Bilag 4

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

TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne
on behalf of the RoB2 Development Group
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Study details

Reference	*Marquez-Chin et al. (2017) Functional electrical stimulation therapy for severe hemiplegia: randomized control trial revisited*

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:	Functional Electrical Stimulation	Comparator:	Conventionel therapy

Specify which outcome is being assessed for risk of bias	Fugl-meyer Assesment
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.	

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☐	“Grey literature” (e.g. unpublished thesis)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?	Deltagerne blev randomiseret via en computeriseret randomiseringsproces, og det blev anvendt forseglede kuverter for at sikre tilfældig tildeling. Der er ingen indikationer på problemer med randomiseringen. Y Randomiseringen blev udført med forseglede kuverter, og der er ingen indikationer på, at randomiseringen blev afsløret, før interventionerne blev tildelt deltagerne. Denne proces skaber en effektiv skjult tildeling af interventioner. Y	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?	Der er betyde forskel i alderen, den er dog beregnet til ikke at være statistisk signifikant. Alder mean score i interventionsgruppen er dog 51 og 65 i control gruppen, derfor vurderes det at det klinisk kan gøre en forskel.	Y / PY / PN / N / NI
Risk-of-bias judgement	Some concerns	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?	Deltagerne kunne muligvis vide, hvilken intervention de modtog, da der var markante forskelle i resultaterne, hvilket gør det svært at opretholde blindhed i denne sammenhæng. PY Terapeuterne, som leverede behandlingen, var også opmærksomme på, hvilken intervention de administrerede, hvilket kan have introduceret bias. Y	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?	Der blev ikke rapporteret om afvigelser fra den planlagte intervention. Der er ikke nogen indikation af, at de ændringer, der blev gjort, skyldtes selve forsøgets kontekst. N	NA / Y / PY / PN / N / NI
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Der blev anvendt en passende analysemetode for at vurdere effekten af interventionen (FES vs. standardrehabilitering), og dataene blev behandlet korrekt. Y	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
Risk-of-bias judgement	Low	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?	To deltagere fra kontrolgruppen og behandlingsgruppen blev ekskluderet (en af medicinske årsager og en pga. Botox), så der er nogle manglende data, men de blev behandlet korrekt. Y	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?	Fugl-Meyer-skalaen (FMA-UE) er velkendt og accepteret måleinstrument til at vurdere funktionelle resultater. N	Y / PY / PN / N / NI
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	Der er ingen indikation af, at målingerne blev udført forskelligt mellem interventions- og kontrolgruppen. N	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?	Der er angivet, at blinding kunne være svær at opretholde, men ikke nødvendigvis at de vidste om interventionen. PN	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?		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
Risk-of-bias judgement	Low	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?	I den artikel nævnes, at de anvendte en prædefineret analyseplan, og der er ingen indikation af, at resultatmålingerne blev ændret undervejs. Der blev gennemført de nødvendige statistiske analyser i henhold til en plan. Y	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?	De brugte de specifikke målinger som FMA-UE, der var forudbestemt i protokollen. N	Y / PY / PN / N / NI
5.3 ... multiple eligible analyses of the data?	Der er ingen tegn på, at de har valgt specifikke analyser baseret på resultaterne. De foretog de nødvendige statistiske analyser for at teste forskellene mellem interventions- og kontrolgrupperne, uden at vælge data post hoc. N	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?	Studiet følger en foruddefineret analyseplan, og resultaterne blev rapporteret baseret på en forudbestemt måling (Fugl-Meyer Upper Extremity (FMA-UE) score), hvilket reducerer risikoen for selektiv rapportering. Der er ingen indikationer i studiedesignet på, at resultater blev udvalgt eller selektivt rapporteret efter dataanalyse. De vigtigste resultater ser ud til at være baseret på en fastlagt analyse-strategi, og der synes ikke at være manipulation af resultaterne baseret på de opnåede data.	NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

	Studiet antyder ikke, at specifikke resultater eller tidspunkter blev valgt for at fremstille et mere fordelagtigt resultat efter dataanalyse, dermed er der ingen væsentlig indikation på selektiv rapportering af resultater.	

Overall risk of bias

Risk-of-bias judgement	Some concerns	Low / High / Some concerns
Optional: What is the overall predicted direction of bias for this outcome?	Baseline alder er stor forskel. Deltager og Terapeuter ikke muligt at blinde. Forsker er forsøgt blindet, men ikke muligt på grund af de store forskelle i resultaterne.	NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable