Supplement 5

Modified ROBINS-I Tool

Signalling questions		Response options
1. Bias due to confounding		
	1.1 Is there potential for confounding of the effect of intervention in this study?	Y / PY / PN / N
	Risk of bias judgement	Low/Moderate/Serious/Critical/NI
2. Bias in selection of participants into the study		
	2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics	Y / PY / PN / N / NI
	Risk of bias judgement	Low/Moderate/Serious/Critical/NI
3. Bias in classification of interventions		
	3.1 Were intervention groups clearly defined?	Y / PY / PN / N / NI
	Risk of bias judgement	Low/Moderate/Serious/Critical/NI
4. Bias due to deviations from intended interventions		
	4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice?	Y / PY / PN / N / NI
	4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome?	NA / Y / PY / PN / N / NI
	Risk of bias judgement	Low/Moderate/Serious/Critical/NI
5. Bias due to missing data		
	5.1 Were outcome data available for all, or nearly all (>80%), participants?	Y / PY / PN / N / NI
	5.2 **If PN/N to 5.1**: Are the proportion of participants and reasons for missing data similar across interventions?	NA / Y / PY / PN / N / NI
	5.3 **If PN/N to 5.1:** Is there evidence that results were robust to the presence of missing data?	NA / Y / PY / PN / N / NI
	Risk of bias judgement	Low/Moderate/Serious/Critical/NI
6. Bias in measurement of outcomes		
	6.1 Could the outcome measure have been influenced by knowledge of the intervention received?	Y / PY / PN / N / NI
	Risk of bias judgement	Low/Moderate/Serious/Critical/NI
7. Bias in selection of the reported result		
	Is the reported effect estimate likely to be selected, on the basis of the results, from... 7.1. ... multiple outcome *measurements* within the outcome domain?	Y / PY / PN / N / NI
	7.2 ... multiple *analyses* of the intervention-outcome relationship?	Y / PY / PN / N / NI
	7.3 ... different *subgroups*?	Y / PY / PN / N / NI
	Risk of bias judgement	Low/Moderate/Serious/Critical/NI
Overall bias		
Risk of bias judgement		Low/Moderate/Serious/Critical/NI

NB: *NA = Not Applicable, Y = Yes, PY = Probably Yes, PN = Probably No, N = No, NI = No Information*

Criteria for overall bias judgement – ROBINS-I	
Judgement	**Criteria**
Low risk of bias (the study is comparable to a well-performed randomized trial);	The study is judged to be at **low risk of bias for all domains**.
Moderate risk of bias (the study appears to provide sound evidence for a non-randomized study but cannot be considered comparable to a well-performed randomized trial);	The study is judged to be at **low or moderate risk of bias for all domains**.
Serious risk of bias (the study has some important problems);	The study is judged to be at **serious risk of bias** in at least one domain, but not at critical risk of bias in any domain.
Critical risk of bias (the study is too problematic to provide any useful evidence and should not be included in any synthesis);	The study is judged to be at **critical risk of bias in at least one domain.**
No information on which to base a judgement about risk of bias.	There is no clear indication that the study is at serious or critical risk of bias *and* there is a lack of information in one or more key domains of bias (*a judgement is required for this*).

(Sterne et al., 2016a)

Revised Cochrane Risk-of-Bias Tool for Randomised Trials (RoB 2.0)

Domain & Signalling Question		Response Options
1. Risk of bias arising from the randomization process		Low / High / Some concerns
1.1	Was the allocation sequence random?	Y / PY / PN / N / NI
1.2	Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y / PY / PN / N / NI
1.3	Did baseline differences between intervention groups suggest a problem with the randomization process?	Y / PY / PN / N / NI
2. Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)		Low / High / Some concerns
2.1	Were participants aware of their assigned intervention during the trial?	Y / PY / PN / N / NI
2.2	Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y / PY / PN / N / NI
2.3	If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	NA / Y / PY / PN / N / NI
2.4	If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA / Y / PY / PN / N / NI
2.5	If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA / Y / PY / PN / N / NI
2.6	Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y / PY / PN / N / NI
2.7	If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA / Y / PY / PN / N / NI
2. Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)		Low / High / Some concerns
2.1	Were participants aware of their assigned intervention during the trial?	Y / PY / PN / N / NI
2.2	Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y / PY / PN / N / NI
2.3	If Y/PY/NI to 2.1 or 2.2: Were important co-interventions balanced across intervention groups?	NA / Y / PY / PN / N / NI
2.4	Were there failures in implementing the intervention that could have affected the outcome?	Y / PY / PN / N / NI
2.5	Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?	Y / PY / PN / N / NI
2.6	If N/PN/NI to 2.3 or 2.5 or Y/PY/NI to 2.4: Was an appropriate analysis used to estimate the effect of adhering to the intervention?	NA / Y / PY / PN / N / NI
3. Risk of bias due to missing outcome data		Low / High / Some concerns
3.1	Were data for this outcome available for all, or nearly all, participants randomized?	Y / PY / PN / N / NI
3.2	If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	NA / Y / PY / PN / N
3.3	If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA / Y / PY / PN / N
3.4	If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA / Y / PY / PN / N

