Research and Development 2019-2020

**By Group**

- Golder S, Scantlebury A, Christmas H. Understanding Public Attitudes Toward Researchers Using Social Media for Detecting and Monitoring Adverse Events Data: Multi Methods Study. JMIR 2019 Aug 29;21(8):e7081. doi: 10.2196/jmir.7081

**Cochrane Methods**

**Adverse Effects**

- Leading development of a tool for addressing conflicts of interest in randomised trials (TACIT) and a tool for assessing risk of bias due to missing results (ROB-ME). (Convenors) Funding sources for both tools: other
- Updating reporting guidelines for protocols for randomised trials (SPIRIT) and randomised trials (CONSORT). In the initial phase, the Bias Methods Group is participating in developing a database with literature relevant to SPIRIT or CONSORT (the SCIP database), a scoping review on suggested changes for SPIRIT or CONSORT, and a systematic evaluation of CONSORT extensions. (Group) Funding source: other
- Leading the work on developing updated versions of the revised Cochrane risk of bias tool (RoB 2) for cluster-randomised and crossover trials. (Group) Funding source: Cochrane and other
- Leading the 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. (Group) Funding source: other
- Participate in the steering committee for a living network meta-analysis of interventions for COVID-19 (https://covid-nma.com/). Funding source: other
- Leading a methodological project involving developing procedures for a quality control on the risk of bias assessments on included trials (done using RoB 2). Funding source: other
- Completed involvement in updating the Cochrane Handbook for Systematic Reviews of Interventions (July 2019). Convenors and members of the Bias Methods Group were Senior Scientific Editors, Associate Scientific Editors, and authors of several Handbook chapters. Funding source: Cochrane and other
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**Comparing Multiple Interventions**
- Leading the development of a reporting guideline for overviews of reviews. We published the protocol for this work in December 2019 (Syst Rev 2019 Dec 23;8(1):335).
- Finalized the updated chapter on Overviews of Reviews for the Cochrane Handbook (version 6, 2019)
- Finalized the updated chapter on Network Meta-Analysis for the Cochrane Handbook (version 6, 2019)

**Economics**
- Aim to incorporate equity components in systematic reviews of economic evidence. This work will be conducted without funding support. However, we will aim to look at potential funding sources in future.

**Equity**
- In 2019, we developed a guideline for when and when not to replicate systematic reviews of interventions. This will be published in 2020 in the BMJ. This was a 4-year project funded by the Canadian Institutes of Health Research.
- In 2020-2021 we will apply for funding to develop guidance for equitable multi-stakeholder engagement in systematic reviews, in collaboration with the Cochrane ACTIVE team. This work complements our Canadian Institutes of Health Research funded project to develop guidance for equitable multi-stakeholder engagement in guideline development.
- In 2020, we developed a GRADE multi-stakeholder survey to support the equitable implementation of clinical guidelines. The Journal of Clinical Epidemiology is reviewing this methods paper.

**GRADEing**
- The methods development of the Cochrane GRADEing Methods Group takes largely place within the GRADE Working Group ([www.gradeworkinggroup.org](http://www.gradeworkinggroup.org)).
- Our funding is primarily received indirectly through support from academic institutions. We continue to advance GRADE methods through grants that group members receive for systematic reviews and guidelines by adding methods projects to these grants. No dedicated funding for methods groups is received.

