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.

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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

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Poll 1

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Poll 2

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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 Authors' declarations of interest

Version published: 28 October 2020
https://doi.org/10.1002/14651858.CD013400.pub2

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,

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

Open in table viewer

Study	Bias: Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Subgroup 1.1.1 Exercise training						
Therrien 2003	✗	✓	✓	~	~	✗
Moalla 2006	~	✓	✓	~	~	~
Madhavi 2011	✗	~	✗	✗	~	✗
Winter 2012	~	✓	~	~	~	~
Westhoff-Bleck 2013	~	✓	~	~	~	~
Duppen 2015	✓	✓	✓	~	~	~
Avila 2016	✓	✓	✓	~	~	~
Novakovic 2018	✓	✓	✓	~	~	~
Opotowsky 2018	✓	✓	✓	~	~	~
Sandberg 2018	✓	✓	✓	✓	~	~

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 — Open in table viewer

Study	Bias: Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Subgroup 1.1.1 Exercise training						
Therrien 2003	High	Low	Low	Some	Some	High
	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.					
Moalla 2006	Some	Low	Low	Some	Some	Some
	There was no information on method of randomisation, there was no baseline imbalance that would suggest a problem with randomisation.					
Madhavi 2011	High	Some	High	High	Some	High
	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	Some	Low	Some	Some	Some	Some
	"Randomization was performed using sealed envelops. 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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Abstract
Plain language summary
Authors' conclusions
Summary of findings
Background
Objectives
Methods
Results
Discussion
Appendices
Information
Authors
History
Keywords
Translation notes
References
Characteristics of studies
Risk of bias
Data and analyses

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 — Open in table viewer

Study	Bias: Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Subgroup 1.1.1 Exercise training						
Therrien 2003	✗	✓	✓	~	~	✗
	Lack of information on randomisation, baseline imbalances and blinding of outcome assessors and no pre-registered protocol / statistical plan.					
Moalla 2006	~	✓	✓	~	~	~
Madhavi 2011	✗	~	✗	✗	~	✗
Winter 2012	~	✓	~	~	~	~
Westhoff-Bleck 2013	~	✓	~	~	~	~
Duppen 2015	✓	✓	✓	~	~	~
Avila 2016	✓	✓	✓	~	~	~
Novakovic 2018	✓	✓	✓	~	~	~
Opotowsky 2018	✓	✓	✓	~	~	~

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Print | Share | Follow
Abstract
Plain language summary
Authors' conclusions
Summary of findings
Background
Objectives
Methods
Results
Discussion
Appendices
Information
Authors
History
Keywords
Translation notes
References
Characteristics of studies
Risk of bias
Data and analyses

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?

0:00 / 3:37

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 | Cochr

methods.cochrane.org/risk-bias-2

Apps | Cochrane Handboo... | Webmail - The Univ... | Cochrane Reviews |... | Citrix Access Gatew... | RAINFORD BROOK... | Cochrane Handboo... | MSU Reviews, prot... | Edit - Risk of Bias 2...

Cochrane Library | Cochrane.org | Admin

Cochrane Methods

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Risk of Bias 2 (RoB 2) tool

- Process for proposing changes to methods or tools used in Cochrane
- Clinical study reports and other regulatory documents
- Data-based predictive distributions for between-study heterogeneity
- Repeated meta-analyses
- Risk of Bias 2 (RoB 2) tool
- ROBINS-I 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

How to propose changes to methods or tools used in Cochrane

CLICK HERE

Implementation statement

Risk of Bias 2 (RoB 2) tool

Implementation statement

CSC members are not responsible for managing implementation of these recommendations which will require an implementation plan to ensure co-ordination for a smooth introduction. This will include launch, timescales and roll out strategy. Therefore, these statements do not signify immediate implementation.

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 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.

