Cochrane Methods

Cochrane Scientific Committee

MINUTES

31 March 2019

Krakow, Poland

ATTENDESS

David Tovey (DT) - Editor in Chief
Ella Flemyng (EF) - Methods Implementation Coordinator
Toby Lasserson (TL) - Senior Editor

Committee members attending:

Corinna Dressler (CD)
Research Associate at the Division of Evidence-Based Medicine (dEBM) at the Charité – Universitätsmedizin Berlin, Germany
Donna Gilles (DG)
Editor for both the Cochrane Developmental, Psychosocial and Learning Problems Group and Diagnostic Test Accuracy Review Group.
Julian Higgins (JH)
Professor of Evidence Synthesis at the School of Social and Community Medicine, at the University of Bristol, Bristol, UK, and current Senior Scientific Editor of the *Cochrane Handbook of Systematic Reviews for Interventions.*
Ana Marušić (AM)
Professor of Anatomy and Chair of the Department of Research in Biomedicine and Health at the University of Split School of Medicine, Split, Croatia and founder of Cochrane Croatia.
Jane Noyes (JN)
Professor of Health and Social Services Research and Child Health, Bangor University, Wales, UK, lead Convenor of the Cochrane Qualitative and Implementation Methods Group, and a UK Cochrane Fellow.
Tomas Pantoja (TP)
Associate Professor, Family Medicine Department, School of Medicine, Pontificia Universidad Católica de Chile and Editor of the Cochrane Effective Practice and Organisation of Care (EPOC) Group.
Philippe Ravaud (PR)
Professor of Epidemiology, Faculty of Medicine, Head of the Clinical Epidemiology Centre, Hôtel-Dieu Hospital, Paris Descartes University, France and Director of Cochrane France.
Rebecca Ryan (RR)
Research Fellow at the School of Psychology and Public Health, La Trobe University, Australia and Joint Co-ordinating Editor of the Cochrane Consumers and Communication Group.
Nicole Skoetz (NS)
Scientific Co-ordinator, Working Group Standard Operating Procedures of the Comprehensive Cancer Centers, Center of Integrative Oncology Köln Bonn, and Co-ordinating Editor Cochrane Haematological Malignancies Group, Department of Internal Medicine, University Hospital of Cologne.
Nichole Taske (NT)
Associate Director (Methodology), Centre for Guidelines, NICE, UK

Committee members' apologies:

AsbjØrn Hróbjartsson (AH)
Professor of Evidence-Based Medicine and Clinical Research Methodology at the University of Southern Denmark, and Head of Research for the Center for Evidence-Based Medicine at Odense University Hospital, which hosts the secretariat of the Cochrane Bias Methods Group.
Johannes Reistma (JR)
Associate Professor at the Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, The Netherlands and a member of both the Cochrane Diagnostic Test Accuracy Working Group and the Screening and Diagnostic Tests Methods Group.
Christopher Schmid (CS)
Professor of Biostatistics, founding member and Co-Director of the Center for Evidence Synthesis in Health, Brown School of Public Health, US, Fellow of the American Statistical Association (ASA) and Founding Co-Editor of *Research Synthesis Methods.*

MINUTES

Chairs of the Scientific Committee - Ana Marušić and Philippe Ravaud

Overview of the day (31 March 2019):

09:00-10:30	Meeting – General business
10:30-11:00	Break
11:00-12:30	Meeting – Scientific Committee set-up
12:30-13:30	Lunch
13:30-15:00	Meeting – New methods discussions
15:00-15:30	Break
15:30-17:00	Meeting – Reflection on previously approved methods

