Cochrane Italia

Risk of bias tool

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Reviewer
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Cochrane Drugs and Alcohol

Cochrane Haematological Malignancies

Cochrane Breast Cancer

Randomised controlled trials :
RoB 2.0

RoB 2.0

Proposta informalmente al Colloquium di Vienna (ottobre 2015)

Primo pilota a Bristol nel febbraio 2016

Lanciato ufficialmente al Colloquium di Seoul (ottobre 2016)

Fase iniziale di sviluppo
RevMan e Covidence dovrebbero essere cambiati per permetterne l'uso

RoB 2.0

Old RoB:

Used simplistically and inconsistently (domains added or removed)

Overuse of «unclear risk»

The item “other” not straightforward

RoB judgements difficult for some domain (incomplete outcome data and selective reporting)

Challenges with open-label trials

Not well suited for cross-over or cluster trials

RoB 2.0

New RoB 2.0:

To allow authors to make a better assessment and to separate for different outcomes

To have a tool with a formulation similar to the other most recent tools (i.e. with signalling questions and overall risk of bias)

New response options without “unclear option”

Different templates for different types of RCTs available:

- Randomized parallel group trials
- Cluster-randomized trials
- Randomized cross-over trials

RoB 1.0	RoB 2.0
Random sequence generation (*selection bias*)	Bias arising from the randomization process
Allocation concealment (*selection bias*)	
Blinding of participants and personnel (*performance bias*)	Bias due to deviations from intended interventions
Incomplete outcome data (*attrition bias*)	Bias due to missing outcome data
Blinding of outcome assessment (*detection bias*)	Bias in measurement of the outcome
Selective reporting (*reporting bias*)	Bias in selection of the reported result
Other bias	N/A
N/A	Overall bias

Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y / PY / PN / N / NI	[Description]
	1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	Y / PY / PN / N / NI	[Description]
	1.3 Were there baseline imbalances that suggest a problem with the randomization process?	Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Low / High / Some concerns	[Support]
	Optional: What is the predicted direction of bias arising from the randomization process?		[Rationale]
Bias due to deviations from intended interventions	2.1. Were participants aware of their assigned intervention during the trial?	Y / PY / PN / N / NI	[Description]
	2.2. Were carers and trial personnel aware of participants' assigned intervention during the trial?	Y / PY / PN / N / NI	[Description]
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	NA / Y / PY / PN / N / NI	[Description]
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome?	NA / Y / PY / PN / N / NI	[Description]
	2.5 Were any participants analysed in a group different from the one to which they were assigned?	Y / PY / PN / N / NI	[Description]
	2.6 If Y/PY/NI to 2.5: Was there potential for a substantial impact (on the estimated effect of intervention) of analysing participants in the wrong group?	NA / Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Low / High / Some concerns	[Support]
	Optional: What is the predicted direction of bias due to deviations from intended interventions?		[Rationale]
Bias due to missing outcome data	3.1 Were outcome data available for all, or nearly all, participants randomized?	Y / PY / PN / N / NI	[Description]
	3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across intervention groups?	NA / Y / PY / PN / N / NI	[Description]
	3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NA / Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Low / High / Some concerns	[Support]
	Optional: What is the predicted direction of bias due to missing outcome data?		[Rationale]
Bias in measurement of the outcome	4.1 Were outcome assessors aware of the intervention received by study participants?	Y / PY / PN / N / NI	[Description]
	4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NA / Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Low / High / Some concerns	[Support]
	Optional: What is the predicted direction of bias due to measurement of the outcome?		[Rationale]
Bias in selection of the reported result	Are the reported outcome data likely to have been selected, on the basis of the results, from...		
	5.1. ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	Y / PY / PN / N / NI	[Description]
	5.2 ... multiple analyses of the data?	Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Low / High / Some concerns	[Support]
	Optional: What is the predicted direction of bias due to selection of the reported result?		[Rationale]
Overall bias	**Risk of bias judgement**	Low / High / Some concerns	[Support]
	Optional: What is the overall predicted direction of bias for this outcome?		[Rationale]

RoB 2.0 - signalling questions

For each domain some signalling question have been proposed

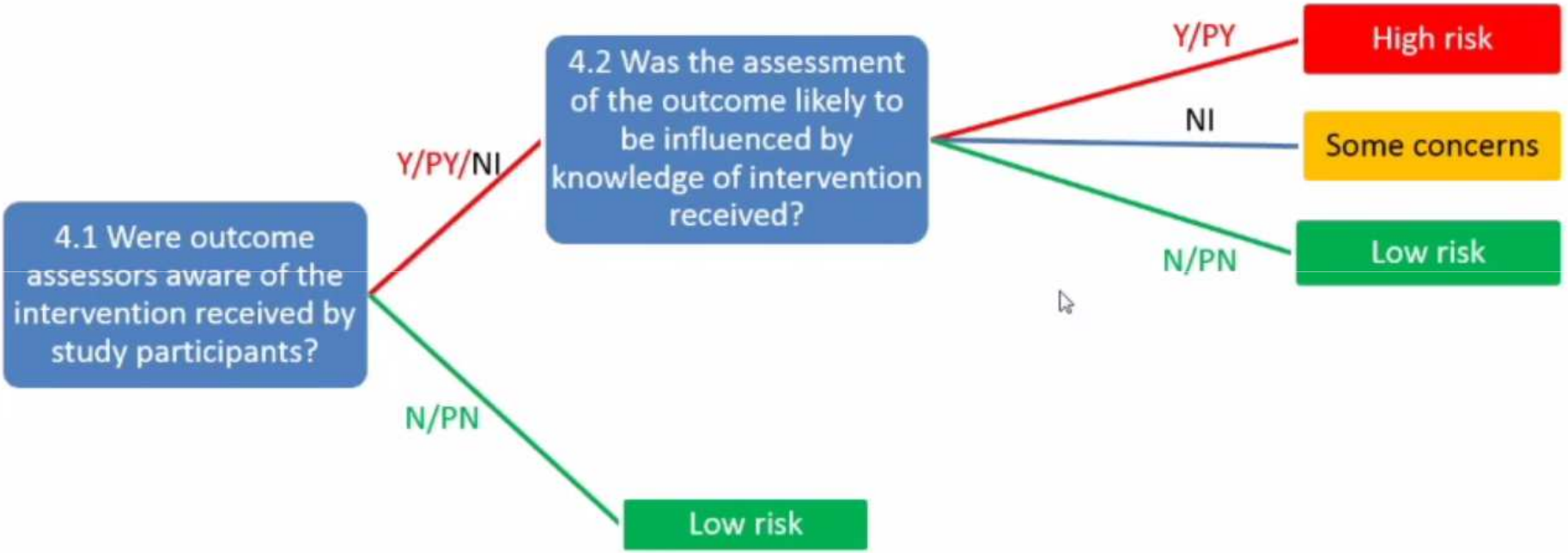
- **Signalling questions**: possible answers:

