This is also true for the disease definitions of interventions of interest. Anticipating various differing definitions is hard, but we try to do our best.

7. Are core outcome sets static? Is there ever a need to update or modify these?

Answer: They should be updated as needed; but there probably should be a good reason to do so.

8. What are resources to find core outcomes for health systems outcomes rather than disease-specific outcomes? Specifically, I've been looking for mHealth or telehealth outcomes

Answer: Do try the COMET database (https://www.comet-initiative.org/). There is a filter for "Effective practice/health systems".

9. How should authors manage if, for an outcome, some studies in their review have data for meta-analysis but a large number of studies do not, should they present a narrative synthesis together with a meta-analysis?

Answer: As best we can, we try to contact the authors of the individual studies for the unreported/inadequately reported data. This doesn't always get us far. In that case, we synthesize those data narratively. If we do conduct a meta-analysis of the available data, we acknowledge and explore the implications of the fact that we don't have all the data from the studies we included. It certainly is not ideal!

10. I have never used those alternative plots as I always push for the meta-analysis, e.g., by estimating standard deviations from a similar study or getting data from graphs (all reported in the Cochrane handbook). In your opinion, what's the limit of data estimation?

Answer: I think meta-analysis has lots of benefits, so if you can impute missing information, then I think this is preferable. Of course, undertaking sensitivity analyses to examine how robust your results are to your imputation choices is important.

11. As systematic reviewers, do you think this analytic question is beyond our scope/responsibility to consider as part of evidence synthesis? I don't have a clear answer myself on this question and wonder if the outcome complexity issue may have the potential to increase the multiple comparison issue in the way that trials are conducted and reported.

Answer: No, it is within scope. Yes, the outcome complexity results in so many analytic results (Mayo-Wilson et al. explore this issue in the MUDS papers. You're right about the complexity problem!

Resources share:

This is a very broad area, but we covered a lot of the key papers in the Cochrane Handbook chapter: https://training.cochrane.org/handbook/current/chapter-17

Also see the series of papers here: https://gh.bmj.com/content/4/Suppl_1/e000963

Recent thinking on systems perspective in public health: https://www.sciencedirect.com/science/article/pii/S0277953621000290?via%3Dihub