Risk of Bias 2
Cochrane Review Group
Starter Pack
For Pilot Groups

July 2020
Background
Up-to-date information from the developers on Risk of Bias 2 (RoB 2) is available via the Risk of Bias tools website: https://www.riskofbias.info/

Up-to-date information on the piloting and implementation of RoB 2 can be found via the Cochrane Methods Website: https://methods.cochrane.org/risk-bias-2

What guidance is available?
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.

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.

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.

Using RevMan Web
RoB 2 is only available in RevMan Web and is not supported by RevMan 5.
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 and the ability to search.

The RevMan Web Practice Platform
RevMan Web offers a practice platform where practice reviews can be created from a RevMan 5 file or a template review. Practice reviews allow users to learn how RevMan Web works without changing the data in the live review. Only one person can work at the same time in a practice review. To create a practice review with RoB 2 enabled click here.

How-to guide for RoB2 data input in RevMan Web
Guidance on how to enter RoB 2 assessments in RevMan Web can be accessed here.
A four-minute video also shows how to input RoB 2 assessments into RevMan Web available here.

What training is available?
Cochrane Learning Live webinars
A Cochrane Learning Live webinar series from May 2020 to December 2020, presented by leading experts, covers an introduction to RoB 2, detailed sessions on the five Risk of Bias 2 (RoB 2) domains, reaching overall RoB judgements, RoB 2 bias in other types of studies (crossover and cluster trials) and editorial considerations. Full details and sign-up here.

A Cochrane Learning Live webinar from November 2016, presented by Dr Matthew Page, explains the development and application of RoB 2. The recording can be accessed here.

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. The previous version from the Editorial Resources Committee has been revised in light of the development of RoB 2. It should be seen as a starting point for developing bespoke data collection forms for reviews, and it should be modified accordingly. The form can be found here.

**RoB 2 Excel tool or Word template**
The developers have created two templates for completing the RoB 2 assessment. It is advised that review groups use one, and both are available via the Risk of Bias tools website here:

1. RoB 2 Excel tool (preferred) – email risk-of-bias@bristol.ac.uk to feedback any issues
3. A browser-based online tool is under development.

As of July 2020, these tools could also help create outcome-level tables with all studies and all domain assessments from the risk of bias tool. This can be uploaded into RevMan Web as an additional table. (Interim solution).

**Other tools**
As of July 2020, for risk of bias assessments, RevMan Web only creates forest plots with traffic lights. Tools for creating other risk of bias figures can be found via the Risk of Bias tools website and can be uploaded into RevMan Web as an additional figure: https://www.riskofbias.info/welcome/robvis-visualization-tool. (Interim solution)

**RoB 2 considerations for protocol development**
There are ten key items to consider when using the RoB 2 tool:

<table>
<thead>
<tr>
<th>What to report</th>
<th>Further details</th>
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<tr>
<td><strong>Methods section</strong> - 'Assessment of risk of bias in included studies'</td>
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<tr>
<td>2. State your effect of interest - effect of assignment or effect of adherence</td>
<td>Guidance: Section 1.3 Detailed guidance (Riskofbias.info); Section 8.2.2 Cochrane Handbook</td>
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<tr>
<td>3. List or refer to the results that will be assessed using RoB 2, inc. outcome(s), outcome measure(s) and timepoint(s)</td>
<td>Guidance: Section 1.3 Detailed guidance (Riskofbias.info); Section 7.3.2, Section 8.2.1 and Section 8.7 Cochrane Handbook</td>
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<tr>
<td><strong>Risk of Bias 2 CRG Starter Pack</strong></td>
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</table>
| **4. (If applicable) State how you will handle cluster RCTs and cross-over RCTs** | As of July 2020, interim guidance on handling cluster and cross-over RCTs is available (see below this table). Variants of the RoB 2 tool are in development for each study design and will be shared when available.  
**Guidance:** See the guidance for cluster and cross-over RCTs below this table. |
| **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 riskofbias.info website)  
**Guidance:** MECIR C54; Section 7.3.2 Cochrane Handbook. |
| **Methods section - ‘Data synthesis’** | **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.  
**Guidance:** MECIR C22; Section 10.11.2 and Section 7.6.2 Cochrane Handbook. |
| **Methods section - ‘Sensitivity analysis’** | **Methods section - ‘Summary of findings and assessment of the certainty of the evidence’**  
(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.  
**Guidance:** MECIR C71; Section 10.14 and Section 7.6.2 Cochrane Handbook. |
| **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. We recommend that the consensus decisions for the signalling questions are available to your readers in the full review so your rational for judgements is transparent. This can be stored as supplemental data or files (see the Editorial and Publishing Policy for full details).  
**Guidance:** MECIR C54; Section 7.3.2 Cochrane Handbook. |
|  | **See this published protocol as an example** |

