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

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Study details

Reference	Uhrbrand P et al. Shared decision-making approach to taper postoperative opioids in spine surgery patients with preoperative opioid use: a randomized controlled trial. PAIN 00 (2021) 1–8

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:	Personalized opiod tapering plan	Comparator:	Standard care

Specify which outcome is being assessed for risk of bias	NRS
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.	Median (IQR)

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
X Trial protocol: ClinicalTrials.gov (NCT04140955)
☐ 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☐ "Grey literature" (e.g. unpublished thesis)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 1.1. Y Quote: "Randomization was computer-generated in Research Electronic Data Capture (REDCap) (a secure web application qualified to capture and store electronic data for research studies20) with a concealed random allocation sequence with a ratio of 1:1 between the 2 groups" (p. 2)	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. N Quote: "(A) Back pain intensity in the intervention group and control group preoperatively and 2 weeks (n 5 105), 1 month (n 5 88) (due to a setup error in the electronic survey, the first 18 patients included in the study were not asked about pain intensity after 1 month. These patients did not differ with regard to baseline characteristics or pain intensity before surgery, at 2 weeks, and at 3 months), and 3 months (n 5 106) after discharge (median NRS 0-100 with interquartile ranges). (B) Radicular pain intensity in the intervention group and control group preoperatively and 2 weeks (n 5 105), 1 month (n 5 88) (due to a setup error in the electronic survey, the first 18 patients included in the study were not asked about pain intensity after 1 month. These patients did not differ with regard to baseline characteristics or pain intensity before surgery, at 2 weeks, and at 3 months), and 3 months (n 5 106) after discharge (median NRS 0-100 with interquartile ranges)" (p. 6).	Y / PY / PN / N / NI

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 2.2. Y Comment: It was not possible to blind the patients or the carers for this intervention.	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 Quote: "The study was not blinded and patients allocated to the control group may have increased attention to opioid tapering simply by being included in the study" p. 7).	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. NI	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 Quote: "Based on a power calculation, we decided to include 110 patients.33 In brief, we expected that a tapering plan and telephone counselling reduced the percentage of patients who exceeded their daily preoperative opioid consumption, ie, were unable to taper, to their preoperative level from 25% to 5% (primary outcome). According to a x2 test comparing 2 independent proportions, based on the premises a5 0.05 and b5 0.2, 49 patients had to be included in each group. To account for dropouts, we decided to include 55 patients in each of the 2 groups. Data were exported from REDCap and DaneSpine to STATA 16 (Stata Corporation, College Station, TX) in which the statistical analyses were conducted. Dichotomous variables were presented as numbers (%) with 95% confidence intervals (CIs) and compared using a x2 test. Ordinal variables and nonnormally distributed continuous variables were presented as medians with interquartile ranges (IQRs) and compared using the	Y / PY / PN / N / NI

	Mann– Whitney U test. All P values were two-sided and considered statistically significant if , 0.05" (p. 3)	
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
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 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 Y Comment: 95,5 % (Figure 1).	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 / 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	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 AIM Quote: "To identify methods that can facilitate opioid tapering after surgery in patients with preoperative opioid use, we conducted a prospective randomized controlled trial (RCT). We hypothesized that the combination of a personalized tapering plan and telephone counselling would reduce postoperative opioid use, reduce contacts with the healthcare system after discharge, increase patient satisfaction, and reduce symptoms possibly related to withdrawal, compared with standard of care. We chose to include patients scheduled to undergo spine surgery because this procedure has been highlighted as a high-risk surgery with regard to persistent opioid use" p. 1 METHOD OF MEASURING THE OUTCOME Quote: "The primary outcome was the number of patients exceeding their daily preoperative opioid consumption by any amount, ie, were unable to taper, 1 month after discharge (yes/no). Secondary outcomes were the number of patients who succeeded in tapering opioids to zero at 3 months after discharge (yes/no dichotomous outcome), pain-related contacts to the primary and/or secondary health care system during the first 2 weeks after discharge (yes/no dichotomous outcome), patient satisfaction with pain treatment over the first 2 weeks after discharge (ordinal scale with 5 options converted to dichotomous outcome, yes [very satisfied, satisfied], no [neither satisfied nor dissatisfied, dissatisfied, very dissatisfied]), and the presence of any symptoms possibly related to withdrawal during opioid tapering in the first month after discharge (yes/no).	Y / PY / PN / N / NI
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	4.2. PN 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 Comment: The outcome assessor is the study participant.	NA / 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?	4.4. PY 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 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 Quote: "The conducted research was preregistered with an analysis plan, which is outlined in the protocol paper published in March 2020" p. 7.	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 N Comment: All eligible reported results for the outcome domain correspond to all intended outcome measurements.	Y / PY / PN / N / NI
5.3 ... multiple eligible analyses of the data?	5.3 N Comment: All eligible reported results for the outcome domain correspond to all intended outcome measurements.	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

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