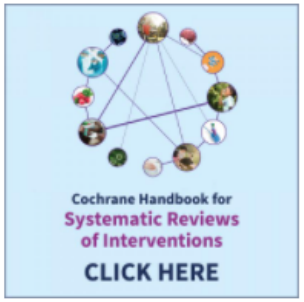
Risk of Bias 2 Webinars

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

How to propose changes to methods or tools used in Cochrane

CLICK HERE



Cochrane Handbook for Systematic Reviews of Interventions

CLICK HERE

Methodological Expectations of Cochrane Intervention Reviews

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

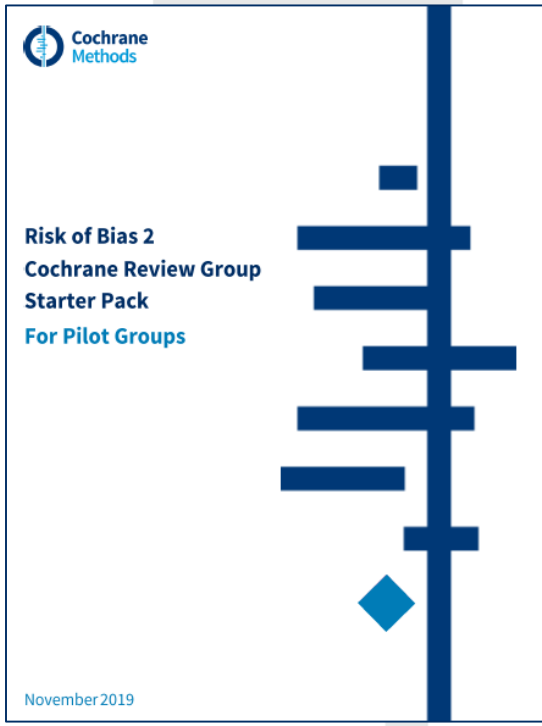
Watch this seven-minute video on RoB 2 considerations for full review reporting

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



Risk of bias tools

riskofbias.info

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

RoB 2 tool

A revised Cochrane risk of bias tool for randomized trials

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:

Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT

MRC Hubs for Trials Methodology Research

This work was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/1- N61). Infrastructure support was provided by the Medical Research Council ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomized controlled Trials In Invasive procedures – MR/K025643/1).

Current version of RoB 2

Current version

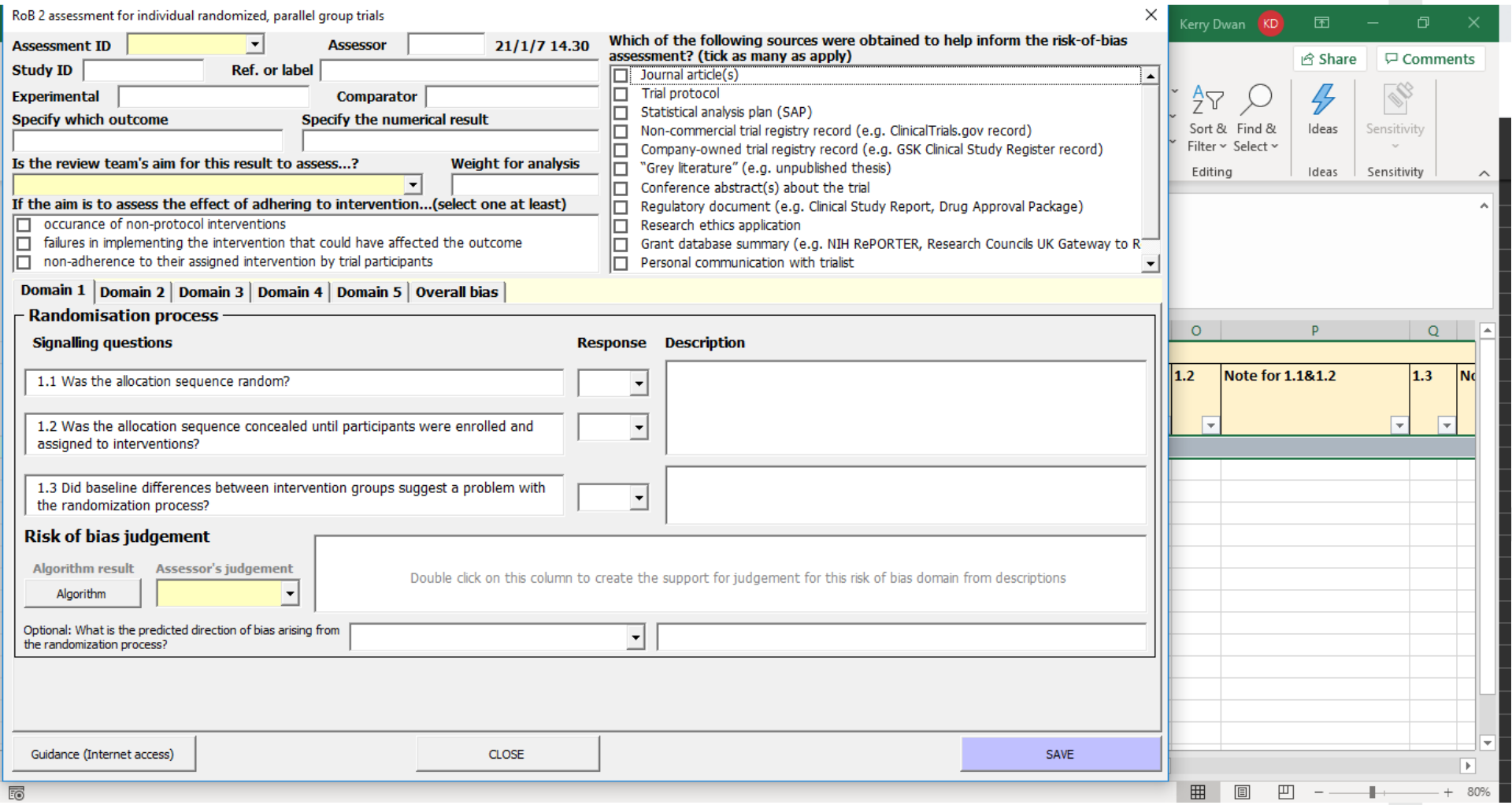
Download the 22 August 2019 version:

- 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.


Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne
on behalf of the RoB2 Development Group


RoB 2 assessment for individual randomized, parallel group trials
Assessment ID
Assessor
21/1/7 14.30
Study ID
Ref. or label
Experimental
Comparator
Specify which outcome
Specify the numerical result
Is the review team's aim for this result to assess...?
Weight for analysis
If the aim is to assess the effect of adhering to intervention...(select one at least)
occurance of non-protocol interventions
failures in implementing the intervention that could have affected the outcome
non-adherence to their assigned intervention by trial participants
Which of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)
Journal article(s)
Trial protocol
Statistical analysis plan (SAP)
Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Company-owned trial registry record (e.g. GSK Clinical Study Register record)
"Grey literature" (e.g. unpublished thesis)
Conference abstract(s) about the trial
Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
Research ethics application
Grant database summary (e.g. NIH RePORTER, Research Councils UK Gateway to R
Personal communication with trialist
Domain 1
Domain 2
Domain 3
Domain 4
Domain 5
Overall bias
Randomisation process
Signalling questions
Response
Description
1.1 Was the allocation sequence random?
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?
Risk of bias judgement
Algorithm result
Assessor's judgement
Algorithm
Double click on this column to create the support for judgement for this risk of bias domain from descriptions
Optional: What is the predicted direction of bias arising from the randomization process?
Guidance (Internet access)
CLOSE
SAVE
Kerry Dwan
KD
Share
Comments
Sort & Filter
Find & Select
Ideas
Sensitivity
Editing
Ideas
Sensitivity
O
P
Q
1.2
Note for 1.1&1.2
1.3
80%