**Cluster RCTs**

For cluster RCTs there are additional considerations for risk of bias. The RoB 2 developers are drafting guidance on this but it is not yet finalised. To help authors with this we suggest you use this interim guidance and describe these methods in your protocol.

For cluster RCTs, our recommendation is to:

1. use the RoB 2 tool as it is **and**
2. add an additional domain specific for cluster RCTs from the archived version of the tool (Domain 1b - ‘Bias arising from the timing of identification and recruitment of participants’) and use the signalling questions from the archived version **and**
3. use the guidance in the Cochrane Handbook (version 6) Chapter 23 (Section 23.1.2 and Table 23.1.a).

**Cross-over RCTs**

For cross-over RCTs there are additional considerations for risk of bias. The RoB 2 developers are drafting guidance on this but it is not yet finalised. To help authors with this we suggest you use this interim guidance and describe these methods in your protocol.

For cross-over RCTs, our recommendation is:

1. use the RoB 2 tool as it is and
2. For Domain 2 “Bias due to deviations from intended interventions” use the signalling questions from Domain 2 in the archived version of the tool for cross-over RCTs and For Domain 3 “Bias due to missing outcome data” use the signalling question 3.2 of the archived version of the tool for cross-over RCTs to inform your answer to question 3.2 of the RoB 2 tool and
3. refer to the guidance in the Cochrane Handbook (version 6) Chapter 23 (Section 23.2.3 and Table 23.2.a) to help you answer the signalling questions.

**Please note:** If you have intended from the OUTSET to ONLY use data from the first period of the cross-over – then you can use the standard version of RoB2 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 and further explanation read section 23.2 of the Cochrane Handbook.

**RoB 2 considerations for reporting the full review**

There are eight key items to consider when reporting RoB 2 in the full review:

**Please note, this checklist ONLY highlights RoB 2 considerations for review reporting**

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<tr>
<th>What to report</th>
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<tr>
<td><strong>Methods</strong> - ‘Assessment of risk of bias in included studies’</td>
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<tr>
<td>1. Include all the RoB 2 considerations from the Protocol.</td>
<td>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).</td>
</tr>
<tr>
<td>2. State the version of the RoB 2 tool that was used.</td>
<td>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, e.g. when this guidance was created the 2019 version was the current version with the full guidance was published on 22 August 2019.</td>
</tr>
<tr>
<td><strong>Results</strong> - ‘Risk of bias in included studies’</td>
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<tr>
<td>3. Refer to the results-level RoB 2 tables.</td>
<td>The results-level RoB 2 tables are located 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. <em>Guidance on how to view these tables in RevMan is below</em>:</td>
</tr>
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</table>

*Guidance on how to view these tables in RevMan is below:*
4. State how to access detailed risk of bias assessments data (with consensus responses to the signalling questions).

These may be referenced in the main text as supplemental data or files (they should not be included within the Review itself).


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 studies should be provided within the ‘Effects of intervention’ section (see Point 7 below).

**Results - ‘Effects of intervention’**

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 (from the Analyses section).

It may be very helpful to stratify forest plots according to overall risk of bias.

