| Section/Topic       | Item No | Checklist item                                                                 | Reported on page No |
|--------------------|---------|--------------------------------------------------------------------------------|---------------------|
| Title and abstract | 1a      | Identification as a randomized trial in the title                              | 2                   |
|                    | 1b      | Structured summary of trial design, methods, results, and conclusions          | 4-5                 |
| Introduction       | 2a      | Scientific background and explanation of rationale                             | 6-8                 |
|                    | 2b      | Specific objectives or hypotheses                                              | 8                   |
| Methods            | 3a      | Description of trial design (such as parallel, factorial) including allocation ratio | 9                   |
|                    | 3b      | Important changes to methods after trial commencement (such as eligibility criteria), with reasons | n.a.                |
| Participants       | 4a      | Eligibility criteria for participants                                          | 9-10                |
|                    | 4b      | Settings and locations where the data were collected                           | 9                   |
| Interventions      | 5       | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | 10-12 (and reference design study) |
| Outcomes           | 6a      | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | 12-14 (and reference design study) |
|                    | 6b      | Any changes to trial outcomes after the trial commenced, with reasons          | n.a.                |
| Sample size        | 7a      | How sample size was determined                                                 | 14 (and reference design study) |
|                    | 7b      | When applicable, explanation of any interim analyses and stopping guidelines   | n.a.                |
| Randomization:     | 8a      | Method used to generate the random allocation sequence                         | 9                   |
| Sequence generation| 8b      | Type of randomization; details of any restriction (such as blocking and block size) | 9                   |
| Allocation         | 9       | 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 | 9                   |
| concealment mechanism|    |                                                                                  |                     |
| Implementation | 10 | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions |
|----------------|----|-------------------------------------------------------------------------------------------------------------|
| Blinding       | 11a| If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how |
|                | 11b| If relevant, description of the similarity of interventions |
| Statistical methods | 12a| Statistical methods used to compare groups for primary and secondary outcomes |
|                | 12b| Methods for additional analyses, such as subgroup analyses and adjusted analyses |
| Results        |    | Reference design study |
| Participant flow (a diagram is strongly recommended) | 13a| For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome |
|                | 13b| For each group, losses and exclusions after randomization, together with reasons |
| Recruitment    | 14a| Dates defining the periods of recruitment and follow-up |
|                | 14b| Why the trial ended or was stopped |
| Baseline data  | 15 | A table showing baseline demographic and clinical characteristics for each group |
| Numbers analyzed | 16 | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups |
| Outcomes and estimation | 17a| For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) |
|                | 17b| For binary outcomes, presentation of both absolute and relative effect sizes is recommended |
| Ancillary analyses | 18 | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory |
| Harms          | 19 | All important harms or unintended effects in each group |
| Discussion     |    | Reference design study |
| Limitations    | 20 | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses |
| Generalizability | 21 | Generalizability (external validity, applicability) of the trial findings |
| Interpretation | 22 | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence |
| Other information |    | Reference design study |
| Registration   | 23 | Registration number and name of trial registry |
| Protocol       | 24 | Where the full trial protocol can be accessed, if available |
| Funding        | 25 | Sources of funding and other support (such as supply of drugs), role of funders |