Research and Development 2020-2021
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- We published evidence that reporting of harms is still sub-optimal.
- We are finishing the CONSORT Harms update and working with senior CONSORT Executive so that enhanced harms reporting is incorporated into the main checklist.

Publication:

Methodological projects initiated and led by the Bias Methods Group:
- The Bias Methods Group actively participated in the implementation and rollout of the revised tool to assess risk of bias in randomized trials (RoB 2) in Cochrane. Funding source: Cochrane and other
- The Bias Methods Group led the work on developing a tool for assessing risk of bias due to missing evidence (ROB-ME). During the past year, a preliminary version of the tool has been made publicly available [link to tool] and the tool has been pilot tested. Funding source: other
- The Bias Methods Group led the work on developing a tool for addressing conflicts of interest in randomised trials (TACIT). A preliminary version of the tool has been developed and during the past year pilot and user testing has been initiated. Funding source: other

Methodological projects with participation from convenors of the Bias Methods Group:
- Convenors of the Bias Methods Group have led the work on updating the reporting guideline for systematic reviews (PRISMA). The updated guideline was published in BMJ in 2021: Page MJ, McKenzie JE, Bossuyt PM, Bouter L, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. Funding source: other
- Convenors of the Bias Methods Group were involved in the process of updating reporting guidelines for protocols for randomised trials (SPIRIT) and randomised trials (CONSORT). The Bias Methods Group was involved in developing a database with literature relevant to SPIRIT or CONSORT (the SCIP database), conducting a scoping review on suggested changes for SPIRIT or CONSORT, and conducting a systematic evaluation of CONSORT extensions. Funding source: other
- Convenors of the Bias Methods Group led the work on developing updated versions of RoB 2 for cluster-randomised and crossover trials. During the past year, test versions of both tools have been made publicly available [link to tools].
Commented [EF1]: Highlight to other MGs for collaboration purposes

Commented [EF2]: Flag to other MGs

Methods research and developments in the year ahead:
In the year to come, the Bias Methods Group will continue the work on implementing and developing core tools to assist authors in conducting systematic reviews. The main priorities will be to participate in the rollout of RoB2 including training activities related to the tool, and to continue the development of ROB-ME and TACIT.

Network meta-analyses:

- Visualizing the evolution of evidence: Cumulative network meta-analyses of new generation antidepressants in the last 40 years, Y Luo, A Chaimani, TA Furukawa, Y Kataoka, Y Ogawa, A Cipriani, ... Research Synthesis Methods 12 (1), 74-85
- Conduct and reporting of individual participant data network meta-analyses need improvement, A Chaimani, BMC Medicine 18 (1), 1-2

Overviews:
Our current efforts are focused on developing a reporting guideline for overviews (Pride). During the last year, we completed our second delphi survey and held a virtual consensus meeting. We are currently working on the manuscript and E&E document, and hope to have this completed and ready to submit for publication by the end of 2021.
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<tbody>
<tr>
<td><strong>Cochrane Methods</strong></td>
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| **Cochrane Methods**                         |
| Not reported.                                |

| **Cochrane Methods**                         |
| **Equity**                                   |
| • In 2020, we published a framework for identifying and mitigating the equity harms of COVID-19 policy interventions. |
| • We are co-investigators on an eCOVID grant in which a living map of COVID-19 recommendations is being developed. This project included developing methodological guidance to support the consideration of equity in reviews and decision making for COVID-19. We also developed a framework for classifying equity-related reviews and piloted this on studies included COVID-END inventory. |
| • In March 2021, we successfully applied for funding to develop guidance for multi-stakeholder engagement in systematic reviews. This project will begin in late 2021. |

| **Cochrane Methods**                         |
| **GRADEing**                                 |


# Research and Development 2020-2021 
By Group

**Completed:**
- Based on a comparison of results based on IPD with those based on aggregate data, a decision tree was developed to help researchers systematically determine when aggregate data MAs have enough information for robust clinical conclusions, and when the IPD approach might add considerable value.
  

- Based on IPD, determined that the association between blood pressure differences and stroke risk multiplication was not the same between individuals, as that within individuals; and within individuals, it was not the same when on diuretics as when on betablockers (final analyses being conducted prior to submission).