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.
### Guidance: Section 7.6 Cochrane Handbook

7. For each outcome, state whether the risk of bias assessments have implication Review’s objective or conclusions.

A summary of the risk of bias assessments should accompany the main results 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). **Highlight any important implications** from the risk of bias assessments that is of particular importance to the review’s objective or conclusions, such as highlighting which effects of the intervention may need to be interpreted with caution due to the risk of bias in the included studies. **Guidance: Section 7.5 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)

8. Discuss any risk of bias judgements that affect the certainty of the evidence along with all other GRADE considerations.

### History – ‘Differences between protocol and review’

(If applicable) State if there were any deviations from the Protocol. **Guidance: MFCIR R107 and R108.**

**Other considerations**
See this **published review as an example (not yet published)**

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**Interim guidance for viewing results-level RoB 2 tables in RevMan**

A pending update to RevMan will remove all RoB 2 risk of bias assessments from the characteristics of results section and into non-interactive versions of the results-level tables. This view will be integrated into RevMan Web when updates to Archie/RevMan occur later this year.

**In the meantime**, authors can view the these results-level tables in RevMan using the following route:

1. Find the review in Archie and right click -> Select ‘View’ -> Select ‘Latest version’
2. The latest version of your review will pop-up and in the Contents bar in the top right, find and select ‘Risk of bias’ **PLEASE NOTE** at the moment, all analyses you have completed that includes risk of bias data for will show as a separate table (inc. sensitivity and subgroup analyses). We know this is incorrect and are working with the RevMan team to update it so only the main outcomes include risk of bias tables. **In the published review, only tables for the main outcome analyses will show.**

What other support is available for review teams in the pilot

**Initial call with pilot group**
Review groups involved in the RoB 2 pilot will be invited to attend an introductory call with representative from the Editorial and Methods Department (Kerry Dwan, Ella Flemyng, Tess Moore) and the Information Technology Support (ITS) Department (Rebecka Hall). This session will outline plans for the pilot and how your review fits into it, showcase RoB 2 functionality in RevMan Web, and showcase early mock-ups of how the tables will render in the Cochrane Library. It will also provide the review group with the opportunity to ask any questions they have.

**Questions via email**
At any point during the pilot you are encouraged to send questions about RevMan Web functionality to Rebecka Hall (rhall@cochrane.org) and questions about RoB 2 assessments, guidance, tools, or other miscellaneous questions, to Kerry Dwan (kdwan@cochrane.org) or Ella Flemyng (eflemyng@cochrane.org).

**Web-clinics for the pilot review groups**
Monthly web-clinics are available to review teams in the pilot using GoToMeeting teleconference software (we are trialling this set-up for the first time so how often the web-clinics occur could be subject to change). All review groups involved in the pilot will be invited to learning and experience can be shared across the pilot groups and details on the web-clinics will be shared in your initial call.

The web-clinics are led by the Methods Support Unit Lead and others within the Methods Support Unit. CRG Editors, Associate Editors, Network Support Fellows, the Methods Implementation Coordinator, and RevMan Owner will be invited to attend. Escalation to specialist methods support will be available as a follow up if any issues with the tool were identified during the pilot phase.

*Recording and notes for past Web Clinics can be found here.*

**Other RoB 2 tips from review teams**

*This section will be developed over the course of the pilot*

These are a few tips for prospective review group from other Cochrane Review Groups, the Editorial and Methods Department and the RoB 2 developers, to facilitate use of the RoB 2 tool:
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.

When planning the data collection form, think about where issues related to risk of bias will be similar or different across outcomes, and arrange to collect information accordingly (for example, 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). These considerations are addressed in the new data collection tool (see the 'What tools are available' section above).

After you have completed data analysis and RoB 2 assessments on outcomes, you can input the data analysis into RevMan 5 and then switch to RevMan Web to add your RoB 2 assessments. Authors must have checked their review into RevMan Web before switching on RoB 2 otherwise the switch doesn’t work and RoB 1 domains remain in the review.

