## RESEARCH & IMPLEMENTATION 2018-2019

**By Group**

### Cochrane Methods Adverse Effects
- In consultation with Elsevier for our surgical adverse effects filter and our medical device filter to be incorporated into OVID Embase and Embase.com.
- Published guidance on searching for adverse effects following the methodologies we proposed in the Cochrane Handbook.

### Cochrane Methods Priority Setting
- Developed reporting guidelines for research priority setting that is under development
- PhD student focusing on evaluating the implementation of the equity lens in priority setting through engaging with stakeholders from a range of ethnicity and socioeconomic backgrounds. This was identified as a methods priority.
- As part of the EVBRES EU COST action funding, we look at how systematic reviews are used as part of the priority setting and decision-making process of the funding agencies.

### Cochrane Methods Bias
- Work on completing and implementing the updated Cochrane Risk of Bias Tool 2.0 (RoB 2.0 Tool) will continue in the year to come. The Bias Methods Group will continue to contribute to completing the updated versions of RoB 2.0 Tool for cluster-randomised trials and crossover trials.
- Work on developing and implementing the tool for addressing conflicts of interest in medical research (TACIT) and the tool for assessing risk of bias due to missing results (ROB-ME) will equally continue.
- Work on developing version 2 of the Risk Of Bias In Non-randomized Studies – of Interventions Tool (ROBINS-I), which has variants in development for different study designs, will continue.
- The Bias Methods Group is hosted by Centre for Evidence-Based Medicine Odense (CEBMO) and receives funding from Odense University Hospital in Denmark.

### Cochrane Methods Comparing Multiple Interventions
- Began developing MECIR standards for network meta-analysis.
- Began developing a plan to implement network meta-analysis in Cochrane reviews.
- Cochrane will fund further development of CIneMA.

### Cochrane Methods Economics
- Updating the new Economics Evidence chapter of the Cochrane Handbook
- Pauline Sobiesuo, a Campbell & Cochrane researcher based at Newcastle University is preparing supplementary material to outline economic concepts, a description of the processes for an integrated full systematic review of economics evidence and a glossary of terms based on chapter 10 of the 2010 book 'Evidence based economics' (Shemilt I, Mugford M, Donaldson C, Vale L, Marsh K. Wiley Books, London, 2010). The description of processes for an integrated full systematic review of economics evidence is intended to be converted into an additional chapter for the Cochrane Handbook.
- Working towards supporting Cochrane Groups and their editorial bases to incorporate economics into their reviews, exemplified by Cochrane Incontinence, who have adopted a position that all new reviews and review updates should include at least a brief economic commentary as standard.
### Cochrane Methods

**Equity**

- Luke Vale and Ian Shemilt have been invited to join a potential GRADE working group looking at a proposal for an economic evidence GRADE project led by Maria X Rojas.
- Ian Shemilt is contributing to a GRADE working group on GRADE for modelled evidence.
- Blogs: Jacqueline Mallender and Rory Tierney examine how we decide on how best to spend resources tackling crime. This includes how economic analysis is becoming increasingly popular in measuring the impact of resource use, looks at government-sponsored projects and systematic reviews in the process. Patricia Aluko blogged how she helped in the process of adding brief economic commentaries (BECs) into eight reviews by Cochrane Incontinence, including how the reviews were chosen, and the methods used in undertaking the BECs.

**GRADEing**

- A 2-day workshop was held in February 2019 to develop guidance for when (and when not) to replicate systematic reviews. Multiple papers based on this work are planned and it will be presented as a workshop at the 2019 Cochrane Colloquium. The project will also be presented as a panel presentation at the What Works Global Summit in October 2019. This work was funded by the Canadian Institutes of Health Research.
- Working with an international team of collaborators and stakeholders to develop guidance for multi-stakeholder engagement in systematic reviews and guideline development. This work has been funded, in part, by the Canadian Institutes of Health Research. This work will be presented as a workshop at the 2019 Cochrane Colloquium.

**IPD Meta-analysis**

- During 2018-19, much of the work has focused on the assessment of evidence and communication of findings from different types of reviews, including intervention reviews, but also reviews including NRS, diagnostic test accuracy reviews, network meta-analyses, and reviews of patient values and preferences. Future work will include focus on reviews of patient values and preferences.
- Members of the Group have published a number of methodological papers on:
  - Meta-analysis methodology
  - Evaluation and validation of failure time surrogate endpoints
  - IPD network meta-analysis using restricted mean survival or hazard ratios
  - Impact of missing IPD on meta-analyses
  - Study designs other than randomised controlled trials:
    - Meta-analysis of prognostic and predictive factors
    - Accuracy and equivalency of depression scales and questionnaires

