RESEARCH & IMPLEMENTATION

By Group

The second edition of the *Cochrane Handbook* will be published mid-2019. Most Methods Groups have contributed updated or novel chapters. Pre-publication chapters will be made available online towards the end of 2018. Please check the Cochrane Methods website for more information.

Cochrane Methods Adverse Effects	• Extensively updated and revised chapter on Adverse Effects for the next edition of the *Cochrane Handbook*. Publication expected early 2019.
Cochrane Methods Priority Setting	• On-going collaboration with an Australian research group on developing a reporting guideline. • The Group works closely with the REWARD, Evidence based Research network and EVIR (Ensuring Value In Research) collaboration on how the methodology of setting priorities needs to be adapted under the concept of reducing research waste.
Cochrane Methods Bias	• Convenors and members of the Group have worked on adjusting the updated Cochrane 'Risk of bias' tool 2.0. The tool was launched at the 24th Cochrane Colloquium in Seoul in October 2016. Since its launch the tool has been monitored by convenors and members of the Group to see how it has been received by the users. • Ongoing participation in the development of a tool for assessing the severity of conflicts of interest in medical research (the TACIT project). • Ongoing development of a tool for assessing risk of bias due to missing results. • Involved in the re-writing of four chapters of the *Cochrane Handbook* covering general aspects of risk of bias assessments, Risk of Bias Tool 2.0, risk of bias due to missing results, and ROBINS-I. The updated version of the *Cochrane Handbook* will be published in early 2019. • The Group receives funding from Odense University Hospital in Denmark and is hosted by Centre for Evidence-Based Medicine Odense (CEBMO).
Cochrane Methods Comparing Multiple Interventions	• Continued methodological research into network meta-analysis, either as part of core academic work or funded by grants (e.g. by Swiss National Science Foundation, Agency for Healthcare and Quality) • Further development of the CINeMA tool with support now being sought to maintain this tool into the future as a valuable resource for Cochrane authors and others. • Completed PhD: Pollock M. Advancing Methods for Overviews of Reviews of Healthcare Interventions (PhD thesis). University of Alberta, 2017
Cochrane Methods Economics	• Development of case studies for Brief Economic Commentaries and Integrated Full reviews of economic evidence. These have been funded primarily by NIHR and the Health Foundation. Details of funding and outputs are in the Key Achievements report.

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Cochrane Methods Equity	• Developed and published an equity extension for the CONSORT reporting guideline for randomized controlled trials (CONSORT Equity). The reporting guideline and the explanation and elaboration were published as one paper in the BMJ. • Authored a chapter on "Equity and Specific Populations" for the Second Edition of the *Cochrane Handbook.* • Awarded funding for a 4-year project to develop guidance for stakeholder engagement in guideline development. This project includes 4 systematic reviews, key informant interviews, a Delphi survey, and consensus meeting. This project also includes the development of an evaluation framework to assess stakeholder engagement in guideline development.

Cochrane Methods IPD Meta-analysis	• Updated IPD reviews chapter for the Second Edition of the *Cochrane Handbook*.
	• Methodological papers published on:
	  • Meta-analysis methodology
	  • Multiple imputation for multi-level data.
	  • Detecting small-study effects in meta-analyses of survival data.
	  • Meta-analytical methods to identify who benefits most from particular treatments.
	  • Framework for identifying treatment-covariate interaction in IPD network meta-analyses.
	  • Study designs other than randomised controlled trials:
	  • Selection of appropriate methods for updating prediction models.
	  • Development of a checklist (CHAMP) for the appraisal of moderators and predictors.
	  • Data sharing:
	  • Principles and recommendations for the sharing and re-use of IPD.
	  • Use and applications of IPD:
	  • Opportunities and limitations created by access to IPD.
	  • Practical implications of using real-world evidence in comparative effectiveness research.
	  • Several IPD meta-analyses have been published in, for example, breast cancer, stroke, epilepsy, trypanosimiasis, peptic ulcers, acute respiratory distress and perinatal care.
	  • Developed a prediction model for motor neurone disease.
	  • Ongoing projects:
	  • Investigating when meta-analyses of published hazard ratios are likely to be reliable, and when individual participant might be required.
	  • Developing methods for the imputation of missing data in IPD meta-analyses, to develop and validate prediction models using IPD and to improve methods for survival analysis based on IPD (with funding obtained from the Netherlands Organisation for Health Research and Development (ZonMw))
	
	Please visit the Group website for further information about IPD meta-analyses and IPD-related methodological publications undertaken.

