Editorial considerations in reviews using Risk of Bias 2

Kerry Dwan, Methods Support Unit Lead and Statistical Editor, Cochrane Editorial and Methods Department.

Rebecka Hall, Product Owner of RevMan.

Tess Moore, Systematic Review Methodological Editor, Cochrane Methods Support Unit.
Outline

1. First published review using RoB 2
2. RoB 2 training resources and support relevant to authors and editors
3. Protocol and Review reporting requirements
4. Entering RoB 2 judgements in RevMan Web
5. Common errors for RoB 2
Poll 1
Poll 2
First published review using RoB 2

Physical activity interventions for people with congenital heart disease
Physical activity interventions for people with congenital heart disease

Craig A Williams, Curtis Wadey, Guido Pieles, Graham Stuart, Rod S Taylor, Linda Long

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Abstract

Background

Congenital heart disease (ConHD) affects approximately 1% of all live births. People with ConHD are living longer due to improved medical intervention and are at risk of developing non-communicable diseases. Cardiorespiratory fitness (CRF) is reduced in people with ConHD, who deteriorate faster compared to healthy people. CRF is known to be prognostic of future mortality and morbidity: it is therefore important to assess the evidence base on physical activity interventions in this population to inform decision making.

Objectives

To assess the effectiveness and safety of all types of physical activity interventions versus standard care in individuals with congenital heart disease.

Search methods

We undertook a systematic search on 23 September 2019 of the following databases: CENTRAL, MEDLINE, Embase, CINAHL, the Cochrane Library, and the Joanna Briggs Institute database.
## Risk of bias

Click on one or more cells to see and compare the Support for judgement for that bias, or click on a bias header to open all bias in that column.

**Legend:** 🟢 Low risk of bias  🔴 High risk of bias  🌐 Some concerns

### Risk of bias for analysis 1.1 Maximal cardiorespiratory fitness

<table>
<thead>
<tr>
<th>Study</th>
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**Therrien 2003**

No information on method of randomisation and significant baseline imbalance between groups. There is a 8 year age gap – the intervention group are younger and age of repair was younger. Right ventricular outflow tract (11 vs 22 mmHg) were half in the intervention group. Daily activity levels were less in the intervention group. This may suggest a problem with randomisation.

**Moella 2006**

There was no information on method of randomisation, there was no baseline imbalance that would suggest a problem with randomisation.

**Madhavi 2011**

Patients were randomly divided into study and control group by simple randomization using the lottery method. However there were substantial differences in patients fitness (as measured by VO2 peak) between the intervention and control group.

**Winter 2012**

“Randomization was performed using sealed envelopes. Each participant chose an opaque envelop from a shuffled stack which contained either ‘yes’ which allocated him to the treatment group or ‘no’ which allocated him to the control group. Randomization was stratified by participating centre.” There were no baseline imbalances that would suggest a problem with randomisation.
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Legend: ✓ Low risk of bias  ✗ High risk of bias  ❏ Some concerns

Lock of information on randomisation, baseline imbalances and blinding of outcome assessors and no pre-registered protocol and statistical plan.
Risk of Bias 2 Assessment Tool: Heart publishes its first review with RoB 2

We are excited to announce that the first Cochrane Review to publish using RoB 2 through the Cochrane pilot, using RoB 2 functionality built into RevMan Web and the Cochrane Library has now been published: Physical activity interventions for people with congenital heart disease.

Authors Craig Williams and Curtis Wadey

Just prior to the publication of the review, we talked with the authors Craig Williams and Curtis Wadey from the Children’s Health and Exercise Research Centre at the University of Exeter, UK, about the tool and their experience of using it. Marianna Kaye, Assistant Managing Editor with Cochrane Heart, is asking four questions which are presented as individual podcasts below.

Firstly, can you give us an overview of what your review was looking at and what the main findings were?

Your review was the first we have published using the new risk of bias 2 tool. What was your experience?
RoB 2 training resources and support relevant to authors and editors
Support and training resources for authors/ editors

Risk of Bias 2 (RoB 2) tool

The Risk of Bias 2 (RoB 2) tool is an update to the original risk of bias tool that launched in 2008. The relevant chapter in the Cochrane Handbook for Systematic Reviews of Interventions Chapter 8, titled ‘Assessing risk of bias in a randomized trial’. The Methodological Expectations for Cochrane Intervention Reviews (MECIR) Manual includes standards for assessing risk of bias in included studies; C52-60. Up-to-date information from the developers on RoB 2 is available via the Risk of Bias tools website: https://www.riskofbias.info/. Key Cochrane resources for using RoB 2 in Cochrane Reviews are:

An Introduction to Risk of Bias 2

The Introduction to RoB 2 is a one-page leaflet with links to short videos that should be watched at different stages of your review, 1) before you start, 2) when writing your Cochrane Review protocol, 3) managing your RoB 2 tool, and 4) reporting your review.
Risk of Bias 2 (RoB 2) tool

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An Introduction to Risk of Bias 2

The Introduction to RoB 2 is a one-page leaflet with links to short videos that should be watched at different stages of your review, 1) before you start, 2) when writing your Cochrane Review protocol, 3) managing your RoB 2 assessments, and 4) when writing your full Cochrane Review.