**IPD Meta-analysis**
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| | • Two research projects on indirect network meta-analyses methods with IPD time-to-event meta-analyses  
• One research project on the restricted mean survival time in an IPD time-to-event meta-analysis  
• Leading a study examining how risk of bias and applicability/generalizability are assessed, reported, and incorporated in IPDMAs. This will review IPDMAs of three types: diagnostic accuracy studies, prediction model studies, and trials, leading to the development of guidance for assessing, reporting, and incorporating risk of bias/applicability into IPDMAs, by developing extensions/adaptations to QUADAS-2, PROBAST, and ROB2 that are tailored to the IPD setting. Brooke Levis & Richard Riley | **Planned** |
| | | • Evaluation of direct and indirect methods for comparing the screening accuracy of the PHQ-9 and HADS-D in an IPD meta-analysis, which will use IPD to adjust for indirectness when comparing accuracy across screening tools (https://osf.io/75v6u/). No specific funding for analyses, but IPD dataset was funded by the Canadian Institutes of Health Research (CIHR). Brooke Levis, Brett Thoms, Andrea Benedetti - DEPRESSD Project  
• Follow-up project with the same dataset as used for the IPD meta-analysis of cerebroplacental ratio in predicting adverse perinatal outcomes note above. No funding. Charlotte Vollgraf Heidweiller-Schreurs | |
| **Clinical Study Reports (CSR)** | **ISSG Search Filter Resource** |
| Following on from the project reported on last year, partly funded by Cochrane under the MIF programme: Interim guidance on the inclusion of Clinical Study Reports and other regulatory documents in Cochrane Reviews, and two publications by Hodkinson et al and Jefferson et al., Julie Glanville and Carol have both joined the Clinical Study Report Working Group. | [https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/home](https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/home)  
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, which 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 |
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<th>NRS for Interventions</th>
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<td><strong>appraisals for some of the filters and published reviews comparing filters. The site continues to be updated monthly.</strong></td>
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| **• SuRe Info web resource**  
[http://vortal.htai.org/?q=sure-info](http://vortal.htai.org/?q=sure-info)  
Julie Glanville and Carol Lefebvre, together with other IRMG members and non-members, continue to maintain and develop the SuRe Info (Summarized Research in Information Retrieval) 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. |
<p>| <strong>• Continued collaboration with the Bias Methods Group to develop / improve tools for assessing the risk of bias in primary studies.</strong> |
| <strong>• Collaboration with Julian Higgins and Jonathan Sterne to develop an application (web database) to apply RoB v2, capturing responses to signaling questions and generating domain judgements and an overall risk of bias classification for an outcome. Completed work was to be showcased at the cancelled Toronto Colloquium.</strong> |
| <strong>• Collaboration with Sandra Eldridge and colleagues on an extension of RoB v2 for cluster RCTs; final manuscript draft being prepared for submission to the BMJ.</strong> |
| <strong>• Collaboration with Julian Higgins and Jonathan Sterne to develop a “version 2” of ROBINS-I for cohort studies, including algorithms to map responses to signaling questions to bias domain judgements. This work is ongoing. The plan is to have a similar application (web database) to the one completed for RoB v2 for ROBINS-I. We are confident that this will make version 2 of ROBINS-I easier to use, although assessing risk of bias in NRSI will still not be a ‘beginner’s’ role.</strong> |</p>
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- Rheumatology trials: an initial qualitative study from an OMERACT Working Group. Ann Rheumatic Dis. This work is continuing.

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<th>Patient Reported Outcomes</th>
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<td>- MID credibility instrument manuscript published in the BMJ in 2020: &quot;Evaluating the credibility of anchor based estimates of minimal important differences for patient reported outcomes: instrument development and reliability study&quot; <a href="https://www.bmj.com/content/369/bmj.m1714">https://www.bmj.com/content/369/bmj.m1714</a></td>
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<td>- Article describing key methodological issues with current MID literature accepted (in press) at Evidence-Based Mental Health (BMJ Journals): &quot;Mind the Methods of Determining Minimal Important Differences – Three critical issues to consider&quot;</td>
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<td>- PROMID website - currently still in development but enough information publicly available on the website to describe the initiative: <a href="http://www.promid.org">www.promid.org</a></td>
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<td>- Development of a MID Reporting guideline - In the planning and development stages</td>
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<td>- Development of principles for selection of a MID estimate when multiple estimates for a PROM exist. This guidance will help clinical trialists, systematic review authors and guideline developers select trustworthy and applicable MIDs for interpretation of PROM data</td>
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<td>- Article describing the extent of reporting issues in anchor-based MID estimation studies submitted to Journal of Clinical Epidemiology: &quot;Serious issues of reporting exist in minimal important difference studies: Current state and suggestions for improvement&quot;</td>
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<th>Cochrane Methods</th>
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<td>- Worked with the EU office of WHO to develop a priority setting framework for national priority setting for countries - this is done on the basis of an overview of reviews. The paper is prepared and submitted for publication.</td>
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**Comments/feedback**

*Conflict of interest in setting priorities for research* is an important topic - we raised it in the guidance but we did not do any research on it.