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Cochrane Methods Information Retrieval	• Interim guidance on the inclusion of clinical study reports and other regulatory documents in Cochrane Reviews (led by Tom Jefferson, Acute Respiratory Infections Group, with input from the Group and a number of other Methods Groups). The team drew on their experience with neuraminidase inhibitors, the first Cochrane Review based entirely on regulatory documents, and others' similar experiences to develop guidance on how to decide whether to incorporate clinical study reports and other regulatory documents into Cochrane Reviews. The project was funded by the Methods Innovation Fund 2 and is now complete. Two papers have been submitted for publication; one paper describing the two surveys that were conducted and a second paper describing the entire project. • SuRe Info web resource continues to be maintained and developed. It provides updated research-based information relating to the information retrieval aspects of producing systematic reviews and health technology assessments. Members of the group are authors of specific sections on the site and also fulfil the roles of site co-lead and member of the Steering Group. • Members of the Group contribute to the editorial team and continue to maintain the InterTASC Information Specialists' Sub-Group (ISSG) 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. • Cochrane Embase OVID RCT Filter has been converted to work in Embase.com. Several technical issues were identified with conversions. These have been submitted to a journal and will be presented at the Colloquium in 2018. The next filter to be developed will be to identify controlled trials in LILACS.
Cochrane Methods NRS for Interventions	• Further development of risk of bias tools including; the revised tool for RCTs and a modification for cluster RCTs; version 2 of ROBINS-I for cohort studies; modifications of ROBINS-I for particular NRSI designs (e.g. time series, controlled before-and-after studies, risk-difference and instrumental variable analyses); and algorithms to reach risk of bias judgements based on the responses to signalling questions.
Cochrane Methods Patient Reported Outcomes	• Providing resources for interpreting results of RCTs included in Cochrane reviews.

Cochrane Methods Prognosis	• Methods Innovation Fund 2
	  o Various approaches for design and analysis of reviews and meta-analysis of prognostic models have been developed and published.
	  o Methods for detecting small-study effects and funnel plot asymmetry in prognostic factor studies have been published.
	• Two comprehensive papers on methods for design and meta-analysis of prognostic factor studies are underway.
	• A formal risk of bias tool for prediction model studies (PROBAST) has been submitted for publication.

Cochrane Methods

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	• The Group is working on a number of projects to explore the uptake of published tools and guidance for carrying out prognostic factor reviews, the generalisability of prognostic review methodology to a variety of clinical specialties, and the efficacy of current search filters for prognostic studies. (supported by non-Cochrane funding).
Cochrane Methods Prospective Meta-analysis	• The group has re-commenced work on a study 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.
Cochrane Methods Qualitative and Implementation	• Continuation of GRADE-CERQual work. The Group contributed to a 3-day methodological retreat at the Brocher Foundation in Geneva in 2017. • Subgroups are investigating: o dissemination bias in qualitative research and; o tools to assess methodological limitations.
Cochrane Methods Rapid Reviews	• Completed the research project related to abbreviated literature searches; and published one chapter in the WHO Evidence Alliance guidance on rapid reviews. Several projects are in the manuscript phase. • Below is a specific list of completed and ongoing research undertaken in 2017 and expected to complete by 2019, specific to rapid reviews methodology and that involve one or more RRMG conveners: o Trading Certainty for Speed - How much uncertainty are decision makers and guideline developers willing to accept when using rapid reviews: an international survey [completed] o Assessing the validity of an ultra-rapid review strategy: four case studies from oncology and public health – A Study protocol. (Project Leads: Cochrane Austria, Cochrane Rapid Reviews Methods Group, & Cochrane Public Health Europe) (March 2017) [study in progress] o 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 – CIHR] [manuscript in progress] o A cross-sectional, comparative methodological study of formatting characteristics of published and unpublished RR reports (Project Lead: C Garritty) [Funded – CIHR] [manuscript in progress] o Evaluation of conduct characteristics of rapid reviews (Project Lead: A Stevens) [Funded – CIHR] [study ongoing – data collection phase] o Developing an extension to PRISMA for rapid reviews (Project Lead: A Stevens) [Funded – CIHR] [study ongoing] o Assessing rapid reviews as an information product according to the BRIDGE criteria: an evaluation pilot study (Project Lead: C Garritty); [Funded – CIHR] [manuscript in progress] o Rapid Reviews 2.0 – A second look at the OHRI approach to conducting rapid evidence summaries. Revisions and updates to our methodology (Project Lead: C Garritty) [Unfunded] [manuscript in progress] o Systematic Prospective Assessment of Rapid Knowledge Synthesis SPARKS (Project Lead: A Tricco; A Stevens and C Garritty – co-investigators) [Funded – CIHR] [project ongoing]

