Cochrane Methods

Risk of Bias 2
Cochrane Review Group
Starter Pack

May 2022

Contents

About Risk of Bias 2

Up-to-date information from the developers on Risk of Bias 2 (RoB 2) is available via the Risk of Bias tools website.

Up-to-date information on the piloting and implementation of RoB 2 can be found via the Cochrane Methods Website.

Watch the six-minute video on RoB 2 guidance, training, and tools here

The RoB 2 tool has two supplemental variants. One for cluster RCTs and one for crossover RCTs. Details of these are listed on via the Risk of Bias tools website. Authors should use the variants where necessary. Interim guidance for presenting cluster and crossover trials in reviews is described below.

The table below gives an overview of how RoB 2 differs from the original Risk of Bias tool (RoB 1).

	RoB1	**RoB2**
Focus of assessment	Study (all studies in the review)	Outcome data with a numerical result– if there is **no numerical result** for an outcome from a specific study, then you do not need to complete a risk of bias assessment as it will not be contributing to the review
Structure	7 standard domains	Preliminary considerations Signalling questions 5 domains plus overall risk of bias
Domains	-Random sequence generation -Allocation concealment -Blinding of participants and personnel -Blinding of outcome assessment -Incomplete outcome data (attrition bias) -Selective reporting (reporting bias)* -Other bias	-Bias arising from the randomization process -Bias due to deviations from intended interventions -Bias due to missing outcome data -Bias in measurement of the outcome -Bias in selection of the reported result Plus 'Overall risk of bias'

Basis of judgement	Author defined	Signalling questions answered Yes; Probably yes; Probably no; No; No information with suggested algorithm for reaching judgement
Judgement options	Low risk – Unclear – High risk	Low risk – Some concerns – High risk (plus optional direction of bias)
*Authors should note that, as a result of the move to outcome-based assessment, selective reporting bias is not part of the revised tool. *Guidance for using RoB 1 is available in v5.2 or v5.1 of the Cochrane *Handbook*.		

What guidance is available?

Resources for RoB 2 in Cochrane Reviews

An Introductory leaflet on RoB 2, the most -up-to-date version of this Starter Pack and the RoB 2 FAQs for Cochrane Reviews can be found via the Cochrane Methods website.

Full guidance on the Cochrane Risk of Bias tool for randomised trials (RoB 2)

Detailed and comprehensive guidance on RoB 2 can be found via the Risk of Bias tools website. Review teams can use this to help answer any question they have about the tool.

RoB 2 cribsheet

This document summarises the RoB 2 tool, providing the fields that need to be completed, brief explanations for help answer the signalling questions within each bias domain, and the key considerations for how to come to risk of bias judgements for each domain and overall. The document can be found via the Risk of Bias tools website here. It is intended to be used regularly as a reference document while completing the tool – particularly to help answer the signalling questions.

Handbook

The *Cochrane Handbook for Systematic Reviews of Interventions* (Version 6) relevant chapter is Chapter 8, titled 'Assessing risk of bias in a randomized trial'. Review teams should ensure they are familiar with contents of this chapter.

MECIR

The Methodological Expectations for Cochrane Intervention Reviews (MECIR) includes nine standards for assessing risk of bias in included studies here (C52-60). Review teams are expected to follow the MECIR standards.

Using RevMan Web

RoB 2 is only available in RevMan Web and is not supported by RevMan 5 (desktop version).
The key resource for RevMan Web is the Knowledge Base here. This includes details on getting started and introductory webinars, as well as step by step guides, the ability to search and how to use the RevMan Web Practice Platform.

How-to guides for RoB 2 data input in RevMan Web

Guidance on how to enter RoB 2 assessments in RevMan Web is set out in this four-minute video.

How to use the RoB 2 tool for randomised trials (RoB 2)

Detailed and comprehensive guidance on RoB 2 can be found via the http://www.riskofbias.info. Review teams can use this to help answer any question they have about the tool.

Monthly methods Web Clinic

Cochrane authors and Cochrane Review Group staff can submit RoB 2 questions to the **monthly Methods Support Unit Web Clinic** for discussion. Information on dates and how to submit questions here.

Training

Cochrane Learning Live webinars

Nine Cochrane Learning Live webinars presented by leading experts are available. Each has been broken into short sections and can be viewed through the links below.

