Using Risk of Bias 2 to assess results from randomised controlled trials: guidance from Cochrane

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Abstract

A systematic review identifies, appraises and synthesises all the empirical evidence from studies that meet prespecified eligibility criteria to answer a specific research question. As part of the appraisal, researchers use explicit methods to assess risk of bias in the results' from included studies that contribute to the review's findings, to improve our confidence in the review's conclusions. Randomised controlled trials included in Cochrane Reviews have used a specific risk of bias tool to assess these included studies since 2008. In 2019, a new version of this tool, Risk of Bias 2 (RoB 2), was launched to improve its usability and to reflect current understanding of how the causes of bias can influence study results. Cochrane implemented RoB 2 in a phased approach, with users of the tool informing guidance development. This paper highlights learning for all systematic reviewers (Cochrane and non-Cochrane) from the phased implementation, highlighting differences between the original version of the tool and RoB 2, consideration of reporting systematic review protocols or full review reports that have used RoB 2, and some tips shared by authors during the pilot phase of the implementation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Assessing risk of bias in the results of included studies of a systematic review is a key step in ensuring our confidence in the review's findings. A new tool for assessing risk of bias in the results from randomised controlled trials was launched in 2019 called Risk of Bias 2 (RoB 2). During the phased implementation of RoB 2 in Cochrane, guidance for authors was developed.

WHAT THIS STUDY ADDS

⇒ This paper details the differences between the original risk of bias tool and RoB 2, as well as guidance developed by Cochrane for authors on using RoB 2 in systematic reviews that include randomised controlled trials which can be applied to non-Cochrane systematic reviews.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This paper provides recommendations for reporting systematic review protocols or full review reports that have used RoB 2, along with additional tips shared by Cochrane authors, to guide authors of any systematic review that includes randomised controlled trials and wants to use RoB 2 to assess the risk of bias in the studies' results.

Introduction

A systematic review identifies, appraises and synthesises all the empirical evidence from studies that meet prespecified eligibility criteria to answer a specific research question. Researchers conducting systematic reviews seek to use explicit, systematic methods that are selected with a view aimed at minimising bias and imprecision to inform decision making. Assessing risk of bias in the design, conduct and reporting of the included studies in the review is a key step. This helps systematic reviewers, and the users of these reviews, to understand whether there is any risk of bias in the included study's results that could distort the review's results. This helps improve our confidence in the review's conclusions and that it accurately represents the truth (that the true effect of the intervention has not been overestimated or underestimated).

Cochrane defines bias in this context as 'a systematic error, or deviation from the truth, in results'.[1] Before the mid-2000s, tools that critically assessed studies within reviews typically considered the broader notion of 'methodological quality' which often involved a combination of risk of bias, imprecision, relevance, applicability, ethics and completeness of reporting. However, this breadth of concepts was not based on any particular underlying theoretical framework for 'quality' assessment and therefore different tool resulted in different assessments for the same study.[2] To address this, in 2008, Cochrane released a risk of bias tool to focus on the single concept of risk of bias in randomised controlled trials (RCTs) included within its reviews of interventions.[3] Other concepts are now considered at

other stages in the review process. For example, precision (the extent to which results are free of random errors) and external validity (directness, applicability or generalisability) are domains of GRADE (Grading of Recommendations, Assessment, Development and Evaluations).[4]

In 2019, a new version of the tool, Risk of Bias 2 (RoB 2), was launched to improve its usability, address some of the limitations of the original version[5 6] and to reflect current understanding of how the causes of bias can influence study results.[7 8] A recent study by Minozzi *et al*[9] found that 69% (95/137) reviews published between 2019 and 2021 adhered to RoB2 by assessing an outcome rather than the study. However, the majority of these reviews only included a single primary outcome and when the analysis was restricted to reviews with at least two primary outcomes, adherence decreased to 29%.

Cochrane used a phased implementation approach to introduce RoB 2 to authors of its systematic reviews. It aimed for a supported and gradual roll-out to observe and address common issues as they arose.[8] Following the publication of the first Cochrane Review from the pilot phase,[10] RoB 2 is now the recommended tool for assessing risk of bias in RCTs in Cochrane Reviews, though the original risk of bias tool is still acceptable (https://community.cochrane.org/news/status-and-expectations-implementation-risk-bias-2-cochrane-intervention-reviews).