09:00-10:30 – General business
Chaired by Ana Marušić

Agenda item	Details and links to documents or appendix
1) Approval of previous minutes	Approved the minutes dated November 2018 without further edits – see **Paper 1**.
2) Updates from Cochrane	Update on methods implementation projects as part of the Content Strategy – see **Paper 2** (presented by Ella Flemyng). Content Strategy 2019 priorities include six main methods implementation projects. 1. Risk of Bias 2 (RoB 2): emphasis on technology and process piloting. Will only be available in RevMan Web (not RM5). Signalling questions still being tweaked and finalised once scientific paper published (submitted to BMJ). 2. Living Systematic Reviews (LSR): Aim to have LSRs initiated across all Networks by end 2019. Likely to publish evaluation and present at the Colloquium. **ACTION EF: Check the publication plans for the living systematic review pilot with Tari Turner (project manager)** 3. Network meta-analysis (NMA): Cochrane Interactive Learning module launched. Need to identify expertise - authors, peer reviews and advisors. Need to develop MECIR extension. Tech development needed for RevMan to support rollout. Linked to project on study centric data. CD has an NMA update and wants to make it living. NS stated a Living NMA will be initiated in the Cancer Network in June 2019. Those interested should contact the LSR Network or EF to ensure they have the most up-to-date guidance

and support. Issues around publishing LSR in Cochrane has created some challenges for peer review and versioning. DT: versioning is common in Cochrane with Update publications. AM: We can learn from other publishers with versioning, where each version has its own DOI and is included in PubMed, e.g. *F1000 Research*.

ACTION ALL: If your CRGs or Networks are considering living systematic reviews or NMAs contact Tari Turner or Ella Flemyng to ensure you have the most up-to-date versions of the guidance and tools available

ACTION EF/TL: Follow up with Harriet MacLehouse to determine how versioning affects publication of LSRs in Cochrane and share with the Scientific Committee

4. Rapid Reviews: Proposal being put to Governing Board later in 2019 for a 'go or no-go' decision on formal rapid reviews in Cochrane but project delayed. Confirmed that this should come to the CSC first for methodological consideration, and then to Governing Board for strategic decision. Discussed that appraisal is a key stage and concerns that RoB would be dropped; DT flagged this is unlikely, rigor will be maintained, and CSC can approve proposal on methodological integrity first. Highlighted that 'rapid reviews' vary hugely, and the term is challenging, which is why this project has been initiated. Discussed that increasing the rapidity of methods is only one part of the process and editorial processes and production should be assessed too, e.g. links to Fast Track. Discussed a need for improving extraction of data from trials, inc. thinking differently about this in a format that can be machine readable and extracted from trial registries; could Cochrane lead a project with trial registries about ensuring aggregate data is in a format for streamlined extraction into a Review? Discussed whether developments in CENTRAL could facilitate aggregate data extraction, which would also be of benefit to LSRs and NMA.

ACTION EF: Feedback to the Rapid Reviews Methods Group with details on the Scientific Committee discussions and request that their proposal is sent first to the Scientific Committee for consideration before the Governing Board

ACTION DT: Follow up with CENTRAL to see what plans, if any, there are to host aggregate data to facilitate NMAs and LSRs in Cochrane

ACTION PR: Share with the Scientific Committee the paper on rapid reviews from Christl Donnelly

5. Prognosis reviews: tools in development, network of experts set up and individuals assigned to new reviews. In-person training is a key next step. 21 reviews initiated across different CRGs. Aiming to publish six by end of year.
6. Clinical Study Reports (CSRs): At an early stage of development, hosting a consultation meeting to discuss feasibility on using CSRs in Cochrane Reviews on 16 May2019. If deemed feasible, a pilot will be initiated in three Reviews in 2019. Discussed the issue around convincing manufacturers to share information with Cochrane. It was highlighted that CSRs for drugs recently approved could be possible, but that after this point availability for CSRs is less likely (generally 5-7 trials pre-approval and <300 trials post-approval). DT stated that the EMA want to work with Cochrane on CSR sharing. It's likely that the impact of this project will affect many Methods Groups so engagement with them, including via the Methods Executive, in CSR implementation would be needed. Discussed that consistency in data structures will facilitate CSR usefulness. DT highlighted the RCT Classifier, part of the TRANSFORM Project, which is 99% sensitive and accurate in identifying an RCT report. It's currently being used within Cochrane Reviews.

ACTION EF: Check whether it's possible for the RCT Classifier to be used by those not associated with Cochrane

Update on the Cochrane Handbook for Systematic Reviews of Interventions (presented by Ella Flemyng).

Intervention Handbook has been submitted to Wiley with publication estimated in Quarter 3 2019. The Handbook will also be publicly available, and PDFs of the chapters are currently available to Cochrane members. Discussed that the Handbook will be versioned, but

not living. All attendees thanked the Handbook Editors and authors for their contribution and the effort that has gone into the new Handbook.