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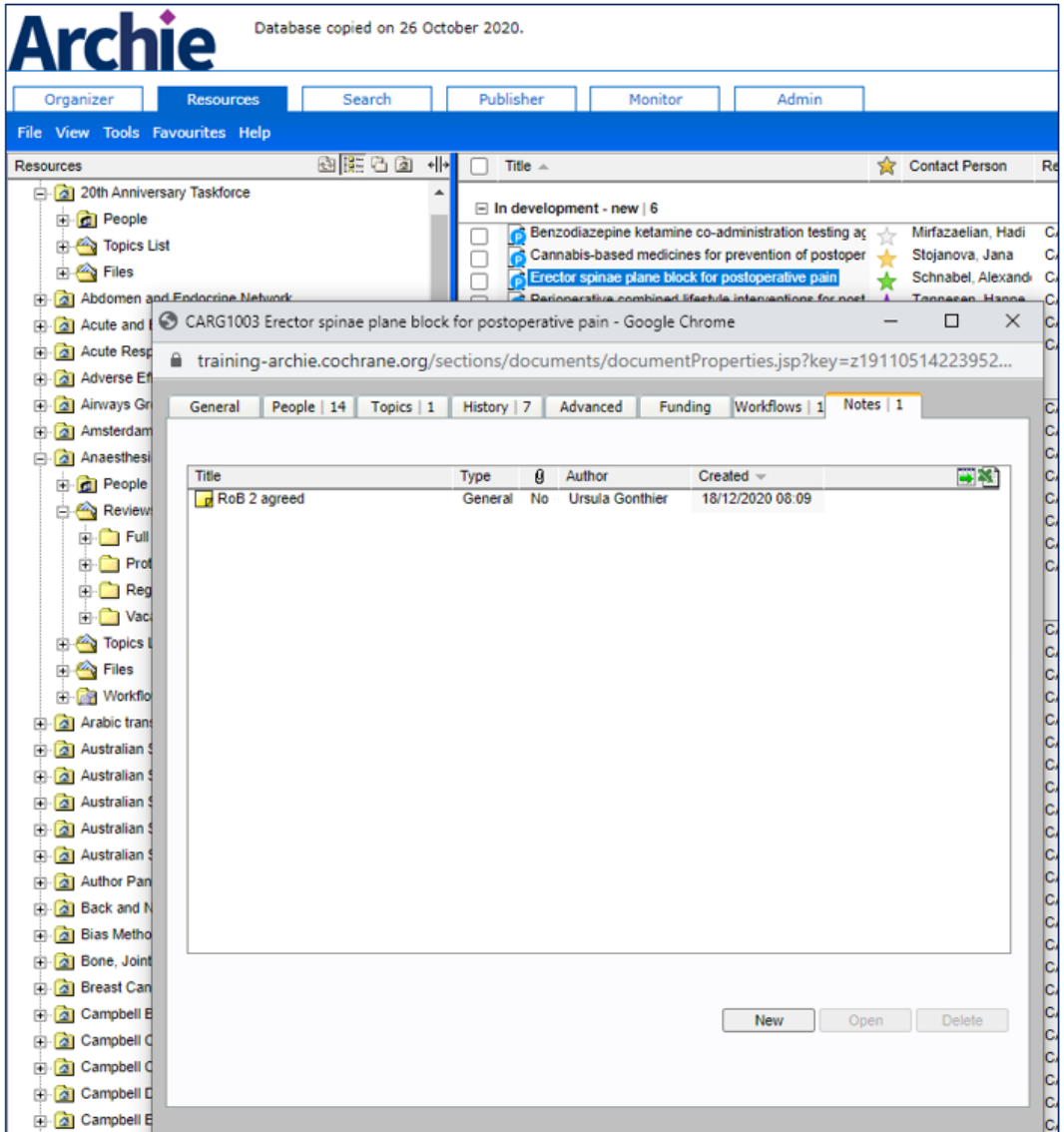
Protocol and Review reporting requirements

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.



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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?

   Subgroup analyses/ Sensitivity analyses
10. 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.