RoB 2: Introducing RoB 2 [May 2020]
RoB 2 Domain 1: Bias arising from the randomisation process [June 2020]
RoB 2 Domain 2: Bias due to deviations from the intended interventions [July 2020]
RoB 2 Domain 3: Bias due to missing outcome data [August 2020]
RoB 2 Domain 4: Bias in measurement of the outcome [September 2020]
RoB 2 Domain 5: Bias in selection of the reported result [October 2020]
RoB2: Reaching an overall RoB judgement and incorporating RoB assessment into analysis and interpretation [November 2020]
RoB 2: Bias in other types of studies: cluster-randomised and cross-over [December 2020]
RoB 2: Editorial considerations and Common errors in using RoB 2 [January 2021]

Cochrane Interactive Learning Module

The Cochrane Interactive Learning (CIL) Module 5 on 'Introduction to study quality and risk of bias' is RoB 2 compliant. Full CIL course can be accessed here.

What tools are available?

Data collection form

A sample data collection form is available that can be seen as a starting point for developing bespoke data collection forms for reviews. It will need to be modified accordingly. The form can be found here.

Tools for managing your RoB 2 assessments

The developers have created two templates for completing the RoB 2 assessment and both are available via the Risk of Bias tools website here:

1. RoB 2 Excel tool (**recommended**) – this tool has a manual embedded within it, with short videos on how to use the RoB 2 excel tool
2. RoB 2 Word template.

Other tools

We advise that Cochrane authors use RevMan Web to create forest plots with traffic lights to visually represent RoB 2 data. If authors want to showcase the RoB 2 assessments in other ways, *robvis* is a tool for creating other risk of bias figures and can be found via the Risk of Bias tools website. These figures can be uploaded into RevMan Web as an additional figure. If you use *robvis*, please ensure you cite it in your review: https://www.riskofbias.info/welcome/robvis-visualization-tool.

RoB 2 considerations for protocol development

Watch the five-minute video about RoB 2 protocol considerations here

There are ten key items to consider when using the RoB 2 tool:

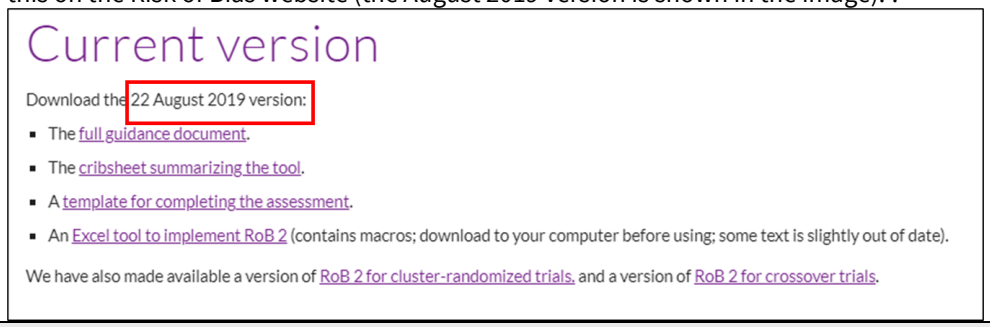
What to report	Further details
Methods section - '**Assessment of risk of bias in included studies'**	
1. State that RoB 2 tool will be used and reference it	Reference Sterne et al 2019 BMJ paper and / or Cochrane Handbook (version 6) Chapter 8. **Guidance**: MECIR PR27
2. State your effect of interest - effect of assignment or effect of adherence	**Guidance**: Section 1.3 Detailed guidance (Riskofbias.info); Section 8.2.2 Cochrane Handbook.
3. List or refer to the results that will be assessed using RoB 2, inc. outcome(s), outcome measure(s) and timepoint(s)	**Guidance**: Section 1.3 Detailed guidance (Riskofbias.info); Section 7.3.2, Section 8.2.1 and Section 8.7 Cochrane Handbook.
4. (If applicable) State how you will handle crossover RCTs and cluster RCTs .	Reference the RoB variant for crossover trials and/ or the RoB 2 variant for cluster trials. **Guidance**: RoB for crossover trials via riskofbias.info and RoB 2 for cluster trials via riskofbias.info ***NB**: Please note, as of December 2020, the cluster and cross trial variants for RoB 2 have not been developed in RevMan Web yet so there is interim guidance on how to display these results. See section below* ***NB**: Please note, if you have intended from the OUTSET to ONLY use data from the first period of the crossover, then you can use the standard version of RoB 2 as it is. However, please be alert to the potential impact of selective reporting of first period of data only when carry over is detected by trialists. Omission of trials which do not report first period data may lead to bias at the meta-analysis level. For details are in Section 23.2 Cochrane Handbook.*
5. State who will assess RoB2 (initials), how many and whether independently and duplicate	**Guidance**: MECIR C53; Section 7.3.2 Cochrane Handbook.
6. List the domains of the tool	**Guidance**: Section 1.3 Detailed guidance (Riskofbias.info); Section 8.2.3 Cochrane Handbook.
7. List the judgment options (High, Some Concerns, Low) and how overall risk of bias is reached, e.g. using the signalling questions/tool algorithms	**Guidance**: Section 1.1, Section 1.2.1 and Section 1.2.3 Detailed guidance (Riskofbias.info); Section 8.2.3 and Section 8.2.4 Cochrane Handbook.
8. State if you plan to use any tools to manage the assessment of bias using RoB 2	For example, the RoB2 Excel tool to implement RoB 2 (available on the riskofbiasinfo.org website) **Guidance**: MECIR C54; Section 7.3.2 Cochrane Handbook.
Methods section - '**Data synthesis'**	
9. State whether the primary analysis will include all eligible studies or only those which have low risk of bias, or low risk and some concerns	This may depend on the number of studies with each risk of bias rating as you will need sufficient numbers for the analyses. It could also be appropriate to pool data from studies at high risk of bias and use a sensitivity analysis to assess the effects of restricting the analysis to RCTs overall 'low' or 'low/some concerns'. **Guidance**: MECIR C21, Section 7.6.2 Cochrane Handbook.
Methods section - '**Subgroup analysis and investigation of heterogeneity'**	