Over 150 Cochrane Reviews are now in development that use RoB 2. In this paper, the team that led the implementation and members of the Cochrane Bias Methods Group share the guidance developed to support authors using RoB 2 in systematic reviews.

Online supplemental appendix 1 details the key resources, training, tools, software and template recommended by Cochrane that are available for systematic review authors to help them learn about and use RoB 2.

Differences between the original risk of bias tool and RoB 2

A comparison of the differences between the two tools can be seen in table 1. One key difference between the two is that risk of bias assessments for RoB 2 are more explicitly associated with a specific result for an outcome from each included study (result-level assessment).

This recognises that different outcomes from one study could have different issues that affect the risk of bias, for example, an objective outcome (eg, maximal cardiorespiratory fitness) versus a subjective outcome (eg, health-related quality of life) as seen in Williams *et al*[10] Cochrane Review on physical activity interventions for people with congenital heart disease. For one of the studies ('Sandberg 2018'), the authors judged the health-related quality of life result to be of high risk of bias because the participants both reported the outcome and were aware of the intervention, and they felt that this knowledge would have likely influenced the outcome (RoB 2, domain 4; blinding of the outcome assessment). In contrast, they judged this same domain in the same study to be at low risk of bias for the maximal cardiorespiratory fitness result because most of the assessors were blinded and for those who were not blinded, the authors felt that this knowledge would not have influenced the measurement as it is an objective outcome.

In addition, RoB 2 recognises that different results for the same outcome from one study could have different issues that affect the risk of bias. As an example, a Cochrane Review by Kew *et al*[11] on increasing the dose of inhaled corticosteroids when asthma symptoms worsen to reduce the need for further treatment included the outcome of treatment failure. This outcome was assessed in two populations; all randomised participants and those participants who started their study inhaler. The result for each outcome (treatment failure in all randomised participants vs treatment failure in only those who took their study inhaler) were different and

Table 1 Differences between the original risk of bias tool and RoB2 for assessing randomised controlled trials

	Original risk of bias tool	RoB 2
Focus of assessment	Outcome level, for example, subjective and objective outcomes should be assessed separately (however, in practice, this tool has often been used at the study level)	Result level, such that a numerical result is specified as the focus of the assessment (if there is no numerical result for an outcome from a specific study, then there is no need to complete a risk of bias assessment as it will not be contributing to the review)
Structure	Seven recommended bias domains, with the option of adding or deleting domains Risk of bias judgement for each domain only	Preliminary considerations Five fixed bias domains Signalling questions Risk of bias judgement for each domain and overall
Domains	► Random sequence generation ('selection bias') ► Allocation concealment ('selection bias') ► Blinding of participants and personnel ('performance bias') ► Blinding of outcome assessment ('detection bias') ► Incomplete outcome data ('ttrition bias') ► Selective reporting ('reporting bias')* ► Other bias†	► Bias arising from the randomisation 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 derived	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)

Guidance for using the original risk of bias tool is available in V.5.2 of the Cochrane Handbook.

*As RoB 2 assesses risk of bias in a numerical result, risk of bias due to missing results (from non-publication of trials or results) is not part of the revised tool. This can be assessed using the Risk of Bias-Missing Evidence; available on the Risk of Bias tools website (https://www.riskofbias.info/welcome/rob-me-tool).

†RoB 2 does not include an 'other bias' domain. All domains within RoB 2 include trial features that directly influence the risk of bias; those that indirectly influence the risk of bias should be assessed in other stages of the review, or example,for conflicts of interest a Tool for Addressing Conflicts of Interest in Trials is in development.[16]

RoB2, Risk of Bias 2.