What to report	Further details
Methods section - **'Assessment of risk of bias in included studies'**	
1. State that RoB 2 tool will be used and reference it	Reference Sterne et al 2019 BMJ paper and / or Cochrane Handbook (version 6) Chapter 8 . **Guidance**: MECIR PR27
2. State your effect of interest - effect of assignment or effect of adherence	**Guidance**: Section 1.3 Detailed guidance (Riskofbias.info); Section 8.2.2 Cochrane Handbook.
3. List or refer to the results that will be assessed using RoB 2, inc. outcome(s), outcome measure(s) and timepoint(s)	**Guidance**: Section 1.3 Detailed guidance (Riskofbias.info); Section 7.3.2, Section 8.2.1 and Section 8.7 Cochrane Handbook.
4. (If applicable) State how you will handle crossover RCTs and cluster RCTs	Reference the RoB variant for crossover trials and/ or the RoB 2 variant for cluster trials. **Guidance**: RoB for for crossover trials via riskofbias.info and RoB 2 for cluster trials via riskofbias.info ***NB**: Please note, as of December 2020, the cluster and cross trial variants for RoB 2 have not been developed in RevMan Web yet so there is interim guidance on how to display these results.* ***NB**: Please note, if you have intended from the OUTSET to ONLY use data from the first period of the crossover, then you can use the standard version of RoB 2 as it is. However, please be alert to the potential impact of selective reporting of first period of data only when carry over is detected by trialists. Omission of trials which do not report first period data may lead to bias at the meta-analysis level. For details are in Section 23.2 Cochrane Handbook.*
5. State who will assess RoB2 (initials), how many and whether independently and duplicate	**Guidance**: MECIR C53; Section 7.3.2 Cochrane Handbook.
6. List the domains of the tool	**Guidance**: Section 1.3 Detailed guidance (Riskofbias.info); Section 8.2.3 Cochrane Handbook.
7. List the judgment options (High, Some Concerns, Low) and how overall risk of bias is reached, e.g. using the signalling questions/tool algorithms	**Guidance**: Section 1.1, Section 1.2.1 and Section 1.2.3 Detailed guidance (Riskofbias.info); Section 8.2.3 and Section 8.2.4 Cochrane Handbook.
8. State if you plan to use any tools to manage the assessment of bias using RoB 2	For example, the RoB2 Excel tool to implement RoB 2 (available on the riskofbiasinfo.org website) **Guidance**: MECIR C54; Section 7.3.2 Cochrane Handbook.
Methods section - **'Data synthesis'**	
9. State whether the primary analysis will include all eligible studies or only those which have low risk of bias, or low risk and some concerns	This may depend on the number of studies with each risk of bias rating as you'll need sufficient numbers for the analyses. It could also be appropriate to pool data from studies at high risk of bias and use a sensitivity analysis to assess the effects of restricting the analysis to RCTs overall 'low' or 'low/some concerns'. **Guidance**: MECIR C21, Section 7.6.2 Cochrane Handbook.
Methods section - **'Subgroup analysis and investigation of heterogeneity'**	
(If applicable) Specify if subgroup analysis is planned based on risk of bias	Consider whether overall risk of bias should be used as the basis for any subgroup analysis. **Guidance**: MECIR C22; Section 10.11.2 and Section 7.6.2 Cochrane Handbook.
Methods section - **'Sensitivity analysis'**	

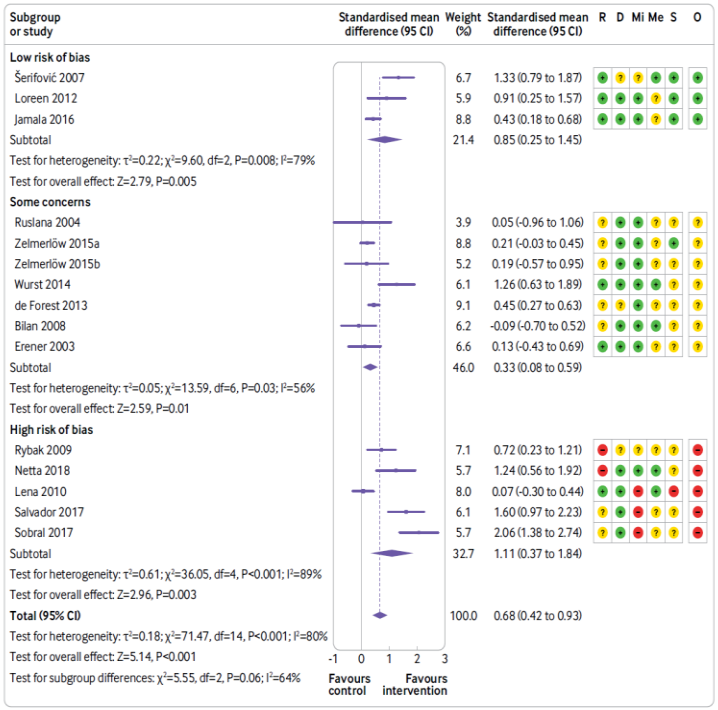
Review reporting requirements

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.

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Investigate sensitivity - 1.1 Headache

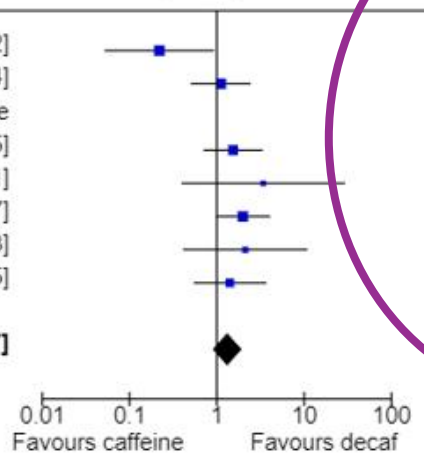
Odds ratio | **Risk ratio** | Risk difference | **Fixed effect** | Random effects | Scale 100 | Save image