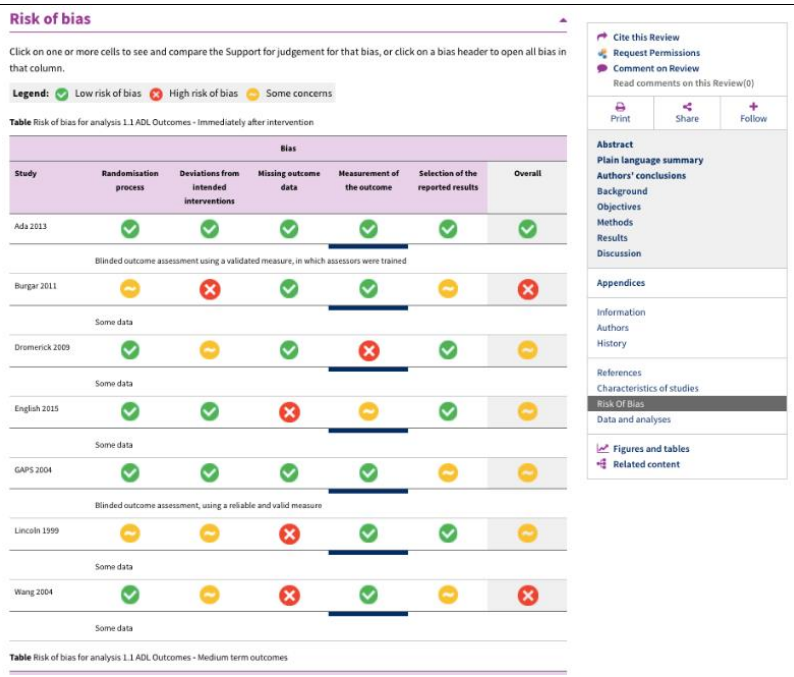
(If applicable) Specify if subgroup analysis is planned based on risk of bias	Consider whether overall risk of bias should be used as the basis for any subgroup analysis. Subgroup analyses may be done as a means of investigating heterogeneous results, or to answer specific questions about particular patient groups, types of intervention or types of study (as well as clinical heterogeneity there is methodological heterogeneity). If you would like to perform subgroup analyses using risk of bias, please discuss with your CRG Managing Editor during protocol development. **Guidance**: MECIR C22; Section 10.11.2 and Section 7.6.2 Cochrane Handbook.
Methods section - '**Sensitivity analysis'**	
(If applicable) Specify if sensitivity analysis is planned based on risk of bias	Consider whether overall risk of bias should be used as the basis for any sensitivity analysis. A sensitivity analysis is a repeat of the primary analysis or meta-analysis in which alternative decisions or ranges of values are substituted for decisions that were arbitrary or unclear. In respect to risk of bias, review authors may perform sensitivity analyses to show how conclusions might be affected if studies at a high risk of bias, or high risk bias and some concerns, were included. **Guidance**: MECIR C71; Section 10.14 and Section 7.6.2 Cochrane Handbook.
Methods section - '**Summary of findings and assessment of the certainty of the evidence'**	
10. State how the RoB 2 assessment will be used to assess the certainty of the evidence/ GRADE/ SoF	State that the *overall* RoB2 judgement will be used to feed into the GRADE assessment. **Guidance**: MECIR C54; Section 7.3.2 Cochrane Handbook.
Other considerations	Authors should not adapt the RoB 2 tool. State how you will store and present your detailed RoB2 data - the RoB 2 tool may generate a large amount of data. These data should be publicly and openly available in a repository, and should be cited and linked to in the main text of the Cochrane review as supplemental data or files (they should not be included within the Review itself). Guidance on how to deposit and link to supplemental data in repositories is available in 'Supplemental data and files'. If authors choose not make their detailed risk of bias assessments publicly and openly available in a repository, they should be willing and able to share data with readers following reasonable requests, and the Cochrane review should state "Detailed risk of bias assessments are available on reasonable request". The detailed assessments must, however, be made available to editors and peer-reviewers on submission of their article to Editorial Manager. Further information on submitting supplemental files to Editorial Manager is available in Submit the first draft of your protocol, review or update to Editorial Manager **Guidance**: MECIR C54; Section 7.3.2 Cochrane Handbook. See this published protocol as an example: • Contraception decision aids to improve care and effective method use (missing Point 8 – whether they have plans to use any tools to manage the assessment of bias using RoB 2)