Once RoB 2 functionality has been switched on in your Review, you’ll need to log out and log in again to see the changes.

We advise data is input and analysed in RevMan in this order:
1) input main results data (see 'How to set up an analysis') ->
2) input RoB 2 data (see ‘How to use RoB 2.0 in RevMan Web’) ->
3) duplicate inputted results and RoB 2 data for sensitivity (see ‘How to do a sensitivity analysis’) – if a main analysis has risk of bias data the default is to create a forest plot with traffic lights for the sensitivity analysis (can select to not show risk of bias data if you wish)
4) duplicate inputted results and RoB 2 data for subgroup analyses (see ‘How to do a subgroup analysis’).

Interview questions for the pilot
As part of the RoB2 pilot in Cochrane we are seeking feedback of your experience of using RoB2. All feedback is useful as we build the infrastructure and support for Cochrane Review groups (CRGs) to use RoB 2. Below are some questions to help us frame your feedback to use to make improvements. We suggest that you make notes on the questions as you proceed through the different stages of the review.

At the end of the pilot we would like to develop these interview questions into Q&A community posts that would be posted on the Cochrane website as a resource for future review groups.

Assessing risk of bias:
1. How did you find the process of selecting outcomes for RoB 2 assessment and did you face any issues with this?
2. How did you find the general process of using RoB 2?
3. How did you store the answers to the signalling questions and do you think it was fit for purpose? If not, what would you advise?

Tools and guidance:
4. Did you use any of the other listed guidance documents and if so, how did you find the usability, and do you have any recommendations for developing the guidance?
5. Did you make use of the updated data collection form on Cochrane.org? What were the main benefits and/or limitations of using the form, and do you have any recommendations for their development?
6. Did you use either the RoB 2 Excel tool or Word template? What were the main benefits and/or limitations of using the tool(s), and do you have any recommendations for its development?

**RevMan Web and Cochrane Library:**
7. How was the process of transferring RoB2 information into RevMan Web? What could facilitate this process?
8. Within the Results section, was the new ‘Risk of bias in included studies’ section fit for purpose? Did the pre-populated subheadings within that section facilitate reporting? Do you have any recommendations that could help facilitate RoB 2 reporting within the review?
9. Please provide feedback on the RoB 2 table in the RevMan Web. What sort of changes do you think are needed or advice would you give to others about using it?
10. Please provide feedback on the RoB 2 table in the Cochrane Library (in the published review). Do you think it is fit for purpose? If not, what do you advise?

**Other questions:**
11. How did you find this RoB 2 CRG Starter Pack and do you think there is any important guidance or information missing?
12. Were there any issues with any software, tools or guidance that haven’t been captured above? If so, please provide details.
13. What do you think should be our key priority to help CRGS use RoB 2 in the future (tools, software, guidance, training etc.)?
14. On reflection, was there anything you would have done differently at the protocol stage to facilitate the RoB 2 assessments?
15. What do you think the key benefit was in using RoB 2 for your review?
16. Any final comments to prospective review groups?

**FAQs**

*The section will continue to be developed over the course of the pilot.*

**Implementation**

**Can I edit my review in RevMan 5 after I choose to use RoB 2 in RevMan Web?**
No, to use RoB 2 you will need to only use RevMan Web. You will not be able to check out the review when you have turned on this feature. It is a strategic decision from Cochrane to only implement new functionality in the new version of RevMan.

**What evidence is there that the reporting of bias is substantially better with RoB 2 compared with RoB 1, i.e. more transparent, more consistent, more reproducible ratings?**
The RoB 2 assessment have been developed to be more transparent because it has much more specific signalling questions and an algorithm to map these to RoB judgements. These developments were necessary following evaluations of the original tool that have low consistency and agreement between raters. We do not have evidence about consistency or reproducibility for RoB 2 at this point though. Cochrane is supporting two Studies Within A Review (SWARs) looking at RoB 2 vs RoB 1, which are due in Q2/Q3 2020.
What was the rationale for changing to RoB 2? The tool was approved as the preferred methodological tool for Cochrane, but how does it ensure better information for decision makers?