Study or Subgroup	Caffeine Events	Caffeine Total	Decaf Events	Decaf Total	Weight	Risk ratio M-H, Fixed, 95% CI
✓ Amore-Coffea 2000	2	31	10	34	21.2%	0.22 [0.05 , 0.92]
✓ Deliciozza 2004	10	40	9	40	20.0%	1.11 [0.51 , 2.44]
✓ Kahve-Paradiso 2002	0	0	0	0		Not estimable
✓ Mama-Kaffa 1999	12	53	9	61	18.6%	1.53 [0.70 , 3.35]
✓ Morrocona 1998	3	15	1	17	2.1%	3.40 [0.39 , 29.31]
✓ Norscafe 1998	19	68	9	64	20.7%	1.99 [0.97 , 4.07]
✓ Oohlahlazza 1998	4	35	2	37	4.3%	2.11 [0.41 , 10.83]
✓ Piazza-Allerta 2003	8	35	6	37	13.0%	1.41 [0.54 , 3.65]
Total (95% CI)		**277**		**290**	**100.0%**	**1.31 [0.92 , 1.87]**
Total events:	58		46			

Heterogeneity: Chi² = 8.66, df = 6 (P = 0.19); I² = 31%

Test for overall effect: Z = 1.51 (P = 0.13)

Test for subgroup differences: Not applicable



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/assessing-risk-of-bias/how-to-use-risk-of-bias-2-0-rob-2-0-tool-in-revman-web

\https://documentation.cochrane.org/revman-kb

Support available for Cochrane Reviews using RoB 2

Key resources

methods.cochrane.org/risk-bias-2

FAQs

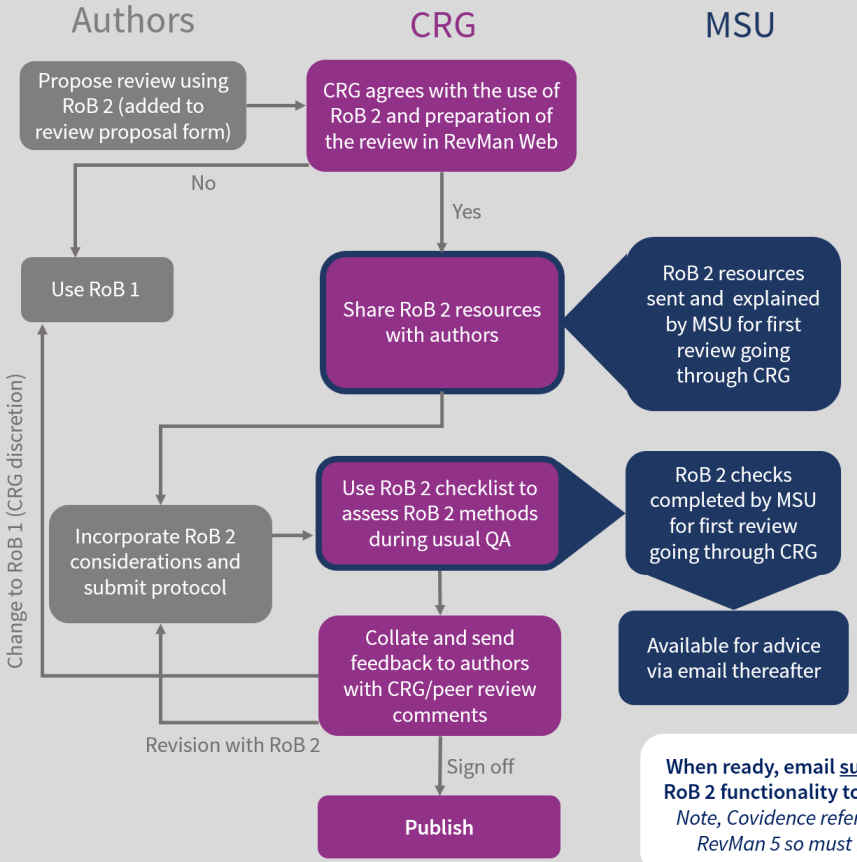
Introductory leaflet
With pre-recorded videos

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

Protocol development



When ready, email support@cochrane.org to ask for RoB 2 functionality to be switched on in RevMan Web
Note, Covidence references can only be imported into RevMan 5 so must be imported before the switch

Review development