RoB 2 considerations for reporting the review

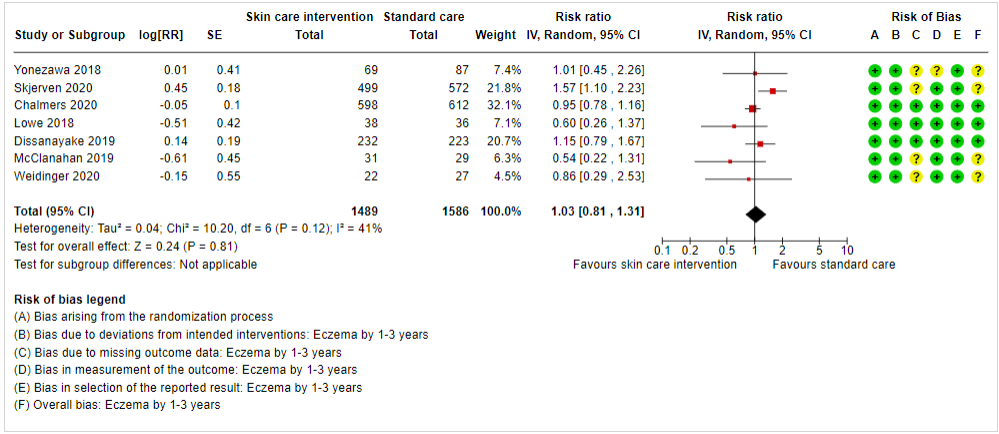
Watch the seven-minute video about RoB 2 review reporting considerations here

There are seven key items to consider when reporting RoB 2 in the full review:
Please note, this checklist ONLY highlights RoB 2 considerations for review reporting.

