# Tool to Assess Risk of Bias in Randomized Controlled Trials

**Contributed by the CLARITY Group at McMaster University**

## 1. Was the allocation sequence adequately generated? *

<table>
<thead>
<tr>
<th>Definitely yes (low risk of bias)</th>
<th>Probably yes</th>
<th>Probably no</th>
<th>Definitely no (high risk of bias)</th>
</tr>
</thead>
</table>

**Examples of low risk of bias:**
- Referring to a random number table
- Using a computer random number generator
- Coin tossing
- Shuffling cards or envelopes
- Throwing dice
- Drawing of lots
- Minimization with or without a random element

**Examples of high risk of bias:**
- Sequence generated by odd or even date of birth
- Sequence generated by some rule based on date (or day) of admission
- Sequence generated by some rule based on hospital or clinic record number
- Allocation by judgement of the clinician
- Allocation by preference of the participant
- Allocation based on the results of a series laboratory test or series of tests
- Allocation by availability of the intervention

* Option to omit this item
2. Was the allocation adequately concealed?

**Examples of low risk of bias allocation concealment techniques:**
- Central allocation (including telephone, web-based, and pharmacy-controlled, randomization)

**Examples of possible low risk of bias:**
- Sequentially numbered drug containers of identical appearance
- Sequentially numbered, opaque, sealed envelopes

**Examples of high risk of bias allocation concealment techniques:**
- Using an open random allocation schedule (e.g. a list of random numbers)
- Assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered)
- Alternation or rotation
- Date of birth
- Case record number
- Any other explicitly unconcealed procedure
3. Blinding: Was knowledge of the allocated interventions adequately prevented? *

<table>
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<tr>
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</tr>
</thead>
</table>

3.a. Were patients blinded?

<table>
<thead>
<tr>
<th>Definitely yes (low risk of bias)</th>
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<th>Probably no</th>
<th>Definitely no (high risk of bias)</th>
</tr>
</thead>
</table>

3.b. Were healthcare providers blinded?

<table>
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<tr>
<th>Definitely yes (low risk of bias)</th>
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<th>Probably no</th>
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3.c. Were data collectors blinded?

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* This global rating is challenging. May want to omit and use only the ratings below.
3. Blinding: Was knowledge of the allocated interventions adequately prevented?

3.d. Were outcome assessors blinded?

- **Definitely yes** (low risk of bias)
- **Probably yes**
- **Probably no**
- **Definitely no** (high risk of bias)

3.e. Were data analysts blinded?

- **Definitely yes** (low risk of bias)
- **Probably yes**
- **Probably no**
- **Definitely no** (high risk of bias)

Examples of low risk of bias:

- No blinding but the review authors judge that the outcome and the outcome measurement are not likely influenced by lack of blinding
- Blinding of participants and key study personnel ensured, and unlikely that blinding could have been broken
- Either participants or some key study personnel were not blinded, but outcome assessment was blinded and the nonblinding of others unlikely to introduce bias

Examples of high risk of bias:

- No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding
- Blinding of key study participants and personnel attempted, but likely that the blinding could have been broken
- Either participants or some key study personnel were not blinded, and the nonblinding of others likely to introduce bias
4. Was loss to follow-up (missing outcome data) infrequent?

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**Examples of low risk of bias:**

- No missing outcome data
- Reasons for missing outcome data unlikely to be related to outcome (for survival data, censoring unlikely to be introducing bias)
- Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have an important impact on the intervention effect estimate
- For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have an important impact on observed effect size
- Missing data have been imputed using appropriate methods

**Examples of high risk of bias**

- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce important bias in intervention effect estimate
- For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size
- 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomization
- Potentially inappropriate application of simple imputation
5. Are reports of the study free of selective outcome reporting? *

**Definitely yes** (low risk of bias)  **Probably yes**  **Probably no**  **Definitely no** (high risk of bias)

**Examples of low risk of bias:**

- The study protocol is available and all of the study’s pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way
- The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon)

**Examples of high risk of bias**

- Not all of the study’s pre-specified primary outcomes have been reported
- One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified
- One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect)
- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study

* This item sufficiently difficult to judge that it may be omitted
6. Was the study apparently free of other problems that could put it at a risk of bias? *

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**Examples of low risk of bias:**
- The study appears to be free of other sources of bias

**Examples of high risk of bias**
- Had a potential source of bias related to the specific study design used
- Stopped early due to some data-dependent process (including a formal-stopping rule)
- Had extreme baseline imbalance
- Has been claimed to have been fraudulent
- Had some other problem

* May omit this item