# 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**

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**Study details**

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|---|---|
| **Reference** | Oosterhuis T. et al. Early rehabilitation after lumbar disc surgery is not effective or cost-effective compared to no referral: a randomised trial and economic evaluation |

**Study design**

X 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: Early rehabilitation Comparator: No referral

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|---|---|
| **Specify which outcome is being assessed for risk of bias** | NRS, ODI, SF12 |
| **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. | Mean (SD) |

**Is the review team's aim for this result…?**

X 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 <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)**

X 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☐ "Grey literature" (e.g. unpublished thesis)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. Y<br>1.2. Y<br>Quote: "To conceal treatment allocation, a computer-randomised list was generated for each hospital by an independent investigator prior to study commencement. To achieve the predetermined sample size for the experimental and control groups, weighted block randomisation (blocks of four) was used. Based on these lists and prior to the start of the study, the independent investigator prepared a set of numbered, opaque and sealed envelopes containing the assigned postoperative strategy for each hospital. Directly after having received the completed baseline questionnaire and prior to surgery, the research nurse opened the next consecutive envelope in order to inform the participant about the assigned postoperative strategy" (p. 145). | 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?** | 1.3. PN<br>Quote: "Baseline characteristics of the experimental (n = 92) and control (n = 77) group are presented in Table 1. Baseline measures were taken a mean of 13 days (SD 15) before surgery. The groups were well matched with respect to demographic characteristics and baseline values of the outcome measures" (p. 148). | Y / PY / PN / N / NI |

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| **Risk-of-bias judgement** | Low | Low / High / Some concerns |
| Optional: What is the predicted direction of bias arising from the randomization process? | | 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*)

| Signalling questions | Comments | Response options |
|---|---|---|
| **2.1. Were participants aware of their assigned intervention during the trial?** | 2.1. Y<br>2.2. Y<br>Quote: "Due to the nature of the intervention, participants and care providers could not be blinded" (p. 149). | 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 trial context?** | 2.3 PY<br>Quote: "Based on the registration forms, the content of the treatment seemed to deviate from the protocol, with a focus on isolated exercises rather than the resumption of activities of daily living. As a consequence, the intervention under study might have been too generic instead of specifically focusing on the activities of daily living needs of the individual participant, and this may have influenced its effectiveness" p. 151. | NA / Y / PY / PN / N / NI |
| **2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?** | 2.4 PY<br>Quote: "Based on the registration forms, the content of the treatment seemed to deviate from the protocol, with a focus on isolated exercises rather than the resumption of activities of daily living. As a consequence, the intervention under study might have been too generic instead of specifically focusing on the activities of daily living needs of the individual participant, and this may have influenced its effectiveness" p. 151. | NA / Y / PY / PN / N / NI |
| **2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?** | 2.5 NI | NA / Y / PY / PN / N / NI |
| **2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?** | 2.6 Y<br>Quote: " The results of the sensitivity analyses were in line with the main analysis, indicating that the findings were robust" (p. 149). | 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** | | NA / Y / PY / PN / N / NI |

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| **the failure to analyse participants in the group to which they were randomized?** | | |
| **Risk-of-bias judgement** | High risk | Low / High / Some concerns |
| Optional: What is the predicted direction of bias due to deviations from intended interventions? | | 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*)

| **Signalling questions** | **Comments** | **Response options** |
|---|---|---|
| **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 applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across intervention groups?** | | NA / Y / PY / PN / N / NI |
| **2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?** | | 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?** | | 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?** | | NA / Y / PY / PN / N / NI |
| **Risk-of-bias judgement** | | Low / High / Some concerns |
| Optional: What is the predicted direction of bias due to deviations from intended interventions? | | 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 PN<br>Comment: 90,5 % of data for this outcome were available. | 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?** | 3.2 Y<br>Quote: "The results of the three sensitivity analyses did not substantially differ from the main analysis" p. 148 | 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 / NI |
| **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 / NI |
| **Risk-of-bias judgement** | Low risk | Low / High / Some concerns |
| Optional: What is the predicted direction of bias due to missing outcome data? | | NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable |

Domain 4: Risk of bias in measurement of the outcome

| Signalling questions | Comments | Response options |
|---|---|---|
| **4.1 Was the method of measuring the outcome inappropriate?** | 4.1 N<br><br>RESEARCH QUESTION:<br><br>Quote: "Is referral for early rehabilitation after lumbar disc surgery effective and cost-effective compared to no referral?" p. 145<br><br>METHOD OF MEASURING THE OUTCOME<br><br>Quote: "The study used standardised instruments with demonstrated validity, reliability and responsiveness … Functional status was assessed by the Oswestry Disability Index … Average pain intensity over the preceding week was measured for leg pain and low back pain on an 11-point numerical rating scale (0 = no pain to 10 = worst imaginable pain). Global perceived effect was evaluated using the sevenpoint Global Perceived Effect scale, ranging from 'completely recovered' to 'worse than ever'. This was dichotomised into success (completely and much recovered) and non-success (slightly recovered, no change, slightly worse, much worse and worse than ever). General physical and mental health were assessed with the Medical Outcome Study Short Form 12 (SF-12). For the cost-effectiveness analysis, the EuroQol (EQ-5D-3L) was administered to assess health-related quality of life" p. 146. | Y / PY / PN / N / NI |
| **4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?** | 4.2. PN<br><br>Comment: Comparable methods of outcome measurement and time points. | 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?** | 4.3 Y<br><br>Comment: The outcome assessor is the study participant. | NA / Y / PY / PN / N / NI |

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| **4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?** | 4.4. PY<br><br>Comment: Knowledge of the assignment could influence participant-reported outcomes. | 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?** | 4.5 PN<br><br>Comment: There is no reason to believe that knowledge of the intervention status could have influenced outcome. | NA / Y / PY / PN / N / NI |
| **Risk-of-bias judgement** | Some 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 Y<br><br>Quote: "Details of the statistical analysis plan available in Appendix 2 and the code used to conduct the analyses in the statistical software are presented in Appendix 3" p. 146. | Y / PY / PN / N / 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 PN<br><br>Comment: All eligible reported results for the outcome domain correspond to all intended outcome measurements.<br><br>Source: Appendix 2 | Y / PY / PN / N / NI |
| **5.3 ... multiple eligible analyses of the data?** | 5.2 PN<br><br>Comment: All eligible reported results for the outcome domain correspond to all intended outcome measurements.<br><br>Source: Appendix 2 | Y / PY / PN / N / NI |
| **Risk-of-bias judgement** | Low | 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

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