Risk of Bias 2 Cochrane Review Starter Pack

The Starter Pack includes all the key resources you’ll need, including guidance, training, tools, RoB 2 protocol considerations, RoB 2 considerations for reporting the full review, and support.

Risk of Bias 2 FAQs

Frequently Asked Questions from authors and editors.

Risk of Bias 2 Webinars

The RoB 2 webinar series covers an introduction of RoB 2, detailed sessions on the five RoB 2 domains, reaching overall RoB judgements, RoB 2 bias in other types of studies (crossover and cluster trials) and editorial considerations.

Editorial checklists for RoB 2
From your perspective as authors, please liaise with your Managing Editor as usual.

Please ensure you familiarise yourself with the RoB 2 Pilot Starter Pack

Before you start:

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

All resources are available in the Starter Pack

When writing your Cochrane Review protocol:
The RoB 2 assessment of bias is specific to a single trial result (and is therefore outcome based). This, together with other key differences, distinguish it from the original risk of bias tool. For these reasons there are some key considerations that must be prespecified in the protocol otherwise you will be at risk of using the tool incorrectly. Your Managing Editor will check the RoB 2 considerations as part of the peer review process. Please ensure you address these comments and ask questions if anything is unclear.

Watch this five-minute video on RoB 2 considerations for protocol development

The full checklist is available in the Starter Pack

Managing your RoB 2 assessments
We recommend authors use the RoB 2 Excel tool to manage your assessments available here.

Watch the RoB 2 Excel tool demo videos for managing your assessments

Watch this four-minute video on inputting RoB 2 data into RevMan Web

RoB 2 functionality has only been built into RevMan Web (not the desktop version) - key points to know include:
- RoB 2 must be switched on manually for your review when you are ready to input your RoB 2 data (this switch breaks compatibility with the desktop RevMan 5 version; if you are using Covidence, you must ensure that you import all data in RevMan 5 (desktop) before you ask for the RoB 2 function to be switched on),
- We advise data is input and analysed in RevMan in this order: 1) input main results data -> 2) input RoB 2 data -> 3) duplicate inputted results and RoB 2 data for sensitivity and/or subgroup analyses.
- Check the RevMan Web Knowledge Base if you have any questions.

When writing your full Cochrane Review

Watch this seven-minute video on RoB 2 considerations for full review reporting
Support and training resources for authors/editors

Support

➢ Methods Support Unit
  ➢ Monthly webinar clinics

➢ RoB 2 FAQs

➢ Cochrane standards and guidance (MECIR and Handbook)

Training

➢ Interactive learning module

➢ Standard author training materials

➢ RoB 2 webinar series

https://training.cochrane.org/rob-2-learning-live-webinar-series
Welcome to our pages for risk of bias tools for use in systematic reviews.

- **RoB 2 tool** (revised tool for Risk of Bias in randomized trials)
- **NEW! RoB ME (Risk Of Bias due to Missing Evidence in a synthesis)**
- **ROBINS-I tool** (Risk Of Bias in Non-randomized Studies - of Interventions)
- **robvis (visualization tool for risk of bias assessments in a systematic review)***

Feedback is welcome to risk-of-bias@bristol.ac.uk

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Email risk-of-bias@bristol.ac.uk with feedback.
A revised tool to assess risk of bias in randomized trials (RoB 2)

Welcome to the website for the RoB 2 tool.

The current version (22 August 2019), suitable for individually-randomized, parallel-group trials.

NEW! A test version for cluster-randomized trials is now available (10 November 2020).

NEW! A test version for crossover trials is now available (8 December 2020).

We are also maintaining an archive of the previous version, which had variants for three different trial designs (see below).

Citing the tool

The revised tool may be cited as:

Current version of RoB 2

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.
Protocol and Review reporting requirements
How to tag the Review as approved for using RoB 2

The Cochrane Review Group can add a note to the review properties in Archie (as seen below). This will be helpful for Community Support, the Methods Support Unit, and copy editors checking the Methods section and Handbook references.