ACTION EF: Ensure the Methods Groups and Methods Executive are included in the implementation plan for the Intervention Handbook

DTA Handbook is ongoing, and prognosis and qualitative Handbooks are being proposed.

Cochrane's data sharing policy – see **Paper 3** (presented by David Tovey).

Discussed that this is an ongoing topic for the Governing Board and policies on Open Access and Open Data will likely be revised; consultations will be set-up for both. Barriers include legal obstacles as Cochrane doesn't own all of the data in its Reviews. Plan S proposes that research funded by certain funders would need to be published in gold open access journals (no hybrid journals); however, NIH, NIHR and MRC haven't signed this. Cochrane will always adhere to funder requirements and will be GDPR compliant. Discussed a need for consistency, according to FAIR data principles. Discussed that it doesn't need to be open but that the policy should be transparent. Scientific Committee to ensure they input into decisions when the consultations open (EF to ensure consultation information is circulated).

11:00-12:30 – Scientific Committee set-up

Chaired by Philippe Ravaud

Agenda item	Details and links to documents or appendix
3) New methods approval process in Cochrane	Discussion to clarify the process, including what roles and responsibilities the Scientific Committee, Methods Executive and Methods Groups have in the process - see **Paper 4**. All agreed that the Scientific Committee only needs to approve methods that meet the following three criteria: 1. Methods with a wide-ranging impact on the conduct of Cochrane Reviews (e.g. built into the structure of the review or methods that became mandatory); 2. Widespread use or mass resources from Cochrane needed (e.g. training required); 3. Controversial methodological topics without community consensus. Agreed that new submissions will be assessed by the Methods Executive, who will triage (those that meet the above criteria will be escalated to the Scientific Committee). The Chairs of the Scientific Committee should also be involved in these initial discussions (once the process becomes standard the Chairs may consider not being involved in the triage). Some submissions may need to be assessed by the relevant Methods Group or liaison with others before decisions can be confirmed. Decisions from the Scientific Committee are recommendations to the Editor-in-Chief, as well as the Governing Board if there are financial implications. If the Editor-in-Chief doesn't endorse the Scientific Committee, this can be appealed to the Governing Board. Highlighted four general areas for new methods – identifying topics, deciding on whether they progress to the Scientific Committee, liaison with the applicants to develop the submission, and implementation. Scientific Committee should be involved in the first

	two/three. If sub-groups are formed to make decisions on new methods, Scientific Committee, Methods Executive and Methods Groups should be involved. Scientific Committee to arbitrate, challenge or request independent review. Discussed the need for a transparent process for methodologists that is publicly available. **ACTION ALL: EF to circulate the current webpage and webform text for comment and feedback on updates to ensure the process for new methods submissions is transparent for applicants and to ensure that the form includes all the information needed for informed decisions** Agreed that all methods submission to Cochrane should be submitted by Methods Groups, methodologists or any other parties, such as CRGs, through the webform to ensure they are archived in one place. Would be useful if submissions and how they are proceeding is publicly, and there is the potential for others to comment on the submissions. Highlighted new questions that would be useful: endorsement vs. permission; proposals vs. requests. Will also need to detail an appeal process for applicants. **ACTION EF: Discuss with the ITS team what functionality Drupal has to make the new methods submission webform open publicly and possible to comment on** Decided that the specific process for new methods should be -> submit method or tool proposal via webform -> Methods Executive and/or Scientific Committee decision -> if yes, the applicants will be encouraged to conduct a pilot on one Review (previously referred to as exemplar but decided to rename to 'pilot'). Methodological quality must be maintained and if low it would be rejected from the Cochrane Library at the Protocol stage (Protocols should have one method and one topic review) -> if Review is published with new method, applicant to submit/update the methods proposal for final consideration for wider roll-out. **ACTION EF: Work with relevant colleagues to develop a diagram on the process for new methods submissions to Cochrane** Discussed that CRGs sometime pilot new methods without submitting to a new methods proposal. EF and TL highlighted they receive non-standard Review title registration alerts, but you cannot assess methods implications from these. Engagement with Methods Groups and CRGs/Networks will be key to the success of this process. **ACTION EF/TL: Discuss within CET and Networks the process for new methods proposals to determine an effective communication plan to inform authors and CRGs about the process**
4) Methods community roles and responsibilities	Discussion to finalise the roles and responsibilities document, which will include the Scientific Committee, Methods Executive, Methods Groups, Methods Support Unit, Methods Implementation Coordinator and other CET roles - see **Paper 4**. Highlighted a wider review of the Execs, which is on hiatus. The roles and responsibilities document will be useful to inform this project. Scientific Committee's remit is methods and scientific issues; Methods Exec is involved in the business infrastructure for methods and methods strategy; Governing Board's remit is Cochrane's strategy and any financial implications. Blue-sky thinking for future methods development or evidence synthesis ecosystem should involve all three (Scientific Committee, Methods Executive and Editorial Board). Discussed that it's useful to have a small overlap (approximately two people) between the Scientific Committee and Methods Executive to help bridge the two groups; however, majority of Scientific Committee should be independent. Agreed on changes to the roles and responsibilities document (Paper 4). **ACTION ALL: Approve the final wording of roles and responsibilities document relating to the Scientific Committee in Paper 4**
5) 2019/2020 strategic priorities for the Scientific Committee	Considering strategic objectives and priorities for the Scientific Committee. Scientific Committee is generally reactive. Discussed that the future of evidence synthesis (in Cochrane) is a shared responsibility between the Scientific Committee, Methods Executive, Editorial Board and Editor-in-Chief. The Scientific Committee would like to feed into Cochrane's future strategies on