- MG members have also published a number of IPD meta-analyses in, for example, breast cancer, oropharyngeal cancer, non-small cell lung cancer and epilepsy.
- Ongoing projects:
  - Funding has been obtained for a commissioned update of a Cochrane IPD Network meta-analysis to inform NICE guidelines entitled: Cochrane priority reviews for NICE. Update of the Cochrane review: Antiepileptic drug monotherapy for epilepsy: a network meta-analysis of individual participant data, which is due to be completed in June 2020.
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<th>Cochrane Methods Information Retrieval</th>
<th>Cochrane Methods NRS for Interventions</th>
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<td>• Visitors to our website <a href="http://methods.cochrane.org/ipdmeta/welcome-ipd-meta-analysis-methods-group">http://methods.cochrane.org/ipdmeta/welcome-ipd-meta-analysis-methods-group</a> can also find further information about IPD meta-analyses and IPD-related methodological publications undertaken by Group members.</td>
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<td>• Clinical Study Reports: Carol Lefebvre participated in a project partly funded by Cochrane under the MIF programme: Interim guidance on the inclusion of Clinical Study Reports and other regulatory documents in Cochrane Reviews. This resulted in two publications listed as Hodkinson et al and Jefferson et al in the Publications section. This project also led to a further Cochrane project to discuss the feasibility and implications of using Clinical Study Reports (CSRs) as the main data sources within Cochrane Reviews of drug interventions. JG and CL have both joined the Clinical Study Report Working Group.</td>
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<td>• ISSG Search Filter Resource: Julie Glanville and Carol Lefebvre, together with Kath Wright, as the editorial team, continue to maintain the InterTASC Information Specialists' Sub-Group (ISSG) Search Filter Resource. This aims to identify, assess and test published and unpublished search filters designed to retrieve research by study design or focus. It also provides information and guidance on how to critically appraise search filters and provides independent appraisals for some of the filters and published reviews comparing filters. The site continues to be updated monthly.</td>
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<td>• SuRe Info web resource: Julie Glanville and Carol Lefebvre, together with other IRMG members and non-members, continue to maintain and develop the SuRe Info web site, providing updated research-based information relating to the information retrieval aspects of producing systematic reviews and health technology assessments. JG is the site lead, together with Jaana Isojarvi, and CL is on the Steering Group. Both CL and JG are also authors of specific sections on the site. The site continues to be updated every 6 months with the latest evidence in information retrieval in the field of evidence synthesis.</td>
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<td>• Work is being done on a key requirement when including NRSI in a Cochrane view of an intervention for which there is currently no guidance. The risk of bias due to confounding is widely recognised as critical in reviewing NRSI and deciding the value of the evidence they contribute. Since 2009, the NRSIMG has recommended that “At the stage of writing the protocol, list potential confounding factors” (NRSIMG chapter 13: Including non-randomized studies in version 5 of the Handbook). Specifically, the NRSIMG advised that reviewers should “Identify the confounding factors that the researchers have considered and those that have been omitted.” These two tasks are central to assessing bias due to confounding with ROBINS-I but no guidance has been given about how to do the first step. An oral presentation in Santiago will present some empirical findings about how this step might be done based on methods used to identify confounding factors for a secondary data analysis.</td>
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**By Group**

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<th>Group</th>
<th>Projects</th>
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| **Cochrane Methods** | - Discussion with members of GRADE about how to reconcile competing algorithms for deciding whether to include NRSI in [Cochrane] reviews and what the implications should be for scoping the available literature and finalising protocols.  
- Collaboration with members of the Bias Methods Group on an extension to RoB v2 for cluster-randomized trials.  
- **Cochrane Methods**  
  - Patient Reported Outcomes  
    - Presentation approaches for enhancing interpretability of patient-reported outcomes (PROs) in meta-analysis: a systematic survey of Cochrane reviews.  
    - Meta-analyses of clinical trials often provide sufficient information for decision-makers to evaluate whether chance can explain apparent differences between interventions. Interpretation of the magnitude and importance of treatment effects beyond statistical significance can, however, be challenging, particularly for patient-reported outcomes (PROs) measured using questionnaires with which clinicians and patients have limited familiarity. The objectives of this study are to systematically evaluate Cochrane systematic review authors’ approaches to calculation, reporting and interpretation of pooled estimates of PRO measures (PROMs) in meta-analyses. Published protocol: Devji T, Johnston BC, Patrick DL, et al. Presentation approaches for enhancing interpretability of patient reported outcomes (PROs) in meta-analysis: a protocol for a systematic survey of Cochrane reviews. BMJ Open 2017;7:e017138. doi:10.1136/bmjopen-2017-017138. Linan Zeng, PhD student from McMaster University, Canada, is leading this work under the joint supervision of Drs. Guyatt and Devji. Results will be available later in 2019.  
    - Reporting and Application of Minimally Important Differences in Randomized Controlled Trials Evaluating Patient Reported Outcomes: A Systematic Survey  
    - The objectives of this project are as follows: 1) Determine Frequency of MID use in RCTs; 2) Among studies that use an MID, how credible are these estimates? 3) Among studies using MIDs, how often are these estimates anchor vs. distribution? 4) Document Investigator’s reasons for using MIDs i.e. interpretability or trial design (e.g. sample size); 5) If MIDs used for interpretation, then how are effect estimates presented in relation to the MID? 6) What inferences about the magnitude of effect, if any, are investigators making about the results of the PROM in relation to the MID. Dr. Tahira Devji is currently leading this project.  
- **Cochrane Methods**  
  - Prognosis  
    - A formal risk of bias tool for prediction modelling studies (PROBAST) has been published.  
    - A guidance paper on how to perform a systematic review and meta-analysis of prognostic factor studies is published.  
    - A paper going into the details of meta-analysis of prognostic factor studies is underway.  
    - Working on guidance for data extraction and critical appraisal for prognostic factor studies (CHARMS-PF), updating the risk of bias tool for prognostic factor studies (QUIPS), and developing GRADE guidance for prognostic factor studies.  
    - Working on projects focusing on the efficacy of current search filters for prognosis studies and meta-analysis of added value studies.  
    - All these projects and deliverables are supported by non-Cochrane funding. |
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**Prospective Meta-analysis**
- The group is conducting research that aims to describe the current landscape and key features of prospective meta-analyses (PMA) in health research by systematically identifying all planned, ongoing and published PMA.
- The group’s research is supported in-kind by each of the convenor’s respective organisations. No other funding is provided.

