Cochrane Scientific Committee

Recommendation statement/report

Date: 12th September 2018

Relates to agenda item and meeting reference: Item 5 5th June 2018

Priority: **Low**

Open access/restricted: **Open**

Data-based predictive distributions for between-study heterogeneity

Lead developers/investigators: **Rebecca Turner and colleagues (including Julian Higgins)**

Abstract:

In small meta-analyses, a conventional random-effects meta-analysis is problematic because between-study heterogeneity is imprecisely estimated, and this imprecision is not taken into account. A Bayesian meta-analysis allows researchers to incorporate external evidence on the likely extent of between-study heterogeneity in their particular research setting. Davey et al[1], found that 75% of meta-analyses reported in Cochrane Reviews included five or fewer studies.

Aim & objective: To assist with implementation of Bayesian meta-analysis, this project set out to provide empirical evidence on how much between-study heterogeneity could be expected in various healthcare settings.

Methods for development: Meta-analyses from the *Cochrane Database of Systematic Reviews* (Issue 1, 2008) were classified according to the type of outcome, type of intervention comparison and medical speciality. The impact of meta-analysis characteristics on the underlying between-study heterogeneity variance was investigated by modelling the study data from all meta-analyses simultaneously. Meta-analyses of binary outcomes and meta-analyses of continuous outcomes were modelled separately.

Predictive distributions were obtained for the between-study heterogeneity expected in future meta-analyses. These distributions can be used directly as data-based informative prior distributions for heterogeneity in Bayesian meta-analyses.

Results: Between-study heterogeneity was found to be strongly associated with the type of outcome measured in the meta-analysis and somewhat associated with the types of interventions compared. For example, between-study heterogeneity variances for meta-analyses in which the outcome was all-cause mortality were found to be on average 17% (95% CI 10% to 26%) of variances for other outcomes. In meta-analyses comparing two active pharmacological interventions, heterogeneity was on average 75% (95% CI 58% to 95%) of variances for non-pharmacological interventions.

We have published predictive distributions for heterogeneity for various settings, defined by type of outcome and type of intervention comparison, separately for meta-analyses of binary outcomes[2,3] and for meta-analyses of continuous outcomes[4]. In addition, we have proposed

accessible methods for implementing Bayesian meta-analysis with informative priors, avoiding the need for specialist Bayesian software[3, 5].

Final product: Guidance will be incorporated into Version 6 of the *Cochrane Handbook for Systematic Reviews of Interventions*.

SUPPORTING DOCUMENTATION

1. Davey J, Turner RM, Clarke MJ, Higgins JPT. Characteristics of meta-analyses and their component studies in the Cochrane Database of Systematic Reviews: a cross-sectional, descriptive analysis. *BMC Medical Research Methodology*; 2011; 11: 160.

2. Turner RM, Davey J, Clarke MJ, Thompson SG, Higgins JPT. Predicting the extent of heterogeneity in meta-analysis, using empirical data from the Cochrane Database of Systematic Reviews. *International Journal of Epidemiology*; 2012; 41: 818-27.

3. Turner RM, Jackson D, Wei Y, Thompson SG, Higgins JPT. Predictive distributions for between-study heterogeneity and simple methods for their application in Bayesian meta-analysis. *Statistics in Medicine*; 2015; 34(6): 984-98.

4. Rhodes KR, Turner RM, Higgins JPT. Predictive distributions were developed for the extent of heterogeneity in meta-analyses of continuous outcome data. *Journal of Clinical Epidemiology* 2016; 68(1): 52-60.

5. Rhodes KM, Turner RM, White IR, Jackson D, Spiegelhalter DJ, Higgins JPT. Implementing informative priors for heterogeneity in meta-analysis using meta-regression and pseudo data. *Statistics in Medicine*; 2016; 35(29): 5495-511.

Key reference: Turner and colleagues: https://academic.oup.com/ije/article/41/3/818/834878

CSC RECOMMENDATION

☐ ***Highly recommended***
Because

☐ ***Recommended with provisions***
Because

☐ ***Recommendation that method/tool etc. is not used***
Because

☒ ***Optional/advisory (one among several options)***
Because it provides an option to improve estimation of the amount of heterogeneity (and hence estimation of intervention effects) in meta-analyses with a small number of studies

☐ ***Not recommended***
Because

CSC STATEMENT

Summary statement

The Committee recommends that Cochrane Review authors consider applying Bayesian meta-analysis with prior distributions for the heterogeneity variance alongside the traditional techniques included in RevMan. Such analyses should supplement standard analyses, offering potentially improved estimation of intervention effects and their uncertainty. This approach is particularly helpful when the number of studies is anticipated to be small, in which case the prior distribution can have a tempering impact, especially if a more conventional estimate of heterogeneity variance is very large or very small. The suggestion to consider these methods will be included in the updated Handbook (version 6).

Credibility & validity: -

Limitations/caveats: **Methods should be used in specific circumstances and are not advised for all reviews.**

Areas of concern/uncertainty: **None noted**

Impact on Cochrane: **Low**

Cochrane resources needed: **No integration expected into RevMan at this point. Training for editors is a consideration. In addition, the Editorial & Methods Department might wish to consider whether any active encouragement is required or whether this is left to Reviewer judgement.**