	methods and help inform decisions, i.e. the next strategy after Strategy 2020. Discussed setting up an annual meeting with the Editorial Board and Scientific Committee to discuss the future of evidence synthesis, which could help inform Cochrane strategy. **ACTION DT: Discuss with the Editorial Board a meeting between the Scientific Committee and Editorial Board (and Methods Executive) at the 2019 Colloquium** **ACTION EF: Add a standing item of 'any new methodological innovations that need to be added to Cochrane's agenda' to the Scientific Committee agenda** Discussed that if there are unanswered methodological review questions we could ask the Methodology Review Group to consider it for a future review. **ACTION EF: Ensure that that any unanswered methodological review questions are flagged to Mike Clarke and the Methodology Review Group to consider it for a future review** Scientific Committee want to feed into any publication ethics or research integrity policies. **ACTION EF: Ensure that any consultation for any publication ethics or research integrity policies are sent to the Scientific Committee**

13:30-15:00 – New methods discussions

Chaired by Ana Marušić

Agenda item	Details and links to documents or appendix
6) New submission(s) for Cochrane Scientific Committee Review	See new submission in **Appendix 1:** Use of interactive analysis framework to facilitate diagnostic test accuracy and network meta-analyses analyses This is a tool and not within the remit of the Scientific Committee. Decided that the application needs to be assessed by the Screening and Diagnostic Tests Methods Group and CMIMG before a decision can be made. Questions around whether they are asking for permission or endorsement. It was highlighted that the guidance or evaluation of the tool should be published. **ACTION EF: Send the new methods submission in Appendix 1 to the Screening and Diagnostic Tests Methods Group and CMIMG for assessment before sending to the Methods Executive for a final decision**
7) Process for receiving new submissions for review	Discussed the general process for submissions and how the Scientific Committee could proactively encourage or request methods submissions from Methods Groups. Discussed that the process needs to be transparent (see notes from Agenda point 3 above). The following methods or tools were highlighted for future consideration: • Risk of Bias due to Missing Evidence (RoBME) • Tool for Addressing Conflict of Interests in Trials (TACIT) • (Semi) automation methods • Prognosis methods

	• Standalone qualitative evidence synthesis (following PHHSN two-year pilot) • Prevalence and causes of disease • Use of IPD in repositories and other types of data Discussed whether the Scientific Committee could have a living paper on its position on different methods that have been considered. Positions on certain methods can change over time as the evidence for the method develops. **ACTION EF: Assess the feasibility of the Scientific Committee having a living paper on its position on different methods that have been considered** Discussed visibility of this process and a need for an engagement and communication plan for Methods Groups, inc. at the Co-Convenors Meeting or Methods Exec Plus meetings. This will be included with the redesign and engagement with Methods Groups with the webform.