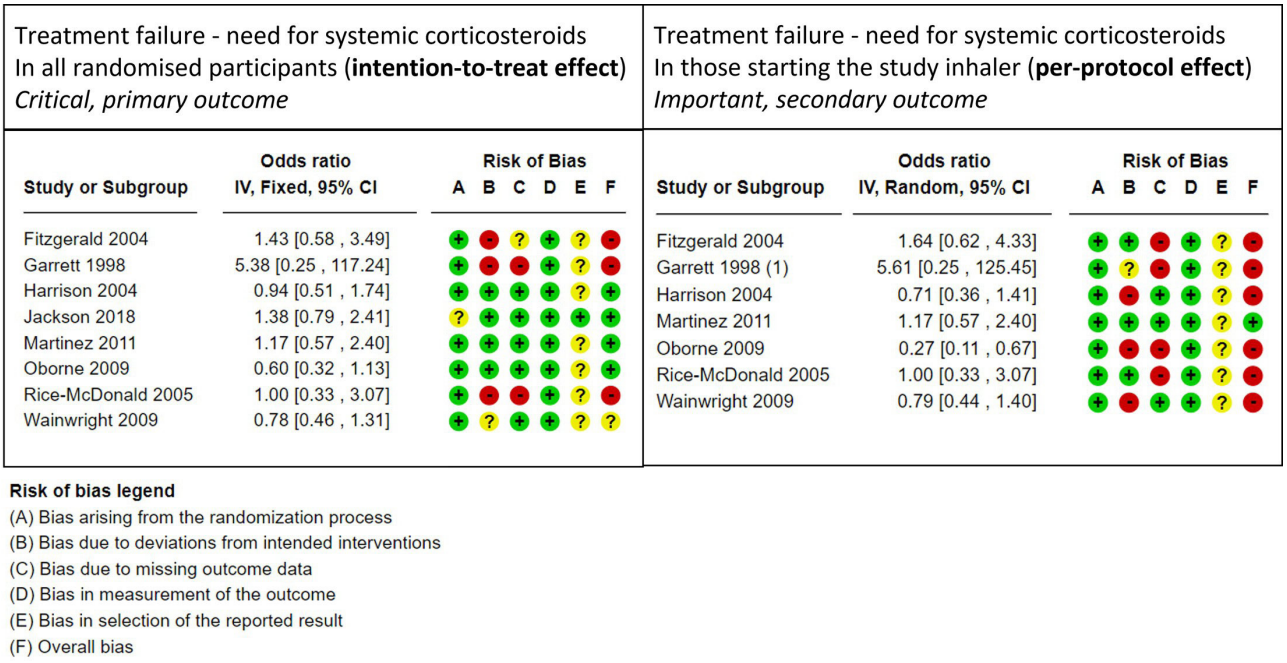

Figure 1 Example of how different results from the same outcome from one study or the effect of interest (intention to treat vs per-protocol) can have implications on risk of bias assessments using RoB 2.[11] ROB 2, Risk of Bias 2.

for each result there were different issues that affected the risk of bias, as seen in figure 1. For one of the studies ('Oborne 2009'), the authors judged the treatment failure in all randomised participants result to be of low risk of bias because all participants contributed data for the intention-to-treat analysis up to the point at which they left the study (RoB 2 domain 3; missing outcome data). In contrast, they judged this same domain in the same study to be of high risk of bias for the treatment failure in only those who took their study inhaler result as this population represents a relatively small, non-randomised proportion of the full cohort, there was an imbalance in the number of people in each group who took the study inhaler, and patients who discontinued who did not use the study inhaler might have done so for reasons relating to their disease worsening. Another hypothetical example is a systematic review interested in a outcome measured at end of treatment, such as 4 weeks, and at longest follow-up, such as months or years later. These two results for the same outcome may theoretically have different risk of biases, that is, a lower risk of bias at end of treatment and higher risk of bias at longest follow-up due to missing outcome data.

Another important development is that RoB 2 requires authors to specify whether the result being assessed is being interpreted as the effect of assigning participants to interventions (the intention-to-treat effect) or the effect of participants adhering to their assigned intervention according to the trial protocol (the per-protocol effect). Authors need to think carefully about the aim of their systematic review, and which is most appropriate for each result. The effect of interest will have implications for the risk of bias due to deviations from the intended intervention (RoB 2, domain 2). An example of this is again seen in Kew *et al* Cochrane Review[11] where, in the included trials, the randomised population only starts the intervention at the onset of treatment failure. The critical outcome for the review was treatment failure in all randomised participants (the intention-to-treat effect), and an important secondary outcome was treatment failure in participants using the study inhaler (the per-protocol effect); the same outcome in different populations resulted in different effects of interest and different risk of bias assessments (see figure 1).

By considering the specific result for each outcome of interest from a study separately, we can more accurately assess bias for those results which will increase our confidence in the evidence presented in the systematic review.

Richter and Hemmingsen[12] compared RoB 2 to the original tool and found that the mean assessment times were comparable and there were few difficulties achieving agreement between raters with both tools. The biggest divergence between the tools was with subjective outcomes in open-label studies, where the original tool was more likely to penalise than RoB 2. The original tool led to harsher judgements due to the options available (high/low/unclear risk) whereas the signalling questions and guidance made RoB 2 easier to work through complexity and context.