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<th>Cochrane Methods</th>
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<td>- Framework for meta-analysis of prediction model studies with binary and time-to-event outcomes has been published in the journal Statistical Methods in Medical Research (see reference list).</td>
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<tr>
<td>- Developing guidance for reporting and quality assessment of prediction models developed using Machine Learning techniques. This will result in TRIPOD-ML and PROBAST-ML. As a starting point, we are performing a</td>
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systematic review aiming to evaluate the reporting quality, the methodological conduct, and the risk of bias of prediction model studies that applied ML techniques for model development and/or validation (PROSPERO CRD42019161764).

- Co-authored many papers on reporting of and methods for primary and meta-prognosis studies, including TRIPOD for abstracts and guidance for sample size calculations for prediction model development (see reference list).
- Developing guidance for using GRADE in systematic reviews of prognosis studies. This has led to the publication of a guidance paper on how to use GRADE for the assessment of evidence of prognostic factor studies (reference below). Guidance on GRADE for prognostic model studies is under way and will be prioritised in 2020-2021.

Papers/publications

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- Riley RD, Ensor J, Snell KIE, et al. Calculating the sample size required for developing a clinical prediction model. BMJ. 2020;368:m441. Published 2020 Mar 18. doi:10.1136/bmj.m441

- Developed a step-by-step guide to conducting a prospective meta-analysis, which was published in the Research Methods and Reporting section of the BMJ
- Updated our scoping review to identify the number of PMA in health research, and describe their key features, methods and reporting characteristics
- Saskia Cheyne continues to make progress on her PhD, for which she aims to develop methods for the conduct and reporting of ‘next generation’ systematic reviews and meta-analyses, including PMA
- Conduct a project on how to search for planned, ongoing, and unpublished studies using trial registries, which is a key early step in building a PMA collaboration (2020-2021)
- Undertake a PMA evaluating mesenchymal stem cells for the treatment of severe COVID-19, for which a grant application has been made (2020)
- The group’s research is supported in-kind by each of the convenor’s respective organisations. No other funding is provided
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| GRADE CERQual celebrates 10 years since its inception. Sub-group work continues on: (i) identifying dissemination bias in qualitative research, (ii) further developing our understanding of methodological limitations in primary studies and development of the CAMELOT tool for use with CERQual and (iii) ongoing CERQual training activities. A 10-year retrospective paper is being prepared for publication.
| WHO is providing some support to develop the 10 year retrospective paper. Cochrane has previously provided a partially funded MIF grant to develop some of the stages of CAMELOT. Other work is undertaken at no cost to Cochrane.

| Completed |
| As part of Cochrane’s Content Strategy to 2020, the RRMG has been exploring the appropriateness of RRs as a formal Cochrane product. To inform this work, the RRMG conducted two formal scoping reviews (projects 1-2) and two methods research projects (projects 3-4). Further, we developed and administered an evidence-informed questionnaire to elicit targeted feedback on the defining features of a Cochrane RR and acceptable RR methods by surveying Cochrane constituents from 20 Cochrane entities (project 5). The information generated from projects 1-5 subsequently informed development of interim Cochrane RR definition and methods (project 6). A brief description of each project is listed below:

1. **Scoping Review of RR Definitions (Hamel et al.)** - This study was a systematic scoping review and thematic analysis of definitions and defining characteristics of RRs. Definitions were captured from 216 RRs and 90 RR methods papers. The top four articles referenced as providing definitions were identified along with eight key themes. Overall, findings from this study have allowed for the creation of a suggested definition for RRs that can be used to seek consensus from the SR community. (Funded by Cochrane)

2. **Scoping Review of Empirical Studies Evaluating RR Methods (Hamel et al.)**: This study was a systematic scoping review to identify research assessing one or more method(s) applicable for undertaking RRs with each other/or with standard SR methods. We then conducted a mapping analysis to see which review conduct key dimensions were evaluated and compared these shortcuts against MECIR criteria. The author identified 90 studies evaluating or discussing RR methodology. Only the 14 formal evaluation studies were mapped to key dimension and MECIR. Four studies were labelled as composite evaluations (i.e., including more than one shortcut concurrently), and the remaining 10 studies evaluated RR methods individually. (Funded by Cochrane)