The following are the reasons a new version was developed:

- More accurate
  - more comprehensive
  - more guidance and structure to improve consistency
  - versions appropriate to cluster-randomized trials, cross-over trials
- More usable
  - clearer guidance, in-built help in reaching judgements
- More current
  - incorporates developments in the science (particularly missing data, unblinded trials)
- More useful
  - overall risk of bias judgement feeds into sensitivity analyses/exploration of heterogeneity
  - allied to ROBINS-I for non-randomized studies

When using the RoB 2 Excel tool, if I have assessed risk of bias for one outcome from a study and have a second outcome that will have (some of) the same domain outcomes and responses to signalling questions, how can I copy these across to the second outcome?

Use the following process:

1. Complete the RoB Assessment Form for the first outcome (e.g. Unique ID “outcome1” and Study ID “study1”) and close the interactive window
2. Go to the Excel worksheet tab “Results”
3. Copy the complete row for outcome1 (should be row 3 if it’s the first assessment)
4. Paste it into the following row (e.g. row 4)
5. Edit the Unique ID for the new row (e.g. cell B4) to a new ID, e.g. “outcome2”
6. Go back to the first Excel worksheet tab (“Intro”) and open up the RoB 2 Assessment Form.
7. In the drop-down box for Unique ID you should now have two identical assessments, but with different Unique IDs. You can amend the second one to match the second outcome in the study.

Choosing outcomes for RoB 2

What outcomes should I chose for RoB 2 assessments?
It is advised that the outcomes listed in your Summary of Findings (SoF) table should have RoB 2 assessments.

Are we supposed to produce reviews that focus only on a few primary outcomes? There seems to be a disincentive to report multiple outcomes as this will require lots of RoB assessments.

Feedback from those who have used it so far include that they found that with RoB2 needed for each outcome – it wasn’t that onerous. Many of the decisions about domains for one outcome may be copied across from one outcome to another. In other words – once you have done one outcome – the majority of the work is done. Then you need only edit those domains for outcomes that are different. E.g. if all your outcomes are subjective, and the analyses by the trial authors are largely similar – then most of the domains will be the same. Differences may be apparent in missing data etc. Also your familiarity with the RCT will mean answering the other domains is easier. This is something we hope to have more clarity on as part of the pilot.

RoB 2 was developed so that people would assess risk of bias in a logical and sensible way. Since risk of bias can be different for different results from the same study, we need to be able to produce different assessments of bias for different results.

Randomisation process domain
When looking at baseline imbalances, how do I know if it’s too unbalanced? For example, do I need to know about prognostic or baseline factors, and how to you judge baseline misbalance for factors such as age?

This signalling question is looking for strong evidence of a problem. If there is not strong evidence of a problem, then answer “N” – this should be considered the default answer. If baseline data are compatible with chance, answer “N”. The signalling question seeks only to identify when there are big differences that do not look to have arisen by chance. Remember that differences at baseline will always occur by chance; these are not sources of bias.

**Deviation from intended interventions domain**

How do I know whether to use intention to treat (ITT) effect or per protocol effect for my RoB 2 assessments?

In your protocol, you should state whether you will analyse RoB 2 against the effect of assignment to the intervention (ITT effect) or the effect of adhering to the intervention (per-protocol effect). The RoB 2 assessment changes slightly depending on which you choose, and most reviews will only select one, though depending on the specific review question(s) you may want to look at both. Most conventional intervention reviews will be assessing the effect of assignment, because this compares the groups as they are randomised (and particularly relevant to a policy-maker who wanted to know the effect of implementing an intervention). The effect of adhering to the intervention answers a question more relevant to an individual patient deciding whether to follow an assigned intervention, and is difficult to estimate appropriately.

What would a deviation from the intended intervention in/not in the experimental context constitute? Is it that to minimise bias, these deviations should be balanced across groups? What are the implications for the many unobservables for which there will be no information and could commonly result in high risk of bias?