15:30-17:00 – Reflection on previously approved methods

Chaired by Philippe Ravaud

Agenda item	Details and links to documents or appendix
8) Reflection on past Scientific Committee decisions	Discuss progress of methods following past decisions – see **Appendix 2** below. It was noted that cumulative methods Bayesian approaches should be considered, rather than should be used. Discussed that prevalence is an important consideration, which wasn't included in the Content Strategy, DG should reassess the submission and consider resubmitting. **ACTION DG: Reassess the submission on meta-analyses of prevalence and risk, and consider resubmitting**
9) Next Scientific Committee meetings	Teleconferences should be held ever three months and aim to meet in person once a year (next one at the 2020 Governance Meetings). Highlighted the need to add 'house rules' at the beginning of calls as feedback can make audio difficult. **ACTION EF: Ask the Methods Liaison Officer to set-up teleconference for the Scientific Committee for the rest of 2019 (every three months)** Will also need to look at current Scientific Committee set-up as three-year tenure that will end in May for some members.
10) Any other business	There was support from the group for Cochrane to have its own publishing platform for methods research, e.g. a Methods Section in the CDSR. Discussed the new Intervention Handbook all were interested in receiving copies of the following chapters, for their information as they have been extensively reworked or are new – 3, 9 and 12. **ACTION EF: Send links to chapters 3, 9 and 12 of the new Intervention Handbook along with the minutes**

APPENDIX 1 – New methods submission(s)

SHORT TITLE OF METHOD OR METHODS RELATED DEVELOPMENT
Use of interactive analysis framework to facilitate diagnostic test accuracy and network meta-analyses analyses

Name: Alex Sutton
Email: ajs22@le.ac.uk
Contact details: Department of Health Sciences, College of Life Sciences, University of Leicester, George Davies Centre, University Road, LEICESTER LE1 7RH UK
Telephone: + 441162297268
Cochrane Affiliation: methods group, bias group, non-randomised group, dementia & cognitive impairment, accident prevention

Lead researchers or developers
Several people from the Complex Review Support Unit (http://www.nihrcrsu.org/) and beyond
A comprehensive list can be supplied later if necessary.

Aims and Objectives
To develop interactive software to facilitate meta-analysis which otherwise requires specialist software routines which are difficult to use by non-statistical experts. Also, to provide a powerful interface so even statisticians will want to use the software for its power, speed, flexibility and ease of use.
This software has been developed, in part, as part of work with the NIHR Complex Review Support Unit which supports UK based Cochrane authors. Experiences through this unit indicated software mas a major barrier for Cochrane reviewers to use the most relevant analysis methods for diagnostic test accuracy and network meta-analyses. This software aims to remove that barrier, and initial feedback suggests it is being successfully used by pilot groups.

Key features
- Point and click interface, removing barrier to entry for non-statistical experts for specialist network meta-analysis and diagnostic test accuracy analysis types. Both of which are not available in Cochrane software.
- Runs in a web browser minimising compatibility problems.
- Underpinned by analysis routines developed in R (by others) ensuring accuracy of results.
- Emphasis given to visual output formats that are clinically relevant
- Some graphics - like the displaying of study quality on an ROC plane - are novel and not available in other software
- All output can be exported and imported into Cochrane Reviews.
- We are open to suggestions for improvements and new features to add to the software
- Individual studies can be excluded in seconds facilitating sensitivity analysis.
- It would be very possible, with amendments to the software, to use the interface to view the data in published Cochrane reviews allowing authors to carry out their own critique of the analysis / conduct alternative analyses and produce alternative views of the data not included in the original review.