3. **Limiting to English-only studies (Nussbaumer-Steit et al.)**: This study assessed whether limiting inclusion criteria solely to English language publications affected the overall conclusions of SRs - based on 59 randomly selected Cochrane Intervention Reviews with no language restrictions (which included 1281 studies). The
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<td>4. <strong>Single Reviewer Screening of RCTs Using Cochrane Crowd (Gartlehner et al.):</strong> This study was an online parallel-group RCT that assessed the accuracy of single-reviewer screening versus dual-reviewer screening using Cochrane Crowd platform. Overall, findings suggest single-reviewer abstract screening misses about 13% of relevant studies. Based on prior research that suggests 10% is a generally accepted level of risk decision-makers are willing to take for missing evidence; the authors concluded this may be a viable approach for RRs. (Funded by Cochrane)</td>
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5. **Cochrane RR methods ‘menu options’ survey (Garritty et al.):** We developed a web-based survey to seek the input of Cochrane members on RR methods primarily focused on major identified streamlined RR methods across the stages of performing a review. Respondents were asked to rank order certain options at various stages of conduct and to solicit their preferences for certain abbreviated approaches. The survey was administered between Sept. 14-Nov. 1, 2019 to a sample of 119 individuals identified from 20 Cochrane entities over a 6-week period. Survey results were analyzed using descriptive statistics. Of those that responded, a large proportion were either extremely/very (38%; n=24) or somewhat (38%; n=24) somewhat familiar with RRs. Further, 62% (n=39) has previously participated in a RR in various capacities. Overall, there was general approval for Cochrane implementing RRs as a product (only one respondent of 59 indicated Cochrane should not undertake RRs). Specific survey results available upon request. (Funded by Cochrane)

6. **Rapid Review Methods Recommendations: Interim Guidance from the Cochrane Rapid Reviews Methods Group (Garritty et al.):** We developed methods guidance for Cochrane Rapid Reviews (RRs) produced in response to requests for timely evidence syntheses for decision-making purposes including, urgent health issues of high priority. Interim recommendations were informed by a scoping review of the underlying evidence, primary methods studies conducted, and a survey sent to 119 representatives from 20 Cochrane entities, who were asked to rate and rank RR methods across stages of review conduct. Discussions among those with expertise in RR methods further informed the list of recommendations with accompanying rationales provided. Based on survey results from 63 respondents, 26 RR methods recommendations are presented for which there was a high or moderate level of agreement or ranked highest in the absence of such agreement have also been recommended. Where possible, how recommendations align with Cochrane methods guidance for SRs is highlighted. Therefore, the Cochrane Rapid Reviews Methods Group offers new, interim guidance to support the conduct of RRs produced within Cochrane. Because best practice is limited by the lack of currently available evidence for some RR methods shortcuts taken, this guidance will need to
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7. Combining abbreviated literature searches with single-reviewer screening: three case studies of rapid reviews (Affengruber et al.): This study assessed the validity of a rapid review approach that combines a substantially abbreviated literature search with a single-reviewer screening of abstracts and full texts using three case studies. We used a convenience sample of three ongoing Cochrane reviews as reference standards. Two reviews addressed oncological topics and one addressed a public health topic. The study concluded that a rapid review approach that combines abbreviated literature searches with single-reviewer screening may be feasible for focused clinical questions. For complex public health topics, sensitivity seems to be insufficient. (Funded by Cochrane and the University of Bremen)

- In addition, co-convenors of the RRMG were involved in the completion of the following RR methods research projects:

8. Assessing the format and content of journal published and non-journal published rapid review reports: a comparative study (Garritty et al.): The purpose of this study was to compare and contrast report format and content features of journal-published (JP) and non-journal published (NJP) RRs including ‘how’ (i.e., visual arrangement) and ‘what’ information was presented. Based on our sample of identified 103 RRs (52 JP and 51 NJP) we found a higher percentage of certain features were observed in JP RRs compared to NJP RRs (e.g., reporting authors; use of a traditional journal article structure; section headers including abstract, methods, discussion, conclusions, acknowledgments, conflict of interests, and author contributions; and use of figures (e.g., Study Flow Diagram) in the main document). For NJP RRs, a higher percentage of features were observed (e.g., use non-traditional report structures; bannering of executive summary sections and appendices; use of typographic cues; and including outcome tables). NJP RRs were more than double in length versus JP RRs. Including key messages was uncommon in both groups. This comparative study highlights differences and that both groups would benefit from better use of plain language, and more clear and concise design to ensure better packaging of RR results to facilitate uptake into policy and practice. (Funded by CIHR)