The majority of changes that happen during an RCT will not fall into the category of ‘Deviations from the intended intervention’. We would expect the majority of RCTs not experience deviations from intended intervention. Deviations from intended intervention are changes that arise purely because the people are in an RCT. Many will be a result of the informed consent process. Examples of this would be – if people changed their intervention because of the study. We have an example of this:

An RCT randomised people to telephone support versus usual treatment for debt (to mitigate the effect of debt on mental health). (It was a social science type review). The “debt telephone counselling” was the intervention. The debt telephone counselling used in the RCT was delivered by a national provider and is free to all citizens of the UK. The authors of the RCT found that 30% of the people randomised to control (no telephone counselling), went and sought out the free telephone counselling, as a result of the informed consent process. This is a source of bias related only to the context of the trial.

The guidance indicates that unless there is good evidence of this – you should answer “No” or “Probably no”. (See Box 6 section 2.3).

As for balance between groups – this is covered in the Algorithm for the domain – see Figure 2 page 33. If the trial is unblinded and there are deviations for context - then if the deviations were balanced between the groups - - that would reduce the level of bias – but if not – then this would lead to high risk of bias.

There are more examples (and medical ones at that) of this in the detailed ROB2 guidance see section 5. Specifically Box 5 which contains 4 examples: [https://www.riskofbias.info/welcome/rob-2-0-tool/current-version-of-rob-2](https://www.riskofbias.info/welcome/rob-2-0-tool/current-version-of-rob-2)

**Applying RoB 2: Evidence synthesis and meta-analysis**

If the default is a high RoB rating overall if one of the 5 domains gets a high-risk rating, how can this in practice be managed editorially? Why would authors continue to perform a full assessment
of the results (what rationale would there be for this)? Why would authors not simply abort the analyses altogether if the results are at high(er) RoB?

As a review author, it is important to know the detail of each study in the review. So that is one reason to complete all domains for all outcomes being assessed. Also, meta-analyses are not only allowed if no domains are high. Authors can use a sensitivity analysis to assess the effects of a judgement of high RoB on the treatment effect.

A look across a set of RCTs in a review as to what aspects of the RCTs are struggling to achieve ratings of ‘Low’ or ‘Some concerns’ is important for both the “implications for research” part of the review. and for transparency in review production. Especially in some reviews - where by default all RCTs could be high because of blinding – and subjective outcome reporting (e.g. psychological interventions, social work interventions etc -) – but low or some concerns for all other domains. It would be important to have data from all domains to see the pattern of bias.

In addition, having all domains completed is arguably important for transparency in review production, in the same way we would prefer to see transparency in RCT reporting, and RCTs following CONSORT, so it’s important to be transparent when producing reviews.

What should I do if my review doesn’t have a meta-analysis?
RoB 2 aims to assess risk of bias in a quantitative result that feeds into a synthesis, whether the synthesis uses meta-analysis or another (‘narrative’) approach. RoB 2 can be used when no specific quantitative result is available, though it may make some signalling questions more difficult to answer. This should not stop people from including outcomes that have a narrative summary rather than a meta-analysis in their Summary of Findings tables. We are planning to add the Risk of Bias domains for results that have been set up as ‘Other data types’ in RevMan Web.

Should only outcomes with low risk of bias be included in the meta-analysis?
This (restricting to ‘Low’) is not the guidance – it is one option, and obviously a sensible one only if there are sufficient studies at low risk of bias. See Handbook V6 Section 7.6.2 (NB: we have realised that it is regretful that the Handbook Section does not refer to studies rated as having “some concerns”. In retrospect we should have explained that one option is to restrict to studies at “low” or “some concerns”, and this might often be the reasonable compromise). It is 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 low or low/some concerns.