This paper concentrates on guidance for parallel RCTs only. The RoB 2 tool has two supplemental variants, one for cluster RCTs and one for crossover RCTs, both available from the Risk of Bias tools website (https://www.riskofbias.info/welcome/rob-2-0-tool).

RoB 2 considerations for systematic review protocol development

It is important to consider carefully at the protocol stage how RoB 2 will be used in a review. As RoB 2 is a result-level tool and does not need to be completed for all the outcomes and all the studies in the systematic review, prioritisation of which outcomes to assess is likely to be needed. Without considering this, reviewers can increase their workload substantially and are at risk of using the tool incorrectly, that is, with a study-level focus instead of the correct results-level focus. Cochrane recommends that review authors limit the RoB 2 assessments to the results for their outcomes planned for inclusion in a summary of findings table, that is, those outcomes deemed to be the most critical and important outcomes for decision making. Table 2 details these considerations.

Rows highlighted green are core to the context of a systematic review and must be prespecified to facilitate the accurate use of

Table 2 10 items Cochrane's evidence production and methods directorate recommends authors consider and report when developing a protocol for a systematic review that plans to use 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*.[7]
2. State the effect of interest—effect of assignment or effect of adherence	Guidance: Section 1.3 of the detailed guidance (available via riskofbias.info); Section 8.2.2 of the Cochrane Handbook.[13]
3. List or refer to the results that will be assessed using RoB 2, including outcome(s), outcome measure(s) and timepoint(s)	Guidance: section 1.3 of the detailed guidance (via riskofbias.info); section 7.3.2[1], section 8.2.1 and section 8.7 of the Cochrane Handbook.[13]
4. (If applicable) State how cross-over RCTs and cluster RCTs will be handled.	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, if it is intended from the OUTSET to use ONLY data from the first period of a crossover RCT, then the standard version of RoB 2 can be used as it is. However, there is 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, see section 23.2 of the Cochrane Handbook.[17]
5. State who will assess RoB2 (initials), how many and whether independently and duplicate	Guidance: section 7.3.2 of the Cochrane Handbook,[1] item 11 of PRISMA 2020[14]
6. List the domains of the tool	Guidance: section 1.3 of the detailed guidance (via riskofbias.info); section 8.2.3 of the Cochrane Handbook.[13]
7. List the judgement options (high, some concerns, low) and how overall risk of bias is reached, for example, using the signalling questions/tool algorithms	Guidance: section 1.1, section 1.2.1 and section 1.2.3 of the detailed guidance (via riskofbias.info); section 8.2.3 and section 8.2.4 of the Cochrane Handbook.[13]
8. State if there are plans to use any tools to manage the assessment of bias using RoB 2	For example, the RoB 2 Excel tool to implement RoB 2 (available via riskofbiasinfo.org) Guidance: section 7.3.2 of the Cochrane Handbook.[1]
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 larger numbers of studies make the analyses more robust. It could also be appropriate to combine results 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: section 7.6.2 of the Cochrane Handbook.[1]
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). Guidance: section 10.11.2[18] and section 7.6.2 of the Cochrane Handbook.[1]
Methods section—'Sensitivity analysis'	
(If applicable) Specify if sensitivity analysis based on risk of bias is planned	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. With respect to risk of bias, review authors may perform sensitivity analyses to show how conclusions might be affected if studies at high risk of bias, or high risk bias and some concerns, were included or excluded. Guidance: section 10.14[18] and section 7.6.2 of the Cochrane Handbook,[1] item 11 of PRISMA 2020[14]
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/ summary of findings	State that the overall RoB2 judgement will be used to feed into the GRADE assessment. Guidance: section 7.3.2 of the Cochrane Handbook,[1] item 15 of PRISMA 2020.[14]
Other considerations	Authors should not make any changes to the RoB 2 tool (Sterne et al 2019).[7] State how detailed RoB2 data will be stored and presented—the RoB 2 tool may generate a large amount of data. We recommend that the consensus decisions for the signalling questions are available to readers in the full review so that the rational for each judgements is transparent. This could be via a repository or as online supplemental file 1 to the review. Guidance: section 7.3.2 of the Cochrane Handbook,[1] item 27 of PRISMA 2020.[14] See this published protocol as an example: Contraception decision aids to improve care and effective method use[19]

GRADE, Grading of Recommendations, Assessment, Development and Evaluations; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomised controlled trial; RoB 2, Risk of Bias 2.

