Cochrane Risk-of-bias training event 2019

Bristol, July 2019

Example assessment of Engerbretsen trial

Signalling questions	Response	Rationale
Bias arising from the randomization process		
1.1 Was the allocation sequence random?	**PY**	"A statistician not involved in data collection or analysis randomly allocated patients to treatment groups in blocks of four to six. Randomisation was stratified by sex. A person not involved in the treatments opened the sealed envelopes and assigned appointments according to treatment group."
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	**PY**	
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	**N**	"The groups were similar at baseline with regard to age, education, dominant arm affected, duration of pain, sick leave, shoulder pain and disability index score, and secondary outcome variables Seventeen (33%) patients in the radial extracorporeal shockwave group and 12 (23%) in the supervised exercise group were on sick leave because of shoulder pain."
Risk of bias judgement	**Low**	Allocation sequence was adequately generated and concealed, and baseline imbalances appear to be compatible with chance.
Bias due to deviations from intended interventions (effect of assignment to intervention)		
2.1. Were participants aware of their assigned intervention during the trial?	**Y**	Patients knew which interventions they could be assigned to: "The patients were referred to the investigator (KE, a physiotherapist), received oral and written information about the two treatments, and gave their informed consent before the baseline evaluation."
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	**Y**	
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	**PN**	"All the patients were asked not to have any additional treatment except analgesics (including anti-inflammatory drugs) … between the start of treatment and the 18 week follow-up." "Thirteen patients in the radial extracorporeal shockwave group and three patients in the supervised exercise group received additional treatment (cortisone injections, chiropractic treatment, physical therapy/supervised exercises) between 12 and 18 weeks (odds ratio 5.5, 95% confidence interval 1.3 to 26.4; P=0.014)."

2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	**NA**	
2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	**NA**	
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	**Y**	"One patient crossed over to the supervised exercise group after one treatment with radial extracorporeal shockwaves". However, authors stated that "We analysed data according to the intention to treat principle, in which the study groups are compared in terms of the treatment to which they were randomly allocated."
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**	
Risk of bias judgement	**Low**	More patients in the radial extracorporeal shockwave group sought unintended co-interventions (13 vs 3), but this could be considered reflective of usual practice.
Bias due to missing outcome data		
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	**Y**	"Two patients [of 52] randomised to supervised exercises did not attend followup at 12 and 18 weeks, and two patients [of 52] in the radial extracorporeal shockwave group did not attend the 18 week follow-up".
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	**NA**	
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	**NA**	
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	**NA**	
Risk of bias judgement	**Low**	Data were available for 96% of participants.
Bias in measurement of the outcome		
4.1 Was the method of measuring the outcome inappropriate?	**N**	"The participants completed a questionnaire including questions on demographics, education, duration of pain, sick leave, emotional distress, and the outcome measures. The main outcome measure was the shoulder pain and disability index (SPADI), a self report questionnaire for patients with shoulder pain."

4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	**PN**	This seems unlikely. It seems like all participants completed the same questionnaires.
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	**Y**	"A blinded physiotherapist made the baseline and follow-up measurements. The patients were instructed not to discuss their treatment with the blinded physiotherapist." However, pain/disability is self-reported by the participants, who were aware of their intervention.
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	**Y**	Participants beliefs about the superiority/inferiority of either intervention could have influenced their assessment of pain/disability. We have no reason to believe that patients would have a strong preference [though it is possible that they would]
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	**PN**	
Risk of bias judgement	**Some concerns**	Pain/disability was self-reported by participants who were aware of their assigned intervention, and participants beliefs about the superiority/inferiority of either intervention could have influenced their assessment of the outcome, but there is no evidence that this was likely
Bias in selection of the reported result		
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?	**NI**	No statistical analysis plan available to us
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?	**PN**	The reported scale (SPADI) and time point (18 weeks) were pre-specified in ClinicalTrials.gov.
5.3 ... multiple eligible analyses of the data?	**NI**	It is unclear if the reported approach to analysing this outcome was pre-specified or influenced by the results.
Risk of bias judgement	**Some concerns**	Unclear if the reported analysis approach was pre-specified or influenced by the results.
Overall risk of bias	**Some concerns**	