

Cochrane Scientific Committee

Teleconference 5th June 2018

Notes and abbreviations

Members of the CSC present

Corinna Dressler (CD)	Present
Donna Gilles (DG)	Apologies
Julian Higgins (JH)	Present
Asbjørn Hróbjartsson (AH)	Present
Ana Marusic (AM)	Present
Jane Noyes (JN)	Present
Tomas Pantoja (TP)	Present
Philippe Ravaud (PR)	Present
Johannes Reitsma (JR)	Present
Rebecca Ryan (RR)	Present
Christopher Schmid (CS)	Present
Nicole Skoetz (NS)	Present
Nichole Taske (NT)	Apologies
David Tovey (DT)	Present

Other attendees

Jackie Chandler	Minutes
Rebecca Turner	Invited speaker

AGENDA ITEM	Minutes
1) Welcome and apologies received	Nicole Taske, Donna Gillies
2) Approval of previous minutes	Minutes dated 28 th February 2018 (Paper 1)
a) Matters arising	<p>5. (2) Expert panel report on whether using sequential methods to adjust P values is necessary in repeated meta-analyses.</p> <p>CS apologised for the delay in completing the position statement based on the outcome of the expert panel discussions. JH, not a panel member, reviewed the current version and proposed some amendments. CS will provide an updated version to the expert panel members to reach a final version to present the Committee for final recommendation.</p> <p>JH commented on the wording asking that the principle recommendation should shift its emphasis to an active recommendation, stating, the 'expert panel recommends against' the use of sequential methods and he articulated six reasons, why:</p>

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- 1) Cochrane Reviews should provide the best summary of **current** evidence
 - 2) Cochrane advocates a preference for reporting confidence intervals, with exact P values, if desired. There is an inappropriate arbitrary division between what determines statistically significance or non-significance which is at the heart of these sequential approaches.
 - 3) The meta-analysis context is not the same as the trial context
 - 4) Decision makers using Cochrane Reviews may not agree with approach chosen by review authors.
 - 5) There are technical problems with these methods.
 - 6) Readers are unlikely to understand these methods.

If reviewers insist on using these techniques Cochrane must be clear on the context in which they can be used. They must not be used for primary analysis. It is permissible to use these methods for secondary analysis to provide an additional interpretation of the data from a specific perspective.

DT raised the issue regarding review sample size and whether enough information is provided, another rationale for using these methods. P value adjustment results in a GRADE downgrading decision, when the review provides sufficient data and confidence in the result if the P value is not adjusted. The EMD (CEU) is addressing a major dispute on this matter with a Review Group who routinely use Trial Sequential Analysis to which they link to the downgrading decisions in GRADE for imprecision/sparse data. Cochrane regard this as inappropriate but it is difficult to convince the Review Group. JH responded that this is covered by the first of the rationales in that meta-analyses should be based around existing evidence. He agreed to add a note to the position statement to clarify further.

The Committee agreed that the guidance should be about the management of effects in relation to uncertainty not the other way around. The Committee's decision on the use of these methods will be final and will be published on the Cochrane Methods website. To enable the community to respond the Committee discussed publishing a Cochrane Editorial or external paper. At this stage the discussion document is to remain within the Scientific Committee and not be widely shared.

Action: DT to send CS a note detailing the sample size issue. JH will make amendments to point 3 to reflect this discussion.

8. Any other business

JH raised an item regarding scientific misconduct and whether there was an expectation to actively search for any errors or misconduct in study reports rather than respond to items that, opportunistically, come to light.

Action: JH to circulate draft section to AM and DT

JC has discussed with Bryony Urquhart the development of a broad misconduct policy for both author and reviewer. This is in development and should be available by the end of 2018. BU has commented on a draft from a new section in the Handbook. The EPPR will include a specific section on misconduct.

AM believes that all linked documents should be examined and cross checked. The Committee should decide what procedures for detecting misconduct should be mandatory and, if reviewers find errors and plagiarism, how they deal with it. If it becomes mandatory, then a tool needs to be provided for reviewers to ensure consistency across reviews.

ACTION: AM will submit her recommendations in writing to the Committee.

3) CSC Business matters	None
4) Submissions	No further submissions
5) Methods for CSC Review	<p>Data-based predictive distributions for between-study heterogeneity</p> <p>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.</p> <p>Rebecca Turner attended and presented at the meeting. (Paper 2)</p>

Following a presentation by Rebecca Turner the Committee had a detailed discussion about the application of Bayesian meta-analysis in Cochrane Reviews which included the following issues:

- Although this work was based on a set of data from 2008 it is still relevant
- Rebecca would advocate that specific priors from the initial paper are used based on the nature of the meta-analysis i.e. narrow vs broad settings
- The priors in the initial paper can be used for any sized meta-analysis not just for those with 5 studies or fewer but the recommendation would be that the methods are likely to have most impact when the number of studies is 10 or fewer
- It was agreed that when there is a small number of studies the estimates of heterogeneity are poor as most authors use the DerSimonian- Laird technique. Given that 75% of Cochrane Reviews have fewer than 5 studies the Committee should recommend which technique to use.
- The QIMG are very interested in Bayesian meta-analysis in relation to Qualitative Evidence Syntheses. Asking authors to

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- add Bayesian meta-analysis alongside traditional syntheses may be a good compromise to compare the techniques.
- The current Cochrane Handbook is clear that Bayesian meta-analysis can be used although it is not included in RevMan so this presents a huge implementation challenge. The new updated Handbook addresses alternatives to DerSimonian-Laird for random effects analyses. There are better methods available than in RevMan and this needs to be made clear to authors

The Committee thanked RT and a summation of decisions will be sent.

ACTION: The Committee recommends that Cochrane Reviewers are encouraged to add Bayesian meta-analysis alongside the traditional techniques included in RevMan to supplement and improve their review. Particularly where there is a very high or low heterogeneity estimate. Therefore, in these situations an additional Bayesian analysis will have the greatest impact. This will be included in the new updated Handbook chapter.

6) Methods for CSC sign off and recommendation	None
7) Special items	
a) Research priorities and strategy	None
8) Any Other Business	Further clarification is needed in the template wording to distinguish between recommendations. In particular, to include the “recommended against” option to be more definitive
<p><i>ACTION: JC will clarify the wording in the templates.</i></p>	
9) Meeting schedule	List of meetings 16 th September 2018 at 7.30am (Colloquium) informal and invite the Methods Executive (overlapping membership). 8 th November 2018 at 11.00am UK GMT