RoB 2 during risk of bias assessments. Includes guidance from chapter 7[1] and chapter 8 of the Cochrane Handbook,[13] as well as PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020.[14]

RoB 2 considerations for reporting the full systematic review

Table 3 details the considerations needed when reporting the full systematic review.

Note that this checklist only highlights RoB 2 considerations for review reporting. Rows highlighted green are core to understanding the risk of bias assessments in the context of a systematic review's conclusions. Some journals may have specific guidance on use of tables and figures, so this guidance may need to be adapted to meet those journal requirements. Includes guidance from chapter 7 and chapter 14 of the Cochrane Handbook.[1 4]

Table 3 Seven items Cochrane recommends authors report in a completed systematic review that used the RoB 2 tool

What to report	Further details
Methods—'Assessment of risk of bias in included studies'	
1. Include all the RoB 2 considerations from the Protocol.	Ensure the review includes all the RoB 2 information from the protocol. If there were any deviations from the protocol, these should be detailed in the review's methods section, along with justification.
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 that the version used is stated.
Results—'Risk of bias in included studies'	
3. Refer to results-level RoB 2 tables, which includes the support for judgement for each domain assessment.	Tables summarising the risk of bias for all results that contribute to an outcome should be included in the review. Each result for the outcomes prespecified for risk of bias assessments (likely to be the reviews' critical and important outcomes) should have a table that includes the risk of bias judgements (high, low or some concerns) and the support each judgement. In certain circumstances, authors may wish to use other figures that best present the risk of bias data, for example, weighted risk of bias bar plots can provide a succinct summary when there are lots of studies in a synthesis. See figure 2 for an example of a risk of bias figure for one result for one outcome created using robvis.[20]
4. State how to access detailed risk of bias assessments data (with consensus responses to the signalling questions).	Authors should state how the data can be accessed, for example, via a online supplemental file 1, repository or other.
5. Provide a brief overview of the risk of bias assessments.	Consider *overall comments on key aspects* of the risk of bias assessments, for example, the quality of randomisation 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—Describing the effects of interventions	
6. Refer to visual representations of the risk of bias assessments in relation to each result.	Using forest plots with traffic lights is highly recommended (see Figure 2-6 in Williams *et al*[10]). For synthesis without meta-analysis, we recommend that a column is added to any visual representation of the data to highlight the overall risk of bias associated with each of the results in the table/figure (see table 1 in Williams *et al*[10]). Guidance: section 7.6 of the Cochrane Handbook.[1]
Results—'Subgroup analysis'	
(If applicable) Discuss any subgroup analysis conducted that relates to the overall risk of bias judgements.	When preparing subgroup analyses it is advisable to use the 'overall' judgement of bias, rather than using bias relating to specific domains. Guidance: section 7.6.2 of the Cochrane Handbook.[1]
Results—'Sensitivity analysis'	
(If applicable) Discuss any sensitivity analysis conducted that relates to the overall risk of bias judgements.	When preparing sensitivity analyses it is advisable to use the 'overall' judgement of bias, rather than using bias relating to specific domains. Guidance: section 7.6.2 of the Cochrane Handbook.[1]
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. These are likely to be the reviews' critical and important outcomes or those included in the summary of findings table. For example, if 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 of the Cochrane Handbook.[1 4]

GRADE, Grading of Recommendations, Assessment, Development and Evaluations; RoB 2, Risk of Bias 2.

RoB 2 tips

In this section, we bring together some of the key takeaways from the RoB 2 pilot phase of implementation.

Create a RoB 2 decision tool following protocol development

While RoB 2 is a result-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. This early investment goes a long way. 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, for example, issues in randomisation 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.[15] The first few assessments may take some time to get right but once done, subsequent assessments naturally become much easier and faster.

Disagreements are no bad thing

Practising 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.