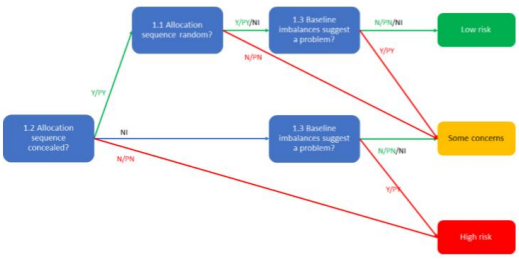
4. Risk of bias in measurement of the outcome		Low / High / Some concerns
4.1	Was the method of measuring the outcome inappropriate?	Y / PY / PN / N / NI
4.2	Could measurement or ascertainment of the outcome have differed between intervention groups?	Y / PY / PN / N / NI
4.3	If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	Y / PY / PN / N / NI
4.4	If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA / Y / PY / PN / N / NI
4.5	If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA / Y / PY / PN / N / NI
5. Risk of bias in selection of the reported result		Low / High / Some concerns
5.1	Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Y / PY / PN / N / NI
5.2	… multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	Y / PY / PN / N / NI
5.3	… multiple analyses of the data?	Y / PY / PN / N / NI

NB: *NA = Not Applicable, Y = Yes, PY = Probably Yes, PN = Probably No, N = No, NI = No Information*

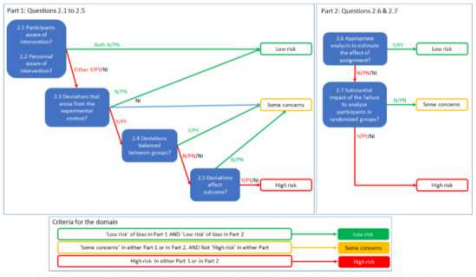
Overall risk of bias	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of bias due to selection of the reported result?	NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Criteria for overall bias judgement – RoB 2.0	
Judgement	**Criteria**
Low risk of bias	The study is judged to be at low risk of bias for all domains.
Some Concerns	The study is judged to raise some concerns in at least one domain for this result, but not to be at high risk of bias for any domain.
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 substantially lowers confidence in the result.

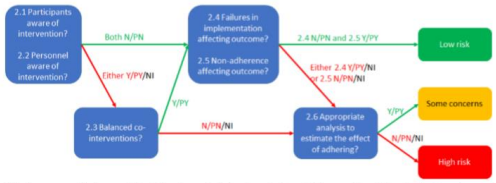
(Higgins et al., 2019)



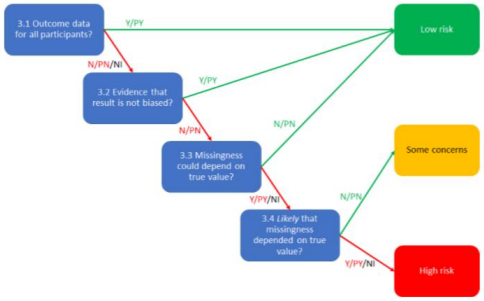
Algorithm for suggested judgment of risk of bias arising from the randomization process



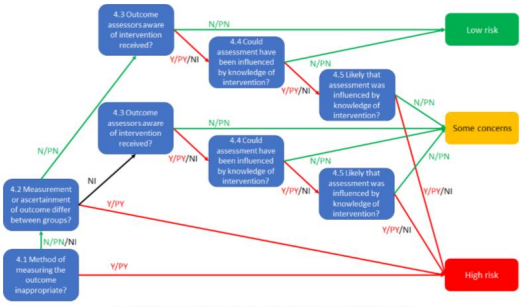
Algorithm for suggested judgment of risk of bias due to deviations from the intended interventions (effect of assignment to intervention)



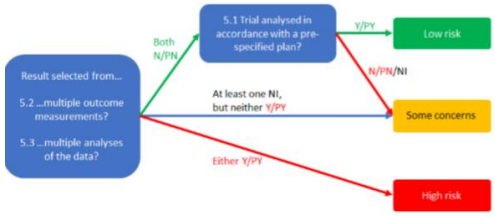
Algorithm for suggested judgment of risk of bias due to deviations from the intended interventions (effect of adhering to intervention)



Algorithm for suggested judgment of risk of bias due to missing outcome data



Algorithm for suggested judgment of risk of bias in measurement of the outcome



Algorithm for suggested judgment of risk of bias in selection of the reported result