- Undertook pilot work exploring potential for developing topic-based IPD repositories (based on depositing data at the end of IPD projects)
  
  

- An IPD network meta-analysis, to examine the comparative efficacy / safety of cognitive enhancers by patient characteristics for managing Alzheimer’s, showed that the choice among different cognitive enhancers may depend on patient’s characteristics (submitted)

- An IPD network meta-analysis, to examine the comparative efficacy / safety of long (detemir or glargine) and intermediate-insulin (NPH) regimens for type 1 diabetes for different patient characteristics, showed that long-acting insulins reduced A1c compared to intermediate-acting insulins and were associated with lower severe hypoglycaemia (submitted)

- Conducted a collaborative meta-analysis to investigate the long-term benefits and risks of adjuvant trastuzumab on breast cancer recurrence and cause-specific mortality, which showed that adding trastuzumab to chemotherapy for early-stage, HER2-positive breast cancer reduces recurrence of, and mortality from, breast cancer by a third, with worthwhile proportional reductions irrespective of recorded patient and tumour characteristics.
  

**Planned:**
- Richard Riley, Jayne Tierney and Lesley Stewart: Following on from the publication of a book on meta-analysis using IPD, a series of individual papers are planned to further expand on specific topics covered by the handbook e.g. embarking on an IPD project

- Larysa Rydzewska, Jayne Tierney, Lesley Stewart and Mike Clarke: Initiating a project, together with members of the Cochrane Prospective Meta-analysis Methods Group, to develop global standards for data sharing. Grant funding is currently being sought for this project

- Sarah Burdett and Jayne Tierney: Ongoing collaborative project, based on IPD collected from bladder cancer trials, to investigate potential surrogate outcomes for overall survival
Research and Development 2020-2021
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- Jayne Tierney and Larsya Rydzewski: IPD collected from prostate cancer trials is being used to identify potential surrogate outcomes for overall survival (as part of the STOPCAP programme to speed up the evaluation of therapies for metastatic hormone-sensitive prostate cancer)
- David Fisher, Peter Godolphin and Jayne Tierney: Building on a previous project [BMJ 2017], which provided guidance (and associated Stata programs) for estimating, reporting and plotting interactions between participant covariates and treatment effects in order to avoid aggregation bias. This work is being extended to estimate within-trials interactions for both aggregate data and for modelling continuous covariates and prognostic modelling in IPD meta-analysis
- Francois Gueyffier: Using IPD to validate a new method (see above) to explore the relationship between blood pressure changes induced by treatment and the associated reduction in the risk of stroke
- Aretil Angeliki Veroniki: Protocol in development for an IPD network meta-analysis compare the effect of prophylactic, intermediate, and therapeutic dose anticoagulation on 28-day all-cause mortality in hospitalized patients with Covid-19
- Brooke Lewis, Brett Thombs and Andrea Benedetti: The DEPRESSD team (https://www.depressd.ca/) was awarded a 3-year grant by the Canadian Institutes of Health Research (CIHR) to develop and test statistical methods for individual participant data meta-analysis in diagnostic test accuracy

ISSG Search Filter Resource:
https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fsites.google.com%2Fsa%2Fyork.ac.uk%2Fissgisssearch.filt-ers-resource%2Fhome%26amp%3Data%3D04%7C01%7Celem%40cochrane.org%7C%7F2a%0857db95495a10d08d958e8aa%7Cbc7c21e4db7453391638e1451c1caah%7C0%7C%7C37634865146887684%7C%7Cunknown%7C0TWFsbGZsb3BeyIWiwMcAgwiAwMDAIIJCjQjBhY2UuMzliJCjBTI6k1haWwiLCjXVCjEmn0%3D%7C3000%26amp%3Ddata%3Dp%7B2BB7EqY4QoGfdVT9953FOgzlAMuUd318U7KoO%3D%26amp%3Dpreserved%3D0

Julie Glanville and Carol Lefebvre, together with Paul Manson, Sophie Robinson, and Naomi Shaw are the editorial team for 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 appraisals for some of the filters and published reviews comparing filters.

The site continues to be updated monthly. New features added during 2021 so far include links to launch filters in PubMed and the addition of comments, correspondence and errata to search filter records.

