Multimedia Appendix 3: Risk-of-bias assessment (based upon the CONSORT checklist [1])

	Aali et al (2020)	Andrade et al (2015)	Cho et al (2020)	Clarke et al (2019)	Dang et al (2020)	du Sert et al (2018)	Falconer et al (2017)	Leff et al (2013)	Pinto et al (2013)	Robinson-Whelen et al (2020)	Rus-Calafell et al (2020)	Stewart et al (2010)	Thomas et al (2019)	Tong et al (2020)	Tongpeth et al (2018)	Triberti et al (2019)	Wonggom et al (2019)	Wonggom et al (2020)
1. Title and Abstract																		
a. identification as a randomized trial in title	0	1	0	0	0	0.5	0	0	0	0	0	0	0	0	0	0	0	1
b. structured summary of trial design, methods, results, and conclusions	1	1	0.75	1	0.5	0.75	0.25	1	0.75	0.25	0.5	0	0	0	0	0	1	0.75
2. Introduction																		
a. scientific background and explanation of rationale	1	1	1	1	1	0.75	0.75	1	1	0.25	1	1	1	0.75	1	0.25	1	0.75
b. specific objectives or hypotheses	1	0.75	1	1	0.75	0.75	0.75	1	1	0.25	1	1	1	1	1		1	0.75
3. Trial design																		
a. description of trial design	0	1	0.75	0	0	0.75	0	1	0.75	0.75	1	0	0	0	0	0	0	0.75
b. important changes to methods after trial commencement (such as eligibility criteria), with reasons	0	0.25	0.25	0	0	0	0	0.75	0	0.75	0.75	0	0	0	0	0	0	1
4. Participants																		
a. eligibility criteria for participants	1	1	0.25	1	1	1	0.75	1	1	1	1	0	0	1	0.75	0.25	1	1
b. settings and locations where the data were collected	0	0.75	0.25	0	0.75	0.75	0.75	0.25	1	1	0.75	0	0	1	0.25	0.75	1	1
5. Interventions Descriptions with sufficient details to allow replication, including how and when they were actually administered	1	0.75	0.5	0	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0	0	0.75	0.75	0.25	1	0.75
6. Outcomes																		
a. pre-specified primary and secondary outcome measures, including how and when they were assessed	1	1	0.75	0	0.75	0.75	0.25	0.75	0.25	1	1	0	0	0.75	1	0.25	1	1
b. any changes to trial outcomes after the trial commenced, with reasons	0	0.25	0	0	0	0.25	0	1	0	1	0	0	0	0	0	0	0	1
7. Sample size																		
a. how sample size was determined	0	1	0	0	0	0	0	1	0	0.75	0	0	0	0	0	0	0	1
b. when applicable, explanation of any interim analyses and stopping guidelines	0	1	0	0	0	0	0	1	0	0.75	0.25	0	0	0	0	0	0	1
8. Randomisation - sequence generation	0	1	0	0	0	0.25	0	1	0	0.5	0	0	0	0	0	0	0	1
a. method used to generate the random allocation sequence																		
b. type of randomisation including details of any restriction	0	1	0	0	0	0	0	1	0	0.25	0	0	0	0	0	0	0	1
9. Allocation concealment mechanism Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	0	0.75	0	0	0	0	0	0.75	0	0.25	0	0	0	0	0	0	0	0.25
10. Implementation Who generated the random allocation sequence, who enrolled participants,	0	1	0	0	0	0	0			0.5	0	0	0	0	0	0	0	0

and who assigned participants to interventions																		
11. Blinding																		
a. if done, who was blinded after assignment to interventions and how	0	0.75	0	0	0	0	0	0	0	0.25	1	0	0	0	0	0	0	0
b. if relevant, description of the similarity of interventions	0	1	0	0	0		0		0	0.25	0	0	0	0	0	0	0	1
12. Statistical methods																		
a. statistical methods used for (primary and secondary) outcomes	0	1	0.75	0	0.75	0.75	0.75	1	0.75	1	1	0	0	0.5	0.75	0.75	0	1
b. methods for additional analyses, such as subgroup analyses and adjusted analyses	0	1	0	0	0	0.75	0.25	1	0.25	1	1	0	0	0	0	0.75	0	1
13. Participant flow																		
a. for each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	1	1	0	1	0.75	0	0	1	0	1	0	0	0	0	0	0	1	1
b. for each group, losses and exclusions after randomization, together with reasons	1	0.75	0	1	0.75	0	0	1	0	1	0.25	0	0	0	0	0	1	1
14. Recruitment																		
a. dates defining the periods of recruitment and follow-up	0	1	0.75	0	0.75	0	0.75	0	1	0.75	0.75	0	0	0.5	0.25	0	0	1
b. why the trial ended or was stopped	0	1	0	0	0	0	0		0	0.25	0	0		0	0	0	0	0
15. Baseline data																		
a. a table showing baseline demographic and clinical characteristics for each group	0	1	1	1	0.75		0	1	0.75	1	1	0	0	1	1	0.75	0	1
b. systematic table of characteristics for each group	0	1	0.25	1	0.75		0	1	0	1	1	0	0	0.75	0.75	0.75	0	1
16. Numbers analyzed																		
For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	1	1	0.75	0	0.5	1	0.25	1	0.25	0.75	0.75	0	0	0.75	0.75	0.75	0	1
17. Outcomes and estimation																		
a. for each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	1	1	0.5	1	0.25	0.25	0.25	0.75	0	1	1	0	0	0	0	1	1	1
b. for binary outcomes, presentation of both absolute and relative effect sizes is recommended	1	0.25	0	1	0	1	0	0.75	0	1	1	0	0	0	0	1	1	1
18. Ancillary analyses																		
Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory	0	1	0	0	0	0.75	0	0.75	0	0.25	0.75	0	0	0	0	0	0	0.75
19. Harms																		
All important harms or unintended effects in each group	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
20. Limitations																		
Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	1	1	1	1	1	0.75	0.5	1	1	1	1	0	0	1	0.75	1	1	1
21. Generalizability																		
Generalizability (external validity, applicability) of the trial findings	0	0.75	0.25	0		0.75	0.25	0.75	0	1	0.75	0	0	0	0.25	0	0	0.75

22. Interpretation Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	0	1	1	1	0.75	1	0.75	1	0.75	1	1	0	1	0.75	0.75	0.75	0	0.75
23. Registration Registration number and name of trial registry	1	0	1	1	1	1	0	1	0	0	1	0	0	0	0	0	1	1
24. Protocol Where the full trial protocol can be accessed, if available	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1
25. Funding Sources of funding and other support (such as supply of drugs), role of funders	1	0	1	0	1	1	1	1	0	1	1	1	1	1	1	0	1	1
Numbers of criteria satisfied	14	25	7	13	5	6	1	21	6	16	18	3	4	6	5	3	15	25

References:

1. Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. PLoS Med 2010 Mar 24;7(3). doi: 10.1371/journal.pmed.1000251. Medline:20352064