

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

TEMPLATE FOR COMPLETION

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on behalf of the RoB2 Development Group

Version of 22 August 2019

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



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Study details

Reference

Fawzy M et al, 2018

Study design

- ☒ Individually-randomized parallel-group trial
- ☐ Cluster-randomized parallel-group trial
- ☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental: Artificial oocyte activation

Comparator: Routine ICSI

Specify which outcome is being assessed for risk of bias

Live birth rate

Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

This will be after pooling the live birth rate from all studies

Is the review team's aim for this result...?

- ☒ to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)
- ☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

- ✓ occurrence 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) with results of the trial
- ✓ 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- ☐ "Grey literature" (e.g. unpublished thesis)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 or Research Councils UK Gateway to Research)
- ☐ Personal communication with trialist
- ☐ Personal communication with the sponsor

Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in **red** are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?	1.1 <u>Yes</u>	<u>Y</u> / <u>PY</u> / PN / N / NI
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	1.2 <u>Yes</u>	<u>Y</u> / <u>PY</u> / PN / N / NI
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	1.3 <u>No</u>	Y / PY / <u>PN</u> / <u>N</u> / NI
Risk-of-bias judgement	<u>Low concerns</u>	Low / High / Some concerns
Optional: What is the predicted direction of bias arising from the randomization process?	Not applicable	NA / Favours experimental / Favours comparator / Towards null / Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*) **participant behaviour contamination**)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	2.1 <u>No</u>	Y / PY / <u>PN</u> / N / NI
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	2.2 <u>Probably yes (while the clinicians were not aware, the embryologist were aware)</u>	Y / PY / <u>PN</u> / N / NI
2.3. If <u>Y/PY/NI</u> to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	2.3 <u>Probably no (no contamination)</u>	NA / Y / PY / <u>PN</u> / N / NI
2.4 If <u>Y/PY</u> to 2.3: Were these deviations likely to have affected the outcome?	2.4 NA	NA / Y / PY / <u>PN</u> / N / NI
2.5. If <u>Y/PY/NI</u> to 2.4: Were these deviations from intended intervention balanced between groups?	2.5 NA	NA / <u>Y/PY</u> / <u>PN</u> / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	2.6 <u>Yes</u>	<u>Y</u> / <u>PY</u> / <u>PN</u> / N / NI
2.7 If <u>N/PN/NI</u> 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?	2.7 NA	NA / Y / PY / <u>PN</u> / N / NI
Risk-of-bias judgement	<u>Low concerns</u>	Low / High / Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?	NA	NA / Favours experimental / Favours comparator / Towards null / Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*) (**performance bias**)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?	2.1 No	Y / PY / PN / N / NI
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	2.2 Yes (while the clinicians were blinded, the embryologist were aware)	Y / PY / PN / N / NI
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across intervention groups?	2.3 Probably Yes	NA / Y / PY / PN / N / NI
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?	2.4 Probably No	NA / Y / PY / PN / N / NI
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?	2.5 No	NA / Y / PY / PN / N / NI
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of adhering to the intervention?	2.6 NA	NA / Y / PY / PN / N / NI
Risk-of-bias judgement	Low concerns	Low / High / Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?	NA	NA / Favours experimental / Favours comparator / Towards null / Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	3.1 Yes	<u>Y</u> / <u>PY</u> / <u>PN</u> / <u>N</u> / NI
3.2 If <u>N/PN/NI</u> to 3.1: Is there evidence that the result was not biased by missing outcome data?	3.2 NA	NA / <u>Y</u> / <u>PY</u> / <u>PN</u> / <u>N</u>
3.3 If <u>N/PN</u> to 3.2: Could missingness in the outcome depend on its true value?	3.3 NA	NA / <u>Y</u> / <u>PY</u> / <u>PN</u> / <u>N</u> / NI
3.4 If <u>Y/PY/NI</u> to 3.3: Is it likely that missingness in the outcome depended on its true value?	3.4 NA	NA / <u>Y</u> / <u>PY</u> / <u>PN</u> / <u>N</u> / NI
Risk-of-bias judgement	Low concerns	Low / High / Some concerns
Optional: What is the predicted direction of bias due to missing outcome data?	NA	NA / Favours experimental / Favours comparator / Towards null / Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome (Detection bias)

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?	4.1 No	Y / PY / <u>PN / N</u> / NI
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	4.2 No	Y / PY / <u>PN / N</u> / NI
4.3 If <u>N/PN/NI</u> to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	4.3 Yes	NA / Y / PY / <u>PN / N</u> / NI
4.4 If <u>Y/PY/NI</u> to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	4.4 Probably no	NA / Y / PY / <u>PN / N</u> / NI
4.5 If <u>Y/PY/NI</u> to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	4.5 NA	NA / Y / PY / <u>PN / N</u> / NI
Risk-of-bias judgement	Low concerns	Low / High / Some concerns
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null / Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
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?	5.1 Probably yes (even though not clearly specified in the trial protocol, the authors have reported all the standard expected outcomes for fertility trial)	<u>Y</u> / <u>PY</u> / <u>PN</u> / <u>N</u> / NI
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	5.2 Probably no	<u>Y</u> / <u>PY</u> / <u>PN</u> / <u>N</u> / NI
5.3 ... multiple eligible analyses of the data?	5.3 Probably no	<u>Y</u> / <u>PY</u> / <u>PN</u> / <u>N</u> / NI
Risk-of-bias judgement	Low concerns	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

Overall risk of bias

Risk-of-bias judgement	Low concerns	Low / High / Some concerns
Optional: What is the overall predicted direction of bias for this outcome?	NA	NA / Favours experimental / Favours comparator / Towards null / Away from null / Unpredictable



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