Does RoB 2 shift the perspective on how decisions are made in relation to meta-analysis and GRADE?
No. GRADE should generally be applied to the synthesis set once decisions have been made about the most sensible synthesis set. GRADE assessments should not necessarily be used to decide how to synthesize. However, several considerations will feed into the decision whether to pool, including whether the studies are all answering the same underlying question, and whether there is evidence of non-reporting bias, as well as RoB judgements.

Does the decision about what can be pooled in a meta-analysis needs to be made independently of the risk of bias assessments – particularly in complex reviews where these decisions are typically made based on consideration of a wide range of factors?
Risk of bias assessment should be one of the factors informing the decision, but does need to be weighed in importance against the other factors.
It is also possible to do sensitivity analyses with” Low”/ “Some concerns” and ‘High’ risk of bias to see the effect of bias on the treatment effect.

Ideally, when should the risk of bias assessments be completed in the review process – before or after data analysis?
Risk of bias can (and should) be assessed before the synthesis itself is conducted. However, this is one aspect to consider as part of the pilot.

**Updating reviews**

When updating a review, should I move from the original risk of bias tool to RoB 2?
RoB 2 will be rolled-out in early 2020 (specific date TBC). From the roll-out date, reviews that have a protocol accepted for publication, and reviews that are being updated do not need to switch from the original risk of bias tool to RoB 2. However, it is desirable that review authors consider switching in these situations, and CRGs can make decisions about moving to RoB 2 on a case-by-case basis. The earlier you are in the review process, the easier the switch will be. For example, if you are yet to publish a protocol, changing to RoB 2 should be more straightforward than if the review has progressed to the analysis stages. If a published review only has a handful of RCTs and you are expecting many more when you update, switching to RoB 2 would probably be best for the quality of the review. However, if the published review includes many RCTs and you are not expecting many new studies the gains will be marginal, and it would be reasonable to continue using the original tool.

I am updating my review, can I use the original risk of bias tool for the old trials and RoB 2 for the new trials?
No, if you to choose to use RoB 2 all results will need to be assessed in the same way. If you are updating your review, there will be a choice to keep the original risk of bias tool.

If my review used the original risk of bias tool and during the updating process, we decided not to switch to RoB 2, can I still access guidance applicable to the original risk of bias tool?
Yes, an archived version of MECIR version 1.07 can be found [here](https://www.mecir.org.uk/downloads/MECIR(version 1.07).pdf) (see the [MECIR versions and changes page](https://www.mecir.org.uk/downloads/MECIRversionsandchangespage.pdf) for all available archived versions) and version 5.2.0 of the Cochrane Handbook for Systematic Reviews of Interventions can be found [here](https://handbook.cochrane.org/handbookversionsandchangespage.pdf) (see the [Handbook versions and changes page](https://handbook.cochrane.org/handbookversionsandchangespage.pdf) for all archived versions).

When I’m considering whether to switch from the original risk of bias tool to RoB 2, are there specific trial characteristics where a RoB 2 assessment will be of significant benefit?
The biggest differences between assessments using the original tool and using RoB 2 are likely to be the areas of deviations from intended intervention (previously known as ‘performance bias’) and selection of the reported result (previously known as selective reporting). RoB 2 provides a more appropriate assessment of bias in trials in which participants and trial personnel are not blinded, and this assessment depends importantly on the effect of interest (ITT effect vs per protocol effect).

**Other FAQs**

Why does RoB 2 not include affiliation bias assessments?
RoB 2 focuses on mechanisms through which bias may arise (e.g. randomisation processes; influences on outcome assessments due to knowledge of intervention received; processes of selecting which outcome data to report). We recognise the importance of affiliation bias, and believe that it may lead to bias in trial results through one or more of the mechanisms covered by the tool. Furthermore, affiliation biases lead to problems other than risk of bias in results: they may lead to inappropriate choice of comparators, or suppression of results, neither of which is covered by RoB 2. A new tool titled Tool for Addressing Conflicts of Interest in Trials (TACIT) is currently under development that will assess affiliation bias of the study’s researchers. More information on this will available in due course. New Cochrane editorial policies will also address bias of reviewers in the review group themselves.