Key publication or guidance document
We have 2 peer reviewed papers re-submitted post revisions and are hoping these will be accepted and published shortly (at which point they will be open access):
The apps (which are free to use and under active development) are available at:

https://crsu.shinyapps.io/dta_ma/
https://crsu.shinyapps.io/metainsightc/

APPENDIX 2 - Methods discussed by the Scientific Committee (2017-2018):

18 May 2017

1. **ROB 2.0 = Highly recommended** - *the recommendation is that it is mandatory for new reviews when officially launched. For updates, it is not reasonable to re-do previously included studies and a strategy is required to handle these situations.*
   Now included in the Content Strategy and a priority project for 20119 to assess the feasibility of implementation.
2. **ROBINS-I = Recommended with provisions** - *the ROBINS-I tool is recommended as the preferred tool for new reviews. It is not mandatory. The importance of competency to use the tool will be highlighted in guidance.*
   Recommended but unsure of implementation or evaluation. Will need to discuss with developers.
3. **Cumulative meta-analysis = Further evaluation required** - *the CSC agreed that further technical examination of the key approaches was required to ascertain whether there is a preferred method, or whether the methods provide value to managing random error and are needed at all, or only in certain scenarios. An expert panel will be asked to consider the work completed by colleagues to date and will report to a future CSC.*
   See points relating to whether using sequential methods to adjust P values is necessary in repeated meta-analyses for decision.

18 October 2017

1. **Inclusion of results from searching study registries in Cochrane reviews: completed but not published studies** = *Not a matter for the CSC but further guidance needs developing.*
2. **Meta-analyses of prevalence and risk** = *This is not currently matter for the CSC and will be considered further in Cochrane's Content Strategy.*
3. **Meta-regression** = *This is a matter for the Editorial Board (possibly Governing Board if it impacts on budgets). This is not a matter for the CSC.*
4. **Timely and Reliable Evaluation of the Effects of Interventions: A Framework for Adaptive Meta-analysis (FAME)** = *this was to be incorporated into the Handbook and not a matter for the CSC.*
5. **Determining when meta-analyses of published time-to-event outcomes reliable enough to form robust clinical conclusions. An evidence-based approach** = *this was to be incorporated into the Handbook and not a matter for the CSC.*
6. **Data-based predictive distributions for between-study heterogeneity** = *CSC not able to make a decision and requested paper and presentation for future meeting.*
   Decision below.

Following methods were highlighted for consideration at a future meeting:

- Intervention Complexity Assessment tool.
- Guidance for when to include Clinical Study Reports and other regularity data in CR's.
- Methods for prognosis reviews.
- Methods for addressing missing participant data.
- Assessing the quality of evidence and presenting the results of Non-randomised Studies in CR'.
- Evaluation and validation of the RCT classifier.

28 February 2018

1. **Interim guidance on how to decide whether to include clinical study reports and other regulatory documents into Cochrane Reviews = Optional/advisory -** *CSC members agreed this data was important in tackling reporting bias. Further development of methods and tools were required that identifies where more evidence is needed as well as where Cochrane should concentrate its energies. The report's findings were accepted in principle by the committee. However, further consideration of roll out and implementation within the main body of Cochrane required the input of both Governing Board (resources) and Editorial Board (implementation requirements).*
   Now included in the Content Strategy and a priority project for 20119 to assess the feasibility of implementation.
2. **Expert panel report on whether using sequential methods to adjust P values is necessary in repeated meta-analyses = Not recommended -** *The CSC concur with the panel's recommendation that these methods should not be used routinely in Cochrane and that only in specifically justified cases is it reasonable to do so.*
   Statement posted on Methods Website. No further action.

5 June 2018

1. **Data-based predictive distributions for between-study heterogeneity = Optional/advisory -** *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.*
   Statement posted on Methods Website. No further action.

8 November 2018

1. **Qualitative evidence synthesis as a standalone review = Decision not made by CSC** – Editorial Board approved a two-year pilot and following the pilot the CSC and Methods Executive would make a decision on whether standalone QES would be endorsed in Cochrane.
2. **Prognosis reviews as standalone review = Decision not made by CSC**.
   Now a formal review type in the Cochrane Library and Prognosis Methods Group have been overviewing the development and implementation.

Following methods were highlighted for consideration at a future meeting:

- Risk of Bias due to Missing Evidence (RoBME).
- Tool for Addressing Conflict of Interests in Trials (TACIT): Cochrane has a COI policy in development currently. AH is a member of the working group on the COI policy. He will ensure there will be good co-ordination between the two approaches.
- Semi automation methods.
- Prognosis methods.