What to report	Further details
Methods **- 'Assessment of risk of bias in included studies'**	
1. Include all the RoB 2 considerations from the Protocol.	Compare the Review to the Protocol to ensure they are consistent (it may be useful to assess the reporting against the protocol checklist for RoB 2 to ensure everything was included originally). If there were any deviations from the Protocol, these should be detailed in the 'Differences between protocol and review' section (see below).
2.State the version of the RoB 2 tool that was used.	The riskofbias.info website lists the current version and archived versions of the RoB 2 tool. Ensure you state which version of the tool you used. The image below shows where to find this on the Risk of Bias website (the August 2019 version is shown in the image). .  Current version Download the 22 August 2019 version: ▪ The full guidance document. ▪ The cribsheet summarizing the tool. ▪ A template for completing the assessment. ▪ An Excel tool to implement RoB 2 (contains macros; download to your computer before using; some text is slightly out of date). We have also made available a version of RoB 2 for cluster-randomized trials, and a version of RoB 2 for crossover trials.
Results **- 'Risk of bias in included studies'**	
3.Refer to the results-level RoB 2 tables, which includes the support for judgement for each domain assessment. For analyses with mixtures of individually randomised RCTs, cluster RCTs or cross-over RCTs see interim guidance below.	The results-level RoB 2 tables are located in the 'Risk of bias' section after the characteristics of studies section. Each outcome prespecified for risk of bias assessments (likely to be the reviews' critical and important outcomes included in the SoF table) should have a table that includes the risk of bias judgements (high, low or some concerns) and the support each judgement. ***NB****: Please note, as of January 2022, the support for each judgement in this table will not be copyedited. Please ensure you spell check and proofread your assessments. It is the authors' responsibility to ensure these are accurate.* **Guidance**: How to create and view the Risk of bias tables is detailed in the RevMan Web Knowledge Base (see RoB 2 in RevMan Web).

	 In certain circumstances, authors may wish to use other figures that best present the risk of bias data, e.g. weighted risk of bias bar plots can provide a succinct summary when there are lots of studies in a synthesis.
4. State how to access detailed risk of bias assessments data (with consensus responses to the signalling questions).	These data should be publicly and openly available in a repository, and should be cited and linked to in the main text of the Cochrane review as supplemental data or files (they should not be included within the Review itself). Guidance on how to deposit and link to supplemental data in repositories is available in 'Supplemental data and files'. If authors choose not make their detailed risk of bias assessments publicly and openly available in a repository, they should be willing and able to share data with readers following reasonable requests, and the Cochrane review should state "Detailed risk of bias assessments are available on reasonable request". The detailed assessments must, however, be made available to editors and peer-reviewers on submission of their article to Editorial Manager. Further information on submitting supplemental files to Editorial Manager is available in Submit the first draft of your protocol, review or update to Editorial Manager
5.Provide a brief overview of the risk of bias assessments.	Consider ***overall comments on key aspects*** of the risk of bias assessments, e.g. the quality of randomization and extent to which blinding was implemented. Consider whether there are ***important differences*** in risk of bias by outcome. If ***risk of bias assessments are very similar*** (or identical) for all outcomes in the review, a summary of the assessments across studies should be presented here. If ***risk of bias assessments are very different*** for different outcomes, this section should be very brief, and summaries of the assessments across results should be discussed with other GRADE considerations in the Discussion (see point 7 below).
***Results* - 'Effects of intervention'**	
6. Refer to visual representations of the risk of bias assessments in relation to each result. For analyses with mixtures of individually randomised RCTs, cluster	Using forest plots with traffic lights is highly recommended (reference this from the Analyses section – you do not need to add additional Figures). **Guidance**: How to create and view forest plots with traffic lights in Analyses is detailed in the RevMan Web Knowledge Base (see RoB 2 in RevMan Web). It may be very helpful to stratify forest plots according to overall risk of bias.

RCTs or cross-over RCTs [see interim guidance below.]



For synthesis without meta-analysis, we recommend that a column is added to any visual representation of the data that highlights the overall risk of bias associated with each of the results in the table/figure, e.g.:

Table 1. Health related quality of life

Author	Sample size	Type of intervention	Questionnaire	Domain	Intervention vs. control at follow up Mean (Standard deviation) & between group P value	Direction of effect	Overall risk of bias
Duppen 2015	73	Exercise training	SF-36 (8 domains)	Physical functioning	94.6 (10.9) 95.0 (8.5) P=0.71	Exercise = control	High
			SF-36 (8 domains)	Bodily pain	96.6 (8.1) 93.2 (17.3) P=0.96	Exercise = control	High
			SF-36 (8 domains)	General health	68.3 (27.9) 67.5(19.1) P=0.94	Exercise = control	High
			SF-36 (8 domains)	Vitality	71.7 (18.0) 70 (17.0) P=0.56	Exercise = control	High
			SF-36 (8 domains)	Role limitations due to physical limitations	100 (0.0) 91.7(21.2) P=0.16	Exercise = control	High
			SF-36 (8 domains)	Social functioning	95.8 (10.0) 100.0 (0.0)P=0.09	Exercise = control	High