SuRe Info web resource:
https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fport.altmetric.com%2F4%7C01%7Celem%40cochrane.org%7C%7F2a%0857db95495a10d08d958e8aa%7Cbc7c21e4db7453391638e1451c1caah%7C0%7C%7C37634865146887684%7C%7Cunknown%7C0TWFsbGZsb3BeyIWiwMcAgwiAwMDAIIJCjQjBhY2UuMzliJCjBTI6k1haWwiLCjXVCjEmn0%3D%7C3000%26amp%3Ddata%3DscDsraSB7REosozKcKzE3PkwσqUGN8088hqTkMXOu0k0%3D%26amp%3Dpreserved%3D0
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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.

The NRSIMG has continued to collaborate with the Bias Methods Group to develop/improve tools for assessing the risk of bias in primary studies.

- Convener (HW and BR) are working on a risk of bias approach for the discontinuity design, an increasingly common approach in social science and public health. One of the Bias Methods Group conveners (Julian Higgins) is aware of this work, and is keen to incorporate the finished product as an extension to ROBINS-I.
- The NRSIMG collaboration with Sandra Eldridge and colleagues on an extension of RoB 2 for cluster RCTs has been finalised (see URL below).
- The NRSIMG has collaborated with Julian Higgins and Jonathan Sterne to develop a "version 2" of ROBINS-I for cohort studies, including algorithms to map responses to signalling questions to bias domain judgements (reported last year). This version will align ROBINS-I more closely with RoB 2 for RCTs, including algorithms to help users proceed from signalling questions to answers to risk of bias judgements.
- NRSIMG conveners (BS, PT, BR) have continued to collaborate with an OMERACT working group on a second paper to define contextual factors in rheumatology studies (two publications are listed below).

Patient Reported Outcomes Minimal Important Difference (PROMID) database in development but website is publicly accessible: the largest database of anchor-based MID estimates for PROs. By providing easy access to available MIDs, including ratings of their credibility, and thus by reducing the time, effort, and likelihood of error in MID estimate identification and selection, the inventory will close the gap between the estimation of MIDs and their subsequent application for facilitating the interpretation of PROs in clinical trials, systematic reviews, and clinical practice guidelines. [Link to the database]

- Development of a criterion to assess construct proximity, an alternative to the correlation between PROM and anchor when establishing the credibility of an anchor-based MID estimate
- Development of principles for selection of an MID estimate for application in clinical trials, systematic review, and guidelines is currently underway. This guidance will help clinical trialists, systematic review authors and guideline developers select trustworthy applicable MIDs for interpretation of PRO data.
- Development of a reporting guideline to improve the completeness and transparency of MID estimation studies and promote higher methodologic standards is in progress.
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• Sumanth Kumbarere is working on a PhD project on how to engage with different ethnicities in a research priority setting exercise - how it affects the process and how their priorities differ. We expect the initial results of the project will be available in 2022 and we can present in relevant Cochrane events
• We worked with the EU office of WHO on an overview of reviews on research priority setting. The overview is submitted for publications.
• Further development of a national evidence gap map for research priority setting:
• Our priority is to develop better guidance on how to develop a more inclusive approach to setting priorities for research.

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• We are currently focusing on developing guidance for reporting and quality assessment of prediction models developed using Machine Learning techniques. We have published the first of a series of articles in which we appraise the methodological and reporting quality of studies developing prediction models using Machine Learning. This will result in TRIPOD-AI and PROBAST-AI. Delphi procedures to develop these tools have started or will start very soon and we will prioritise this the coming year.
• We’ve also coauthored many papers on reporting and methods for primary and meta-prognosis studies, including guidance for sample size calculations for prediction model development and validation (see reference list in ‘defining best practice’).
• Currently we focus, amongst other things on developing guidance for using GRADE in systematic reviews of prognosis studies. Guidance on GRADE for prognostic model studies has been approved by the GRADE working group and will be published in the coming year.

There is no funding for any of these projects.
• Furthermore, we are developing a risk of bias tool for Overall Prognosis studies. A protocol for this is published on the Open Compliance Framework: https://euro01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fosf.io%2FEdfk2r&amp;data=b4%7C01%7Ce6femyn%5Dcochrane.org%7C0483c5a03a143ea6530bd952b99e4c%7C6b62e21e4db74533916938c1451c1ca%7C0%7C1%7C6
3763157327889801%7CUnknoww%7C7WFpbGz%3d%3d8vWliiojMC4wLIAwMDA1LjQjoiV2uMzilLCJBTiI6Ik1hWklCJXV
C8Mn0%3D%7C0000&amp;data=Kc5WgtdI8sEWQONJlaf%2BzaToVknb9bn1hMZxe7dnk%3D&amp;reserved=0. This
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Methods / guidance papers:


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Publications:

Presentations:
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<tr>
<td><strong>Australian and New Zealand Obesity Society (ANZOS) Annual Meeting, July 2021.</strong> <em>Won Best ANZOS Early Career Researcher Oral Presentation Award, Public Health</em></td>
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<td><strong>Seidler AL, Hunter KE, Johnson BJ. Early prevention of childhood obesity - moving the field forward through collaboration. Webinar for the Centre of Research Excellence in the Early Prevention of Obesity in Childhood (CRE EPOCH), 17th December 2020</strong></td>
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<tr>
<td><strong>Other:</strong></td>
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<td>• Anna Lene Seidler was awarded a PhD for her thesis entitled, ‘Next generation systematic review methodology’</td>
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<td><strong>Future plans:</strong></td>
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<td>• Manuscript nearly ready for submission on how to search for planned, ongoing, and unpublished studies using trial registries, which is a key early step in building a PMA collaboration</td>
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<tr>
<td>• Methods projects focusing on data sharing standards, data integrity and processing</td>
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<td><strong>Funding:</strong></td>
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<td>• The group’s research is supported in-kind by each of the convenor’s respective organisations. No other funding is provided.</td>
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<th>Cochrane Methods Qualitative and Implementation</th>
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<td><strong>GRADE CERQual - celebrates 10 years since publication of the first use and we have conducted a review of the application and fidelity of CERQual. This will be completed this year and submitted for publication. Sub group work continues on:</strong></td>
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<td>(i) identifying dissemination bias in qualitative research</td>
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<td>(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. 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.</td>
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<tr>
<td>• In the next year we focus on development of the Cochrane Campbell QES Handbook.</td>
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<th>Cochrane Methods Rapid Reviews</th>
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<td><strong>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 that have been published within the last year:</strong></td>
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<td><strong>In addition, members of the RRMG published the following RR methods papers:</strong></td>
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## Research and Development 2020-2021

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<tr>
<td>Cochrane Methods</td>
<td>Searches led to identical or very similar effect estimates: meta-epidemiological study, Journal of Clinical Epidemiology, <a href="https://doi.org/10.1016/j.cej.2020.08.002">https://doi.org/10.1016/j.cej.2020.08.002</a>.</td>
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| Ongoing Projects | - Systematic Prospective Assessment of Rapid Knowledge Synthesis SPARKS (Project Lead: A Tricco; A Stevens and C Garrity – co-investigators) (Funded by CIHR)  
- Developing an extension to PRISMA for rapid reviews (Project Lead: A Stevens) (Funded by CIHR)  
- Systematic review and methods study on falsely excluded studies in the literature screening process (Project Lead: L Affengruber) (Funded by NFB Science Call 2017) |

### Priority Methods Research and Development Planned for the Year Ahead

The Cochrane RR MG has outlined a specific preliminary workplan to establish RR as a new evidence format within Cochrane. Unfortunately, this workplan did not receive any funding from Cochrane. Nevertheless, we will pursue methods research in the area of RR in the year ahead. Specifically, we plan to:

- Collaborate with Cochrane Crowd and validate the accuracy of the Screen4Me approach within RRs.  
- To seek 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.  
- Prepare a series of papers providing guidance on several steps and aspects of the RR process that will be published in the journal BMJ EBM.

Note: The RR MG is also in search of funding in order to develop guidance on when to do and when not to do rapid reviews.

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| Cochrane Methods Screening and Diagnostic Test | - Development of QUADAS-C, extension to QUADAS2 for appraising the risk of bias of comparative accuracy studies included in test accuracy reviews. Paper soon to be published. Related paper:  
- PRISMA-DTA for abstracts and the explanation and elaboration paper for PRISMA-DTA published.  
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<td>An empirical study comparing the impact of using different statistical methods for random effects meta-analysis applied to meta-analyses in the Cochrane reviews is nearing completion. Specifically, we have examined the impact of using different heterogeneity variance estimators (Paule-Mandel, Restricted Maximum Likelihood, and DerSimonian and Laird) and different methods for confidence interval calculation for the summary effect estimate (Hartung-Knapp-Sidik-Jonkman (and variants), Wald-type). This study has informed recommendations for proposed additional random effects meta-analysis methods to be included in RevMan.</td>
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