	• In 2018/2019 funding will be sought for the following:
	  o Assessing independent versus single researcher and the impact of automated searching
	  o Detecting differences between Cochrane systematic reviews and rapid reviews at varying stages of conduct
	  o Assessing the utility of speeding up the abstract screening process using online collaborative tools
	  o Exploring an optimal rapid review format for Cochrane
	  o Developing an evidence-informed rapid review process map to guide development
	  o A comparison between Cochrane Systematic Reviews and Rapid Reviews
	  o Assessing the performance of rapid reviews against MECIR standards
	  o Developing search strategies to assist in the identification and indexing of rapid review reports
	  o Exploring strategies to involve patient partners (consumers) in rapid reviews
	• The Group will also further explore links with other Cochrane products including: living systematic reviews; updates/targeted updates; and overview of overviews.
	• Development of guidance on when to do and when 'not' to do rapid reviews.

Cochrane Methods Screening and Diagnostic Tests	• The PRISMA-DTA Group are preparing an "Elaboration and Explanation" document to accompany the PRISMA-DTA Statement published in January 2018. This document will include examples and explanation to facilitate the use and understanding of the PRISMA-DTA Statement. • QUADAS-2 is the methodological quality assessment tool recommended by Cochrane for DTA reviews. Developers of the tool recognised its limitation in appraising comparative test accuracy studies (i.e. studies that directly compare the accuracy of two or more index tests in the same study population either by giving patients all the tests or randomising patients to one of the tests). A Steering Group and an Advisory Group involving many members of the original QUADAS Group have been convened to lead and support the process of developing an addition to QUADAS-2: QUADAS-2C for comparative test accuracy studies. The work has begun but lacks funding - look out for future updates.
Cochrane Methods Statistics	• Methods Innovation Fund 2 o "Statistical methods for updating meta-analyses" has now concluded. The results of this project were discussed at a collaborative meeting in November 2017 and the conclusions from this meeting passed to the Cochrane Scientific Committee. This research will support decisions as to how to perform meta-analyses when undertaking updates in Cochrane Reviews. • A comprehensive overview of "*The available methods in the methodological literature for calculating a confidence interval for the overall effect size under the random-effects model*" has been conducted and this work is currently under review. In this paper the authors indicate whether some methods are preferable by considering the results of comparative simulation and real-life data studies, as well as examining potential issues surrounding the computation of prediction intervals under the random-effects model. Although the DerSimonian and Laird method is the most frequently used approach and is the default method for meta-analyses with random effects, it has been long challenged due to its unfavourable statistical properties. Several alternative methods have been proposed that have

	better statistical properties in specific scenarios. Overall, the Hartung-Knapp-Sidik-Jonkman method is one of the best alternatives, as it performs well in meta-analyses with fewer than ten studies (which are common in Cochrane reviews). However, caution is required in meta-analyses with rare events, in meta-analyses with fewer than five studies and when the data are highly homogeneous.