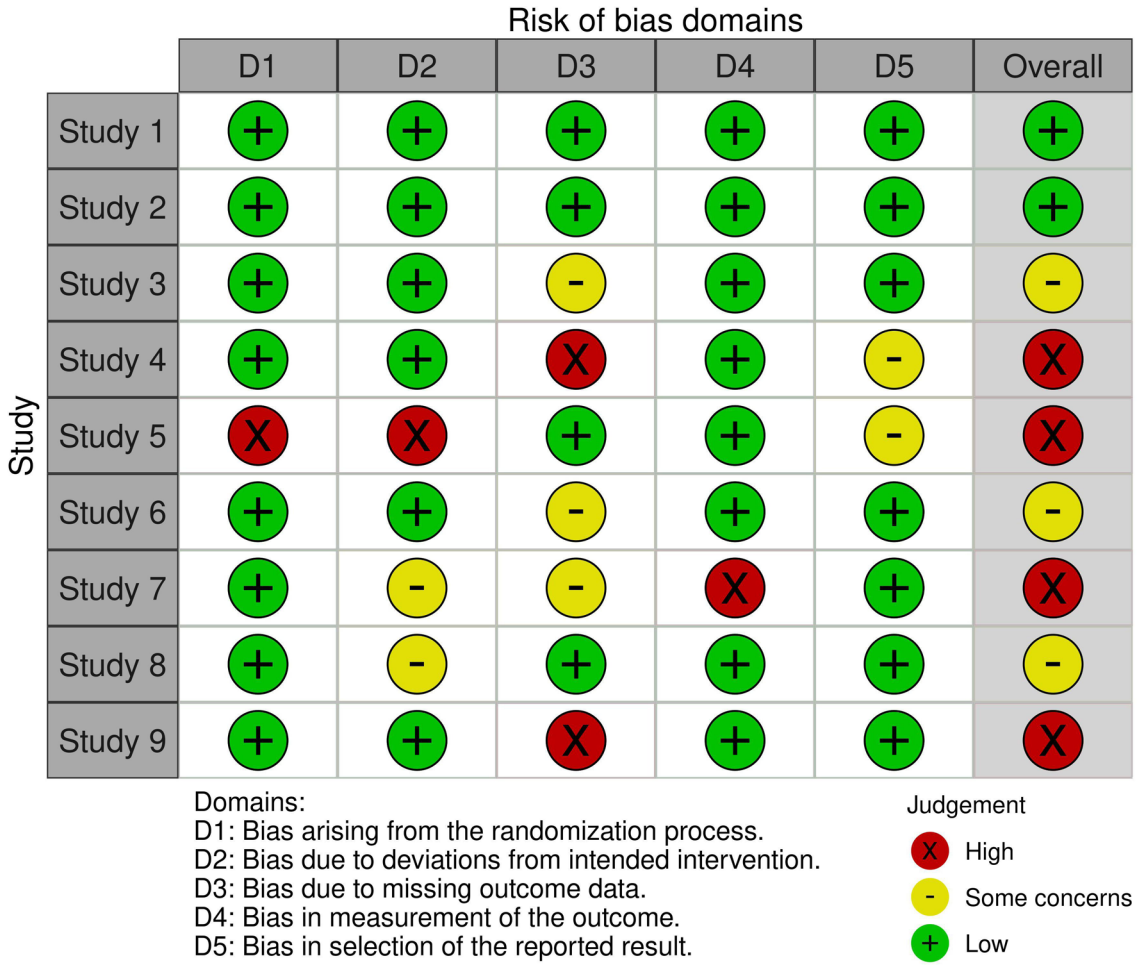

Figure 2 Example of a risk of bias figure for one result for one outcome. Generated using robvis software.[20]

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 systematic reviews. RoB 2 provides a framework for building meaningful bias considerations through reviews, from protocol planning to writing up results and implications for practice.

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 tables; however, this will depend on the review question and protocol, which may have specified other outcomes for risk of bias assessment.

Conclusions

RoB 2 is the recommended tool to assess the risk of bias of specific results included in a systematic review. It has some fundamental differences from the original Cochrane risk of bias tool and these need to be understood before the tool is applied. This includes whether the authors are interested in the effect of assignment or adherence and which results they plan to assess. Prespecifying some items from RoB 2 can aid implementation of the tool. Transparency is key and all supporting material should be submitted alongside the full review and for peer review. An Excel tool is available on the risk of bias website (www.riskofbias.info) to facilitate completion of the assessments. Assessing the risk of bias for specific results allows us to see the impact this has on a synthesis or meta-analysis, whereas previously a study was usually judged for bias overall and might have left some results with a worse assessment of bias than was warranted.