9. Assessing how information is packaged in rapid reviews for policymakers and other stakeholders: a cross-sectional study (Garritty et al.): The aim of this project was to assess how well RRs convey useful information in a format that is easy to understand so decision-makers can make best use of evidence to inform policy and practice. We assessed a diverse sample of 103 RRs against the BRIDGE criteria, originally developed for communicating clearly to support healthcare policymaking. We modified the criteria to increase assessability and to align with RRs. We assessed each RR on 26 factors (e.g., organization of information, lay language use).
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Certain criteria were well covered across the RRs (e.g., all aimed to synthesize research evidence, and all provided references of included studies). Further, most RRs provided detail on the problem or issue (96%; n=99) and described methods to conduct the RR (91%; n=94), while several addressed political or health systems contexts (61%; n=63). Many RRs targeted policymakers and key stakeholders as the intended audience (66%; n=68), yet only 32% (n=33) involved their tacit knowledge, while fewer (27%; n=28) directly involved them reviewing the content of the RR. Only six RRs involved patient partners in the process. Only 23% (n=24) of RRs were prepared in a format considered to make information easy to absorb (i.e., graded entry) and 25% (n=26) provided specific key messages. Readability assessment indicated the text of key RR sections would be hard to understand for an average reader (i.e., would require post-secondary education) and would take 42 (± 36) minutes to read. Overall, conformity of the RRs with the modified BRIDGE criteria was modest. By assessing RRs against these criteria, we now understand possible ways they could be improved to better meet information needs of healthcare decision-makers, and their potential for innovation as an information-packaging mechanism. (Funded by CIHR)

### Ongoing

10) Systematic Prospective Assessment of Rapid Knowledge Synthesis SPARKS (Project Lead: A Tricco; A Stevens and C Garritty – co-investigators) (Funded by CIHR)

11) Developing an extension to PRISMA for rapid reviews (Project Lead: A Stevens) (Funded by CIHR)

12) Systematic review and methods study on falsely excluded studies in the literature screening process (Project Lead: L Affengruber) (Funded by NFB Science Call 2017)

### Planned

- Moving forward, the Cochrane RRMG has outlined a specific preliminary workplan developed for stage two activities (with additional funds provided). They are as follows:

  **Stage 2 Objectives:**
  1) Formalize the Cochrane RR Definition (i.e., refinements to the interim definition that has been proposed; and will seek endorsement from relevant Cochrane entities)
  2) Develop Cochrane RR standards (MECIR-RRs) (e.g., Delphi or adaptation)
  3) Write the Cochrane Handbook Chapter
  4) Validate the accuracy of the Screen4Me approach
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<td><strong>5) Collaborate in the development of training modules for Cochrane RRs</strong>&lt;br&gt;Further, in light of the development of Cochrane COVID-19 RRs, we would like to pursue the following activities (with additional funding provided):&lt;br&gt;6) To see formal feedback and input from those research teams that have applied the interim Cochrane RR methods guidance as part of the response to COVID-19.&lt;br&gt;7) Adapt the interim Cochrane RR Methods Guidance for review types beyond ‘intervention reviews’ (e.g., diagnostic or screening RRs).&lt;br&gt;8) Work towards development of criteria as to when it is appropriate to undertake a RR vs. standard Cochrane SR or a living SR.</td>
<td><strong>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.</strong></td>
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<th><strong>Ongoing</strong></th>
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<td><strong>Our Methods group does limited Methods research and development for Cochrane. We do methods research and development as individuals and publish with our home base affiliations. This approach facilitates collaborations with key methodologists from a range of institutions to inform Cochrane DTA Methods.</strong></td>
<td><strong>An empirical study comparing the impact of using different statistical methods for random effects meta-analysis applied to meta-analyses in the Cochrane reviews. Specifically, we are examining the impact of using different heterogeneity variance estimators (Paule-Manel, Restricted Maximum Likelihood, and DerSimonian and Laird) and different methods for confidence interval calculation for the summary effect estimate (Hartung-Knapp-Sidik-Jonkman, Wald-type).</strong></td>
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