Yes - Probably yes - Probably no - No –

No information

Responses of 'Yes' and 'Probably yes' (also of 'No' and 'Probably no') have similar implications.

The former (yes, no) would imply that firm evidence is available in the study in relation to the signalling question; the latter (probably…) would imply that a judgment has been made


4.1 Were outcome assessors aware of the intervention received by study participants?
Y/PY/NI
N/PN
Low risk
4.2 Was the assessment of the outcome likely to be influenced by knowledge of intervention received?
Y/PY
NI
N/PN
High risk
Some concerns
Low risk

RoB 2.0 judgment

Table 1. Reaching an overall risk of bias judgement for a specific outcome.

Overall risk of bias judgement	Criteria
Low risk of bias	The study is judged to be at **low risk of bias for all domains** for this result.
Some concerns	The study is judged to be at **low or risk of bias or some concerns for all domains** for this result.
High risk of bias	The study is judged to be at **high risk of bias** in at least one domain for this result. Or The study is judged to have **some concerns** for **multiple domains** in a way that subtantially lowers confidence in the result.

Declaring a study to be at a particular level of risk of bias for an individual domain will mean that the study as a whole has a risk of bias at least this severe (for the result being assessed). Therefore a

Bias arising from the randomization process (selection bias)

3 signalling questions:

- **1.1** Was the allocation sequence random?
- **1.2** Was the allocation sequence concealed?
- **1.3** Were there baseline imbalances that suggest a problem with randomization?

Bias due to deviation from intended interventions (performance bias)

Important distinction between two types of intervention effect that review authors might be interested in quantifying. These are:

(1) the **effect of assignment to the interventions** at baseline (regardless of whether the interventions are received);

(2) the **effect of receiving the interventions** as specified in the protocol.

Bias due to deviation from intended interventions (performance bias)

1. **effect of assignment to intervention**

5 signalling questions

(blinding of participants and providers, deviation reflecting the usual practice, ITT analysis)

2. **effect of initiating and adhering to intervention**

6 signalling questions

(blinding of participants and providers, success of implementation, compliance, co-interventions)

Bias due to missing outcome data (attrition bias)

3 signalling questions

(Amount of missing data, balance between groups, reasons , handle of missing data in the analysis)

Bias in measurement of the outcome (detection bias)

Only 2 signalling questions

But….

Before assessing this domain, it is important to determine:

- who is the outcome assessor;
- whether the outcome measure is likely to be influenced by knowledge of intervention received.

Bias in measurement of the outcome (detection bias)

Some suggestions are provided:

Patient-reported outcomes: likely to be influenced by knowledge of intervention received

Observer-reported outcomes not involving judgment (e.g. mortality, laboratory tests) : not likely to be influenced by knowledge of intervention received

Observer-reported outcomes involving some judgment (e.g. clinical examination, radiograph) : likely to be influenced

Treatment provider decision outcomes (e.g. hospitalization, discharge) : likely to be influenced

Composite outcomes: Assessment should take into account the frequency of each component of the composite outcome and the risk of bias of the most frequent components

Bias in selection of the reported result (selective reporting bias)

Three levels of assessment:

1. **Outcome domain**: when the outcome domain is not reported or partially reported: Outcome non-reporting bias: does not bias study results (outcome not reported) , but biases meta-analysis. **NOT TO BE ASSESSED BY RoB 2.0**
2. **Outcome measurement**: when multiple measurement instruments (e.g. pain scales) and only reporting data for the instrument with the most favourable result: Selective reporting of a particular outcome measurement
3. **Outcome analysis**: when only change from baseline or only difference in post intervention scores : Selective reporting of a particular analysis

3 signalling questions

https://sites.google.com/site/riskofbiastool//welcome/rob-2-0-tool

RoB 2.0 - Conclusions

Not all review authors are experts methodologists

PROS:

Completely new approach that asks reviewers to think more deeply, to reason, to interpret and to formulate a subjective judgment; good because the risk of bias assessment will become more accurate and precise and less “automatic”

Very stimulating for methodologists…….

Definitely right to assess the risk of bias at the outcome level

CONS:

Much more complex and very time consuming

More room for subjective judgment: useful but also dangerous