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References

1 **Boutron I**, Page MJ, Higgins JPT. Chapter 7: Considering bias and conflicts of interest among the included studies. In: **Higgins JPT**, Thomas J, Chandler J, *et al*, eds. *Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022)*. Cochrane, 2022. www.training.cochrane.org/handbook
2 **Jüni P**, Witschi A, Bloch R, *et al*. The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA* 1999;**282**:1054–60.
3 **Higgins JPT**, Altman DG, Gøtzsche PC, *et al*. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;**343**:d5928.
4 **Schünemann HJ**, Higgins JPT, Vist GE. Chapter 14: Completing 'Summary of findings' tables and grading the certainty of the evidence. In: **Higgins JPT**, Thomas J, Chandler J, *et al*, eds. *Cochrane Handbook for systematic reviews of interventions version 6.2 (updated February 2021)*. Cochrane, 2021. www.training.cochrane.org/handbook
5 **Savović J**, Weeks L, Sterne JAC, *et al*. Evaluation of the Cochrane collaboration's tool for assessing the risk of bias in randomized trials: focus groups, online survey, proposed recommendations and their implementation. *Syst Rev* 2014;**3**:37.
6 **Jørgensen L**, Paludan-Müller AS, Laursen DRT, *et al*. Evaluation of the Cochrane tool for assessing risk of bias in randomized clinical trials: overview of published comments and analysis of user practice in Cochrane and non-Cochrane reviews. *Syst Rev* 2016;**5**:80.
7 **Sterne JAC**, Savović J, Page MJ, *et al*. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;**366**:l4898 https://www.bmj.com/content/366/bmj.l4898
8 **Flemyng E**, Dwan K, Moore TH, *et al*. Risk of bias 2 in Cochrane reviews: a phased approach for the introduction of new methodology. *Cochrane Database Syst Rev* 2020;**10**:ED000148.
9 **Minozzi S**, Gonzalez-Lorenzo M, Cinquini M, *et al*. Adherence of systematic reviews to Cochrane RoB2 guidance was frequently poor: a meta epidemiological study. *J Clin Epidemiol* 2022;**152**:47–55.
10 **Williams CA**, Wadey C, Pieles G, *et al*. Physical activity interventions for people with congenital heart disease. *Cochrane Database Syst Rev* 2020;**10**:CD013400.
11 **Kew KM**, Flemyng E, Quon BS, *et al*. Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children. *Cochrane Database Syst Rev* 2022;**9**:CD007524.
12 **Richter B**, Hemmingsen B. Comparison of the Cochrane risk of bias tool 1 (RoB 1) with the updated Cochrane risk of bias tool 2 (RoB 2). cochrane.org. Available: RoB1_2_project_220529_BR KK formatted.pdf [Accessed Dec 2022].
13 **Higgins JPT**, Savović J, Page MJ. Chapter 8: Assessing risk of bias in a randomized trial. In: **Higgins JPT**, Thomas J, Chandler J, *et al*, eds. *Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022)*. Cochrane, 2022. www.training.cochrane.org/handbook
14 **Page MJ**, Moher D, Bossuyt PM, *et al*. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ* 2021;**372**:n160.
15 **Minozzi S**, Dwan K, Borrelli F, *et al*. Reliability of the revised Cochrane risk-of-bias tool for randomised trials (RoB2) improved with the use of implementation instruction. *J Clin Epidemiol* 2022;**141**:99–105.
16 **Lundh A**, Boutron I, Stewart L, *et al*. What to do with a clinical trial with conflicts of interest. *BMJ Evid Based Med* 2020;**25**:157–8.
17 **Higgins JPT**, Eldridge S, Li T. Chapter 23: Including variants on randomized trials. In: **Higgins JPT**, Thomas J, Chandler J, *et al*, edseds. *Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022)*. Cochrane, 2022. www.training.cochrane.org/handbook
18 **Deeks JJ**, Higgins JPT, Altman DG. Chapter 10: Analysing data and undertaking meta-analyses. In: **Higgins JPT**, Thomas J, Chandler J, *et al*, edseds. *Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022)*. Cochrane, 2022. www.training.cochrane.org/handbook
19 **Buckingham P**, Amos N, Saha SK. Contraception decision aids to improve care and effective method use. *Cochrane Database Syst Rev* 2020;**7**:CD013659.
20 **McGuinness LA**, Higgins JPT. Risk-of-bias visualization (robvis): an R package and shiny web app for visualizing risk-of-bias assessments. *Res Syn Meth* 2020:1–7.