Table 1. Health related quality of life *(Continued)*

Westhoff-Bleck 2013	40	Exercise training	KCCQ	KCCQ	NR	Exercise = control	High
Winter 2012	46	Exercise training	SF-36	Mental component	P=0.17	Exercise = control	High
			SF-36	Physical component	P= 0.20	Exercise = control	High
			Con-HD-TAAQOL	Symptoms	85 (10.79) 83 (10.47) P=0.31	Exercise = control	High
			Con-HD-TAAQOL	Worries	77 (15.4) 84.5 (9.21) P=0.30	Exercise = control	High
			Con-HD-TAAQOL	Impact	84 (7.19) 85.25 (6.20) P=0.91	Exercise = control	High

Each study's outcome of health related quality of life was individually assessed using risk of bias 2; all studies were judged as a high risk of bias under the domain 'Measurement of the outcome'. SF-36, 36-Item Short Form Health Survey; HRQoL, Health related quality of life; QoL, Quality of life; MLHFQ, Minnesota living with heart failure questionnaire; TACQOL, TNO/AZL child quality of life questionnaire; ConHD TAAQOL, The congenital heart disease - TNO/AZL adult quality of life questionnaire; EQ5D VAS, EuroQol Vertical Visual Analogue Scale; KCCQ, Kansas City Cardiomyopathy Questionnaire.

Physical activity interventions for people with congenital heart disease (Review)
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Guidance: Section 7.6 Cochrane Handbook

(If applicable) Give results of additional analyses (e.g., meta-regression).

***Results* - 'Subgroup analysis'**

(If applicable) Discuss any subgroup analysis conducted that relates to the risk of bias judgments.

***Results* - 'Sensitivity analysis'**	
(If applicable) Discuss any sensitivity analysis conducted that relates to the risk of bias judgments.	
***Discussion* -'Certainty of the evidence' (previously the 'Quality of the evidence' section**	
7. Discuss any risk of bias judgements that affect the certainty of the evidence along with all other GRADE considerations.	Along with the other GRADE considerations, ***highlight any important implications*** from the risk of bias assessments for each of the outcomes prespecified for risk of bias assessments (likely to be the reviews' critical and important outcomes included in the SoF table), such as whether the risk of bias assessments results in downgrading the certainty of the evidence for a specific outcome and whether the effects of the intervention may need to be interpreted with caution. **Guidance**: Section 7.5 and Section 14.2.2 Cochrane Handbook
***History* – 'Differences between protocol and review'**	
(If applicable) State if there were any deviations from the Protocol.	**Guidance**: MECIR R107 and R108.
Other considerations	See this published review as an example: • Physical activity interventions for people with congenital heart disease

Interim guidance for presentation of RoB 2 in RevMan Web for mixtures of individually randomized, cluster randomized and cross over RCTs

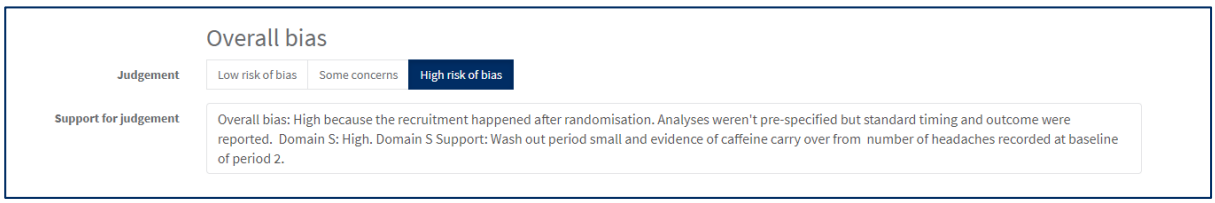
For authors using RoB 2 that include either cluster or cross over RCTs we are recommending that support for judgment regarding the cluster domain (Domain 1.b) or the crossover domain (Domain S) is placed within the overall risk of bias text box. Also in this text box should be the support for judgement for the overall risk of bias. The judgement for overall risk of bias should be displayed. This overall judgement should take into account of the risk of bias for all the domains including the cluster RCT domain (1.b), or the crossover RCT Domain S.