**Qualitative and Implementation**
- Completion of methodological work with WHO to define context and create a new question formulation framework for complex health system wide interventions and qualitative evidence synthesis.
- Continuation of GRADE-CERQual work. The Group contributed to various training opportunities in 2018. E.g. Booth and Garside delivered training to NICE on 6th July 2018.
- Subgroups are investigating:
  - dissemination bias in qualitative research and;
  - tools to assess methodological limitations.
- A methodological review of current appraisal tools (CAMELOT) was published in 2019 (see also publication section).

**Rapid Reviews**
- Completed research project related to English-only searching; crowd screening; and two scoping reviews on RR methods/definitions. Several projects are in the manuscript phase.
- Completed and ongoing research undertaken in 2018-19 specific to rapid reviews methodology and that involve one or more RRMG conveners:
  - A cross-sectional, comparative methodological study of formatting characteristics of published and unpublished RR reports. Project Lead: C Garritty, funded by CIHR, manuscript under journal consideration
  - Assessing rapid reviews as an information product according to the BRIDGE criteria: an evaluation pilot study. Project Lead: C Garritty, funded by CIHR, manuscript under journal consideration
  - What is the relation of completeness of reporting of rapid reviews to publication status? A comparative, cross-sectional methodological study. Project Lead: A Stevens, Funded by CIHR, manuscript in progress
  - Evaluation of conduct characteristics of rapid reviews. Project Lead: A Stevens, funded by CIHR, study ongoing – data collection phase
  - Developing an extension to PRISMA for rapid reviews. Project Lead: A Stevens. Funded by CIHR, study ongoing
  - Systematic Prospective Assessment of Rapid Knowledge Synthesis (SPARKS). Project Lead: A Tricco; A Stevens and C Garritty – co-investigators. Funded by CIHR, project ongoing
- If the RRMG is able to secure funding in 2019/2020, the following projects are of priority:
  - Modifying MECIR standards for Cochrane Rapid Reviews
  - Developing search strategies to assist in the identification and indexing of rapid review reports
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<th><strong>Screening and Diagnostic Tests</strong></th>
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| o Exploring strategies to involve patient partners (consumers) in rapid reviews  
  • In addition, the RRMG will continue to explore links with other Cochrane products including the following: living systematic reviews; updates/targeted updates; and overview of overviews. The RRMG is also in search of funding in order to develop guidance on when to do and when 'not' to do rapid reviews. |
| **Development of QUADAS-2C**, an extension of QUADAS for assessing risk of bias and applicability concerns in studies comparing the accuracy of two or more index tests. The QUADAS-2C Advisory Group is meeting in Birmingham on the 28th of August 2019 to finalise a draft of the checklist for piloting.  
  • The new PLS guidance has been adopted for Cochrane DTA reviews. The PLS project was funded by the Methods Innovation Fund (MIF).  
  • Future work includes implementation of DTA meta-analysis methods that allow inclusion of multiple thresholds from each study. |

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<td><strong>An empirical study comparing the impact of using different estimation methods (Paule-Manel, Restricted Maximum Likelihood and Knapp Hartung) than the DerSimonian and Laird method for the random effects model in Cochrane reviews is ongoing with Kerry Dawn (research associate of the group) as the lead author.</strong></td>
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