Database copied on 26 October 2020.
Assessment of risk of bias in included studies

For all users of RoB 2:

1. State RoB 2 will be used and provide a reference to it
2. State effect of interest — Your choice
3. State which results will be assessed — Usually those in SoF table
4. State plans for design variants (cluster, crossover) if needed
5. Detail assessors (how many? who? independently? consensus?)
6. List the domains in the tool (these can’t be modified)
7. List the judgement options: High, Low, Some concerns; overall RoB
8. Tools to manage assessments
9. Primary analysis: all studies or low risk?
10. Subgroup analyses/ Sensitivity analyses

GRADE: state how RoB2 will be used

Storage
RoB 2 considerations for protocol development

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

A list of these items in a format that is easy to copy and paste to send to authors is at the end of this document.

When assessing these points in Cochrane Protocols, some Cochrane Review Group have added a third column to note whether the point has been completed or what is missing.

<table>
<thead>
<tr>
<th>What to report</th>
<th>Further details</th>
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</thead>
<tbody>
<tr>
<td><strong>Methods section - ‘Assessment of risk of bias in included studies’</strong></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, including outcome(s), outcome measure(s), and timepoints</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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</tbody>
</table>
| 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 Review Web yet so there is interim guidance on how to display these results.

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: MECP C53; Section 7.3.2 Cochrane Handbook. |
| 6. List the domains of the tool | Guidance: Section 1.3 Detailed guidance (riskofbias.info); Section 8.2.4 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.org website). Guidance: MECP 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: MECP 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. Guidance: MECP C22; Section 10.11.2 and Section 7.6.2 Cochrane Handbook. |

**Methods section - ‘Sensitivity analysis’**
Review reporting requirements

Methods
1. Include all the RoB 2 considerations from the Protocol. (If applicable). State if there were any deviations from the Protocol.
2. State the version of the RoB 2 tool that was used.

Results
1. Refer to the results-level RoB 2 tables.
2. State how to access detailed risk of bias assessments data (with consensus responses to the signalling questions).
3. Provide a brief overview of the risk of bias assessments.
4. Refer to visual representations of the risk of bias assessments in relation to each result.
5. (If applicable) Discuss any subgroup analysis/ sensitivity analysis conducted that relates to the risk of bias judgments.

Discussion
1. Discuss any risk of bias judgements that affect the certainty of the evidence along with all other GRADE considerations.
Investigate sensitivity - 1.1 Headache

Risk of Bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions: Headache
(C) Bias due to missing outcome data: Headache
(D) Bias in measurement of the outcome: Headache
(E) Bias in selection of the reported result: Headache
(F) Overall bias: Headache


https://documentation.cochrane.org/revman-kb
Support available for Cochrane Reviews using RoB 2

**Key resources**

- [methods.cochrane.org/risk-bias-2](http://methods.cochrane.org/risk-bias-2)

**FAQs**

**Introductory leaflet**
With pre-recorded videos

**RoB 2 Starter Pack**
- Online training
- Tips and timesavers
- Tools for using RoB 2
- Example reviews
- Protocol checklist
- Review checklist

*MSU Web Clinic webform:* [methods.cochrane.org/methods-support-unit-web-clinic](http://methods.cochrane.org/methods-support-unit-web-clinic)

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**Protocol development**

**Authors**

1. Propose review using RoB 2 (added to review proposal form)
   - Change to RoB 1 (CRG discretion)
   - Use RoB 1
   - Incorporate RoB 2 considerations and submit protocol

2. CRG agrees with the use of RoB 2 and preparation of the review in RevMan Web
   - Use RoB 2 checklist to assess RoB 2 methods during usual QA
   - CRG checks completed by MSU for first review going through CRG
   - Available for advice via email thereafter
   - Revision with RoB 2
   - Sign off
   - Publish

**CRG**

- Share RoB 2 resources with authors
- RoB 2 resources sent and explained by MSU for first review going through CRG
- Available for advice via email thereafter

**MSU**

- RoB 2 checks completed by MSU for first review going through CRG
- Available for advice via email thereafter

**Review development**

**Authors**

- Conduct RoB 2 assessments
- Submit RoB 2 issues and queries via the webform* for discussion with MSU
- Submit issues and queries via the webform* for discussion
- Submit RoB 2 assessments before write-up for checks
- CRG checks the RoB 2 ‘support for judgements’ are included
- MSU available for RoB 2 ’support for judgement’ checks
- MSU available for RoB 2 checks completed by MSU for first review going through CRG
- Available for advice via email thereafter

**CRG**

- CRG checks the RoB 2 ‘support for judgements’ are included
- Use RoB 2 checklist during usual QA
- Collate and send feedback to authors with CRG/peer review comments
- Sign off
- Publish

**MSU**

- Monthly Web Clinics hosted by MSU
- CRG checks the RoB 2 ‘support for judgements’ are included
- Use RoB 2 checklist during usual QA
- Collate and send feedback to authors with CRG/peer review comments
- Sign off
- Publish

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When ready, email support@cochrane.org to ask for RoB 2 functionality to be switched on in RevMan Web

*Note: Citations references can only be imported into RevMan 5 so must be imported before the switch*