This workaround will mean that the bias judgement and reason for that judgement for these two domains (1.b cluster RCTs and S crossover RCTs) will be included in the risk of bias tables. Unfortunately, the judgement specific to those domains are not able to be displayed in the forest plot. We would ask authors to present a footnote information explaining the location of the judgement and support for judgement for the domains 1b and S.

We believe this is the best workaround. And will allow for authors to present risk of bias for cluster RCTs and crossover RCTs study designs.

Example text as entered in RevMan web for cluster RCTs

Example text as entered in RevMan web for crossover RCTs



What support is available?

Cochrane Learning live webinar on RoB 2 Editorial considerations

This webinar is in three parts. It takes you through what is expected in a protocol and a review, how to input data into RevMan Web and describes the common errors we have seen. It is available here

Protocol and Review development support from the Methods Support Unit

The Methods Support Unit are available to support Cochrane Review Groups with Reviews using RoB 2. Cochrane Review Groups are encouraged to seek hands-on support for the first protocol and review using RoB 2 that goes through their group and training to manage subsequent reviews. The Methods Support Unit will provide advice and guidance on an ongoing basis but will not routinely review the application of RoB 2, unless additional support is needed (e.g. for large network meta-analyses or reviews including a range of study designs).

Guidance on how RoB 2 is applied

Cochrane authors: You may send in examples of your completed risk of bias assessments to your Cochrane Review Group to check before you finish your review write-up, e.g. the consensus agreed completed RoB 2 Excel tool.
Managing Editors and Editors: As you learn RoB 2 you may ask the Methods support Unit to check examples of authors' completed risk of bias assessments to see if the RoB 2 is being applied according to the guidance. Once you become familiar with the tool you may decide to make these checks yourselves.

Using RevMan Web

Your main source of support is the RevMan Web Knowledge Base [available here]. This includes details on getting started and introductory webinars, as well as step by step guides. It includes specific advice on RoB 2.

FAQs

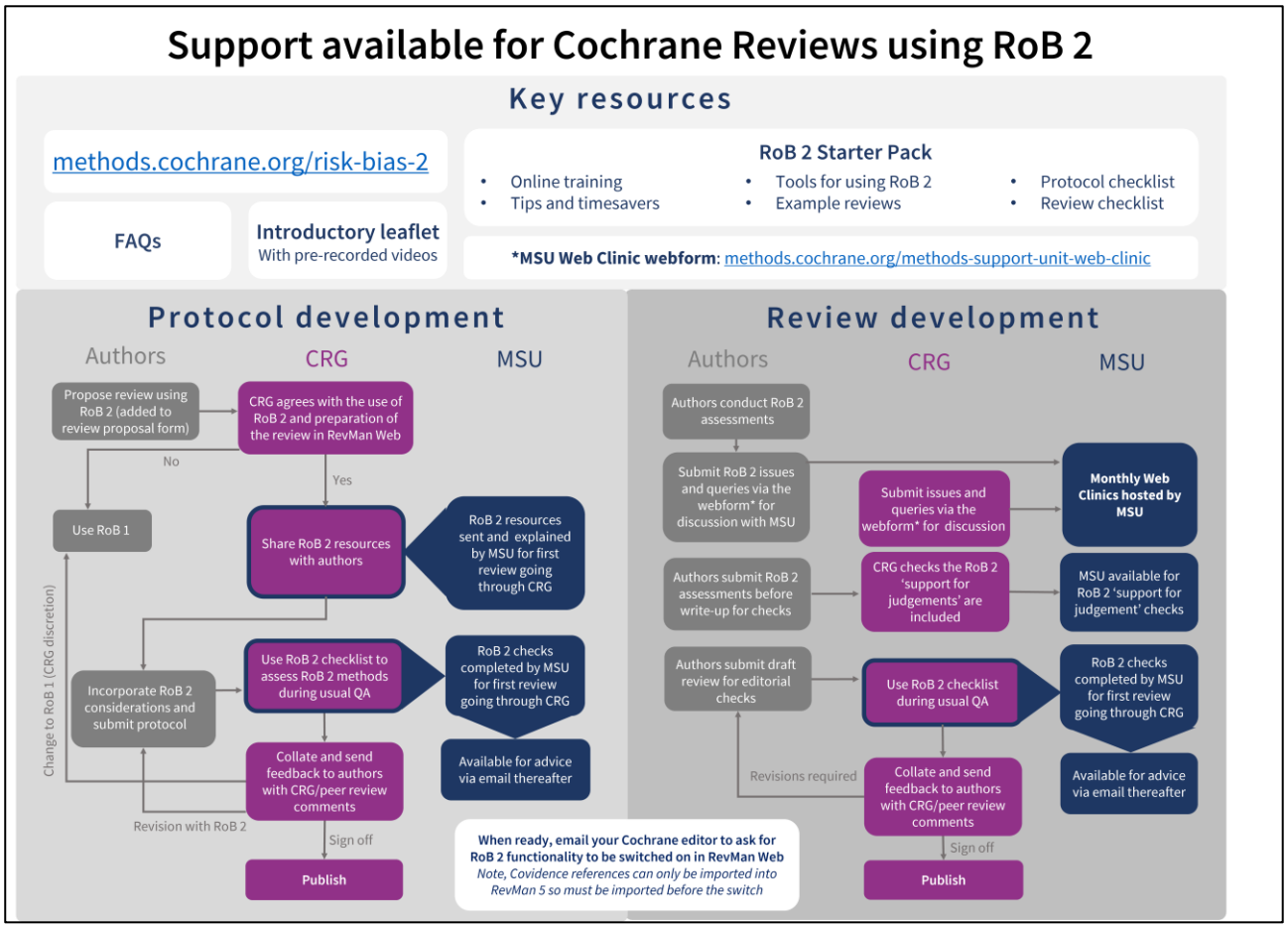
We have developed a list of our most frequently asked questions raised by authors, Managing Editors and editors. support

Monthly Web Clinics

Cochrane authors and Cochrane Review Group staff can submit RoB 2 questions to the **monthly Methods Support Unit Web Clinic** for discussion – read more and submit questions here.

Questions via email

Questions about RevMan Web functionality can be sent to support@cochrane.org and questions about RoB 2 assessments, guidance, tools, can be directed to Kerry Dwan (kdwan@cochrane.org).



RoB 2 tips from review teams

We have brought together some of the key takeaways from our RoB 2 pilot project and encourage all members of the community to send additional tips and feedback to their CRG.

Worked examples are key. Training courses and webinars are most helpful when they include or reference high-quality examples illustrating how to carry RoB 2 through the text, figures, and tables of a review. Example protocols and reviews using RoB 2 will be added to the protocol and reviews consideration sections above, respectively, as they become available.

Disagreements are no bad thing. Practicing a couple of assessments will always highlight differences that can be ironed out, but inter-rater discrepancies beyond that should be expected and may even improve the review. The signalling questions in RoB 2 provide a clearer framework for discussing differences in judgements and justifications than the old tool, and the process of doing so is a key part of gaining understanding and interrogating the evidence.

Early investment goes a long way. While RoB 2 is an outcome-based assessment, considering which domains are expected to be consistent across results within a study and designing the data-collection form accordingly can save a lot of time. Some teams have created a Risk of bias decision tool that is specific to their review, to help reviewers make consistent decisions and to ease the process of assessing bias e.g. issues in randomization will be common to all outcomes, issues of missing data may differ for

outcomes at different time points, and issues of outcome assessment may be different between patient-reported outcomes and outcomes derived from routine data sources. The first few assessments may take some time to get right but once done, subsequent assessments naturally become much easier and faster.

Back to bias assessment as it was always intended. Shifting from assessing studies to assessing results may initially feel like a daunting task but, once a rhythm is found, it can refocus the mind on why bias assessment is so important in Cochrane reviews. RoB 2 provides a framework for building *meaningful* bias considerations through reviews, from protocol planning to writing up results.

The authors are not expected to assess risk of bias for all results from all included studies: The risk of bias assessment should focus on results of studies that contribute information to outcomes that users of the review will find most useful. This will generally correspond to the results that are used to populate outcomes in 'Summary of Findings' (SoF) tables; however, this will depend on your review question and protocol, which may have specified other outcomes for risk of bias assessment. If there is no explicit link described here between the risk of bias and the SoF outcomes, then editorial teams should ask for clarification in any feedback provided to the author teams. Also consider whether the number of outcomes intended for the SoF table is manageable.